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# HealthMED

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## Clivarin® U PROFILAKSI I LIJEČENJU DUBOKE VENSKE TROMBOZE



Clivarin® 1750 (0,25 ml)

<b>BOLESNIK</b>	<b>S NISKIM I SREDNJIM RIZIKOM</b>
<b>DOZA</b>	0,25 ml = 1750 i. j. = 1432 IU anti-Xa
<b>PREOPERATIVNA PROFILAKSA</b>	1 x 0,25 ml sc. 2" prije operacije, najmanje 7-14 dana
<b>POSTOPERATIVNA PROFILAKSA</b>	1 x 0,25 ml sc. 8-12" nakon operacije zanim 1x0,25 ml sc. na dan najmanje 7-14 dana

gotova šprica - 1 x 0,25 ml sc. na dan

Lijek se primjenjuje u zdravstvenim ustanovama.



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<b>DOZIRANJE U LIJEČENJU DUBOKE VENSKE TROMBOZE</b>	
Ovisno o tjelesnoj masi sljedeća se šema doziranja pokazala djelotvornom	
<b>TJELESNA TEŽINA</b>	<b>DOZIRANJE Clivarina</b>
35 - 45 kg	2 x na dan 0,50 ml (0,25 ml = 1432 IU anti-Xa)
46 - 60 kg	2 x na dan 0,60 ml (0,60 ml = 3436 IU anti-Xa)
> 60 kg	2 x na dan 0,90 ml (0,90 ml = 5153 IU anti-Xa)

Gotova šprica - 1 x 0,90 ml sc. na dan.

Uječenje Clivarinom mora se provoditi barem 5-7 dana.  
Lijek se primjenjuje u zdravstvenim ustanovama.



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# Evaluation of the body composition, blood lipids and health life-style in employment and unemployment women

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## Abstract

**Aim:** The aim of the study was to establish the effects on blood lipids, body compositions and healthy lifestyle behaviors of unemployed and employed women.

**Method:** 797 subjects were participated to this study (HW: 383, 42.60±8.65; EW: 414, 41.83±6.31 years). Life style behavior was questioned by using HPLP-II scale of Walker& Pender. Body composition was measured by bioelectric impedance (BIA) analysis method. Blood lipids and blood pressure were measured by using standard methods.

**Results:** There was found significant difference weight, body mass index (BMI), waist-to-hip ratio (WHR), waist circumference (WC), age matched of body (AMB), percent of body fat and mass of body fat (MBF) in EW. Soft lean mass (SLM) and total body water (TBW) were observed difference in HW ( $p < 0.001$ ). No significant difference was found in spiritual growth, interpersonal relations and stress management from HPLP-II scales, ( $p > 0.05$ ). A significant difference was found for health responsibility, exercise and nutritional habits and HPLP-II score in EW ( $p < 0.05$ ). HDL, LDL, TG, T-Cholesterol and glucose values were observed in moderate levels. Number of children of HW and EW was found as 3.0±0.8 and 2.0±0.80 (respectively), ( $p < 0.001$ ).

**Conclusion:** HPLP-II means score was found higher in EW. As body type of HW and EW included in overweight class. The increase in the number of children determined the rise to advantage obesity in body type. Regular diet habits and educational level were observed to be important factor in the control of weight body.

**Key words:** Women, body composition, obesity, blood lipids, health lifestyle.

## Introduction

There are several criteria that determine the healthy lifestyle among women. One of that obesity is evident on the body composition. Obesity is a public problem in global terms and also it is an economic problem. The prevalence of obesity has been increased in the entire world and there is more effect of obesity on women<sup>[1,2,3]</sup>. Obesity, the presence of excess body fat, has been clearly associated with adverse health consequences<sup>[1]</sup>. It is associated with negative health impact and elevated mortality<sup>[4]</sup>. The deleterious effects of extreme obesity on quality of life (QoL) and psychosocial functioning have been well described. Obese women are particularly susceptible to diabetes and diabetes, in turn, puts women at dramatically increased risk of cardiovascular disease (CVD)<sup>[3,5,6]</sup>. In developed or developing countries obesity is an outstanding health problem. Lack of employment outside home and being traditionally unaccustomed to sporting activities are additional factors for the development of obesity for Turkish women<sup>[7]</sup>.

Recently, many methods have been developed which measured local fat distributions in body. As common in estimated of obesity prevalence was used body mass index (BMI) method<sup>[8]</sup>. This method was not a significant determinant fat mass in body and fat distribution. Currently, the bioelectric impedance (BIA) analysis obtains information about the electrical properties of obesity tissue mass and fat tissue<sup>[9,10]</sup>. BIA devices were reliable and could be recommended as valid

field measures of mass and percentage body fat (BF%). Waist hip ratio (WHR), anthropometric methods were used as indicators distribution of body fat in epidemiological research<sup>[1]</sup>. It has been observed that women face changes in the composition of their bodies and suffer obesity because of extreme nourishment or being overweight in post natal periods. In our study, we aimed to investigate the composition of the bodies and health life-style behaviors of (housewives) HW and (employed: official) EW.

## Materials and Methods

### Participants

Participants were divided into two groups according to having an employment (employed group; official working: 414) and being unemployed (housewife group: 383 subjects). The mean age was  $42.60 \pm 8.65$  years and  $41.83 \pm 6.31$  (mean  $\pm$  SD). Healthy HW and EW with similar physical characteristics like age and height were chosen randomly. Written informed consent was obtained from all subjects. The experiments were performed in accordance with the Helsinki Declaration. Society-demographic data was obtained by question form. Under mentioned parameters were compared in both groups.

### Measurement of Health Promotion Lifestyle Profile-II (HPLP-II)

A scale<sup>[11]</sup> was used to measure the health life-style behaviors of women. Validity and reliability of questionnaire in Turkey was done<sup>[12]</sup>. 48 items in 52 items were adopted to Turkish society and applied. All of them were positive and prepared as 4 likert-type scale. All items were pointed as 1 (*never*), 2 (*sometimes*), 3 (*often*), 4 (*regularly*). The HPLP-II measured six aspects of health promotion behaviors: *health responsibility, physical activity, nutritional habits, spiritual growth, interpersonal relations, and stress management*. HPLP-II has high internal consistency with a Cronbach's alpha ranging from 0.79-0.94 and the lowest point is 48, the highest point is 192. An increase in the

points of the measure shows that the individuals health behaviors in a high rate.

### Measurement of Anthropometric Parameters

Anthropometric variables in participants according to standard methods were measured<sup>[13]</sup>. Body height (m) was measured using a stadiometer to the nearest 0.01 m (*Holtain Ltd*). Waist circumferences-WC (cm) was measured to the nearest 0.01 m using a flexible metric tape. Abdominal circumference was defined as the horizontal distance around the abdomen at the umbilicus. Weight and body compositions measures of volunteers BMI ( $\text{kg}/\text{m}^2$ ), WHR (%), BF%, mass of body fat-MBF (kg), soft lean mass-SLM (kg), basal metabolic rate-BMR (kcal), age matched of body-AMB (year) and total body water-TBW (kg) parameters were held by BIA analysis method (*Jawon Segmental Body Composition Analyzer, model AVIS 333 Plus-in Korea*). BIA is a kind of analysis which depends on the electric permeability difference between non adipose tissue and adipose tissue<sup>[9,10]</sup>. The volunteer's measures were held between 8:30 and 12 without intake of liquid or food, following the night hanger. Volunteers didn't have any metal objects or jeweler. Volunteers wore a light cloth, asked to step barefoot on the aluminum steps of the analysis device and to hold the hand electrode. Data was recorded by a computer which was connected to the body composition analyzer. Volunteers who take diuretic or antihypertensive and have kidney disease were not taken to the research. Measures were postponed related to (menstrual cycle) position of the women.

### Classification of BMI

The following BMI categories recently adopted by the World Health Organization were used, these are<sup>[8,14]</sup> *low* ( $<18.5 \text{ kg}/\text{m}^2$ ), *normal* ( $18.5$  to  $24.9 \text{ kg}/\text{m}^2$ ), *overweight* ( $25.0$  to  $29.9 \text{ kg}/\text{m}^2$ ), *obesity I* ( $30.0$  to  $34.9 \text{ kg}/\text{m}^2$ ) and *obesity II* ( $35.0$  to  $39.9 \text{ kg}/\text{m}^2$ ), and *obesity III* ( $\geq 40 \text{ kg}/\text{m}^2$ ). Body type to perceive was evaluated with those questions: *When humans can meet at same society-economic level with you, how do you evaluate body type?* Body type to

perceive score of subjects were determined as *very good* for (1), *good* (2), *low* (3) and *overweight* (4).

### Measurement of Blood Parameters

Blood samples were put into EDTA-treated collection tubes via venipuncture early in the morning (08:00÷10:00 h) at least after 12-14 hours fasting state. Plasma total cholesterol (TC), high density lipoprotein-cholesterol (HDL), low density lipoprotein-cholesterol (LDL), and triglycerides (TG) concentrations were determined from standard enzymatic colorimetric techniques (*Cobas Integra 800, Roche Diagnostics, USA*). Plasma glucose was measured with automated glucose analyzer (*Cobas Integra 400, Roche Diagnostics, USA*). Analyses were done in the accredited Ulus Health Biochemistry Laboratory in Elazig. In sitting position the person's blood pressure by using stethoscope and sphygmomanometer measured and registered as value of mmHg.

### Statistical analyses

The SPSS statistical package program (SPSS Inc, Chicago, IL) was used to evaluate the results of the study. The data are presented as the mean  $\pm$  SD independent samples *t*-test was applied to determine the statistically significant differences between the HW and EW group. Significant levels were adjusted at  $p \leq 0.01$ , 0.05 and 0.001. The relation between variables evaluated with  $\chi^2$  test and the regression analysis method was used for the linear regression matrix correlation between parameters. The  $R^2$  scores were noted, and the significance levels were determined. The graphics and regression linear curves were additionally drawn in the error bar graphic mode in SSPS.

## Results

### Body Composition and Demographic Characteristics

As shown in Table 1, no statistical difference was observed among the physical parameters such

as age, height of HW and EW ( $p > 0.05$ ). Weight, BMI, WC, WHR, AMB, PBF and MBF to advantage of EW meaningful, SLM and TBW to advantage of HW meaningful difference was found ( $p < 0.001$ ). In our study, no significant differences were found with respect to BMR between HW and EW ( $p > 0.05$ ). There was found significant differences between age and body type in HW ( $R^2 = 0.40$ ;  $p < 0.001$ ), EW ( $R^2 = 0.35$ ;  $p < 0.001$ , Fig. 1). Populations mean age limit were found as  $42.36 \pm 7.31$  (Table 1, Fig. 1) Overweight and obese I-II-III body types have been seen high ratio in women in over of this age limit (about 42 years) and it observed increasing in body type with age in HW (Fig. 1).

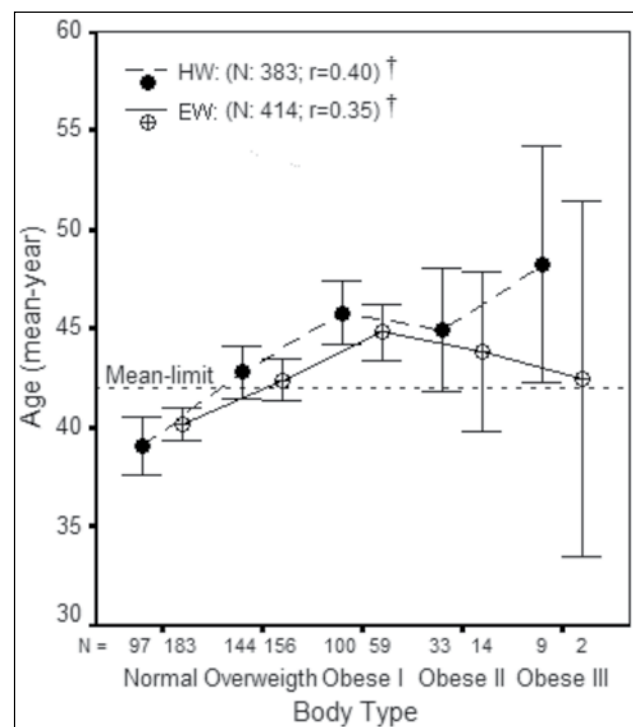


Figure 1. The relationship levels between age and body type according to the HW, EW.

The body type of the EW and HW which evaluated according to BMI presented in table 2. According to BMI classification it hasn't been found any *low person* in body type. Body type in HW as *overweight* (37.6%), EW as *normal* (44.2%) and in general population as *overweight* (37.6%) was observed in this study. In addition, obesity limit of HW was determined high level than EW (Table 2,  $\chi^2 = 51.127$ ,  $p < 0.05$ ; Fig. 2, 3, 4)

Characteristics of perceived body type were summarized in table 2. It have been seen as *overweight* 58.5% of HW, 51.3% of EW and 54.7% of

Table 1. Body composition, blood and HPLP II subscale parameters and number of children of HW and EW

	HW	EW	Total		
Body Composition Parameters	(n:383)	(n:414)	(N:797)	t	p
Age (year)	42.60 ± 8.30	41.85 ± 6.23	42.36 ± 7.31	1.358	0.175
Height (cm)	158.91 ± 6.29	159.23 ± 6.17	158.99 ± 6.32	0.665	0.506
Weight (kg)	71.55 ± 11.46	66.23 ± 11.14	69.18 ± 11.63	6.640	0.001‡
AMB (year)	45.20 ± 9.60	41.62 ± 7.85	43.71 ± 8.99	5.255	0.001‡
BMI (kg/m <sup>2</sup> )	28.77 ± 4.92	26.19 ± 4.24	27.43 ± 4.76	7.938	0.001‡
PBF (%)	35.53 ± 5.13	32.88 ± 4.92	34.26 ± 5.22	6.797	0.001‡
MBF (kg)	26.03 ± 7.33	22.19 ± 6.68	24.16 ± 7.31	7.109	0.001‡
SLM(kg)	41.97 ± 4.66	40.34 ± 4.82	41.11 ± 4.76	4.469	0.001‡
TBW(kg)	33.14 ± 3.75	31.75 ± 3.86	32.41 ± 3.83	4.757	0.001‡
WC (cm)	88.92 ± 11.03	82.74 ± 10.50	85.78 ± 11.14	7.701	0.001‡
WHR (%)	0.87 ± 0.06	0.84 ± 0.061	0.86 ± 0.064	6.162	0.001‡
BMR (kcal)	1200 ± 78.34	1192 ± 74.58	1194 ± 75.74	1.602	0.110
<b>Blood Pressure, Lipids and Glucose</b>					
sBP-Systolic (mmHg)	119.63 ± 19.02	113.33 ± 17.70	116.20 ± 18.33	4.319	0.001‡
dBp-Diastolic(mmHg)	77.18 ± 13.50	73.16 ± 12.62	74.91 ± 12.62	3.809	0.001‡
HDL-Cholesterol (mg/dl)	54.50 ± 8.32	54.28 ± 6.55	54.78 ± 7.95	0.172	0.864
LDL-Cholesterol (mg/dl)	150.39 ± 38.88	145.95 ± 47.20	148.52 ± 41.29	0.544	0.588
TC-Total Cholesterol (mg/dl)	212.44 ± 41.03	210.21 ± 44.75	211.07 ± 41.60	0.284	0.777
TG-Triglyceride (mg/dl)	166.71 ± 79.97	158.57 ± 96.75	161.32 ± 82.22	0.578	0.564
Glucose (mg/dl)	105.64 ± 30.98	101.64 ± 38.21	104.64 ± 33.22	0.738	0.472
<b>The Health Promotion Life-style Profile-II (HPLP-II) Subscale Score</b>					
Physical Activity	7.59 ± 2.70	8.10 ± 2.94	7.87 ± 2.85	2.292	0.05†
Nutritional Habits	16.91 ± 3.93	17.48 ± 3.48	17.21 ± 3.71	2.357	0.05†
Health Responsibility	22.82 ± 6.37	23.65 ± 6.18	23.26 ± 6.28	2.055	0.05†
Interpersonal Relations	20.21 ± 4.18	20.21 ± 4.08	20.23 ± 4.11	0.262	0.793
Stress Management	16.36 ± 4.19	16.18 ± 4.05	16.21 ± 4.12	0.186	0.853
Spiritual Growth	36.64 ± 6.92	36.88 ± 6.80	36.80 ± 6.84	0.374	0.709
Total HPLP-II Score	119.89 ± 20.63	123.75 ± 20.74	122.05 ± 20.78	2.016	0.05†
Difference of Total Scala Score (%)*	72.2 (62.4 %)	68.3 (64.5 %)	70.0 (63.6 %)	2.180	0.05†
<b>Number of children</b>	3.0 ± 1.28	2.0 ± 0.96	2.0 ± 1.9	8.691	0.001‡

Abbreviations: HW: Housewives, EW: Employment women, WHR; Waist to hip ratio, WC; Waist circumference, BMR; Basal metabolic rate, AMB; Age matched of body, PBF; Percent of body fat, MBF; Mass of body fat, SLM; Soft lean mass, TBW; Total body water, sBP; Systolic blood Pressure, dBp; Diastolic blood Pressure.

\*Difference of Total Scala Score (%): calculated by formula ( $Difference = 192 - Total\ HPLP\ II\ score$ ). Maximum score in HPLP-II scale is 192. Data was expressed as mean ± SD, significant level †p<0.05, ‡p<0.001 (Independent samples t test was used)

total population, the proportion of pleased from body type in HW were similar to EW (26 %). In term of child number of HW and EW were found as 3.0±1.28 and 2.0±0.96, respectively (p<0.001, Table 1). As shown figure 3, by increasing number of the child in EW, HW and total population occurs in body types as obesity I, II, III increasing continues. The correlation between number of the child and body type were observed as  $R^2=0.69$  in HW and  $R^2=0.60$  in EW (p<0.001, Fig. 2).

In this study, educational level ratio of HW was observed as *primary school* by 49.1% and *university* level of 61.8% in EW (Table 2). Educational level ratio of EW were determined in high ratio than HW ( $X^2=270.46$ ; p<0.001). As shown in figure 3, the HW ( $R^2=0.26$ ; p<0.01) and EW ( $R^2=0.27$ ; p<0.001) were found significant relation between BMI and educational levels. In addition to, *obesity* showed very high at *primary school* level in HW, EW were determined too small (Fig. 3).

Table 2. Comparison of the HW and EW according to body type, body type to perceive educational level and diet practice habits.

	HW	EW	Total		
<b>Body Type* n (%)</b>	<b>(n:383)</b>	<b>(n:414)</b>	<b>(N:797)</b>	<b>X<sup>2</sup></b>	<b>p</b>
Normal	97 (25.3 %)	183 (44.2 %)	280 (35.1 %)	51.127*	<0.05
Overweight	144 (37.6 %)	156 (37.7%)	300 (37.6 %)		
Obese I	100 (26.1 %)	59 (14.2 %)	159 (19.9 %)		
Obese II	33 (8.7 %)	14 (3.4 %)	47 (6.0 %)		
Obese III	9 (2.3 %)	2 (0.5 %)	11 (1.4 %)		
<b>Body type to perceive n (%)</b>					
Very good	100 (26.1 %)	109 (26.3 %)	209 (26.2 %)	9.678*	<0.05
Good	47 (12.3 %)	83 (20.0 %)	130 (16.3 %)		
Low	12 (3.1 %)	10 (2.4 %)	24 (2.8 %)		
Overweight	224 (58.5 %)	212 (51.3 %)	436 (54.7 %)		
<b>Education Level n (%)</b>					
Primary School	188 (49.1 %)	26 (6.3 %)	214 (26.9 %)	270.46*	<0.001
Secondary School	32 (8.4 %)	13 (3.1 %)	45 (5.6 %)		
High School	114 (29.8 %)	119 (28.7 %)	233 (29.2 %)		
University and upper	49 (12.8 %)	256 (61.8 %)	305 (38.3 %)		
<b>Dietary habits n (%)</b>					
Never	230 (60.0 %)	261 (63.0 %)	491 (61.6 %)	8.306*	<0.05
Sometimes	132 (34.5 %)	127 (30.7 %)	259 (32.5 %)		
Often	16 (4.2 %)	10 (2.4 %)	26 (3.3 %)		
Regularly	5 (1.3 %)	16 (3.9 %)	21 (2.6 %)		

\* In this study, volunteers with low body type are not found

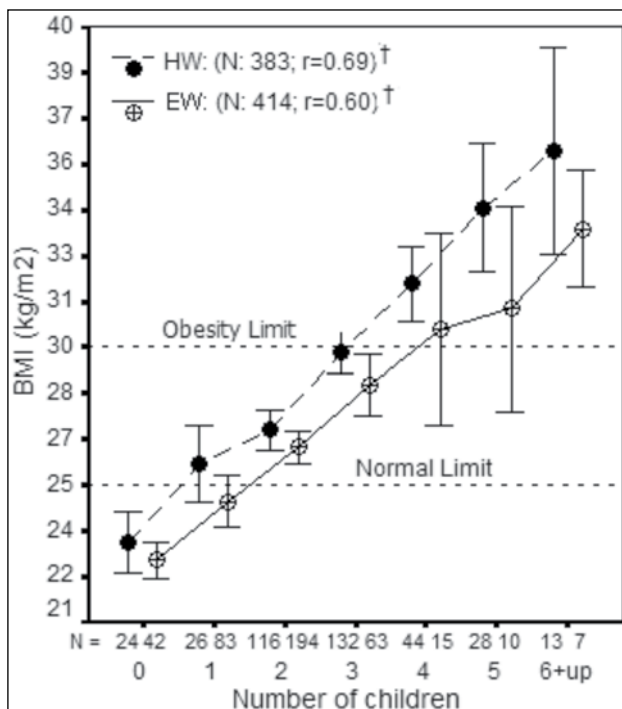


Figure 2. The relationship levels between BMI and child number according to the HW, EW

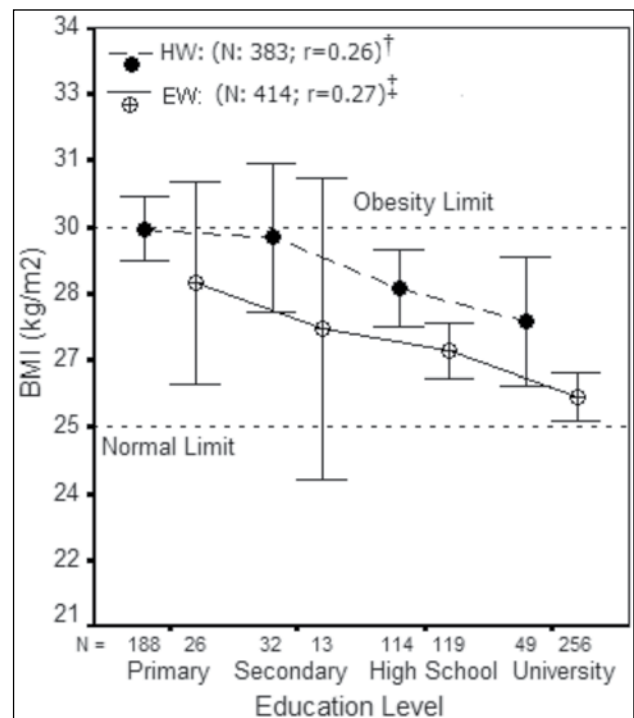


Figure 3. The relationship levels between BMI and education level according to the HW, EW



The ration of diet practice habits of the women shows never applied in HW 60.0%, EW 63.0% and in general totally is 61.6%. Regularly dietary habits were much more (3.9%) in EW than HW (1.3%), (Table 2). No significant differences were found both in BMI and ration of diet practice habits of HW ( $R^2=0.10$ ;  $p>0.05$ ). But, significant differences were found both in BMI and ration of diet a practice habits of EW ( $R^2=0.25$ ;  $p<0.01$ , Fig. 4). In this group were observed reaching to BMI normally limit level with regularly dietary habits (Fig. 4).

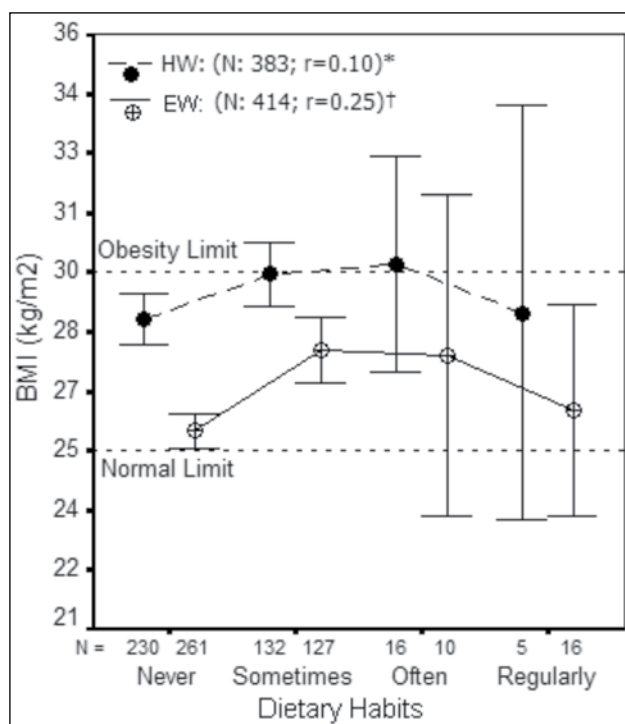


Figure 4. The relationship levels between BMI and dietary habits according to the HW, EW.

### Blood pressure and lipids profile

There was found a significant difference between sBP and dBP values in EW ( $p<0.001$ ), but no found any significant in HDL, LDL, TG, TC from blood lipid parameters and glucose values ( $p>0.05$ , Table 1). In this study observed as normally HDL, LDL, TG, TC, glucose values and up level of TC values (Table 1). As shown in table 3, linear regression matrix in HW, EW and total population were observed correlational relationship a positive between body composition (age, BMI, WC, VHR, PBF, AMP, TBW) and blood pressure parameters (sBP, dBP) ( $p<0.01$ ). Also correla-

tional relationship were observed between body composition (WHR, PBF, AMP) and blood parameters (TG, glucose) ( $p<0.01$ ,  $p<0.05$ ). Correlational relationship were observed between blood lipid (HDL, LDL, TG, TC) and body composition parameters (age, BMI, WC, VHR, PBF, TBW) ( $p<0.01$ ,  $p<0.05$ , Table 3).

### The Health Promotion Life-style Profile II (HPLP-II)

No significant differences were found *spiritual growth, interpersonal relations, stress management* scale score from HPLP-II scale in HW and EW ( $p>0.05$ , Table 1). But significant differences were found between *physical activity, nutritional habits, health responsibility* and *total HPLP-II score* in EW in comparison to HW ( $p<0.05$ , Table 1). According to HW was observed be in good condition on account of *health responsibility* behavior and *physical activity, nutritional habits* of EW by total HPLP-II scale score ( $p<0.001$ ). In according to HW (62.4%) showed higher proportion among total scale score difference calculated ( $\text{Difference} = 192 - \text{Total HPLP-II score}$ ) by consideration of maximum 192 score which obtained in HPLP-II scale in EW (68.5%) in term of health life-style behavior ( $p<0.05$ , Table 1). However, in health life-style behaviors of HPLP-II scale scores of both study groups according to maximum were observed as middle (approximately 65%) level (Table 1). As shown in figure 5a, correlational relationships were found between body type and *physical activity habits* from principal parameters of *health responsibility* behavior (HW:  $R^2=0.25$ , EW:  $R^2=0.29$ ;  $p<0.05$ ). However, correlation relationship were found between total HPLP-II scale mean and body type (Fig. 5b; HW  $R^2=0.35$ , EW  $R^2=0.39$ ;  $p<0.05$ ). Proportion between physical activity and total HPLP-II decreased with increasing of obesity limit (Fig. 5a, 5b).

Table 3. The relationship body composition, blood lipid and blood pressure parameters as linear regression matrix

		R <sup>2</sup>													
Study		Body Composition Parameters							Blood Parameters					Blood Pressure	
	Groups <sup>a</sup>	Age	BMI	WC	WHR	PBF	A.M.P	TBW	HDL	LDL	TG	TC	Gluc	sBP	dBP
	HW	1	0.28‡	0.35‡	0.53‡	0.34‡	0.95‡	0.03	0.20†	0.51‡	0.12	0.60‡	0.17	0.34‡	0.24‡
Age	WW	1	0.27‡	0.29‡	0.45‡	0.30‡	0.87‡	0.05	0.16†	0.39‡	0.10	0.27†	0.03	0.25‡	0.20‡
	Total	1	0.29‡	0.33‡	0.50‡	0.33‡	0.88‡	0.05	0.16†	0.40‡	0.11	0.50‡	0.12	0.31‡	0.25‡
	HW	0.28‡	1	0.79‡	0.85‡	0.91‡	0.48‡	0.57‡	-0.26†	0.45‡	0.24‡	0.32‡	0.17	0.42‡	0.41‡
BMI	WW	0.27‡	1	0.79‡	0.83‡	0.89‡	0.57‡	0.64‡	-0.29†	0.50‡	0.22‡	0.43‡	0.07	0.34‡	0.29‡
	Total	0.29‡	1	0.81‡	0.85‡	0.91‡	0.55‡	0.62‡	-0.26†	0.28‡	0.23‡	0.22‡	0.10	0.41‡	0.37‡
	HW	0.35‡	0.79‡	1	0.75‡	0.73‡	0.52‡	0.56‡	-0.26†	0.29‡	0.34‡	0.31‡	0.05	0.42‡	0.39‡
WC	WW	0.29‡	0.80‡	1	0.69‡	0.71‡	0.51‡	0.62‡	-0.23‡	0.43‡	0.33†	0.44‡	0.06	0.34‡	0.27‡
	Total	0.33‡	0.81‡	1	0.74‡	0.74‡	0.54‡	0.61‡	-0.24‡	0.35‡	0.34‡	0.35‡	0.06	0.41‡	0.35‡
	HW	0.53‡	0.85‡	0.75‡	1	0.84‡	0.71‡	0.42‡	-0.15†	0.28‡	0.28‡	0.32‡	0.24†	0.40‡	0.37‡
WHR	WW	0.45‡	0.83‡	0.69‡	1	0.79‡	0.74‡	0.48‡	-0.17†	0.50‡	0.50‡	0.48‡	0.27†	0.33‡	0.27‡
	Total	0.50‡	0.85‡	0.74‡	1	0.83‡	0.74‡	0.47‡	-0.15†	0.37‡	0.37‡	0.37‡	0.23†	0.39‡	0.34‡
	HW	0.34‡	0.91‡	0.73‡	0.84‡	1	0.55‡	0.33‡	-0.25†	0.21†	0.27‡	0.22†	0.12	0.36‡	0.35‡
PBF	WW	0.30‡	0.89‡	0.71‡	0.79‡	1	0.61‡	0.38‡	-0.24†	0.52‡	0.22‡	0.47‡	0.05	0.32‡	0.29‡
	Total	0.33‡	0.91‡	0.74‡	0.83‡	1	0.60‡	0.39‡	-0.24‡	0.33‡	0.25‡	0.31‡	0.13	0.36‡	0.34‡
	HW	0.95‡	0.48‡	0.52‡	0.71‡	0.55‡	1	0.12†	0.11	0.49‡	0.17†	0.57‡	0.22†	0.39‡	0.31‡
AMP	WW	0.87‡	0.57‡	0.51‡	0.74‡	0.61‡	1	0.23‡	-0.02	0.43‡	0.23‡	0.48‡	0.22†	0.33‡	0.27‡
	Total	0.88‡	0.55‡	0.54‡	0.74‡	0.60‡	1	0.20‡	0.08	0.47‡	0.19‡	0.54‡	0.25†	0.38†	0.31†
	HW	0.03	0.57‡	0.56‡	0.42‡	0.33‡	0.12†	1	-0.14	0.23†	0.28†	0.01	0.04	0.28‡	0.32‡
TBW	WW	0.04	0.64‡	0.62‡	0.48‡	0.38‡	0.23‡	1	-0.22	0.38‡	0.31†	0.30	0.01	0.21‡	0.14‡
	Total	0.05	0.62†	0.61†	0.47†	0.39†	0.20†	1	-0.15	0.24†	0.27†	0.12	0.03	0.27‡	0.25‡
	HW	0.20†	-0.26‡	-0.26‡	-0.15†	-0.25‡	0.11	-0.14	1	0.00	-0.38‡	0.10	0.05	-0.11	-0.09
HDL	WW	0.06	-0.29†	-0.23‡	-0.17†	-0.24‡	-0.02	-0.22	1	0.01	-0.19‡	0.12	0.02	-0.10	-0.16
	Total	0.16†	-0.26‡	-0.24‡	-0.15†	-0.24‡	0.08	-0.15	1	0.01	-0.29‡	0.11	0.03	-0.10	-0.10
	HW	0.51‡	0.45‡	0.29‡	0.28‡	0.21†	0.49‡	0.23†	-0.00	1	0.18†	0.91‡	0.05	0.22†	0.10
LDL	WW	0.39‡	0.50‡	0.43‡	0.50‡	0.52‡	0.43‡	0.38‡	-0.01	1	0.15†	0.90†	0.18	0.02	0.02
	Total	0.40‡	0.28‡	0.35‡	0.37‡	0.33‡	0.47‡	0.24‡	-0.01	1	0.17†	0.91‡	0.04	0.14	0.07
	HW	0.12	0.24‡	0.34‡	0.28‡	0.27‡	0.17†	0.28†	-0.38‡	0.18†	1	0.30‡	0.30‡	0.26†	0.20‡
TG	WW	0.10	0.22‡	0.33†	0.50‡	0.22‡	0.23‡	0.31†	-0.19‡	0.15†	1	0.28‡	0.12	0.20†	0.15†
	Total	0.11	0.23‡	0.34‡	0.37‡	0.25‡	0.19‡	0.27†	-0.29‡	0.17†	1	0.29‡	0.23‡	0.20‡	0.18†
	HW	0.60‡	0.32‡	0.31‡	0.32‡	0.22†	0.57‡	0.01	0.10	0.91‡	0.30‡	1	0.03	0.28‡	0.23†
TC	WW	0.27†	0.43‡	0.44‡	0.48‡	0.47‡	0.48‡	0.30	0.12	0.90‡	0.28‡	1	0.27	0.18†	0.03
	Total	0.50‡	0.22‡	0.35‡	0.37‡	0.31‡	0.54‡	0.12	0.11	0.91‡	0.29‡	1	0.11	0.22‡	0.16
	HW	0.17	0.17	0.05	0.24†	0.12	0.22†	0.04	0.05	0.05	0.30‡	0.03	1	0.10	0.14
Gluc	WW	0.03	0.07	0.06	0.27†	0.05	0.22†	0.01	0.02	0.18	0.12	0.27	1	0.22	0.30†
	Total	0.12	0.10	0.06	0.23†	0.13	0.25†	0.03	0.03	0.04	0.23†	0.11	1	0.01	0.01
	HW	0.34‡	0.42‡	0.42‡	0.40‡	0.36‡	0.39‡	0.28‡	-0.11	0.22†	0.26†	0.28‡	0.10	1	0.70‡
sBP	WW	0.25‡	0.34‡	0.34‡	0.33‡	0.32‡	0.33‡	0.21‡	-0.10	0.02	0.20†	0.18†	0.22	1	0.77‡
	Total	0.31‡	0.41‡	0.41‡	0.39‡	0.36‡	0.38‡	0.27‡	-0.10	0.14	0.20‡	0.22‡	0.11	1	0.74‡
	HW	0.24‡	0.41‡	0.39‡	0.37‡	0.35‡	0.31‡	0.32‡	-0.09	0.10	0.20‡	0.23†	0.14	0.70‡	1
dBP	WW	0.20‡	0.29‡	0.27‡	0.27‡	0.29‡	0.27‡	0.14‡	-0.16	0.02	0.15†	0.03	0.20	0.77‡	1
	Total	0.25‡	0.38‡	0.35‡	0.34‡	0.34‡	0.31‡	0.25‡	-0.10	0.07	0.18†	0.16	0.11	0.74‡	1

Abbreviations: HW: Housewives, EW: Employment women, BMI (kg/m<sup>2</sup>); Body mass index, WHR (%); Waist to hip ratio, WC (cm); Waist circumference, A.M.P (year); Age matched of body, PBF (%); Percent of body fat, TBW (kg); Total body water, HDL (mg/dl); High density lipoprotein, LDL (mg/dl); High density lipoprotein, TG (mg/dl); Triglyceride, TC; Total cholesterol, Gluc (mg/dl); Glucose, sBP (mmHg); Systolic blood Pressure, dBP (mmHg); Diastolic blood Pressure.

<sup>a</sup>There were 383 subjects in the HW group; 414 in the EW group, and 797 total populations. Significant level †p<0.05, ‡p<0.01 (linear regression analysis was used).

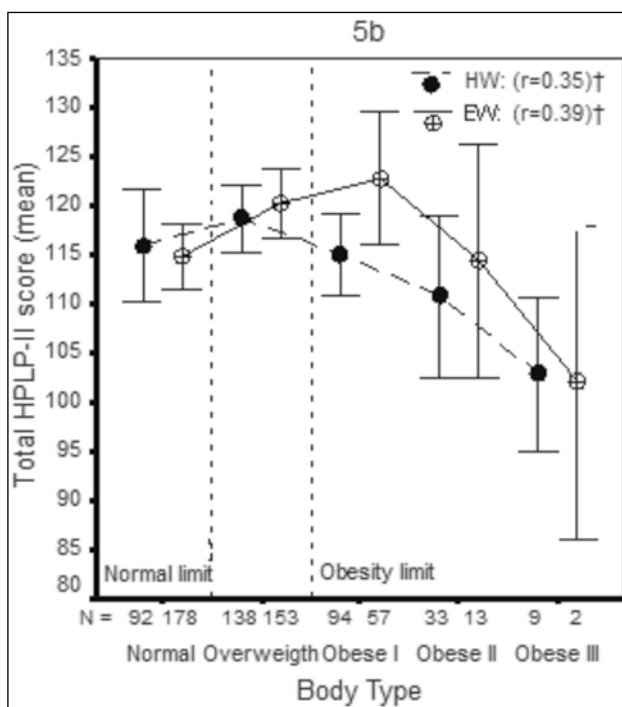
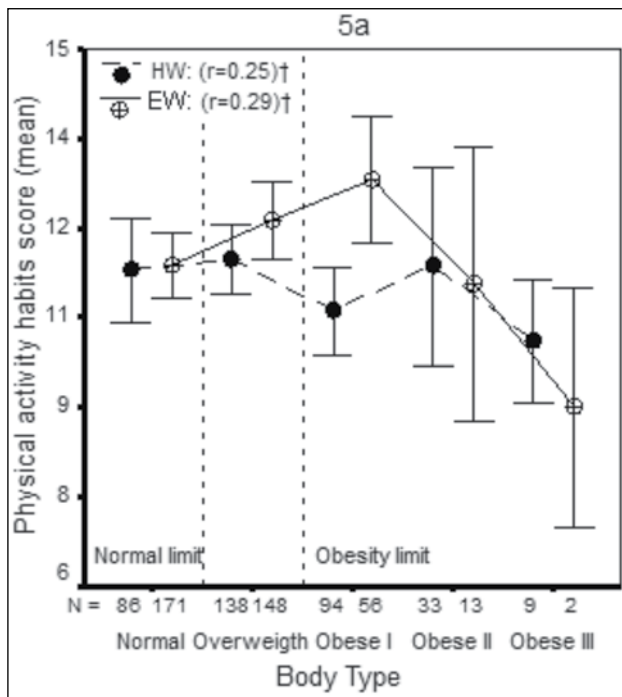


Figure 5. The relationship levels between HPLP-II subscales physical activity habits score (5a), total HPLP II mean score (5b) and body type according to the HW, EW

**Discussion**

Body composition of individuals might vary with factors as height and age<sup>[15,16]</sup>. Therefore we aimed the find the differences on blood lipids,

body compositions and healthy lifestyle behaviors of unemployed and employed women has similar physical characteristics. With reference to no differences were found in height and age parameters on two groups ( $p > 0.05$ ). In this study, while weight, BMI, WC, VHR, AMB, PBF and MBF parameters were found in favor of EW ( $p < 0.001$ ), SLM and TBW parameters were found significantly in favor of HW ( $p < 0.001$ , Table 1).

The incidence of obesity has been rapidly increasing during the past decades<sup>[1,3]</sup>. The big differences have been observed in developed and developing countries where matters like meagerness and obesities excluded from normal weight limits<sup>[17,18]</sup>. In according to populations can change to interpret prevalence of obesity and anthropometric assessment<sup>[2]</sup>. Furthermore, ethnic differences could be showed in body composition<sup>[19]</sup>. In previous studies, the obesity prevalence has been showed differences among regions and this ratio was found very high all of them. Obesity prevalence was determined to be 45.2 %<sup>[20]</sup> and 27.4% in<sup>[21]</sup> in women over of age 20 years, 34.1% in women over of age 40 years<sup>[22]</sup>, 51% in women aged between 25 and 64 years<sup>[23]</sup>. We observed as *obesity I-II-III* of 27.3% and *overweight* of 37.6%, *normal* 35.1% of body type in women. The prevalence of overweight and obesity in the general population have been estimated as 74.9% (Table 2). A few studies, prevalence of obesity were higher 2 to 2.5 fold in HW than in EW<sup>[24]</sup>. The prevalence of obesity varies from 50.0 % to 75.7 %<sup>[18]</sup>. At a study from Turkey, it is reported that ratio of obesity in women of 23888 inhabitants was 36.17%<sup>[25]</sup>.

Incidence of excess weight increased with age for male and female. The increasing of WHR occurred in conjunction with increase of age and BMI<sup>[26]</sup>. Obesity onset age in individual can constitution risk factors for patient and aged of 40 years limit was accepted as critic<sup>[27]</sup>. In Our study, mean obesity limit of women have been determined as aged of 42 years. The EW and HW was found a positive correlation relationship (HW;  $R^2=0.40$ , EW;  $R^2=0.35$ ,  $p < 0.001$ , Fig. 1). Obesity prevalence was observed to increasing with age (Fig. 1). Our results are consistent with literature. Obesity is the most common nutritional disorders and major health problem for the advanced ages. According to their perception of subjects, it has

been seen as *overweight* of HW (58.5 %), of EW (51.3%) and of general population (54.7%). HW and EW have been seen as *low* of 3.1% and 2.4%. It has been seen as approximately *very good* 26 % all of them (Table 2). There was parallelism between body perception and type in their opinion about body composition.

WHR which measured distribution of fat in body is an anthropometric method as independent from BMI is description as abnormal in over of 0.72 and is associated with increased risk of complications if it is  $\geq 1$  in men and  $\geq 0.9$  in women. WC measurement reflects body fat and it doesn't including most of bone structure exception for backbone and big muscle mass. Therefore variability among individual can't influence of false ratio [28]. WC in women was defined as increased risk of  $\geq 80$  cm, CVD and metabolic complications of  $\geq 88$  cm [29]. In our study, WHR was determined as 87% in HW and 84% in EW. Also, WC was determined as 88.92 cm in HW and 82.74 cm in EW (Table 1). When WC and WHR were considered was observed in EW better than in HW but values of both groups will be compose risk level for heart and metabolic complications. When WC was measured, prevalence of abdominal type obesity was determined as 34.9% [30]. Increased of WHR and WC might visible as fatten in region abdominal. Abdominal (central) obesity has greater risks because of the visceral fat, which means that there is an active fat depot in the body [31]. In this study was found a significant correlation between BMI, PBF, AMP, TBW and WHR, WC (Table 3).

Alteration was taken places in abdominal obesity and level of blood cholesterol, which in the high TG; low HDL cholesterol dyslipidemia is also found in obesity patients [32,33]. However, in an earlier study reported a relationship between hypertension and diabetes mellitus, insulin resistance, level of elevated blood glucose with abdominal obesity [1,3,31,34]. Depending on increase of WHR ratio, the relationship between obesity and diabetes mellitus is so closely related that it is worth questioning the possibility of obesity being more than just one diabetes risk. Finally, the evolution of obesity to diabetes leads to a decrease in insulin secretion [28,35]. There was found negative relationship between HDL with WHR and WC. A significant correlation was found between WHR,

WC and LDL, TG, TC, glucose, sBP, dBP. There was found a negative significant in the BMI and HDL, significant correlation among BMI and level of LDL, TG, TC (Table 3). Our study is consistent with previous studies.

Excess body weight is associated with deleterious changes in level of the plasma TG negative correlation between body weight and level of the plasma HDL cholesterol have been reported in literature [33,36,37,38]. Obesity was also associated with other risk factors like high blood pressure, high triglyceride level, and low HDL cholesterol level and diabetes [39]. Our study, although there was not found any significant difference between level of the blood and fat of EW and HW ( $p > 0.05$ ), levels of the HDL, LDL, TG and glucose of women have been observed be normal limit. TC values were determined be high from normal limit (Table 1). sBP and dBP increased with age [23]. There was found a statistical significance association between sBP and dBP with age in study groups ( $p < 0.01$ , Table 3).

By increasing number of the child in total population, EW and HW occurred also weight increased (obesity I-II-III) in body type. The positive correlation between number of the child and BMI were observed (Fig. 2). Overweight and obesity are common findings in women of reproductive age. In a previous study from Japan by Wen and Cournot et al, the risk degree of obesity increases with the more number of the child and pregnancy [40,41]. Furthermore, in women we would have to consider various pregnancy-related circumstances because body composition has been shown to increase with the number of pregnancies. This increasing is advantage 1kg. Indeed, it suggested that association among reproductive and weight gain could be affected from social and behavioral factors [42].

Educational level ratio of EW was determined high ratio than HW. The HW and EW were found correlation relationship between BMI and educational levels (HW:  $R^2=0.26$ , EW;  $R^2=0.27$ ,  $p < 0.01$ , Fig. 3). When level of education was considered, an inverse relationship was observed between level of education and prevalence of obesity. In this study, educational level ratio of HW was observed as *primary school* by 49.1% and in *university level* of 61.8% in EW (Table 2).

As education level increased, the prevalence of obesity decreased. Both BMI and WC in women

showed an inverse gradient with educational level and the rest of the socio-economic variables<sup>[43]</sup>. Prevalence of obesity was highest in the groups of HW at level of the primary school education. EW was not obese but they were observed as overweight (Fig. 3). This case could be result from discipline of work site of EW. Body types keep fit EW than better HW.

As shown figure 4, significant differences were found between BMI and ratio of diet practice habits among EW ( $R^2=0.25$ ;  $p<0.01$ ) but correlation was not determined among HW ( $R^2=0.10$ ;  $p>0.05$ ). In study groups, ratio of regularly and irregularly dietary habits was observed as 2.6 % and 61.6 % respectively (Table 2). BMI ratio of women regularly dietary habits was observed down of obesity limit and made be successful diet of EW than HW (Fig. 4).

The behaviors of healthy lifestyle define the importance of the cognitive processes which have influenced on the conducts and developing his health of the individual. The developing health is a process which included in factors influenced alteration processes and way providing to change their conducts to reach a high health level and a social environment<sup>[33,43]</sup>. Significant differences were found *physical activity*, *nutritional habits*, *health responsibility* and total HPLP-II score from health life-style behaviors in EW in comparison to HW ( $p<0.05$ , Table 1). According to HW was observed good condition on account of health responsibility behavior habits and physical activity, nutritional habits of EW by HPLP-II scale score.

The women's participation in labor power dramatically increases. Based on the protection of the body composition, EW who got higher education level and has work's life discipline is more successful than HW (Table 2, Fig. 3, 5a, 5b). It is reported that the women has a positive effect on the physical fitness without making any physical activities when they take place in the work life<sup>[44]</sup>. The QoL is proportional to participation in health promoting activity (sport, exercise, recreation etc.) and provided free time services. HW who regularly attend to a woman's at-home day, are mostly object to imbalanced nutrition as a cause of the insufficiency of free time services. In many studies it is proved that the experimental studies improve various aspects of QoL of the exercises,

maintenance or strengthening of cardiovascular system, reduce stress, mood elevations of person with relax emotional<sup>[45,46,47]</sup>.

Obesity is a widespread condition, with different etiologist, that is usually treated only symptomatically through lowered energy intake. The chose television viewing as a form of leisure activity more often than non-obese individuals and as a result they could significantly reduce other forms of physical activities and total daily energy expenditure in modern society. In individual could be caused to accumulation as fat of this energy<sup>[27,48]</sup>. Especially in subjects between 25-30 age years, the physical inactivity and unbalance nutrition habits caused to increases in obesity prevalence in Turkey. It is reported that the rate of responsibility of the physical inactivity in the obesity prevalence is 67.5%<sup>[27]</sup>. As shown in figure 5a, positive correlational relationship were found between body type and physical activity habits from principal parameters of health responsibility behavior habits (Fig. 5a; HW;  $R^2=0.25$ , EW;  $R^2=0.29$ ,  $p<0.05$ ). However, correlation relationship were found between total HPLP-II mean score and body type (Fig. 5b; HW  $R^2=0.35$ , EW  $R^2=0.39$ ;  $p<0.05$ ). According to these results, there is an inverse relationship between obesity and physical activity, health life style. Prevalence of obesity found to be decreased with increased physical activity level and health life style (Fig. 5a, 5b).

As conclusion, prevalence of obesity is higher frequency of obesity among HW. The loss of energy decreases in accordance to the repeating and monotonous exercises of house works in HW or EW and protecting the composition of the body has become more difficult. The variety in composition of the body is a major risk factor for development of several disease types. Educational level is seen as an important factor in controlled of weight body. For a long and healthy life, everyone should include a healthy diet, a regular exercise program and a normal weight. To be successful in making all of those, it is not necessary to be wealthy, educated, it is important become well informed, intelligent consumer. In this subject, the people, government, media and food industry must be in collaboration for reducing the obesity prevalence.

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# Correlation between neuropathy score and electroneurographic parameters values in patients with painful diabetic polyneuropathy before and after the low intensity laser therapy

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## Abstract

**Introduction:** Low intensity laser therapy (LILT) is one of methods used in physical medicine for pain reduction in different medical conditions. There are only a few studies about LILT treatment of painful DPN with different results, because pain reduction was not significant in all studies. Some other effects of LILT in painful DPN, as on Neuropathy score and electroneurographic (ENG) parameters values, was not precisely defined yet.

**Aims of research:** To define the effect of LILT on Neuropathy score and ENG parameters values in patients with painful DPN and also to consider correlation between those parameters before and after LILT.

**Patients and methods:** We analysed 31 patients with clinical and ENG signs of painful DPN, average age 54.77 years (54.77±11.39). All analysed patients received 30 LILT treatments during the period of 12 weeks. Prior to and after the 12 weeks period of LILT treatment, Diabetic Neuropathy Examination (DNE) score and Michigan Neuropathy Screening Instrument (MNSI) total score were determined. For ENG examination we used surface electrodes, and we registered motor (MCV) and sensory conduction velocities (SCV) values (in m/s) of peroneal (PN) and ulnar nerves (UN) and their minimal F-wave (PNFL and

UNFL) latencies (in ms) after 40 repetitive stimulations of those nerves. SCV (in m/s) of PN and UN was determined by antidromic technique. Control group consisted 31 patients with painful DPN, corresponding ages, who received only vasoactive therapy. For statistical analysis we used t-test and Pearson bivariate correlation (sig. 2-tailed).

**Results:** We registered statistical significant difference ( $p < 0.001$ ) between MNSI values before (5.61±1.76) and after LILT (4.23±1.67), and also ( $p < 0.001$ ) between DNE values before (7.68±2.27) and after LILT (5.61±1.89), but those differences were not significant ( $p > 0.05$ ) in control group. We didn't register significant difference ( $p > 0.05$ ) between analysed ENG parameters values before and after LILT (applied during the period of 12 weeks) in patients with painful DPN. We didn't register significant correlation ( $p > 0.05$ ) between MNSI total score and analysed ENG parameters values before and after LILT. We registered statistical significant negative correlation ( $p < 0.05$ ) between DNE score and PN MCV before LILT and also in control group. We registered statistical significant positive correlation ( $p < 0.05$ ) between DNE score and PN FL values and statistical significant negative correlation ( $p < 0.01$ ) between DNE score and UN SCV values after LILT. We didn't register any adverse and/or side effect of LILT treatment in patients with painful DPN.



**Conclusion:** In our study LILT had a significant effect ( $p < 0.001$ ) on MNSI total score and DNE score values reduction, but we didn't register significant effect ( $p > 0.05$ ) of LILT on analysed ENG parameters values in patients with painful DPN. We didn't register significant correlation ( $p > 0.05$ ) between MNSI total score and analysed ENG parameters values before and after LILT. There was statistical significant negative correlation ( $p < 0.05$ ) between DNE score and PN MCV values before LILT and also in control group. It indicates that registration of PN MCV values and it's following is important for diagnosis and evaluation of neuropathy severity in patients with painful DPN. There was statistical significant positive correlation ( $p < 0.05$ ) between DNE score and PN FL values after LILT and it indicates that registration of this electrophysiologic parameter value might be useful for evaluation of possible direct effect of LILT on impulse conduction along the whole length of PN motor axons, particularly their proximal parts, including corresponding roots and spinal segments. There was statistical significant negative correlation ( $p < 0.01$ ) between DNE score and NU SCV values after LILT and it indicates that registration of this electrophysiologic parameter value might be useful for evaluation of possible indirect ("remote") effect of LILT on impulse conduction along ulnar nerve sensory axons. Further clinical double-blind randomized controlled studies of LILT treatment in patients with painful DPN is necessary.

**Key words:** laser, low intensity, painful, diabetic polyneuropathy, neuropathy score, electroneurographic parameter

## Introduction

Diabetic neuropathies are the most common types of neuropathies world-wide (1). Diabetes is the leading cause of neuropathy in North American and likely in the most of the developed world and distal, predominantly sensory polyneuropathy is the most common form of neuropathy associated with diabetes (2). Diagnosis of painful diabetic polyneuropathy (DPN) is a clinical one and relies on the patient's description of pain. That pain is distal, symmetrical, often associated with noctur-

nal exacerbations, and commonly described as prickling, deep aching, burning, sharp or like an electric shock. Pharmacologic management of painful DPN consists of symptomatic therapies (antidepressants, anticonvulsants etc.) with, in some cases, many side effects, but no sufficient evidence exists for any nonpharmacologic therapy (3).

The pharmacologic or nonpharmacologic treatment of chronic painful diabetic neuropathy remains a challenge, and the current state of treatment remains unsatisfactory and far from being able to eradicate pain (1). Low intensity laser therapy (LILT) or low level laser therapy (LLLT) as a part of light therapy is one of methods used in physical medicine. These low level lasers are currently being used in the United States and other countries for wounds and soft tissue healing and for pain relief (4). LILT is not associated with any adverse reactions or troublesome side effects (5). This is one of physical therapies which have been proposed and do have support from small controlled trials in the treatment of painful diabetic neuropathy (6, 7).

We analysed Medline database with key words low intensity laser therapy and diabetic neuropathy and we found only two articles considering this problem (8, 9), beside two other articles about neuropathic ulcer healing (10, 11). In both previous studies (8, 9) neuropathic pain reduction was registered in patients with painful DPN treated with LILT compared with placebo. But in randomized, double-masked, sham therapy controlled clinical trial, pain reduction as a result of placebo response was observed in all analysed patients with additional 16% pain score reduction in patients treated with LILT. That suggested some efficacy of this treatment, but did not provide sufficient evidence to recommend it for painful symptoms of diabetic sensorimotor polyneuropathy. Also, in this study LILT had no effect on the Toronto Clinical Neuropathy Score, nerve conduction studies, sympathetic skin response or quantitative sensory testing (8). In our previous studies we registered significant decrease of spatial perception threshold in patients with DPN after LILT (9) and also considered electrophysiological aspect of this problem (12). In this study, we shall analyse the correlation between Neuropathy Score (other than Toronto Clinical Neuropathy Score)

and electroneurographic (ENG) parameters values in patients with painful DPN before and after LILT, to consider other possible influences of this treatment.

### Objective of the study

We analysed Neuropathy Score values in patients with painful DPN and considered correlation between this values and ENG parameters before and after LILT. The aim of this study is to consider the effect of LILT on Neuropathy score and ENG parameters values in patients with painful DPN.

### Methods

We analysed 31 patients (17 males) with clinical and electroneurographic (ENG) signs of painful DPN, average age 54.77 years ( $54.77 \pm 11.39$ ). All analysed patients received 30 LILT treatments at Clinic for physical medicine and rehabilitation Clinical Centre of Niš during the period of 12 weeks. The LILT device had a wavelength of 904 nm and a total power of 60 mW. All LILT treatments lasted for one minute per site (four paravertebral points in the lumbosacral period, three points along ischiadic nerve and two points on the dorsum of the feet). Prior to and after the period of 12 weeks of LILT treatment, the neuropathy score and ENG parameters values were registered. Diabetic Neuropathy Examination (DNE) score (0-16 points) (13) and Michigan Neuropathy Screening Instrument (MNSI) total score (0-10 points) (14) were determined. For ENG examination we used surface electrodes, and we registered motor (MCV) and sensory conduction velocities (SCV) values (in m/s) of peroneal (PN) and ulnar nerves (UN) and their minimal F-wave (PN FL and UN FL) latencies (in ms) after 40 repetitive stimulations of those nerves, using standardised methods (15, 16). SCV of PN and UN was determined by antidromic technique. Control group consisted of 31 patients (17 males) with painful DPN, average age 53.82 years ( $53.82 \pm 12.06$ ) who received only vasoactive drug (Pentoxifylline, 800 mg daily) therapy per os during 12 weeks, and we analysed the same parameters (neuropathy score, ENG pa-

rameters) before and after vasoactive drug treatment. Skin temperature of the patients hands and feet were maintained at 32°C. The patients with some other diseases (uremia, systemic illness, malignant tumor) and those who were using drugs which can cause neuropathy, were excluded from this study. Contraindications for LILT treatment were malignant tumor, pregnancy, epilepsy, vein thrombosis, light hypersensitivity and application over the thyroid gland (17).

### Statistical evaluation

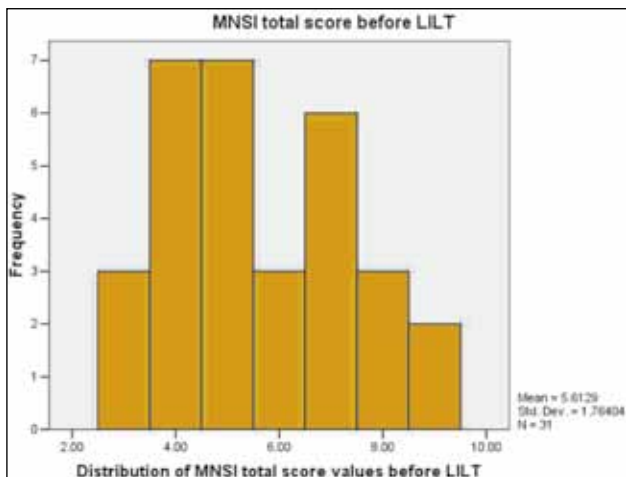
We evaluated registered data by statistical analysis using the computer program SPSS.

We used t-test and Pearson's bivariate correlation (sig. 2-tailed). All tests and analyses are considered statistically significant on the level of significance of  $p < 0.05$ . Results we obtained will be presented on the tables and histograms.

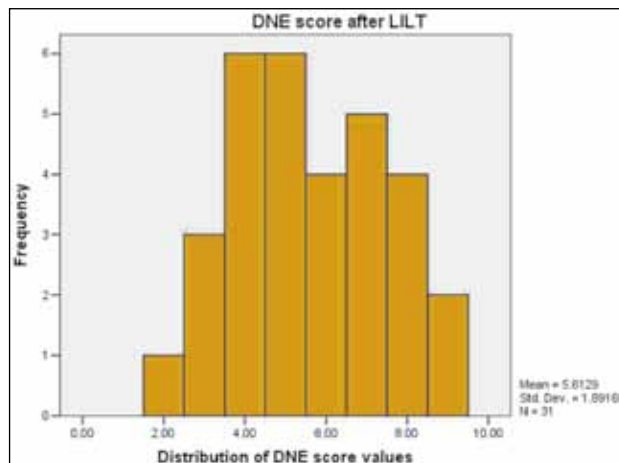
### Results

#### 1. The mean values ( $X \pm SD$ ) of neuropathy score (DNE, MNSI) values in patients with painful diabetic polyneuropathy before and after LILT and in control group

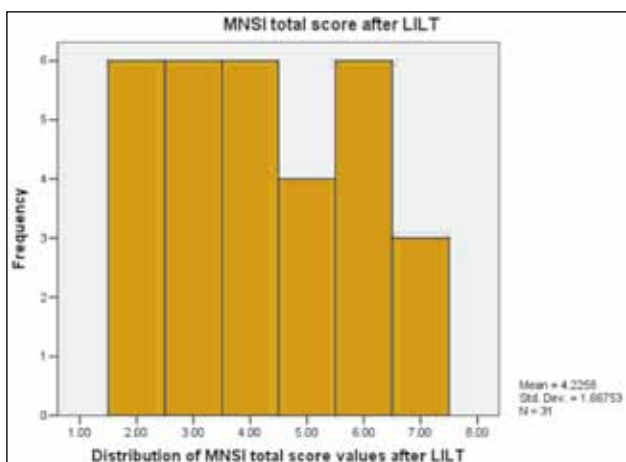
We registered statistical significant difference ( $p < 0.001$ ) between MNSI values before ( $5.61 \pm 1.76$ ) and after LILT ( $4.23 \pm 1.67$ ), and also ( $p < 0.001$ ) between DNE values before ( $7.68 \pm 2.27$ ) and after LILT ( $5.61 \pm 1.89$ ). Distribution of DNE and MNSI values before and after LILT are presented on histograms 1-4. The difference between MNSI and DNE score values in patients with painful DPN before and after vasoactive drug treatment during the period of 12 weeks were not significant ( $p > 0.05$ ). In this group of patients MNSI score mean value was  $6.12 \pm 2.02$  (before vasoactive drug treatment) and  $5.88 \pm 2.27$  (after vasoactive drug treatment) and DNE score mean value was  $7.82 \pm 2.41$  and  $7.65 \pm 2.34$ , respectively.



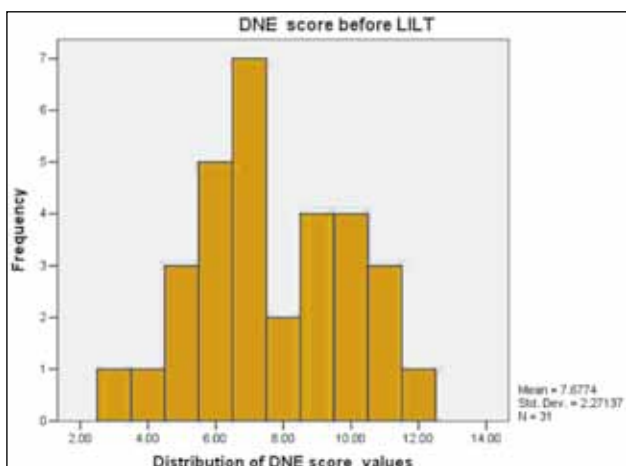
Histogram 1. Distribution of MNSI total score values before LILT



Histogram 4. Distribution of DNE score values after LILT



Histogram 2. Distribution of MNSI total score values after LILT



Histogram 3. Distribution of DNE score values before LILT

**2. The mean values ( $X \pm SD$ ) of ENG parameters in patients with painful diabetic polyneuropathy before and after LILT and in control group**

The difference between ENG parameters values before and after LILT in patients with painful DPN and in control group were not significant ( $p > 0.05$ )- table 1.

**3. Pearson's correlation (sig.2-tailed) between neuropathy score (MNSI, DNE) values and analysed patients age and the duration of diabetes**

We didn't register statistical significant correlation ( $p > 0.05$ ) between neuropathy score (MNSI, DNE) values and analysed patients age and the duration of diabetes.

**4. Pearson's correlation (sig.2-tailed) between neuropathy score (MNSI, DNE) values and electroneurographic parameters values in patients with painful diabetic polyneuropathy before and after LILT and in control group**

The results of correlation study are presented in table 2.

Table 1. The mean values ( $X \pm SD$ ) of ENG parameters in patients with painful diabetic polyneuropathy before and after LILT and in control group

Number	Patients (number of analysed)	ENG parameters	Before LILT	After LILT	p
1.	31 (LILT)	PNMCV (m/s)	39.19±8.87	40.52±6.92	nss
		PNSCV (m/s)	36.32±4.99	36.34±5.28	nss
		PNFL (ms)	57.03±6.59	56.03±7.22	nss
		UNMCV (m/s)	49.96±6.70	50.54±4.89	nss
		UNSCV (m/s)	51.92±11.99	54.07±10.50	nss
		UNFL (ms)	30.88±3.05	30.86±2.64	nss
2.	31 (Control group)		Before VDT	After VDT	
		PNMCV (m/s)	40.23±7.35	40.41±6.98	nss
		PNSCV (m/s)	37.96±6.72	37.62±7.02	nss
		PNFL (ms)	56.12±7.86	56.37±7.19	nss
		UNMCV (m/s)	50.17±7.23	50.31±6.99	nss
		UNFL (ms)	31.12±4.13	31.16±3.97	nss

nss=not statistical significant

LILT=low intensity laser therapy

VDT=vasoactive drug therapy

PNMCV= motor conduction velocity of peroneal nerve

PNSCV= sensory conduction velocity of peroneal nerve

PNFL= minimal latency of F wave after stimulation of peroneal nerve

UNMCV= motor conduction velocity of ulnar nerve

UNSCV= sensory conduction velocity of ulnar nerve

UNFL= minimal latency of F wave after stimulation of ulnar nerve

Table 2. Pearson's correlation (sig.2-tailed) between neuropathy score (MNSI, DNE) and electroneurographic parameters values in patients with painful diabetic polyneuropathy before and after LILT

Number	Neuropathy score before LILT	Electro-neurographic parameter	r	p	Neuropathy score after LILT	Electro-neurographic parameter	r	p
1.	MNSI-b	PNMCV-b		nss	MNSI-a	PNMCV-a		nss
		PNFL-b		nss		PNFL-a		nss
		PNSCV-b		nss		PNSCV-a		nss
		UNMCV-b		nss		UNMCV-a		nss
		UNFL-b		nss		UNFL-a		nss
		UNSCV-b		nss		UNSCV-a		nss
2.	DNE-b	PNMCV-b	-0.418	0.022*	DNE-a	PNMCV-a		nss
		PNFL-b		nss		PNFL-a	+0.438	0.037*
		PNSCV-b		nss		PNSCV-a		nss
		UNMCV-b		nss		UNMCV-a		nss
		UNFL-b		nss		UNFL-a		nss
		UNSCV-b		nss		UNSCV-a	-0.556	0.005**

nss=not statistical significant

\*= $p < 0.05$

\*\*= $p < 0.01$

LILT=low intensity laser therapy

MNSI-b(a)=Michigan neuropathy screening instrument score-before(after) LILT

DNE-b(a)= Diabetic Neuropathy Examination score before(after) LILT

PNMCV-b(a)= motor conduction velocity of peroneal nerve before (after) LILT

PNFL-b(a)= minimal latency of F wave after stimulation of peroneal nerve before(after) LILT

PNSCV-b(a)= sensory conduction velocity of peroneal nerve before(after) LILT

UNMCV-b(a)= motor conduction velocity of ulnar nerve before (after) LILT

UNFL-b(a)= minimal latency of F wave after stimulation of ulnar nerve before(after) LILT

UNSCV-b(a)= sensory conduction velocity of ulnar nerve before(after) LILT

In control group, we registered statistical significant negative correlation ( $p < 0.05$ ) between DNE score and PN MCV values.

## Discussion

Analysed patients with painful DPN had LILT treatments at four paravertebral points in the lumbosacral region, three points along ischiadic nerve and two points on the dorsum of the feet during the period of 12 weeks. We registered statistical significant difference ( $p < 0.001$ ) between MNSI values before and after LILT, and also ( $p < 0.001$ ) between DNE values before and after LILT. Hence, LILT has some influence on reduction of neuropathy score (MNSI, DNE) at patients with painful DPN. The precise mechanism of this influence is unknown, but it is suggested that the primary response takes place at cellular level and consists of increased microvasculature flow and lymphatic drainage, with increased macrophage and fibroblast activity and collagen synthesis what improves healing. The secondary phase comprises the release of endorphins, enkephalins and prostaglandins which have antinociceptive effect (5). Analgesic effect of LILT is caused by activation of neuron metabolism with endorphin level growth and increase of pain threshold (17). In previous study, The Toronto Clinical Neuropathy Score was unchanged during the LILT over the four weeks period, but authors in cited article didn't present this data (8). LILT in our study was applied in three times longer period than in previous cited study and we suppose that it might had an influence on neuropathy score change in patients with painful DPN.

We didn't registered significant difference ( $p > 0.05$ ) between analysed ENG parameters values in patients with painful DPN before and after LILT what indicates that LILT didn't have significant influence on ENG parameters values of PN and UN. All MCV and SCV of PN and UN had a little higher values after LILT than before LILT, but this changes are not significant.

We didn't register statistical significant correlation ( $p > 0.05$ ) between MNSI total score and analysed ENG parameters values before and after LILT, but we registered statistical significant correlation

( $p < 0.05$ ) between DNE score and MCV PN values (in m/s) before LILT and between DNE score and PN FL values (in ms) as well as between DNE score and UN SCV values (in m/s) after LILT. MNSI total score (0-10 points) is a composite measure of sensory and motor symptoms and signs and also peripheral vascular examination signs and we suppose that this is a cause for absence of significant correlation between this neuropathy score values and ENG parameters values before and after LILT in analysed patients with painful diabetic polyneuropathy. DNE score (0-16 points) includes measure of motor and sensory symptoms and signs only, without peripheral vascular examination signs and we registered significant correlation between DNE score values and MCV PN values (in m/s) before LILT, and also in control group. This indicates that registration of PN MCV value is important for diagnosis and evaluation of neuropathy severity in patients with painful DPN. After LILT we registered statistical significant correlation between DNE score and PN FL values (in ms), and also between DNE score and UN SCV values (in m/s). The question is why does DNE score after LILT have a significant correlation with this ENG parameters, when in the same period the differences between the mentioned ENG parameters values before and after LILT were not significant? We suppose that LILT has different effects on peripheral nerve motor and sensory axons function, and that it might have influenced DNE score change after LILT. Our results indicate that registration of PN FL value might be useful for evaluation of possible direct effect of LILT on impulse conduction along the whole length of PN motor axons, particularly their proximal parts, including corresponding roots and spinal segments. We also registered significant correlation between DNE score and UN SCV values (in m/s) after LILT. This indicates that registration of UN SCV values might be useful for evaluation of possible indirect ("remote") effect of LILT on impulse conduction along UN sensory axons. We suppose that "remote" effect of LILT might be associated with reflexogenic mechanism. LILT can cause stimulation of nerve endings with excitation of nerve centres and enhancement of physiological function. Additional research is needed to obtain optimal length of exposure, frequency of treatments and related therapeutic protocols (17).

## Conclusion

1. We registered significant difference ( $p < 0.001$ ) between MNSI total score and DNE score values before and after LILT (applied during the period of 12 weeks) in patients with painful diabetic polyneuropathy.
2. We didn't register significant difference ( $p > 0.05$ ) between analysed ENG parameters values before and after LILT (applied during the period of 12 weeks) in patients with painful diabetic polyneuropathy.
3. We didn't register significant correlation ( $p > 0.05$ ) between MNSI total score and analysed ENG parameters values before and after LILT (applied during the period of 12 weeks) in patients with painful diabetic polyneuropathy.
4. We registered statistical significant negative correlation ( $p < 0.05$ ) between DNE score and PN MCV (in m/s) before LILT and also in control group. It indicates that registration of this electrophysiological parameter and it's following is important for diagnosis and evaluation of neuropathy severity in patients with painful DPN.
5. We registered statistical significant positive correlation ( $p < 0.05$ ) between DNE score and PN FL values (in ms) after LILT (applied during the period of 12 weeks). It indicates that registration of this electrophysiological parameter value might be useful for evaluation of possible direct effect of LILT on impulse conduction along the whole length of PN motor axons, particularly their proximal parts, including corresponding roots and spinal segments.
6. We registered statistical significant negative correlation ( $p < 0.01$ ) between DNE score and NU SCV values (in m/s) after LILT (applied during the period of 12 weeks), so the registration of this electrophysiological parameter value might be useful for evaluation of possible indirect ("remote") effect of LILT on impulse conduction along ulnar nerve sensory axons.

7. We didn't register any adverse and/or side effect associated with LILT treatment (applied during the period of 12 weeks) in patients with painful DPN.
8. Further clinical double-blind randomized controlled studies of LILT treatment in patients with painful diabetic polyneuropathy is necessary.

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# Relation of the Infundibulopelvic angle with the anatomy of the large Renal Calyces

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## Abstract

In this work we have tested the variations of the calyces-pelvic kidney system and have done so on three-dimensional preparations of the calyces-pelvic kidney system, which we obtained through injections and corrosive methods. Fifteen preparation pairs (30 kidneys), taken from adult cadavers, have been anatomically stuffed and injected with a solution of plastic matter after which they were dissolved in nitric acid in order to get corrosive preparations of the calyces-pelvic kidney system.

Based on the angle under which the calyx inferior instilled into renal pelvis, two types of calyces-pelvic kidney systems have been defined. Type I has been defined as a shape where the angle between the longitudinal axis of large lower calyx and the longitudinal axis of renal pelvis is higher than 90°, is marked as the descendant shape and has been found in the amount of 33,3%. Type II has been defined as a shape where the same angle is bellow 90°, is marked as the ascendant shape and has been found in the amount of 66,7%. Based on the measurement of large renal calyces' dimensions, it has been noted that a positive correlation between the calibres of upper renal calyces on the right and on the left side ( $r = 0,68$ ;  $p < 0,05$ ) had existed. At the same time the calibre of middle renal calyces and lower renal calyces on the right side have not shown a statistically relevant correlation with the one on the left side ( $r = 0,19$ ;  $p < 0,05$ ).

The ascendant shape, at average, has wider infundibula (large lower calyx) and longer upper large calyx from those in the descendant shape. The length of infundibula in the ascendant and descendant shape has shown almost equal average

values. These parameters can be a good indicator in determining calculosis and stasis in the lower calyces of the kidney.

**Key words:** renal calyces, infundibulopelvic angle, variations.

## Introduction

According to the recent data found in literature these changes are so common that every fifth human has a smaller or bigger kind of malformation on his/her urinal organs. Still this state is not considered as an abnormality, but as an 'anatomical variation' (1, 2, 3).

Aside from the variations in height, shape, number and position, kidneys also show variations in the inner macroscopic form such as variable shapes of the pelvic kidney system. Kaneto at al. (1997) have described the kidney without its renal calyces which is a very rare anomaly of the urinal system (4).

The examination of large renal calyces variations in position and size gives very important parameters which are, besides everything else, good indicators in determining calculosis and stasis, especially in the lower calyces of the kidney (5, 6, 7, 8, 9, 10, 11, 12).

*The aim* of this research is to examine and to determine the variations of the infundibulopelvic angle and large kidney calyces. We have determined the following by using three-dimensional preparations, which we obtained through the corrosive method:

- The calibre of large renal calyces,
- The length of large renal calyces,



- The infundibulopelvic angle (the angle between the longitudinal axis of large lower calyx and renal pelvis)

### Research methods and materials

Fifteen preparation pairs (30 kidneys), taken from adult cadavers, have been anatomically stuffed and injected with a solution of plastic matter after which they were soaked in water for 24 hours. Later they are soaked into concentrated nitric acid in order to get corrosive preparations of the calyces-pelvic kidney system.

Morphometric measuring has been conducted twice and average values were taken.

Out of statistical methods we have used the coefficient of the correlation from which the statistical significance was considered relevant for  $p < 0,05$ . For measured sizes which can be found in a statistically significant dependence, we have calculated the parameters of the regression axis  $y=ax + b$ .

### Results

It was noted that the longitudinal axis of upper large calyx and middle large calyx in all the preparations were covering an angle of renal pelvis bigger than  $90^\circ$  with their longitudinal axis in the preparations obtained through the corrosive technique. On the basis of the angle under which lower large calyx is being instilled into renal pelvis, two main types of the calyces-pelvic kidney system have been defined. Type I is marked as a shape where the angle between the longitudinal axis of lower large calyx and renal pelvis is over  $90^\circ$ . It is also marked as a descendant shape and has been found in 33,3% (Picture 1). On the other hand, Type II is marked as a shape where that same angle is below  $90^\circ$ , marked as an ascendant shape and has been noticed in 66,7% (picture 2).

Type I (descendant shape) has been noted in the amount of 23,3% on the right and 10% on the left side. On the other hand Type II (ascendant shape) has been noted in the amount of 26,7% on the left and 40% on the right side.



Picture 1. Type I – Descendant shape of lower large calyx



Picture 2. Type II – Ascendant shape of lower large calyx

Through morphometric measuring of preparations obtained by the corrosive method we calculated the lengths of large renal calyces which are stilled into each renal pelvis where the ratio between the measured dimensions was statistically processed.

The average number of large calyces of right kidneys was  $2,33 \pm 0,12$ . The average number of large calyces of left kidneys was  $2,26 \pm 0,11$ .

The average value of lower large calyx's length is 15% longer than the average length of upper large calyx in the descendant shape, whi-

le the same ratio in the case of ascendant shapes was reversed and goes to the benefit of lower large calyx. After all the measuring we came to the conclusion that the average length of upper large calyx for 12,85% longer than the length of lower large calyx. The average length of middle large calyx kidneys is as almost equal as in both calyces-pelvic system shapes. Average values for the calibre of lower large calyx in ascendant shapes are for 24,06% higher than the same values taken from the descendant shapes of calyces-pelvic system.

There had also existed a positive correlation between the calibres of upper large calyx on the right and left side ( $r = 0,68$ ;  $p < 0,05$ )

Calibres of middle and lower large calyces on the right side have not shown a statistically relevant correlation with the same calibres on the left side ( $r = 0,19$ ;  $p < 0,05$ ).

## Discussion

Burykh (1988) had observed the calyces-pelvic system on 157 human kidneys through the injection method and formed a geometrical kidney model according to 3 parts of the kidney: upper, middle and lower part (13). Sampaio and Aragao (1993) analyzed the collecting system's anatomy of the lower-half of a kidney on 146 three-dimensional corrosive preparations of the calyces-pelvic system. Their results have shown that the lower half of the kidney was drained with two calices in 56,8% and with one middle calyx in 43,2%. In 60,3% of cases the lower calyx (infundibula) had the same or bigger calibre than 4mm, and in 39,7% it was smaller than 4mm. In 74% the angle that covers lower large calyx and the axis of renal pelvis is bigger than  $90^\circ$ , and in 26% it is smaller (14). Throughout our research, which was also done with the injection method, we have defined two types of calyces-pelvic kidney system according to the angle under which lower large calyx is being instilled into renal pelvis. Type I is defined as a shape where the angle between the longitudinal axis' of lower large calyx and renal pelvis is bigger than  $90^\circ$ , is marked as the descendant shape and is noted in 33,3% of cases (picture 20). Type II is defined as a shape

where the same angle is smaller than  $90^\circ$ , is marked as the ascendant shape and is noted in 66,7%. The average calibre value of lower large calyx was showing some higher values that those found in the results of Sampaio and Aragao (1993). The effects of anatomical factors, such as: infundibulopelvic angle, the diameter of the lower infundibula (lower large calyx) and its length, on the renal calculosis were examined by Gokalp and all. (1999) on 40 healthy kidney donors. The same parameters were measured on 119 patients with unobstructive calculosis of calyx inferior. The calibre of the lower calyx and its length were significantly bigger from those in the control group. On the other hand the differences in the infundibulopelvic angle of these two groups were not significant. It has been concluded that both the calibre and the length of lower large calyx are good indicators in determining calculosis and stasis in the lower calyces of kidneys (16). The ratio between the length and the diameter of the big lower calyx plays a great role in eliminating stones in the lower half of the kidney by using litotripsy. If the ratio between these two values smaller than 7 than the efficiency of removing the stones is much higher than when that same ratio is 7 or higher (17, 18, 19).

The results of our research have shown a significant dependence of the lower large calyx calibre on the angle under which it is being connected to renal pelvis, because the calibres in the ascendant shape (angle smaller than  $90^\circ$ ) have, in a percentage of 24,06 %, shown a higher value from the value of the measurements taken from the calibres in the descendant shape. It has also been established that the average length of lower large calyx is the same in both, the descendant and ascendant shape, but when compared to the average length of upper large calyx it shows the following variations. Namely, the average length value of lower large calyx is 15% percent longer than the average length of upper large calyx in the descendant shape, while in the ascendant shape that ratio is reversed to the benefit of upper large calyx. According to this fact the average length value of upper large calyx is 12,85 % longer than the same measurement taken for lower large calyx.

## Conclusion

The variable space layout of large renal calyces is defined in relation to the position of lower large calyx whether it is in a descendant or ascendant shape. The representation of the ascendant type is bigger in the amount of 66,7%. The average calibre of lower large calyx in the ascendant shape is larger than the calibre of lower large calyx in the descendant shape in the amount of almost 25% and the average length of upper large calyx in the ascendant shape is 25% bigger than the same length in the descendant shape. Therefore, we can say that the ascendant shape has, in average, wider infundibulas (lower large calyces) and longer upper large calyx from those in the descendant shape. The lengths of the infundibula in the ascendant and descendant shape have roughly shown the same average values. These anatomical parameters can serve as good indicators in determining calculosis and stasis in the lower kidney calyces.

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# Organizational conflict types and the investigation of resolution approaches in nurses

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## Abstract

**Objectives:** This study has been planned as a descriptive study to determine what kind of conflicts the nurses have and which methods are being used in the resolution of these conflicts and to compare whether the demographic factors are effective in determination of the types of conflicts and their resolution methods and to find whether there is a relation between conflict types and their resolution methods.

**Methodology:** The subjects were 603 nurses working at Ege University Faculty of Medicine Research and Application Hospital between January 2004 and June 2004.

**Results:** According to the results, it has been determined that nurses have conflicts at medium levels within themselves (point average is 15.62), within the group (point average is 22.96) and between the groups (point average is 15.80). It has been determined that nurses use completion methods (point average 27.85), commanding method (point average 16.12), adaptation method (point average 18.93), agreement method (point average 15.65), and avoidance method (point average 18.93) at medium levels). It has been found that there is a relation between the conflict types and their resolution methods.

**Key words:** Nurse, Conflict Types, Conflict Resolutions

## Introduction

We live in close connections with various types and dimensions of organizations that perform dif-

ferent social, cultural, technical and scientific functions. The quality of life is substantially shaped by the activities of large scale organizations. Words like 'efficiency' and 'quality' emphasized almost in every field are the goals that occupy a significant place in the agenda related to organization activities and play a gradually increasing role in the development of societies. Specific emphasis is given to the individual in the realization of these goals (1,2). Any organization, in which individuals exist in mutual interaction, contains within itself an environment of potential conflict. Health Care Institutions include several interaction groups. This interaction may occur between institutions and other institutions, institutions and patients, institutions and families, institutions and visitors, and institutions and doctors. Such interactions are often likely to lead to conflicts (3). The existence of conflicts in these environments lays bare the requirement for qualified managers who are capable of managing conflicts in an effective way (4).

Conflicts may differ from person to person or from situation to situation due to the diversity of human nature and inter-personal interactions. Human interactions and the conflicts emerging from these interactions are shaped and diversified by factors such as personality structure of every individual, environment and conditions that constantly affect him/her for the life, personal experiences, adopted values, attitudes and behaviors, needs, objectives and expectations (2).

In organizational conflicts, while conflicts may lead to an awareness of many important issues in an organization, and thus, a search for solutions, development of creative and new ideas and for-

mations as well as effective and permanent decisions; it should be noted that excessive and severe conflicts may have destructive effects for the organizations. The diverse and complicated nature of conflicts imposes a critical and important role on conflict management; because conflicts may contribute to the improvement of organizational effectiveness when they are managed well, but may have destructive effects on the organizations when managers fail to manage and control conflicts in an effective way (1,2,5,6,7,8,9).

An ambiguous atmosphere is created in the health care environment by the change in employees' status in health care organizations, formation of new health care classes and the undefined relationships among the personnel working in these classes, role-based relationships between the conventional health care personnel, changing roles, increasing uncertainties, and rapid changes in health care. Therefore, emergence of conflicts becomes indispensable under these conditions (3).

Consequently, it is possible to say that conflicts contribute to dynamism in an environment and they become an integral part of the development when appropriate approaches are employed. The major factor in resolving conflicts is the attitude and skills of those who manage conflicts. Thus, nurses play a significant role in this matter (10,11).

## Methodology

The study included 603 nurses who worked at Ege University, Faculty of Medicine, Research and Application Hospital between January 2004 and June 2004. As all the head nurses and clinical nurses were included in the research, no additional sampling method was applied. The research was conducted with 603 nurses who accepted to participate in the study. Participation rate was 63.47%.

Research data were collected by using the personal information form prepared by the researcher, and the Rahim Organizational Conflict Inventory I and the Rahim Organizational Conflict Inventory II (A,B,C Forms). The assessment values were  $\mu=.75$  for the first part inventory,  $\mu=.76$  for Form A,  $\mu=.73$  for Form B and  $\mu=.80$  for Form C in the second part inventory.

Percentage, one-way analysis of variance (ANOVA), Pearson's Moment Product Correlation Analyses and Tukey-HSD and Tamhane'T2 Post Hoc test were used in the evaluated of the collected data.

**Table 1** demonstrates some descriptive characteristics of the nurses. It was determined that 31.5% of the nurses were from the age group of 25-29 years, 53.7% were married, 63.2% were university graduates, and 55.1% had no children. *Table 1. Distribution of Nurses According to Their Socio-Demographic Characteristics*

Characteristics	Number	%
<b><u>Group of Age</u></b>		
20-24 years	108	17.9
25-29 years	190	31.5
30-34 years	117	19.4
35-39 years	97	16.1
40 years and older	91	15.1
<b><u>Marital Status</u></b>		
Single	251	41.6
Married	324	53.7
Widow/Divorced/Separated	28	4.7
<b><u>Education Status</u></b>		
Vocational School of Health	66	10.9
Associate Degree	131	21.7
Bachelor Degree	381	63.2
Masters/Doctorate Degree	25	4.2
<b><u>Number of Children</u></b>		
None	332	55.1
1 Child	174	28.9
2 Children and more	97	16.0
<b>Total</b>	<b>603</b>	<b>100.0</b>

It was detected that the age group of nurses did not affect the conflict they experienced within themselves, but affected the conflict within the group and between the groups ( $p<0.05$ , Table 2). No statistical difference was found between the education status of nurses and the types of conflict ( $p>0.05$ , Table 2). According to working years, it was also determined that the nurses who had been working for 11-15 years experienced conflict within themselves and within the group. Years of experience had no effect on the conflict experienced between the groups (Table 2). The nurses who loved their profession were observed to experience less conflict within themselves, within the group and between the groups ( $p<0.05$ , Table 2).

Table 2. Distribution of the Point Averages of the Conflict Type Experienced by Nurses within Themselves, within the Group and between the Groups with respect to their Descriptive Characteristics (N=603)

Descriptive Characteristics	Conflict within Themselves N x ± SS	Conflict within the group N x ± SS	Conflict between groups N x ± SS
<b>Group of Age</b>			
20-24	108 15.07 ±2.83	108 22.50 ±4.05	108 15.25 ±3.65
25-29	190 15.77 ±3.83	190 23.44 ±3.77	190 16.26 ±3.94
30-34	117 15.96 ±3.34	117 23.36 ±3.70	117 16.29 ±3.93
35-39	97 15.71 ±3.37	97 22.74 ±3.39	97 15.34 ±3.03
40-44	91 15.46 ±2.99	91 22.25 ±3.86	91 15.35 ±3.23
	F=1.175, p>0.05	F=2.403, p<0.05	F=2.662, p<0.05
<b>Education Status</b>			
Vocational School of Health	66 15.39 ±3.37	66 22.89 ±3.95	66 15.92 ±3.29
Associate Degree	131 15.77 ±2.89	131 23.11 ±3.39	131 15.97 ±3.35
Bachelor Degree	381 15.56 ±3.49	381 22.94 ±3.78	381 15.65 ±3.70
Masters/Doctorate Degree	25 16.44 ±4.02	25 22.76 ±5.25	25 16.84 ±5.40
	F=0.716, p>0.05	F=0.104, p>0.05	F=0.998, p>0.05
<b>Years of Working Experience</b>			
1-5 years	224 15.26 ±3.09	224 23.09 ±3.86	224 15.62 ±3.85
6-10 years	153 15.98 ±4.00	153 23.00 ±3.94	153 16.49 ±3.85
11-15 years	86 16.48 ±3.20	86 23.87 ±3.26	86 15.91 ±3.53
16-20 years	74 15.33 ±3.20	74 22.14 ±3.83	74 15.13 ±3.23
20 years and more	66 15.24 ±2.95	66 22.18 ±3.47	66 15.40 ±3.04
	F=2.856, p<0.05	F=2.909, p<0.05	F=2.336, p>0.05
<b>Professional Attitude</b>			
Truly love it	88 13.59 ±3.54	88 22.45 ±4.45	88 14.40 ±3.54
Love it	378 15.21 ±2.84	378 22.66 ±3.67	378 15.71 ±3.54
Uncertain	110 17.66 ±3.12	110 24.07 ±3.30	110 16.67 ±3.66
Don't love it	21 18.80 ±3.41	21 24.80 ±3.99	21 18.19 ±3.60
Don't love it at all	6 23.00 ±2.60	6 23.00 ±3.28	6 17.66 ±6.28
	F=38.925, p<0.05	F=4.722, p<0.05	F=7.687, p<0.05

### Opinions of the Nurses, Who Participated in the Research, on Conflict Resolution Methods

A statistically significant difference was found in the relationship between the professional attitude of the nurses and the completion method they used to resolve the conflicts they experience with their superiors (F=5.508, p<0.05). There was also a statistically significant difference between the education status of the nurses and the adaptation method they used to resolve the conflicts with the-

ir subordinates (F=3.417, p<0.05). A statistically significant difference was observed also between the nurses' years of working experience and the avoidance method they used to resolve the conflicts with their peers (F=4.487, p<0.05).

A negative relationship was found between the conflict experienced by nurses within themselves, within the group and between the groups, and the completion method they used to resolve the conflicts with their superiors, subordinates and peers (Table 3).

Table 3. Relationship between the Types of Conflicts Experienced by Nurses and the Resolution Methods They Use in Resolving Conflicts with Their Superiors, Subordinates and Peers

	Superiors			Subordinates			Peers		
	Conflict within themselves	Conflict within the group	Conflict between groups	Conflict within themselves	Conflict within the group	Conflict between groups	Conflict within themselves	Conflict within the group	Conflict between groups
Completion	r	r	r	r	r	r	r	r	r
Commanding	-.284*	-.168*	-.259*	-.286*	-.110*	-.266*	-.210*	-.141*	-.157*
Agreement	-.019	-.012	.032	.047	.049	.063	.039	.055	.042
Adaptation	-.205*	-.066	-.209*	-.199*	-.051	-.212*	-.117*	-.012	-.176*
Avoidance	-.118*	-.006	-.020	-.117*	.010	-.060	-.043	-.002	-.017

\*0.01 level of significance

## Discussion

Regarding the effect of nurses' age on the type of conflict they experienced within themselves, no statistically significant difference was determined between the age of nurses and the total point average of experiencing conflict within themselves ( $F=1.175$ ,  $p>0.05$ ) (Table 2). Therefore, the age of nurses had no effect on the conflicts they experienced within themselves.

Ünver (12), in his study on the evaluation of organizational conflict and resolution approaches in bank employees, noted that individuals in the age group of 19-25 years experienced conflict within themselves.

The evaluation of the relationship between the nurses' years of working experience and type of conflict they experienced within themselves revealed a statistically significant difference and this difference was observed to stem from the nurses who had a point average of 16.48 and a working experience of 11-15 years ( $F=2.856$ ,  $p<0.05$ ) (Table 2). Accordingly, this finding may be associated with the concerns and efforts of the nurses in establishing a position for themselves within the organization and building a career with the knowledge and skills they obtained and would obtain from 11-15 years of working experience.

The evaluation of the relationship between the nurses' professional attitudes and type of conflict they experienced within themselves revealed a statistically significant difference and this difference was observed to stem from the nurses who had a point average of 13.59 and who truly loved

their profession and the nurses who had a point average of 15.21 and who loved their profession ( $F=38.925$ ,  $p<0.05$ ) (Table 2). This result demonstrates that the nurses who loved their profession experienced less conflict within themselves compared to those who were uncertain about their professional attitude, who did not love their profession, and who did not love their profession at all.

The evaluation of the relationship between the nurses' age and type of conflict they experienced within the group revealed a statistically significant difference and this difference was observed to stem from the nurses with a point average of 23.44 and from the age group of 25-29 years and the nurses with a point average of 22.25 and from the age group 40-44 years ( $F=2.403$ ,  $p<0.05$ ) (Table 2). Accordingly, nurses experienced less conflict within the group as they got older.

The evaluation of the relationship between the nurses' years of working experience and type of conflict they experienced within the group revealed a statistically significant difference and this difference was observed to stem from the nurses with a point average of 23.87 and a working experience of 11-15 years and the nurses with a point average of 22.14 and a working experience of 16-20 years ( $F=2.909$ ,  $p<0.05$ ) (Table 2). Thus, the nurses who had been working for 11-15 years experienced many conflicts within the group.

Regarding the relationship between the nurses' professional attitudes and the type of conflict they experienced within the group, a statistically significant difference was found and this difference caused from the nurses who had a point average



of 22.66 and who loved their profession and the nurses who had a point average of 24.07 and who were uncertain whether they loved their profession ( $F=4.722$ ,  $p<0.05$ ) (**Table 2**). According to this result, the nurses who were uncertain about their love of profession experienced more conflicts within the group compared to the nurses who truly loved their profession.

In terms of the relationship between nurses' age and the type of conflict experienced between the groups, there was a statistically significant difference which stemmed from the nurses with a point average of 15.25 and from the age group of 20-24 years and the nurses with a point average of 16.29 and from the age group of 30-34 years ( $F=2.662$ ,  $p<0.05$ ) (**Table 2**). Based on this result, it is possible to say that the nurses from the age group of 30-34 years experienced more conflicts between the groups.

Regarding the relationship between the nurses' love of profession and the type of conflict experienced between the groups, there was a statistically significant difference which stemmed from the nurses who had a point average of 14.40 and who truly loved their profession ( $F=7.687$ ,  $p<0.05$ ) (**Table 2**). Accordingly, the nurses who truly loved their profession experienced less conflict between the groups.

### **Opinions of the Nurses, Who Participated in the Research, on the Methods of Conflict Resolution**

Regarding the relationship between the nurses' love of profession and the completion method they employed to resolve the conflicts with their superiors, there was a statistically significant difference which stemmed from the nurses who truly loved their profession ( $F=5.508$ ,  $p<0.05$ ).

In terms of the relationship between the nurses' education status and the adaptation method they employed to resolve the conflicts with their subordinates, a statistically significant difference was found and this difference was observed to stem from the nurses who graduated from the vocational school of health and those who had bachelor's degree ( $F=3.417$ ,  $p<0.05$ ).

Çıtak (13), in the study conducted on the effect

of conflict resolution education on nurses' conflict resolution skills, methods and level of burnout, determined a statistically significant difference between the education status of nurses and the adaptation method they used, and noted that this difference stemmed from the nurses who graduated from the vocational school of health. This finding is comparable with the results of the present research.

There was also a statistically significant difference between the nurses' years of working experience and the avoidance method they employed to resolve the conflicts with their peers, and this difference stemmed from the nurses who has a working experience of 16-20 years and more than 21 years ( $F=4.487$ ,  $p<0.05$ ).

### **The Relationship between the Types of Conflict Experienced by Nurses and the Resolution Methods Employed**

A negative relationship was found between the conflict experienced by nurses **within themselves** and the methods of completion, adaptation and agreement they used to resolve conflicts with their superiors and subordinates. The points of the conflict experienced by nurses within themselves tended to increase with the decrease in the points of using completion, adaptation and agreement methods. This finding indicates that individuals use the methods of completion, adaptation and agreement to a lesser extent as they experience more conflicts within themselves (**Table 3**).

A negative relationship was found between the conflict experienced by nurses **within themselves** and the methods of completion and agreement they used to resolve conflicts with their peers. The points of using completion and agreement methods tended to decrease with the increase in the points of conflict experienced by individuals within themselves. This finding indicates that individuals use the methods of completion and agreement to a lesser extent as they experience more conflicts within themselves (**Table 3**).

A negative relationship was found between the conflict experienced by nurses **within the group** and the method of completion they used to resolve conflicts with their superiors, subordinates and

peers. The points of using the method of completion tended to decrease with the increase in the conflict experienced within the group. This finding indicates that individuals use the method of completion to a lesser extent as they experience more conflicts within the group (**Table 3**).

A negative relationship was found between the conflict experienced by nurses **between the groups** and the methods of completion and agreement they used to resolve conflicts with their superiors, subordinates and peers. The points of using the methods of completion and agreement tended to decrease with the increase in the conflict experienced between the groups. This finding indicates that individuals use the methods of completion and agreement to a lesser extent as they experience more conflicts between the groups (**Table 3**).

### Conclusion and suggestions

It was determined that nurses experienced conflict at a medium level within themselves, within the group and between the groups.

Nurses used completion, commanding, adaptation, agreement and avoidance methods at a medium level for conflict resolution.

☞ In line with these results, it may be suggested that:

“Conflict Management” education programs should be organized for nurses,

Hospital managers should be educated about the reasons of conflict experienced in organizations and the strategies to be employed for resolving these conflicts.

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# Burnout Status of Health Care Personnel Working in Oncology and their Coping Methods

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## Abstract

**Background:** Working in oncology leads health care personnel (HCP) to feel stress, lack of satisfaction and to have psychological and physical problems and to be unproductive, estranged from job and to experience burnout.

**Objective:** The aim of this study was to determine burnout state and the coping methods in HCP working in oncology.

**Methods:** Interview Form, Maslach Burnout Inventory and Ways of Coping Inventory were administered to total 444 HCP.

**Results:** At the result of study HCP scored 1.76 in emotional exhaustion, 1.05 in depersonalization and 2.25 in lack of personal accomplishment [score range: 0-4]. These scores demonstrate that HCP experience moderate level burnout. It was established that HCP utilize mostly search for social support approach (X: 2.04) and they were least frequently found to use submissive approach (X: 0.97) [range: 0-3] in coping with burnout.

It was established that, for emotional exhaustion nurses, other HCP who consider their income inadequate and feel they have excessive work load form a risk group and for depersonalization with high education level, males, physicians, other HCP who find their income inadequate run higher risk. It was also found that physicians and HCP with higher level of education, HCP who feel themselves under excessive work load have a higher risk of experiencing lack of personal accomplishment.

**Conclusion:** Our study demonstrated that it was not possible to avoid burnout in oncology clinics. The administrators should rapidly put into effect projects and regulations which may protect personnel from burnout.

**Key words:** Cancer, burnout, physician, health care personnel

## Introduction

Working in oncology necessitates an energy adequate to cope with all probable outcomes and self devotion. It is not easy to give care to cancer patients. This process may lead to stress, dissatisfaction, alienation from work and burnout in health care personnel [HCP] (physician, nurse, social worker, psychologist). Investigations demonstrate that factors causing burnout in HCP working in oncology are severity of the condition of the patients, increase in the expectations of the patients, not giving satisfactory care, being unable to control the outcome of efforts exerted, death of patients, feeling of helplessness against death, problems experienced with the relatives of patients, work load, working conditions, low level of income and social opportunities, ending of career and inadequacy of approval by patients and supervisors.<sup>1-7</sup>

In many studies, it has been reported that in health personnel working in the field of oncology, anxiety, depression at clinically significant level and high level of burnout is present. In the study

of Catalan et al.<sup>8</sup>, the rate of burnout was found to be 44% in personnel working in oncology while it was 40% in personnel working in HIV. In a study comparing the burnout status of nurses working in hospices and hospitals, it was established that nurses working in hospices experience less burnout than those working in hospitals and that the quality of the social support system at work in one of the most important parameters in job satisfaction.<sup>9</sup> Oncology nurses involved with the care of patients in the process of dying carry the risk of psychological fatigue. Strategies providing information on the signals of burnout and sources of stress are important for such personnel.<sup>10</sup>

Skilbeck and Payne,<sup>11</sup> suggest that the experience of stress produces very different stress sources for the patients and their families. The duty of HCP is to offer support to the patients and their families in this difficult process. It should be acknowledged that stress is experienced in this support process. Vachon<sup>12</sup> stated that anxiety is a feature of the course of cancer starting from diagnosis to the latest stage of the disease. Complex emotional problems related to physical, psychological, social and spiritual issues are a part of the experiences in this difficult area. HCP are obliged to spend time to determine the worries of patients and their care givers and to relieve these worries. This emotional aspect of the work may deplete both professional and personal sources. The cost of working on this emotional tangle repeatedly may lead to high levels of stress and if not alleviated to burnout.<sup>13</sup> HCP may give different reactions to the difficulties experienced at work. These reactions are usually psychosocial and physical and manifests with 'job related stress', being tired of job' and 'burnout'. Some reports stress that the syndrome of burnout is a disorder resulting from chronic stress and presents frequently with tiredness, sleep problems and chronic fatigue syndrome. This disorder is sometimes mistaken for chronic fatigue syndrome and sometimes they may be concurrent.<sup>14</sup>

Burnout reflects the move from 'providing care and support of the patient to the lack of feeling and interest towards the patient'.<sup>15</sup> Burnout is observed in more than 50% of physicians treating cancer patients. In a study including 598 oncologists, 56% of the oncologist reported experiencing burnout and 53% of these attributed burnout to

working on fatal diseases.<sup>16</sup> 42% of the physicians express their burnout as the feeling of sorrow and ruin. Low rates of success in treatment contribute significantly to their experience of burnout. In this study, it was reported that giving care to patients whose disease has progressed to final stage is the single most important factor contributing to burnout among oncologists.

It is not very clear how sources for coping influence the behavior and cognitive process of someone confronted with a threatening and distressing event. It has been proposed that constant personality and environmental characteristics such as the feeling of self, supportive social relations and high level of socio economic sources.<sup>15</sup> Although offering care to patients about to die has adverse effect on the health of physicians and other HCP, according to the studies on coping and burnout, HCP engage in coping behaviors such as considering their job as a kind of duel, getting a feeling of success from their duty.<sup>8-17</sup>

Although there is concern about the stress sources of health personnel and their effects and this is known by administrators, the issue of burnout in oncology is among the subjects studied rarely in our country.<sup>6</sup> This investigation has been carried out with the aim of determining the burnout status and coping methods of HCP working in oncology. It is very important to recognize and define the burnout risk factors affecting HCP in order that adverse outcomes of burnout, which are of individual and organization origin, can be controlled and managed effectively. The fact that investigations carried out in Turkey on burnout status of HCP are very few in number and have limited samples<sup>4-6</sup> enhances the significance of this study.

This study aiming to determine the burnout status and coping methods of HCP working in oncology attempt to find answers to the following questions:

1. Is there any relation between the scores of HCP from emotional exhaustion (EE), depersonalization (D) and lack of personal accomplishment (LPA), which are subscales of Maslach Burnout Inventory (MBI) and their socio-demographic characteristics.
2. Is there any relation between between the scores of HCP from emotional exhaustion (EE), depersonalization (D) and lack of

personal accomplishment (LPA) which are subscales of Maslach Burnout Inventory (MBI) and characteristics of their work life?

3. What are the important health problems arising in relation to burnout in HCP?
4. Which methods are employed by HCP in order to cope with stress?

## Materials and methods

### - Study Population

In the present study, survey model was used. Study population comprises HCP employed in the radiation and medical oncology clinics of 6 training and investigation hospitals affiliated with the Ministry of Health (Düzce University Hospital, Dr. Abdurrahman Yurtaslan Oncology Hospital, Dr. Sami Ulus Children's Health Hospital, Ankara Numune Hospital, Ankara Atatürk Hospital, Atatürk Respiratory Diseases and Surgery Hospital and Ankara Dışkapı Yıldırım Beyazıt Hospital). As all of the HCP employed in these hospitals were considered without any need for sampling 645 HCP working in these hospitals were included in the study.

Before the administration of data collection tools, necessary permission was obtained from the general Directorate of Treatment Services, Ministry of Health. Social workers (SW) employed in these hospitals helped the investigator in the process of the administration of data collection tools. They were administered between January 14 2008 and May 30 2010. Data collection tools were administered to 478 HCP by face to face interview method and collected. After this process was completed, interview forms collected from 478 HCP were examined and 34 forms were excluded from evaluation since some HCP did not fill all scales and left some questions unanswered. In conclusion, data obtained from 444 HCP were regarded as valid and reliable. (**physician:** 137, **nurse:** 290, **social worker:** 11, **psychologist:** 6). In the end of the study, 444 of the 645 HCP, namely 68% was reached.

### - Data Collection Tools

Information on the data collection tools used in the study is presented below.

### - Interview Form

Interview form developed in view of the relevant literature, includes questions on the hospital where HCP work, profession, sex, age, marital status, education status, overall duration of work, and work load, in order to consider their relation with burnout. In addition, it was tried to determine health problems emerging because of burnout.

### Maslach Burnout Inventory (MBI)

MBI was used in order to determine the burnout levels of HCP included in the study. MBI, developed by Maslach and Jackson<sup>18</sup> is a scale utilized commonly in investigations on burnout. MBI, which was adapted to our country by Ergin<sup>19,20</sup>, was also tested for reliability and validity by Çam.<sup>21</sup> It includes overall 22 articles. After scoring, overall score and subscale scores are obtained. In the present study, when hypotheses are tested, mean scores obtained from subscales were taken into account. When mean scores obtained by the division of overall score from subscales into the number of questions in the scale were divided into three groups with regard to burnout level. The evaluation was made as follows. For emotional exhaustion (EE), depersonalization (D) subscales, mean score 1.3 or lower no burnout 1.4-2.7 moderate level of burnout 2.8 or over severe burnout. In lack of personal accomplishment (LPA), subscale the evaluation was made contrarily. In MBI, the ideal result is 0, score for subscales EE and D, which consists of negative questions and 4 for LPA consisting of positive questions.

### Ways of Coping Inventory

This scale was adapted from Ways of Coping Inventory developed by Folkman and Lazarus<sup>22</sup> and its reliability and validity study was carried out by Hisli and Durak<sup>23</sup>. This scale has two dimensions namely effective ways directed towards problem and ineffective ways directed to emotions. They are reduced to five factors: Self confident approach, optimistic, submissive, helpless and seeking social support. This scale included overall 30 items and is scored between 0-3. Scores for each factor are evaluated separately and overall score is not calculated. If scores approach 3, this means that that coping way is used efficiently and if scores are far from 3, that coping method is not used.

## Data Analysis

At the end of the study, overall interview form and information obtained from scales were transferred to computer. For the analysis of the data, SPSS 12.0 was used. Data were expressed as tables, number, percentage and means. For the testing of hypothesis, depending on the characteristics of variables, t test, Kruskal Wallis Variance Analysis (ANOVA) F and Pearson Moment Correlation (r) were used. Differences in means, which are significant, were demonstrated in tables.

## Results

When the means cores of HCP from MBI were examined, EE mean score was found to be 1.76, D: 1.05, and LPA: 2.25. These scores demonstrate that HCP has moderate level of burnout (0-4 range [Table 1]).

When socio demographic characteristics and work life of HCP are evaluated, it was established that a large majority (79.5%) of HCP were female, mean age was 35.69, majority was married (79.5%) and 39.9% was the graduate of a school or university lasting four years or more. The majority of HCP included nurses (65.3%), they served for mean 13.4 years, considered their income inadequate (73%) and thought that their work load was to much (77%) [Table 1]. The most frequently mentioned problem in relation to burnout was headache (21.80%). In addition, HCP used mostly seeking social support method in order to cope with stress at work environment ( $X=2.04$ ) and submissive approach was used the least ( $X: 0.97$ ) [Table 2].

## Discussion

Conflict between delivering high quality health care and coping with environmental stresses leads to a syndrome termed as 'burnout'. Maslach and Jackson<sup>18,24</sup> defined burnout as 'the index of the discrepancy between what human being are and what they have to do' emotional exhaustion (EE), which is one of the most important characteristics of burnout forming its three subscale, is defined as

depletion of the emotional sources of the individual and decrease of energy, depersonalization (D) as negative, unserious attitude of the working individual towards the people they give care and lack of personal accomplishment (LPA), as the tendency of the person to evaluate oneself adversely and considering oneself inadequate in the profession. Following these three stages experienced as process, HCP can not give themselves to their job emotionally, experiences dissatisfaction thinking that they are unsuccessful in their job and turn to activities outside their work.<sup>25</sup> In the study, mean score of HCP from three subscales of MBI was attempted to be learned.

Average points that the HCP under the scope of our study took from three dimensions of MBI are found as follows: EE average point: 1.76, D average point: 1.05 and LPA average point: 2.25 [Table 1]. These results we have achieved in our study are parallel to the results found by Lee and Henderson<sup>26</sup>, Isikhan et al.<sup>6</sup> When the evaluation criteria of the sample is considered, it is found that HCP face with a moderate level of burnout from EE, D and LPA perspectives. As the emotional exhaustion level of HCP increases, depersonalization increases as well but the sense of personal achievement decreases. This might be caused by personal characteristics of the HCP studied, their ability to cope with problems arising from working with fatal diseases like cancer and the positive feedbacks they receive from patients for their work performance.

### *Social and Demographic Characteristics of HCP and Their Comparison with the Points Obtained from MTI [Table 1]*

**Gender** appears as an important variable in studies on burnout. As a result of a research study using MTI; it is found that gender is an important variable for emotional exhaustion and women experience emotional exhaustion more than men do. Although there is no difference between different genders in terms of depersonalization, it is observed that the sense of achievement is higher in men compared to the women from the lack of personal accomplishment dimension.<sup>19</sup> While there is no statistically significant diffe-

Table 1. Comparison of social and demographic and work related characteristics of hcp and the points they obtained from three subscales of MBI

	Emotional Exhaustion (EE)			Depersonalization (D)			Lack of Personal Accomplishment (LPA)		
	X	SS	Test	X	SS	Test	X	SS	Test
<b>Points Obtained from MBI</b>	1.76	0.74	-	1.05	0.73	-	2.25	0.51	-
<b>Social and demographic and work related characteristics</b>									
<b>Sex (N=444)</b>	<b>X</b>	<b>SS</b>	<b>Test</b>	<b>X</b>	<b>SS</b>	<b>Test</b>	<b>X</b>	<b>SS</b>	<b>Test</b>
Female (N= 338; 76.1%)	1.78	0.77	t = 1.15	0.99	0.74	t = -2.74*	2.25	0.49	t = -0.51
Male (N= 106; 23.9%)	1.69	0.65		1.22	0.67		2.28	0.55	
<b>Age</b>	r = -0.36			r = -0.64			r = -0.76		
<b>Marital Status</b>									
Married (N= 353; 79.5%)	1.75	0.71	F=0.74	1.02	0.73	F= 1.24	2.25	0.51	F= 0.42
Single (N= 73; 16.4%)	1.76	0.86		1.10	0.75		2.25	0.54	
Widowed- Divorced (N= 18; 4.1%)	1.97	0.79		1.27	0.74		2.36	0.36	
<b>Educational Status</b>									
Secondary High School (N= 139; 31.3%)	1.79	0.79	F=0.19	0.97	0.77	F= 5.32 **	2.23	0.53	F= 3.97**
Four-year or more college and undergraduate (N= 177; 39.9%)	1.74	0.77		0.98	0.74		2.20	0.50	
Graduate (N= 128; 28.8%)	1.76	0.64		1.22	0.50		2.25	0.67	
<b>Profession</b>									
Physician (N= 137; 30.8%)	1.73	0.65	F=2.64*	1.24	0.69	F= 6.62**	2.34	0.50	F= 2.16*
Nurse (N= 290; 65.3%)	1.80	0.78		0.98	0.74		2.22	0.51	
Social Worker (N= 11; 2.5%)	1.31	0.58		0.63	0.57		2.19	0.37	
Psychologist (N= 6; 1.4%)	1.27	0.35		0.50	0.46		2.04	0.43	
<b>Work Experience</b>	r = -.022			r = -.060			r = -.050		
<b>Perception on the Wage Level</b>									
Satisfied with Wage Level (N=120; 27%)	1.44	0.66	t=-5.82**	1.00	0.74	t= -0.73	2.24	0.56	t= -0.44
Not satisfied with Wage Level (N=324; 73%)	1.88	0.73		1.06	0.73		2.26	0.48	
<b>Perception on Workload</b>									
High Workload (N=342; 77%)	1.89	0.72	t=7.08**	1.12	0.74	t= 4.22**	2.29	0.51	t= 2.38*
Low Workload (N=102; %23)	1.33	0.64		0.78	0.64		2.15	0.49	

\* p&lt;0.05 \*\* p&lt;0.01

Table 2. Main health problems of HCP arises from burnout

Main Health Problems	Number	%
Headache	259	21,80
Sleep disorders	229	19,29
Complaints like ulcer and gastric	198	16,68
Excessive nervousness	160	13,46
Constipation	94	7,91
Allergic reactions	83	6,98
Indigestion	60	5,05
Hypertension	55	4,62
Cardiovascular diseases	31	2,60
Dither	19	1,61
Total	1188 *	100

\*Total Score (There are more than one options).

rence between groups in terms of **gender** in subgroups of EE and LPA in our study ( $p>0.05$ ), it is seen that men HCP shows a more negative picture compared to the women HCP in D subgroup ( $p<0.05$ ). One of the findings of our study that the women have obtained higher EE average points compared to the men in our study can be attributed to the fact that a major part of the research group is formed from nurses and women. It seems especially true when the life of women outside the work and their ongoing responsibilities related to their homes and children is considered. This finding of the study seems to be parallel to the findings of the studies of Ergin<sup>19</sup> and Aslan et al.<sup>27</sup> but contrasting to the finding of the study conducted by Turkish Medical Association [TMA]<sup>28</sup>. It is found that there is a moderate level of burnout among HCP in terms of LPA. It is also observed that women physicians experience higher level of burnout compared to their colleagues in the other gender from the point of lack of personal accomplishment. The reason behind this fact might be again the responsibilities assumed by the women outside of the work which seem to be higher compared to the men, and the conflicts and uncertainties in roles assumed in the working life. When depersonalization is considered, the difference between averages shows that depersonalization is more common among men compared to the women. In summary, it can be said that women are under risk in terms of EE and LPA, and men are under risk in terms of D.

It is known that young and inexperienced workers are more inclined to **experience** burnout. The research conducted by Isikhan et al.<sup>6</sup> has shown that as the age of HCP increases the stress level he/she experiences decreases. In the study conducted by TMA<sup>28</sup> the physicians with the ages of 35-44 years have obtained the highest emotional exhaustion point among all physicians. In our study the average age of HCP is recorded as 35.69 years, the youngest HCP under the scope of our study is at the age of 18 and the oldest one is at the age of 60. It can be said that a major part of HCP under the scope of our study is at an age bracket which is considered as highly productive in terms of working life. It is found in our study that there is a strong negative correlation between the age variable and EE, D and LPA.

In other words, as the age increases, EE, D and LPA decreases. This finding of the study seems to be contrary to the findings of the study conducted by Aslan et al.<sup>27</sup> but similar to those of the studies conducted by Ullrich and Fitzgerald<sup>29</sup>, Richardson and Burke<sup>2</sup>, Heim<sup>30</sup>, and Isikhan et al.<sup>6</sup> In conclusion it is found that the age variable is not correlated to EE, D and LPA.

When it comes to the **marital status** of HCP, it is recorded that a major part of them are married (79.5%). D, EE and LPA points obtained by HCP as of their marital status show that these personnel experience a moderate level of burnout. It is found that marital status is a variable which does not make a difference among HCP in terms of their burnout level ( $p>0.05$ ). This finding of the study is contrary to the findings of the studies conducted by Isikhan et al.<sup>6</sup>, and Aslan et al.<sup>26</sup> but in line with those of the study conducted by TMA<sup>28</sup>. In conclusion, it is observed that HCP who are widowed or divorced have obtained higher EE and D points compared to other groups but lower LPA points compared to HCP in other marital statuses. When the status of HCP is considered in terms of the level of **educational attainment**, it is seen that a major part of HCP under the scope of the study (39.9%) is graduated from at least four-year colleges or universities. When the fact that 65.3% of the survey population is formed from nurses is considered, it can be said that HCP is not a homogeneity group in terms of their educational attainment levels. D, EE and LPA points obtained by HCP as of their educational attainment levels show that these personnel experience a moderate level of burnout. It is observed that the variable of educational attainment level does not make a difference among these personnel for their EE points but as the educational attainment levels of HCP increases their D and LPA points increase as well. In other words, while EE and LPA average points of HCP who are graduated from secondary or high schools are higher compared to those of other HCP in other categories, D average points of HCP who have graduate level degrees are higher compared to those of other groups. In conclusion, it is found that the variable of educational attainment level makes a difference among HCP in terms of their D and LPA points ( $p<0.01$ ).



### Job Related Characteristics of HCP and Their Comparison with the Points Obtained from MTI [Table 1]

The **profession** of medicine requires a high level of face-to-face communication with other people. The level of emotional reactions that occur in people engaged with these kinds of professions can even reach to the degree of emotional exhaustion. Providing health care to patients of oncology leads to conflicts which are clear for other chronic illnesses. Limited level of medical knowledge, that can change the course of illness, leads to a feel of despair in the personnel. These facts channel physicians and nurses to build deeper relations with patients. While they begin to provide more tense empathetic responses to their patient, this situation leads them to assume additional emotional burden. It is observed that, in addition to physicians and nurses, social workers and psychologists, as well, who hold a profession which engages in the field of oncology, experience burnout because they work under a strong time pressure and emotionally hard work burden, and they face with role conflicts and uncertainties.<sup>7,31,32</sup>

When it comes to EE average points of HCP under the scope this study, it is found that the highest points are obtained by nurses (X: 1.80) and there is a statistically significant difference between average points received by HCP ( $p < 0.01$ ). This finding of our study is in line with the findings of the studies conducted by Ullrich<sup>29</sup>, Richardsen and Burke<sup>2</sup>, and Heim.<sup>30</sup> It is observed that profession is a variable which makes difference among HCP under the scope of the study in terms of their EE average points. When D average points of HCP are considered, it is recorded that the highest point is obtained by physicians (X: 1.24). HCP experience a moderate level of burnout in terms of D points. This finding of our study is found to be parallel to the findings of the study conducted by Kalliath and Morris.<sup>33</sup> When we look at the LPA average points of HCP it is seen that LPA average points are 2.34 for physicians, 2.22 for nurses, 2.19 for social workers and 2.04 for psychologists ( $p < 0,01$ ). These findings of the study are close to those of the studies conducted by Graham et al.<sup>34</sup>, and Grunfeld et al.<sup>35</sup> These findings achieved by the study can be accepted in general as a na-

tural consequence of the care provided for cancer patients. Because of the nature of their work and the special characteristics of the patients they serve for, they frequently experience stress in clinic environments, even though they try to maintain a distance relationship with their patients. The process of providing health care to cancer patients is the most important factor that can affect the stress level HCP experience. In addition, it can be said that other factors like increasing number of patients, workload, low level of wages, problems faced with patients and their relatives, the lack of equipments and etc. might also have affected the burnout experienced by HCP. In summary, it is found that nurses are under risk in terms of EE, physicians are under risk in terms of D and psychologists are under risk in terms of LPA.

The probability of a newly recruited HCP to experience feelings related to cancer and the nature of its work will change depending on his/her ability to cope with and his/her personal characteristics. However it is expected that as the years went by HCP will acquire a higher level of expertise in his/her profession and he/she will feel the sense of being valuable to people when he/she does his/her job. **Seniority** makes HCP to become more controlled in arranging his/her workload and experienced in adjusting to various pressures in time.<sup>36</sup> Senior physicians are able to cope with pressures like increasing demands of patients and the lack of resources. It is observed that physicians with more experience and higher status face with a less level of stress compared to their colleagues with less experience with regards to high workload, problems in diagnosis and treatment, and professional information requests.<sup>37</sup> Seniority appears to be the most significant variable that affects burnout HCP face with. As a result of our study, it is found that seniority is not a statistically significant variable that makes difference between HCP in terms of their EE, D and LPA average points ( $p > 0,05$ ). *Accordingly, it is seen that there is a negative but weak relationship between the variable of seniority and EE, D and LPA.* As the seniority of HCP increases, the EE, D and LPA points they obtain decrease. This finding of our study is found to be parallel to those of the studies conducted by Hinds<sup>37</sup>, Tattersal et al.<sup>5</sup>, Fielden and Peckar<sup>36</sup>, and Isikhan et al.<sup>6</sup>

It is found that many stressors faced by physicians are related to job stress. Literature review shows that low level of **wages** is an important stressor for personnel.<sup>2,6,34</sup> It is tried to understand if the perception of HCP under the scope of our study on the adequacy of their wage levels, leads to a difference for the average points they obtained from three subgroups of MTI. As a result of the study, it is observed that there are differences between the EE average points of HCP depending on their perception on the adequacy of their wage levels and EE average points of HCP who regards their wage levels as unsatisfactory are higher compared to those of other HCP ( $p < 0.01$ ). Sense of regarding the wage level as unsatisfactory might lead HCP to maintain a lower level of life standard compared to the one he/she expects for himself/herself, children and family. This situation will lead HCP to serve his/her patient groups in a discontented, careless and insensible manner. It is observed that there is no statistically significant difference among D and LPA points obtained by HCP depending on their perception on the adequacy of their wage levels ( $p > 0.05$ ). These findings of our study are contrary to those of the studies conducted by Molassiotis and Haberman<sup>38</sup> and Isikhan et al.<sup>6</sup> In summary, it is found that HCP, who consider their wage level as unsatisfactory, are under risk in terms of EE and D, and HCP, who consider their wage level as satisfactory, experience the sense of achievement less frequently.

It is observed that the common point of the jobs which have high level of burnout is the **excessive workload**.<sup>5</sup> Responding to a high number of demands of a high number of patients in a very short time causes the feeling of burnout. High case load and high number of patients are the main stressors faced by physicians working in hospitals. The issue of how the limited time available will be distributed among patients may cause significant tensions among HCP. As a result of our study, it is found that workload is an important variable for the EE, D and LPA points of HCP ( $p < 0.01$ ), [Table 1]. This finding of our study is found to be similar to the findings of the studies conducted by Richardsen and Burke,<sup>2</sup> Tattersal et al.<sup>5</sup>, Graham et al.<sup>34</sup>, and Grunfeld et al.<sup>35</sup> The facts that HCP have a very high workload in job environment, he/she is required to assume more than one role and

responsibility, and supervisors give them works other than their routine works, may cause HCP to have a low level of the sense of personal accomplishment and to feel burnout. In conclusion, it is found that HCP, who consider their workload as high, assume risk for EE, D and LPA.

### Main Health Problems of HCP Arising from Burnout [Table 2]

The burnout syndrome may have physical, emotional and mental symptoms. Physical burnout symptoms include various problems and complaints like chronic fatigue, weakness, loss of energy, frazzling, becoming more sensitive to illnesses, frequent headaches, nausea, muscular cramps, backaches and sleep disorders.<sup>22</sup> Health care related burnout reflects physical and psychological symptoms that affect general welfare of the personnel. Oncologists, who have reported that they experience a significant burnout, have also reported that they use more alcohol, they experience sleep disorders more frequently and they would like to quit the profession of physician in the following 10 years. Furthermore, it is found that physicians, who experience burnout, are less satisfied with their relationships with patients, family and hospital workers.<sup>39,40</sup>

Burnout, which is caused by excessive workload, leads to serious threats especially on the physical health of employees. In our research main health problems experienced by HCP have been inquired. An investigation of the responses given to the questions asked in this regard has shown that a major part of HCP (21.80%) reports headache as their most important health problem, sleep disorders follows headache with 19.29% and gastric ulcer takes the third order by (16.68%) [Table 3]. These physical symptoms of burnout, whose long term effects have been rarely investigated, as reported by HCP, are meaningful for us. In order to help HCP, who are mainly at their middle ages, in their efforts to cope with burnout, it is required to provide them training and exercises on how it is possible to cope with work-related stress. It can be said that the findings of our study are close those of the study conducted by Isikhan et al.<sup>6</sup> This question has been asked to HCP in an open ended

form, as well. When the responses given to this question is analyzed, it is seen that there are several various health problems affecting HCP:

1. Main Health Problems Faced by Physicians: Hair loss, anxiety disorder, backache, pulse, hemorrhoids, excessive fatigue, disorders in body shape (based on continuously using microscope), aches (backache) and complaints because of using non-ergonomic chairs and table and fibromyalgia (soft tissues rheumatism, pains in the back and the neck).
2. Main Health Problems Faced by Nurses: Experiencing frequent infections, herpes, depression, asthma, diabetes, epilepsy, anxiety attack, hearing losses, hernia of the loins and the neck, stomach ache, psychiatric problems, modular goiter, knee pain, varicose, fatigue, anorexia, urethra infections, excessive fatigue, amnesia and having problems in aesthesis, high cholesterol, spasms and hypotension. While social workers do not report any major health problem, it is observed that high cholesterol is widespread among psychologists. In summary, these results show us that HCP, who are experiencing a moderate level of burnout, face with important health problems caused by burnout.

### **Comparison of the Points of HCP Used in the Measurement of Coping with Stress**

It is thought that burnout, which is a sub category of stress, stems from imbalances between the capability of the individual to cope with and the demands of workplace. Interaction with patients, particularly the need for coping with the fact of death, is a major stressor for these personnel.<sup>41</sup> Some coping mechanisms used by HCP have been identified. Among these, there are negative coping mechanisms like depersonalization, the thought of quitting the job, mentally leaving the workplace and non-functional competition.<sup>26</sup> Interpersonal relations, motivation, excessive workload, and the ability of the individual to cope with might be related to burnout. Many patients and relatives of them sometimes reflect their stress, anxiety and depression to HCP. The finding of our study that HCP experience a moderate level of burnout can be accepted as an evidence of this.

In our study, it is observed that HCP experience a moderate level of EE, D and LPA. When the coping mechanisms used by HCP against stress is considered, it is found that HCP use the most healthy coping mechanism of searching for social support the most (X: 2,04), and use submissive approach the least (X: 0,97) [point range: 0-3]. It can be said that HCP do not refrain from facing with the problem and take steps to cope with burnout in a right manner. The finding of the study is parallel to the findings of the study conducted by Isikhan et al.<sup>6</sup>

In sum, in our research, it is found that HCP working in the field of oncology have a moderate level of burnout; nurses and HCP who consider his/her wage level as low and who think that his/her workload is high are under risk in terms of emotional exhaustion; and physicians, and HCP who are men, who have a high level of educational attainment, and who think that his/her workload is high are under risk in terms of depersonalization. It is observed that the risk for physicians and HCP, who have a high level of educational attainment, and who think that his/her workload, to experience lack of personal accomplishment is higher than the one for other groups. In addition, it is found that HCP use the mechanism of searching for social support the most while coping with burnout, and submissive approach the least. Our study has shown that it is impossible to refrain from burnout in oncology clinics. It is required for administrators to take immediate measures, which will prevent personnel to experience burnout, like reducing patient density, increasing the quality and quantity of personnel, raising wage levels, and improving working conditions.

### **Conclusion**

It is impossible to refrain from stress or burnout in oncology clinics. But its treatment and prevention is available. Joint efforts of individuals and institutions are needed in this regard. In order to prevent the burnout of HCP, several short but important steps might be taken, like reducing long working hours, eliminating the problem of low wages, increasing opportunities for recreational and social activities, removing the lack of adequ-

ate number of personnel, making job descriptions clear and precise, arranging regular team meetings, providing continuous training opportunities, increasing opportunities for promotion in the job, making hard works rotated among personnel, making regular turns arranged in a fair and regular way, and respecting for break times. While these methods will decrease the burnout experienced by HCP on the one hand, and they will increase the motivation in the workplace on the other hand.

In the future, if the data collecting tools in these kinds of studies are organized shorter, number variables tried to be measured are reduced and qualitative studies are conducted with a less number of personnel instead of conducting quantitative studies, it might be found that there are several other problems faced by personnel which are in the minds of the personnel but could not have been reported adequately. In addition, a study towards investigating how all personnel working in the field of oncology are coping with the stress can also been done. Moreover, it might also be investigated in the prospective studies that the effects of factors like personal life style of HCP outside of the work, social support and personnel characteristics, and participation which are listed among non-institutional burnout factors on the formation of burnout. Investigating the effects of burnout on the quality of process or health care provided might appear a new field of research area in a period in which stress in the system of health care is pronounced more.

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# Evaluation of health related quality of life among perimenopausal Turkish women

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## Abstract

**Introduction:** This study aimed to evaluate life quality and the related factors among women in menopause in Edirne, Turkey.

**Methods:** A questionnaire querying socio-demographic features and menopause status together with the SF-36 inventory and women's health questionnaire to evaluate life quality were applied to 410 women aged between 40 and 59 years living in Edirne, Turkey.

**Results:** Mean natural menopause age of the participants was 46.24 years. Bone mineral density was measured in 50.5%, mammography was performed in 52.4%, Pap smear was obtained in 52.7% and breast exam was performed in 54.1% of the participants. Among the menopausal and postmenopausal women, only 4.9% were using hormone replacement therapy currently. However, past hormone replacement therapy usage history was 23.6%. Women using medications to prevent osteoporosis made 25.6% of the sample. Advanced age, having less education, low socioeconomic level and being at the peri- or post-menopausal phase demonstrated a negative effect on the quality of life. Tobacco use, obesity and presence of chronic diseases were also found to adversely effect the quality of life, as well.

**Conclusion:** Improving education and socioeconomic level with initiating preventive health care at earlier ages would improve health related quality of life among postmenopausal women.

**Key words:** Edirne, health related quality of life, menopause

## Introduction

Menopause can be defined as complicated changes in women's life composed of biological, psychological, social and cultural factors (1). Menopause also effects health related quality of life. Hot flashes, sleeping disorders, fatigue, mood swings, urinary and sexual problems occurring with the changes in hormonal levels poorly effects the quality of life in women (2). The life expectancy is increasing progressively, leading to rise in the number of women in menopause. In 1990 there were an estimated 467 million women aged  $\geq 50$  years in the world. This number is expected to increase to 1200 million by the year 2030 (1). In certain studies average age of menopause in Turkey is 47-50 years (3-10). Life expectancy in women is 71,5 years. Therefore almost one third of life is spent in menopause. As the duration of life expectancy and expectations of quality in life increases, women in peri- and postmenopause and their problems cannot be underestimated.

There are limited epidemiological studies about menopause in our country. In this consequence in our study we aimed to have knowledge about the problems, expectations and needs of women during menopause in Edirne.

## Materials and methods

This study includes women between 40-59 years of age living in Edirne during 15.08.2006 and 15.03.2007. This is an observational, descriptive

and analytical prevalence study designed to determine the menopausal status and health related quality of life in women at this age group.

452 women were visited and informed about the study in Edirne. Only 410 participants accepted to take part. The only criteria to be included in this study was to be between 40-59 years old.

The data obtained with a questionnaire inquiring demographic and menopausal status together with Woman's Health Questionnaire (WHQ) and SF-36. The duration of the interview took 25 minutes and done face to face with each women.

For the WHQ, permission is obtained from Mapi Research Trust and Turkish validity and reliability was done by Cetinay and Gulseren (11). Turkish validity and reliability of Life Quality Scale SF-36 was performed by Kocyigit et al (12).

In this study participants having menstruation regularly in the last twelve months accepted as in premenopause, having irregular menstruation in last twelve months accepted as in perimenopause and having no menstruation in last twelve months accepted as in postmenopause period.

The convenience of normal variables coherence is analyzed by single sampling Kolmogorov Smirnov test. Where compliance in normal distribution is not established Mann-Whitney U and Kruskal-Wallis ANOVA is used to compare the groups (In the presence of statistically significance the origin of difference then is analyzed by Bonferroni). To determine the effects of factors on quality of life, backward stepwise logistic regression analysis is used.

## Results

The mean age of participants was  $48.18 \pm 5.41$ . Concerning marital status 3.3% (n=13) was single, 81.5% (n=334) was married, 2.2% was divorced and 3.2% (n=54) was widower. 4.4% (n=18) was uneducated, 48.3% (n=198) was primary school graduate, 37.8% (n=155) was secondary and higher secondary school graduate and 9.5% (n=39) had university degree.

Concerning socioeconomical status 2.5% (n=10) had higher, 18.5% (n=76) had upper middle, 29% (n=119) had lower middle and 50% had lower income.

55.9% was overweight (BMI between 25-29.9), and 26.6% was obese (BMI  $\geq 30$ ). 19% was active smoker and 9.3% (n=38) had quit smoking and 7.8% (n=32) was consuming alcohol. Only 29% (n=119) had mentioned about presence of at least one chronic disease.

The average number of pregnancy rate of the participants was 2.89 and their birth rate was 2.3. Average menarche age was 13.04.

In 30.2% (n=124) symptoms of premenstrual syndrome was either still occurring or was present in the perimenopausal period. 47.3% (n=194) had no menses, 40% (n=164) was having periods regularly and 12.7% (n=52) was having irregular periods since last twelve months.

In 38.3% (n=157) participants entrance to menopause was natural and 9% (n=37) was due to surgical reasons.

The mean age of the participants in menopause (n=194) was 45.35 years; median being 46 years. The mean age of the participants naturally and surgically entering menopause was 46.24 and 41.51 years respectively. The mean age of the women at perimenopausal stage with regular periods in last twelve months (n=52) was 46.33 years.

23.6% had used hormone replacement therapy (HRT).

Among the participants in perimenopause and postmenopause (n=246), 30.1% (n=74) had treatment for osteoporosis and only 4.9% (n=12) was currently using HRT and 25.6% (n=63) was currently having treatment for osteoporosis.

62% (n=256) had used contraceptive methods previously and the most preferred one was hormonal methods (26.8%) The percentages of using contraceptive methods in premenopause and perimenopause were 55.5% and 28.8% respectively.

Bone density measurement had only done once in 49.5% (n=178). 52.6% (n=215) had mammography and 52.7% had pap smear. Only 54.1% had breast examination by the physician and the rate of breast examination showed similarity with breast self-examination.

Only 78% (n=320) of the participants accepted menopause as a natural event.

### Comparison of SF-36 Subscales With Independent Variables

Education and menopause was statistically significant in all the subscales of SF-36. Marital status was statistically significant in subscales of SF-36 except in physical functioning and general health perception. Socioeconomic status showed significant difference in only physical functioning, bodily pain, social role-functioning and mental health subscales. Age was also statically significant in the subscales except emotional role-functioning and mental health.

### Comparison of WHQ Subscales With Independent Variables

Correlation with age groups and somatic symptoms, memory-concentration, vasomotor symptoms, sexuality and attractiveness subscales was statistically significant.

Correlation of educational status with all of the subscales was statistically significant except menstruation.

Correlation of marital status with somatic symptoms and menstruation had no significant difference while sexual behavior cannot be evaluated because unmarried group did not answer the questions concerning sexual behavior. The rest of the subscales showed statistical significance with marital status.

Table 1. Comparison of menopausal situation of participants with WHQ subscales

WHQ subscales	Menopausal Situation	N	Mean	SD	Mann-Whitney U	P
Depression	Premenopause	164	0,15	0,14	17598	0,021
	Peri/postmenopause	246	0,21	0,20		
	Total	410	0,19	0,18		
Somatic symptoms	Premenopause	164	0,23	0,23	13375	<0,001
	Peri/postmenopause	246	0,37	0,26		
	Total	410	0,32	0,26		
Memory/ concentration	Premenopause	164	0,18	0,28	17095	0,004
	Peri/postmenopause	246	0,27	0,32		
	Total	410	0,24	0,31		
Vasomotor symptoms	Premenopause	164	0,11	0,20	7870	<0,001
	Peri/postmenopause	246	0,44	0,27		
	Total	410	0,31	0,30		
Anxiety	Premenopause	164	0,19	0,21	17615	0,02
	Peri/postmenopause	246	0,26	0,28		
	Total	410	0,23	0,26		
Sexual behaviour	Premenopause	141	0,08	0,20	7510	<0,001
	Peri/postmenopause	185	0,31	0,32		
	Total	326	0,21	0,30		
Sleep problems	Premenopause	164	0,17	0,26	15281	<0,001
	Peri/postmenopause	246	0,33	0,35		
	Total	410	0,26	0,32		
Menstrual symptoms	Premenopause	164	0,26	0,20	18305	0,103
	Peri/postmenopause	246	0,28	0,22		
	Total	410	0,27	0,22		
Attractiveness	Premenopause	164	0,26	0,27	13847	<0,001
	Peri/postmenopause	246	0,43	0,28		
	Total	410	0,36	0,29		

SD: Standart Deviation



Correlation of socioeconomic status with somatic symptoms, memory-concentration, vasomotor symptoms and sleep problems showed significant difference and menopausal status with all the subscales showed significant difference except menstruation (Table 1).

### Comparison of SF-36 and WHQ Subscale With Other Independent Variables

Smoking showed significant difference in only physical role-functioning subscale of SF-36. The group which quit smoking had significant poor values in physical role-functioning of SF-36 compared to the other two groups.

There was significant difference in between the groups smoking and depressed mood, somatic symptoms, memory-concentration, vasomotor symptoms, sleep problems, menstrual symptoms and attractiveness subscales of WHQ.

Being under treatment of osteoporosis showed statistical significance in physical functioning, bodily pain, social role-functioning subscales of SF-36. The mean values of the group not using medication for osteoporosis was better than the

group on medication in all these three subscales (Table 2, Table 3).

Correlation between treatment of osteoporosis and memory-concentration, vasomotor symptoms, sexual behavior and menstrual symptoms subscales were statistically significant. The mean values in sexual behavior and memory-concentration subscales was poorer, vasomotor symptoms and menstrual symptoms subscales was better in users of osteoporosis treatment.

BMI showed significant difference among the groups with emotional role-functioning, general health perception, social role-functioning and vitality subscales of SF-36.

Correlation with BMI and somatic symptoms, memory-concentration, sexual behavior and attractiveness subscales of WHQ showed statistical significance between the groups.

All subscales of SF-36 except social role-functioning had significantly better mean values in the group who did not have chronic disease.

All subscales of WHQ except menstrual symptoms had significantly better mean values in the group who did not have chronic disease.

Accepting menopause as a natural phenomenon showed significant difference in all subscales of SF-36 except social role-functioning.

Table 2. Comparison of SF-36 subscales with medical treatment for osteoporosis

SF-36 subscales	Medical treatment for osteoporosis	N	Mean	SD	Mann-Whitney U	P
Physical functioning	No	134	77,83	23,19	3052,0	0,007
	Yes	60	69,16	24,94		
Physical role-functioning	No	134	76,11	39,12	3565,5	0,140
	Yes	60	70,00	39,54		
Emotional role-functioning	No	134	76,61	38,35	3867,0	0,600
	Yes	60	78,33	38,24		
Bodily pain	No	134	68,63	19,03	3235,0	0,026
	Yes	60	61,95	15,97		
General health perception	No	134	64,85	17,36	3924,5	0,791
	Yes	60	64,41	16,02		
Social role-functioning	No	134	78,82	17,89	2934,0	0,002
	Yes	60	71,45	13,82		
Mental health	No	134	73,16	12,29	3949,0	0,843
	Yes	60	72,53	12,24		
Vitality	No	134	64,17	16,47	3476,0	0,130
	Yes	60	67,08	13,87		

SD: Standard deviation

Table 3. Comparison of WHQ subscales with treatment for osteoporosis

WHQ subscales	Medical treatment for osteoporosis	N	Mean	SD	Mann-Whitney U	P
Depression	No	134	0,18	0,19	3914,0	0,759
	Yes	60	0,19	0,18		
Somatic symptoms	No	134	0,37	0,24	3691,0	0,364
	Yes	60	0,33	0,21		
Memory/concentration	No	133	0,26	0,32	3299,0	0,031
	Yes	60	0,15	0,23		
Vasomotor symptoms	No	134	0,45	0,26	3148,0	0,005
	Yes	60	0,56	0,20		
Anxiety	No	134	0,23	0,26	3753,0	0,433
	Yes	60	0,25	0,23		
Sexual behaviour	No	95	0,38	0,33	1584,0	0,016
	Yes	44	0,25	0,31		
Sleep problems	No	134	0,31	0,34	3850,0	0,615
	Yes	60	0,28	0,32		
Menstrual symptoms	No	134	0,24	0,18	3187,5	0,011
	Yes	60	0,30	0,16		
Attractiveness	No	134	0,43	0,29	3938,5	0,810
	Yes	60	0,43	0,26		

SD: Standard deviation

Table 4. Backward Stepwise Logistic Regression Analysis of SF-36

Independent variables OR		Physical functioning		Bodily pain		General health perception		Social functioning		Mental Health		Vitality	
		p	OR	p	OR	p	OR	p	OR	p	OR	p	OR
Age	40-44 years	R				R	0,111	R				R	
	45-49 years	1,12	0,734			2,15	0,018	0,69	0,155			2,66	0,003
	50-54 years	0,64	0,265			1,52	0,271	0,72	0,270			2,06	0,076
	55-59 years	0,28	0,005			1,90	0,119	0,17	<0,001			4,59	0,001
Education	Uneducated	R		R		R				R		R	
	Primary	3,15	0,075	7,58	0,002	5,35	0,005			2,28	0,178	3,09	0,064
	Secondary-higher sec	7,14	0,003	15,0	<0,001	6,18	0,003			4,96	0,010	4,83	0,011
	College-university	5,04	0,034	19,2	<0,001	4,46	0,02			4,05	0,041	2,87	0,122
Marital Status	Not married	R						R		R		R	
	Married	0,574	0,089					1,67	0,080	2,56	0,001	1,71	0,062
Socioeconomical status	Higher-upper middle	R	0,057					R					
	Lower middle	1,97	0,068					0,86	0,620				
	Lower	1,06	0,857					0,42	0,001				
Working in a job	Working or worked												
	Not worked												
Menopausal status	Premenopause	R		R		R				R		R	
	Peri/postmenopause	0,24	<0,001	0,30	<0,001	0,30	<0,001			0,46	0,001	0,18	<0,001

OR: Odds Ratio, R: Referans category

Table 5. Backward Stepwise Logistic Regression Analysis of WHQ

Independent variables OR	Depression		Somatic symptoms		Memory-Concentration		Vasomotor symptoms		Anxiety		Sexuality		Sleep		Menstruation		Attractiveness			
	p	OR	p	OR	p	OR	p	OR	p	OR	p	OR	p	OR	p	OR	p	OR		
Age	40-44 years		R		R		R		R		R	0,054			R		R		0,958	
	45-49 years		2,4	0,015	1,9	0,036	1,3	0,533	2,1	0,049	1,1	0,869			2,8	0,004	1,6		0,577	
	50-54 years		2,7	0,016	1,5	0,208	1,5	0,322	4,0	0,002	0,4	0,040			3,0	0,008	1,3		0,723	
55-59 years			3,9	0,003	5,4	<0,001	4,4	0,001	3,1	0,015	0,6	0,319			2,7	0,025	1,7		0,997	
Education	Uneducated	R	0,058		R		R		R		R		R				R			
	Primary	1,4	0,545		4,3	0,011	0,5	0,248	2,2	0,137			4,6	0,021			29,5		0,001	
	Secondary-higher sec	2,4	0,097		6,3	0,002	0,3	0,042	3,6	0,024			5,7	0,010			85,6		<0,001	
Marital Status	College-university	1,1	0,884		4,7	0,028	0,2	0,023	3,8	0,047			2,2	0,292			645		<0,001	
	Not married	R							R				R							
Socioeconomical status	Married	2,4	0,001						2,6	0,002			1,8	0,035						
	Higher-upper middle			R	0,066	R		R	0,095						R	0,078	R			
	Lower middle			2,1	0,037	1,5	0,208	0,6	0,151						2,2	0,025	5,0		0,043	
Working in a job	Lower			1,	0,718	2,4	0,005	1,0	0,905						1,4	0,302	17,9		0,002	
	Working or worked																R			
Menopausal status	Not worked																		0,2	0,038
	Premenopause	R																		
	Peri/postmenopause	0,7	0,079	0,2	<0,001	0,4	0,001	9,9	<0,001	0,2	<0,001	0,2	<0,001	0,5	0,002	0,3	<0,001	0,1		0,019

OR: Odds Ratio, R: Referrans category

Accepting menopause as a natural phenomenon showed significant difference in all subscales of WHQ except depressed mood and menstrual symptoms.

### **Backward Stepwise Logistic Regression Analysis**

#### **Backward Stepwise Logistic Regression Analysis of SF-36 with independent variables:**

To specify confounding factors which effects quality of life Backward Stepwise Logistic Regression Analysis were performed. Lower one third of subscales were compared with other two third. In SF-36 high score shows better quality of life. Age, marital status, education, socioeconomic status, having a job and menopause were considered as confounding factors. The results were shown in Table 4.

#### **Backward Stepwise Logistic Regression Analysis of WHQ with independent variables:**

To specify confounding factors which effects quality of life Backward Stepwise Logistic Regression Analysis were performed. Upper one third of subscales were compared with other two third. In WHQ high score shows poor quality of life. Age, marital status, education, socioeconomic status, having a job and menopause were considered as confounding factors. In the subscale of sexual behaviour 326 participants who had sexual partner were evaluated. The results were shown in Table 5.

### **Discussion**

Absolute attention was paid that the participants should represent the 40-59 years old women population. Therefore stratification is done according to age and power of sampling was 80% The distribution of the age groups were in correlation with the Turkish Census Statistics of 2000 (13).

Having a job or salary had an important role in promoting the status of women especially when income is the question. In our study 67% of the

participants were housewives and the rate of working women was lower than the data obtained from TDHS-2003 because TDHS-2003 data did not include women 50-59 age group. Women with personal income had better share of household income compared to the average income in Turkey (14).

Education is another component effecting women's status as well as health quality. In our sample educational status was higher among women despite being old aged when compared to Turkish Demographic Health Survey (TDHS) conducted in 2003. When compared with the data of Turkstat 2000 for Turkey in general our sample showed primary school graduates were less and secondary and higher- secondary school graduates were more (13,14). In Özdemir's study the majority were uneducated (40.9%), the rate of primary school graduates was nearly similar and the rate of higher education was low (14.9%) compared to our study (15).

Socioeconomical status is associated with income, educational status, profession and social status (16). Socioeconomical status of the most of the participants were low. Whereas according to Gross Domestic Products (GDP), Edirne city stays among the first 20 cities with above Turkey's average (17). The reason of the distinction is that scale prepared by Neyzi et al. shows social development rather than economic indicators (18). Absence of social security only in a small population also predicts economic prosperity. In the thesis of Eker where the center of Edirne is considered as the population the same scale is used and similar results are obtained (19).

Obesity is still an important problem in the world as well as in Turkey. In our study over 80% of our participants' BMI was over 25 and this showed correlation with the studies of Yalçın and Kılınçer (20,21). Our results showed lower outputs than TDHS-2003 data because TDHS is carried out by 15-49 years of women (14).

Smoking and cessation of smoking rates in our study were higher than the studies done in Samsun and Ankara (15,21). 71% of the participants did not have any chronic disease. This data showed similarity with the results of the studies done by Öner'in Edirne and Vehid et al. in Silivri (22,23).

The rates of conception and live births were higher than studies performed in Ankara and Samsun. This could be due to the high standards of

socioeconomic status which leads to decreasing in birth rate. TDHS-2003 data showed that among 40-49 years old women the average live birth rate in west part of Turkey is 2.9 (14). This data was close to our findings ( $2.3 \pm 1.27$ ).

Age of menarche is important because it effects the age of entering menopause and a risk factor for certain hormone dependent cancers like breast cancer. In our study age of menarche was  $13.04 \pm 1.33$  years. In our country other studies showed that menarche age was 12.4 years in Ankara, 13.7 years in Samsun and 13.45 years in Silivri (15,21,23). The menarche age was found to be 13.3 years in United Kingdom, 13.3 years in Austria, 13.5 years in Croatia (24-26). The menarche age in Europe shows similarity with our country.

The age of onset in menopause is effected by many factors. The age of onset of menopause showed similarity with the various studies done in our country (8,23,27-29). In various countries age of entrance to menopause shows differences (30,31-33). But generally the age of onset in menopause is higher in developed countries and is lower in developing countries (1).

In our study 19.1% had surgical menopause and 80.9% had natural menopause. These rates showed similarity with the study of Kilincer and Muderris et al (21,27).

Studies and discussions are still continuing on HRT and attitudes towards HRT is continuously changing. In our study only 4.9 % was still using HRT and 23.6% had used HRT previously. These rates were lower than the rates of the studies done by Özdemir and Biri et al (15,34). In past 5-6 years doctors as well as patients' are selective in using HRT, and this leads to decrease in HRT usage.

Osteoporosis and osteoporotic fractures are the major causes of morbidity in postmenopausal period. In our study only 25.6% of the participants were having treatment for osteoporosis. This rate was higher than the rates in Kilincer's study (21). Women in premenopausal period still carries the risk of becoming pregnant. Irregularity in menses during this period prevents seeing amenorrhoea as a sign of pregnancy and leaves women to come up with unwanted pregnancies. Therefore it is important to inform women about contraception (35,36). In our study 45.5% of the participants did not use any contraceptive methods. Commonly used contraceptive

methods were intra-uterine device (49.5 %), condom (19.8%) and bilateral tubal ligation (15.4%).

In our country referring to a physician for menopausal symptoms creates good opportunity for women to have preventive health care (37). In our study mammography, pap smear, bone mineral density, breast examination and self-breast examination rates are over 50%. Pap smear rates showed similarities with the study of Akyuz et al (38). In the study of Bezircioglu et al. 73.3% did not have any mammography screening and 82.7% did not have bone mineral density measured (39). Higher rates in our study is probably due to the emphasis on screening tests recently and presence of cancer research center which can be reached easily.

78% of the participants accepted menopause as a natural phenomenon and 52.4% defined it as "cessation of menses". Other answers for defining menopause were "end of fertility", "natural phenomenon", "physical change", "new period in life", and "beginning of old age" respectively. These answers having positive and negative meaning shows that Turkish women perceive menopause different than Asian and European women (40).

In menopausal and postmenopausal period apparently health related quality of life in women is effected poorly. Two separate scales SF-36 and WHQ are used for this purpose. The age had more effect on physical health in quality of life in SF-36. A study done in Italy by Genezzani et al. showed that physical components of SF-36 was mostly effected by age (41).

In relation with the educational status quality of life in all SF-36 subscales was poor in low educational status. In the studies done by Genezzani et al. and Brzyski et al. showed that mental health subscales were more effected than physical health subscales in low educational status (41,42).

Mental health subscales were significantly affected by marital status and mean values were higher in married participants.

A study in USA showed that physical health was better in married women and another study in Italy showed that physical health was not effected but instead mental health is effected poorly (41,42). Conde et al. in their study showed that there was no significant difference between marital status with physical and mental health subscales of SF-36 (43).

Occupation had no statistically significance on SF-36 subscales. A study in USA showed that physical health was better in participants having a job (42).

In the state of socioeconomical status physical role-functioning, bodily pain, social role-functioning and emotional role-functioning was seen to be effected. Genazzani et al. in their study determined that women with low economical status had poor quality of life Likewise Brzyski et al. had also shown that women with low economic status had poor quality of life (41,42).

In our study mental and physical subscales mean values in perimenopausal and postmenopausal women were poorer than premenopausal women. Similarly in their study Fuh et al. showed that life quality was much better in premenopausal women (44).

WHQ is an instrument to evaluate health related quality of life among women. Although it is mostly used in evaluation of HRT on life quality, it is also used in field studies (45). Correlation of age with WHQ was statistically significant in somatic symptoms, memory, vasomotor symptoms, sexual behavior and attractiveness subscales. The mean value of memory-concentration subscale on the contrary showed higher values in the group 55-59 years old. This could be due to the tendency not to admit as weakening of the memory occurs with ageing. Relation between age and WHQ subscales was also shown in two studies done in Italy (41-46).

Comparison of educational status with WHQ showed that all the subscales except menstrual symptoms was poorly effected in uneducated group and showed statistical significance.

Genazzani et al. also indicated that women educated for 5 years or less than 5 years had poorly effected quality of life (41). Amore et al. in their study showed a similar relation between educational status and quality of life (46).

In our study depressed mood, vasomotor symptoms, anxiety, sleep problems and attractiveness subscales showed poor mean values in the unmarried group. Amore et al. in their study showed that there were no statistical significance between marital status and WHQ subscales (46).

In our study there was no statistically significance between occupation and WHQ subscales which showed similarity with the study done by Amore et al (46).

In our study low socioeconomical status poorly effected menstrual symptoms, memory-concentration, somatic symptoms and sleep problems subscales. Genazzani et al. showed that socioeconomic levels effected 7 out of 9 subscales of WHQ (41).

In our study menopause showed statistical significance on all subscales of WHQ except menstrual symptoms. Hunter also indicated that menopause has effect on health related quality of life (47).

Studies show that smoking effects the age of entrance to menopause (31,48). Smoking also together with high LDL, sedentary lifestyle, obesity and high blood pressure increases the risk of cardiovascular disease. In our study smoking only effected physical role-functioning in SF-36 and most of the subscales in WHQ. Quality of life was higher among nonsmokers. A study done in Neatherlands showed that being a nonsmoker positively effects psychological health in postmenopausal women (49).

Postmenopausal osteoporosis is an important factor on morbidity and quality of life. While apparent fractures due to osteoporosis having effects like pain, treatment and health care needs, hidden fractures has poor effect on life quality and functions (50). In our study mean values of SF-36 subscales of physical functioning, pain and social functioning subscales was significantly poor. This could be due to not having specific complaints among the participants not using drugs. The mean values of vasomotor symptoms of WHQ beeing poor also supports this opinion in the group having treatment for osteoporosis.

Obesity is a risk factor for many diseases such as cardiovascular disease, diabetes and arthritis. In our study mean value of general health perceptions was poor in obese participants.

Somatic symptoms, memory-concentration, sexual behavior and attractiveness showed poor mean values in obese participants. Studies done in Neatherlands and Equator show that obesity poorly effects quality of life (49,51).

Presence of chronical disease had prominent effect on the evaluation of both SF-36 and WHQ. Quality of life was poorly effected by the presence of chronical disease. The two studies done in Neatherlands and Italy showed that presence of chronical disease poorly effected women in menopausal stage (42,49).

Perception of menopause also effects severity of the symptoms in menopausal stage. In populations where menopause is accepted as a natural phenomenon menopausal complaints show less severity (40). In our study as well women who accepted menopause as a natural phenomenon subscales showed better mean values.

In our study SF-36 showed that the quality of life in women was mostly effected by age, educational status and menopausal status. Advanced age, low educational status, being in peri- or postmenopausal stage had poor effect on quality of life. These findings showed resemblance with the literature (41,42,46,52).

In health related quality of life WHQ showed that age, educational status, marital status, socioeconomical status and menopause were the influencing factors. Advanced age had poor effect on health quality. Effect of educational status had differed. Low educational status while having preventive effect on depression mood, sleep problems, attractiveness and memory-concentration subscales, it was poorly effecting vasomotor symptoms. Participants with better educational status showing poor effectiveness in memory-concentration and attractiveness subscales could be due to having high expectancy. In one of the studies done in Italy it was shown that the lower educational status had effected poorly the vasomotor subscale (41).

Being unmarried had preventive effect on depressed mood, anxiety and sleep problems subscales. As a result of regression analysis although this data seems to be in conflict with the previous data, married participants mostly taking place in the upper one third of the marital seems to be the reason in general.

In our study high socioeconomical status effected positively memory-concentration and attractiveness subscales of quality of life. On the other hand these two subscales were poorly effected in higher educational status. This could be due to the socioeconomic scale which is developed by Neyzi et al. which holds the job and education of men in the foreground (18). Lebrun et al. in their study showed that the educational status of the partners of postmenopausal women especially effected mental components of life quality (49). To be in premenopausal period showed significance on

preventive effect in all the subscales except depression. The poor effect of entering menopause was shown in many studies (42,44,47,53,54).

When we were studying quality of life in women for menopause we came across with expected and unexpected results. It is clear that quality of life is adversely effected but influential reasons show a complicated pattern during this period.

One of the important factors taking place in woman's health is education and socioeconomic status. As the educational status increases women will have more rights on themselves and their health. Improvement in educational and socioeconomic status of women will have positive effect on life quality during menopause and for the community as well.

In the context of continuous and holistic approach family physicians are the people who could suspect and detect the symptoms of menopause and provide help easily. Treating menopausal symptoms and giving recommendations to cope with these changes will be helpful during this period.

Again life events such as illnesses or deaths of the parents, separation of children from home and retirement all coincides with this period. At the end woman starts feeling old and useless. Family physician should understand the distresses of woman, should offer help and support so that they should begin to this new period with hope.

Another task of family physician is to provide healthier life during menopause which covers one third of life of women. Preventive health care starts from childhood by promoting healthy life style and is followed by periodic health examination, determination of risk factors, screening of these risk factors, prevention of the diseases and prevention from the complications of the diseases.

## Conclusion

Advanced age, having less education, low socioeconomic level and being at the peri- or postmenopausal phase demonstrated a negative effect on the quality of life. In this regard in the light of these findings we conclude that improving education and socio-economic level with initiating preventive health care at earlier ages would improve health related quality of life among postmenopausal women.

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# Effect of the education given to the patients undergone kidney transplantation on the life quality and compliance to treatment and anxiety and depression levels

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## Abstract

The aim of this study was to assess the effect of patient education on the quality of life and compliance to treatment and anxiety and depression levels in kidney transplantation patients. The study was carried on patients undergone kidney transplantation registered in nephrology polyclinic of hospital in Erzurum, Turkey. The SF-36 Life Quality Scale, the Kidney Transplantation Adaptation Assessment Scale and the Hospital Anxiety and Depression Scale were used, in addition to sociodemographic data collection questionnaire. It was found that there was a significant difference between pre-education and post-education mean scores of all the subscales of the quality of life and global quality of life, and there was an increase in the scores after the patient education. It was detected that the compliance to treatment of patients increased in Kidney Transplantation Adaptation Assessment Scale after education. The level of anxiety and depression was found to have decreased after the patient education.

**Key words:** Kidney transplantation, quality of life, compliance, anxiety, depression.

## Introduction

Renal transplantation is considered to be the best treatment available for restoring renal functions in patients with end-stage renal disease(1). In the past two decades, researchers have mainly focused on comparing the quality of life (QOL) among patients undergoing renal transplantation, haemodialysis and peritoneal dialysis. The results

have indicated that successful renal transplant recipients have better QOL than those receiving other treatments (2).

Renal transplantation eliminates many limitations from dialysis and can improve the quality of life. However, long-term immunosuppressive drug use may cause problems such as infections, obesity, coronary heart disease, hyperlipidaemia, predisposition to hypertension, protein catabolism, osteoporosis, hyperkalemia, hepatotoxic effects and malignancy in the late period of transplantation (3).

The prevalence of psychiatric disorders, such as anxiety and depression are somewhat higher after kidney transplantation. One study reported that about 50% of kidney transplant recipients suffered from anxiety and 25% from depression after transplantation (4,5).

Compliance with medications after organ transplantation is emerging as a major healthcare issue with implications for chronic rejection and graft loss. Patients who lose their transplants due to non-compliance result in a significant drain on finances, as they are placed back on dialysis, a more expensive modality of treatment than a functioning transplant (6). Therefore, patient compliance and rehabilitation is extremely important for effective treatment and care. The nurses' role within the multidisciplinary team is aimed at prevention of problems and health promotion for this population. The concepts of health promotion and disease prevention can easily be applied to renal transplant recipients, because preventive care and ongoing patient education are imperative to ensure positive outcomes (7).

The main aims of patient education following renal transplantation are to help patients acquire

the required skills for daily living without problems and to help patients cope with physiological and psychosocial problems (8,9). The aim of this study was to assess the effect of patient education on the quality of life and compliance to treatment and anxiety and depression levels in kidney transplantation patients.

## Material Method

### Design

The study was planned and carried out as one group pretest-posttest semi-experimental design with the aim of this study was to assess the effects of patient education on the quality of life and compliance, anxiety and depression levels in kidney transplantation patients.

### Sample and setting

The study was carried out in nephrology polyclinic of a university hospital in Erzurum, Turkey between the dates March 2008 and December 2008. Turkey has a total of 23 kidney transplant centers and conducted in Erzurum is one of them. This center is serving four years and the number of patients registered in the center is only 44 people. Follow-up of patients after discharge is done in the nephrology polyclinic.

The study context is made up of the total 44 patients in whom kidney transplantation was applied to and were registered in nephrology polyclinic of related hospital. The sampling of the study in the process of data collection, kidney transplantation was applied to, not having any current or previous psychiatric disorders, being cooperative and communicative, not having any hearing loss or loss of vision, being at least a primary school graduate, being  $\geq 18$  years of age, and being followed-up in the nephrology polyclinic of this university hospital. In the dates when the study was carried out 42 of 44 patients undergone kidney transplantation and registered in nephrology polyclinic were included in the study content. Two of the patients were excluded from the study as they had the problem of seeing and hearing.

### Data collection

In the data collection of the data, SF-36 Life Quality Scale (SF-36), Kidney Transplantation Adaptation Assessment Scale (KTAAS) and Hospital Anxiety and Depression Scale (HAD) were used in addition to the sociodemographic data collection questionnaire

*SF-36 Quality of Life Scale: Short Form-36 for Health Status:* The SF-36 was developed by Ware and colleagues (10) and adapted to Turkish by Pinar (11) SF-36 measures the following eight dimensions of health: physical functioning, role limitations due to physical problems, bodily pain, general health perceptions, vitality, social functioning, role limitations due to emotional problems, and mental health. We also analyzed four summary scores of SF-36: the functional status, well-being, general health perception and global quality of life scores.

*Functional capacity:* Role limitations due to physical or emotional problems, social functioning limitations due to emotional and social problems, and physical functioning limitations due to health problems.

*Well-being:* Mental health, bodily pain, vitality.

*General health perception:* Changes in the health status since the previous year.

*Global quality of life:* All raw scale scores were linearly converted to 0 (worst possible health status or quality of life) and to 100 (best possible health status or quality of life). The score of the subgroups, as well as the final global score of the SF-36 range between 0 and 100, respectively. All eight SF-36 scales are standardized to range from 0 to 100, with the higher score indicating better health status. The total Cronbach alpha parameter was determined as 0.94; the alpha parameters of the sub-dimensioned Cronbach were determined as 0.89 for functional status, 0.90 for well-being, and 0.75 for general health perception.

*Kidney Transplantation Adaptation Assessment Scale (KTAAS):* This scale was developed by Sagduyu et al. (12), and has five items. The patient with transplantation or his/her relative is asked to complete the form including patient compliance towards diet/medications/physicians, visits/health recommendations and the items for the

general adaptation assessment as poor/moderate/good/very good/excellent/no idea.

*Hospital Anxiety and Depression Scale (HAD):* This scale was developed by Zigmond and Snaith (13) and had reliability and validity studies. The reliability and validity studies for the Turkish version were performed by Aydemir et al (14). Cut-off points were 10 for anxiety and 7 for depression. The scale has 14 items; seven items for depression and seven items for anxiety symptoms. The Cronbach alpha coefficient for anxiety was found as 0.85 and 0.77 for depression in the reliability study. In this study, the Cronbach alpha coefficient was 0.65 for anxiety and was 0.67 for depression.

### **The patient education brochure**

This brochure was created as a nurse intervention tool by the researcher after review of literature (9,15-17). It covers topics such as the kidneys and their functions, end-stage renal failure, its causes and treatment options, information on renal transplantation, discharge, medications, infection prevention, diet and nutrition, social life, sexual life and pregnancy after renal transplantation.

### **Procedure**

After the physical examination, the patients were given pre-tests in the meeting room of the nephrology polyclinic prior to the patient education. All the patients completed the socio-demographic questionnaire, the SF-36 Life Quality Scale, KTAAS and HAD scale. The educations were implemented on a one-to-one basis in the meeting room lasting for approximately 45 minutes per patient. The educations covers topics such as the kidneys and their functions, end-stage renal failure, its causes and treatment options, information on renal transplantation, discharge, medications, infection prevention, diet and nutrition, social life, sexual life and pregnancy after renal transplantation. Visual and verbal teaching methods were used in the question and answer style by the researcher. Each patient was given a education brochure at the end of the education. Three months after the patient education, the scales were re-completed.

### **Data analysis**

The data were coded, installed and analyzed using the SPSS 15.0 pocket program. Percentages and paired-samples t test were used. We set the significance level at  $p \leq 0.001$ .

### **Ethical considerations**

The study was approved by the Ethical Committee of the Health Science Institute of the University and informed consent was obtained from each participant. The patients were informed about the aim of the study and were assured that they had the right to refuse to participate or to leave the study whenever they wished.

### **Findings**

The sociodemographic and transplantation details of the patients have been presented in Table 1. Of the patients, 33.3% were  $\geq 36$  years of age, 59.5% were female, 66.7% were married, 42.9% were employee, 47.6% had graduated from secondary or high school. of patients, 33.3% had a post-transplantation period of 2-5 years, and 83.3% had living donor transplants. It was found that 47.6% of patients did not have adequate information after the transplantation (Table 1).

Patients' mean scores for the pre-education and post-education for the SF-36 quality of life scale are presented in Table 2. There was a significant difference between the mean scores of all dimensions of the quality of life and the mean scores of the global quality of life with higher scores in the post-education ( $p < 0.001$ ) (Table 2).

The numbers and percentages of scores in the pre-education and post-education for the patients and their relatives who scored "good-very good-excellent" for compliance to treatment in KTAAS have been presented in Table 3. The increase was significant for compliance to treatment (Table 3).

The mean scores of pre-education and post-education for Hospital Anxiety and Depression Scale have been displayed in Table 4. The difference was significant ( $p < 0.001$ ) the level of anxiety and depression decreased after the patient education (Table 4).

Table 1. Sociodemographic and transplantation details of the patients

Sociodemographic Details (n = 42)	n	%
<b>Age</b>		
18-23	7	16.7
24-29	9	21.4
30-35	12	28.6
≥36	14	33.3
<b>Gender</b>		
Male	25	40.5
Female	17	59.5
<b>Marital status</b>		
Married	28	66.7
Single	14	33.3
<b>Working state</b>		
Employee	18	42.9
Housewife	10	23.8
Pensioner	8	19.0
Student	4	9.5
Unemployed	2	4.8
<b>Level of education completed</b>		
Primary school	14	33.3
Middle/ High school	20	47.6
University	8	19.0
<b>Transplantation Details</b>		
<b>Duration of transplantation</b>		
1-3 month	6	14.3
4 -6 month	9	21.4
7 month -1 year	5	11.9
2- 5 year	14	33.3
≥6 year	8	19.0
<b>Donor source</b>		
Living donor	35	83.8
Cadaver donor	7	16.7
<b>Postoperative information state</b>		
Did receive	3	7.1
Did not receive	19	45.2
Did not receive adequate	20	47.6

Table 3. The percentages of scores in the pre-education and post-education for KTAAS

	Compliance to treatment pre-education post-education			
	S	%	S	%
<b>Compliance to diet restrictions</b>				
According to the patient	14	33.4	40	95.3
According to the relative	12	28.6	40	95.3
<b>Compliance to medications</b>				
According to the patient	24	57.2	40	95.2
According to the relative	20	47.6	40	95.2
<b>Compliance to physician visits</b>				
According to the patient	26	62.0	41	97.6
According to the relative	23	54.8	41	97.6
<b>Compliance to health behavior recommendations</b>				
According to the patient	22	52.4	41	97.7
According to the relative	20	47.7	41	97.7
<b>General adaptation</b>				
According to the patient	19	45.2	40	95.3
According to the relative	18	42.9	40	95.3

**Discussion**

Renal transplantation is the best method of treatment for improvement of renal functions in patients with end-stage renal failure. However, there are certain challenges such as continuous risk of rejection, adverse effects of medications and continuous obligatory follow-up of the transplant patient (17,18). Besides, the risk for infection, re-hospitalizations and changes in body image are stressful for the patients. The mental and behavioral efforts to overcome these stresses have a significant impact on the quality of life in these patients (19,20). It is well-known that patient education provided by the health personnel has a significant influence on the quality of life in patients (21).

It was found that there was a significant difference between pre-education and post-education

Table 2. Comparison of pre-education and post-education mean scores of the SF-36 Quality of Life Scale of the patients

SF-36 Quality of Life Scale	Pre-education X±SS	Post-education X±SS	t	p
Functional capacity	53.24±21.19	74.02±13.67	5.521	p<0.001
Well -being	66.02±11.67	75.92±12.54	3.996	p<0.001
General health perception	64.02±18.18	74.09±12.15	3.186	p<0.001
Global quality of life	61.07±12.63	74.76±9.11	5.521	p<0.001

Table 4. Comparison of the mean scores of pre-education and post-education for Hospital Anxiety and Depression Scale (n=42)

Hospital Anxiety and Depression Scale	Pre-education X±SS	Post-education X±SS	t	p
Depression	4.85±3.14	2.28±2.42	4.370	p<0.001
Anxiety	5.95±2.84	2.52±2.83	6.110	p<0.001

mean scores of all the subscales of the quality of life and global quality of life, and there was an increase in the scores after the patient education. These findings were consistent with the other studies in the literature (22-24).

Many national studies in Turkey have revealed that most of the renal transplant patients had not been adequately informed regarding life before and after transplantation by the healthcare personnel (25,26). It has been emphasized in many studies that compliance to treatment is a very important factor affecting the prognosis after transplantation and that special attention should be paid to patient information (27,28).

Research results show that there has been a significant increase in the number and percentage of patients and patient relatives scoring "good-very good-excellent" in compliance to treatment in all the subscales of KTAAS after patient education. Various studies have shown that inadequate patient information on treatment has a negative effect on the patients' compliance to treatment in patients with renal transplants, and that compliance to treatment increases in patients who have had patient education (7,27,28).

Deterioration in perception of the body image, sexual dysfunctions, anger, incivility, addiction, passive aggressive behaviour, anxiety and depression are common in transplant patients. The psychiatric symptoms may affect patients' communication with the healthcare team and the treatment success (29,30). It was found in surveys that psychiatric problems in transplant patients were mainly due to probability of rejection and adverse effects of immunosuppressive treatment (4,14,31).

With the patient education on treatment and care, it is possible to decrease anxiety and depression by enabling them to use effective coping skills for compliance and to re-structure the dynamic balance when their health is threatened in unexpected situations. It is possible to see that the depression and anxiety scores decreased af-

ter patient education in our study. In a study by Tsay et al. (32) it was found that patient education had a positive impact on the levels of anxiety and depression. In a national study, it was shown that anxiety and depression scores decreased after patient education on disease and coping with stress in hemodialysis patients (33).

Therefore, it may be suggested that: Continuous education and consulting should be provided by the healthcare team for patients. An education consultant or education nurse should be trained to work in the transplantation unit, as these patients will have to manage their life-long disease by themselves and as they may forget what was taught at hospital, they should have periodic refreshment trainings, although it was found that a considerable percentage of patients and their relatives scored compliance to treatment as good-very good-excellent after patient education, it may be suggested that studies should be conducted in which compliance to treatment is followed and assessed by monitoring objective measures such as medical records, blood biochemistry and body weight.

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# Determining the nurse's health problems and work stress level in Turkey

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## Abstract

**Objectives:** This study was planned to descriptively determine nurses' health problems and the relations between job stress, socio-economic status, smoking and the hospital they work in.

**Material and methods:** A sample was made up of 225 nurses. Data were collected by a questionnaire and the work-related stress scale. Percentage, chi-square and logistic regression analysis tests were used for evaluation of the data.

**Results:** A total of 41.8% of nurses are prelicence graduated and 31.6% of them have been working for 5-9 years as nurses. Thirty-six per cent of nurses in this study have a health problem. Cardiovascular diseases were seen first, disc hernia were seen second in nurses. A total of 67.1% of nurses who have health problems said that their health problems affect their work. Otherwise job stress was seen in all nurses. Smoking differences between the groups according to stress were found to be significant, and nurses who have a high job stress level smoke more ( $p < 0.05$ ).

**Conclusions:** The findings of this study show that job stress was seen in all nurses, stress does not affect having a health problem in nurses, and nurses who have high job stress levels smoke more.

**Key words:** Nursing, job stress, health problems

## Introduction

Recent research has introduced the view that shift working has negative effects on health workers' physiological and psychological health and this situation has a negative effect on patient safety. Shift working affects the social life negatively and leads to problems such as insomnia, nutri-

tion problems, lack of interaction between family members and changes in exercise habits (1,2).

Hospitals carry important risks in terms of environmental factors. Kılıç et al. (2008) established that injuries to nurses by sharp implements is 84.5% (3). Çalışkan and Akdur (2001) reported that 94.2% of nurses think that they work in a risky environment because of infections, stress levels and long working hours (4). Tel et al. (2003) reported that the job stress scores of nurses and physicians are higher than those of other health workers (5).

Job stress is an inevitable experience that occurs in the work environment and its adverse effects on individuals are increased with its frequency and duration. The causes of job stress in the work environment are listed as organizational changes, excessive workload, communication problems, and working with dying patients who need intensive care (5). The field of health care is accepted as being a high stress field as a consequence of caring for highly stressed patients and of the health workers' own job stress. Nurses constitute a risk group in terms of job stress with these features. It is stated that recurrent job stress in the work environment causes migraine, coronary artery disease, muscle tension, insomnia, fatigue, psychological problems, smoking, alcohol abuse and decrease in work efficiency (5).

Nurses are health workers with an important role in the protection and promotion of the health of individuals and the community. When health problems in nurses are not solved and they cannot cope with job stress properly, this leads nurses to be harmed and the quality of service and the care they give may decrease. Therefore, the aim of this study was to determine the health problems and job stress levels of nurses and the relationship between the nurses' health problems and job stress levels.



## 1. Methods

### 1.1. Participants

This descriptive study aims to determine the health problems and job stress levels of nurses working in Gazi University Hospital and Ministry of Health Ankara Training and Investigation Hospital. The scope of the study consists of all nurses working in the Gazi University Hospital and Ministry of Health Ankara Training and Investigation Hospital. The sample of the study was determined by using sample calculation formulae in known situations (6) and included overall 225 nurses. Nurses were stratified according to whether they work in the university or the state hospital. After the weight of the stratum was determined, the sample consisted of 125 nurses from Ankara Hospital and 100 from Gazi University Hospital. All of the nurses answered the questionnaire. The questionnaire form was filled in by face to face interviewing.

### 1.2. Intervention

The data of the study were collected by using a questionnaire form prepared by the investigators in view of the relevant literature and job stress scale (4,5,7,8). The questionnaire form was drawn up by the researchers. The questionnaire form consists of 28 questions in two parts. In the first part, there are questions attempting to determine the demographic characteristics of the nurses and in the second part there are questions regarding health problems.

#### *Job Stress Scale*

This was developed by Haynes and Feinleib (9). The reliability and validity study of the scale in Turkey was carried out by Aktaş (7). The scale contains overall 10 questions. For each question, there are five answers, which are scored from 1 to 5 starting from a to e. The score may range from 10 to 50. In the evaluation of the scale, if the score is lower than 12, the interpretation is that the individual experiences no job stress, if between 12-30, they experience moderate job stress, and if it is 30 or higher, job stress is severe.

### 1.3. Ethical Considerations

This investigation was carried out in accordance with the principles of the Helsinki Declaration. Necessary written approval was obtained from the relevant institutions prior to the application of the study. Before filling in the questionnaire form, nurses were informed as to the aim of the study and their verbal consent was taken.

### 1.4. Statistical Analyses

In the analysis of the data, data obtained from the study were used and a database was formed using SPSS 11.0. Socio-demographic characteristics, smoking status, and coping methods used by nurses were taken as independent variables, health problems both as independent and dependent variables and job stress scores as dependent variables. In the determination of the relation between dependent and independent variables, percentage, chi square and logistic regression analysis tests were used.

## 2. Results

It was established that 46.2% of the nurses were in the 30-39 age group, 60.9% were married, 55.1% did not have children, 80.4% lived in 'nuclear' families and 66.7% evaluated their economic status as middle income. A total of 41.8% of the nurses have a pre-graduate degree, 60.4% started their profession when they were younger than 29 and 31.6% have been working actively as nurses for 5-9 years. A total of 55.6% of nurses are employed in the Ministry of Health Hospital and 66.2% work as clinical nurses. Nurses' mean work hours in a week were 43.19, 67.0% of nurses have night duties and 44.4% of nurses' night duties are 32 hours in a week.

When smoking status was investigated, it was established that 40% were smokers, 32.2% have smoked for 10-14 years and 31.1% consumed a mean of half a packet of cigarettes a day. Of the nurses who are non-smokers at present, 26.9% were ex-smokers and 25.7% of smokers smoked over a packet of cigarettes in a day.

*Table 1. Health Problems of the Nurses and the Difficulties They Face With*

	n	%
<b>Diseases they had after nursing</b>		
No	146	64,9
Yes	65	28,9
No answer	14	6,2
<b>Total</b>	<b>225</b>	<b>100,0</b>
<b>Present diseases (n:65)*</b>		
Cardiovascular**	16	24,6
Disk hernia	16	24,6
Thyroid diseases	12	18,5
Psychosomatic diseases***	9	13,8
Asthma	5	7,7
Other****	21	32,3
<b>Total</b>	<b>65</b>	<b>100,0</b>
<b>Whether present disease influences work power (n:65)*</b>		
Influences	43	66,2
Does not influence	22	33,8
No answer	65	100,0
<b>Treatment status of the present disease (n:65)*</b>		
Receives treatment	44	67,7
Does not receive treatment	21	32,3
No answer	65	100,0
<b>Difficulty faced with at treatment stage(n:65)*</b>		
Difficulty faced with	40	61,5
Does not faced with difficulty	25	38,5
No answer	65	100,0
<b>Total</b>	<b>43</b>	<b>66,2</b>
<b>Difficulty faced with (n:40)*</b>		
Rest	34	85,0
Getting leave from the job for treatment	14	35,0
Getting appointment	13	32,5
Difficulty in diagnosis	4	10,0
<b>Total</b>	<b>40</b>	<b>100,0</b>

\* n was multiplied as there was more than one answer percentages were taken over n

\*\*Arytmia, tachycardia, hypertension, hyperlipidemia, varice

\*\*\*Migraine, gastritis,ulcer

\*\*\*\* Epilepsy, sinusitis, FMF, TBC, kidney stone, myopia, B12 vitamin deficiency, loss of hearing, facet syndrome etc.

As seen in Table 1, 28.9 % of the nurses have indicated that they have had a disease since being a nurse. Leading the health problems is cardiovascular diseases, with 24.6%, to be followed by disc hernia (24.6%). Of the nurses with health problems, 67.7% receive treatment for it and 61.5% are fa-

cing various difficulties at the treatment stage. Of the nurses faced with difficulty during the treatment process, 85% have difficulty in being able to rest, 35% in getting leave for treatment, and 32.5% in getting appointments for treatment. A figure of 66.2% of nurses with health problems stated that their disease influences their ability to work.

*Table 2. Operation Status of Nurses*

	n	%
<b>Operation status</b>		
Underwent operation	108	48,0
Did not undergo operation	106	47,1
No answer	11	4,9
<b>Total</b>	<b>225</b>	<b>100,0</b>
<b>Operation which they underwent (n:106)*</b>		
Caesarian	42	39,6
Appendectomy	14	13,2
Rhinoplasty	9	8,5
Orthopedics	9	8,5
Cystectomy-myomectomy	8	7,5
Tonsillectomy	7	6,6
Lumbar disk hernia	6	5,7
Other**	20	18,9
No answer	10	9,4
<b>Total</b>	<b>106</b>	<b>100,0</b>

\*n was multiplied because there was more than one answer for one question, percentages were taken according to n.

\*\*Tympanoplasty, pilonidal cyst, colon perforation, hemorrhoids, tube ligation, tumor, gall bladder, kidney stone.

A total of 48.0% of the nurses had an operation, caesarean was the leading one at 39.6%, to be followed by other operations (tympanoplasty, pilonidal cyst, colon perforation, haemorrhoids, tube ligation, tumor, gall bladder, kidney stone) with 18.9% and appendectomy with 13.2%. Eighty per cent of the nurses stated that they were using drugs for their diseases while 18.7% were not.

It was established that all nurses experience job stress, 58.2% of nurses have moderate stress, 41.8% of nurses have high job stress and the average job stress score was found to be 29.58%.

In Table 4, the relation between job stress levels and disease status is illustrated. Twenty-nine per cent of the nurses at moderate job stress level and 28.7% of those at high stress levels were found to have health problems. The relation between job stress levels and health problems was found to be statistically insignificant (p>0.05).

Table 3. Job Stress Levels of the Nurses

Job stress score	n	%	Average	SD	Min	Max
Moderate	131	58,2	29,58	5,48	15	46
High	94	41,8				
<b>Total</b>	<b>225</b>	<b>100,0</b>				

Table 4. Distrubution of Nurses Health Problems According To Job Stress Levels

Job Stress Level	Health Problem						Total	
	Yes		No		No answer		n	%
	n	%	n	%	n	%		
<b>Moderate</b>	38	29.0	86	65.6	7	5.3	131	100.0
<b>High</b>	27	28.7	60	63.8	7	7.4	94	100.0

X<sup>2</sup>: 0.419 p: 0.811

Table 5. Methods Used by Nurses for Coping With Stress

Coping methods	n*	%
Thinking for solution	141	62.7
Staying alone	62	27.6
Smoking	37	16.4
Walking	26	11.6
Listening to music	21	9.3
Communicating with friends	15	6.7
Shouting to the people around	12	5.3
Other**	7	3.1

\*n was multiplied because there was more than one answer for a question and percentages were taken according ton.

\*\*Doing house works, crying, sleeping

Among the coping methods used by nurses, the most frequently used method is thinking of finding a solution with 62.7%. It is followed by being on their own (27.6%), smoking (16.4%), having a walk (11.6%) and listening to music (9.3%).

It has been identified that nurses who perceived their socio-economic status as ranging from bad to very bad have a higher level of job stress than nurses who perceived their socio-economic status as being moderate to good. Perception of socio-economic status increased the high job stress level 3.519 times and the relation between job stress level and perceived socio-economic status was found to be statistically significant (p<0.05).

Table 6. Factors Affecting the Nurse's Job Stress Levels

		Job Stress						Chi-Square	p	OR
		Stres		Yüksek Stres		Toplam				
		n	%	n	%	n	%			
<b>Socio-economical status</b>	Moderate-Good	120	62.5	72	37.5	192	100	8.075	0.004	3.519
	Poor- Very poor	9	32.1	19	67.9	28	100			
	Total	129	58.6	91	41.4	220	100			
<b>Graduate Level</b>	Bachelor's degree-Master	55	73.3	20	26.7	75	100	10.561	0.001	2.678
	High School- Pregraduate	76	50.7	74	49.3	150	100			
	Total	131	58.2	94	41.8	225	100			
<b>Smoking Status</b>	No	88	65.7	46	34.3	134	100	7.100	0.008	2.091
	Yes	43	47.8	47	52.2	90	100			
	Total	131	58.5	93	41.5	224	100			
<b>Hospital</b>	University Hospital	82	65.6	43	34.4	125	100	6.294	0.012	1.985
	State Hospital	49	49.0	51	51.0	100	100			
	Total	131	58.2	94	41.8	225	100			
<b>Asthma</b>	No	129	59.4	88	40.6	217	100	Fisher's Exact	0.07	4.398
	Yes	2	25.0	6	75.0	8	100			
	Total	131	58.2	94	41.8	225	100			

It was revealed that high school and pre-graduate graduated nurses have higher rates of job stress than other nurses and school-graduated nurses increased the high job stress level 2.678 times and the relation between job stress level and being school graduated was found to be statistically significant ( $p < 0.05$ ) (Table 6).

It has been identified that state hospital nurses' have higher job stress levels than other nurses and the type of hospital increased the high job stress level 1.985 times and the relation between job stress level and the type of hospital was found to be statistically significant ( $p < 0.05$ ) (Table 6).

It was revealed that nurses who smoke have higher job stress levels than other nurses and smoking increased the high job stress level 2.091 times, but the relation between job stress level and type of hospital was not found to be statistically significant ( $p > 0.05$ ) (Table 6).

It has been identified that nurses who were asthma patients have higher job stress levels than other nurses and having asthma increased the job stress level 4.398 times, but the relation between job stress level and having asthma was not found to be statistically significant ( $p > 0.05$ ) (Table 6).

### 3. Discussion

As seen in Table 1, 28.9% of the nurses said that they had had a disease since being a nurse. The most common disease is cardiovascular disease with 24.6%, to be followed by disc hernia with 24.6%. Studies demonstrate that the rate of coronary disease is higher in those who work in shifts (2,10,11,12). The prevalence of back injuries among nurses is well documented (2,11). In a review of over 80 studies, Hignett (1996) concluded that nursing is among high-risk occupations with respect to lower back injury (13). Nelson et al. (2003) claimed that the prevalence of work-related back injuries in nursing is among the highest of any profession internationally (14). A total of 66.2% of nurses said that their diseases influenced their ability to work. Physical and mental health problems have negative effects on nurses' quality of life and this situation decreases the quality of patient care. In addition nurses' taking days off with health reports is constituted as a problem for institutions that do not have enough staff (15).

When the attitude of nurses to their diseases is considered, 67.7% reported that they had received treatment. According to the study of Yalçinkaya et al. (2007) 82.3% of health workers seek medical help when they have a health problem and 7.6% pay no attention to their problems (16). In our study, it is striking that the rate of nurses who prefer not being treated is higher than in the study of Yalçinkaya et al. (2007).

In the present study, 61.5% of nurses stated that they faced difficulties during the treatment process. Eighty-five per cent of nurses said that they had difficulty in getting rest when they were ill. This was followed by difficulties in leaving for treatment and getting appointments. It can be seen from Table 1 that disease influences workload in 66.2% of nurses.

Work environment is one where stressful moments are experienced from time to time (17). As seen in Table 3, almost all of the nurses experience job stress and stress levels were moderate in more than half of them and high in approximately half of them. In the studies it was revealed that health workers experience job stress in varying proportions (18,19). In the study of Çalışkan and Akdur (2001) it was reported that stress has an adverse effect on the working life of nurses (4). Studies conducted in England demonstrated that health personnel experience high levels of stress (20).

Stress due to work influences the health of nurses adversely, indirectly having an adverse effect on the health of patients as well. As seen in Table 4, 29% of the nurses with moderate stress levels have health problems while 28.7% of the nurses with high stress levels have health problems, the difference between groups being statistically insignificant ( $p > 0.05$ ). This result is the opposite of the literature. We recommend that research might be done on nurses' health problems and job stress levels.

In the present study, when methods of coping with stress were considered, it is seen that the majority of nurses use positive coping methods, such as thinking of solutions to the problem, being on their own, having a walk and listening to music. It is important that they use positive methods for coping with stress. It is known that stress that cannot be coped with in the work environment results in problems such as burnout and health problems (21).

Only 16.4% of the nurses in our study used smoking and 5.3% used shouting at people, which are negative coping methods. These results indicate that positive methods were used more commonly, which reflects a positive development for coping with job stress and preventing burnout.

It has been identified that nurses who perceived their socio-economic status as bad and very bad have a higher level of job stress than other nurses. There are a number of factors which enable some people to experience stress and cope more effectively than others. Some of these are structural features of the individuals' social environment, some are personality characteristics, and some are acquired coping strategies. A social environmental factor is the family socio-economic status (22). Socio-economic status is an established factor of well-being in social life. While socio-economic status increases, so also are the social resources of individuals increased. Low socio-economic status limits the opportunities for a social life for the individual and constitute situational stress. In this case, coping with problems in the work environment can have a negative effect and it is thought that it could increase job stress.

It was found that master degree nurses' high level job stress is 26.7%, license and pre-license degree nurses' high level job stress is 49.3%. Job stress level differences between the groups were found to be statistically significant ( $p < 0.05$ ). A study done by Golubic and colleagues (2009) indicates that a higher level of education has positive effects on the preservation of good working ability (23).

In the present study, it was revealed that nurses who smoke have higher job stress levels than other nurses. Kouvonen et al. (2005) reported that stress increased smoking. Yalçinkaya et al. (2007) established that health workers who do not smoke develop a healthier way of life and coped with stress (16,17). It can be stated that these findings support ours.

In the present study, it was established that one third of nurses have health problems, of which cardiovascular disease is the leading one, to be followed by disc hernia. In addition, nurses frequently complain about varicose veins, excessive fatigue and lower back pain. It was also established that more than half of the nurses with

health problems face difficulties in the treatment process. The most frequently encountered difficulties are being able to rest, make appointments and getting leave from work for treatment. Approximately two thirds of the nurses with health problems stated that health problems influenced their ability to work. In addition, all nurses were found to have job stress. However, a relationship was found between insignificant job stress levels and health problems of nurses. It was also determined that nurses usually use positive methods in coping with health problems. In view of these findings, it is thought that health problems and job stress stem from work conditions and it is recommended that work conditions should be improved in order to prevent this.

#### 4. Conclusion

Nursing is one of the stressfull jobs. In the present study, our findings show that job stress was seen in all nurses. Nursing stress level's does not affect having a health problem in nurses but nurses who have high job stress levels smoke more.

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# Child abuse and neglect among health workers: a study in Erzurum, Turkey

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## Abstract

**Objectives:** To analyze child abuse and neglect among health workers, and the factors leading to this behavior in Erzurum, Turkey.

**Materials and Methods:** The study was conducted as descriptive in a state-run hospital and two hospitals run by a university. 334 health workers participated in the study. A questionnaire was used to collect data. The data were analyzed using percentage distributions and chi-square test.

**Results:** It was found out that 81.8% of health workers applied abuse and neglect physically to their children. According to age, economic situation, and undergoing to misbehavior of fathers and mothers in the childhood, the situation of abuse and neglect of the workers' their children physically was found statistically significant. It was found out that 75.1% of the health workers neglected their children emotionally. According to age, education, profession, family type, economic status, undergoing to misbehaviors of the parents in the childhood, alcohol, the situation of abuse and neglect of health workers' their children emotionally was found statistically significant.

**Conclusions:** The present study in Turkey showed that health workers abused and neglected their children. It is a worrying situation that health workers are risk group for child abuse and neglect. Therefore, the health workers should be scanned as regards abuse and neglect of the children; the risky situations should be determined; some training programmes should be held about the cause, effect and prevention of children abuse and neglect; and similar studies should be carried out in different countries.

**Key words:** Health Staff; Child Abuse and Neglect; Nursing

## Introduction and Background

Child abuse and neglect is defined as the subjection of children by their parents or persons responsible for their upbringing and education or by strangers to attitudes or behaviors that hinder their physical, emotional, mental, or social development [1].

The number of children abused worldwide is very high. A study focusing on Europe and Asia has found that 6 out of every 10 children between 9 and 17 years of age are beaten by their parents when they do something wrong [2]. In the UK, four children a week die because of abuse and neglect, and one in every 1000 children under four years of age is physically abused [3]. The frequency of child abuse between ages 0 to 4 is two times higher than the figure for ages 5 to 14 [4]. A 1997 study conducted in the United States focusing on 35 different countries, found that 330 out of every 1000 children are subjected to bad treatment; of those, 52 percent are neglected and 26 percent are physically abused [5].

It was found that 45 percent [6] to 46 percent [7] of children in Turkey are subjected to abuse and neglect.

Child abuse and neglect is a health problem with tragic results; it damages children's health and well-being leaving life-long, indelible marks on them. Children who are subject to abuse and neglect experience problems such as depression, behavioral disorders, learning disabilities, frequent use of alcohol and addictive substances, aggression towards others and themselves in adult life, delayed speech, failure at school, low self-respect and weak identity, and low future expectations [8]. Studies conducted so far show that the most important risk factor for child abuse and neglect is serious economic hardships faced by the family

[9,10]. Other risk factors for child abuse and neglect include too many children, unemployment, having a foster parent, and the family receiving insufficient social support [10,11]. It was also found that parents who were themselves subjected to abuse and neglect in childhood are more likely to abuse their children [12].

Child abuse and neglect needs to be considered as a problem and health issue that can be prevented via a multi-disciplinary approach [13]. All health workers, regardless of their specialized area of work, have a responsibility in the early diagnosis and treatment of bad treatment and neglect, and the education of family and society on this issue. Health workers consider the family as a whole, provide training for families with regards to the health, care, nutrition and education of children, help improve intra-family relations, and support families with their cooperation [14].

It is important that we have more information about child abuse and neglect among nurses and other health workers [13]. Neglect and abuse is an obstacle to having healthy generations and a healthy society and parents who are also health workers, and therefore responsible for diagnosing and preventing child abuse and neglect, can abuse and neglect their own children. Currently, there are no studies or findings on this subject in health literature.

This study aims to analyze child abuse and neglect among health workers, and the factors leading to this behavior.

## Method

The study was conducted in a state-run hospital and two hospitals run by a university between October 2008 and August 2009.

A total of 1125 health workers were employed in the hospitals where the study was conducted; 609 of them nurses, 281 physicians, 129 technicians, 59 health officers, 19 laboratorians, 11 emergency medical technicians (EMTs), 7 biologists, 3 dieticians, 3 chemists, and 1 bacteriologist.

The universe for the study consisted of the 872 health workers employed in these three hospitals and who had at least one child under the age of 18. Eventually, 334 health workers participated in the study, with 285 nurses, 176 physicians, 48 te-

chnicians, 19 health officers, and 10 laboratorians declining to do so.

The data for the study was gathered using a questionnaire consisting of questions copied verbatim from health literature [1,15]. The questionnaire contained 10 closed ended questions on age, gender, level of education, occupation, family type, economic status, number of children, presence of disabled children in the family, being subjected to bad treatment by parents in childhood, and alcohol use, and 14 closed ended questions designed to measure child abuse and neglect.

After a brief description of the study, participating health workers were given the questionnaires to be filled out. The data was gathered in environments and conditions suitable for participants. Average completion time for the questionnaire was 15 minutes.

The data was analyzed using the SPSS software package. Percentage distributions were used to examine the socio-demographic characteristics of the health workers and their abuse and neglect behaviour patterns, and chi-square analysis to compare the characteristics and abuse and neglect behavior patterns of health workers.

## Results

The mean age of the participants was  $34.70 \pm 6.94$ , and about half (49.4%) were in the 30-39 age group. 68% of the participating health workers were male, 54.5% were college graduates, 59% nurses, 87.4% were part of a nuclear family, and 64.7% had balanced budgets. 84.7% of the health workers had one or two children, 1.5% had a disabled child, 13.2% were subjected to bad treatment in childhood by their parents, and 8.7% consumed alcohol (Table 1). It was found that 81.1% of health workers physically abuse or neglect their children. 23.7% of the participants reported slapping their children in the face, 22.2% beating or pinching, 59.0% neglecting the wishes of their children, 44.9% not taking their kids to the hospital in case of an illness, and 37.4% not attending meetings with the managers of their kids' schools. It was found that health workers who are in the 40 and over age group (86.9%), who are male (83.2%), who have a masters degree (93.8%),



who are in the “other” health workers category (83.8%), who have large families (90.5%), and who have lower earnings than expenses (90.2%) abused or neglected their children more frequently.

The age ( $p < 0.05$ ) and the economic status ( $p < 0.005$ ) of health workers were factors with a statistically significant effect on abuse and neglect behavior patterns (Table 1).

Table 1. The situations of physical abuse and neglect their children according to the characteristics of health workers

Characteristics	The Situation of Physical Abuse and Neglect						Test
	Present		Absent		Total		
	n	%	n	%	n	%	
<b>Age (34.70±6.94, years)</b>							
20-29	60	70.6	25	29.4	85	100.0	
30-39	138	83.6	27	16.4	165	100.0	$X^2=8.680$
40 and over	73	86.9	11	13.1	84	100.0	<b>P&lt;0.05</b>
<b>Gender</b>							
Female	182	80.2	45	19.8	227	100.0	$X^2=.428^*$
Male	89	83.2	18	16.8	107	100.0	$p>0.05$
<b>Education level</b>							
High school	88	80.7	21	19.3	109	100.0	
University	146	80.2	36	19.8	182	100.0	
Master	15	93.8	1	6.3	16	100.0	$X^2=1.777$
Doctorate	22	81.5	5	18.5	27	100.0	$p>0.05$
<b>Profession</b>							
Nursing	159	80.7	38	19.3	197	100.0	
Physician	41	80.4	10	18.4	51	100.0	
Technician	40	81.6	9	21.5	49	100.0	$X^2=.219$
Other	31	83.8	6	16.2	37	100.0	$p>0.05$
<b>Family Type</b>							
Nuclear Family	233	79.8	59	20.2	292	100.0	$X^2=2.737^*$
Large Family	38	90.5	4	9.5	42	100.0	$p>0.05$
<b>Economic status</b>							
Income over expenditure	45	67.2	22	32.8	67	100.0	
Income equivalent to expenses	180	83.3	36	16.7	216	100.0	$X^2=11.963$
Revenue less expense	46	90.2	5	9.8	51	100.0	<b>p&lt;0.05</b>

\* Fisher Chi-square

Table 2. The situations of physical abuse and neglect their children according to the characteristics of health workers

Characteristics	The Situation of Physical Abuse and Neglect						Test
	Present		Absent		Total		
	n	%	n	%	n	%	
<b>Number of children</b>							
1 and 2	227	80.2	56	19.8	283	100.0	$X^2=1.038$
3 and over	44	86.3	7	13.7	51	100.0	$p>0.05$
<b>Being of children with disabilities</b>							
Present	4	80.0	1	20.0	5	100.0	$X^2=.004^*$
Absent	267	81.2	62	18.8	329	100.0	<b>P&lt;0.05</b>
<b>Underwent to abuse and neglect in the childhood</b>							
Yes	41	93.2	3	6.8	44	100.0	$X^2=4.803^*$
No	230	79.3	60	54.7	290	100.0	<b>P&lt;0.05</b>
<b>Alcohol-making</b>							
Yes	25	86.2	4	13.8	29	100.0	$X^2=.533^*$
No	246	80.7	59	19.3	305	100.0	$p>0.05$

\*Fisher Chi-square

It was found that health workers who have three or more children (86.3 %), who do not have a disabled child (81.2 %), who were subjected to bad treatment in childhood by their parents (93.2 %) and who consume alcohol (86.2 %) abuse or neglect their children more frequently. Being subjected to bad treatment in childhood by parents was a statistically significant factor in child abuse and neglect among health workers ( $p < 0.05$ , Table 2).

Another finding of the study was that 75.1 % of the health workers emotionally abused or neglected their children. 28.4 % of the health workers did not express their feelings of love to their children, 65.6 % yelled at them, 24.5 % left them alone at home, 13.5 % intimidated their children, 18.3 % threatened, 18.9 % scolded, 4.8 % behaved as if there were no children at home, and 3.9 % locked their children in their rooms. It was also found that none

of the health workers tied the hands or the feet of their children. Health workers who are forty years of age (82.1%), who are female (77.5%), who have a master's degree (93.8 %), who are nurses (80.2 %), who have large families (90.5 %) and whose earnings are less than their expenses (80.4 %) more frequently engaged in behavior that was emotionally abusive or negligent. The age ( $p < 0.01$ ), level of education ( $p < 0.05$ ), occupation ( $p < 0.001$ ), family type ( $p < 0.05$ ) and economic status ( $p < 0.01$ ) of health workers were statistically significant factors in emotional abuse and neglect (Table 3).

Health workers who have three or more children (88.5 %), who have children with disabilities (100.0 %), who were subjected to bad treatment in childhood by their parents (90.9 %), and who do not consume alcohol (76.7 %) were found to engage in emotionally abusive and negligent beha-

Table 3. The situations of emotional abuse and neglect their children according to the characteristics of health workers

Characteristics	The Situation of Emotional Abuse and Neglect						Test
	Present		Absent		Total		
	n	%	n	%	n	%	
<b>Age</b> (34.70±6.94, years)							
20-29	51	60.0	34	40.0	85	100.0	
30-39	131	79.4	34	20.6	165	100.0	$X^2=14.238$
40 and over	69	82.1	15	17.9	84	100.0	<b><math>p &lt; 0.01</math></b>
<b>Gender</b>							
Female	176	77.5	51	22.5	227	100.0	$X^2=2.155^*$
Male	75	70.1	32	29.9	107	100.0	$p > 0.05$
<b>Education level</b>							
High school	89	81.7	20	18.3	109	100.0	
University	127	69.8	55	30.2	182	100.0	
Master	15	93.8	1	6.3	16	100.0	$X^2=8.258$
Doctorate	20	74.1	7	25.9	27	100.0	<b><math>p &lt; 0.05</math></b>
<b>Profession</b>							
Nursing	158	80.2	39	19.8	197	100.0	
Physician	26	51.0	25	49.0	51	100.0	
Technician	39	79.6	10	20.4	49	100.0	$X^2=19.170$
Other	28	75.7	9	24.3	37	100.0	<b><math>p &lt; 0.001</math></b>
<b>Family Type</b>							
Nuclear Family	213	72.9	79	27.1	292	100.0	$X^2=6.043^*$
Large Family	38	90.5	4	9.5	42	100.0	<b><math>p &lt; 0.05</math></b>
<b>Economic status</b>							
Income over expenditure	40	59.7	27	40.3	67	100.0	
Income equivalent to expenses	170	78.7	46	21.3	216	100.0	$X^2=10.773$
Revenue less expense	41	80.4	10	19.6	51	100.0	<b><math>p &lt; 0.01</math></b>

\*Fisher Chi-square

Table 4. The situations of emotional abuse and neglect their children according to the characteristics of health workers

Characteristics	The Situation of Emotional Abuse and Neglect						Test
	Present		Absent		Total		
	n	%	n	%	n	%	
<b>Number of children</b>							
1 and 2	206	72.8	77	27.2	283	100.0	X <sup>2</sup> =5.427
3 and over	45	88.5	6	11.8	51	100.0	p>0.05
<b>Being of children with disabilities</b>							
Present	5	100.0	-	-	5	100.0	X <sup>2</sup> =1.679*
Absent	246	74.8	83	25.2	329	100.0	p>0.05
<b>Underwent to abuse and neglect in the childhood</b>							
Yes	40	90.9	4	9.1	44	100.0	X <sup>2</sup> =6.739*
No	211	72.8	79	27.2	290	100.0	<b>p&lt;0.05</b>
<b>Alcohol-making</b>							
Yes	17	58.6	12	41.4	29	100.0	X <sup>2</sup> =4.646*
No	234	76.7	71	23.3	305	100.0	<b>p&lt;0.05</b>

\*Fisher Chi-square

avior more frequently. Being subjected to parents' bad treatment in childhood ( $p<0.01$ ) and avoiding alcohol consumption ( $p<0.05$ ) were statistically significant factors for emotional abuse and neglect among health workers.

## Discussion

This study examined child abuse and neglect among health workers and the factors leading to such behavior. The study is limited in that it focuses only on the physical and emotional dimensions of child abuse and neglect. The economic dimension of child abuse was left out with the expectation that the study group would not engage in this kind of abuse, and sexual abuse was left out because the study group is not expected to give accurate information on the subject. As the research was conducted with the participation of health workers from three hospitals, the results of the study can only be generalized for this group. The findings of the study were discussed with reference to the findings of similar studies on different groups, for the lack of similar studies on the same group.

The study found that 81.1% of health workers abused or neglected their children at least once (Table 1). In their study on mothers' physical and emotional abuse and neglect of their children, Güler et al

found that 87.4% of mothers physically abused or neglected their children at least once [1]. In Bulut's study on young mothers' abuse of children, it was found that 78% of mothers physically abused their children [7]. The findings of the present study thus parallel those of earlier studies. Another finding of the present study was that as the age of the health workers increased, the percentage of those engaging in physically abusive or negligent behavior significantly increased as well ( $p<0.05$ , Table 1). This finding parallels the results of Güler et al [1] and Bulut's [7] studies. Bilir et al, in their study on trauma among children, found that younger mothers abuse or neglect their children more frequently [16]. It is known that children of very young mothers are likely to be abused or neglected [17,18]. The present study also found that male health workers were more likely to engage in physically abusive or negligent behavior (Table 1). Males are identified as the group with the most frequent engagement in behavior that results in fatal head injuries and fractures, and other fatal injuries in children [19,20]. It has found that women are more likely to use physical disciplining methods compared to men [21]. Yet, another study has found that females display violent behavior towards their children more frequently than males [22]. Also among the findings of the present study is that health workers with a masters degree or a PhD are more likely to physically abuse or neglect their children

(Table 1). In other studies, mothers with lower levels of education were found to utilize abuse and neglect against children more frequently [1,6,17,18,23,24], and a lower level of education was found to increase the likelihood of applying physical violence against children [19,25-27,28]. It was found that health workers who live with large families physically abuse or neglect their children more frequently (Table 1). In previous studies, different conclusions were reached with regards to the association between family type and physical abuse or neglect towards children. Güler et al found that mothers in nuclear families engage in more physical abuse and neglect towards their children, but that the difference is not statistically significant [1]. In health literature, general findings parallel those of the present study, with violent behavior being more prevalent in large families [26,29,30]. Another finding of the study was that those who earn less than they spend abuse or neglect their children more frequently, with a very high level of statistical significance ( $p < 0.005$ , Table 1). Other findings in health literature that parallel this one cite financial problems at home as causing the neglect and insufficient satisfaction of a child's emotional and physical needs [7], as well as the fact that families with low economic status levels will engage in physically abusive and negligent behavior towards their children more frequently [1,18,23,31,32]. They also cite low income as a factor for increasing the likelihood of physical violence against children [19,25-28].

The present study found that health workers with three or more children abuse or neglect their children more frequently (Table 2). Previous studies have found that a large majority of mothers who have too many children to look after physically abuse or neglect their children, and that families with four children or more use more violence against children, compared to families with less children [1,17,18,23,33]. Health workers who do not have children with disabilities physically abused or neglected their children more frequently (Table 2). However, previous studies suggest that children with disabilities are at a greater risk of being abused [17,18,23,33]. The inconsistency within the findings of earlier studies may have resulted from the fact there were very few health workers in our sample who had children with disabilities. Health workers who were subjected to bad treatment in childhood

by their parents were significantly more likely to engage in abusive or negligent behavior ( $p < 0.05$ , Table 2). This parallels the findings of earlier studies which found that parents who were abused or neglected are more inclined to engage in such behavior themselves [17-19,23,33,34]. It was found that health workers who consume alcohol physically abuse or neglect their children more frequently (Table 2). Previous studies report that alcohol consumption is a factor leading to physical abuse and neglect towards children [6,35]. One study claims that almost all mothers whose spouses consume alcohol physically abuse or neglect their children but that the difference is not statistically significant [1]. Children of parents who consume alcohol are reported to be at risk of being abused or neglected [17,18,23].

The study also found that 75.1% of health workers engaged in emotionally abusive or negligent behavior (Table 3). In another study, the percentage of mothers who emotionally abuse or neglect their children was found to be 93% [1]. 90% of physical abuse and neglect cases involve emotional abuse and neglect as well [36]. One finding of the present study was that health workers who are forty years of age or older, female, nurses, have master's degrees, have large families, and earn less than they spend engage in emotionally abusive or negligent behavior more frequently. Age ( $p < 0.01$ ), level of education ( $p < 0.05$ ), occupation ( $p < 0.001$ ), family type ( $p < 0.05$ ), and economic status ( $p < 0.01$ ) were found to be significantly associated with emotional abuse and neglect (Table 4). Health workers who have three children or more, who have children with disabilities, who were subjected to bad treatment in childhood by their parents, and who do not consume alcohol emotionally abuse or neglect their children more frequently. Being subjected to bad treatment in childhood by parents ( $p < 0.01$ ) and avoiding alcohol consumption ( $p < 0.05$ ) were found to be factors that have a statistically significant relationship to emotional abuse and neglect among health workers (Table 4). When we consider the findings of the study as a whole, we can see that both physical and emotional abuse and neglect are similarly associated with age, level of education, family type, economic status, number of children, and being subjected to bad treatment in childhood by

parents. Health literature also has it that the factors leading to physical and emotional abuse and neglect by mothers towards their children are similar [9,24], that emotional abuse and neglect may be observed in cases where physical abuse and neglect is not present, and that emotional abuse and neglect are the most prevalent types of abuse and neglect that children face [37].

### Conclusion and recommendations

The present study in Turkey showed that health workers abused and neglected their children. It is a worrying situation that health workers are risk group for child abuse and neglect. Therefore, the health workers should be scanned as regards abuse and neglect of the children; the risky situations should be determined for health workers; professional support should be provided for health workers who underwent to abuse and neglect in the childhood, and abused and neglected their children; some training programmes should be held about the cause, effect and prevention of children abuse and neglect; these programmes should be repeated regularly; results of the study should be announced health workers in the hospitals that the study is carried out; and similar studies should be carried out in different countries.

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### Ethical approval

It was received permission from the hospital administrations for the study. numaralı etik kurul kararı ile araştırmaya başlanmıştır. The study started with ethics committee approval date 24. 12. 2008 and number "2008.5.1/L". One of the researchers contacted all of the health staff, and written informed consent was obtained from each participant after the purpose and nature of the study had been fully explained.

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# Rapid assessment of community awareness, attitude and acceptance about voluntary HIV counseling and testing for rural-to-urban migrants in Shanghai, China

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## Abstract

**Objectives:** To quickly understand rural-to-urban migrants' knowledge and acceptance of voluntary counseling and testing (VCT) for HIV/AIDS and community attitudes to providing VCT service to migrants in Shanghai, China.

**Study design:** A rapid assessment consisting of in-depth interviews and focus group discussions was conducted.

**Methods:** A total of 101 in-depth individual interviews and four focus group discussions were administered in 2008. The interviews were audiotaped or taken note and then transcribed. Collected data were analysed according four impact domains on VCT uptake among rural-to-urban migrants: knowledge of HIV/AIDS and VCT (Impact domain I), self-perceived risk of HIV infection (Impact domain II), accessibility and confidentiality of VCT service (Impact domain III), and social environment (Impact domain IV).

**Results:** Current barriers to getting VCT among rural-to-urban migrants included misconceptions about HIV/AIDS, limited to no knowledge about VCT, extremely low self-perception of HIV risks, limited accessibility of VCT service for rural migrants, worrying about disclosure of HIV infection status, and community leaders' or stakeholders' negative attitudes to rural migrants living with HIV and even those attending VCT.

**Conclusions:** It indicates that much greater effort is needed to remove barriers to accessing

VCT for rural-to-urban migrants. Community mobilizations, mass media programs to improve HIV/AIDS and VCT knowledge and awareness, and anti-stigma associated with taking VCT or HIV infection are among the priorities.

**Key words:** VCT, HIV, rapid assessment, rural-to-urban migrants, community

## Introduction

As an effective strategy for changing behavior and preventing sexually transmitted diseases,<sup>1-3</sup> HIV voluntary counseling and testing (VCT) has been one key component of the National "Four Frees and One Care" policy for HIV/AIDS prevention and control in China since 2003. More than 4000 VCT clinics have been established all over the country.<sup>4</sup> However, among 700,000 people living HIV in China, the majority were still not identified.<sup>4</sup> This underscores the urgent need for increasing acceptance and utilization of HIV testing especially VCT. Such need is extremely obvious for rural-to-urban migrants as they have played important roles in HIV transmission in China,<sup>5-8</sup> On the other hand, Migrants are in danger of being marginalized and have no entitlement to urban health cares and services accorded to most urban dwellers due to their non-urban residence.<sup>9</sup>

Shanghai is the most developed city in China and has about 5 million rural-to-urban migrants. By the end of 2007, 3,010 HIV/AIDS cases had been re-

ported, 70% of them were migrants (Shanghai CDC HIV/STDs surveillance Data, 2007), indicating that migrants play a critical role in the HIV epidemic in Shanghai. However, very few migrants have ever received HIV testing and counseling. Both individual- and community-level determinants for the low uptake of VCT service by rural migrants need to be identified, which will be very useful for developing effective programs to improve the uptake of VCT service among rural migrants. Therefore, here we reported a rapid assessment of migrants' and community awareness, attitude and acceptance about VCT for rural migrants in Shanghai, China. A rural migrant was defined for this study as someone born and registered as a permanent resident in a rural area but who worked in Shanghai.

## Methods

### *Study site and participants*

This study was conducted in Shanghai in the spring of 2008. All study participants were 18 years old or above and were recruited from four categories: (1) 74 rural migrants employed in construction sites, vegetable/grocery markets, factories, community service sectors and entertainment establishments; (2) 27 employers and supervisors of rural migrants; (3) 15 community government officials from the departments of family planning, public safety (i.e., police department), women's federation and administration of migrant affairs; and (4) 8 community health care providers. Rural migrants and their employers and supervisors were recruited through community volunteers working with rural migrants in areas known to have large migrant populations. Government officials and health care providers in the same areas were directly approached and invited by researchers to participate in this study. All participants received cash incentives for participating and travel expense reimbursements.

### *Data Collection*

This study consists of two parts: (1) in-depth individual interviews to rural migrants and their

employers or supervisors; and (2) focus group discussions among community government officials and health care providers. A total of 101 in-depth individual interviews were administered: 74 migrants and 27 employers or supervisors. Interviewees were asked whether they were willing to be audio-taped, but very few agreed. For those who explicitly refused to be audio-taped, field notes (recorded as verbatim as possible) were taken by two independent note takers. Each interview lasted for approximately a half hour and took place in a private place. A total of four focus group discussions were held and audio-taped: three for government officials and one for health care providers. Each discussion had five to eight participants, lasted for 60-90 minutes, took place in a closed meeting room, and held in a non-evaluative environment. Epidemiologists with qualitative research experience were invited to conduct focus group discussion in this study.

Five broad categories with closed- and open-ended questions were used to guide in-depth interviews and group discussions: (1) sociodemographic characteristics, (2) knowledge about HIV/AIDS and VCT, (3) attitude towards people living with HIV/AIDS (PLWHA) and those seeking HIV counseling and/or testing, (4) HIV risks among rural migrants, and (5) acceptance of and access to VCT among rural migrants. Specific terms such as VCT were explained in a plain language to help participants to understand.

### *Data management and analysis*

The tapes and/or notes of in-depth interviews and focus group discussions were first compiled and transcribed into word transcripts. The transcripts were read and coded independently by two researchers with qualitative research experiences. Quote excerpts and summaries were then categorized by participant characteristics and the coding domains; they were further reviewed and discussed within the research team until a consensus reached.

A conceptual model was generated from the data disclosing four impact domains on VCT uptake among rural-to-urban migrants (Fig.1): (I) knowledge of HIV/AIDS and VCT, (II) self-perceived risk of HIV infection, (III) accessibility



and confidential of VCT service, and (IV) social environment. Therefore, the study results are presented according to these four domains.

## Results

### Sociodemographic characteristics of the participants

Table 1 presents the sociodemographic characteristics of the study participants. Rural migrants were younger and less educated than other participants. They also had a broad range of occupations and more than two-thirds of them were married. Nearly one half of the employers and supervisors of rural migrants and all local government officials and health care providers were permanent residents of Shanghai.

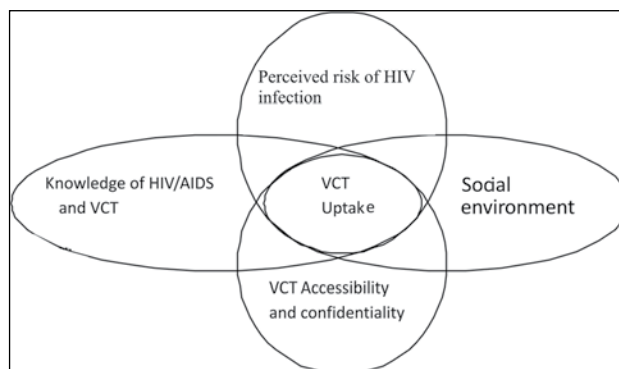


Figure 1. VCT uptake and four impact domains among rural-to-urban migrants

Impact domain I: Knowledge of HIV/AIDS and VCT among Rural Migrants.

Impact domain II: Perceived risk of HIV infection among rural migrants.

Impact domain III: Accessibility and Confidentiality of VCT for rural migrants

Impact domain IV: Social Environment about HIV/AIDS & VCT.

Table 1. Socio-demographic characteristics of study participants

	Rural migrants No. (%)	Employers/ supervisors No. (%)	Government officials No. (%)	Health care providers No. (%)
Gender				
Male	38 (51.4)	16 (59.3)	6 (40.0)	2 (25.0)
Female	36 (48.6)	11 (40.7)	9 (60.0)	6 (75.0)
Age (years)				
18-20	5 (6.8)	0	0	0
21-30	35 (47.3)	9 (33.3)	2 (13.3)	1 (12.5)
31-40	30 (40.5)	6 (22.2)	7 (46.7)	6 (75.0)
41-	4 (5.4)	12 (44.5)	6 (40.0)	1 (12.5)
Education				
Illiterate or primary school	12 (16.3)	1 (3.8)	0	0
Middle school	38 (51.4)	10 (37.0)	4 (26.7)	0
High school	21 (28.4)	13 (48.1)	7 (46.7)	3 (37.5)
College	3 (4.0)	3 (11.1)	4 (26.7)	5 (62.5)
Marital status				
Married	51 (68.9)	5 (18.5)	13 (86.7)	6 (75.0)
Unmarried	23 (31.1)	22 (81.5)	2 (13.3)	2 (25.0)
Working site				
Factory	15 (20.3)	6 (22.2)	---	---
Market	15 (20.3)	5 (18.5)	---	---
Community service	15 (20.3)	5 (18.5)	---	---
Entertainment establishment	15 (20.3)	6 (22.2)	---	---
Construction sites	14 (18.9)	5 (18.5)	---	---
Permanent residence				
Shanghai	0	13 (48.2)	15 (100.0)	8 (100.0)
Other provinces	74 (100.0)	14 (51.8)	0	0

## **Impact domain I: Knowledge of HIV/AIDS and VCT among Rural Migrants**

### ***Knowledge of HIV/AIDS***

All rural migrants participating in this study had heard of HIV/AIDS and most of them realized that HIV/AIDS was an infectious disease, incurable, very serious, and only detectable by a blood test. They were knowledgeable of sexual and blood transmission of HIV but not well aware of mother-to-child transmission of HIV. About 30% of rural migrants thought that other irrelevant routes could transmit HIV, and HIV-infected individuals should look differently from others (data not shown).

Rural migrants rarely used condoms especially while having sex with their spouse or a regular sex partner, or they used condoms primarily for contraception. Although a few female sex workers acknowledged that condom use could prevent HIV infection, they did not use condoms if their male clients insisted on no condom use or paid more for no condom use.

'For safety, I have used condoms every time when I was working, but I did not use it when I had sex with my boy friend' (A 25 year old female sex worker)

'Mostly, we used condoms .... But if he (client) refuses to use this (condom) and would like to pay more money, we will check his body and smell its odors, disinfect (the penis) with alcohol and then make sex without condom' (A 31 year old female sex worker)

### ***Knowledge of VCT***

Most of participating migrants had never heard of VCT for HIV. Even among those having heard of VCT, many didn't know where to go for a VCT service. None of the study participants could describe the concept and procedures of VCT.

*'I have never heard of free HIV testing service (VCT).'* (A 35 years old female migrants working for community service)

*'I don't know VCT. I came from a rural area. I could say nothing about these things.'* (A 34 years old female market vendor)

*'I have heard of free testing of HIV, but I don't know the detail of VCT or where to go for this.'* (A 30 years old male market vendor)

## **Impact domain II: Perceived risk of HIV infection among rural migrants**

Most participating migrants thought that they were unlikely to get infected with HIV. Three participants had previously received HIV testing but none of them took the HIV testing at a VCT site. The main reason for not taking VCT was self-perception of no risk of HIV infection.

*'Generally, I would not get infected, although I am taking this kind of job (sex work), I will protect myself very well, and so I would not get infected with HIV/AIDS.'* (A 23 years old female sex worker)

*'I won't get infected, so I don't care about this (VCT).'* (A 34 years old female sex worker)

*'I would never be infected with HIV; I feel AIDS is very far away from us. Furthermore, there was nobody around who was infected with HIV/AIDS.'* (A 30 years old male market vendor)

Three (7.8%) out of 38 participating male rural migrants reported that they had purchased commercial sex and not often used condoms because they did not think the prostitutes could be HIV positive.

*'I didn't use condoms while having sex with prostitutes because they looked very healthy. Although AIDS is terrible, nobody was infected'* (A 32 years old male construction worker)

## **Impact domain III: Accessibility and Confidentiality of VCT for rural migrants**

Many migrants stated that convenience was a key point for accessibility of VCT service.

*'It may be too far to get a VCT service. Should I spend so much time going for VCT? I think it is unnecessary to do this'* (A 26 years old male market vendor)

*'It is not convenient to take an HIV test. I do not have time to go to a hospital or a VCT clinic because I am very busy'* (A 28 years old male construction worker)

Confidentiality was another important concern among rural migrants for taking VCT. Rural migrants believed that health care providers would disclose their VCT behavior and HIV testing results to others especially their employers despite assurances of confidentiality by health care providers.

*'...But because it (VCT) is a policy of government, it must be open but not confidential service.'* (A 35 years old male construction worker)

*'If the doctors tell my test results or my visiting to the VCT site to my friends, they would look down upon me.'* (A 32 years old male market vendors)

*'If it is possible, I will go to the VCT site to do HIV test, but I am afraid that I would probably encounter acquaintances. They will think I have AIDS'* (A 22 years old female sex worker)

#### **Impact domain IV: Social Environment for HIV/AIDS & VCT**

##### ***Migrants' attitudes towards VCT and PLWHA***

Most rural migrants held negative attitudes or stigma to those taking VCT and PLWHA. They would associate the behavior of visiting VCT with a disgraceful behavior such as visiting a prostitute, doing something immoral, or simply being HIV-infected. They also didn't want to work with an HIV-infected individual.

*'Only riff-raffs would go for VCT, a good man would not go there to do VCT.'* (A 37 years old male migrant working for community service)

*'If I found someone here did HIV test, I would keep away from him and protect myself from being transmitted.'* (A 35 years old male market vendor)

*'If someone had accepted VCT, he must have done something wrong outside his family.'* (A 23 years old male construction worker)

*'If it is possible, I will never talk to an HIV-infected individual. If I have to chat with him, I will keep my face away from him, and won't use things that he has touched.'* (A 34 years old female factory worker)

*'If I know who is infected with HIV/AIDS, I would be reluctant to work with him. Because HIV/AIDS is transmissible, I would get worrisome, even if I had taken precautions measures'* (A 26 years old male construction worker)

#### **Employers' and supervisors' attitudes towards VCT and PLWHA among rural migrants**

Employers and supervisors of rural migrants thought that their employees were unlikely to get HIV infected and it was unnecessary for their employees to get VCT or to test for HIV even if the service was free.

*'It is absolutely impossible for my employees to get HIV/AIDS, because they have been very careful and have paid attentions to prevention of the disease. They can protect themselves.'* (A 30 years old female employer of commercial sex workers)

*'All of our migrant employees have sanitary inspection certificate or health certificate (which did not test HIV), they could not be infected with HIV'* (A 56 years old male market supervisor)

*'I think it is impossible that our workers could get infected with HIV. I trust them. I think they have no problems, so it is unnecessary to get the VCT service'* (A 47 years old female construction administrator).

However, almost all participating employers and supervisors refused to accept an HIV-infected rural migrant to work in their venues. They also had negative attitudes to those having taken VCT even if the testing results were negative.

*'If he was HIV positive, he could no longer work in my factory, because I think it would be a threaten to others.'* (A 37 years old male factory administrator)

*'If we found that he was HIV-infected, he must be isolated; we would turn to related government office to take him away. He could not work here anyway. It would have a very bad impact here.'* (A 58 years male construction work administrator)

*'If someone had taken VCT, he must have done something ignominious. If not, why did he go for VCT?'* (A 62 years old female factory administrator)

#### **Government officials' attitudes towards VCT and PLWHA among rural migrants**

Most government officials held supportive attitudes towards VCT for rural migrants. They believed that some rural migrants were engaging in risky behaviors of HIV and thus, the VCT service

for HIV targeting on rural migrants was very useful. Nevertheless, government officials displayed discrimination against PLWHA.

*'When a rural migrant wants to stay and work here, he needs residence permission. But if he is an HIV carrier, we can't give him residence permission' (A 45 year old male official)*

*'If we know this (a positive HIV result), we will trace him, and notify his hometown, and ask them to take him back.' (A 38 year old female official)*

### **Health care providers' attitudes towards VCT and PLWHA among rural migrants**

Participating health care providers reported that very few rural migrants had come to take VCT. They thought that VCT should be provided to rural migrants only if a long-term and sustainable antiretroviral therapy is available which serves as a benefit to taking VCT.

*'...and what will happen to them afterwards, if they are tested positive for HIV? Could they get antiretroviral therapy, or could they work in his work place any more?' (A 31 years old female health care worker)*

### **Discussion**

VCT has proved to be a major preventive strategy in the fight against HIV/AIDS.<sup>2-3</sup> From view of public health, It is important to assess the level of VCT-related knowledge, attitude, and acceptance among rural to urban migrants in China. The rapid assessment procedure is a practical public health tool. It has been used in the implementation of public health intervention programs as well as HIV/AIDS prevention, where it is necessary to make informed decisions quickly.<sup>10-12</sup> In the present study we used qualitative methodology to rapidly assess migrants' and community's awareness of, attitudes to and acceptance of VCT for rural-to-urban migrants in Shanghai. To our knowledge, this is the first study to use a rapid assessment methodology to assess HIV/AIDS-related health service for rural-to-urban migrants in China. The knowledge gained from this study is valuable for developing community-based HIV/

AIDS intervention programs tailored for rural-to-urban migrants.

The present study indicates that very few rural-to-urban migrants had ever heard of VCT. Such a low awareness of existing VCT service highlights the urgent need for more mass media programs introducing concepts, procedures and availability of VCT in China. Meanwhile, almost none of the study participants including those having engaged in HIV-related risky behaviors had taken VCT before. The low practice of VCT uptake was probably due to the extremely low awareness of HIV risks observed among migrants participating in this study. Studies in other countries do indicate that risk awareness is the main determinant of readiness for VCT<sup>13-15</sup>. Moreover, limited accessibility was another important barrier to taking VCT among rural-to-urban migrants. This observation is in agreement with studies conducted among residents in rural counties of Guizhou province in Southwest China.<sup>16-17</sup> It might be impractical and not cost-effective to increase the accessibility of VCT service by simply building up new VCT clinics or sites in a community. Instead, it is important and would be sustainable to integrate VCT service with other community health services and non-government organizational activities.<sup>18-19</sup>

For community-based HIV/AIDS programs to be implemented successfully they must be accepted and supported by community leaders or stakeholders.<sup>20-22</sup> This is particularly true for rural-to-urban migrants residing and working in urban areas. The negative attitudes towards migrant's HIV infection status and/or VCT behaviors among employers and supervisors of rural migrants, government officials and health care providers participating in this study underscores the importance of motivating community stakeholders to accept VCT for rural migrants, to remove stigma to HIV/AIDS, and to create a supportive community or environment for HIV/AIDS prevention and control especially targeting rural migrants.

In conclusion, findings from this study have important implications for developing intervention programs targeting rural-to-urban migrants in Shanghai as well as other metropolitan areas in China. First, a much greater effort is needed to improve HIV/AIDS and VCT knowledge and awareness of HIV risks.<sup>23</sup> Second, it is important to

integrate voluntary HIV counseling and/or testing with routine community services and activities so that VCT is sustainable, accessible and more acceptable for rural migrants. Third, urban communities must be mobilized to remove barriers to accessing VCT for rural migrants.

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# Psychosocial adjustment and affecting factors in Turkish patients with cancer

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## Abstract

**Aim:** this study aimed to determine the psychosocial adjustment and affecting factors in cancer patients. The results of this study can be used in planning psychosocial support programs to increase the psychosocial adjustment levels of the cancer patients.

**Methods** This study included 105 patients with cancer who presented to the outpatient unit of a medical oncology clinic to receive outpatient chemotherapy between December 2005 and February 2006. A two part survey was used to collect the data. The questionnaires included a demographic questionnaire and the Turkish version of the Psychosocial Adjustment to Illness Scale-Self-Report-PAIS-SR

**Results:** The findings obtained from the study were analysed, the PAIS-SR total point average was found to be  $57.1 \pm 14.8$ . When the points that patients receive from PAIS-SR were evaluated in terms of psychosocial adjustment, it was determined that the psychosocial adjustment levels of 64.8% of the patients were “poor”, 28.6% were “medium”, and 5.7% were “good”. This study is the knowledge level of the cancer patients regarding their diseases is the most important variable that affects psychosocial adjustment.

**Conclusion:** The research results showed that the psychosocial adjustments of the cancer patients were poor, and the psychological adjustments, especially regarding the professional and social life dimensions, were affected more.

**Key word:** cancer, psychosocial adjustment, nursing

## Introduction

Cancer is a life threatening illness that can challenge the experience of life. A diagnosis of cancer is a stressful event and may result in a wide range of physical, psychological, and social effects that may influence a patient's needs ( Landmark et al., 2001; Farrell et al., 2005; Çam et al., 2009). The physical and mental problems, problems about family and business life, uncertainties about the future, and social and moral problems that arise with cancer and its treatments negatively affect the moral state of the patients with cancer and their psychosocial adjustment to the disease. The affecting factors in psychosocial adjustment to the disease are determined as personality structure, sociocultural characteristics, psychosocial stressors, tendencies of the disease, negative feelings about the disease (like seeing the disease's negative aspects such as a loss or a threat), coping methods, past experiences, lifestyle, and hereditary characteristics (Spiegel, 1997; Brennan, 2001; Kocaman et al., 2007; Çam & Babacan Gümüş, 2009).

Psychological and social adjustment (psychosocial adjustment) is an important factor in evaluating a patient's psychosocial status. For cancer patients, psychosocial adjustment involves making life adjustments to adapt to these altered roles and mental changes resulting from the experience of cancer. Poor adjustment has negative effects on the patient's physiological and social status (Northouse et al. 1995; Brennan, 2001; Kocaman et al. 2007; Adaylar, 1995; Armstrong, 1996; Tan & Karabulutlu, 2005; Erci & Karabulut, 2007 Çam & Babacan Gümüş, 2009). Previous studies have

indicated that patients with poor psychosocial adjustment are at a high risk of developing depression or anxiety (Ateşci et al., 2003; Bahar, 2007). When other studies about the subject in Turkey were analysed, it was found that the psychosocial adjustment of 33% of the patients with breast cancer was at the “poor” level of acceptance, 40.7% were at the “medium” level, and 26.3% at the “good” level (Babacan Gümüş, 2007). And in another study conducted to analyse emotion support oriented nursing initiatives and their effect on psychosocial adjustment in patients whose disease was diagnosed as breast cancer, it was determined that the psychosocial adjustment of all the patients before emotional support oriented nursing initiatives was “poor”, and after these types of initiatives their psychosocial adjustment levels rose (Çam et al., 2009).

The term “Adjustment Deficiency” is present in the nursing diagnosis of the North American Diagnosis Association (NANDA) and is described as the situation in which the patient is unable to change his lifestyle and his behaviors to suit his present medical condition (Carpenito, 1997). Understanding adjustment is also a central concern of nurses working with people with cancer. Because of this, understanding the patients, evaluating how the patients adapt to the disease psychosocially, and facilitating their adjustment to the present situation are of great importance (Northouse et al., 1995; Northouse et al., 2001; Kocaman et al., 2007). The fact that cancer creates a wide range of problems in patients, treatment and care should be handled with versatile approaches. Because of this, all health professionals, and especially the nurses who are in more close contact with patients, should approach cancer patients with a holistic approach, evaluate their psychosocial adjustments inclusively, and plan and apply support initiatives within the scope of this information (Çam et al., 2009).

In Turkey, researches that analyse psychosocial adjustment in general cancer patients do not appear to have been conducted. So, this study will be a guide in evaluating the psychosocial adjustment and affecting factors in general cancer patients.

## Materials and methods

This study included 105 patients with cancer who presented to the outpatient unit of a medical oncology clinic to receive outpatient chemotherapy between December 2005 and February 2006. The study was conducted in a large hospital in Eastern Turkey and almost all the patients with cancer in this region, particularly those living in the vicinity of Erzurum, received cancer treatment in that hospital.

## Sample

The study design involved cross-sectional and descriptive analyses. The inclusion criteria were:

1. Awareness of the illness.
2. No known psychiatric or neurological disorders that would interfere with the completion of the measurements.
3. Stages I–III (i.e. a prediction of at least 6 months to live and not in the terminal phase of the disease).
4. Receiving curative chemotherapy.
5. Able to read the Turkish language.

Of the 137 patients who met the inclusion criteria, 13 patients refused to participate and 19 patients did not complete all the questionnaires. Thus, only 105 cases (75% participation rate) were used for the final data analysis.

## Procedure and data collection

A two part survey was used to collect the data. The questionnaires included a demographic questionnaire and the Turkish version of the Psychosocial Adjustment to Illness Scale-Self-Report-PAIS-SR (Adaylar, 1995).

## Questionnaire Form

The demographic questionnaire obtained information on the age, education, sex, marital status, employment, and income of the patients. Medical information on the duration of treatment, frequency of treatment, stage of cancer, and type of cancer was obtained from the patients’ medical records.



## Psychosocial Adjustment to Illness Scale-Self-Report (PAIS-SR)

This is a multi-dimensional scale that was developed by Derogatis and Lopez in 1983 to evaluate psychosocial adjustment to the disease (27). PAIS-SR measures the interaction of individuals with other individuals and institutions that compose the sociocultural environment. Scale is composed of 46 articles. The questions in the scale are divided into 7 fields of psychological adjustment to the disease. These 7 fields compose the sub-scales of the scale. The sub-scales are as follows.

1. Adjustment to Health Care (8 articles)
2. Professional Environment (6 articles)
3. Family Environment (8 articles)
4. Sexual Relations (6 articles)
5. Large Family Relations (5 articles)
6. Social Environment (6 articles)
7. Psychological Pressure (7 articles) (23, 27)

For each question in the scale, four descriptive expressions that determine the changing levels of adjustment are used. The subject can select the answer that best, and most closely, describes his/her personal experience. By giving points ranging between 0 and 3 to the articles in the scale, the answers are converted into numerical values. For each article in the scale, the large negative changes since the disease occurred are valued with 3 points and no change or positive changes are valued with 0 points. In the PAIS-SR scale, the low points indicate "good psychological adjustment" to the disease and high points indicate "poor psychological adjustment". In PAIS-SR, points lower than 35 mean a "good psychological adjustment", points between 35 and 41 mean a "medium psychological adjustment", and points over 51 mean a "poor psychological adjustment" (Adaylar, 1995; Derogatis, 1986). PAIS-SR was adapted for use in Turkey, and its validity and reliability were tested by Adaylar (1995). In this study, the internal consistency of the scale in patient samples with acute and chronic physical diseases is introduced as 0.94. In this study, the general psychosocial adjustment internal consistency coefficient of the scale was found as 0.87.

## Procedure

Each patient was contacted by a research assistant and provided with a detailed explanation of the aim and conduct of the study. The questionnaire was given to the patients in a separate quiet room of the oncology clinic. The patients were provided with questionnaires before a chemotherapy session that they filled out by themselves. If the patients were unable to complete the questionnaire on their own, the researcher read the questionnaire items to the patient and recorded the answers. The questionnaires took 20-30 mins to complete.

## Ethics

The researchers obtained an approval from the medical oncology department of Yakutiye Hospital, Atatürk University, and informed consent was obtained from each patient. The aim of the research was explained to the patients and they were informed that if they preferred not to continue, they could withdraw from the study any time they wished. After these explanations, 105 patients consented to participate in the study voluntarily.

## Data analysis

Statistical analyses were performed using the Statistical Package Version 11.5. In the evaluation of the data, percentages, T tests, the Kruskal-Wallis test, posthoc advanced analysis and the internal coherence test were used. A *P* value of less than .05 was adopted as the significance level in all of the statistical analyses.

## Results

The socio-demographic and medical characteristics of the patients are summarized in Table 1. It is observed that 48.6% of the subjects are female, 78.1% are married, 30.6% are primary school graduates, 50.5% perceived his/her economical status as an average amount, and 44.8% had partially sufficient information on their illne-

ss. The average age of the patients was  $48.5 \pm 14.3$ , the average duration of the illness was  $17.0 \pm 15.2$  (months). Patients had been diagnosed with various types of cancer. Frequently reported diagnoses included gastrointestinal cancer (34.3%), respiratory cancer (23.8 %), breast cancer (21 %), and other cancers (21%).

Table 1. Characteristics of Patients

Characteristics	N	%
<b>Sex</b>		
Female	51	48.6
Male	54	51.4
<b>Marital Status</b>		
Married	82	78.1
Single	23	21.9
<b>Age (average)</b>	48.5±14.3	
<b>Education</b>		
Elementary school education	50	47.6
Secondary school	43	41.0
High school	12	11.4
<b>Economic Status</b>		
High	22	21.0
Average	53	50.5
Low	30	44.4
<b>Duration of treatment</b>		
6–12 months	47	44.7
12–24 months	27	25.7
≥24 months	31	29.6
<b>Type of cancer</b>		
Respiratory	25	23.8
Breast	22	21.0
Gastrointestinal	36	34.3
Other	22	21.0
<b>Stage of cancer</b>		
I	25	23.8
II	54	51.4
III	26	24.7
<b>Information on the Illness</b>		
Sufficient	26	24.8
Partially Insufficient	47	44.8
Insufficient	32	30.5

When the PAIS-SR sub-scale point averages of the patients that participated were analysed, the social care adjustment point average was determined as  $9.1 \pm 3.7$ , the professional environment point average as  $12.6 \pm 3.0$ , family environment point average as  $7.1 \pm 3.9$ , sexual relation point average as  $7.2 \pm 4.8$ , large family relations point average as  $6.8 \pm 4.8$ , social environment point average as  $10.8 \pm 4.2$ , and the psychological pressure point average was determined as  $7.3 \pm 4.1$ . And the ge-

neral psychosocial adjustment average of the patients was found to be  $57.1 \pm 14.8$ . When the points that the patients receive from PAIS-SR were evaluated in terms of psychosocial adjustment, it was determined that the psychosocial adjustments of 64.8% of the patients were “poor”, 28.6% were “medium”, and 5.7% were “good”.

Table 3. Psychosocial Adjustment scores regarding in relation to demographic and medical characteristics

Characteristics	N	Total Psychosocial Adjustment Mean ± SD
<b>Sex</b>		57.7±13.1
Female	51	56.5±16.4
Male	54	t = 0.670; P = 0.388
<b>Marital Status</b>		57.5±15.7
Married	82	55.5±11.1
Single	23	t = 0.566; P = 0.105
<b>Education level</b>		56.9±15.0
Elementary school	50	55.5±12.7
Secondary school	43	63.4±20.2
High school	12	F = 0.960; P = 0.415
<b>Economic Status</b>		61.1±16.2
High	22	57.1±11.9
Average	53	52.8±18.6
Low	30	F = 1.549; P = 0.217
<b>Duration of treatment</b>		52.3±15.0
6–12 months	47	49.5±12.7
12–24 months	27	51.8±20.2
≥24 months	31	F = 1.214; P = 0.348
<b>Information on the Illness</b>		48.1±13.1
Sufficient	26	58.1±11.7
Partially Insufficient	47	62.8±17.1
Insufficient	32	F = 8.164; P = 0.001
<b>Type of Cancer</b>		62.0±11.0
Respiratory	25	52.6±15.1
Breast	22	57.8±12.4
Gastrointestinal	36	54.9±20.3
Others	22	F = 0.947; P = 0.421
<b>Stage of cancer</b>		54.1± 16.2
I	25	57.3 ± 11.9
II	54	56.8± 18.6
III	26	F = 1.129; P = 0.326

The level of information patients had on their illness created statistically significant differences on their psychosocial adjustment. The patients with insufficient knowledge on their illness had a psychosocial adjustment mean of  $62.8 \pm 17.1$  and it was observed that the adjustment level among these patients was poor ( $p < 0.01$ ). In the conducted advanced analyses, it was determined that the statistical difference resulted from groups that receive adequate information and those that did not.

It was determined that variables about demographics and disease did not create a significant difference on the sub-scale point averages in terms of statistics (data not shown).

## Discussion

When the findings obtained from the study were analysed, the PAIS-SR total point average was found to be  $57.1 \pm 14.8$ . When the points that patients receive from PAIS-SR were evaluated in terms of psychosocial adjustment, it was determined that the psychosocial adjustment levels of 64.8% of the patients were “poor”, 28.6% were “medium”, and 5.7% were “good”. In the studies conducted with breast cancer patients in Turkey, the psychological adjustments of the patients were generally stated as “poor” (Çam et al., 2009; Babacan Gümüş, 2007). The results of the conducted studies were similar to the results of this study. When these results were considered, it was seen that the psychosocial adjustment levels of the Turkish cancer patients were poor, and there is a need to take some action regarding this issue.

It was also clear that the sub-dimensions of the psychosocial adjustments of the patients who participated to the study which were most affected were professional environment and social environment, and it was also found that the psychological adjustments in these fields are worse than in other sub-dimensions. This result shows that the cancer causes negative results, especially in the professional and social lives of the patients. Similar to the results of the study, the other conducted studies also indicated that cancer negatively affects professional and social lives (Çam et al., 2009; Babacan Gümüş 2007) The intense and long-term treatments for cancer and the severe

side effects of these treatments cause a decrease in the working skills of patients and a decrease in their performance. Also, a long treatment period can mostly prevent the patients finding the energy required to continue their social relations. For this reason, it has been considered that the psychosocial adjustment levels of patients in terms of their professional and social fields are worse.

In conclusion, it was seen that the psychosocial adjustment dimension that was least affected in cancer patients was large family relations. The researches conducted on cancer patients in Turkey revealed the fact that the highest level of support comes from family and close relatives (Özyurt, 2007; Tan & Karabulutlu 2005; Özbek et al., 2003). A general characteristic of Turkish family structures is the increased closeness of family relations during hard conditions such as illnesses or loss, especially in the Eastern Anatolia region where this study was conducted, where this characteristic is more widely seen. It can be stated from the results that the least affected field is large family relations, which may be a result of cultural characteristics. In the studies conducted in other cultures, psychosocial adjustment was valued as poorer in terms of large family relations (Herranz & Gavillan, 1999; Ramirez et al., 2003). In line with these results, it can be stated that cultural characteristics are affective in psychosocial adjustment.

The demographical variables of patients did not create a significant difference on the total psychosocial adjustment and its sub-dimensions in terms of statistics. In other studies, psychosocial adjustment was not affected to any great degree by age, sex, marital status and economical status (Courts & Beyonce, 1998; Adaylar, 1995; Butler et al., 2006; Kocaman et al., 2007).

The knowledge level variables do affect total psychosocial adjustment. It can be seen that the psychosocial adjustments of patients who stated that they did not have sufficient knowledge about their diseases and treatment periods were worse. And in different studies conducted in Turkey, it was determined that the information provided to the patients about their diseases and treatment processes is not adequate. Informing the patients and their families about the disease, treatment processes and side effects of the treatment will facilitate adjusting to the disease and coping with the problems (Atıcı et al., 2009; Kocaman et al., 2007;

Wolf, 2004). This result shows the importance of informing patients adequately about the disease. In this respect, health personnel have important roles, especially the nurses who have closer relations with patients and should be aware of the importance of informing patients.

### Conclusion

The research results showed that the psychosocial adjustments of the cancer patients were poor, and the psychological adjustments, especially regarding the professional and social life dimensions, were affected more. A result that attracts attention in this study is the fact that the knowledge level of the cancer patients regarding their diseases is the most important variable that affects psychosocial adjustment. Our findings may have important implications regarding the care of Turkish cancer patients. The results of this study can be used in planning psychosocial support programs to increase the psychosocial adjustment levels of the cancer patients. It will be very helpful to integrate these programs into routine practices and for nurses to play a role in such applications.

### Limitations

This study was conducted in only one city in Turkey, and only the individuals who lived in the city centre were included in the study. The results of this study may be generalized to the sample group in this study. The sample in this study reflects only one area of Turkey. The findings therefore cannot be generalized to all patients with cancer in Turkey. Thus, further studies with larger Turkish sample sizes are needed. However, we believe that because our study is the first to investigate the associations of psychosocial adjustment in patients with cancer in Turkey, it will provide a foundation for future studies.

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# Is this heart attack worse than the other? Use of D-dimer levels in non-ST elevation myocardial infarction

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## Abstract

**Background:** Non-ST Segment Elevation Myocardial Infarction (NSTEMI) is an elusive diagnosis in patients presenting with chest pain in the emergency department (ED). The role of D-dimer in the diagnosis used as an additional tool is unclear.

**Objective:** The present study is designed to investigate the role of D-dimer levels in the initial management of patients diagnosed with Troponin-positive NSTEMI admitted to the University-based ED.

**Methods:** A prospective, observational study was conducted in the ED of a major tertiary university-affiliated center in the six-month study period. Fifty-eight patients diagnosed with NSTEMI in the six-month study period were enrolled in the study. All patients were observed for 12 hours in ED and serial ECGs were obtained. Creatinin Phosphokinase-MB fraction (CK-MB), Myoglobin and Troponin-T were measured three times for each patient. Patients with elevated Troponin-T levels were diagnosed as NSTEMI and then D-dimer levels were assayed.

**Results:** Mean age of the 58 patients was 69.7±11.8 and 34 (58.6%) were male. D-dimer levels were found high in 35 (60.3%) of 58 patients diagnosed with NSTEMI. Coronary angiography (CAG) was performed in 46 patients (79.3%) and significant coronary atherosclerosis was detected in 44 (95.6%) of them. Mean D-dimer levels of patients with only 1 or 2 involved vessels were found to be lower than those with 3 or more involved vessels (p=0.001).

**Conclusion:** D-dimer levels may have a role in predicting more severe coronary artery disease in

the emergency setting in patients presenting with chest pain and NSTEMI.

**Key words:** Non-ST Segment Elevation Myocardial Infarction, D-dimer, Acute Coronary Syndromes, diagnosis

## Introduction

There is a relationship between coronary events and haemostatic abnormalities with elevated levels of fibrinogen, D-dimer, von Willebrand factor, factor VII, and plasminogen activator inhibitor<sup>1,2</sup>. Plasma D-dimer levels, the primary degradation product of cross-linked fibrin, have shown elevated in acute coronary syndromes (ACS) in some of the studies<sup>1,3-5</sup>. Wakai et al. assigned patients into three categories regarding D-dimer levels and concluded that coronary heart disease risk is approximately 70% greater in those in the group with the highest D-dimer levels compared to those in the bottom third<sup>6</sup>.

However, the role of D-dimer in patients presenting to the emergency department (ED) with Non-ST Segment Elevation Myocardial Infarction (NSTEMI) is unclear<sup>1</sup>. This study is designed to investigate the role of D-dimer levels in patients diagnosed with NSTEMI admitted to the University-based ED.

## Methods

After approval of the Institutional Review Board was obtained, a prospective, observational

study was conducted in the ED of a major tertiary university-affiliated center in the six-month study period between December 1, 2004 and May 31, 2005. The study included 58 patients who presented to the ED with NSTEMI. Patients with probable false high D-dimer level (patients with cancer, systemic infection, coagulopathy/anticoagulant therapy, renal and/or liver failure, suspected pulmonary embolism, cerebrovascular disease) were excluded from the study.

All patients were observed for 12 hours in ED and serial ECGs were obtained. Cardiac markers (Creatinin phosphokinase MB fraction-CK-MB, Myoglobin and Troponin T) were analyzed and recorded three times in all patients according to Advanced Cardiac Life Support (ACLS) protocol established and updated by American Heart Association (AHA) in 2005. When Troponin T levels were elevated, patients were diagnosed with NSTEMI and new blood samples were drawn and D-dimer levels were analyzed. In this study, D-dimer levels were measured with Cardiac D-dimer Diagnostic Kits® and Diagnostic CardiacReader®. D-dimer levels  $\geq 500 \mu\text{g/L}$  were considered as positive result.

The present data were analyzed using the Statistical Package for Social Sciences for Windows, version 11.0. Mean values were given with  $\pm$ standard deviation (SD) values. Categorical data were analyzed using Pearson's  $\chi^2$  and Fisher's exact test.

## Results

Sixty patients were eligible for the study. After one patient with carbonmonoxide intoxication and one patient with myocarditis were excluded from the study, 58 patients were taken into consideration for statistical analysis. The mean age is  $69.72 \pm 11.88$  (range: 41 to 95 years) and 34 (58.6%) are male.

Patients with NSTEMI were admitted with different main complaints. The most common complaint was chest pain in 37 (63.8%) patients (Table 1). Patients' complaints reportedly ensued on average 4 hours before admission (range: 1 to 96 hours).

Forty-six (79.3%) of 58 patients underwent diagnostic CAG, while the others received medical

treatment. In 44 (95.6%) of 46 patients, critical lesions in coronary arteries were detected with CAG. *Table 1. Distribution of patients with respect to D-dimer levels and chief complaints on presentation into the ED.*

Chief complaints on admission	D-Dimer	
	Normal	Positive
Chest Pain	21	16
Dyspnea		8
Syncope	1	5
Vertigo		1
Pain in left arm	1	
Weakness		1
Hypertension		1
Abdominal pain		1
Back pain		1
Palpitation		1
<b>Total</b>	<b>23</b>	<b>35</b>

CAG procedure could not be performed in 12 patients, i.e., 2 patients left against medical advice to undergo CAG in another center, 4 patients died before the procedure and 6 patients refused procedure.

Mean level of D-dimer in 58 patients was  $849 \mu\text{g/L} \pm 788.99$  (range 50 – 3240  $\mu\text{g/L}$ ). D-dimer level was found positive (i.e.,  $\geq 500 \mu\text{g/L}$ ) in 35 (60.3%) patients. Among all patients, the mean values of D-dimer in the subgroups of patients with high and normal D-dimer values were calculated as  $1256 \mu\text{g/L} \pm 778.17$  and  $230 \mu\text{g/L} \pm 110.29$  respectively. Mean D-dimer value of 44 patients with positive CAG was found to be  $830 \mu\text{g/L} \pm 822.50$  (range 100-3240  $\mu\text{g/L}$ ). On the other hand, mean value of 12 patients who did not undergo to CAG was  $846 \mu\text{g/L} \pm 666.97$  (range 50–2230  $\mu\text{g/L}$ ).

While D-dimer levels were elevated in only 16 (43.2%) of 37 patients with chest pain, it was elevated in all of 8 (100%) patients with dyspnea ( $p=0.06$ ). D-dimer levels were significantly raised in 17 (70.8%) of female patients, vs. 18 (52.9%) male patients, though the difference was not statistically significant ( $p=0.170$ ).

Distribution of lesions identified in CAG regarding normal and high D-dimer levels were shown in (Table 2). The highest number of patients were in the group with three-vessel disease ( $n=16$ ).

Table 2. Distribution of lesions detected in CAG with respect to the groups of normal and high D-dimer levels.

Number of vessels with lesion in CAG	D-dimer		Frequency (%)
	Normal	High	
0	0	2	2 (4.3)
1	3	1	4 (8.7)
2	9	2	11 (23.9)
3	6	10	16 (34.8)
4	2	9	11 (23.9)
5	0	2	2 (4.3)
<b>Total</b>	<b>20</b>	<b>26</b>	<b>46 (100)</b>

Regarding the relationship between the extent of lesions detected by CAG and D-dimer levels, it is apparent that D-dimer levels were significantly increased as the number of involved vessels increased ( $p=0.013$ ) (Table 2). Of 44 patients with coronary vascular lesions, 21 (72.4%) of 29 patients with 3 or more affected vessels had high D-dimer levels while only 3 (20%) of 15 patients with 1 or 2 affected vessels had high D-dimer levels. Mean D-dimer levels of patients with only 1 or 2 involved vessels were found to be lower than the levels of those with 3 or more involved vessels ( $p=0.001$ ). (Sensitivity:72.4%, Specificity: 80%, Positive predictive value (PPV):87.5%, Negative predictive value:40%).

Among 58 patients, 10 patients died (i.e., 2 refused to undergo CAG, 4 died before CAG and 4 died after CAG procedure). Of those, all patients (100%) had high D-dimer levels. ( $p=0.005$ ) (Sensitivity 100%, specificity: 47.9%, PPV:28.5%) The difference between two groups regarding D-dimer positivity was found to be statistically significant.

Among 10 died patients, only 4 patients underwent CAG, and all patients had 3 or more lesions in coronary vessels (Fisher's exact test,  $p=0.175$ )(Sensitivity:100%).

Ischemic ECG changes were recorded in 30 patients among 58. There was no statistically significant difference between patient with high and normal D-dimer levels respecting ischemic ECG changes ( $p=0.259$ ).

## Discussion

The "miss" rate for acute myocardial infarction in patients evaluated in the ED is currently about two percent<sup>7</sup>. In some studies, D-dimer was found as an early diagnostic marker of coronary ischemia in patients with chest pain besides other cardiac markers.

Bayes et al found an approximately five-fold increase in D-dimer level in patients with unstable angina pectoris and with an acute myocardial infarction than in nonischemic patients<sup>8</sup>. Researchers also found as an independent diagnostic value for acute coronary disease the D-dimer level which has greater than  $500 \mu\text{g/L}$ <sup>8-10</sup>. Kruskal et al. showed that D-dimer was elevated in patients with unstable angina pectoris, whereas it was generally found within normal limits in patients with stable angina pectoris<sup>3</sup>. Baraket et al. found higher D-dimer levels in patients with NSTEMI than patients with stable angina pectoris<sup>11</sup>. Koernig et al. found plasma D-dimer levels are strongly and independently associated with the presence of CAD in patients with stable angina pectoris<sup>12</sup>.

Alcalai et al. studied to determine the predictors for the diagnosis of ACS in the presence of an abnormal Troponin level<sup>13</sup>. The overall PPV of Troponin T for ACS diagnosis was only 56% (95% CI, 52%-60%).

Wakai et al emphasized that although D-dimer levels were defined to be useful in identification of high risk ACS patients, it has been reported not to be specific for diagnosis and D-dimer levels should be used along with Troponin values<sup>6</sup>.

Tello-Montoliu et al. conducted a study to define the utility of the combined measurement of Troponin T, C-reactive protein (CRP), N-Terminal Pro-B-Type Natriuretic Peptide (NT pro-BNP) and D-dimer as biomarkers to predict adverse events in non-ST elevation ACS<sup>14</sup>. They found that Troponin T, NT pro-BNP and CRP were predictors of adverse events in the multivariate analysis, but not D-dimer levels.

D-dimer levels were found positive only in 35 (60.3%) patients with NSTEMI in the present study. Baraket et al. found a positive correlation between level of d-dimer and complexity of coronary lesions in their prospective study in 22 patients<sup>11</sup>.



Lui et al. investigated the relationship between serum advanced fibrinogen, total cholesterol (TC), triglycerides (TG), low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C) and D-dimer and the severity of coronary artery stenosis in 195 patients and revealed that elevated fibrinogen level is related to the severity of CAD<sup>15</sup>. Likewise, Pachenko et al. found D-dimer was the highest in patients with the most extensive atherosclerosis<sup>16</sup>.

Turker et al studied the relationship between culprit lesion severity and thrombotic and fibrinolytic parameters (D-dimer, fibrinogen, thrombin-antithrombin III complex (TAT), and prothrombin fragment 1 \_ 2 (PF 1 \_ 2)) in patients who had non-ST elevation ACS (NSTEMI-ACS) in 95 patients. They revealed that the severity of culprit lesion may be associated with plasma D-dimer, TAT, and PF 1 \_ 2 levels in NSTEMI-ACS patients<sup>17</sup>.

Shitrit AB et al. conducted a prospective, observational study in a major tertiary university-affiliated center in 124 patients with ACS and normal cardiac enzymes<sup>1</sup>. They found ELISA D-dimer levels were positively correlated with catheterization findings and they revealed D-dimer levels may add important clinical data concerning patients with ACS and normal cardiac enzymes. Alzarka et al. found that the incidence of abnormal D-dimer levels was not significantly higher in any of four groups (filling defects, extrinsic lesions with irregular borders and total occlusions with or without staining) than in the two groups with normal coronaries or with smooth lesions and the majority of patients (64%) had normal D-dimer levels in their study with 136 patients undergoing CAG<sup>18</sup>.

Shitrit D et al. studied sensitivity, specificity, PPV and NPV of the D-dimer assay for the diagnosis of CAD in 54 patients with unstable angina pectoris in a prospective, observational study<sup>19</sup>. They found a statistically significant correlation between ELISA D-dimer levels and age, male sex, hypertension, use of beta-blocker, fibrinogen levels and catheterization findings while no correlation was noted between ELISA D-dimer levels and degree of the CAD (sensitivity 70%, NPV 72%, and overall accuracy 67%). In the present study, D-dimer levels were significantly increased as number of involved vessels detected by CAG increased. Considering relationship between num-

ber of vascular lesions and D-dimer levels, mean D-dimer levels of patient with 2 or less lesions were higher than those with 3 or more lesions. (Sensitivity:72.4%, Specificity: 80%, PPV:87.5%).

Menown et al. studied the independent predictive value of d-dimer and inflammatory markers for the risk of recurrent adverse events in patients with acute chest pain with normal levels of cardiac troponin I (cTnI) in 391 patients<sup>20</sup>. They revealed that D-dimer and inflammatory markers (sP-selectin) may improve risk stratification for death/MI.

In the current study, mortality rate was significantly higher in patients with high D-dimer levels. It is important to note that no patient with a normal D-dimer level was belonged to the group with fatal consequences. On the other hand, findings of the present study failed to show any statistical significant relationship regarding the relationship between ischemic ECG changes and D-dimer levels.

### Limitations

In the present study, D-dimer levels were studied only in Troponin T-positive patients. If this study had included all chest pain patients in ED, the comparison of D-dimer vs Troponin T values according to CAG results would be more sound. Small sample size and confinement to a single center are also considered a major drawback for the study.

### Conclusion

D-dimer levels may have a role in predicting more severe coronary artery disease in the emergency setting in patients presenting with chest pain and NSTEMI.

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# The effect of Caesarean delivery care on postpartum problems and satisfaction

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## Abstract

**Introduction and Objective:** Standardized and qualified nursing care is of crucial importance in resolving postpartum problems and adapting to the new role after caesarean delivery. A healthy postpartum period affects women's satisfaction with the care they receive. The research was designed as a quasi-experimental study with a post-test control group in order to evaluate the effect of caesarean delivery care on postpartum problems and satisfaction with nursing care.

**Material and Method:** The research was conducted with 160 individuals (80 experimental, 80 control) who gave caesarean delivery in gynaecology clinics and who met the research criteria. Erzurum Nenehatun Hospital was chosen as the site of the control group, and the gynaecology clinic of Aziziye Research Hospital was chosen as the site of the experimental group. The women in the experimental group were given care in line with the care management guide and monitored by using nursing follow-up forms. The women in the control group were followed up in accordance with the routine applications of the hospital. Descriptive characteristics form, post-caesarean nursing care and follow-up form prepared by the researchers in line with the literature, and satisfaction with nursing care scale were used as data collection tools.

**Findings:** It was determined that post-caesarean nursing care reduced the prevalence rate of postpartum problems in the experimental group compared to the control group. The women in the experimental group stayed in the hospital for 3.6

days on average in post-caesarean period, while the women in the control group stayed in the hospital for 4.2 days. Nursing care satisfaction in the experimental group (78.83±9.44) was found to be significantly higher than that in the control group (48.11±10.12).

**Conclusion and Suggestions:** Consequently, it was detected that post-caesarean care and follow-up reduced the rate of postpartum problems and increased the nursing care satisfaction. In line with these results, it is suggested that necessary arrangements are made in gynaecology clinics to meet the needs and expectations of women who deliver a baby by caesarean section, and women should be followed up by using nursing follow-up forms in nursing care applications and women's satisfaction with nursing care should be evaluated on a routine basis.

**Key words:** Caesarean delivery, nursing care, satisfaction

## Introduction and objective

In recent years, delivery by caesarean section is the most frequently applied major surgical intervention both in the world and in our country. According to the Turkish Population and Health Survey (TNSA), the rate of caesarean delivery in Turkey was 21.1% in 2003 and increased to 36.7% in 2008 [1,2]. The World Health Organization, taking the maternal and perinatal mortality rates into consideration, recommends that the caesarean section rate should not be higher than 15%. Caesarean section rates reported in our country are much higher than

15%, the rate recommended by the World Health Organization (WHO) within the scope of their slogan "Health for Everyone in 2000".

Caesarean delivery is a beneficial obstetric intervention which saves the life of both the mother and the baby; however, like other major surgical interventions, it brings along many risks associated with anaesthesia and surgical procedure, as well as some physical and psychosocial problems and complications in postpartum period [3-7]. Previous researches show that women and families having their first delivery by caesarean section need information, support, communication, encouragement and comprehensive care in the postpartum period and they require help to adapt to their new roles [5-9].

Nursing care services play a significant role in helping the mother to recover and perform all her roles and functions in the postpartum period. In this period, women and their families should be provided with sufficient information and nursing care [5,9,10]. Since caesarean deliveries are a powerful source of stress effective on both expectant mothers and all family members, caesarean care should be both mother- and family-centred. Postpartum nursing care is based on effective, individual and qualified care for defining and meeting the physical and psychosocial needs of the mother, the newborn and the family. Standardized, comprehensive and qualified nursing care in caesarean deliveries plays a significant role in resolving problems and adapting to the new role in this period [3,11].

Education and care given in caesarean deliveries enables the mother to develop competence in self- and baby-care, positive health behaviours, self-confidence, problem-coping skills and adaptation to the new life and roles, and to increase in breast-feeding success, and therefore provides the mother with a problem-free, comfortable and healthy postpartum period and a safer future [3,11]. This care has a positive effect on the mother's satisfaction with the provided service. The studies conducted so far on this subject demonstrate that caesarean care increases mothers' overall satisfaction [12,13].

Aim of the research was to evaluate the effect of caesarean care on postpartum problems and nursing care satisfaction by using nurse follow-up forms in line with the care management guide.

Research Hypotheses:

- Caesarean care reduces postpartum problems.
- Caesarean care reduces the hospitalization period after delivery.
- Caesarean care increases the satisfaction with nursing care.

## Material and method

### Research Design

The study was performed with a quasi-experimental model with post-test control group in order to determine the effect of caesarean care on postpartum problems and satisfaction.

### Research Site and Period

The research was conducted in 2007 in the province of Erzurum located in eastern Turkey, in the gynaecology clinic of Atatürk University Aziziye Research and Application Hospital and in the gynaecology clinic of Erzurum Nenehatun Hospital.

### Research Population and Sample

The population of the research included 160 women who gave birth by caesarean section in the two institutions at the time of the research and who accepted to participate in the study. Sampling method was not used in the study. The minimum sample size for experimental studies is estimated to be not less than 30 individuals [14].

Nenehatun Hospital was used as the control group, and Aziziye Research Hospital was used as the experimental group. The reason for choosing Aziziye Research Hospital as the site for the experimental group was its convenience for transportation, and the fact that it provided an atmosphere for working in cooperation with the nurses in the clinic, for a researcher to work in this clinic and following up the patients in accordance with the care management guide (continuous follow up).

The women in both the experimental and control group consisted of conscious individuals who did not experience serious medical complications. The control group included 80 women who met

these criteria and who were receiving nursing care in accordance with routine applications performed in the gynaecology clinic of Nenehatun Hospital. The experimental group included 80 women who met the same criteria but who were followed up by care management guide.

### Research Variables

Health problems experienced after caesarean delivery and levels of satisfaction with nursing care were determined as the dependent variable of the research, and nursing care was determined as the independent variable. Women's descriptive and obstetric characteristics were taken as the control variables of the research. No difference was found between the experimental group and control

group in terms of the control variables, and both groups were observed to be similar (Table 1).

### Data Collection Tools

Descriptive characteristics form prepared by the researchers, post-caesarean nursing care and follow-up form prepared in line with the literature in accordance with care management guide, and satisfaction with nursing care scale were used as data collection tools.

**Descriptive Characteristics Form:** This form includes questions about the women's demographic (age, education status, occupation status and economic level) and obstetric (parity, reason for having caesarean delivery, previous delivery method) characteristics.

Table 1. Comparison of The Experimental and Control Groups for The Equality

Characteristics	Experimental Group (n=80)		Control Group (n=80)		Significance
	n	%	n	%	
<b>Age</b>					
< 24	28	35.0	18	22.5	
25-34	36	45.0	51	63.7	$\chi^2=5.686$
35 >	16	20.0	11	13.8	P>0.05
<b>Education level</b>					
Illiterate	44	55.0	44	55.0	
Primary-secondary	14	17.5	13	16.3	
High school	6	7.5	15	18.7	$\chi^2=6.561$
University	16	20.0	8	10.0	P>0.05
<b>Employment status</b>					
Housewives	75	93.8	68	85.0	$\chi^2=3.225$
Employed	5	6.2	12	15.0	P>0.05
<b>Economic level</b>					
Income less than expenditure	20	25.0	29	36.3	
Income equivalent to expenditure	20	25.0	22	27.4	$\chi^2=3.502$
Income more than expenditure	40	50.0	29	36.3	P>0.05
<b>Parity</b>					
Primiparous	30	37.5	37	46.2	$\chi^2=1.258$
Multiparous	50	62.5	43	53.8	P>0.05
<b>Reason for caesarean delivery</b>					
Medical indications	55	68.8	59	73.8	$\chi^2=0.488$
Personal decision	25	31.2	21	26.2	P>0.05
<b>Previous delivery method</b>					
Caesarean section	28	54.9	29	69.0	$\chi^2=1.943$
Vaginal delivery	23	45.1	13	31.0	P>0.05

**Nursing Care and Follow-up Form:** This form was prepared by the researcher in line with the literature data. The aim of the nursing care form is to measure by follow-ups the efficacy of the integrated care given after caesarean delivery in line with the care management guide. This form evaluates the women's self-care, baby care, mobilization, breast-feeding condition, breast problems, and complaints like gas, pain, constipation, anxiety, fatigue and sleep withdrawal. Follow-up form included follow-ups scheduled every 15 minutes between 1-2 hours, every 30 minutes between 2-4 hours, and once an hour between 4-6 hours.

**Satisfaction with Nursing Care Scale:** This scale is used to assess the patient's satisfaction with nursing care. The patients define their satisfaction with various aspects of nursing care by using 5-point likert scale consisting of 19 items. Patient satisfaction is measured on a scale of 1 to 5 (1= Not satisfied at all, 2=Rarely satisfied, 3=Satisfied, 4=Very satisfied, 5=Truly satisfied). Higher scores indicate patient's satisfaction with nursing care in all aspects. Cronbach's alpha internal consistency coefficient of the scale was reported as .94 [15]. In this research, Cronbach's alpha internal consistency coefficient was found as .97.

### Nursing Intervention

Following the ethical principle, permission was obtained from relevant authorities and the individuals who participated in the research on voluntary basis were informed about the research before the initiation of the study. In the hospitals where the research was conducted, there was no written education guideline and care plan prepared for patients to undergo caesarean section. In addition, the hospitals did not have any follow-up form to enable a systematic follow-up. Nurses monitored the patients on the basis of routine applications and activities the patients request from them. In the research, no intervention was made in the control group which received a routine follow-up and care applied in the clinic. The women in the experimental group received information and support before caesarean section operation, and post-caesarean nursing interventions and follow-ups were performed in line with the nursing care management guide.

### Intervention Material

"Nursing Care Management Guide" was used as the intervention material for the women in the experimental group who underwent caesarean section operation. The Nursing Care Guide includes information about nursing care to be given before, during and after the operation.

*Interventions of pre-caesarean care* include interventions for increasing deep breathing and coughing ability, reducing anxiety and pain, achieving early recovery, regaining the ability to perform daily life activities, and having psychological improvement in order to reduce the risk of post-caesarean complications.

*Interventions for care during caesarean section* involve the obstetrics team and the performed procedures as well as the support services.

*Interventions of post-caesarean care and follow-ups* include the prevention of problems and complications that may arise after caesarean section.

This guide comprises the routine applications in the clinic besides the maternal and baby care and education for integrated care. The care guide was prepared in line with the literature [5-7,11,12,16,17]. The topics in the Nursing Care Guide include the follow-up of vital signs, lochia, incision, involution, breast care and breast-feeding, diuresis, GIS control, deep breathing and coughing exercises, mobilization, personal hygiene, self-care applications (general body, perineum, breast), activity, position, mother-baby interaction, psycho-social condition, education, and planning the discharge. In line with the Nursing Care Management Guide, the individuals in the experimental group were given integrated post-caesarean care. Follow-ups were performed every 15 minutes between 1-2 hours, every 30 minutes between 2-4 hours, and once an hour between 4-6 hours.

### Data Collection

In order to collect data, descriptive characteristics form, nursing care and follow-up form, and satisfaction with nursing care scale were applied to the women in the control and experimental group before they were discharged.

**Statistical Analysis**

Statistical analysis of the data was carried out by using Statistical Package for Social Sciences (SPSS 11.0) package program. Mean, standard deviation, range frequency of response variables,  $\chi^2$  test and the *t* test in independent groups were reported.

**Findings**

When the post-caesarean problems experienced by the experimental and control groups were compared, it was observed that the women in the experimental group who received the specified care had fewer problems in self-care, baby care, breast-feeding and walking compared to

Table 2. Comparison of The Problems Experienced by The Experimental and Control Groups

Problems Experienced	Experimental Group (n=80)		Control Group (n=80)		Significance
	n	%	n	%	
<b>Women's self care</b>					
Present	16	20.0	29	36.3	$\chi^2=5.225$
Absent	64	80.0	51	63.7	P=0.022
<b>Baby care</b>					
Present	31	38.8	45	56.3	$\chi^2=4.91$
Absent	49	61.2	35	43.7	P=0.027
<b>Breast-feeding</b>					
Present	44	55.0	56	70.0	$\chi^2=3.840$
Absent	36	45.0	24	30.0	P=0.050
<b>Breast Problem</b>					
Present	7	8.8	13	16.3	$\chi^2=2.057$
Absent	73	91.2	67	83.7	P=0.151
<b>Pain</b>					
Present	64	80.0	65	81.3	$\chi^2=0.040$
Absent	16	20.0	15	18.7	P=0.841
<b>Gas</b>					
Present	26	32.5	45	56.3	$\chi^2=9.141$
Absent	54	67.5	35	43.7	P=0.002
<b>Constipation</b>					
Present	15	18.8	21	26.3	$\chi^2=1.290$
Absent	65	81.2	59	73.7	P=0.256
<b>Mobilization</b>					
Present	21	26.2	36	45.0	$\chi^2=6.132$
Absent	59	73.8	44	55.0	P=0.013
<b>Anxiety</b>					
Present	13	16.3	30	37.5	$\chi^2=9.191$
Absent	67	83.7	50	62.5	P=0.002
<b>Fatigue</b>					
Present	22	27.5	46	57.5	$\chi^2=14.731$
Absent	58	72.5	34	42.5	P=0.000
<b>Sleep</b>					
Present	13	16.3	25	31.3	$\chi^2=4.970$
Absent	67	83.7	55	68.7	P=0.026

Table 3. Comparison of The Means of Length of Stay in Hospital between The Experimental and Control Groups

	Experimental Group X±SD	Control Group X±SD	Significance
Length of Stay (day)	3.61±1.39	4.23±2.84	t:-1.734 p>0.05

Table 4. Comparison of The Score Means of Satisfaction with Nursing Care between The Experimental and Control Groups

	Experimental Group X±SD	Control Group X±SD	Significance
Satisfaction with Nursing Care	78.83±9.44	48.11±10.12	t:19.851 p<0.001

the women in the control group. In addition, the experimental group had fewer problems of gas, anxiety, fatigue and sleep withdrawal compared to the control group, and the difference between the groups was found to be statistically significant ( $p<0.05$ ). In the experimental group in which nursing intervention was applied, an increase was observed in the rates of early recovery, providing self-care and baby care, early and continued breast feeding, and a decrease was determined in fatigue and sleep withdrawal.

The women in the experimental group stayed in the hospital for 3.6 days on average in post-caesarean period, while the women in the control group stayed in the hospital for 4.2 days. The statistical evaluation revealed no difference between the two groups ( $p>0.05$ ).

The score means of satisfaction with nursing care were statistically different in the experimental and control group. The score mean of satisfaction with nursing care in the experimental group (78.83±9.44) was significantly higher than the score mean of satisfaction with nursing care in the control group (48.11±10.12) ( $p<0.001$ ).

## Discussion

In the research, the rate of postpartum problems experienced in the experimental group taking the care was determined to be lower than that of the control group, and the difference between the groups was found to be statistically significant

( $p<0.05$ ). Spradlin, in his study on the implementation of a couplet care program for families after a caesarean birth, reports that the care given to patients has a positive effect on recovery, protects the mother and the baby, facilitates family bonding, supports successful breastfeeding and reduces postpartum depression [18]. Altuğ-Özsoy notes that the pre-operation education given to mothers who are to undergo caesarean section is effective in postpartum period [16]. Gözüm et al. have examined the effects of early and frequent postpartum follow-up on the mother and the baby, and concluded that early and frequent follow-up has positive effects on both the mother and the baby and increased the mother's satisfaction [19]. The results of this study support the hypothesis "Caesarean care reduces postpartum problems". This result demonstrates the importance of nursing care services in maternal recovery as well as in enabling the mother to perform all her roles and functions in caesarean deliveries.

The women in the experimental group stayed in the hospital for 3.6 days on average in post-caesarean period, while the women in the control group stayed in the hospital for 4.2 days, and the difference between the two groups was found to be statistically insignificant ( $p>0.05$ ). Staying in the hospital for 1-3 days after delivery is important for the health of the mother and the baby. The Ministry of Health specifies a minimum 48-hours hospitalization period for cases who do not develop any post-caesarean complications [20]. The findings of this study for both the experimental



and control group comply with the post-caesarean hospitalization period specified by the Ministry of Health. Although the hospitalization period was shorter in the experimental group compared to the control group, the difference between the groups is insignificant and does not support the hypothesis “*Caesarean care reduces the hospitalization period after delivery*”.

In the research, the score mean of satisfaction with nursing care was observed to be higher in the experimental group compared to the control group ( $p < 0.001$ ). Akay and Kömürcü (2004) also reported a significantly higher rate of satisfaction with nursing care in mothers of the experimental group that received care in comparison with the those in the control group [12]. Patient satisfaction is an important indicator of the quality of nursing services [15]. There is a close relationship between patient satisfaction and high-quality care. It is reported in previous researches that the information, education, and communication provided about caesarean delivery improves the efficacy of the given service and increases patient satisfaction [12,13]. In the study conducted by Eryılmaz (1999), it is emphasized that providing the mother with the attention and care she expects from nurses and giving her adequate information about self- and baby-care are important parameters in evaluating nursing care [17]. In the present study, the care given to women having caesarean delivery increased their satisfaction with nursing care. The obtained results comply with those in the literature. In line with these results, the study findings support the hypothesis “*Caesarean care increases the satisfaction with nursing care*”.

### Conclusion and suggestions

Consequently, it was detected that post-caesarean care and follow-up reduced the prevalence rate of postpartum problems and increased the nursing care satisfaction in the experimental group compared to the control group. On the other hand, no significant difference was observed between the experimental group and control group in terms of the effect of nursing care on hospitalization period. Based on these results, the following suggestions may be introduced:

- Standard care plans with systematic application convenience should be prepared and used in postpartum clinics in order to increase the quality of postpartum nursing care and patient satisfaction
- Satisfaction and expectations of the mother and her relatives regarding postpartum services should be evaluated on a regular basis
- Motivating studies should be performed to increase the performance of nurses working in postpartum services
- Satisfaction status of the employees should also be investigated.

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# Determination Of The Types Of Conflict Experienced By Student Nurses

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## Abstract

**Objectives:** The objective of this study is to identify the types of conflict experienced by university students and to determine whether demographic factors have an effect on the types of organizational conflicts.

**Methodology:** The population of the study included 387 students from the Nursing School of Atatürk University between April 2009 and June 2009. The sample group consisted of 323 students who volunteered to participate in the research. Data were collected by using a questionnaire form that included questions about the age, gender, grade level and marital status of the students and educational level of their parents, and applying "Rahim's Organizational Conflict Scale".

**Results:** According to the results, 27.9% of the students who participated in the research were first-year students, 25.7% were second-year students, 26.3% were third-year students and 20.1% were fourth-year students. The total score mean that the students obtained from the organizational conflict scale was  $55.13 \pm 7.76$  and the highest mean was obtained from the subscale of intra-group conflict. When the scores of intra-group conflict subscale and their distribution according to grade levels were examined, a statistically significant difference was found between the grade levels.

**Conclusions:** It was demonstrated that the organizational conflict score of the students was of medium level and that the organizational conflict level was affected by characteristics such as age, grade level, and the individuals whom the students experience conflict with. These results indicate that the level of organizational conflict is determined by some individual characteristics, and reveal

the necessity of taking these characteristics into consideration in future studies.

**Key words:** Conflict, Conflict Types, Student Nurse

## Introduction

Conflict is not an event peculiar only to humans. All living beings are in continuous interaction with their environment and they are obliged to get into conflict when necessary in order to survive. If a living organism meets with an obstacle when trying to satisfy a vital need, this situation causes discomfort and, in turn, stress. As for humans, conflict is experienced in states of tension caused by the pressures preventing an individual from satisfying both his/her physiological and socio-psychological needs. However, conflict is one of the difficult concepts to define, because there are different reasons for its emergence and there exist various types of conflicts depending on how it is formed or processed (Eren 2000; Elma and Demir 2000). Due to this fact, the concept of conflict has been defined in different ways by different scientists.

When the concept of conflict is considered on general terms, it is possible to say that the conflict arises from an individual's rejection of a person, group, idea or event, or his/her dislike of the mentioned factors. For an individual and group, the change in one's goals in a certain period of time and the emergence of contradicting goals lead the individual to experience conflict while trying to choose one of these goals. Conflict may sound scary as a concept, since it is generally associated with negativities imprinted on our memory, as

well as pains, hostilities and even disastrous wars. There will always be conflict as long as there are differences in the preferences, desires, values, beliefs and interests of social parties that communicate and interact with one another. Since conflict is unavoidable, it is necessary to use the benefits of the emerging conflict and manage conflict in an efficient way to prevent its possible destructive effects. Although differences may be a source of progress and development, in cases of uncertainty about how to cope with certain problems that stem from differences, these differences lead to violence which have destructive consequences for individuals, groups, organizations and even countries **(Hall 1985)**.

Since organizations consist of different individuals with different goals, perceptions, personalities and needs, conflict is inevitable and managers should have knowledge about conflict. Therefore, it is possible to say that management is, in a sense, identified with conflict management. The managers of successful organizations are those who can keep conflicts at an optimal level as soon as possible or at nearly optimal point and who can effectively sustain this approach **(Rahim 1999)**. Any organization in which individuals are in mutual interaction contains a potential environment of conflict within itself. Health Care Institutions include several interaction groups. This interaction may occur between institutions and other institutions, institutions and patients, institutions and families, institutions and visitors, and institutions and doctors. Such interactions often lead to conflicts. Thus, the existence of such environments of conflict requires the presence of managers with qualifications of effective conflict management **(Rahim 1983, Akkirman 1998)**. Consequently, conflicts breed dynamism in an environment and become an indispensable part of progress when appropriate approaches are used. The attitude and skills of the manager is the primary factor in solving conflict problems. From this perspective, nurses play a very important role in this matter. The purpose of this study is to identify the types of conflict experienced by university students and to determine whether demographic factors have an effect on the types of organizational conflicts.

## Methodology

This research was designed as a descriptive study and the study population included 387 students from the Nursing School of Atatürk University in the 2008-2009 academic year between April 2009 and June 2009. Sampling method was not used in the research which aimed to reach the entire population. Since 64 students could not be reached due to reasons such as illness, absenteeism and reluctance to participate in the study, the research sample comprised a total of 323 students. Participation rate was 83.46%. Written permission was received from the ethics committee of the Nursing School and verbal permission was received from the students during the implementation of the research.

Research data were collected by using "Rahim's Organizational Conflict Scale" and the two-section questionnaire form which included socio-demographic characteristics in the first section and which was prepared by the researchers after the review of relevant literature. "Rahim's Organizational Conflict Scale" consists of three subscales measuring three dimensions of conflict: intrapersonal conflict, intra-group conflict and inter-group conflict. The dimension which reveals the highest/lowest conflict is determined by looking at the score means of each subscale. The scale consists of 20 items, and the highest and lowest scores in the scale are 100 and 20, respectively. The scale was developed by Rahim M.A. in 1997. The total Cronbach's alpha coefficient of the "Rahim's Organizational Conflict" scale was .78 for this study. Since the scale did not have any cut point, average score was used in statistical assessment. Data were analyzed by percentage, average, one way variance analysis, and Tukey HSD test.

## Results

Among the student nurses who were included in the research, 27.9% were first-year students, 25.7% were second-year students, 26.3% were third-year students and 20.1% were fourth-year students. 87.6% of the students were female and 61.9% of the students were from the age group of 21-23 years. Most of the students (96.9%) were

single, 44.9% lived in the city centre for the longest time, 80.2% came from a nuclear family, 27.2% lived with their parents, and 54.5% stayed in the dormitory at that time. 46.4% of the students had 4 or more siblings, 54.5% lived in a dormitory or hostel, 65.6% had an income equal to their expenses, and 63.8% lived off bursaries and student loans. 87.3% of the students had a democratic and supportive family structure, 66.3% experienced some problems within the family, 62.5% experienced problems with their friends and these conflicts decreased their success level (44.3%). Students' mothers were mostly primary school graduates (51.4%) and unemployed (87.9%), while education level was higher among fathers (38.4% were high school graduates) and a considerable number of fathers was retired (34.4%).

Table 1 illustrates the distribution of students' subscale scores obtained from "Rahim's Organizational Conflict" scale. Total score mean of the organizational conflict scale was  $55.13 \pm 7.76$ , and it was determined that students experienced a medium level of intrapersonal ( $16.39 \pm 3.32$ ), intra-group ( $22.34 \pm 3.99$ ) and inter-group ( $16.39 \pm 3.59$ ) conflict. As shown in Table 1, a statistically significant difference was found between the student scores obtained from the subscales ( $F = 1.417$   $p < 0.05$ ).

Table 1 demonstrates Comparison of the organizational conflict subscale scores and grade levels of students. There was no significant difference between the students' grade level and the

subscale of inter-group conflict ( $p > 0.05$ ); whereas a significant difference was found in comparison with the subscale of intrapersonal and intra-group conflict ( $p < 0.05$ ).

It was determined that 62.5% of the students experienced conflict with their friends, and these conflicts did not affect the success level in 47.4% of the students. When the subscale scores of the organizational conflict scale were compared with students' grade levels, a statistically significant difference was found between intra-group conflict score means ( $F = 8.503$   $p < 0.05$  Table 2). As demonstrated by a further analysis (Tukey HSD test), this difference was associated with the lower score mean of fourth-year students compared to the score means of other grades.

There was no significant relationship between the attitudes of families and the score means of the conflict scale ( $p > 0.05$ , Table 1). A significant difference was found between the total score means of intrapersonal conflict about the students' choice of profession ( $F = 1.724$ ,  $p < 0.05$ ). No significant difference was detected between the groups which the students experience conflict with, and the total scale score and the score means of intrapersonal and inter-group subscales ( $p > 0.05$ ), whereas a significant difference was found with respect to the intra-group subscale ( $p < 0.05$ ). As revealed by a further analysis performed to determine the reason of this difference, the reason is that the conflict score means were high among those who experience conflict with their fri-

Table 1. Distribution of students' subscale score means of organizational conflict

Subscale	N	X±SD	F	P
Intrapersonal Conflict	323	16.39 ± 3.32	F= 1.417	p<0.05
Intra-group Conflict	323	22,34 ± 3,99		
Inter-group Conflict	323	16,39 ± 3,59		

Table 2 Comparison of the organizational conflict subscale scores and grade levels

Subscale	Grade Level								F	P
	1 (n=90)		2 (n=83)		3 (n=85)		4 (n=65)			
	X	SD	X	SD	X	SD	X	SD		
Intrapersonal Conflict	16.04	3.71	17.44	3.34	15.91	2.95	16.16	2.96	F=0.734	P=0.393
Intra-group Conflict	22.85	4.59	23.13	3.33	21.78	3.85	21.36	2.83	F=8.503	P=0.04
Inter-group Conflict	23.13	3.33	16.53	3.23	15.80	3.63	16.10	3.54	F=2.273	P=0.134

ends. No significant difference was found between the total score means of answers given about how the conflicts affected students' success ( $F=0.996$ ,  $p>0.05$ ). The students who needed bursary or economic support had higher total score means of conflict scale compared to other students ( $p<0.05$ ). In this study, the highest score in the conflict scale was obtained from students whose mothers were primary school graduates ( $17.32 \pm 2,12$ ); yet, the difference between the groups was not significant ( $p>0.05$ ). On the other hand, a significant difference was detected between intra-group score means in terms of the education level of mothers ( $p<0.05$ ). Although the students whose fathers were high school graduates obtained the highest total scores in all subscales, this finding was not considered statistically significant ( $p>0.05$ ). The total conflict scale scores of students who spent most of their lives in the city centre were high in inter-group subscale but not statistically significant ( $p>0.05$ ).

## Discussion

Conflict is not only an event individuals may experience in every environment throughout their lives, but also a concept which inevitably brings positive and negative consequences in organizational environments and whose presence cannot be denied. In conflict-free environments, innovation, change, creativity and success may be affected negatively; while continuous and major conflicts experienced in organizations have a negative effect on success due to reasons such as delays in decisions or even inability to make decisions, and failure in solving problems by compromise; thereby, the existence of the organization will fall into jeopardy (**Bingöl 1990**). Among the students who participated in this study, 66.3% experienced some problems and 62.5% experienced conflict with their friends. In previous studies **Adrian-Taylor (2007)** reported that 22% of the students experienced conflicts with instructors; **Mamchur and Myrick (2003)** reported that 28.2% of students and 24% of nursing students experienced conflicts with their preceptors, 51% of the students frequently and 84% occasionally experienced conflicts.

Individuals in mutual interaction show differences in their tendencies and value judgments in line

with their personalities. These differences are followed by other factors such as education differences, emotional factors, jealousy, desire to be promoted and accepted, and differences in social background. Above mentioned differences turn into contradictions and excessive discordance in time and create interpersonal conflicts (**Eren 2000; Koçel 1999**). Research findings demonstrated a medium level of conflict in "Organizational Conflict Scale" and the subscales of intrapersonal, intra-group and inter-group conflict. Intra-group conflict arises when individuals fail to comply with the objectives, traditions, habits and rules of the group; while inter-group conflict is caused by the clash between two or more interacting groups (**Şimşek 1987**). When the organizational conflict subscale scores of the students were compared to their grade levels, it was found that intrapersonal and intra-group conflict was high among second-year students and inter-group conflict was high among first-year students. Conflicts of various levels experienced within an organization and the approaches used to resolve these conflicts are among the issues that consume students' time and energy. Therefore, topics on conflict-solving approaches should be included in undergraduate curricula. The review of international literature has demonstrated that topics related to conflict-solving are given very limited space in the curricula of nursing education programs (**Deary et al. 2003; Smith et al. 2001**). **Haydenberg et al. (2003)** demonstrated that conflict management education decreased the time that educators spent dealing with conflicts, had positive influences on the school's atmosphere and the development of students'.

In their study, **Seren and Baykal (2007)** reported that conflict-solving skills were higher among nursing students compared to medical students. Interpersonal relationships, communication and interaction should be a part of the curriculum in nursing education programs. In addition, evaluating patients as a whole, identifying their needs and communicating with them during student practices are effective in developing conflict-solving skills (**Kocaman 1998; Velioglu 1994**). Many of the conflicts arise as a result of uncertainties, perceptual deficits and misuse of communication channels during the process of communication and interaction (**Özcan 1996**). In the present study, female students were observed to experien-

ce more conflicts compared to male students. It is reported in other studies that female students had higher scores of conflict-solving skills compared to male students. The main limitation of this study are, unfortunately, the study included only one school and a limited number of students, the research results cannot be generalized to all nursing students. Because the students' organizational conflict types were limited to those with faculty members they may not reflect how they deal with conflict they experience with managers, peers and their family members.

### Conclusion

The school environment has an important role in the socialization of students in the organizational conflict types. Therefore, students need to be supported and encouraged in their use of effective conflict management styles. Thus, students will be facilitated in coping with conflict in their future work and private lives in an effective. In future studies it is recommended that the study be repeated with a larger sample

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# Focal Adhesion Kinase: A key Mediator of Cancer Pathogenesis

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## Abstract

Focal adhesion kinase (FAK) is a 125 KDa non-receptor protein tyrosine kinase. FAK is localized to focal adhesion plaques where its association with several signalling proteins enables it to work as a scaffold protein. It was implied that FAK exhibits a crucial role in the up-regulation of several cellular signalling responses including spreading, proliferation, migration, and invasion. FAK is implicated in apoptosis through the inhibition of the tumour suppressor protein, p53, also activated FAK functions to up-regulate cell adhesion and migration. Besides that, FAK signalling stimulates the production of matrix metalloproteinases (MMPs), mainly MMP-2 and MMP-9, which have a basic role in cancer invasion and metastasis. Recent research focuses on decoding several signalling pathways involving elevated FAK levels and activated status in the up-regulation of several cellular activities. However, the data obtained are still not well elucidated and need further investigation. Here, we review briefly FAK structure, activation and inhibition, FAK signalling impact on several cellular activities and expression and activation levels in several malignancies. FAK appeared to contribute to the activation of several signalling cascades which are mostly over activated in cancer.

**Key words:** Focal Adhesion Kinase; p53; matrix metalloproteinases; invasion

## Introduction

Focal adhesion kinase (FAK) has been indicated in the development of many types of cancers

(Schaller, 1992, Owen *et al.*, 1995). FAK plays a dual function; it works as kinase and scaffold protein which associates with several signalling molecules controlling several signalling pathways (Schaller, 1996; Beviglia *et al.*, 2003). Two research groups headed by Steve Hanks, Jun-Lin Guan and Michael Schaller discovered FAK independently in 1992. Prior to FAK discovery, previous researches were conducted to examine the involvement of Src in cancer signalling. FAK was identified as a substrate of the viral Src oncogen, and was known to localize at cell adhesion contacts where integrins assemble (Mitra *et al.*, 2005). Following activation FAK was thought to promote tyrosine activation of substrates such as paxillin, and amplify mitogen activated protein kinase (MAPK) signalling in transformed cells. However, FAK inhibition was unable to restore transformed cells original phenotypes (Schaller, 2001; McLean *et al.*, 2005).

Recently, reports have indicated tyrosine kinases in neoplastic development and cancer progression. FAK may contribute to the unrestrained proliferation of cancer cells, tumor development, and progression of metastatic cancers (Olayioye *et al.*, 2000; Demetri *et al.*, 2002). However, despite the crucial contribution of FAK to our present understanding of several cellular signalling pathways, and its recent disclosed involvement to the field of tumor biology, only a limited role for the activated FAK in cancer has been determined. Here, the mechanisms by which FAK activation may participate in malignant transformation and play prominent roles in cancer signalling will be reviewed.



## FAK Structure

FAK is encoded by PTK2 genes in humans (Gabbarrá-Niecko *et al.*, 2003). The encoded protein consists of three main domains, a non catalytic N-terminal domain, a central catalytic domain and a C-terminal domain. C-terminal domain consists of the focal adhesion targeting (FAT) sequence (Mon *et al.*, 2006). There are also docking sites for proteins with SH3 domain, located between catalytic domain and FAT sequence (Parsons, 2003). The N-terminal domain of FAK shows strong homology with structurally conserved FERM domains, which are present in various families of structural proteins like talin and protein 4.1, ezrin-radixin-moesin (FERM), as well as in JAK family kinases (Sun *et al.*, 2002). FERM domains were thought to mediate protein-protein interactions. Some binding partners of FAK-FERM domain have been reported, among others are  $\beta$ 1 integrin and growth factor receptors (EGFR and PDGFR) (Sieg *et al.*, 2000). The N-terminal domain was thought to direct FAK interaction to signalling proteins and integrins clusters to regulate its catalytic activity (Parsons *et al.*, 2003). FERM domain-mediated interactions were also thought to have a role in the regulation of cell motility (Streblov *et al.*, 2003).

FAK tyrosine phosphorylation with subsequent activation was increased when FAK N-terminal domain was released from binding to FAK kinase domain. N-terminal domain truncation is followed by assembly of Src family of protein tyrosine kinases (PTKs), and binding of Src-SH2 domains to FAK at Tyr 397. FAK N-terminal domain truncation was thought to initiate Src-FAK Tyr 397 association leading to successive FAK phosphorylation at other tyrosine residues. These events were thought to fully activate FAK molecule (Lietha *et al.*, 2007). Additionally, mutant cells with truncated N-terminal domain exhibited an increased level of cell migration (Schaller, 2001).

Previous report suggested a role of FAK N-terminal domain in the suppression of p53 transcription, thus the N-terminal domain could have an anti-apoptotic activity leading to increase cell survival (Mittra and Schlaepfer, 2006). On the other hand, the N-terminal domain was shown to induce cell adhesion loss followed by apoptosis. The N-terminal domain appeared to be involved in

FAK nucleocytoplasmic translocation, which may lead to cellular rounding, detachment and then proceeding in apoptosis (Beviglia *et al.*, 2003).

The FAK C-terminal domain has many proteins interaction sites through which FAK can be localized and directed to adhesion complex regions. FAT domain is a part of the FAK C-terminal region which binds to paxillin and talin proteins, and contributes to supporting FAK localization to focal adhesions (Martin *et al.*, 2002). FAK-related-non-kinase domain (FRNK) an autonomously expressed C-terminal domain of FAK was thought to inhibit FAK kinase activity contributing to the inhibition of cell spreading as well as chemotactic and haptotactic migration (Hildebrand *et al.*, 1993; Hildebrand *et al.*, 1995). Besides that, it was implied that FRNK suppresses growth-factor-stimulated signals transduction to MAPK (Hauck *et al.*, 2001; Taylor *et al.*, 2001; Parson, 2003).

## FAK Phosphorylation, Activation and Inhibition

FAK tyrosine phosphorylation leads to the stimulations of different cellular responses (Schwartz & Assoian, 2001). Conversely, disrupting FAK association with ECM signalling molecules dephosphorylates FAK specifically at tyrosine residues, inhibits its activity and downregulates several cellular activities (Hynes, 2002; Sawai *et al.*, 2003).

FAK-integrins association at focal adhesions causes Tyr 397 phosphorylation and recruits Src kinases leading to FAK phosphorylation at other residues (Mittra & Schlaepfer, 2006). FAK phosphorylation at tyrosine residues is an essential event for FAK activation, cell attachment to the ECM, cell adhesion, cell proliferation and contribution to pathological transformation (Gabbarrá-Niecko *et al.*, 2003; Siesser & Hanks, 2006). The phosphorylation of FAK tyrosine residues is followed by the phosphorylation of intracellular proteins, creation of binding sites for many signalling proteins (Vuori, 1998) and forming signalling complexes at the focal adhesion regions (Ma *et al.*, 2001). Dephosphorylation of FAK tyrosine residues was reported to terminate FAK activity leading to inhibition of specific cellular activities such as migration, invasion and growth (Tamura

*et al.*, 1999; Schaller, 2001). FAK activation does not exclusively happen as a result of integrin clustering to focal adhesion plaques, instead, growth factors, neuropeptides and bioreactive lipids are known of activating FAK in integrin-independent manner (Sieg *et al.*, 1999). FAK activation can also be stimulated by platelet derived growth factors (PDGF), and human growth factor (HGF) (Chen *et al.*, 1998; Cospedal *et al.*, 1999). FAK association with Grb2, PI3-Kinase, and p130C signalling molecules enables it to work as a switchable adaptor protein, situated at a cross junction, controlling different signalling pathways and regulating different cellular activities (Hauck *et al.*, 2002; Beviglia *et al.*, 2003).

Unlike tyrosine phosphorylation serine phosphorylation appeared to have a negative regulatory effect on FAK. It was observed that serine phosphorylation is normally accompanied by deactivation and dephosphorylation of FAK tyrosine residues and FAK disassembly from signalling complexes (Yamakita *et al.*, 1999). It was reported that mitotic cells or cells at the interphase stage of cell cycle expressed elevated levels of FAK phosphorylated at serine residues (Yamaguchi *et al.*, 1997; Yamakita *et al.*, 1999). Therefore, serine phosphorylation appeared to be involved in cell cycle progression while it may have a downregulatory function on tyrosine phosphorylation.

Generally, FAK phosphorylation at different tyrosine residues has been associated with the development of various types of tumours (McLean *et al.*, 2005). FAK Tyr 397 which is located upstream of the kinase domain is important for supporting adhesion strength, and recruitment of signalling proteins following integrin binding (Michael *et al.*, 2009). Tyr 397 was correlated with higher potencies of cellular migration, proliferation and apoptosis protection (Mon *et al.*, 2006). FAK Tyr 397 has been considered as the only autophosphorylation site on FAK and its phosphorylation initiated FAK phosphorylation at various residues. It has been thought that the phosphorylation of this site is critically required in integrin-mediated FAK signalling (Siesser & Hanks, 2006). One possible explanation about FAK Tyr 397 activation role in cancer is that through the activation of MAPK pathway. Following phospho-FAK Tyr 397-Src association, FAK activation at Tyr 925

creates binding site for Grb2-SOS complex, and consequently involves FAK in MAPK signalling (Schlaepfer & Hunter, 1996). MAPKs act as switches for breast cancer angiogenesis during the development of breast tumour (Luo *et al.*, 2009). Specifically, ERK-MAPK plays a significant signalling role in tumour cell invasion, and may regulate Rho and Rac GTPases signalling pathways. Thus, MAPK-FAK association could contribute to signals convey downstream of Ras oncogene, which is involved in cancer cell proliferation, motility, survival and invasion (Vial *et al.*, 2003). The rest of tyrosine residues are thought to be phosphorylated following Src kinases binding to FAK through Src-SH2 binding domain (Mon *et al.*, 2006). For these reasons, autophosphorylation of FAK Tyr 397 may be considered as the most important event in FAK activation.

FAK association with Src proteins is required for FAK activation. FAK-Src binding is essential for FAK phosphorylation at Tyr 407, Tyr 576, Tyr 577, Tyr 861, and Tyr 925 leading to maximal FAK activation (Schaller, 2001; Mon *et al.*, 2006). Following FAK-Src binding, several signalling molecules will be recruited and activated. FAK-Src association triggers signalling pathways output amplification leading to the stimulation of various cellular responses (Siesser & Hanks, 2006; Caron-Lormier & Berry, 2005).

FAK Tyr 407 phosphorylation appeared to have a negative effect on cell adhesion, spreading, migration and proliferation (Jeon *et al.*, 2007). Elevated levels of phospho-FAK Tyr 407 were observed when cells were grown under stress conditions, such as during serum starvation, cell cycle arrest and contact inhibition. FAK Tyr 397 phosphorylation was suppressed as a result of FAK Tyr 407 phosphorylation, thus FAK Tyr 407 may negatively affect FAK kinase activity and reduce total FAK activation (Lim *et al.*, 2007). According to other report findings, concurrent activations of FAK, Tyr 407 and Tyr 397 residues were directly correlated with more differentiated colon tumour with less malignant status (Matkowskyj *et al.*, 2003). On the contrary, endothelial cells expressed elevated levels of phospho-FAK Tyr 407 following exposure to vascular endothelial growth factor. Therefore, FAK Tyr 407 could be involved in the transduction of vascular endothelial growth

factor signalling, as it stimulates recruitment of focal adhesion molecules with the increase of endothelial cells migration (Le Boeuf *et al.*, 2004).

FAK Tyr 861 role in cancer was more prominent in breast cancers than any other cancers. FAK Tyr 861 activation was implicated in FAK- $\alpha\beta 5$  integrins association, and was thought to work downstream of Src kinases. Moreover, FAK Tyr 861 was implicated in triggering signalling pathways leading to vascular development and angiogenesis (Eliceiri *et al.*, 2002). Previous study western blots analysis showed co-expressions of phospho-FAK Tyr 861 and HER2 proteins in breast cancer (Schmitz *et al.*, 2005). This could indicate a role of FAK phosphorylation, especially at Tyr 861, in regulating cell signalling of human breast cancer.

FAK Tyr 576 and Tyr 577 are located in the kinase domain. Phosphorylation of these tyrosine residues is highly required to attain optimum FAK kinase activity (Jacamo *et al.*, 2007). FAK Tyr 576 and Tyr 577 phosphorylations are important events for restoring autoinhibited conformational FAK activity resulting in increasing FAK phosphorylation (Cox *et al.*, 2006). FAK Tyr 925 phosphorylation creates binding site for Grb2 protein through FAT sequence of the C-terminal domain, and was thought to have a role in cancer cell proliferation (Zhao & Guan, 2009). Besides that, FAK Tyr 925 was implicated in the induction of Ras signal transduction pathway through its association with Src family kinases. Activation of Ras pathway was expected to happen independently of integrin clustering (Schlaepfer & Hunter, 1996). Therefore Tyr 925 could be involved in the signal transduction pathway in integrin independent manner.

Tyrosine dephosphorylation is as crucial as tyrosine phosphorylation in modulating events happening at focal adhesions. PTP-PEST is one of the important phosphatases secreted at the focal adhesions. Cells lacking of PTP-PEST exhibited a decrease in focal adhesions with migrational defects (Angers-Loustau *et al.*, 1999). However, elevated levels of PTP-PEST resulted in impaired associations and phosphorylation of many focal contacts signalling proteins (Garton & Tonks, 1999). Therefore, PTP-PEST is secreted in a proper balance, and it acts as a key regulator for focal adhesion molecules phosphorylation (Sastry *et*

*al.*, 2002). FAK inactivation can also happen by a tumour suppressor gene known as PTEN which inhibits FAK phosphorylation leading to FAK deactivation (Lipinski *et al.*, 2003).

### **FAK as a Scaffold and Src Stimulator Protein**

FAK has also been considered as a scaffold protein which has the capability of nucleating multivalent scaffold complex at adhesion plaques (Carlucci *et al.*, 2008). FAK involvement in the regulation of multiple signalling pathways is through to happen through its homology (SH2 and SH3) binding to different signalling proteins like paxillin, p130Cas, Src-family PTKs, p85 subunit of phosphatidylinositol 3-kinase (P13-kinase), Shc and Grb2 proteins (Schlaepfer *et al.*, 1999; Jacamo *et al.*, 2007). However, FAK stimulation of these signalling molecules mainly happen due to the employment of FAK N-terminal domain. This domain helps in connecting FAK with integrins receptors whereby signals will be transmitted downstream triggering FAK activity (Sun *et al.*, 2002; Parsons *et al.*, 2003). Both FAK and integrins especially  $\beta$ -integrin participate in signalling cascades initiation that transmits signals to downstream targets. FAK-integrins association is required for Focal adhesion complex (FAC) establishment within sites of focal adhesions. FAC supports FAK performance as docking site for binding to several pathways mediator molecules (Ilic *et al.*, 1997; Mitra *et al.*, 2005). Apart from that, recruitment of focal adhesion molecules and growth factor receptors such as EGFR and PDGFR to the site of adhesion further stimulates FAK signalling activity (Cohen & Guan, 2005).

FAK involvement in Src activation is not fully understood. It was shown that Src can be activated by integrins independent of FAK. That is,  $\alpha 4\beta 1$  integrins stimulate Src activation, and restore motility defects in FAK-null fibroblasts (Hanks *et al.*, 2003; Mitra and Schlaepfer, 2006). Src stimulation also leads to the activation of p130Cas-associated motility-promoting signalling pathway which is proposed to have a critical function in modulating cellular motility regardless of Src mode of activation (Hanks *et al.*, 2003; Mitra and Schlaep-

fer, 2006). In other words, it can regulate cellular motility either by  $\alpha 4\beta 1$  integrins or by FAK dependent manner.

### FAK Involvement in Cell Adhesion and Migration

FAK was implicated in cellular force, stress and contraction, also morphological changes were noticed when cells showed marked decrease in FAK activation, and cellular death increased as a result of cellular cytoskeleton defects in FAK deficient cells (Mitra *et al.*, 2005). FAK depletion in endothelial cells produced cells that appeared rounded in shape with less polarity. In addition, FAK deficient cells showed broad lamellipodia with extended protrusions (Braren *et al.*, 2006). According to previous report (Michael *et al.*, 2009), FAK role in adherent cells survival is based on its kinetic role in the formation of adhesive forces. FAK activity was thought to be governed by time-dependent adhesive force mechanosensing responses, where integrin binding and activation are regulated by FAK up-regulatory manner.

FAK was also implicated in protecting ECM-detached cells from undergoing anoikis, and by the virtue of its association with integrin clusters FAK was thought to play a regulatory function in cell adhesion strengthening (Haier & Nicolson, 2000).

Cell migration is a coordinated process resultant from rapid dynamic changes of actin filaments (Mitra *et al.*, 2005). Cell filopodia are formed by parallel bundles of actin, whereas lamellipodia are formed of dense actin meshwork arrangements. Both actin structures are involved in guiding cell motility at cell leading edge, and creating driving forces that enhance forward movement (Etienne-Manneville, 2004). FAK's role in migration was proven both *in vivo* and *in vitro* (Hauck *et al.*, 2002; Braren *et al.*, 2006). FAK as a scaffold protein enables it to regulate a range of intracellular signalling molecules namely such as Grb7, Rac, PI3K and others. Therefore it has been implicated in actin and microtubule filaments polymerization (Hanks *et al.*, 2003), thus directs membrane protrusion and cell polarity toward forward movements. In previous study, FAK levels increased in migrating cells when wound repair assay had

been performed. However, FAK-null mice fibroblast cells failed to migrate but restored migration capacity following FAK transfection (Owen *et al.*, 1999; Lipinski *et al.*, 2003).

### FAK Involvement in Cancer Invasion and Metastasis

Several studies have proposed that tumour cells that have the tendency to invade adjacent tissues and metastasize *in vivo* usually showed increased levels of FAK (Gabarra-Niecko *et al.*, 2003; Hsia *et al.*, 2003). Cancer metastasis requires but not always shared function of matrix metalloproteinases (MMPs) for ECM barriers destruction to allow invasion. MMPs are localized and stimulated at actin-rich cellular points, where association with ECM took place. These contact places termed as invadopodia or podosomes are constitutively distinct from focal adhesions (Siesser and Hanks, 2006). Increased expressions of MMPs such as MMP-2, MMP-7, MMP-9 and MMP-13 have been implicated in various types of cancer (Sternlicht *et al.*, 1999; Coussens *et al.*, 2002; Egeblad and Werb, 2002).

For MMPs-dependent invasion, FAK is involved in MMPs secretion and is known to localize at invasive fronts. Invasion can also happen independent of MMPs secretion but depended on FAK to regulate or promote different mechanisms of tumour invasions (McLean *et al.*, 2005). MMP-9 secretion is thought to be stimulated through FAK upstream regulation. MMP-9 secretion requires cell attachment to ECM where variety of signalling proteins including FAK are of importance (Sein *et al.*, 2000). MMP-2 activation was thought to happen following the stimulation of a cell surface protein known as membrane-type 1 matrix metalloproteinase (MT1-MMP) which is implicated in the cleavage of pro-MMP-2 to its active form, and was thought to be partially governed by FAK/ Src signalling pathway (Wu *et al.*, 2005).

### FAK Regulates a dynamic Balance between Cell Survival and Apoptosis

Intracellular signalling pathways that regulate and maintain cellular growth and survival are

governed by shared signalling networks involving growth factor receptors, integrins and transmembrane receptors (Gilmore, 2005). It is thought that survival or growth signalling pathways interruption through FAK inhibition can stimulate cell cycle arrest and execution (Xu *et al.*, 1996; Cance *et al.*, 2000). Besides that, FAK translocation between cytoplasm and nucleus has been implicated in cell survival (Sein, 2000; Hauck *et al.*, 2002; Hsia *et al.*, 2003; Mon *et al.*, 2006), though the relation between FAK localization and apoptosis is still not well clarified.

In reference to FAK structural functions, FAK N-domain in was shown to regulate FAK kinase activity and associate with SUMO protein (Parsons *et al.*, 2003; Cox *et al.*, 2006). SUMO is a FAK modifier which adapts FAK function through its binding to the FAK N-domain, SUMO-FAK association led to FAK localization to nuclei (Golubovskaya *et al.*, 2005; Stewart *et al.*, 2002). However, only recently, the signals that promote or regulate FAK shuttling in and out of the nucleus were limitedly revealed. FAK nuclear localization was also shown to be putatively governed by sequences of leucine-rich nuclear export signals (NES). NES signalling, mainly NES1 and NES2, instigates nuclear protein translocation to cytoplasm (Terry *et al.*, 2007). NES1 sequence is ubiquitously located in the F1 lobe of FAK-N domain, whereas NES2 is situated in the kinase domain of FAK. Both signals are proposed to enable FAK nucleocytoplasmic shuttling (Ossovskaia *et al.*, 2008). Given that NES2 sequence is not affected by the structural alterations that take place in the FAK kinase domain (Lietha *et al.*, 2007) it could play a crucial role in the regulation of FAK nucleocytoplasmic shuttling (Ossovskaia *et al.*, 2008).

p53 is considered as one of the most powerful apoptosis triggers upon its activation (Reddig and Juliano, 2005). Usually, when cells are subjected to stabilized growth conditions p53 is maintained at low levels (Vousden, 2002). Cells exposure to stress conditions can enhance p53 stability leading to the stimulation of cell cycle targets like p21<sup>Cip</sup>/WAF1 (p21), a cyclin-dependent kinase inhibitor which is stimulated following the exposure to cell death triggers (Oren, 2003; Harris and Levine, 2005). ECM-integrin association was shown to maintain cell survival and stimulate p21

degradation with abrogated p53. The correlation between cell survival and integrin, p21 and p53 is not completely understood but is thought to be regulated through FAK nucleocytoplasmic shuttling (Stromblad *et al.*, 1996; Bao *et al.*, 2002). FAK has been implicated in p53 inhibition (Golubovskaya *et al.*, 2005; Cance & Golubovskaya, 2008). Lim *et al.* (2008) has discussed FAK role in nuclear localization on mouse embryonic fibroblasts cells (MEFs), and suggested that nuclear FAK enhanced cell survival through the degradation of p53 by FAK kinase-independent manner. It was shown that nuclear FAK N-domain works as a scaffold to embrace and stimulate Mdm2 function leading to p53 ubiquitination (Lim *et al.*, 2008). Mdm2 (Murine double minute-2) is one of the p53 regulatory members which regulates p53 level in living cells (Iwakuma and Lozano, 2003).

Receptor interacting protein (RIP) is a serine/threonine kinase which embraces a death domain (Hsu *et al.*, 1996). RIP has been considered as an important member of the death receptor complex, and was considered as a possible switch between survival and apoptosis (Martinon *et al.*, 2000). FAK binding to RIP has been reported to play an important role in apoptosis signalling for both breast cancer cell lines and mouse embryonic fibroblasts (Kurenova *et al.*, 2004). However signalling involving FAK and RIP in apoptosis is not completely understood. It was reported that anoikis stimulated by Fas/CD95 signalling stimulated Fas association with RIP and detached RIP-FAK binding (Kamarajan *et al.*, 2010). RIP creates proapoptotic signals that induce apoptosis, while RIP binding to FAK was thought to inhibit its activity (Kurenova *et al.*, 2004).

FAK signalling contribution to cell cycle progression has received some attention, FAK was shown to enhance the progression of cell cycle and induce proliferation through the acceleration of G1 phase-M phase transition (Zhao *et al.*, 2009). Besides that, FAK stimulated cyclins D1 and E but inhibited p27<sup>Kip1</sup> and p21<sup>Waf1</sup> which are required in the regulation of the cell cycle. Importantly, FAK deactivation at the autophosphorylation tyrosine site Tyr 397 inhibited cell cycle progression and lead to p27<sup>Kip1</sup> and p21<sup>Waf</sup> activation which inhibited proliferation (Ding *et al.*, 2004).

## Focal Adhesion Kinase and Cancer

FAK expression in cancer cells was shown to increase dramatically along with cancer progression, normal tissues and benign tumours expressed low amounts of FAK, while invasive and metastatic tumours expressed high FAK levels (Owens *et al.*, 1995; Gabarra-Niecko *et al.*, 2003). Malignancies usually require overactivation of intracellular signalling pathways for the progression of cancer (Tilghman & Parsons, 2008), besides that FAK activation has been implicated in the activation of diverse signalling molecules which are more activated in cancer. Therefore, FAK has been considered as a key factor which upregulates several cellular functions (Niwa *et al.*, 2005).

According to previous reports, FAK was overexpressed in various types of cancers like colon, breast, ovarian, thyroid, prostate, mesenchymal tumours (Owens *et al.*, 1995; Tremblay *et al.*, 1996), head, neck, and esophagus (Lark *et al.*, 2005). Equally important, at early stages of blood tumourigenesis adhesion to marrow stromal cells protects acute myeloid leukaemia cells (AML) from undergoing apoptosis, and prolongs their survival (Burger *et al.*, 2003). In patients diagnosed with AML FAK expression was frequently detected at protein and gene levels in about 50 % of AML patients (Recher *et al.*, 2004). In an ovarian cancer study analysis, elevated FAK levels were significantly associated with more invasive and metastatic tumours (Sood *et al.*, 2004). FAK expression has been correlated to the development of breast cancer from normal to non invasive and invasive phenotypes (Luo *et al.*, 2009). Based on past study, the progressive increase of FAK level accompanied colon tumour development into invasive and metastatic tumours (Owens *et al.*, 1995).

One possible elucidation of phospho-FAK role in supporting cancer cells proliferation and survival, specifically breast, is through the involvement in BRCA1-STAT1 pathway. BRCA1 (also called breast cancer type 1 protein) is a tumour suppressor gene which regulates several functions of normal cells (Smalley *et al.*, 2008). It has been shown that BRCA1 mutation could be associated with breast cancer progression, induced proliferation and protection from apoptosis (Somasundaram *et al.*, 1997). Based on previous report (Zhang *et al.*, 2010), FAK phosphorylation initiated its interaction with Signal

transducers and activators of transcription (STATs). Through this association, the FAK-STAT1 pathway was expected to regulate cell apoptosis, invasion and metastasis (Cáceres *et al.*, 2005; Zheng *et al.*, 2009). Abnormal BRCA1 may interact with STAT1 to induce proliferation and prolong survival (Zhang *et al.*, 2010), similarly FAK-STAT1 activation is involved in apoptosis protection (Cáceres *et al.*, 2005; Zheng *et al.*, 2009).

To summarize, the correlation between FAK signalling and signal transduction of cancerous diseases is not well understood. Further work is necessary to dissect the mechanisms used by tumour cells and non-tumour cells to activate FAK besides other signalling proteins. Decoding FAK signalling seems to be essential to design targeted therapies directed to specific signalling molecules. This will yield an important new cancer therapy which could be utilized as effective compounds to inhibit tumour progression.

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## Abbreviations

FAK (Focal Adhesion Kinase),  
 MAPK (Mitogen Activated Protein Kinase),  
 FAT (Focal Adhesion Targeting Domain),  
 FRNK (FAK Related Non-kinase Domain),  
 ECM (Extracellular Matrix),  
 EGFR (Epidermal Growth Factor Receptor),  
 PDGFR (Platelet Derived Growth Factor Receptor),  
 MMPs (Matrix Metalloproteinases),  
 NES (nuclear export signals),  
 RIP (Receptor Interacting Protein),  
 AML (Acute Myeloid Leukaemia).

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# Knowledge level of patrons attending community pharmacies in Pakistan: Is it a threat to rational use of drugs?

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## Abstract

**Background:** Knowledge on drug use is important for patient compliance and in achieving the desired therapeutic outcome of the medicines. The information on drug use is received by the patient or its care giver through counselling while dispensing medications.

**Objectives:** The study evaluated the knowledge of patrons regarding drug use attending community pharmacies in three major cities of Pakistan.

**Methods:** A total of 1113 patrons were interviewed from a randomly selected sample of 371 pharmacies and the patrons were selected by using convenient sampling technique when patronaged these pharmacies in the three respective cities namely Islamabad (n=118), Peshawar (n=120) and Lahore (n=133). A structured questionnaire was developed and finalized by focused group discussions and through pilot testing. Knowledge assessment scale was used to measure the knowledge of patrons regarding drug use. Kruskal-Wallis and Mann-Whitney tests were performed to find out differences among the knowledge of patrons regarding drug use.

**Results:** Less than three quarter of the respondents were aware regarding the medicines they were buying. Only, thirty five percent were aware of the name of the drug, 6.9% knew the name of drug along with the condition while 6.8 % knew that they were buying analgesic, 2 % flu remedy and 4.3% antibiotics. Significant differences were observed in the knowledge of patients in the three cities and rural/urban settings.

**Conclusions:** The overall knowledge of patrons on medicine use attending community pharmacies is inadequate. Patrons attend pharmacies to purchase medicines suggested by different individuals who may at times are not qualified dispensers. The pharmacies are somehow failing to play their effective role in enhancing consumer knowledge.

**Key words:** Community pharmacy, Drug use, knowledge, Patron, Pakistan

## Background

Majority of the population depends on community pharmacies to buy medicines in countries where health care is largely provided by the private sector [1-2]. Knowledge on drug use is important for the patrons for achieving compliance and desired therapeutic outcome of the medicines. The information on drug use is received by the patrons or its care giver through the process of counselling by the doctor or pharmacists. The quality of information provided is directly proportional to the compliance and better use of medications by the patrons. Thus it becomes important to see the quality of information provided to the patrons and the patron's knowledge on drug use [3]. The perception of community pharmacies as advisors on general health care does not appear to be shared by the public. Most consumers have previous experience of their ailments and use pharmacies as one of several resources available to them to treat their minor illness, having made their own diagnosis and assessment before entering the pharmacy. Thus, the scope for giving new advice is therefore limited [4].

Community pharmacies in developed countries are providing pharmaceutical care services to their patrons to improve the quality of life. The pharmacies in these countries pay special emphasis on improving patrons knowledge regarding drug use and consider patrons counselling as an important component of pharmaceutical care services [5]. The role of community pharmacies as an essential component of health care system is well established and is recognized by the general population in developed countries. People expect information regarding medicine use and their possible side effects from the pharmacies.

On the other hand in most developing countries, community pharmacies rarely take into account any patrons related services which can enhance patrons knowledge and satisfaction regarding drug use. The emphasis is more business oriented rather than on addressing health needs in an equitable and effective manner [6]. This decreases the credibility of pharmacies and consumers consider these pharmacies simply as drug sale outlets. People take medications according to their own wish or based on the advice of a drug seller, neighbour, friends or relatives, availability of wider range of drugs at low cost depending on their purchasing power they can get full or half dose, without any restrictions from the drug sellers [7]. This is a common practice in most developing countries where drugs are sold over the counter with or without prescriptions [8].

People's beliefs and knowledge about medicines influence the way they take medications as prescribed to them. Gaps have been identified by various studies in training, knowledge and qualification of dispensers working at community pharmacies in Pakistan. This in turn impacts the quality of information given to the patrons and ultimately on their drug use [9-11]. The present has been designed to assess the knowledge of patrons/customers regarding drug use, attending community pharmacies in the three major areas of Pakistan namely Islamabad (national capital), Peshawar (capital of Khyber *Pakhtoonkhwa*) and Lahore (capital of Punjab province) and highlights the importance of patrons counselling to achieve better outcomes of therapy.

## Methodology

A survey was conducted between April-June 2008. A total of 1113 patrons/customers interviews were conducted from a randomly selected sample of 371 pharmacies by using convenient sampling technique in the three respective cities namely Islamabad (118), Peshawar (120) and Lahore (133). The study population included all community pharmacy outlets in Islamabad, Lahore and Peshawar cities selling allopathic medicines, or homeopathic or herbal medicines if sold alongside allopathic medicines. Any community pharmacy meeting this definition constituted the sampling unit.

The data collection tool was developed by focused group discussions and using the references of Drug Act of Pakistan 1976 and relevant rules under, Good Pharmacy Practice guidelines, International Pharmaceutical Federation (FIP) guidelines and inspection book of pharmacies. Focus group discussions were carried out with four different groups i.e. community pharmacist, drug inspectors, academia and members of consumer groups, each comprising of 3-4 participants for development and finalization of data collection tool. The study was approved by the panel of experts at Research & Development section of Drug Control Organization at Ministry of Health, Government of Pakistan.

A structured questionnaire with coded responses and few open ended questions was used to get information regarding patrons/customers knowledge regarding drug use attending community pharmacies. Face and content validity was built through panel of pharmacy research experts, community pharmacists, statistician and pilot testing. The value of Cronbach's alpha was 0.843 which was applied to assess the reliability and internal consistency of the tool used to collect data. The questionnaire included a total of seventeen questions which included information on demographics, about what drug was bought, for whom it was bought, who suggested the drug, prior experience of use of drug, provision of written and oral information and expectation and satisfaction from the pharmacy. A scale including five parameters on drug identification its dose, frequency, duration and administration relation to diet was conside-

red as a minimum standard of patrons/customers knowledge. The score of scale was between 5-10 and lower scores referred to better knowledge of patrons/customer.

Three teams, one in each city comprising of ten data collectors in each team were trained by the group of experts including principal investigator. In Islamabad and Lahore, data collectors were both male and females however due to the gender barriers in Peshawar only male data collectors were engaged. Local chapters of chemist and druggist association were also contacted and informed regarding the study. Informed and verbal consent for participation was taken from the respondents. Respondents were ensured for the confidentiality of information verbally as well as confidentiality under taking signed by the principal investigator was shown.

After the data collection, data was cleaned, coded and entered in SPSS 16 version. Kruskal-Wallis test ( $p < 0.05$ ) was used to compare patron's/customer's knowledge among cities and by whom medicine was recommended. Mann Whitney test ( $p < 0.05$ ) was used to compare patron's/customer's knowledge among rural and urban setting and provision of oral or written information among cities on the knowledge of patron's/customers.

## Results

A total of 1113 patrons/customers visiting at 371 community pharmacies for purchase of medicines

were interviewed in three main cities of Pakistan namely Islamabad, Peshawar and Lahore. Out of 371 pharmacies (118) 31.8% were in Islamabad, (120) 32.3% in Peshawar and (133) 35.8% were in Lahore. The urban rural distribution of pharmacies was 77 and 23 percent respectively. The mean age of respondents was 35 years out of which 79% were male while remaining 21% were female.

Forty eight percent of respondents visited the pharmacies to buy medicines for their family members, 46% came to buy their own medicines, 5.3% bought for someone else while 0.6% do not know for whom they were purchasing the medicines. Thirty five percent of respondents were aware of the name of the drug while 6.9 % were aware of the name of drug along with the condition, 6.8 % reported that they came to buy analgesic, 2 % bought flu remedy and 4.3% bought antibiotics. When asked that who has decided for them to buy this medicine, 74.8% responded that the drugs were recommended by doctor, 17.3% by themselves while 5.5% were suggested by the drug seller.

Eighty one percent of respondents claimed that they knew how to use the purchased medicines. Written information was received by only 1.3% of the respondents while only 29.8% received verbal information from the drug sellers. Majority of respondents (90.7%) thought that pharmacy is a place to buy medicines only while 1.7% thought that they can also seek drug information. When asked whether they were satisfied with the performance of the pharmacies 70.7% were fully satisfied, 8 % were satisfied to some extent and 4.9% were

Table 1. Knowledge of patrons regarding drug use attending community pharmacies in the three cities

Sr. No	Indicator	Description	Islamabad n = 354		Peshawar n = 360		Lahore n = 399		Composite n = 1113	
			F	%	F	%	F	%	F	%
1	Drug identification	Know correctly	246	69.5	172	47.8	294	73.7	712	64
2	Dose of drug	Know correctly	243	68.6	232	64.4	288	72.2	763	68.6
3	Frequency of drug	Know correctly	222	62.7	282	78.3	276	69.2	780	70.1
4	Duration of drug	Know correctly	146	41.2	139	38.6	218	54.6	503	45.2
5	Administering relation with diet	Know correctly	66	18.6	69	19.2	106	26.6	241	21.7

not satisfied. Sixty four percent of the respondents were able to identify the drug correctly, 68.6% respondents were aware of the correct dose of the drug, 70.1% respondents told correct frequency of the drugs, and 45.2% respondents told correct duration of the drug use while 21.7 % of the respondents were aware of the administration of drug with relation to diet.

The composite median of knowledge assessment scale of patrons/customers among the three cities was found to be 7 (6-9). While the median obtained in individual city was 7 (6-9) Islamabad, 7 (6-9) Peshawar and 7 (6-9) Lahore. Significant difference at ( $p < 0.05$ ) was seen in the knowledge of patrons/customers purchasing drugs from the community pharmacies in the three cities. The knowledge of patrons/customers was found to be relatively better in Lahore as compared to Islamabad and Peshawar.

*Table 2. Comparison of knowledge of patrons/ customers regarding drug use attending community pharmacies in three cities*

Indicator	Knowledge about drug use
No of exit interview	1113
No of drugs bought	Islamabad = 606 Peshawar = 819 Lahore = 621
H	22.757
P value	0.000*

\*Kruskal Wallis Test at  $p = 0.05$ , Significant at ( $p < 0.05$ )

Significant difference ( $p < 0.05$ ) was seen regarding the knowledge of patrons/customers purchasing drugs from the community pharmacies in the rural/urban setting. Patrons/customers attending

community pharmacies in urban settings had comparatively better knowledge as compared to those in rural setting.

Significant difference ( $p < 0.05$ ) was seen among recommendation from different providers on the knowledge of patrons/customers purchasing drugs from the community pharmacies. The knowledge of patrons/customers on drug use was better for those who were self medicating as compared to those who were prescribed by physicians or suggested by the drug seller.

Significant difference at ( $p < 0.05$ ) was seen in the knowledge of patrons/customers purchasing drugs from the community pharmacies when oral information was provided. The results of the present study showed that the provision of oral information if provided had a significant impact on the knowledge of the patrons/customers regarding drug use.

## Discussion

Knowledge of patrons/customers attending community pharmacies in Pakistan is inadequate. A large number of patrons attend community pharmacies as it is economical to seek treatment for their minor ailments in lesser time [8]. But it is an undeniable fact that the community pharmacies has failed to provide all the patron oriented services in most of the countries [12]. Community pharmacists had failed to balance between professionalism and business needs. Lack of adequate knowledge of patrons/customers refers to their low demand for the provision of information from the dispensers working at community phar-

*Table 3. Comparison of knowledge of patrons/customers attending community pharmacies in rural/ urban settings between cities regarding drug use*

Indicator	Islamabad	Peshawar	Lahore	Composite
	Knowledge about drug use	Knowledge about drug use	Knowledge about drug use	Knowledge about drug use
No of exit interviews	Urban= 294 Rural = 60	Urban= 204 Rural = 156	Urban= 363 Rural = 36	Urban= 861 Rural = 252
No of drugs bought	Urban = 497 Rural = 109	Urban = 448 Rural = 331	Urban = 572 Rural = 49	Urban = 1557 Rural = 489
U	22176.500	71110.00	8603.500	304924.500
P value	0.002*	0.001*	0.000*	0.000*

\*Man Whitney Test at  $p = 0.05$ , Significant at ( $p < 0.05$ )

Table 4. Comparison of recommendation of medication by different individuals on knowledge of patrons/customers attending community pharmacies in the three cities

Indicator	Islamabad n= 354	Peshawar n= 360	Lahore n= 399	Composite n= 1113
	Knowledge about drug use	Knowledge about drug use	Knowledge about drug use	Knowledge about drug use
Recommendation of drug	By physician = 261 By myself = 70 By drug seller = 23	By physician =285 By myself =49 By drug seller =16 Others =10	By physician =287 By myself =74 By drug seller =22 Others =16	By physician =833 By myself =193 By drug seller =61 Others =26
No of drugs bought on recommendation	By physician = 481 By myself = 88 By drug seller = 37	By physician = 694 By myself = 79 By drug seller = 28 Others = 18	By physician = 469 By myself = 102 By drug seller = 28 Others = 22	By physician = 1644 By myself = 269 By drug seller = 93 Others = 40
H	12.721	23.169	19.540	31.315
P value	0.000*	0.000*	0.000*	0.000*

\*Kruskal Wallis Test at  $p = 0.005$ , Significant at ( $p < 0.05$ )

Table 5. Comparison of provision of oral information by the drug seller on knowledge of patrons/customers attending community pharmacies in the cities

Indicator	Islamabad n=354	Peshawar n= 360	Lahore n= 399	Composite n= 1113
	Knowledge about drugs	Knowledge about drugs	Knowledge about drugs	Knowledge about drugs
Oral information	Received =77 Not received =277	Received =211 Not received =149	Received =44 Not received =355	Received =332 Not received =781
U	10232.00	11096.00	6589.00	119976.500
P value	0.056	0.000*	0.007	0.000*

\*Man Whitney Test at  $p = 0.05$ , Significant at ( $p < 0.05$ )

macies [13]. It has been reported by many studies that dispensers working at community pharmacies in developing countries lack knowledge and proper training for handling the patrons thus in terms translating into poor knowledge of patrons/customers regarding drug use [9, 11, 14].

The result of the study highlights that the overall knowledge of patrons/customers in the three cities was low but the knowledge of patrons/customers was found to be better in Lahore as compared to Islamabad and Peshawar. On the other hand patrons/customers attending community pharmacies in urban settings had better knowledge as compared to those in rural setting. Similar pattern of better knowledge from urban setting was reported in a study from Lao PDR in which people living in urban areas had better knowledge regarding drug quality and its use [15]. This better knowl-

edge may also refer to the higher literacy rates in urban centres as compared to rural areas. Better knowledge have been found to be associated with higher levels of education of patrons [16, 17].

Availability of medicines with out prescription is an issue in developing countries. The results of the study highlights that only a smaller proportion of patrons/customers were self-medicating, while a larger population of patrons/customers claimed that they were taking medicines on the advice of the physician but did not carry any prescription. This claim of patrons/customers reflects their previous experience of consulting a physician. The knowledge of patrons/customers on drug use was better for those who were self medicating as compared to those who were prescribed by physicians or suggested by the drug seller. This better knowledge can be due to their previous experience of using the



medicine and when the patrons/customers are buying medicines for themselves are more concerned to acquire knowledge. Similar results had been reported indicating that the consumers seek knowledge about drug use to assess the effects of their medicine, in particular the side effects. This is more common among those consumers who self-medicate for themselves and their families [18].

It is a common observation that most of the pharmacies do not provide any information to the patrons/customers and if any information given is usually in form of verbal communication and occasionally in written form [19]. The results of the present study showed that the provision of oral information if provided had a significant impact on the knowledge of the patrons/customers regarding drug use while the provision of written information was missing. This largely reflects on the approach of community pharmacies only as drug sellers and not as professionals with a responsibility to enhance safe use of medicines and poor knowledge of drug sellers about medicine use [13, 20].

### **Implications on practice**

The present study is significant and contributes in this aspect as it has assessed the knowledge of the patrons/customers about drug use attending community pharmacies across three major cities of Pakistan and will serve as a baseline to design future interventions to assess how patrons/customers knowledge about drug use can be improved by focusing on patrons counseling for the desired therapeutic outcomes.

### **Study recommendations**

The need of promoting public awareness should be recognized by the community pharmacies and priority must be accorded to provision of appropriate patron information including its dose, frequency, use, administration with diet and side effects. This can be achieved through proper legislation and its implementation by involving different concerned stakeholders. Mass media awareness should be involved to inform the general

public of the potentials of community pharmacies in promoting safe and effective drug therapy. The presence of qualified persons can ensure better handling of patients at community pharmacies thus helping them to know their medicines in a way, which can improve compliance and reduce the related adverse effects.

### **Limitations of the study**

These findings are important in giving information on the current level of knowledge of patrons/customers but no information about the educational level of the customers or socio-economic data was obtained.

### **Conclusion**

The overall knowledge of patrons/customers on medicine use attending community pharmacies is far beyond acceptable. Patrons/customers attend pharmacies to purchase medicines suggested by different individuals who may at times are not qualified prescriber. The patrons/customers attending community pharmacies may claim that the medicine has been suggested by a prescriber but may not carry a prescription which reflects on their previous experience of consulting a physician. The pharmacies are somehow failing to play their effective role in enhancing consumer knowledge. The provision of information at community pharmacies is scanty and reflects on the poor communication of dispenser working at community pharmacies.

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# The determination of women's fatigue levels in the third trimester of pregnancy and in the postpartum period

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## Abstract

**Objective:** To determine women's level of fatigue in the 3rd trimester of pregnancy and in the postpartum period.

**Subject and methods:** A descriptive and prospective study. The participants were 121 women who came to the obstetric clinic for prenatal control in the 3rd trimester of their pregnancy. All of them were followed up at the end of the first postpartum month. A Visual Analogue Scale for Fatigue (VAS-F) was used to measure fatigue levels.

**Results:** Older and unemployed women had more fatigue. Gravidity, parity, the number of living children and pregnancy interval did not affect mean fatigue score. The mean fatigue score for the pregnant women in the 3rd trimester was  $70.22 \pm 20.7$ , and their mean energy score was  $24.61 \pm 7.7$ . The mean fatigue score at the end of the first postpartum month was  $66.82 \pm 20.9$ , and their mean energy score was  $25.39 \pm 8.6$ . It was determined that the severity of fatigue was higher in the 3rd trimester than in the postpartum period. There was a positive correlation between 3rd trimester fatigue and postpartum fatigue ( $P < 0.01$ ).

**Conclusion:** All the women in this study experienced fatigue both in the 3rd trimester and in the postpartum period. The severity of fatigue was higher in the 3rd trimester than during the 1st postpartum month.

**Keywords:** Postpartum fatigue, pregnancy fatigue, VAS-F.

## Introduction

Pregnancy and the postpartum period are physiological and psychological changing processes for

every woman. During these two periods of time there are changes in several systems in women [1]. There are also very rapid and complex physiological changes and repairs that occur in the body in the postpartum period, as there were in pregnancy. Women may have some complaints as a result of the changes occurring during pregnancy and in the postpartum period. Fatigue is one of the common complaints experienced by women [2-5].

Fatigue can affect a woman's general health and it can lead to some problems. The previous studies have revealed that fatigue experienced in pregnancy leads to some complications such as spontaneous abortion, preterm birth, early membrane rupture and increase in caesarean birth [5-8]. The fatigue experienced in pregnancy and in the postpartum period can affect women's mental health, their social activities, women's sexual life and fulfillment of their responsibilities [9-11]. Fatigue not only affects women's activities but also their families' quality of life. Fatigue can interfere with the new mother's ability to care for her infant and with the mother's daily activities (self-care, infant care and household tasks) [3]. It was been reported that the care of newborns and other siblings is affected by fatigue in the mother [9,12]. For these particular reasons, midwives and nurses who care for women in pregnancy and in the postpartum period need to focus on the problem of fatigue. They also need to give consideration to the preservation and maintenance of the mother's and baby's health. If fatigue in the pregnancy and postpartum period is eliminated, the mother's and baby's health can improve and the mother can return to her normal life early.

Fatigue levels has not been evaluated in pregnant and postpartum women in East of Turkey. The aims of this study were to determine the level

of fatigue in the 3rd trimester of pregnancy and during the first postpartum month.

## Methods and materials

### Study design and sample

This is a descriptive and prospective study. The study was carried out in the Obstetrics and Gynecology Clinic at Atatürk University Research Hospital between April 2003 and April 2004. The study population consisted of pregnant women in the 3rd trimester of pregnancy who presented to the Obstetrics and Gynecology outpatient clinic for antenatal control. Using a random sampling method 150 pregnant women were chosen. All of the women were scheduled for follow up during the first postpartum month. However 29 of the women did not come for postpartum follow up and they excluded from the study. Therefore the study was conducted with the remaining 121 women. All the women included in the study gave birth to a healthy infant and they were their infant's caretaker. There were no pregnant women who refused to participate in the study.

### Measures

A questionnaire designed for this study and a Visual Analogue Scale for Fatigue (VAS-F) were used in the collection of data. The questionnaire form consisted of questions about sociodemographic details and obstetric history, and about when they started to experience fatigue.

Fatigue and energy levels in pregnancy and in the postpartum period were measured by the VAS-F. The scale was developed by Lee, Hicks, and Nino-Murcia [13]. It was adapted for Turkish by Yurtsever and Bedük [14], and its validity and reliability were examined. The VAS-F contains two subscales, 13 items measuring fatigue and 5 items measuring energy. The women indicated how they felt by making a mark on a line from 0 to 100 mm. The high point of the fatigue subscale and the low point of the energy subscale show that the intensity of fatigue is high.

In previous research [13] Cronbach's alphas for the fatigue subscales were .96(A.M) and .91(P.M.),

and for the energy subscales were .95(A.M.) and .94(P.M.). Yurtsever and Bedük [14] reported Cronbach's alpha for the VAS-F fatigue subscale was .90 and VAS-F fatigue subscale was .74. For this study Cronbach's alpha for the VAS-F fatigue subscale in pregnancy was 0.83, and VAS-F energy subscale was 0.63. In the present study Cronbach's alpha for VAS-F fatigue subscale in the postpartum period was 0.87, and Cronbach's alpha for VAS-F energy subscale was 0.77.

The data were collected from the pregnant women who came for prenatal control in the 3rd trimester of pregnancy and the same women at their fourth week postpartum. The data were collected using face-to-face interview technique in the morning.

The questionnaire was administered to the pregnant women and to the women at their 1st postpartum month in a separate room. Before data collection, women were informed about how to fill out the scale. Women who were illiterate were helped to fill in the questionnaire form and VAS-F by the researcher. It took them 15–20 minutes to fill in the VAS-F. Women participating in the study were telephoned by the researcher at the third week of their postpartum period and they were reminded to come for a follow up visit at the fourth week of the postpartum period. When the women in the postpartum period came for a follow up in the fourth week, data about the postpartum period were collected. After obtaining formal consent, in order to understand whether the questions were comprehensible or not, a pilot test was conducted with 15 pregnant women and then these pregnant women were excluded from the study.

Independent variables were the sociodemographic details and obstetric characteristics of the pregnant women, and when they started to experience fatigue.

Dependent variables were the level of fatigue in pregnancy and the postpartum period.

### Procedure

A formal written consent was received from the Ethics Committee of Atatürk University Medical Faculty in order to carry out the study in the Obstetrics and Gynecology Department of Atatürk University Hospital. After providing information

to the pregnant women participating in the study, their verbal consent was taken. The pregnant women were told that they were free to participate in the study, and that their names and other personal data would be kept confidential.

### Data analysis

The statistical analysis of the data was conducted using SPSS 11.0 statistical packet program. The data were evaluated using average and percentage, Pearson correlation analysis, Kruskal Wallis Variance analysis, one-way Variance Analysis and Bonferroni correction analysis.

### Results

The age of the women ranged from 20 to 38 and their mean age was  $27.53 \pm 4.1$  years. The participants' educational levels were as follows: 3.4% illiterate, 38.8% primary school, 31.4% secondary school, and 26.4% university graduates. Most of the women (81%) were unemployed. The age of the pregnant women affected the fatigue score and older women ( $\geq 35$  years) had a higher fatigue score (KW=16.421  $p < 0.001$ ). Unemployed women also had a significantly higher fatigue score than employed women ( $t = 2.127$ ,  $p < 0.005$ ). All the women in the study had health insurance and their monthly average income was  $551 \pm 272$  US\$. The obstetric characteristics of the participants are shown in Table 1. The obstetric characteristics (gravidity, parity, the number of living children and pregnancy interval) did not affect the mean fatigue score.

It was determined that 39.7% of the pregnant women started to experience fatigue in the first trimester, 24% in the second trimester and 36.3% in the last trimester, and that all the pregnant women in the 3rd trimester experienced fatigue. No significant difference was found between the time of beginning of experienced fatigue and mean VAS-F values (for fatigue  $F = 0.184$   $p > 0.05$ ; for energy  $F = 1.038$   $p > 0.05$ ).

They answered the question "what was the degree of fatigue you felt during the third trimester?" as follows: 9.9% felt mild, 47.9% felt moderate

and 42.2% felt severe fatigue. Mean VAS-F score was also high in women who felt severe fatigue. All the women stated that they had experienced fatigue both in the 3rd trimester and at the end of the first postpartum month.

Table 1. Obstetric characteristics of pregnant women's (n=121)

Obstetric characteristics	n	%
Number of pregnancies		
1	36	29.8
2	37	30.6
3	22	18.1
4 and over	26	21.5
Number of births		
None	40	33.1
1	46	38.0
2	21	17.3
3 and over	14	11.6
Number of miscarriages		
None	100	82.6
1	15	12.4
2 and over	6	5.0
Number of living children		
None	41	33.9
1	48	39.7
2	19	15.7
3 and over	13	10.7
The interval of pregnancy (n=85)		
12 months or less	8	9.4
13 to 24 months	12	14.1
25 months and over	65	76.5

As shown in Table 2, it was found out that the mean fatigue score of the pregnant women in the 3rd trimester was  $70.22 \pm 20.7$ , and that their mean energy score was  $24.61 \pm 7.7$ , and that the mean fatigue score at the end of the first postpartum month was  $66.82 \pm 20.9$ , and that their mean energy score was  $25.39 \pm 8.6$ . It was determined that the fatigue was higher in the 3rd trimester than at the end of the first postpartum month.

There was a positive correlation between the fatigue level in the 3rd trimester of pregnancy and the fatigue level at the end of the first postpartum month ( $r = 0.348$   $p < 0.01$ ). There was also a negative correlation between the energy level in the 3rd trimester of pregnancy and the fatigue level at the end

Table 2. The mean VAS-F score in the 3rd trimester and at the end of the 1st postpartum month

Periods	VAS-F	
	Fatigue Sub Scale	Energy Sub Scale
3rd trimester of pregnancy	70.2±20.7	24.6±7.7
1st postpartum month	66.8±20.9	25.3±8.6

Table 3. Correlation between VAS-F in the 3rd trimester of pregnancy and VAS-F in the postpartum period

3rd Trimester of Pregnancy VAS-F	Postpartum Period VAS-F	
	Fatigue SubScale	Energy SubScale
Fatigue SubScale	r= 0.348**	r= -0.165
Energy SubScale	r= -0.199*	r= 0.176

of the first postpartum month, ( $r = -0.199, p < 0.05$ ). No significant correlation was found between the fatigue level in the 3rd trimester and the energy level at the end of the first postpartum month ( $r = -0.165, p > 0.05$ ). Also, no significant correlation was determined between the energy level in the 3rd trimester and the energy level at the end of the first postpartum month ( $r = 0.176, p > 0.05$ ) (Table 3).

## Discussion

The results of this study demonstrated that older women and unemployed women experienced more fatigue. Gravidity, parity, the number of living children and pregnancy interval did not affect mean fatigue score. Almost all women in this study experienced fatigue, therefore obstetric characteristics did not affect the fatigue score.

In a previous study Chou et al. [15] found that 43.4% of the women occasionally experienced fatigue in the 1st trimester and 53.1% of them frequently experienced fatigue in the 1st trimester. Similarly, Lee and Zaffke [11] indicated that the fatigue in the 3rd trimester was not different from the fatigue in other trimesters. In this study, 39.7% of the pregnant women had started to experience fatigue in the 1st trimester and all of them experienced fatigue in the last trimester. This study revealed that fatigue was experienced throughout the pregnancy, and the time when fatigue was first experienced did not affect the 3rd trimester fatigue and energy scores.

In a study by Catty et al. [4] it was reported that 59% of the pregnant women had a moderate level of fatigue and that 18.1% of them had a severe level of fatigue. In our study most of the women

stated that they felt moderate or severe fatigue and this finding showed that fatigue is a very common complaint in pregnancy. Catty et al. [4] reported that the mild fatigue experienced in the postpartum period was increased in the 3rd trimester and that severe fatigue decreased. In the present study, all the women stated that they felt fatigue at various degrees at the end of the first postpartum month. All the participants were breastfeeding their infants. Because the women had to wake up at night to breastfeed their infants, this may have contributed to their fatigue. The study carried out by Lee and Zaffke [11] documented that the mean fatigue score were  $64.5 \pm 18.1$  at the 3rd trimester and  $68.2 \pm 17.7$  at the end of the first postpartum week, and it was reported that their mean energy scores were  $27.9 \pm 15.3$  in the 3rd trimester and  $24.7 \pm 14.1$  at the end of the first postpartum week. In our study, mean fatigue scores in the 3rd trimester of the pregnancy were higher than mean fatigue scores at the end of the first postpartum month, but mean energy scores were similar. In the current study, mean fatigue scores in the 3rd trimester were higher and mean energy scores were lower than the findings of Lee and Zaffke [11]. We conclude from this result that women who live in this region felt more fatigue. This area has a high altitude (about 1870 meters) and O<sub>2</sub> concentration is relatively low 16. As the altitude gets higher, the total and partial pressure of oxygen decreases. As a result of this drastic decrease, reduction in the performance of exercise and fatigue inevitably results due to hypoxia. So the women may have felt severe fatigue [17].

In the present study, while a positive correlation was found between the mean fatigue scores

in the 3rd trimester and the mean fatigue scores at the end of the first postpartum month, a negatively correlation was found between the mean energy scores in the 3rd trimester and the mean fatigue scores at the end of the first postpartum month. These results have shown that 3rd trimester fatigue increased postpartum fatigue. No significant correlation was found between the mean fatigue and energy scores in the 3rd trimester and the mean energy scores in the postpartum period. We cannot compare this result with other studies because no information was available in the literature.

Since almost all the women felt fatigue in the 3rd trimester and at the end of the first postpartum month, nurses need to caution pregnant women about fatigue and provide better assistance to those in need.

### Recommendations

The following recommendations are presented in light of the current study's findings:

- Women who are in the 3rd trimester and postpartum period need to be taught to manage fatigue
- Pregnant women need to be supported during the 3rd trimester while they carry out household responsibilities,
- Early postpartum women need to be supported to carry out their daily activities and care for their infants.

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# Critical thinking dispositions of nursing students and influencing factors in Turkey

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## Abstract

**Objectives:** To evaluate the critical thinking dispositions of undergraduate, master and doctoral students of nursing and to examine the influencing factors.

**Materials and Methods:** The research was conducted in the nursing departments of the Faculty and Health Science Institute at a university. The population of the study included 362 students. A question form and California Critical Thinking Disposition Inventory were used as data collection tools. Means, percentages, student-t test, variance analysis and Cronbach's Alfa coefficient calculation were used for data analysis.

**Results:** Critical thinking levels were found to be low among undergraduate and master students and medium among doctoral students, and the difference between the groups was statistically significant. It was also determined that critical thinking levels were higher in female students and those who were 28 years of age and older, married, living in the city centre, participating in social and scientific activities and who had nursing experience. According to these variables, the difference between the students' critical thinking levels was statistically significant.

**Conclusions:** It was an expected result that the highest level was observed in doctoral students; yet, critical thinking dispositions of students in all three programs were below the desired level. Reorganizing the curriculum in a way to improve students' critical thinking skills may be helpful. In addition, young and single male students who live in towns and villages, who do not participate in

social and scientific activities and who do not have nursing experience should be provided with more support to improve their critical thinking skills and they should be encouraged to participate in activities.

**Keywords:** Nursing Students; Critical Thinking; Factors

## Introduction and Background

Critical thinking is an essential process of thinking that involves skills like collecting and organizing information from sources, deciding on the needs, choosing one of possible approaches, applying the chosen approach, and evaluating the process results [1].

In fields of health care, critical thinking is one of the fundamental requirements to provide health care in the highest level [2]. The importance of critical thinking in nursing, as in all professional occupations, is emphasized by national and international nursing institutions, and critical thinking capability is considered as one of the primary components of nursing applications [3,4].

Today, a professional nurse is expected to exhibit critical thinking in all her/his roles and functions [5]. Providing nurses with critical thinking skills plays a significant role in enabling the nursing profession to become a discipline believing in science and practiced through scientific research and evidence-based applications [6,7].

Lack of critical thinking skills, which add dynamism to the content and quality of nursing care, has a negative effect on service quality, efficacy



and sufficiency, professionalism, autonomy and power in the practice of nursing [5]. Thus, national and international nursing institutions and accreditation institutions emphasize the importance of including critical thinking in education programs, and consider critical thinking as one of the evaluation criteria [8]. Accordingly, it is important to provide the future nurses with critical thinking skills during their education [15].

There are several studies in the literature which evaluate the critical thinking dispositions and skills of nurses [9-12]. In our country, studies conducted on nurses' critical thinking dispositions and skills are very limited [13,14]. Studies carried out with undergraduate nursing students have investigated the students' critical thinking skills and dispositions [15-18] and the effects of problem-based learning on developing critical thinking skills [19]. The studies conducted in our country have focused on the critical thinking dispositions of undergraduate and master students of nursing and influencing factors [5,20,21].

The literature does not include any research that examines the critical thinking dispositions of undergraduate, master and doctoral students of nursing in a single study. The objective of this research is to evaluate the critical thinking levels of undergraduate, master and doctoral students of nursing as well as influencing factors.

## Methods

### Design and Setting

The research was designed as a descriptive study and conducted in the nursing departments of the Faculty and Health Science Institute at a university.

### Participants

The research population consisted of 295 undergraduate students studying at the department of nursing, and 33 master and 38 doctoral students registered in the nursing program in the academic year 2008-2009. As the entire population was included in the research (n=366), no sampling was

applied. Although there was no student who refused to participate in the research, there were four baccalaureate students who have health problem on the day that the tools were administered. The study was carried out with 362 students and the response rate was 98.9%.

### Data collection and analysis

The research data were collected between 15 May and 15 June 2009. A question form and California Critical Thinking Disposition Inventory (CCTDI) were used as data collection tools. It took approximately 20-25 minutes to complete the forms.

*Question Form:* This form, prepared by the researchers based on the relevant literature, was comprised of questions to reveal subject's characteristics such as, age, gender, education level, marital status, family's settlement, scientific activity and nursing experience [5,20,21].

*CCTDI:* This inventory was used to measure students' critical thinking disposition. The CCTDI was developed by Facione et al in 1998 and the Turkish version of the tool was tested for validity and reliability by Kökdemir (2003c) [22]. The tool's internal consistency coefficient has been determined to be .88 [22]. The CCTDI is a 51 item tool with a 5-point Likert type scale. The points given for each item are considered the score. However the negative items (5, 6, 9, 11, 15, 18, 19, 20, 21, 22, 23, 25, 27, 28, 33, 36, 41, 43, 45, 47, 49, 50) are scored in the reverse. In the evaluation of CCTDI the students' level of agreement with the item is totaled for every item and the result evaluated out of the total possible of 306 points. In the scores a total score less than 240 is considered low, scores between 240-300 are considered average and scores over 300 are considered to represent a high level of critical thinking skills. The tool's internal consistency coefficient was determined to be .88 in this study.

The data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 10.0. Means and standard deviations were determined for quantitative data and frequency determined for categorical variables. Cronbah alpha coefficient calculation, Student-t test and variance

analysis (parametric statistics-Fisher test; nonparametric statistics-Kruskal Wallis test) were used for comparison between multiple means. P value<0.05 was considered statistically significant.

## Results

### Participants' characteristics

The majority of the students who participated in the research (80.4%) were receiving undergraduate education (Table 1). The age average of the students was  $22.06 \pm 3.74$ , 71.6% of the students were from the age group of 18-22 years, and 83.4% were

women. 11.3% of the students were married and 54.7% lived in the city centre. Most of the students participated in social (87.8%) and scientific activities (64.9%). 19.1% of the students had nursing experience and the average period of their nursing experience was  $4.22 \pm 3.81$ , years (Table 1).

### Critical thinking level

In the research, critical thinking level of doctoral students ( $243.13 \pm 21.75$ ) was higher than that of the master students ( $231.36 \pm 23.76$ ) and undergraduate students ( $217.43 \pm 23.97$ ), and the difference between the groups was statistically significant

Table 1. Student's critical thinking levels according to their characteristics

Characteristics	n	%	CCTDI Mean $\pm$ SD	Test and p
<b>Age, yrs (<math>22.06 \pm 3.74</math>)</b>				
18-22	259	71.6	217.94 $\pm$ 23.49	
23-27	66	18.2	222.81 $\pm$ 26.51	F=17.843
28 and over	37	10.2	243.08 $\pm$ 23.19	<b>P=.000</b>
<b>Gender</b>				
Female	302	83.4	222.83 $\pm$ 24.79	t=2.452
Male	60	16.6	214.18 $\pm$ 25.82	<b>P=.015</b>
<b>Marital status</b>				
Married	41	11.3	236.87 $\pm$ 23.08	t=4.287
Unmarried	321	88.7	219.42 $\pm$ 24.72	<b>P=.000</b>
<b>Family's settlement</b>				
City	198	54.7	224.00 $\pm$ 24.33	
Town	126	34.8	221.41 $\pm$ 26.59	F=6.822
Village	38	10.5	207.81 $\pm$ 19.85	<b>p=.001</b>
<b>Social and scientific activity</b>				
Yes	235	64.9	223.40 $\pm$ 25.07	t=2.077
No	127	35.1	217.68 $\pm$ 24.91	<b>P=.039</b>
<b>Nursing experience</b>				
Yes	69	19.1	236.01 $\pm$ 24.63	t=5.558
No	293	80.9	217.95 $\pm$ 24.02	<b>P=.000</b>
<b>Nursing experience, yrs (<math>4.22 \pm 3.81</math>)*</b>				
<1	25	36.2	228.16 $\pm$ 24.61	
1-5	32	46.4	237.65 $\pm$ 22.34	KW=3.944
6 and over	12	17.4	248.00 $\pm$ 26.80	P=.139
<b>Education level</b>				
Baccalaurate	292		217.43 $\pm$ 23.97	
MSc	33		231.36 $\pm$ 23.76	F=22.896
Doctorate	38		243.13 $\pm$ 21.75	<b>P=.000</b>
<b>Total</b>	<b>362</b>	<b>100.0</b>		

\*The number of students who have experience in nursing is sixty nine.

( $p < 0.001$ ), (Table 1, Figure 1). According to these results, critical thinking levels of undergraduate and master students were low, while doctoral students' critical thinking levels were medium. Critical thinking levels were determined to be higher among female students who were 28 years of age and older, who were married, who lived in the city centre, who participated in social and scientific activities and who had nursing experience (Table 1). The difference between the students' level of critical thinking in terms of their age ( $p < 0.001$ ), gender ( $p < 0.05$ ), marital status ( $p < 0.001$ ), place of residence ( $p < 0.01$ ), participation in social and scientific activities ( $p < 0.05$ ) and nursing experience ( $p < 0.001$ ) was also statistically significant (Table 1).

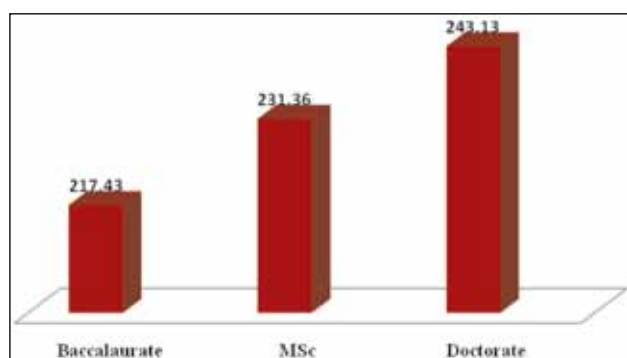


Figure 1. Students' critical thinking levels according to the educational level

## Discussion

In the research, critical thinking dispositions of undergraduate, master and doctoral students of nursing were evaluated and influencing factors were examined.

Critical thinking dispositions were found to be low among undergraduate and master students and medium among doctoral students. The difference between the groups was statistically significant ( $p < 0.001$ ) (Table 1, Figure 1). The levels of critical thinking disposition observed among undergraduate students comply with results of similar studies previously conducted in our country [5,20,21]. As to the studies carried out in different societies, critical thinking dispositions of undergraduate students were determined to be of medium level in Hong Kong [16] and high level in Canada [15] and USA [18]. The levels of critical thinking disposition observed among master

students were found to be lower than the results reported in a similar study previously conducted in our country. In the study carried out by Öztürk and Ulusoy (2008), critical thinking dispositions of master students were detected to be of medium level [5]. In our research, critical thinking dispositions among doctoral students were found to be of medium level. When the score means of students were examined on an overall basis, the level of critical thinking disposition was determined to increase in direct proportion to education. The increase in critical thinking levels with the increase in education level is considered to be an expected result [5]. This finding obtained in our research is comparable to the findings of other studies conducted with undergraduate, and master students of nursing [5,17]. On the other hand, in some studies which examined the development of critical thinking among students in different stages and programs of academic education, critical thinking scores were observed to increase at the end of the programs, but the difference was found to be insignificant [4,10,23].

It is an expected result that critical thinking skills are improved with age due to the increase in students' experience [5]. In the present research, it was determined that students' critical thinking levels increased with the increase in their age and the difference between the groups was found to be significant ( $p < 0.001$ , Table 1). This finding is consistent with the results obtained in similar studies [4,5,9]. In contrast, some studies did not reveal any relationship between age and the level of critical thinking [13,14,21]. In this research, it was found that female students ( $p < 0.05$ ) and married ( $p < 0.001$ ) students had higher levels of critical thinking and the difference between the groups was significant (Table 1). This result may have stemmed from the high number of female and married students. In the study of Walsh and Hardy (1999), it was found that gender did not have an effect on critical thinking [11]. Furthermore, in our research, critical thinking levels were higher also among students living in town compared to those living in villages, and higher among student living in cities compared to those living in towns; and the difference was found to be significant ( $p < 0.01$ , Table 1). A similar result was obtained in the study conducted by Öztürk and Ulusoy (2008). It has

been reported that living in cities or big cities and benefiting more from educational opportunities, which provide individuals with more experience and stimulus, improve individuals' mental processes such as problem solving skills, and therefore, increase their critical thinking levels [5]. In this research, students who participated in social and scientific activities had higher critical thinking levels, and the difference between the groups was significant ( $p < 0.05$ , Table 1). Similarly, Eşer et al. (2007) reported that nurses who participated in certificate and in-service training programs had higher critical thinking levels and that the difference between the groups was significant [13]. Arslan et al. (2009) also detected a higher level of critical thinking among nurses who participated in scientific activities, but their study did not reveal a significant difference between the groups [14]. In our research, critical thinking levels were higher in students who had nursing experience and whose nursing experience was more than 6 years, and the difference between the groups according to having nursing experience was found to be significant ( $p < 0.001$ , Table 1). It is reported in some studies that clinical experience does not affect nurses' critical thinking levels [9,13,24,25]. However, in one of the studies on the subject, it was determined that analytical thinking disposition increased with the increase in occupational experience [12]. This result shows parallelism with the results obtained in our study. The first dimension of critical thinking is vocational education as the basis of nursing, and the second dimension is the occupational experience of nurses. Critical thinking increases with the increase in experience, and critical thinking levels of nurses are improved by clinical practice, and involvement in decision making in patient care [21].

## Conclusion

In the research, critical thinking dispositions of undergraduate, master and doctoral students of nursing were evaluated and influencing factors were examined. Critical thinking levels were found to be low among undergraduate and master students and medium among doctoral students, and the difference between the groups was signifi-

cant. It was an expected result that the highest level was observed in doctoral students; yet, critical thinking levels of students in all three programs were below the desired level. Reorganizing the curriculum of all three programs in a way to improve students' critical thinking skills may make contribution. It was also determined that critical thinking levels were higher in female students and those who were 28 years of age and older, married, living in the city centre, participating in social and scientific activities and who had nursing experience; and the difference between the groups was statistically significant. Accordingly, it is considered important that young and single male students who live in towns and villages, who do not participate in social and scientific activities and who do not have nursing experience should be provided with more support to improve their critical thinking skills and they should be encouraged to participate in activities.

## Ethical considerations

After having the necessary written approval from the university's relevant authorities of the university, for the administration of the data collection tools in the study, the researchers went to every class, and explained the purpose of the study to the students in the classrooms and emphasized that participation was voluntary. Students were assured that their privacy and confidentiality would strictly be protected as no personal identifiers were included in the questionnaire and any information given will only be used for research purpose. In the study students' informed consents were received. It was also explained that non-participation to the study would cause no disadvantage for the students. The students completed the forms without indicating their names on the forms.

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# The Effects of Performance Based Supplementary Payment on Physician Practice; A Cross Sectional Questionnaire Study

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## Abstract

**Aim:** The aim of this study is to assess the effects of performance based supplementary payment (PBP) on work conditions, relations among health workers, income level, and use of health care services.

**Method:** In this cross sectional survey, 654 physicians who had been practicing for at least ten years filled in a questionnaire to obtain opinions on the PBP.

**Results:** Mean age and standard deviation of the physicians were 43.26±6.8. In terms of relationship among physicians, 67.6 % reported 'negative effect' of PBP. In terms of solidarity and competition, 68.8% responded that PBP decreased solidarity, and 84.1% responded that PBP increased competition among health care workers. Of the subjects, 56.1% reported an increased work load during PBP. More than two third of physicians thought that performance method increased unnecessary procedures and overuse of the services. More than half of the subjects responded that waiting time for physical examination reduced, and 60.9% reported that spending time per examination also decreased. More than half of the physicians had negative opinion about the PBP, 70.2% implied a negative effect on peace at work. With regard to effect of PBP on social life, 44.8% responded 'no effect' while 40.7% responded 'negative effect', and 60.6% reported that holiday activities were affected negatively.

**Conclusion:** Increased income level of physicians, and increased accessibility to health care are main positive effects of PBP. Great incentives with fixed low salary may cause increased overuse of health services, increased competitions, decreased solidarity, conflict among physicians, inefficient use of resources, loss of ethical values, and decreased quality of service.

**Key words:** pay for performance, reimbursement mechanism, incentives, working conditions, physicians

## Introduction

Globalization has a great impact on various issues around the world. Social values, economical relationship, consumer and producer behaviours are constantly changing. Governments are moving from social state or social market economy to liberal market economy. With regard to health sector, one of the main results of globalization is commercialization of healthcare services<sup>(1)</sup>. As a result of this, payment methods, working conditions, financing of health care, service providers, and behaviour of health workers have remarkably changed. Performance-based payment (PBP) is spreading around the world<sup>(2, 3, 4, 5)</sup>. However, results of studies about effectiveness of PBP are not consistent<sup>(3,5,6,7, 8, 9)</sup>. Kalk et al, reported considerably negative effects in Rwanda with regard to PBP<sup>(3)</sup>. Metthew acknowledged many concerns about

PBP in terms of medical ethics and professionalism<sup>(10)</sup>. Finally some studies reported positive effects on quality of health care<sup>(6,7)</sup>.

Since early 1980s, globalization has been introducing many changes in health care systems. In Turkey, the government narrowed its role, and it took responsibility for planning and regulating of healthcare. Management of the hospitals, management and structure of social security organizations, financing of healthcare, reimbursement and payment models were significantly changed. Nearly all public hospitals in Turkey have become for-profit organizations by initiating revolving funds. With regard to payment to health workers, fixed salaries were replaced with mixed payment methods which included fixed salaries, revolving funds, and performance based payment (PBP)<sup>(11)</sup>. By these means, health workers' income was strongly associated with the income of their institution. In this method, physician can take performance based incentives as much as seven fold of fixed salary<sup>(12)</sup>.

Probably, these changes have some effects on relations among the health workers, quality of services, work load, income level of health workers, motivation of the workers, social life of workers, continuous medical education, job satisfaction, and work conditions. However, little is known about the effects of payment method on these issues in Turkey. The purpose of this study is to assess the effects of PBP on work conditions, relations among the health workers, income level, and use of health care services.

## Material and Methods

**Study sample and population:** The study population were 1280 physicians who had at least ten years working experience in four provinces in 2009. A total of 876 physicians were reached; 222 physicians did not respond. The sample size was 654 physicians who filled in the questionnaire and the response rate was 74.7%. This is a cross sectional, self report questionnaire survey. The performance system was launched in 2004. Therefore, these physicians accustomed to two models; 1-Fixed salary method 2- Mixed payment method. Therefore they can compare two models.

**Performance based supplementary payment:** PBP was initiated as a pilot implementation in ten hospitals in the second half of the year 2003, and it has been implemented across Turkey from 2004. In this method, a physician takes fixed salary from the budget of the Health Ministry and PBP (incentives) from revolving fund of the hospital. According to performance of physician, the additional payments vary from zero to seven fold of the fixed salary<sup>(12)</sup>. In this payment method, fixed salary is lower than PBP. At the beginning, performance criteria were based on individuals, institutional, managerial, financial and clinical indicators were added in 2005<sup>(11)</sup>. This intervention includes 975 hospitals, 6400 local health centers, and 310 staff. Processes were scored and scores were calculated for institutions and individuals. Calculation method of PBP is complex<sup>(11)</sup>.

**The questionnaire:** It includes 50 questions; main categories in the questionnaire were socio-demographic variables, professional experience, payment methods, income level, relations among the physicians, relations among the other health workers, solidarity, competition, patient-physician relationship, satisfaction with pay for performance, social life, continuous medical education, over use of health care services, unnecessary use of service, peace at work, relations among health care services at different steps, and quality of services.

**Statistical analysis:** The statistical procedures were carried out using Epi Info version 3.3.2, developed by the Centers for Disease Control and Prevention. Frequencies, percentages and confidence intervals are presented in the tables. Verbal informed consent was obtained from the subjects.

## Results

Socio-demographic characteristics of the physicians are presented in Table 1; 74.8% are male, 51.8% work in a primary care unit, and 43.6% work in a hospital. Of the physicians, 92.2% had been working with an official contract. With regard to payment, most of the physicians (91.5%) took mixed payments including a fixed salary and incentives. Mean age and standard deviation were  $43.26 \pm 6.8$ , and mean years for work experience  $17.97 \pm 6.35$ .

Table 1. Socio-demographic characteristic of the physicians (n= 654)

	n	%	Confidence interval 95%
Gender			
Male	489	74.8	71.4-78.1
Female	165	25.2	21.9-28.5
Work place			
Hospital	285	43.6	39.8-47.4
Primary care unit	339	51.8	48.0-55.6
Other	30	4.6	2.9-6.2
Provinces			
Diyarbakir	75	11,5	9.0-13.1
Hatay	214	32,7	29.1-36.3
Kayseri	77	11,8	9.3-14.2
Mersin	288	44,0	40.2-47.8
Type of contract			
Official	603	92.2	90.1-94.3
Contractual	50	7.6	5.6-9.7
Other	1	0.2	-0.1-0.4
Payment methods			
Salary	46	7.1	5.1-8.9
Salary- Revolving fund	473	72.3	68.9-75.7
Salary-Performance	80	12.2	9.7-14.7
Salary-Revolving fund- Performance	46	7.0	5.1-8.9
Other	9	1.4	0.5-2.3
	Mean	Std. Deviation	
Age (year)	43.26	6.80	42.7-43.8
Work experience (year)	17.97	6.35	17.5-18.5
Average working hours per week	43.03	8.12	42.4-63.6

Table 2 shows opinions of the physicians about the effects of performance on their working conditions. With regard to relationship among the physicians, 67.6 % reported negative effect of performance. Similarly, 59.5 % thought that PBP had a negative effect on relationship between physicians and other health workers. In terms of solidarity, 68.8% responded that PBP decreased the solidarity among the health workers, 66.4% reported 'decreased solidarity' with regard to healthcare service institutions. At the same time, 84.1 % responded that PBP increased competition among health care workers. With regard to relationship between physician and patients, 36.2% reported 'negative', while 35.2% reported 'no effect'. In terms of income, 69.0% responded that PBP increased their income, and 55.5% of the subjects reported 'no effect on work time'. More than half of the subjects (56.1%) reported an increased work load while 38.4% reported 'no effect'. In terms of joi-

ning the scientific activities such as seminar, conference, 46.2% responded no effect while 42.7% said negative effect. With regard to professional development, 51.1% said 'no effects' while 34.7% said 'negative effect'.

Table 3 shows the effects of performance method on using healthcare services. More than two third of physicians thought that performance method increased unnecessary work, and the percentage of the subjects who responded 'increased overuse' was 81.7. With regard to unnecessary procedures, 77.1% reported increased unnecessary diagnostic procedures and 81.5% reported increased unnecessary procedures. With regard to surgical procedures, 62.4% responded 'Negative effects' while 14.8% responded 'Positive effect'.

The opinions of the subjects about effect of performance on service quality are presented in Table 4. More than half of the subjects responded that waiting time for physical examination redu-



Table 2. The effects of the pay for performance on work conditions(n= 654)

According to your opinion, how did the performance effect ...	n	%	Confidence Interval 95 %
on relationship among your colleagues?			
No effect	150	22.9	19.7-26.2
Negative	442	67.6	64.0-71.2
Positive	46	7.0	5.1-9.0
Other	7	1.1	0.3-1.9
No response	9	1.3	0.5-2.3
relationship between physicians and other health workers?			
No effect	184	28.1	24.7-31.6
Negative	389	59.5	55.7-63.2
Positive	76	11.6	9.2-14.1
Other	2	0.3	-0.1-0.7
No response	3	0.5	-0.1-0.9
solidarity among the health workers?			
No effect	122	18.7	15.7-21.6
Increased solidarity	74	11.3	8.9-13.7
Decreased solidarity	450	68.8	65.3-72.4
Other	5	0.8	0.1-1.4
No response	2	0.4	-0.1-0.7
competition among the health workers?			
No effect	76	11.6	9.2-14.1
Increased competition	550	84.1	81.3-86.9
Decreased competition	10	1.5	0.6-2.5
Other	17	2.8	1.4-3.8
No response	1	0.2	-0.1-0.4
Relationship with patient and patient relatives			
No effect	230	35.2	31.5-38.8
Negative	237	36.2	32.6-39.9
Positive	179	27.4	23.9-30.8
Other	5	0.8	0.1-1.4
No response	3	0.5	-0.1-0.9
solidarity between health care institutions in different level			
No effect	155	23.7	20.4-26.9
Increased	25	3.8	2.3-5.3
Decreased	434	66.4	62.7-69.9
Other	23	3.6	2.1-4.9
No response	17	2.6	1.4-3.8
your income?			
No effect	113	17.3	14.4-20.2
Negative effect	84	12.8	10.3-15.4
Positive effect	451	69.0	65.4-72.5
Other	2	0.3	-0.1-0.7
No response	4	0.7	0.1-1.2
your work time?			
No effect	363	55.5	51.7-59.3
Increased	265	40.5	36.8-44.3
Decreased	22	3.4	1.9-4.7
Other	1	0.2	-0.1-0.4
No response	3	0.5	-0.1-0.9
your work load?			
No effect	251	38.4	34.6-42.1
Increased work load	367	56.1	52.3-59.9
Decreased work load	29	4.4	2.8-6.0
Other	2	0.3	-0.1-0.7
No response	5	0.8	0.1-1.4
activities like seminar, meeting, and conference?			
No effect	302	46.2	42.4-50.0
Positive effect	63	9.6	7.4-11.9
Negative effect	279	42.7	37.7-47.5
Other	4	0.6	0.1-1.2
No response	6	1.0	0.4-3.8
your professional development?			
No effect	334	51.1	47.2-54.9
Positive effect	84	12.8	10.3-15.4
Negative effect	227	34.7	31.1-38.4
Other	4	0.6	0.1-1.2
No response	5	0.8	0.1-1.4

Table 3. Effects of performance on using healthcare services (n= 654)

According to your opinion; how did the performance effect...	n	%	Confidence Interval 95%
Unnecessary work?			
No effect	152	23.2	20.0-26.5
Increased unnecessary work	463	70.8	67.3-74.3
Decreased unnecessary work	30	4.6	2.9-6.2
Other	5	0.8	0.1-1.4
No response	4	0.7	0.1-1.2
... Overuse of healthcare services?			
No effect	103	15.7	12.9-18.5
Increased overuse	534	81.7	78.7-84.6
Decreased overuse	11	1.7	0.7-2.7
Other	1	0.2	-0.1-0.4
No response	5	0.8	0.1-1.4
Unnecessary use of radio-diagnostic procedures?			
No effect	105	16.1	13.2-18.9
Increased	504	77.1	73.8-80.3
Decreased	13	2.0	0.9-3.1
Other	11	1.7	0.7-2.7
No response	21	3.1	3.1-6.4
Unnecessary procedures?			
No effect	88	13.5	10.8-16.1
Increased	533	81.5	78.5-84.5
Decreased	16	2.4	1.3-3.6
Other	1	0.2	-0.1-0.4
No response	16	2.5	1.3-3.6
Surgical procedures?			
No effect	71	10.9	8.5-13.2
Positive effect	97	14.8	12.1-17.5
Negative effect	408	62.4	58.7-66.1
Other	30	4.6	2.9-6.7
No response	48	7.3	5.3-9.3

ced. On the other hand 60.9% reported that time spending per examination decreased, and 64.2% reported that time spending per patient decreased. In terms of examined patient number, 76.0% responded 'Increased'. More than half of the subjects reported that performance method increased malpractice while 31.8% reported 'no effect'. With regard to effects on preventive medicine, 58.7% responded 'negative effect' while 12.1% reported 'positive effect'.

Table 5 shows some opinions of the physicians on performance method. Related to community perception, 65.7% thought that performance method decreased respect to physicians, while 24.2 reported 'no effect'. Of the physicians, 54.1% had

negative opinion about the PBP. Although 52.9% thought that performance criteria were not objective, 7.8% thought it was objective.

With regard to effect of performance method on peace at work, 70.2% responded 'negative' while 11.0% responded 'positive'. In terms of general feeling about performance method, 1 in 3 responded 'happy' while 2 in 3 responded 'not happy'. With regard to effect of PBP on social life, 44.8% responded 'no effect' while 40.7% responded 'negative effect', and 60.6% reported that holiday activities were affected negatively.

Table 4. Effect of the performance method on quality of service (n= 654)

According to your opinion; how did the performance effect...	n	%	Confidence Interval 95%
Waiting time of the patient for examination			
No effect	150	22.9	19.7-26.2
Increased	120	18.3	15.4-21.3
Decreased	378	57.8	54.0-61.6
Other	1	0.2	-0.1-0.4
No response	4	0.6	0.1-1.2
spending time per examination			
No effect	177	27.1	23.7-30.5
Increased	68	10.4	8.1-12.7
Decreased	398	60.9	57.1-64.6
Other	6	1.0	0.4-3.8
No response	5	0.8	0.1-1.4
Spending time per patient			
No effect	161	24.6	23.6-30.5
Increased	62	9.5	7.2-11.7
Decreased	420	64.2	60.5-67.9
Other	1	0.2	-0.1-0.4
No response	10	1.6	0.6-2.5
Examined patient number			
No effect	127	19.4	16.4-22.4
Increased	497	76.0	72.7-79.3
Decreased	23	3.5	2.1-4.9
Other	1	0.2	-0.1-0.4
No response	6	0.6	0.4-3.8
Malpractice			
No effect	208	31.8	28.2-35.4
Increased	383	58.6	54.8-62.3
Decreased	31	4.7	3.1-6.4
Other	15	2.3	1.1-3.4
No response	17	2.6	1.4-3.8
Preventive medicine			
No effect	172	26.3	22.9-29.7
Negative	384	58.7	54.9-62.5
Positive	79	12.1	9.6-14.6
Other	6	0.9	0.4-3.8
No response	13	2.0	0.9-3.1

## Discussion

The data on this study based on the opinions of the physicians who had been practicing for at least 10 years. Therefore, it was assumed that they had known two periods; before and after the PBP.

Most of the physicians indicated that PBP increased competition and decreased solidarity among health workers. A similar result was reported in another study<sup>(13)</sup>. This is consistent with

the nature of performance, and it is an expected result. Two third of the physicians responded that PBP had a negative effect on relationship among their colleagues. Similarly, more than the half reported that there was a negative effect on relation between physicians and other health workers.

In this study, PBP was found to have a negative effect on peace at work. Violence at work was stated as a negative result of PBP<sup>(14)</sup>. Previous studies in recent years reported that violence at workpla-

Table 5. Opinions of the physicians on the performance method(n= 654)

	n	%	Confidence Interval 95%
<b>Community perception for the physician</b>			
No effect	158	24.2	20.9-27.4
Increased respect	54	8.3	6.1-10.4
Decreased respect	430	65.7	62.1-69.4
Other	7	1.1	0.3-1.9
No response	5	0.8	0.1-1.4
<b>What is your opinion about the performance method?</b>			
Neutral	125	19.1	16.1-22.1
Positive	133	20.3	17.2-23.4
Negative	354	54.1	50.3-57.5
Other	39	6.0	4.1-7.8
No response	3	0.5	-0.1-0.9
<b>What do you think about the objectivity of performance criteria?</b>			
Not objective	346	52.9	49.1-56.7
Partially objective	251	38.4	34.6-42.1
Objective	51	7.8	5.7-9.7
Other	4	0.6	0.1-1.2
No response	2	0.4	-0.1-0.7
<b>Peace at work</b>			
No effect	113	17.3	14.4-20.2
Negative	459	70.2	66.7-73.7
Positive	72	11.0	8.6-13.4
Other	3	0.5	-0.1-0.9
No response	7	1.1	0.3-1.9
<b>What is your general feeling about performance method?</b>			
Very happy	33	5.0	3.4-6.7
Happy	171	26.1	22.8-29.5
Not happy	290	44.3	40.5-48.1
Extremely not happy	149	22.8	19.6-25.9
No response	11	1.7	0.7-2.7
<b>Social life</b>			
No effect	293	44.8	40.9-48.6
Positive	80	12.2	9.7-14.7
Negative	266	40.7	36.9-44.4
Other	8	1.2	0.4-2.1
No response	7	1.1	0.3-1.9
<b>holiday and entertainment habits</b>			
No effect	223	34.1	30.5-37.7
Negative	396	60.6	56.8-64.3
Positive	27	4.1	2.6-5.7
Other	4	0.6	0.1-1.2
No response	4	0.6	0.1-1.2

ces in health care was common in Turkey<sup>(15,16,17)</sup>. Nearly half of the health workers face violence per year. Unmet needs of patients, work overload, and social values such as competition or solidarity are likely associated with violence in health care services. Increased value of competition and decreased value of solidarity in health care settings may contribute to violence. However, it is difficult to

establish a relationship between PBP and violence by the methodology of this study. Violence is a complex and multi-factorial issue.

Holiday activities of the physicians were affected negatively by the PBP. Similar finding was reported in the study of TMA<sup>(13)</sup>. In the current PBB, physicians are forced to work continuously, because performance of a physician is negatively

affected by holiday activities.

With regard to income of physicians, they reported that PBP increased it. This result is consistent with another study from Turkey<sup>(14)</sup>. It is clear that PBP increases income of physicians, at least for most of them.

They reported that their work load was also increased. Although more than half of the physicians said that working duration per day was not changed, significant amount of the physicians said that it was increased during the PBP. We think that PBS may stimulate overtime.

In terms of joining scientific activities and professional development, the most frequent choice was no effect of PBP while the second frequent choice was negative effect. It is not easy to find out a definitive result based on these findings. Our results are not consistent with the study of TMA regarding joining scientific activities<sup>(13)</sup>.

Most of the physicians thought that PBP increased unnecessary work; unnecessary diagnostic procedures, surgical and service use. Balci reported similar findings; PBP increased unnecessary and dangerous diagnostic or surgical interventions<sup>(14)</sup>. In another study carried out by TMA, 63.8% of the physicians reported that the number of diagnostic procedures was increased<sup>(13)</sup>. In this study, most of the physicians thought that percentage of the interventions without indication were increased<sup>(13)</sup>. It is another expected result because PBP stimulate the physicians to perform more procedures.

Waiting time for a patient was reduced, and average time for examination per patient was also reduced. Similarly, it was reported that examination time per patient was reduced after the performance application<sup>(13)</sup>. It was reported that the waiting period had become shorter<sup>(11)</sup>.

PBP increased examined patient numbers per physician in a day. Similar result was reported by previous studies<sup>(11,14)</sup>. These findings are consistent with the desire for examining more patients and increasing performance.

More than half of the subjects indicated that PBP increased malpractice. In the study of TMA, 52.8% of the physicians sad that PBP increased malpractice<sup>(13)</sup>. PBP may contribute to overworking and therefore may contribute to malpractice.

In this study, most of the physicians thought

that PBP has a negative effect on preventive medicine. Health Ministry suggested that, there had been improvement in vaccination rates, pregnancy and infant monitoring numbers compared to previous years, as a result of score supports towards protective health services<sup>(11)</sup>. There might be improvement in the selected and supported targets by the incentives. In general, significant amount of the health efforts and incentives of the PBS are related to treatment issues in Turkey. Despite some improvements, it is difficult to imply that PBP had a significant effect on preventive medicine. Water borne, food borne diseases, induced abortion etc. are still important in Turkey<sup>(18)</sup>.

More than half of the physicians had negative opinions about the PBP. On the other hand, the main aim of this method was to improve motivation and productivity of health personnel<sup>(12)</sup>. Our findings suggest that intrinsic factors were negatively affected while extrinsic factors were forced to work more.

It seems that most of the unwanted results are associated with low salary and high additional payment to physicians. High amount of performance based incentives may produce pressure on physicians and stimulate physicians to do negative things as well as positive things. Our suggestion is that the problems may be solved by reversing this situation. Fixed salary, not additional payment, must constitute a great part of total income. Chung et al, implied that small financial incentives (maximum, \$5000/year) based on individual physicians' performance might have led to continued or enhanced improvement in well-established ambulatory care measures<sup>(19)</sup>. Khon suggested that if physicians and hospitals become focused on the metrics, they might lose sight of the global goals of healthcare<sup>(20)</sup>.

### Limitations of the study

The study based on respondents of the physicians and spans a long period. Therefore the results may be affected by the memory.

## Conclusion

It is clear that some things are changed with positive or negative direction during the PBP. Increased income level of physicians, and increased accessibility to health care are main positive effects of PBP.

On the other hand, it seems that great incentives with a fixed low salary may cause increased overuse or unnecessary use of health services, increased competitions, decreased solidarity, conflict among physicians, inefficient use of resources, loss of ethical values, and decreased quality of service.

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# Nursing student the critical thinking development of the critical thinking education

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## Abstract

**Objectives:** The research is planned as a “design study with a time series and nonequivalent control group” conducted in order to apply and evaluate the course “Critical Thinking in Nursing” prepared for contributing to the development of critical thinking skills of student nurses.

**Methodology:** Research was conducted in Ege University School of Nursing in fall semester 2007- 2008 academic year and the research population were total 318 students who were registered second and third classes. The sample of the research was set of total 78 students, 39 were experimental group and 39 control group. 39 voluntary students were control group who were chosen with simple random method. It is provided that matching the students in both groups on parameters like 2006- 2007 academic year final grade success points mean and “Critical Thinking in Nursing” course in the sample selection. Socio demographic Features Data Form and, Following Tests (scenario exam assessments of 11 units’) and Level Defining Tests were used as data collection tools. SPSS 15.0 package software program were used in evaluation of data and numbers, percentage estimation, arithmetic mean, t test and Pearson correlation analysis were used. A project support was taken from Adnan Menderes University Scientific Fund in this research. At the end of the research, course education materials were reorganized and carried a course book. Skill based critical thinking education program were conducted 14 week (two credit), 11 units, every unit theoretical knowledge, scenario studies, exercises and homework in the content of the course.

**Results:** There was not statically significant difference between discussing and control groups about socio-demographic features of students who attended the research, it was seen that both of the group were homogenized. There was not statically significant difference between groups on academic success levels of students before course ( $p>0.05$ ); there was not statically significant difference after the “Critical Thinking in Nursing” course ( $p<0.05$ ). This difference originated from experimental group that had higher academic success scores from control group. It is observed that experimental group students had explicit increase on final grade success through the first unit to last unit in the course period. Students had finished the course successfully with the  $71.37\pm 8.36$  final grade point mean.

**Conclusions:** It is concluded that to improve the students’ critical thinking course was helpful. To improve students’ critical thinking presenting theoretical knowledge, scenario studies and making exercises, giving homework can be suggested, as implemented in this research. It can be developed tools for nurses for scale the critical thinking in our country.

**Key Words:** Critical thinking, critical thinking in nursing education, nursing student

## Introduction

Critical thinking has been defined by many noted educators during the past century (Brookfield, 1991; Dewey 1910; Mezirow, 1990; Norris and Ennis, 1989; Paul, 1993; Watson and Glaser, 1964), with each definition emphasizing different aspects. As a result, the nature of critical think-

ing lacks consensus across academic disciplines (Myrick, 2002) Through a Delphi method with 46 experts, the American Philosophical Association developed a cross-disciplinary conceptual definition: We understand critical thinking to be purposeful, self-regulatory judgement which results in interpretation, analysis, evaluation, and inference, as well as the expiations of the evidential, conceptual, methodical, criteria logical, or contextual, considerations upon which that judgement was based (Facione, 1990).

Bandman and Bandman (1995) conceptualized critical thinking in nursing as: The rational examination of ideas, inferences, assumptions, principles, arguments, conclusions, issues, statements, beliefs, and actions. This examination covers scientific reasoning, includes the nursing process, decision making, and reasoning in controversial issues. Besides these definitions, Beyer (1987) also brings out a new term for critical thinking: *evaluative thinking*. He indicates that critical thinking is evaluative in nature, because it entails precise, persistent, and objective analysis of any claim, source, or belief to judge its accuracy, validity, or worth. According to Yıldırım (2011), critical thinking is “the process of searching, obtaining, evaluating, analyzing, synthesizing and conceptualizing information as a guide for developing one’s thinking with self-awareness, and the ability to use this information by adding creativity and taking risks”.

Nowadays, all of the members of the profession should adapt easily to the developments and innovation, eliminate information wisely and have modern and professional quality. In order to be attuned to the innovations of the times, these qualities can be brought in student nurses through a modern education which aims at making the student to internalize the basic notions and fitting them with qualities that enables the students to solve the problems using critical thinking (Çıkrıkçı, 1992; Kaya, 1997; Öztunç, 1999). Universities, which are defined as the environment for the universally thinking people, are of crucial importance in realizing this (Kaya, 1997; Kökdemir, 2003). Since the changes in the health care system is rapid and dynamic, the nurses should use critical thinking in addition to the traditional nursing approaches in providing optimal patient care and clinical decision making (Yıldırım, 2010; Yıldırım, 2011).

As it is the same in all professional occupations, the importance of critical thinking has been emphasized by national and international nursing institution and critical thinking is accepted as one of the basic tenets of nursing practices (Angel, et al., 2000; Facione, et al., 1994; Martin, 2002). Nurses’ developing their critical thinking skills is of great importance for nursing being a discipline that believes in science, investigates and implements the scientific facts and realize its applications based on evidence (Taşocak, 1997; Özer 2002; Karageleş, 2003; Yıldırım, 2010). Adams argues that the ability of critical thinking increases as the work years increase, and the critical thinking skills can be improved during nursing education (Adams, 1999; Yıldırım, 2010). Be rapid and dynamic change in the health care system, nurses, nursing student in providing optimal patient care, problem solving, ethical decision making, determine priorities and trends in clinical decision making and critical thinking skills you need to use (Yıldırım, 2010).

The need to think critically for functioning in today’s society has resulted in examination of the role education plays in preparing individuals with critical thinking skills (Godfrey, 1995; La Bar and Wright, 1986; McEwen, 1994; Quina, 1989). Educators have recognized the need for students to acquire critical thinking ability as a skill for life. The current emphasis on critical thinking in education has occurred as a direct results of national reports which indicate that first, scholastic aptitude scores are declining and second, students have poor thinking skills. California was the first state to recognize a lack in its curriculum related to development of critical thinking skills. In 1980, California mandated all junior and senior colleges and universities to require a course in critical thinking as part of the general education requirements for graduation. Eventually, high schools, junior high and middle schools, and elementary schools included critical thinking in their curricula as well (Paul and Adamson, 1990). From this beginning in California, the critical thinking movement has spread to the rest of the United States. Many schools from elementary through college have placed emphasis on critical thinking within their curricula. Instructional strategies for teaching critical thinking require the use of scientific inquiry rather than a strict didactic approach (Hahnemann, 1986; Hudgins and Edelman,



1988). Paul (1993) develops the argument that all educational systems must foster learning of critical thinking skills through their curriculum and instructional process. Regarding the current education on critical thinking in the nursing schools of the universities in Turkey, we see that critical thinking courses are offered only in the Faculty of Nursing at Istanbul University, the Nursing School of Dokuz Eylul University, the Nursing School of Ege University and the Nursing School of Adnan Menderes University, and that different methods are applied in these courses to provide the students with better critical thinking skills.

### Methodology

The research is planned as a “design study with a time series and nonequivalent control group” conducted in order to apply and evaluate the course “Critical Thinking in Nursing” prepared for contributing to the development of critical thinking skills of student nurses.

### Participants

This research is a “design study with a time series and nonequivalent control group” with an objective to evaluate the program to be applied to nursing students to improve their critical thinking skills. In the Nursing School of Ege University, in the Fall Semester of 2007-2008 academic year, there were 155 students in the integrated 1<sup>st</sup> year program, 152 students in the integrated 2<sup>nd</sup> year program, 166 students in the integrated 3<sup>rd</sup> year program, and 169 4<sup>th</sup> year students receiving education in the classical system. There weren't any integrated 4<sup>th</sup> year students. The review of international studies on the critical thinking skills of nursing students revealed that 2<sup>nd</sup>, 3<sup>rd</sup> and 4<sup>th</sup> year students had higher levels of critical thinking compared to 1<sup>st</sup> year students. (Bullen, 1997; Bullen, 1998; Fresseman, 1990; Goodin, 2005; Janiszewski, 2005; Studley, 2005). Thus, the research population included 318 students from the 2<sup>nd</sup> and 3<sup>rd</sup> years of the program.

A total of 39 students, 21 students in the 2<sup>nd</sup> class and 18 students in the 3<sup>rd</sup> class, were registe-

red to the “Critical Thinking in Nursing” course in the Fall Semester of 2007-2008 academic year in the Nursing School. The students who selected this course comprised the experimental group. In the Nursing School, there were 138 students whose academic success grades were close to that of students in the experimental group. The control group included 39 volunteer students, who were selected among these 138 students by simple random sampling method according to their academic success grades. At the end of this process, students in the experimental and control groups were matched according to their academic success grades and class ranks. The research sample consisted of 78 students in total, 39 students in the experimental group and 39 students in the control group.

### Intervention and Measures

The students in the control group were assessed by using their socio-demographic data and final academic success grades. The students in the experimental group were assessed by using the socio-demographic data, grades they obtained from the “Critical Thinking in Nursing” course, and their final academic success grades. Moreover, the “Critical Thinking in Nursing” course attended by the students in the experimental group was a 14-week course with 2 credits. In the course, student assessment was made with exams in the middle (Mid-term Exam) and at the end of the semester (Final and Make-up Exams). In addition, the scenarios prepared in line with the content and objective of the course “Critical Thinking in Nursing” were applied to the experimental group's students at the end of the course. The scenarios were evaluated to determine the learning deficiencies of the students and the challenges causing these deficiencies. The answers given to the questions in the scenarios were evaluated according to the answer key prepared for each scenario. Assessment was made over 100 points. Units were evaluated with the scenarios prepared in accordance with the content and objectives of the units from 1 to 11. At the end of these evaluations, the score calculated by taking the arithmetic average of the grades obtained from the scenarios of 11 units were accepted as the 2<sup>nd</sup> midterm grade. The average of the 1<sup>st</sup> and 2<sup>nd</sup> midterm gra-

des of the student was taken as the midterm grade. The success grade was calculated by adding 40% of the midterm grade and 60% of the final grade. Students with a final grade and course success grade of at least 60 were considered successful (Figure 1). Student assessment of “Critical Thinking in Nursing” course was made according to Article 17 in the Education Regulations of Ege University which specifies exam assessment methods, and taking into consideration the Guidelines on the Absolute Assessment Method included in the Education Regulations of Ege University as well as the Education and Exam Directives of the Nursing School of Ege University (Ege University, 2007).

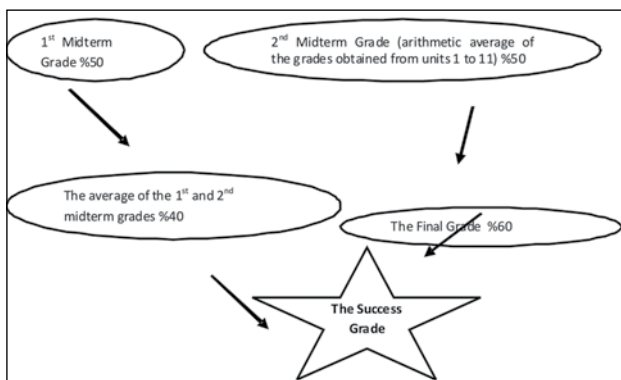


Figure 1. Calculation of the Success Grade obtained from “Critical Thinking in Nursing” course.

### Statistical Analysis

Data were analysed using the SPSS for Windows, Version 15.0 (SPSS, Inc., Chicago, IL). Data were analyzed using numbers, percentage, chi-square, arithmetic average, t-test, and Pearson’s correlation analysis.

### Ethical Consideration

The Research Ethics Committee at the Ege University, School of Nursing approved the study design and research protocol.

### Results

Socio-demographic characteristics of the students in the experimental and control groups were

determined. Table 1 illustrates the distribution of data related to characteristics such as class, marital status, number of siblings, education level of parents, family structure and income status of the students in both groups. There was no statistically significant difference between the socio-demographic characteristics of the students in the experimental and control groups ( $p>0.05$ ). Table 1 illustrates, both groups were homogeneous in terms of descriptive characteristics (Table 1).

The students in the experimental and control groups could not adequately define the concept of critical thinking at the beginning of “Critical Thinking in Nursing” course, and no statistically significant difference was found between the critical thinking definitions of the students in both groups ( $p>0.05$ ). The homogeneity test revealed no difference between the groups. Yapılan homojenlik testinde gruplar arasında fark yoktur (Table 2).

At the end of the “Critical Thinking in Nursing” course, 89.7% of the students in the experimental group defined the concept of critical thinking adequately, while this rate was 7.7% in the control group. A statistically significant difference was determined between the students’ definitions of the concept of critical thinking at the end of the semester, and this difference was associated with the adequate level of definition provided by the students in the experimental group ( $p<0.05$ ) (Table 3).

The point averages of the first and second midterm exams and final exam of the “Critical Thinking in Nursing” course were determined to be  $70.05\pm 9.14$ ,  $72.88\pm 8.19$ , and  $71.30\pm 8.05$ , respectively, while the success grade average was determined as  $71.37\pm 8.36$ . The mean of each unit of the course exam: Critical Thinking in Nursing  $54.69\pm 14.93$ , Problem Solving in Nursing  $66.64\pm 5.11$ , Decision Making in Nursing  $65.20\pm 10.26$ , Priority Setting in Nursing  $72.79\pm 9.32$ , Nursing Process  $72.79\pm 7.55$ , Delegation in Nursing  $77.61\pm 8.71$ , Communication in Nursing  $80.38\pm 6.95$ , Patient Teaching in Nursing  $80.12\pm 7.29$ , Clinical Practice in Nursing  $78.71\pm 6.95$ , Ethical Decision Making in Nursing  $80.89\pm 6.87$ , Applying Nursing Judgement in Clinical Setting  $82.30\pm 6.16$  dir. This distribution of the grade averages of the students is present in Table 4.

The academic success grade averages of the students were found to be  $74.00\pm 3.79$  in the experimental group and  $74.00\pm 3.73$  in the control group

Table 1. Distribution of Socio-Demographic Characteristics of Students

Characteristics	Experimental Group (n=39)		Control Group (n=39)		x <sup>2</sup> p
	Number	%*	Number	%*	
<b>Class</b>					
2.class	21	53.8	21	53.8	x <sup>2</sup> =0.00 p>0.05
3.class	18	46.2	18	46.2	
<b>Age Group</b>					
17-19	4	10.3	8	20.5	x <sup>2</sup> = 1.70 p>0.05
20-22	32	82.1	29	74.4	
23-25	3	7.7	2	5.1	
<b>The Mean Age of Student</b>	20.87±1.08		20.84±1.24		
<b>Marital Status</b>					
Single	37	94.9	36	92.3	x <sup>2</sup> =0.21 p>0.05
Married	2	5.1	3	7.7	
<b>Number of Siblings</b>					
A Sibling	19	48.7	19	48.7	x <sup>2</sup> = 1.08 p>0.05
Two Siblings	7	17.9	9	23.1	
Three Siblings	8	20.6	5	12.8	
Four and more sinlings	5	12.8	6	15.4	
<b>Mother Education Level</b>					
Illiterate	3	7.6	3	7.6	x <sup>2</sup> = 1.02 p>0.05
Primary Education	32	82.1	28	71.8	
High School	4	10.3	8	20.6	
<b>Father Education Level</b>					
Primary Education	23	59.0	21	53.9	x <sup>2</sup> = 1.76 p>0.05
High School	10	25.6	10	25.6	
University	6	15.4	8	20.5	
<b>Income</b>					
Low	3	7.7	5	12.8	x <sup>2</sup> =0.55 p>0.05
Medium	36	92.3	34	87.2	
<b>Total</b>	<b>39</b>	<b>100.0</b>	<b>39</b>	<b>100.0</b>	

\*Column Percentage

Table 2. Students' Defining the Concept of Critical Thinking "Critical Thinking in Nursing" Pre-Course

Critical thinking concept	Experimental Group (n=39)		Control Group (n=39)		x <sup>2</sup> p
	Number	%*	Number	%*	
<b>Enough</b>	0	0	0	0	x <sup>2</sup> =0.147 p>0.05
<b>Moderate Enough</b>	17	43.6	16	41.0	
<b>Inadequate</b>	22	56.4	23	59.0	
<b>Total</b>	<b>39</b>	<b>100.0</b>	<b>39</b>	<b>100.0</b>	

\*Column Percentage

Table 3. Students' Defining the Concept of Critical Thinking "Critical Thinking in Nursing" Post-Course

Critical thinking concept	Experimental Group (n=39)		Control Group (n=39)		x <sup>2</sup> p
	Number	%*	Number	%*	
<b>Enough</b>	35	89.7	3	7.7	x <sup>2</sup> = 12.443 p<0.05
<b>Moderate Enough</b>	3	7.7	24	61.5	
<b>Inadequate</b>	1	2.6	12	30.8	
<b>Total</b>	<b>39</b>	<b>100.0</b>	<b>39</b>	<b>100.0</b>	

\*Column Percentage

Table 4. Students' Distribution of Course Exam Mean "Critical Thinking in Nursing"

Course Exam Averages (n=39)	$\bar{X}$	$\pm$ SD
The average of the 1 <sup>st</sup> Midterm Grade Min-max (60-90)	70.05	9.14
The average of the 2 <sup>nd</sup> Midterm Grade Min-max (65-88)	72.88	8.19
Critical Thinking in Nursing Unit	54.69	14.93
Problem Solving in Nursing Unit	66.64	5.11
Decision Making in Nursing Unit	65.20	10.26
Priority Setting in Nursing Unit	72.79	9.32
Nursing Process Unit	72.79	7.55
Delegation in Nursing Unit	77.61	8.71
Communication in Nursing Unit	80.38	6.95
Patient Teaching in Nursing Unit	80.12	7.29
Clinical Practice in Nursing Unit	78.71	6.95
Ethical Decision Making in Nursing Unit	80.89	6.87
Applying Nursing Judgement in Clinical Setting Unit	82.30	6.16
The Final Grade Min-max (60-87)	71.30	8.05
The Success Grade	71.37	8.36

Table 5. Students' Distribution of the average of Academic Achievement Note

Students' Academic Achievement Note Averages	Experimental Group (n=39)		Control Group (n=39)		t*	p
	$\bar{X}$	SD	$\bar{X}$	SD		
2006-2007 Academic Year of The Average Academic Achievement Note	74.00	3.79	74.00	3.73	6.10	1.02
2007-2008 Academic Year of The Average Academic Achievement Note	77.38	5.26	74.23	3.90	<b>3.00</b>	<b>0.00</b>

in the 2006-2007 academic year, and  $77.38 \pm 5.26$  in the experimental group and  $74.23 \pm 3.90$  in the control group in the 2007-2008 academic year. While no statistically significant difference was found between the final academic success grades of the students before the "Critical Thinking in Nursing" course in the 2006-2007 academic year ( $p > 0.05$ ); there was a statistically significant difference between the students' final academic success grades after the completion of the course in the 2007-2008 academic year ( $p < 0.05$ ). This significant difference was associated with the higher grades of the students in the experimental groups compared to those in the control group. Table 5 illustrates the results.

A positive and statistically significant difference of medium level was detected between the final academic success grade averages of the students in the experimental group in the 2007-2008 academic year and grade averages of the "Critical Thinking in Nursing" course ( $r = 0.497$   $p = 0.001$ ).

## Discussion

High level of adequacy in the definitions of the students in the experimental group was the reason for the statistical difference between the students in the experimental and control groups in terms of the definitions of critical thinking after the completion of the "Critical Thinking in Nursing" course. Defining the concept of critical thinking is a cognitive aim and this was an expected result at the end of the 14-week and 28-hour course.

The complexity of the problems experienced in social life and health services requires that nurses and student nurses are equipped with necessary skills to cope with these problems. In order to meet the health-related needs of society, student nurses are expected to search for information, to have self-confidence, to be honest, to take risks, to be investigative, to obtain information when a problem arises, to rely on their instincts and expe-

riences, to introduce different options for the solution of a problem, to make use of other people's opinions, to experience themselves clearly, to use language properly, and to avoid taking steps on impulse without thinking (Pitts, 2001). Therefore, it is important to include critical thinking courses in the curriculum and investigate the progress of students in this matter.

Critical thinking has become both the basic concept and key power of today's societies. The transition from industrial society to information society has brought along features necessary to become one of the powerful societies. These features include the ability to think critically and use critical thinking to cope with the complexity of modern life. The attention and preferences of employers, educators and executive managers have, therefore, focused on individuals who can effectively use their critical thinking skills (Pitts, 2001). In line with these developments, the education programs offered in universities need to be evaluated and reorganized to integrate critical thinking into the education process.

Success grade averages of the "Critical Thinking in Nursing" course in the experimental group were observed to be high. Gadzella et al. (1997) and Sesow (1991) have noted that the development of critical thinking is a complicated method, and the researches concerning the education on critical thinking demonstrated that these skills may be acquired by a well-prepared education program. Different education methods were used in different studies to improve the critical thinking skills of nursing students. Study results revealed an increase in the level of critical thinking among students. As reported in some studies, students who participated in these studies were introduced to the concept of critical thinking for the first time within the scope of a program and their level of success was found to be medium at the end of the program, indicating the success of the researches (Duphorne, 2000; Ellermann, et al., 2006). In the present study, the high grade averages were the success of the students, the researchers and the education program.

Kökdemir (2003) reported an increase in the final academic success grades of the students in the experimental group. Stewart and Dempsey conducted a case study in 2005 based on theoretical in-

formation in order to improve the critical thinking skills of nursing students, and observed a positive increase in the final success grades of students at the end of the study. Ellermann et al. (2006), who conducted researches in 2004 with nursing students, tried to improve the critical thinking skills of students by using concept map in class, and the students were observed to be more successful in their courses at the end of the semester compared to beginning of the semester. Morey, who carried out a study in 2008 with nursing students, observed an increase in the success levels of students in the experimental group compared to those in the control group in terms of their success both in their courses and practices. The above mentioned literature findings support our study results. In our study, no statistical difference relationship was found between the academic success grade averages of the experimental and control students before the "Critical Thinking in Nursing" course and the between the grade averages were not significant. This result was associated with the fact that the students in the control group were selected with the simple random sampling method among volunteer students who had academic final grade averages similar to those of the experimental group's students at the end of the previous academic year. On the other hand, a statistical difference was found between final academic success grade averages of experimental and control students after the completion of the "Critical Thinking in Nursing" course, and this difference was associated with the higher scores obtained by experimental students compared to those in the control group, indicating that the "Critical Thinking in Nursing" course improved the critical thinking skills of the students in the experimental group and contributed to the increase in their final academic success grade averages.

Authorized bodies in the United States emphasized the need to include courses and methods developing critical thinking such as critical thinking courses, group activities on critical thinking, active class participation in the curricula of nursing education (Shin et al., 2006). Furthermore, the necessity of assessing the results of critical thinking education is highlighted by the American National Association of Nursing (Tarh, 1999; Valiga, 2003).

The students who participated in the study were asked three questions about their opinions on the

“Critical Thinking in Nursing” course and their answers were collected in writing. Concerning the first question “What are the developmental contributions of the ‘Critical Thinking in Nursing’ course?”, all the students in the experimental group noted that the course improved their critical thinking skills as well as problem-solving skills, 37 students noted that they no longer experienced conflict while making decisions in case of problematic situations, 36 students noted an improvement in their nursing process skills and process capability in cases they encounter in practice, and 35 students noted an increase in their ability to think systematically against an event. 34 students expressed opinions such as “I behave more sensitively in situations of conflict” and “I try not to develop prejudices against my friends and the situations I encounter”. More than half of the class stated that their self-confidence increased after the completion of this course, while half of the class reported an increase in their empathy skills and time management skills as well as in their love of profession. Less than half of the class noted that they developed a better comprehension of what it meant to make ethical decisions and that they tried to apply this comprehension in their training practice.

The distribution of the answers given to the second question “What are the difficulties of the ‘Critical Thinking in Nursing’ course?” is as follows: 27 students mentioned the difficulty caused by examinations not based on rote-learning, 20 students mentioned the intensity of theoretical information which they had not expected in the “Critical Thinking in Nursing” course. 7 students expressed their dislike of exercises, scenarios and written homework assignments.

As a response to the third question “What are your suggestions about the ‘Critical Thinking in Nursing’ course?”, 37 students suggested that this course should be offered as a compulsory course on a yearly base in both semesters to be taken by all students in the School of Nursing. 15 students suggested that more discussions on the topic should be made in class, and 7 students suggested that more scenarios, exercises and homework should be assigned.

According to Main and Eggen (1991), students “use their critical thinking skills by applying the knowledge they gain through self-experience in a communicative and open environment

and through meaning formation process by prescriptive interrogation, and therefore, they build the foundations of thinking”. In his studies published in 2002-2003, Zimmerman states that scenario-based education has a major contribution to critical thinking, because students express themselves better in cases related to life. Abel and Freze (2006), Hill (2006), Ferrario (2004), Chaill and Fonteyn (2000) also report that the techniques used in the development of critical thinking dispositions and skills have a considerable contribution to this development, and that these techniques as well as the instant feedback given to students improve their critical thinking skills and help them to express themselves more openly and freely. Morey (2008), Trap (2005), Motolla and Murphy (2001) highlight the importance of critical thinking education and state that the quality of education programs and especially the feedbacks received from students contribute to the development critical thinking.

### Conclusion

In the definitions of the concept of critical thinking provided by experimental and control group students at the end of the “Critical Thinking in Nursing” course, it was observed that the rate of students who defined critical thinking adequately was higher in the experimental group compared to the students in the control group. In addition, academic success grades were higher in the experimental group after the completion of the course. According to the evaluations of all the students in the experimental group who were registered to “Critical Thinking in Nursing” course, all the students improved their critical thinking and problem solving skills, and almost all the students no longer experienced conflict while making decisions for resolving problems. 37 students in the discussion group mentioned that this course should be offered on a yearly base in two semesters as a compulsory course and that all the students in the School of Nursing should take the course. Consequently, the opinions of students on “Critical Thinking in Nursing” course were evaluated and education material was reorganized and collected in a book.

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# Evaluation of clinical effectiveness and direct drug costs of different antipsychotics in inpatient settings

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## Abstract

The treatment of schizophrenia is a complex issue. Considering the costs of disease this is one of the most expensive psychiatric disorders.

To evaluate clinical effectiveness and direct drug costs of different antipsychotics after one month therapy in patients with acute psychotic episodes of schizophrenia.

One hundred patients with acute psychotic episodes of schizophrenia were included. PANSS scores were assessed in two time points, at baseline and one month later.

In group receiving only typical antipsychotics the reduction in Positive and Negative subscale score is numerically and statistically significant with average cost per patient of 45.81 EUR. In the group that received only atypical antipsychotics percentile reduction of both scores, was the greatest (-44.7%, -22.3, respectively) with average cost per patient of 63.07 EUR. Different combinations of antipsychotics are the most expensive treatment with average cost per patient of 82,41 EUR.

Typical antipsychotics are clinically and cost-effective in the treatment of Positive and Negative symptoms of schizophrenia in patients with acute psychotic episodes during first month therapy in inpatient settings with lowest direct drug cost per patient and with acceptable adverse effects profile.

**Key words:** schizophrenia, antipsychotics, PANSS, cost-effectiveness

## Introduction

Schizophrenia occurs in 1% of the world's population, regardless of country and culture (1). As a disease it is characterised by complex clinical picture associated with impairment of different domains of psychological functions (disturbances of perception, cognitive functions, loss of motivation, disturbances of formal and conceptual fraction of thinking, impaired affect) and somatic impairment as diabetes mellitus, hyperlipoproteinemias, hypertension and other diseases. Clinical picture varies from person to person and sometimes individually during different life periods.

Same as clinical picture the treatment outcomes are different in different patients. According to treatment outcomes three basic groups of schizophrenic patients are distinguished: nonresponders, partial responders and responders. For prediction of general prognosis there are certain prognostic factors ranked as factors of "good" and "bad" prognosis (2). Positive and Negative Symptoms Scale – PANSS scale is often used for evaluation of current psychiatric condition (measuring symptom severity) as a relatively brief interview. It is based on the fact that the symptoms of schizophrenia (SCH) usually segregate into semi-independent symptom complexes: positive symptoms and negative symptoms. Positive symptoms comprise delusions and hallucinations, usually auditory. The presence and severity of negative symptoms are more critical to the prognosis than the positive symptom complex; negative symptoms include blunted, abnormally unresponsive mood, reduced willpower, reduced amount of spontane-

ous speech and loss of self-care skills. Negative symptoms can become progressively more severe and often persist to a degree even when positive symptoms have improved so these symptoms represent a great problem in the treatment of patients suffering from SCH. Men, however, are slightly more likely to develop enduring negative symptoms than women, who have greater representation in the good prognosis group.

As clinical picture and treatment outcomes vary amongst patients, the treatment of SCH is a complex issue. The main goal of treatment is control of the symptoms and social rehabilitation of patient. The non-compliance to the antipsychotic treatment is a major problem with people suffering from SCH leading to a poor stabilization of disease. Compliance is influenced by many various causes as clinical features of disease, adverse drug effects, social support etc.

### **Antipsychotic drug treatment**

The optimal maintenance treatment of schizophrenia involves the integration of physical, psychological and social care. Drugs used for treatment of SCH are divided in two groups: 1) conventional or typical antipsychotics as promazine, chlorpromazine, levomepromazine, tioridazine, fluphenazine, perazine, haloperidol, and 2) second generation - atypical antipsychotics as risperidone, clozapine, olanzapine, quetiapine, ziprasidone.

The conventional or typical antipsychotics are characterised by very good efficacy in treatment of positive symptoms but have several critical limitations: a) around 20–25% of people with schizophrenia treated with the conventional antipsychotics fail to show a satisfactory response; b) the drugs have a limited effect on the negative symptoms; c) these drugs are associated with a numerous adverse effects as sedation and acute extrapyramidal side-effects (EPS).

Second generation antipsychotics – atypical antipsychotics, compared to typical, have a wider spectrum of activity as they are effective in the treatment of both, positive and negative symptoms with lower incidence of adverse effects (3). This reduced risk of EPS is a major advance, as acute EPS have undesirable motor and psychological

manifestations, and often require treatment with antiparkinsonic or anticholinergic agents, which have their own side-effects and hazards. However, based on data from clinical trials it is estimated that percentile decrease of SCH symptoms after treatment with typical or atypical antipsychotics, compared to baseline values, ranges between 12% i 18% (4).

In clinical practice, the lack of a satisfactory response to a single antipsychotic often prompts the addition of another. In the majority of cases the reason given for this polypharmacy was that a single antipsychotic had not been effective.

Considering the costs of disease SCH is one of the most expensive psychiatric diseases (5) because of high direct and indirect costs associated with specific clinical features that vary from person to person, because of its resistance to treatment, non-compliance and adverse drug reactions.

Literature data indicates that the new atypical antipsychotics including clozapine are cost-effective compared with chlorpromazine or haloperidol (6). Overall, the economic evidence suggests that the new atypical antipsychotics are associated with improved outcomes compared with conventional antipsychotics and with cost savings or small increases in costs although these drugs can induce some metabolic disturbances as secondary hypertriglyceridemia (7). Nearly all the evaluations found that the new atypical antipsychotics were cost-effective. The majority of comparisons of new atypical antipsychotics and conventional drugs considered risperidone or olanzapine.

Nevertheless, since their introduction almost 50 years ago, the conventional or typical antipsychotic drugs have formed the mainstay of both acute and long-term treatment for schizophrenia, and have been invariably used as first line therapy.

### **Objectives**

The primary objective of our investigation was to evaluate clinical effectiveness and direct drug costs of different antipsychotics after one month therapy in patients with acute psychotic episodes of SCH, based on assessment of Positive and Negative scores of PANSS scale as a direct outcome measure.

## Methods

The investigation was conducted as open-label study in inpatient settings of everyday clinical practice. In total, 100 patients with acute psychotic episodes of SCH were included by consecutive order as they were admitted to Psychiatric Clinic. Patients were considered „withdrawn“ if they did not appear on last visit ( after one month). In accordance to basic principles of contemporary psychopharmacotherapy patients were individually treated as in routine practice. PANSS scores was assessed in two time points, at baseline and one month later.

### Inclusion/exclusion criteria

Inclusion criteria: clinically verified schizophrenia, admittance to Psychiatric Clinic, age above 18 years.

Exclusion criteria: substance abuse; age below 18 years.

### Eligibility

Eligibility criteria were that patients were eligible in the context of 1 month's history.

### Primary outcome measure

Clinical evaluation is based on Positive and Negative Symptoms Scale – PANSS scale. The PANSS is a well-validated, widely used schizophrenia rating scale, containing 30 items divided into three subscales (positive, negative and general psychopathology). A 20% change in total score is considered clinically important. Positive and Negative subscale are extracted for evaluation as a main difference between typical and atypical antipsychotics efficacy in treating SCH. Adverse effects were assessed by psychiatrist.

Only direct drug costs were included in the analysis, based on average costs of drugs used. The drug costs were valed from Drug Registry (2009), average cost for every drug and every unit (tablet, capsule, ampoule) was calculated, than multiplied

by prescribed daily dose. If patient received more than one drug daily, doses were added, than multiplied by number of treatment days. The switching from one to another drug(s) was calculated by the same method. Detailed information about medication included dose, duration and route of administration. The cost of medicines did not include the costs of dispensing or administration. Total drug cost and average cost per patient are presented in local currency – convertible mark (KM) and in euros (EUR) with conversion factor 1.95.

### Individual drugs

The following drugs were considered to be conventionals and were available to prescribing clinicians for patients: haloperidol tbl, haloperidol amp., haloperidol depot , fluphenazine depot, promazine drag., promazine amp., levomepromazine tbl., sulpiride caps., risperidone tbl., clozapine tbl., olanzapine tbl., as well as diazepam tbl., diazepam amp., nitrazepam tbl., sertraline tbl., maprotiline tbl., clomipramine drag., biperiden tbl., biperiden amp. and bisacodyl dragee.

Statistical evaluation was performed by statistical tests incorporated in computer programs Excel 7.0, Sigma Stat 3.5.

### Results

In total, 100 patients with acute psychotic episodes of SCH were included by consecutive order as they were admitted to Psychiatric Clinic. The mean age was 40.7 years and the majority (79%) were female. The mean duration of SCH was 9.8 years, 27% patients with chronic course of SCH, 34% progredient, 32% intermittent and 7% with first episode. Only 6 were non-smokers. After one month 91 patient was eligible for analysis (9% withdrew) as presented in Table 1.

Conventional antipsychotics were prescribed to 65 (71.4%) patients and atypical were prescribed to 12 (13.2%) patients. Forteen patients (15.4%) were receiving different combinations of typical and atypical (Table 2.). From 91 patient 24 (26.4%) received depot preparations. Biperiden was prescribed to 15 (16.5%) patients but there

Table 1. Baseline demographic and disease characteristics

Characteristic	(n=100)	%
Male	21	21
Female	79	79
Mean age (years)	40.7	
Mean duration of SCH (years)	9.8	
Smoking	6	6
First episode	7	7
Intermittent	32	32
Proгредиant	34	34
Chronic	27	27
Withdrew	9	9

Table 2. Antipsychotics prescribed and costs

Antipsychotics	Number of patients	Percent %	Total drugs cost KM/EUR	Average cost per patient KM/EUR
All antipsychotics	91	100	9531.71/4888.06	104.74/53.71
Received only typical antipsychotics	65	71.4	5806.39/2977.636	89.33/45.81
Received only atypical antipsychotics	12	13.2	1475.7/756.77	122.98/63.07
Received combination of typical and atypical	14	15.4	2249.62/1153.65	160.69/82.41

Table 3. PANSS score Positive and Negative subscale (all antipsychotics)

Statistics	Positive subscale		Negative subscale	
	Baseline	After 1 month	Baseline	After 1 month
N = 91				
Mean	34.5	19.6	31,2	25.2
Min	16	8	15	9
Max	48	42	49	49
Median	35	20	31	24
Std Dev	6.49	6.69	8.80	8.81
Difference	14.9		6.0	
t = 15.290 with 180 degrees of freedom. (P = <0.001)*			T = 9839.500 (P = <0.001)**	
Statistical significance	Significant		Significant	
Percentile reduction by (%)	- 43.2		- 19.2	

\* t-test; \*\* Mann-Whitney Rank Sum Test

Table 4. PANSS score Positive and Negative subscale (typical antipsychotics)

Statistics	Positive subscale		Negative subscale	
	Baseline	After 1 month	Baseline	After 1 month
N = 65				
Mean	34.9	19.7	31	25
Min	16	8	15	9
Max	48	42	47	47
Median	35	20	31	24
Std Dev	6.79	6.93	8.58	8.79
Difference	15.2		6.0	
t = 12.592 with 128 degrees of freedom. (P = <0.001)*			T = 5035.000 (P = <0.001)**	
Statistical significance	Significant		Significant	
Percentile reduction by (%)	- 43.6		- 19.4	

\* t-test; \*\* Mann-Whitney Rank Sum Test

were no cases of switching therapy or withdrawal because of adverse effects as in most cases (12) biperiden was prescribed „as needed“ and only in 3 cases biperiden was administered (2 cases tablets; 1 case injection). There were 3 cases of obstipation reported, requiring drug therapy.

After one month total decrease in Positive subscale of PANSS score for 91 patients and therapy with all antipsychotics was estimated to be from 34.5 to 19,6 (- 43.2%) and in Negative scale from 31.2 to 25.2 (- 19.2%) (Table 3.) achieved with 9531.71 KM (4888.06 EUR) total drug cost and 104.74 KM (53.71 EUR) average direct drug costs per patient. In both, Positive and Negative subscale, the difference in score reduction one month from baseline was statistically significant.

After one month total decrease in Positive subscale of PANSS score for 65 patients treated only with typical antipsychotics was estimated to be from 34.9 to 19.7 (- 43.6%) and in Negative scale from 31 to 25 (- 19.4%) (Table 4.) achieved with 5806.39 KM (2977.636 EUR) total drug cost and 89.33 KM (45.81 EUR) average direct drug costs per patient. In both, Positive and Negative subscale, the difference in score reduction one month from baseline was statistically significant.

In group of patients receiving only atypical antipsychotics after one month total decrease in Positive subscale of PANSS score for 12 patients was estimated to be from 30.9 to 17.1 (- 44.7%) and in Negative scale from 34.5 to 26.8 (- 22.3%) (Table 5.) achieved with 1475.7 KM (756.77 EUR) total drug cost and 122.98 KM (63.07 EUR) average direct drug costs per patient. Although the score reduction for Negative subscale was by 22.3% after one month from baseline it was statistically not significant. The difference in score reduction for Positive subscale after one month from baseline was statistically significant.

After one month from baseline combination of different antipsychotics used in treatment of 14 patients with SCH resulted in total decrease in Positive subscale of PANSS score from 36 to 21.1 (-41.4%) and in Negative subscale of PANSS score from 29.3 to 24.6 (- 16%) (Table 6.) achieved with 2249.62 KM (1153.65 EUR) total drug cost and 160.69 KM (82.41 EUR) average direct drug costs per patient.

The greatest clinical and statistically significant

difference in Positive subscale score (15.2) after one month of treatment compared to baseline values was for group receiving only typical antipsychotics. In this group the reduction in Negative subscale score is numerically and statistically significant (6.0; - 19.4%) with average cost per patient of 45.81 EUR . In the group that received only atypical antipsychotics percentile reduction of both, Positive and Negative subscale scores, was the greatest (- 44.7%, - 22.3, respectively) with average cost per patient of 63.07 EUR. But, only percentile reduction in Positive subscale score was statistically significant. Different combinations of antipsychotics are, by numerical data, more effective in reduction of positive subscale score than atypical antipsychotics (14.9 vs 13.8, respectively) with average cost per patient of 82.41 EUR (Table 7.).

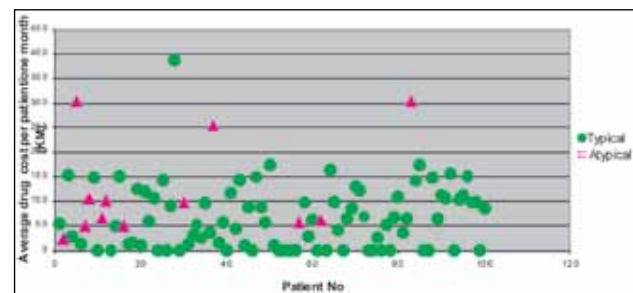


Figure 1. Direct drug costs (typical vs atypical antipsychotics) distribution (n=77)

As presented in Figure 1. one quarter (25%) of atypical antipsychotic direct drug costs (3/12) ranges above limit of 200.0 KM (102.6 EUR) while only 1.5% (1/65) of typical antipsychotic direct drug costs ranges above this limit. These observations has to be considered with caution regarding number of patients in two groups (12 vs 65).

Although biperiden was prescribed to 15 (16,5%) and bisacodyl to 3 (3,3%) patients, total of 6 adverse effects (6,6%) were reported: 3 cases required anticholinergic therapy with biperiden (2 cases of mild and 1 case of moderate EPS) and 3 cases required laxative bisacodyl (2 mild and 1 moderate case of obstipation), all in patients receiving typical antipsychotics.

Table 5. PANSS score Positive and Negative subscale (atypical antipsychotics)

Statistics	Positive subscale		Negative subscale	
	Baseline	After 1 month	Baseline	After 1 month
N = 12				
Mean	30.9	17.1	34.5	26.8
Min	23	9	17	12
Max	41	27	49	49
Median	31	15	32.5	23.5
Std Dev	5.29	5.64	9.48	10.63
Difference	13.8		7.7	
	t = 6.187 with 22 degrees of freedom. (P = <0.001)*		t = 1.864 with 22 degrees of freedom. (P = 0.076)*	
	Statistical significance		Not significant	
	Percentile reduction by (%)		- 22.3	
	- 44.7			

\* t-test

Table 6. PANSS score Positive and Negative subscale (combination of antipsychotics)

Statistics	Positive subscale		Negative subscale	
	Baseline	After 1 month	Baseline	After 1 month
N = 14				
Mean	36	21.1	29.3	24.6
Min	28	11	17	14
Max	44	30	49	42
Median	36	20	29	23
Std Dev	5.06	6.13	9.15	7.61
Difference	14.9		4.7	
	t = 6.984 with 26 degrees of freedom. (P = <0.001)*		t = 1.482 with 26 degrees of freedom. (P = 0.150)*	
	Statistical significance		Not significant	
	Percentile reduction by (%)		- 16	
	- 41.4			

\* t-test

Table 7. Comparative reduction in Positive and Negative subscale and drug costs

Antipsychotics	All	Typical	Atypical	Combination
Difference Positive scale	14.9	<b>15.2</b>	13.8	14.9
Difference Negative scale	6.0	6.0	<b>7.7</b>	4.7
Positive scale reduction by %	- 43.2	- 43.6	<b>- 44.7</b>	- 41.4
Negative scale reduction by %	- 19.2	- 19.4	<b>- 22.3</b>	- 16
Statistical significance Positive scale	significant	significant	significant	significant
Statistica significance Negative scale	significant	significant	<b>Not significant</b>	<b>Not significant</b>
Total drugs cost KM/EUR	9531.71/4888.06	5806.39/2977.64	1475.7/756.77	2249.62/1153.65
Average cost per patient KM/EUR	104.74/53.71	89.33/ <b>45.81</b>	122.98/ <b>63.07</b>	160.69/ <b>82.41</b>

Table 8. Cost-effectiveness analysis

	Positive scale reduction by %	Statistical significance	Negative scale reduction by %	Statistica significance	Cost KM/EUR
Typical	43.6%	Yes	19.4%	Yes	89.33/45.81
Atypical	44.7%	Yes	22.3%	No	122.98/63.07

## Discussion

The majority of efficacy studies of the atypical antipsychotics that have been reported relate to symptom improvement in short-term clinical trials, of less than 12 weeks in duration. However, schizophrenia is often both a chronic and recurrent disorder and hence information on efficacy and safety in long-term maintenance treatment is important. Thus far, there are only a few studies assessing longer term outcome in terms of maintaining early symptom improvement, relapse prevention, tolerability, medication compliance and quality of life. A recent systematic review suggests that the conclusions that could be drawn about the relative effectiveness of the newer antipsychotics were limited because of problems with the validity of the trials in terms of inclusion and exclusion criteria, dose used, sample size and duration of trials, outcome measures used and methods of reporting symptoms (8,9).

From total of 100 patients included in our investigation after one month 91 patient was eligible for analysis (9% withdrew) what is far less than 28% reported in other studies with small number of patients (10).

In our investigation the majority (71.4%) of patients with acute psychotic episodes of SCH in inpatient settings were treated with typical antipsychotics what is comparable with results from other investigations claiming that conventional, typical, antipsychotics still have a place in the treatment of patients suffering from SCH (11). The greatest clinical and statistically significant difference in Positive subscale score (15.2; - 43.6%) after one month of treatment compared to baseline values was for group receiving only **typical** antipsychotics. In this group the reduction in Negative subscale score is numerically and statistically significant (6.0; - 19.4%) with average cost per patient of **45.81 EUR**. In the group that received only **atypical** antipsychotics percentile reduction of both, Positive and Negative subscale scores, was the greatest (- 44.7%, - 22.3, respectively) with average cost per patient of **63.07 EUR**. But, only percentile reduction in Positive subscale score was statistically significant. Different combinations of antipsychotics are, by numerical data, more effective in reduction of positive subscale score than atypical antipsychotics (14.9 vs

13.8, respectively) with average cost per patient of 82.41 EUR. It is well known that, compared to typical antipsychotics, atypical antipsychotics are more effective in the treatment of negative symptoms (3, 9, 12, 13).

Total of 6 adverse effects (6%) were reported: 3 cases of EPS and 3 cases of obstipation what is far less than incidence reported by other authors (14).

## Conclusion

SCH is one of the most expensive psychiatric diseases because of high direct and indirect costs associated with specific clinical features that varies from person to person and sometimes in person during different life periods, because of its resistance to treatment, non-compliance and adverse drug reactions.

In our investigation the majority (71.4%) of patients with acute psychotic episodes of SCH in inpatient settings are treated with typical antipsychotics. Based on results from our investigation typical and atypical antipsychotics have equal clinical effectiveness in treatment of Positive SCH symptoms in routine inpatient practice. Typical antipsychotics are clinically and cost-effective in the treatment of Positive and Negative SCH symptoms in patients with acute psychotic episodes of SCH during first month of therapy in inpatient settings, with lowest direct drug cost per patient and with acceptable adverse effects profile. Atypical antipsychotics are clinically effective in reducing Positive and Negative SCH symptoms but with no statistical significance in reducing Negative symptoms compared to baseline values, with higher direct drug cost per patient than typical antipsychotics. Different combinations of antipsychotics are the most expensive treatment for SCH based on average cost per patient (82,41 EUR) with no statistically significant difference in reduction of Negative subscale score. but with greater numerical reduction in Based on our results typical antipsychotics are clinically and cost-effective in the treatment of Positive and Negative SCH symptoms in patients with acute psychotic episodes of SCH during first month of therapy in inpatient settings. This can also include the possibility that an intervention is associated with no



differences in effectiveness, and is cost saving. Further planned analyses of this data set include an examination of the effects of injectables, depot preparation, the impact and determinants of polypharmacy, and an examination of PANSS total score and other subscales in schizophrenia as well as further investigations with larger number of patients for a longer time.

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# Impact of hemoglobin level on the development of ischemic heart disease

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## Abstract

The acute coronary syndrome is a clinical condition based on a sudden critical myocardial ischemia and it implies the three entities: unstable angina pectoris, acute myocardial infarction and a sudden cardiac death. The development of acute coronary syndrome is affected by a number of factors and the presence of comorbid conditions which significantly affect the prognosis and the course of therapy.

Low hemoglobin level is an independent risk indicator of ischemic developments especially if it is caused by acute bleeding; and is also important for chronic state of anemia, which patients usually endure quite well but they require special treatment.

The aim of this study was to attest the influence of anemia on the development of acute ischemic heart disease. The study included 93 patients observed at our cardiology department, they all suffered anemia, 67 patients or 72.04% had outpatient treatment, and 26 patients or 27.96% had outpatient treatment after being hospitalized at the Tuzla Internal Medicine Clinic. Two thirds of the patients were elderly and they suffered anemia caused by chronic disease (malignant neoplasm, rheumatoid arthritis, chronic renal insufficiency, idiopathic myelofibrosis) and to a lesser extent the anemia due to the acute bleeding, which was more frequent with the middle aged patients.

The patients have been administered peroral and parenteral preparations of iron, and a satisfactory effect of the therapy has been achieved reducing the symptoms of angina discomforts and heart failure.

We have concluded that low hemoglobin level significantly contributes to the deterioration of the

clinical picture, and influence the prognosis and the course of the ischemic heart disease.

**Key words:** acute coronary syndrome, anemia, hemoglobin.

## Introduction

Acute coronary syndrome is a clinical condition based on a sudden critical myocardial ischemia and it implies the three entities: unstable angina pectoris, acute myocardial infarction and a sudden cardiac death. The development of acute coronary syndrome is affected by several risk factors such as age, sex, obesity, hypertension, diabetes, high blood lipid levels, consumption of tobacco, family tendency towards heart diseases, as well as comorbidity. Reasons for low hemoglobin level may be acute bleeding (gastrointestinal, menstrual, etc.) and anemia of chronic disease (malignant disease, rheumatoid arthritis, chronic renal insufficiency, idiopathic myelofibrosis, etc.).

Hemoglobin is the iron-containing oxygen-transport metalloprotein in the red blood cells. Its reference value for men is 138-170 g/L, and for women 120-150 g/L. Low hemoglobin level impacts the oxygen transport in our body. The metabolic processes of the myocardium are almost exclusively aerobic, therefore they need oxygen. Low hemoglobin level, which accompany some diseases, impact metabolism in myocardium, and along with the primary cardiovascular disease, ischemia occurs. We have anaerobic metabolism in heart muscle, in which several non-oxygenated metabolic products are developed, which then activate sensory nerve endings of the sympathetic in the myocardium, creating severe visceral pain - angina.

## The aim of the study

The aim of the study was to show the impact of hemoglobin level on the development, course and prognosis of acute coronary syndrome.

## Materials and methods

In a retrospective study we processed a group of 93 patients - 47 men and 46 women; 25 to 75 years of age; which were monitored at the Lukavac Health Center cardiology outpatient department from January 2006 to December 2007. 67 patients (72.04%) were monitored and treated at the outpatient department, and 26 patients (27.96%), were, after hospitalization, treated at the Tuzla Internal Medicine Clinic.

They had come in our outpatient department, where we, according to anamnesis data, clinical examination, EKG result, lab test results and previous medical documentation, had determined whether they would be treated at the outpatient department or should be hospitalized. All the patients had had low hemoglobin level compared to the reference values for men and women; and besides that they had had other risk factors of ischemic heart disease. 15 patients (16.12%) had suffered hypertension, 18 (19.35%) had suffered diabetes, 33 (35.48%) had suffered high blood lipid levels, and 14 (15.05%) had had positive family history for coronary disease.

Reason for low hemoglobin level had been different: One third of the patients had suffered anemia as a result of acute bleeding, mainly gastrointestinal. Two thirds of the patients had suffered anemia as a result of a chronic disease such as malignant neoplasm, rheumatoid arthritis, chronic renal insufficiency, idiopathic myelofibrosis. There had been two patients who suffered idiopathic anemia.

We used the data from the Lukavac Health Center laboratory and from the hospital discharge summaries issued by the Tuzla Internal Medicine Clinic.

We divided all the patients into two groups; the ones whose hemoglobin level was below 100 g/L (13 patients) and those whose hemoglobin level was above 100 g/L (80 patients).

## The results

Of the total of 93 patients, 26 or 27.95% of them had been referred to the Tuzla Internal Medicine Clinic for hospital treatment, under the clinical picture of acute coronary syndrome, whom we monitored even after the hospitalization. There were 17 (65.38%) men and 9 (34.62%) women. (Chart 1.)

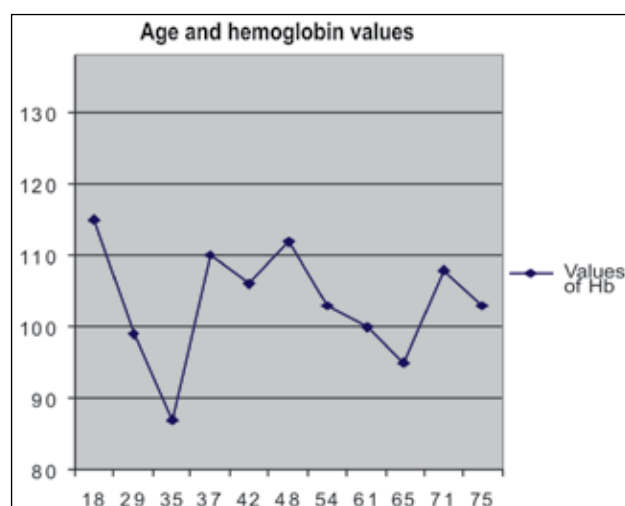


Chart 1. Correlation between the age of the patients and anemia

All the patients had had one more or more risk factors for cardiovascular disease, such as hypertension, diabetes, obesity, high blood lipid levels, chronic renal insufficiency (but had not been chronic hemodialysis patients), consumed tobacco, and apart from that had had lab test results indicating low hemoglobin level with normal or low level of red blood cells, as well as medical history.

The patients have been administered iron preparations parenterally and perorally. We have obtained satisfactory results with one half of the patients - 46 (49,46%) of them, in other words the anemia was cured. With 33 (35,48%) patients we have obtained a good result - but they have still demanded regular monitoring and occasional usage of iron preparations. 14 (15,05%) patients have reached the maximum level of hemoglobin of up to 120 g/L.(Chart 2.) The medical conditions of majority of the patients have improved, which means they have suffered angina discomforts and heart failure less frequently.

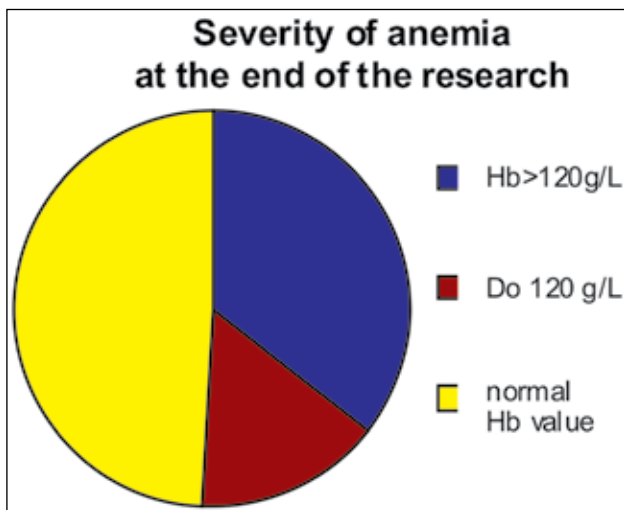
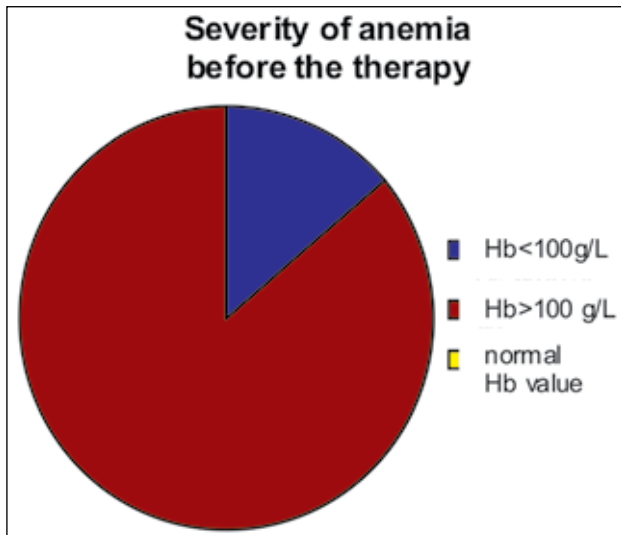


Chart 2.

In our study, all the patients suffered anemia, in other words they had low level of hemoglobin, accompanied by certain symptoms and signs of acute coronary syndrome. After the treatment with peroral and parenteral iron preparations, along with an adequate therapy for the cardiovascular disease, in the two-year monitoring study, one half of the patients have reached the level of hemoglobin within the reference values for men and women.

### Conclusion

Low hemoglobin level significantly contributes to the deterioration of the clinical picture of patients suffering ischemic heart disease, and affects the prognosis and the course of the disease itself.

It is very important to recognize and search for the cause of low hemoglobin level on time, in order to adequately treat the disease; because myocardial hypoxia as a secondary disease along with a primary cardiovascular disease has a worse prognosis.

With an adequate iron therapy and the therapy for ischemic heart disease, medical condition of most of the patients has improved; there have been less angina discomforts and heart failures.

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# TOT tape in the treatment of stress urinary incontinence with coexisting anterior vaginal wall prolapse

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## Abstract

**Introduction and Hypothesis:** The aim of the survey is the presentation of surgical technique in the treatment of stress urinary incontinence joined with anterior vaginal vault prolapse (cystocele grade II 57,2 % and III 42,8 %), evaluation of obtained results and complications of the treatment.

**Methods:** At 13 patients, we performed surgical correction of cystocele (Gynemesh PS - 6, tobacco pouch - 7) and then suburethral placement of Gynecare TVT Obturator System (Johnson & Johnson Company) by “inside-out” method in the same act. Urodynamic examinations were carried out at all patients prior the operation and 24 months after surgery.

**Results:** Cystocele and stress incontinency recurrence occurred at 2 (14.2 %) patients two years after the surgery, while 13 (92.9 %) patients are dry. Other complications (mesh erosion, de novo urgency), which occurred at 3 (21,5 %) patients, are similar to those which appear after separate cystocele correction and TOT tape placement.

**Conclusions:** Urinary stress incontinency and anterior vaginal wall prolapse require surgical correction of these two disorders in the same act.

**Key words:** Trans-obturator surgery, Stress urinary incontinence, Cystocele.

## Brief Summary

At 13 patients, we performed surgical correction of cystocele and then suburethral placement of Gynecare TOT by “inside-out” method in the same act.

## Introduction

Anterior vaginal wall defect (cystocele) is a common condition in women which may be associated with urinary stress incontinence and voiding difficulty (1). Many surgical procedures by vaginal route for treating different types of cystocele have been proposed with recurrent rate between 30-50 % (2,3). Prosthetic meshes ( marlex, prolene, polypropylen ) have been advocated as a replacement of natural structure in the treatment of cystocele (4,5,6). The minimally invasive midurethral slings have changed the treatment approach for female stress incontinence and become a new gold standard with good surgical outcome after 7 years of follow up (7). Delorme developed the trans-obturator tape as a new operation for stress urinary incontinence in 2001 and de Leval introduced “inside-out” route for placement of trans-obturator tape in 2003 (8,9). Rather small number of patients applies for the treatment with the isolated problem of urinary stress incontinence and absence of even minimal disorder of anterior vaginal wall and uterus position. Surgical procedures for the treatment of cystocele and stress incontinency are most commonly separately presented in the literature, although these two disorders are often associated, and demand surgical treatment in the same act (10). In our study, in the treatment of stress urinary incontinency and anterior vaginal wall prolapse correction ( cystocele grade II-III) we use TOT tapes ( inside-out technique), combined with nonabsorbible prolene sof mesh (Gynecare PS) or tobacco pouch, as well as complications and the results of 2-year follow-up at 14 patients.

## Materials and methods

In the period from 2004 to 2006, 14 women (mean age 60,2 years, range 45-69) were operated at University Clinic of Gynecology and Obstetrics (Novi Sad, Serbia) for urinary stress incontinence and anterior vaginal wall prolapse. During preoperative treatment, laboratory blood and urine analyses, as well as urinoculture examination were carried out. All patients underwent the complete physical and gynecological examination, and cystoscopic, urodynamic and ultrasound examinations of kidneys were performed. Urodynamic examinations consisted of urethral pressure profilometry and filling cystometry with cough. The physical exam consisted of a pelvic examination with stress in supine and standing positions and Boney test. If physical findings did not correspond to symptoms, or if the maximum extent of the prolapse could not be confirmed, the woman was reexamined in the standing position. The grading systems for anterior vaginal wall prolapse are described using criteria from the Organ Prolapse Quantitation (POPQ) system (11). Using the above listed diagnostic procedures, stress type of urinary incontinence and anterior vaginal wall prolapse were confirmed at all women: cystocele grade II (8 – 57,2 %) and grade III (6 - 42,8 %). At 5 (35,7 %) patients with grade III cystocele, initial uterus prolapse (grade I) was recorded. At 2 patients decreased bladder capacity below 200 ml and abnormal detrusor activity were proven by cystometry, and therefore 10 series of functional electrical stimulation (FES), oxybutynin tablets orally and intravaginal estrogen cream locally 3 times a week were administered to these patients.

## Surgical technique

A vaginal incision for TOT midurethral sling is made 10 mm from the external urethra meatus, and extending approximately for 10-15 mm. Before helix needle placement TOT tape alignment, surgical correction of cystocele is made by leaving the “bridge” of vaginal mucosa between the posterior end of the incision for TOT and vaginal incision for cystocele correction, 5 mm in length. Afterwards, vaginal mucosa is infiltrated by saline solutions

and incision is made on the whole length of anterior vaginal wall. As the vagina is incised, the edges are grasped with Allis clamps and drawn laterally for further mobilization. Dissection of the vaginal flaps is then accomplished by turning the clamps back across the forefinger and incising the vaginal muscularis with a scalpel. The procedure is performed bilaterally until the entire extent of the anterior vaginal prolapse has been dissected. Using sharp dissection is also important to mobilize the bladder base from the vaginal apex. At 7 patients, after the vaginal mucosa and pubocervical fascia were dissected, tobacco pouch was placed at the area of urinary bladder wall using synthetic absorbable material 2/0 of thickness. At 6 patients, cystocele correction was made using synthetic nonabsorbable prolene soft mesh (Gynemesh PS, Gynecare, Somerville, NJ, USA). After the vesicovaginal space has been opened and the full thickness of the anterior vaginal wall has been reflected from the midline laterally for the full extent of the vesicovaginal space, a pattern of sterile cardboard is cut to fit the estimated size of the defect. This serves as the pattern from which a rhomboid-shaped piece of Gynemesh can be fashioned. The mesh is then tacked to the capsular connective tissue underlying the bladder by three or four sutures on either side along the lateral margins of the vesicovaginal space, from as high in the vaginal vault as can be reached to the area beneath the vesicovaginal junction. For the inside-out transobturator approach (TOT) a Gynecare TVT Obturator System (Johnson & Johnson Company) were used by applying the technique described by De Leval in 2003 (9). Successful needle placement through the obturator region and correct position of the patient on surgical table is essential, gynecological position with bent legs at the angle of 110 degrees. With the patients under either spinal or general anesthesia, surgical site preparation and Foley catheter placement, incision points are marked at the thigh fold, where the needle tips will pass. Foley catheter is removed after 48 hours.

## Results

All 14 women were available for follow-up for a mean period of 25,0 months (range 24-27). At all patients, control urodynamic examination (profi-

lometry-UPP and cystometry) were performed 12 and 24 months after the surgery. For the confirmation of recurrent anterior vaginal wall prolapse are described using criteria from the Organ Prolapse Quantitation (POP-Q) system (11). Results and complications of the treatment are shown in table 1. Complications appeared at 6 (42.8 %) patients and they consisted of: urinal retention, Gynemesh erosion, cystocele and stress incontinency recurrence, as well as post-operative urgency-freaquency syndrome. Recurrence of stress incontinency (1) and anterior vaginal wall prolapse (1) were recorded at 2 ( 14.2 %) patients.

## Discussion

For women with potential or occult stress incontinence associated with advanced anterior vaginal wall prolapse, placement of TVT results in significantly higher objective postoperative continence rate compared with suburethral plication (92 vs. 56 %) (12). In a study of surgical repair of large cystoceles by Gardy et al. stress incontinence resolved in 94 % , urge incontinence in 87 % and approximately 5% of patients developed a recurrent anterior vaginal prolapse (13). Thus, placement of TVT or transobturator sling, is recommended for all women with potential stress

incontinence. In our study, we have shown the surgical treatment of stress incontinence and anterior vaginal wall prolapse in the same act, by first performing the correction of cystocele (Gynecare soft mesh or placement of tobacco pouch), and then the placement of TOT tape.

Urinary retention after surgery emerged at the first patient where only TOT tape was placed, without the correction of cystocele grade II. Three months after the surgery, due to the void difficulty and residual urine quantity over 150 ml, complete excision of the TOT tape below urethra was performed, with the anterior colporrhaphy with bladder neck Kelly plaction using Vicryl 2/0 sutures along with the correction of cystocele. Two years after the first operation, patient was continent and without difficulties. This case of urinary retention where we have not made the correction of anterior vaginal wall prolapse and the position of vesicourethral angle in the same act, induced us to change the surgical concept for successive 13 patients and correct cystocele first, and then place TOT tape below the middle part of the urethra. No intraoperative and early postoperative complications (bleeding more than 300 ml, hematoma, injury of urethra or bladder, infection, pain in the area of thighs etc.) were recorded in our sample of 14 operated women. Complications were recorded at 6 (42.8 %) patients (urinary retention, Gynemesh

Table 1. Patient information – results and complication of the treatment

Patient number	Age (years)	TOT and surgical repair techniques for cystocele	Follow-up (months)	Complications	Repeated surgery
1	65	TOT only	25	Urinary retention Mesh erosion	Excision of TOT tape + Kelly plaction + TP
2	58	TOT + Gynemesh PS	24	+ De novo urgency	Partial mesh excission
3	61	TOT + Gynemesh PS	24	-	-
4	57	TOT + Gynemesh PS	26	-	-
5	62	TOT + Gynemesh PS	24	-	-
6	45	TOT + TP	25	-	-
7	51	TOT + TP	27	Recurrent SUI	TOT
8	63	TOT + Gynemesh PS	25	-	-
9	69	TOT + TP	24	-	-
10	59	TOT + TP	27	Recurrent cystocele	Gynemesh PS
11	63	TOT + TP	25	-	-
12	67	TOT + TP	24	-	-
13	56	TOT + TP	26	-	-
14	68	TOT + Gynemesh PS	25	+ Urgency	-

TOT transobturator tape, TP tobacco pouch, SUI stress urinary incontinence, Gynemesh PS nonabsorbible prolen soft mesh

erosion, recurrence of cystocele and stress incontinency, appearance of urgency-frequency syndrome after the surgery).

Vaginal erosion of the mesh is a common complication of polypropylene mesh placement for cystocele repair by vaginal route with a need for subsequent revision or removal in 2-12 % cases (12). Milani and Dabodinance have reported high erosion rates up to 13-17,5 % associated with vertical vaginal incision (15,16). Erosion of Gynemesh occurred 12 months after the surgery at 1 (7.1 %) patient, which was resolved by partial excision of the mesh and vaginal suture above the erosion. Urinary incontinence recurrence occurred at 1 (7.1 %) patient 19 months after the first operation, and was treated by the replacement of TOT tape. Remaining patients (13-93.9 %) were dry, which is the result similar to the results of other authors where 72-92 % of patients were satisfied with the results of the application of TOT tapes in the treatment of urinary incontinence (17,18,19). Recurrence of cystocele after the tobacco pouch placement was recorded at 1 (7.1%) patient 18 months after the surgery. In the second act, Gynemesh was placed and the patient was continent and well 24 months after the first surgery. Postoperative detrusor overactivity and irritative symptoms with urgency, frequency, urge incontinence or dysuria occur in 2-50 % of patients after various operations for stress incontinence. De novo detrusor overactivity is usually transient and responds well to bladder retraining and anticholinergic therapy (20). Urgency-frequency syndrome developed at 2 (14,2 %) patients during 3-6 months after the surgery, and was dealt with by local application of estrogen cream, Oxybutynin and functional electrical stimulation for pelvic floor muscles.

### Conclusion

Urinary stress incontinency and anterior vaginal wall prolapse require surgical correction of these two disorders in the same act. Method of choice is correction of cystocele (Gynemesh or tobacco pouch) and then placing suburethral support using TOT tape. Two years after the surgery, 13 ( 92.9 %) patients are dry while the recurrence of cystocele and stress incontinency occurred at 2

(14.2 %) patients, and was resolved by the second surgery. Other complications of the treatment are identical to those which occur after the cystocele correction and the placement of TOT tape (mesh erosion, urinary retention, de novo urgency).

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# Transportation of heavily exsanguinated patients – a personal experience

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## Abstract

**Introduction:** The significant cause of death at traumatized persons is active bleeding which lead on haemorrhagic shock and exsanguinations, which is defined as the most extreme form of hemorrhage, with an initial blood loss of >40% .

**Aim:** The goal of this study was to point to the problems observed in the out-of-hospital treatment and transportation of the heavily exsanguinated patients at out-of-hospital conditions and to describe our experience at threatment of the heavily exsanguinated patients.

**Matherial and methods:** Study was performed in Clinical Centre of Vojvodina, Institute of Surgery, Clinic of Anaesthesiology and Intensive Care in Novi Sad, Serbia and Emergency Medical Services of Vojvodina region, Serbia, as prospective, randomized and controlled study from 2002 to 2009 year. The study included traumatized victims who had symptoms and signs of haemorrhagic shock and exsanguinations with an estimated blood loss of >40%. The approach, blood loss estimation and threatment for all victims were standardised by *Advanced Trauma Life Support for doctors*. All patients were administered multiple large bore intra-venous catheters (IV) (<17 gauge). Prompt liquid compensation was administered in the following manner: 4 liters of balanced crystalloid solution, 1 liter of 5% Albumin (which is given after first bolus of 1-2 liters of crystalloids) and 1 liter of colloid solution due to need, until arterial pressure and hart rate were normalized with goal of systolic pressure from 90 to 100 mmHg- permissive hypotension. During tran-

sportation all patients were sedated, intubated and artificialy ventilated by lung protective strategy. In the study we followed: Causes, transportations, urine output, vital signs, biochemical parameters, outcome to hospital, 1 day and 30 day outcome, pregnant victims outcome to hospital, 1 and 30 day.

**Results:** Thirty four traumatized persons, aging from 23 to 35 ( $28 \pm 2$  on average), were primary assesed and threated in the above mention conditions. All thirty four evacuated patients survived the out-of-hospital threatment and transportation. During the transportation no incidents occurred and all patients were satisfactory hemodynamic stabile with an average urine output of 0,89 ml/kg/h. All patients had the following observed blood test results: hematocrit levels between  $0.099 \pm 0.02$ ; average blood lactate  $3.02 \pm 0.6$  mmol/l; and pH-  $7.23 \pm 0.11$ . Two patients died (5,42%) 24 hours after being admitted Clinical Centre of Vojvodina and 12(34,8%) victims didn't survive first 30 days. Overall mortality after 30 day was 40,12% (14 victims). All three pregnant woman survived first 24 hours after admission at Clinical Centre of Vojvodina and surrvied after 30 days.

**Conclusion:** Early out-of-hospital insensive threatment of exsanguinated victim, which goal is hemodinamic stabilisation by fluid resuscitation and providing advanced ventilation, during the appropriate and rapid transportation can improve outcome. Threatment of exsanguinated injurys by anaesthesiologists, emergency or special educated physicians in out-of-hospital condition can contribute also to improved outcome. Particularlyly skills are needed.

**Key words:** exsanguinations, hemorrhagic shock, out-of-hospital threatment, transportation.

## Introduction

Trauma is the leading cause of death for people aged 1-44 years. Uncontrolled post-traumatic bleeding is the leading cause of potentially preventable death among trauma patients.<sup>1,2</sup> Adequate trauma care and rapid transportation in out-of-hospital conditions is essential for surviving of injured victims. The significant cause of death at traumatized persons is active bleeding which lead on haemorrhagic shock and exsanguinations. Asensio<sup>3</sup> has described it as the most extreme form of hemorrhage, with an initial blood loss of >40% and ongoing bleeding that, if not surgically controlled, will lead to death.

According to the Serbian medical doctrine the aim of prehospital care of bleeding trauma patients is to deliver the patient to a trauma facility for definitive care within the shortest amount of time (the goal is one hour- "the golden hour") by rapid transport, stopping the external bleeding, airway management and ventilation, fluid resuscitation and restoration of the volume, which is essential to treatment of haemorrhagic shock. Fluid resuscitation should prevent further deterioration and subsequent exsanguinations and also allow for preservation of vital functions without increasing the risk for further rebleeding and 'permissive hypotension' may be the goal to achieve.

The goal of this study was to point to the problems observed in the out-of-hospital treatment and transportation of the heavily exsanguinated patients at out of hospital conditions and to describe our experience at threatment of the heavily exsanguinated patients.

## Material and methods

Study was performed in Clinical Centre of Vojvodina, Institute of Surgery, Clinic of Anaesthesiology and Intensive Care in Novi Sad, Serbia and Emergency Medical Services of Vojvodina region, Serbia, as prospective, randomized and controlled study from 2002 to 2009 year.

The study included traumatized victims who had symptoms and signs of haemorrhagic shock and exsanguinations with an estimated blood loss of >40% (>2000 ml) and ongoing bleeding. The

approach, blood loss estimation and threatment for all victims were standardised by *Advanced Trauma Life Support for doctors (ATLS)*<sup>4</sup> guidelline and the Guideline of Prehospital Trauma Life Support (PHTLS)<sup>5</sup> except parts of fluid resuscitation.

During the primary and secondary survey and transportation, hemodynamic parameters (hart rate, sistolic and mean arterial pressure, ECG, oxyhemoglobim saturation), clinical signs and urine output were monitored. For monitoring we use ZOO<sup>R</sup> and M-class defibrillator and monitoring system: Non-invasive blood pressure, ECG, pulse-oximeter. Biochemical parameters were taken upon arrival to Clinical Centre of Vojvodina: hematocrit levels, blood lactate and pH.

In prehospital condition and transportation hemorrhage control of penetrating injurys were by standard prehospital methods<sup>5</sup> (digital compression, compressive bandage etc.). Temperature controle and prevention of hypothermia by blankets and optimal warmed fluids had been done.

All patients were administered multiple large bore intra-venous catheters (IV) (<17 gauge), and some of victims central venous catheters. Prompt liquid compensation was administered in the following manner: 4 liters of balanced crystalloid solution, 1 liter of 5% Albumin (which was given after first bolus of 1-2 liters of crystalloids) and 1 liter of colloid solution due to need, until arterial pressure and hart rate were normalized with goal of systolic pressure from 90 to 100 mmHg- permissive hypotension. All patients also received 150 – 200 ml of 8.4% NaHCO<sub>3</sub> per liter of estimated blood loss and opiate analgetics.

During transportation all patients were sedated, intubated and artificialy ventilated by lung protective strategy with tidal volume 4-6 l/min and PEEP 5-10 mmH<sub>2</sub>O with Drager<sup>R</sup> 1000 and 3000 portable ventilator. Standard methods and methods of endotracheal intubation in restrained condition and "Novi Sad" method by Gavrilovic et al.(1998)<sup>6,7</sup> were also used.

All emergency medicine doctors who were on the field and participate in this study were educated at Clinical Centre of Vojvodina and they use this stand metod of threatment. Data were collected in standard documents, designed for this study.

In the study we followed: Causes, transportations, urine output, vital signs, biochemical pa-

rameters, outcome to hospital, 1 day and 30 day outcome, pregnant victims outcome to hospital, 1 and 30 day.

## Results

Thirty four traumatized persons, aging from 23 to 35 ( $28 \pm 2$  on average), were primary assessed and threatened in the above mention conditions. The etiology of the wounds was one of the following: head and neck injuries with prolapsed large blood vessels 4 (11.76%), extremity injuries and concussion 8 (23.54%), combined injuries more than two anatomic regions including spine injuries 4 (11.76%), pelvic injuries 4 (11.76%) and thoraco-abdominal injuries 14 (41.19%). Causes of injuries were: blunt trauma by motor vehicle accident and falls from height 11 (32,35%) and penetrating trauma by fire-arm related trauma and sharp object trauma 23 (67,65%). The average duration of transport were from 27 to 75 (average  $48 \pm 8$ ) minutes. Three victims were pregnant woman at 7, 13, 34 gestational week.

All thirty four evacuated patients survived the out-of-hospital treatment and transportation. During the transportation no incidents occurred and all patients were satisfactory hemodynamic stable with an average urine output of 0,89 ml/kg/h (Table 1).

Upon admittance to Clinical Centre of Vojvodina- Institute of Surgery, all patients had the following observed blood test results: hematocrit levels between  $0.099 \pm 0.02$ ; average blood lactate  $3.02 \pm 0.6$  mmol/l; and pH-  $7.23 \pm 0.11$ . 91.18% of patients had an increase in blood lactate levels, while metabolic acidosis was found in 100%.

Two patients died (5,42%) 24 hours after being admitted Clinical Centre of Vojvodina and

12(34,8%) victims didn't survive first 30 days. Overall mortality after 30 day was 40,12% (14 victims). All three pregnant woman survived first 24 hours after admission at Clinical Centre of Vojvodina and survived after 30 days. One child which was delivered by cesarean section survived.

## Discussion

Although the main topic of this paper is the initial out-of-hospital assessment and transportation of the heavily exsanguinated patients, it is necessary to describe the actions that preceded the event in question.

The struggle to prevent respiratory insufficiency and shock begins as early as admittance and triage stages. All patients have their vitals checked and one or more large bore venous cannulas are placed (depending on the estimated loss of blood and the demands of the intervention to follow). Also, one or more Ringer-lactat solution are pushed, as well as the powerful analgesics. The rate of IV delivery depends on the initial values of the vitals. With the most critical patients 5% Albumin and/or Hema-cel® or another type of gelatin plasma substitutes is administered through another venous cannula. It is considered that one liter of Ringer-lactat solution given within the first ten minutes upon admittance is far more efficient than more liter of fluids given in the following few hours.

The function of the fluid input was to compensate for the fluid loss, including urine output, bearing in mind that crystalloids are eliminated from the blood stream up to 2 hours, and plasma expanders up to 6 hours.

By Cochrane Injuries Group (1998)<sup>8</sup>, there is no evidence that albumin administration reduces

Table 1.

	Vital signs, Initially (average)	Average Vital signs- at reaching in hospital (average)	% of victims with non-satisfactory vital signs at admission to hospital
HR (/min)	118( $\pm 23$ )	87( $\pm 14$ )	8,82
SAP (mmHg)	73( $\pm 12$ )	108( $\pm 14$ )	2,94
SaO <sub>2</sub> (%)	90( $\pm 4$ )	97( $\pm 4$ )	0

\*Non satisfactory vital signs: HR > 100/min, SAP < 90 mmHg, SaO<sub>2</sub> < 92%

mortality in critically ill patients with hypovolemia, burns, or hypoalbuminaemia. The our aim of using 5% Albumin is rapid volume expansion, achieving better colloid-osmotic pressure and decreasing early acute coagulopathy associated with traumatic injury which is significant problem in haemorrhagic shock<sup>9,10</sup>. By Jansen J. et al. (2009)<sup>11</sup> plasma substitution can be beneficial for preventing early acute coagulopathy. Our experience and results of using 5% Albumin in initial fluid resuscitation in out-of-hospital condition, when we have not blood products, is that Albumin and colloids could be beneficials. Our opinion is that further investigation is needed.

The given therapy leads to dilutive hypo coagulation. Consequently, administering preserved blood is strictly counter indicated in the course of treatment to follow. The additional blood given must be fresh or given in the form of decanted erythrocytes and fresh frozen plasma since such blood and/or derivatives best maintain their physiological function.

During the phase of the cellular distress, and the onset of shock, cellular ischemic anoxia occurs and anaerobic metabolism starts. The existing quantities of glucose and oxygen are depleted, which leads to the accumulation of end products of the anabolic metabolism (lactates)<sup>12</sup>. The decreased levels of glucose are insufficient to provide enough energy for the basal metabolic requirements. Therefore, adequate oxygenation and gas exchange can decrease further damages in haemorrhagic shock and maintain victims physiologic functions. Also, it is essential to lower metabolic demands. This is achieved through complete sedation and volume controlled mechanical ventilation with lung protective strategy, as soon as, optimum without delay, in the place of accident.

Ventilation can affect the outcome of severe trauma patients<sup>13</sup>. Ventilation with low tidal volume is recommended in patients with acute lung injury. In patients with normal lung function, the evidence is scarce, but some observational studies show that the use of a high tidal volume is an important risk factor for the development of lung injury<sup>14,15</sup>. Also, we consider that maintaining volemia in pulmonary capillars during lung protective ventilation decrease alveolar dead space and therefore improve ventilation and oxigenaion.

During the shock, metabolic acidosis is present (the consequence of anaerobic metabolism). For that reason, a solution of 8.4% sodium bicarbonate (NaHCO<sub>3</sub>) is administered in the minimal dosage of 250 ml until the clinical signs of shock have dissipated. Although the patients have been repeatedly administered the solution, upon admittance to Clinical Centre of Vojvodina, all of them had metabolic acidosis. It is safe to conclude that no fluid compensation without transfusions was adequate, but we don't know whether and how much sodium bicarbonate buffered acidosis. None of the administered doses were sufficient to combat cellular distress syndrome. Current opinions<sup>16</sup> do not support administrating of sodium bicarbonate without laboratory tests except in prolonged cardiopulmonary resuscitation, but our opinion is that sodium bicarbonate was "t harmful in this situation.

We observed most significant biochemical parameters which were available and routine in praxis. Biochemical parameters which we observed (pH and serum lactate) is recommended<sup>17</sup> and by Asensio JA et al.<sup>18</sup> (2001) pH represent predictors of outcome (pH < or =7.2 predict poor outcome). Our average value of pH was 7,23 which is consistent with our outcome (40% death). The results we achieved could indicate that less acidemia is repercussion of threatment measures which are performed and it results in better outcome but it is still insufficient to conclude it.

Exsanguination mortality is very high and it is between 40-90%<sup>1,19</sup>. Asensio and colleagues (2003) reported a 6-year retrospective study involving 548 patients admitted with the diagnosis of exsanguination with a mortality rate of 63%<sup>20</sup>. How do we explain the difference compared to our mortality rate of 40% ?

The first group of reasons is that injured persons who are admitted in hospital were hemodynamically stable, were better ventilated and prognostic factors were favourable (pH, blood pressure, heart rate, penetrating injuries). It could be concluded that fluid resuscitation (maybe Albumin), advanced ventilation and optimal oxygenation, which were started without delay results in favourable prognostic factors which probably contribute to better outcome.

The second group of reasons is that Serbian Emergency Medical Service which is consist of

physician in the field. In our cases, exsanguinated victims were threatened by emergency medicine physicians-specialists with adequate and modern equipment (vehicles-reanimobils, ventilators..etc.) who were capable to perform advanced prehospital intensive threatment procedures: Intubation, ventilation, canullation, fluid resuscitation etc. Simply, emergency medicine physicians were started earlier with intensive care support and presented victims in better condition in emergency room.

Pregnancy can worsen exsanguination, and exsanguination is very danger condition for fetus. Major trauma can also cause other types of new hemorrhage which is related to pregnancy and can complicate basic injury. In major trauma in pregnancy, placental ablation, placenta previa and coagulopatya can occur as consequence of hypoxic and hypovolemic placental damage and perforation of utherus, new intrauterine and intraabdominal bleeding can occur as as consequence of direct trauma. In additon to hypoxia, hypovolemia and acidosis, surgical threatment and medicaments can seriously damage the fetus. Major trauma and traumatic hypovolemic and hypoxic states often lead to placental oedema and placental dysfunction. Many congenital defects can be caused by trauma, hypovolemic shock and traumatic placental dysfunction. Therefore, if fetus survive, our opinion is that all survivors should undergo to all invasive and non-invasive techniques of prenatal diagnostics<sup>21,22,23</sup>.

During the threatment of a pregnant woman, we have 2 potential patients: the mother and the fetus. The best hope of fetal survival is maternal survival. In our case, the pregnant woman in 34 gestational week had exsanguinated extremity injuries by motor vehicle accident. In additon to out standard threatment we used and specific threatment options, like as left lateral transport position and gynecologist team in hospital were alarmed. Specific problem of airway management had ocured which was solved by using different technique of inubation. The pregnant woman was undergo at immediate surgery, cesarean delivery and surgical threatment of blleding were performed, and both, mother and children survived. Doctors who perform advanced trauma life support eider in the prehospital or hospital conditions in their departments must be aware of the circumstances and

criteria that emergency delivery or section may be saving therapeutic option for the mother and child. Also they must be aware of specific circumstances related to pregnancy and educate to solve that kind of problems.

Limitations of our study are no control group existing and small number of patients. We recommend further investigations.

## Conclusion

Early out-of-hospital intensive threatment of exsanguinated victim, which goal is hemodynamic stabilisation by fluid resuscitation and providing advanced ventilation, during the appropriate and rapid transportation can improve outcome.

Threatment of exsanguinated injurys by anesthesiologists, emergency or special educated physicians in out-of-hospital condition can contribute also to improved outcome. Particularly skills are needed.

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# Neoplanta score for acute Appendicitis diagnosis in pediatric patients

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## Introduction

The suspicion of acute appendicitis is the most common reason for urgent laparotomy in pediatric patients. [1,2] The diagnosis of acute appendicitis based on the anamnesis, physical examination, laboratory and additional methods - ultrasound, abdominal plain X-ray, CT, peritoneal aspiration and laparoscopy.[3] Symptoms of acute appendicitis in children often differ from the usual clinical description and varies in a wide range of minimally expressed discomfort to the intestinal obstruction and septic shock. Intraoperative findings vary in the range of unaltered appendix up to old perforation with the presence of adhesions and intraansal abscess.[4]

Definitive diagnosis of acute appendicitis during the initial examination is only 50% to 70 % pediatric patients. Delayed treatment leads to progression of disease with increased risk of perforation [5], inflammatory complications-wound infection (11%) and intraabdominal abscess (1-5%), postoperative adhesions and intestinal obstruction. Incidence of negative appendectomy due to the false positive diagnosis of acute appendicitis in different series ranges from 10% to 30%.[6,7,8,9,10]

Diagnostic score systems are useful models that facilitate the rational surgical decision. [11] They combine clinical, laboratory and ultrasound parameters in order to increase the security of diagnosis.[12] Most of the diagnostic score systems were originally designed for the adult population - Teicher 1983[13], Alvarado 1986 [14], Fenyő 1987[15], Christian 1992 [16], Ohman1995 [17], Tzanakis 2005[18]. Lintula [2, 19] and Samuel [20] make the attempt to introduce pediatric appendicitis score. Although most authors report on high predictive values, only some score systems confirmed their applicability in prospective randomized trials. [13,16]

The ideal score system would have sensitivity, specificity and the predictive value of 100%, without false positive and false negative results, the absolute probability of 100% and the diagnostic index 1. The criteria for validity of score systems in the diagnosis of acute appendicitis are negative appendectomy rate below 15%, the risk of perforation below 35%, overlooked perforation below 15% and the missed appendicitis rate below 5%. The application of score systems in surgical practice increased diagnostic reliability from 58% to 71%, with a significant decline in the frequency of appendix perforation from 27% to 12,5%. However, the negative appendectomy rate still remains and is 11.5%.[20]

The aim of study is to evaluate prognostic value of clinical, laboratory and ultrasound parameters in the diagnosis of acute appendicitis in the pediatric patients and validation of the existing score systems. The ultimate goal is to create an original Neoplanta score that includes a valid clinical, laboratory and ultrasound variables and its testing on a sample of pediatric patients. This will improve the diagnosis, help to determine the high-risk patients group with suspected acute appendicitis and reduce the negative appendectomy rate.

## Material and methods

A case-control clinical study was designed and conducted at tertiary care Children hospital between from 1<sup>st</sup> October, 2008 to 1<sup>st</sup> January, 2010. The study included 150 patients aged 4 to 18 years with acute abdominal pain and symptoms, which included acute appendicitis as a differential diagnosis. From the study were excluded patients who had previously had appendectomy.

All patients were examined clinically, with laboratory and ultrasound tests performed. The met-



hodological procedure was the same for the entire sample. The study evaluates the value of the score system and their result did not effect the indicated operative treatment. Patients with a positive clinical presentation of acute appendicitis were hospitalized. Non hospitalized patients were also controlled. Only the first clinical decision was observed and compared with the result of the treatment. Operative treatment is indicated if even after conservative measures taken, the symptoms of acute appendicitis persist. The evidence of acute appendicitis was confirmed on histopathology report.

For the statistical analysis all patients are grouped as follows:

*Appendicitis group* are those patients in whom the intraoperatively macroscopically and histopathologically was set the diagnosis of acute appendicitis.

- 1) true positive - admitted on time, operated and with confirmed acute appendicitis (SPOA);
- 2) false negative - initially unrecognized, missed appendicitis but treated surgically, confirmed appendicitis (LNOA);

*Non appendicitis group*

- 1) true negative - on the basis of diagnostic procedures performed the acute appendicitis ruled out and in the course of the study were not reported with a similar problem (SNNA);
- 2) false positive
  - operated - rulled out the existence of acute appendicitis (LPONA);
  - hospitalized, but not operated (LPNO);
  - false negative, undergone surgery, no appendicitis (LNONA).

Algorithm of treatment is presented at Figure 1.

Primary variables of interest were divided into categories of demographic information, hospital admission, clinical variables and ultrasound findings. Table 1

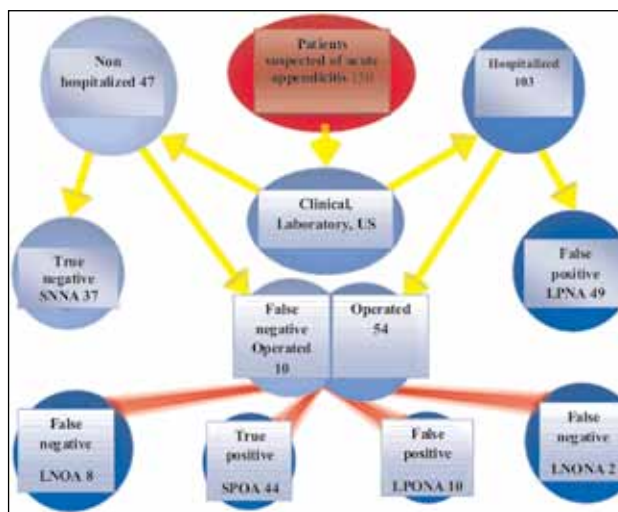


Figure 1. Diagram of algorithm treatment

Table 1. Primary variables of interest

Demographic data	age, sex, body weight
Hospital admission data	
Anamnesis	
Pain duration <24h,> 24h	
Localisation - RLQ pain, periumbilical, epigastrium, diffuse	
Decreased appetite Y / N	
Nausea Y / N	
Vomiting Y / N	
Diarrhea Y / N	
Fever Y / N (Temperature> 38.5 o C)	
Clinical examination	
Antalgic position Y / N	
Accelerated pulse Y / N	
Coated tongue Y / N	
Pain localisation - ileocecal, periumbilical, diffuse, epigastrium	
Palpation Tenderness - none, local, diffuse	
Guarding RLQ Y / N	
Palpable signs of acute appendicitis	
Bloomberg Y / N	
Grossman Y / N	
Perman Y / N	
Rosenstein Y / N	
Rovsing Y / N	
Lanz Y/N	
Kuster Y/ N	
Douglas Y / N	
White blood cells per microliter in 1000 (in range)	

Ultrasound is an imaging technique widely used in diagnosis of acute appendicitis in pediatric patients. The ultrasound examinations were performed

with Siemens sonoline sienna ultrasound color Doppler with 7.5MHz linear transducer. Ultrasound findings of acute appendicitis are test compressible, outer diameter and appendiceal wall thickness, hyperechogenic and anechogenic contents around the appendix, appendicolith, fluid-filled abscess, circumferential color-flow identified around the appendix, free fluid noted in the right low quadrant of the abdomen and ultrasound grade. Table 2

Table 2. *Ultrasound signs of acute appendicitis*

positive test compressible (with appendix incompressible the finding was defined as positive and vice versa);
outer diameter of appendix (positive findings lumen width is greater than 7 mm);
appendiceal wall thickness is a positive finding is the appendix wall thickness over 2mm);
hyperechogenic and anechogenic contents around the appendix (engaged omentum, fibrin deposits, massive adhesions);
appendicolith
fluid-filled abscess
circumferential color-flow identified around the appendix
free fluid noted in the right low quadrant of the abdomen and the pelvis
ultrasound grade

Ultrasound grades emerged as new criteria in diagnosis of acute appendicitis. Attempts to correlate ultrasound and patohystological findings are reported. Severity was classified into four grades based on the appearance of intramural appendiceal structure. [21]

The prognostic value of clinical, laboratory and ultrasound parameter is then examined in relation to the further clinical course of disease. Sensitivity, specificity, negative and positive predictive value were specified for each parameter. The validity of the existing representative score system in the diagnosis of acute appendicitis was tested at all patients (Alvarado, Madan Samuels, Lintula, Ohman, Eskelinen, Christian, Tzanakis). For each score individually the groups of patients with low and high risk of developing acute appendicitis were isolated and compared with the clinical course of the disease. The next phase of the testing included the creation of the score system made up of valid clinical and ultrasonographic parameters. The prognostic score system was originally named The Neoplanta Score.

The evaluation of The Neoplanta score values was performed throughout the sample.

### Statistical analysis

The data collected were synthesised in the database formed in the Excel software package ver. 2007. Descriptive statistical methods were used for the processing of demographic characteristics of the population. Processing of basic statistical parameters was carried out by using the software package Statistica, ver. 8.0. Encoded conditions are imported into the basic modules of the software package Statistica, ver. 8.0 for the correspondent canonical analysis. The correspondent canonical analysis was used in order to present the impact of the condition, anamnestic, clinical, laboratory and ultrasound parameters to define the difference between the studied groups as well as the mutual influence of the subgroups. Achieved results are shown in the coordinate space of the correspondent axis with the help of dendograms obtained by the cluster analysis of correspondent scores of patient groups studied. Conditions positions of the investigated parameters represented the basis for the selection of features that will be included in the new proposed score for the appendicitis evaluation. All acquired features were tested in the space of correspondent axis with the highest degree of significance. The newly created score was also finally tested together with the other scores, but in the same time on it's own in relation to the frequency of appendicitis occurrence in the examined sample. Multivariate statistical analysis was performed by using the software package Statistica, ver. 8.0, Statsoft Inc., Tulsa, OK, USA. It was performed at the Department of Biology and Ecology, Faculty of Natural Sciences, University of Novi Sad. The collected data were grouped and presented in tables and graphs.

### Results

The study included 150 patients aged 4-19 years (11,53 years) with acute abdominal pain and symptoms, which included acute appendicitis as a differential diagnosis. Sex ratio of the sample was 89 girls (59.33%) and 61 boys (40.66%). The hi-

ghest frequency of clinical conditions with a suspicion of acute appendicitis is at the age of 12 to 15 years, especially among girls. Figure 2

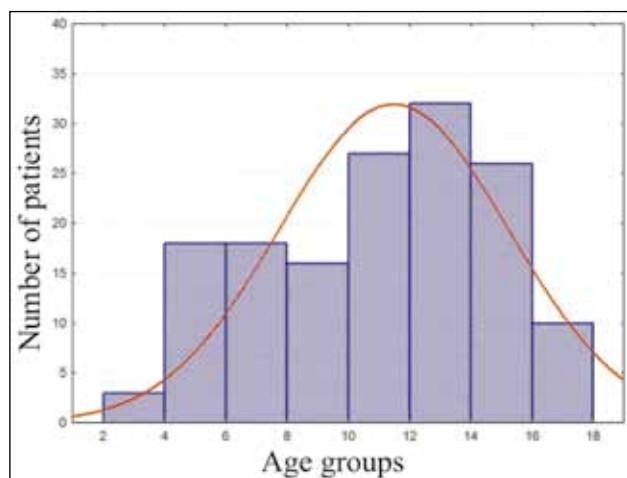


Figure 2. Distribution of the analyzed patients according to age groups

After completion of standard diagnostic algorithm 103 patients were hospitalised. Among non hospitalised patients ( $n = 47$ ) the existence of appendicitis was definitely ruled out at 37 patients-true negative group (24.66%). In this group there were also 10 false negative patients (6,66%) that the initial check up were not recognised, but were hospitalised and sent to surgery after the control examination. Out of 103 admitted patients, 49 were not operated (false positive) and after the release did not re-emerged with signs of acute appendicitis. The total sample had 64 operated patients (42.66%). In the operated group, acute appendicitis was confirmed in 53 patients (82.8%). This was the group of true positive, while in 11 the appendicitis wasn't confirmed (negative appendectomies rate) -17.18%. In the group of operated patients 10 of them were not hospitalized initially - missed appendicitis (15.62%). Out off 11 negative appendectomies 2 were initially returned and after reoccurrence they were hospitalized and operated, but pathohistologically acute appendicitis was not confirmed. The degree of appendicix inflammation was confirmed by the pathohistological examination. **Table 3** Anamnestic data results includes six standard symptoms that showed different frequencies and diagnostic values. A negative trend in frequencies of appearances of symptoms is noticed so it's represented in descending. **Table 4** The

results of the study in terms of clinical signs in all subjects are shown in **Table 5**. Diagnostic value of palpable signs is partially unbalanced. (**Table 6**) The ultrasound examination of the abdomen and the appendix were performed in all patients included in the study. This analysis was conducted due to the high diagnostic value of ultrasound in the diagnosis of acute appendicitis. [15] **Table 7**

Table 3. Patohistological examination results

Form of inflammation	Number	%
Non appendicitis	11	17,18
Appendicitis catarrhalis	6	9,37
Appendicitis phlegmonosa	17	26,56
Appendicitis gangraenosa	16	25
Appendicitis perforativa	13	20,31
Abscessus periappendicularis	1	1,56
Total	64	100

### Scores results comparative review

As a number of scores for the evaluation of acute appendicitis is already known in literature, the comparison of the well-known representative scores is performed on our sample. (**Table 8**) By evaluating the diagnostic significance, the data obtained in our sample showed high predictivity in Ohman, Lintula, Eskelinen and Tzanakis scores. The worst prediction of appendicitis shows Madan Samuels score. In the final phase of the study is formed the pediatric appendicitis score system, originally named The Neoplanta score. It contains three anamnesis data, two physical signs and ultrasound criteria of acute appendicitis. Each of these criteria is, based on it's position in the evaluation system at the group level, given the appropriate value ("force") which is expressed quantitatively. Neoplanta score components and their numeric values are represented in Table 9. Score validation is determined and the break points for which the Neoplanta score system has the highest sensitivity and specificity in recognizing acute appendicitis pediatric patients. Also, the score clearly defines and gives a recommendation for further treatment modality (**Table 10**). Neoplanta score is tested independently on the current sample and the results obtained show a high sensitivity and positive predictive value. (**Table 11**)

In addition to independent testing the new score was subjected to the entire set of cross-checks.

By the use of correspondent analysis with all-made scores, we got the results that are in favour for the use of Neoplanta score. Within the first two correspondence axes the position of Neoplanta score in diagnostic phase of the disease, found in the vicinity of the SPOA group centroids and surrounded by positions of state scores that proved to be the best in previous work. Also in the opposite area of the same correspondent axis, the negative Neoplanta score is in the vicinity of the SNNA group's

centroids, but also the negative values of individual old scores. (Figure 3). Within the second and third correspondent axis it's emphasized the agglomeration centroid subgroups and condition due to reduced levels of variability in the sample. In this environment the positions of the relevant points of the Neoplanta score shows the accuracy of given values for all elements. Neoplanta score 0 is in the close range to SNNA group, while Neoplanta score 2 is close to SPOA group. Neoplanta score 1 cen-

Table 4. Diagnostic value of the analyzed anamnestic data

Symptom	sensitivity	specificity	positive predictive value	negative predictive value
Pain in RLQ	0.816	0.407	0.455	0.786
Anorexia	0.816	0.417	0.816	0.750
Nausea	0.841	0.321	0.507	0.708
Vomitus	0.811	0.277	0.469	0.650
Fever	0.794	0.250	0.692	0.364
The change of stool	0.800	0.568	0.296	0.926

Table 5. Diagnostic value of the analyzed elements of the physical examination

Symptom	sensitivity	specificity	positive predictive value	negative predictive value
Antalgic position	0.860	0.442	0.457	0.760
Coated tongue	0.875	0.143	0.583	0.455
Ileocolic tenderness	0.824	0.350	0.447	0.758
Muscle defence	0.971	0.500	0.825	0.500
Percussion	0.900	0.193	0.439	0.733

Table 6. Diagnostic value of the analyzed palpable signs

Palpable sign	sensitivity	specificity	positive predictive value	negative predictive value
Blumberg	0.854	0.122	0.449	0.500
Grossmann	0.833	0.136	0.612	0.500
Perman	0.867	0.071	0.667	0.200
Rosenstein	0.921	0.107	0.461	0.625
Krüger	0.850	0.111	0.680	0.250
Rovsing	0.872	0.045	0.619	0.167
Lanz	1.000	0.100	0.526	1.000
Küster	0.933	1.000	0.636	1.000
Douglas	0.760	0.290	0.463	0.600

Table 7. *Ultrasound examinations results*

Ultrasound examination	sensitivity	specificity	Positive predictive value	Negative predictive value
positive test compressible	0.840	0.143	0.636	0.333
outer diameter ( $\geq 7$ mm)	0.941	1.000	1.000	1.000
Appendiceal wall thickness ( $> 2.5$ mm)	0.854	0.375	0.538	1.333
hyperechogenic and anechogenic contents	0.923	0.364	0.632	0.800
appendicolith	1.000	0.167	0.615	1.000
Appendix aperistaltic	1.000	0.000	0.714	0.000
fluid-filled Abscess	0.833	0.100	0.556	1.000
The presence of free liquids	0.824	0.100	0.609	0.250
Ultrasound grade	0.971	1.000	0.971	1.000

Table 8. *Diagnostic value of the representative scores for acute appendicitis*

Score	sensitivity	specificity	positive predictive value	Negative predictive value
Alvarado	0.827	1.000	0.524	1.000
Madan Samules	0.872	0.073	0.519	0.333
Lintula	0.971	1.000	0.694	1.000
Ohman	0.913	1.000	0.778	1.000
Eskelinen	0.955	1.000	0.667	1.000
Christian	0.884	0.154	0.535	0.545
Tzanakis	0.870	0.042	0.635	0.143

Table 9. *Neoplanta score, components and their numeric values*

Variable	Number of points
Lower right tenderness	1
Loss of appetite	1
Nausea, vomiting	1
Fever $> 37.5^\circ$	2
Abdominal muscle defance	1
positive test compressible	1
Appendiceal wall thickness ( $> 2.5$ mm)	1
Ultrasound grade (III ili IV)	1
outer diameter of appendix ( $\geq 7$ mm)	1
Indirect US signs of appendicitis	1

Table 11. *Neoplanta score*

The element of the clinical significance	value
Sensitivity	0.915
Specificity	1.000
The positive predictive value	0.977
Negative predictive value	1.000

troid is surrounded by centroids different in origin and with no clear orientation and as far as the studied groups are concerned, they are close to the set of centroids, whose origin is not absolutely defined. **Figure 4.** If we test the new score alone, we get the same results. Any proposed boundary module has its close subgroups. The subgroup SPOA is oriented towards the value of score 2, and they are joined at an appropriate distance, by the subgroup LNOA. The opposite side is reserved for the nonappendicitis group in which the SNNA subgroup is surrounded by a zero score value. A condition that requires further observation and examination (NEOPLANTA: 1) gathers the undefined group of patients by status.

## Discussion

The diagnosis of acute appendicitis still remains a controversy. Multicentric studies confirm the maximum incidence of disease in the second decade and in later years the incidence declines

Table 10. Neoplanta score and recommendation

Score value	Status	Recommendation	MARK
0-4	Non apendicitis	release	0
5-7	Possible apendicitis	observation	1
8-11	Apendicitis	surgery	2

[22,23]. In the performed study the greatest frequency of clinical conditions that raise a suspicion of acute apendicitis is between 12 to 15 years which is especially evident in girls. In the false positive group dominate girls aged 16-19 years with the higher body weight (> 60 kg). This can be interpreted by a higher frequency of discomfort in the right lower quadrant of in girls due to juvenile physiological and pathological gynecological conditions. The greater body mass followed by coincides with the more difficult clinical and ultrasonographic examination.

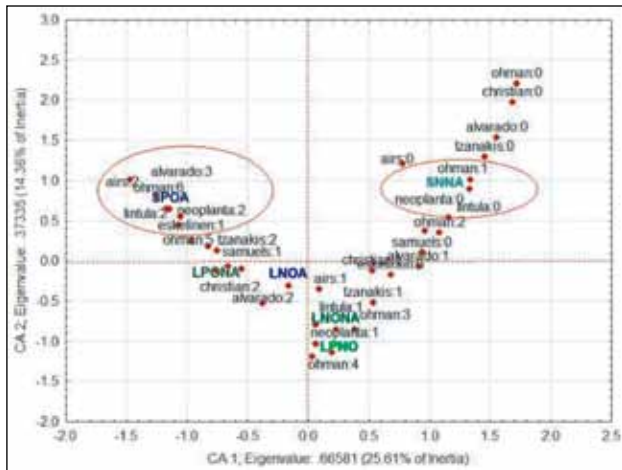


Figure 3. The positions of centroids subgroup of patients and the status of all scores in the space of the first and second correspondence axis

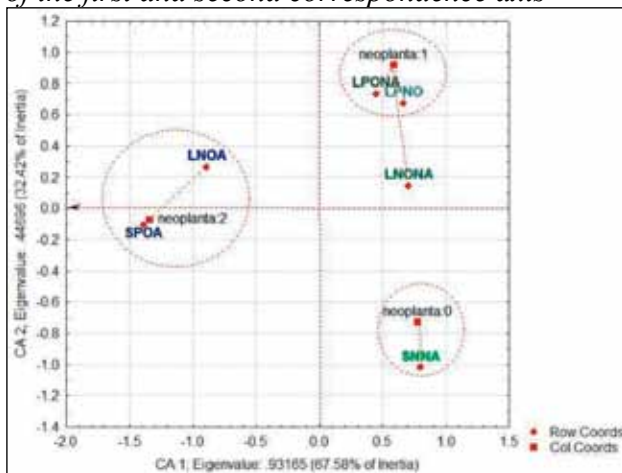


Figure 4. Subgroup patients centroid positions and the NEOPLANTA score status in the space of the first and second correspondence axis

Appendix perforation is the most common in young children, 82% under 5 years and 100% in infants.[24,25] In the performed research the incidence of appendix perforation is the largest in the youngest age group, 56.25%. The delay in diagnosis and treatment of acute apendicitis leads to the subsequent morbidity increase, length of hospitalization and increased costs of treatment. [26,27,28] Respecting the risk of complications arising due to delay in recognising and treatment leads to early surgical explorations and the increase in the number of negative appendectomies.

The significance of ultrasound examination in the diagnosis of acute apendicitis is undeniable [2,29], with the sensitivity of this method up to 100%. The first study that establishes ultrasound criteria in the diagnosis of acute apendicitis was performed by Puylaert at 1986.[30] A number of subsequent studies have confirmed that ultrasound is a valid method in the diagnosis of acute apendicitis. [31,32, 33]

Previously established score systems, including the Alvarado score as the most famous, are not widely accepted because they did not show their importance in prospective studies. A score system would ideally be constructed from variables that have the strongest independent discriminative capacity to identify groups of patients suspected of acute apendicitis. All the previous score systems lose their capacity of discrimination because most of them are made of dichotomy variables. Also, the failure of some score system lies in the use of inadequate mathematical models for their constructions. The criteria for assessing the validity of score system in the diagnosis of acute apendicitis are well known and mentioned before. [34] By analyzing ten score systems, Ohman found that only the Alvarado score meets all four criteria, while Fenyö and Christian score meet two criteria. [17,35]

Most score systems define the breaking point with a high sensitivity to detect apendicitis, whereas the specificity is low in order to define and bring the decision on surgical treatment. The ratio-

nal approach is based on defining the three diagnostic test zones and the accompanying high-sensitive surgical decision (surgery, observation, discharge).

On the basis of our sample the high predictivity scores were given by Ohman, Lintula, Eskelinen and Tzanakis. Madan Samuels score shows the worst appendicitis prediction. The string of diagnostic scores for the correct positive prediction of the definite appendicitis is as follows: Lintula-Ohman-AIRS- Alvarado-Tzanakis. As far as negative prediction is concerned Lintula-Ohman are outstanding in that order. Curran in the one-year prospective study evaluated and compared the diagnostic value of a modified Alvarado score and ultrasonographic examination of adult patients with clinical suspicion of acute appendicitis. They found no significant differences in the safety of these diagnostic algorithms individually, but together can only increase the safety of diagnosis. [36, 37] Modern score system for acute appendicitis, in addition to clinical and laboratory parameters includes the ultrasonographic criteria. Tzanakis created the original score that included clinical, laboratory and ultrasonographic parameters and tested it prospectively in adult patients. [18] However, in children's surgical practice, such a score system has not yet been implemented.

As a result of research is created the original prognostic score system that incorporated representative clinical and ultrasonographic criteria, determined their factors of significance and prognostic safety. The Neoplanta score clearly defines the three diagnostic areas (without appendicitis, possible appendicitis, appendicitis), and is also one of the few systems that besides the recognition of acute appendicitis provides recommendations for further treatment modality. The Neoplanta score is independently tested on the current sample, and the results show a high degree of its sensitivity and high positive predictive value. The value of successful prediction of the patient's condition is almost 1 and thus shows a high correlation module with selected features and elements of their expression. The Neoplanta score system proved to be very practical, simple and multidisciplinary. It sublimed the most important variables significant for identifying patients with acute appendicitis. Data for its creation were obtained from clinical and ultrasonographic parameters. By applying an

adequate score system its possible to provide for all patients, an optimal form for further treatment, timely recognition of acute appendicitis and reducing the number of negative appendectomies.

## Conclusion

In the conducted study the Neoplanta score proved to be very applicable, fast, reliable and practical. Neoplanta testing on the complete sample of studies confirmed the sensitivity 0.915, specificity 1.000, positive predictive value of 0.977 and negative predictive value of 1.000. Any contribution towards a safer diagnosis of acute appendicitis in the pediatric patients is scientifically and socially justified.

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# The use of Dynamic Electromyography in Gait analysis

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## Abstract

**Background.** Normal gait is a harmonious, energetically economic motoric activity resulting from a sequence of a human body steps in space. Each gait cycle includes the Support Phase, and the Swing Phase. Many factors may induce a gait disorder, which can be observed at a clinical examination of a patient, and by electromyography, too.

**Objective:** To apply and evaluate dynamic electromyography holter system in gait analysis.

**Material and Methods:** Dynamic electromyography (EMG) gait analysis was performed in a pilot study at the Clinic for Children's Habilitation and Rehabilitation, in cooperation with the Faculty of Technical Sciences. The signal recording was performed by the EMG holter system designed at the Department for Systems and Signals of the Faculty for Technical Sciences of Novi Sad, providing for recording of up to four EMG signals, and eight signals from different sensor types. The recorded signals were saved in the USB flash memory. Within a pilot study at the Clinic for Children's Habilitation and Rehabilitation, gait analysis was performed in one patient with a normal gait, and two patients with cerebral palsy (diplegia and hemiparesis). This EMG holter system provided high-quality scans, suggesting that one leg gait stages could also be assessed by this system, on the basis of the obtained force-sensing resistors signals from both legs

**Results:** The results included the gait scans from a healthy child (m. tibialis ant. and m. gastrocnemius contractions), scans of the same muscle contractions in a girl with hemiparesis, and scans of m. gastrocnemius contractions in another girl with diplegia, taken prior to and in a month following the botulinum toxin type A injection.

**Conclusion:** Dynamic EMG gait analysis provides the information about a patient's functional status which may be useful in evaluating the patients themselves, as well as in selecting the therapy mode and monitoring its effects. The dynamic electromyography device designed at the Faculty of Technical Sciences in Novi Sad is one of possible technical solutions suitable for wide clinical application.

**Key words:** dynamic electromyography, gait, cerebral palsy

## Introduction

A motion is generally defined as an act or ability of moving from one location to another by one's own mechanisms, or by some kind of aid (1). Other authors define gait as a form of motion in which one's leg foot is positioned on the ground before separating the foot of another leg (2). Normal, regular gait is a useful, energetically economic, harmonious, rational motor activity enabling a body to move in space (3). Normal gait includes a sequence of even and coordinated movements of the extremities and trunk, composed of the sequence of steps. The intact locomotor system, with normally functioning central and peripheral nervous systems, as well as the cardiovascular and sensory ones, are necessary for the normal gait. If one link (muscle, joint, nerve...) of the chain is altered, it will be clinically manifested by a deviation and pathological gait patterns. The Gait Cycle is the period from the moment of an initial contact of the foot and ground, to the moment the contact is repeated by the same foot (4).

Each gait cycle is composed of two basic phases: the Support phase or Stance, and the Swing

phase. At the normal speed of gait, the Support Phase makes 60% of the total Gait Cycle period, while the Swing Phase makes another 40 %. Increasing the gait speed, the Support Phase is reduced (5). Each gait phase can be further subdivided into a few sub phases. The Stance includes the Initial Heel Contact, Loading Response, Mid Stance, Terminal Stance, which is succeeded by the Pre-Swing.

The Swing Phase starts as the back leg foot is entirely separated from the ground, and it also includes a few subphases: Initial Swing, Midswing, and Terminal Swing. The leg moves forward, and the front leg becomes the back one. While walking, movements are also registered at the level of the pelvis (rotation, leaning, lateral movement), hip joint, knee, ankle, toe joints, accompanied with reciprocal movements of the upper limbs. In the Swing Phase, the ankle almost reaches the neutral position, the knee joint is flexed at 40-60 degrees, and the hip joint at 20-30 degrees flexion. In the Support Phase, these flexion and extension ranges alter, depending on the current sub phase of the lower extremity. The gravity centre moves ahead, laterally left-right, and cyclically up and down, depending on whether the support is in one or both legs. The relevant factors which may affect gait features include the sex, age (the gait of a child who has recently begun to walk differs from the adult gait), height and weight, clothes, shoes, walking ground type, tiredness... (4,5).

The energy consumption will depend on the type of the activity performed by the body. Thus, for example, a 70 kg-weighting person in a lying position uses 1 kcal/min. The energy consumption depends on the gait speed. If a person walks at the speed of 27 m/min, he/she uses 2,3 kcal/min, but if the gait speed is doubled to 54m/min, the energy consumption will amount to 3,1 kcal/min on the average. At "light walking", amounting to 80 m/min in a normal healthy adult, the energy consumption is rationalized depending on the taken distance. The energy consumption may be expressed in the form of the metabolic equivalent (MET), equal to 3,5 ml O<sub>2</sub> per kg/bm/min (6). All gait deviations significantly elevate the energy consumption. The walking-engaged musculature uses 4-5 as much blood

as the common 15% of the minute volume used at rest. The cardiovascular system responds to exertion by the systolic volume increase, elevated frequency, blood pressure variations, as well as by accelerated breathing (the common frequency of 14-16 respirations in a minute may increase to even 50), and elevated respiratory volume (5,6).

A deviated gait pattern develops as a result of the sum of simultaneous disorders at the level of one or more body segments (e.g., the weakness of foot dorsiflexors may develop as a single phenomenon, or associated with excessive knee flexion or leg circumduction). Gait ceases to be energetically economic and is often slower than the normal common gait. If there exists pain in any segment of the lower extremities, the Stance of the affected leg is shortened, accompanied with a reduced step length (7). The gait of children with cerebral palsy is characterized with abnormalities in all body segments. At the level of extremities, the following abnormalities may be observed: arm adduction, elbow joint flexion, forearm pronation, volar wrist flexion, and adduction with internal rotation of upper leg, knee joint extension and planar foot flexion (8).

The gait assessment includes measurements of the body movements in space (kinematics), power, i.e. force engaged in movement/gait performance (kinetics), and electromyography. The kinematic gait assessment includes monitoring of certain body parts' movements by observing certain points on the examined subject's body. A patient may be repeatedly evaluated in certain time intervals, before the treatment and after therapy (e.g., botulinum toxin type A administration), when changes in the active movement of the treated body segments may be detected (9). The kinetic gait assessment includes the pressure force registered and altered at the contact of a subject's foot and the ground, depending on the phase of the gait cycle (10).

Dynamic electromyography (EMG) is a method of EMG screening at functional movements (walking, catching ...). To improve the examined subjects' mobility and adjust the method to the clinical conditions, dynamic electromyography may take the holter system form. It is a specific portable system carried by the patient him/her-

self, thus eliminating the problem of long patients' cables connecting the electrodes with a stationary EMG device (11). This device registers the electrical activity of a few muscles, concurrently with the signals from other types of sensors, and the obtained findings can be saved in the database for further processing and analysis. The gait assessment may involve all large muscles of the lower extremities, but the following ones are most frequently examined: m.rectus femoris (a part of m.quadriceps), m.semitendinosus, m.gastrocnemius (caput laterale and caput mediale), and m.tibialis anterior. Specific adhesive electrodes (also used in electrocardiography) are applied to the intact skin above the muscle whose activity is followed during patient's walking. The electrodes are placed above the muscle motor point. The analysis may be performed for barefoot walking, or walking in corrective orthopedic footwear, with or without aiding devices. The dynamic EMG holter system is accompanied with a video camera screening of a patient for the purpose of further detailed gait analysis and evaluation of other body segments (head, neck, trunk, upper limbs) (9,10).

### Objective

The objective of the study was to apply and evaluate dynamic electromyography (in form of specific portable system) for gait assessment.

### Material and Methods

In a pilot study, the gait was analyzed in one normal subject and two cerebral palsy (diplegia and hemiparesis) patients at the Clinic for Children's Habilitation and Rehabilitation. After a clinical examination and evaluation, which included the range of movement in all lower extremities' segments, manual muscle test, spasticity assessment by modified Ashworth Scale, the examined patient's gait was analyzed. A more detailed gait analysis was performed by dynamic electromyography.

Signal recording was performed by EMG holter system designed in the Department for Sy-

stems and Signals of the Faculty for Technical Sciences of Novi Sad, as a pilot study. This device enabled the recording of up to 4 EMG signals and 8 signals from different sensor types, The recorded signals were saved in the USB flash memory with speed of 1000 per second, with a minimal processing which included the anti aliasing filter. Signal processing was performed subsequently on a PC, applying the MATLAB program (11). Synchronization of the EMG signals and gait phases was based on recording a subject's heel contact with the ground. In our system, it was performed by two force-sensing resistors (FSR), applied to the metatarsal region of both legs, thus providing a very precise information about the initiation of the Stance (the moment when a leg loses the contact with the ground – FSR signal fails to zero); to precisely establish the start of the Stance, it would be necessary to place the FSR sensors on the heel region as well. As this method was in particular designed for cerebral palsy patients whose gait was characterized by a lacking contact of the heel region and the ground due to anti gravitation musculature, and having also wished to make the method clinically acceptable by reducing the number of sensors, we did not apply the FSR sensors to the subjects' heels, so the Support Phase was estimated on the basis of the available information.

The recording protocol: the electrodes were first placed on one leg, and than onto the other one, followed by applying the neutral electrode and FSR sensor onto the metatarsal foot region. The electrodes and sensor were then connected by the patient's cables with the holter device. After turning the appliance on, a patient stood at one spot for five seconds, and then walked at usual speed along a pre-defined 10 m path (the taken distance may even be longer). When a patient came to the end of the path, he/she kept standing on the spot for five seconds, and then the EMG monitoring was discontinued. Recording was continued in the same sequence but in the opposite direction, until a patient was back to the start.

**Results**

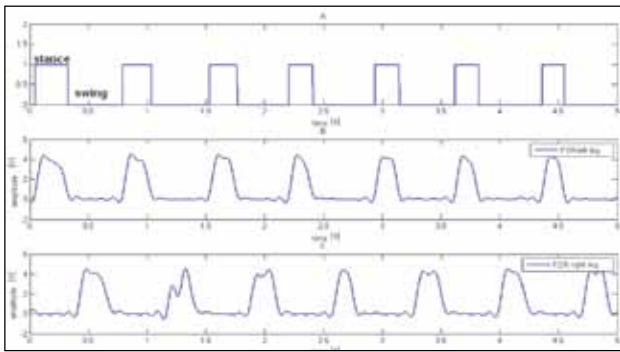


Figure 1. Evaluation of gait (left leg) by dynamic electromyography using signals from FSR of left (B) and right (C) leg.

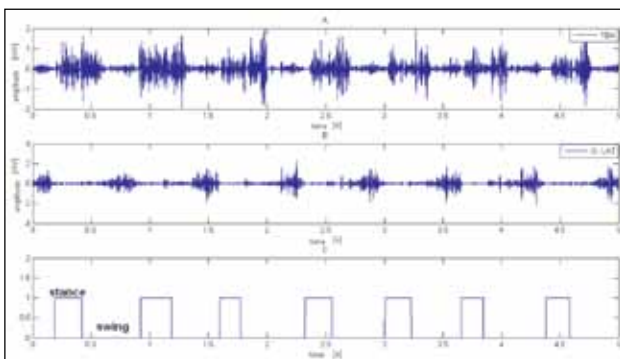


Figure 2. Gait analysis in healthy 12 years old boy: A- EMG signal of m. tibialis anterior (TBA), B- EMG signal of m. gastrocnemius (caput laterale) (G. LAT), C- evaluation of gait cycles using signals from FSR sensors.

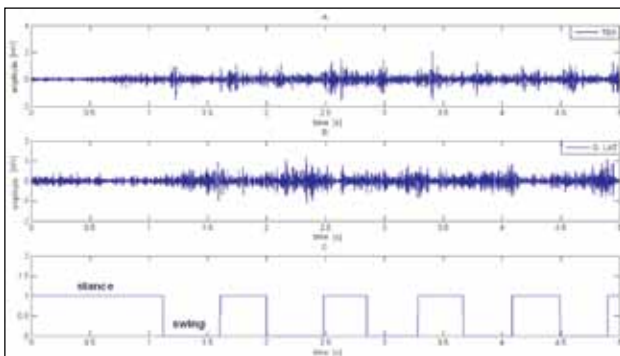


Figure 3. Gait analysis in patient with right hemiplegia: A- EMG signal of m. tibialis anterior (TBA), B- EMG signal of m. gastrocnemius (caput laterale) (G. LAT), C- evaluation of gait cycles using signals from FSR sensors.

Gait analysis in healthy 12 years old boy showed two main phases: stance and swing phase. In stance phase main contractures are from m. tibialis ant., and in swing phase were from m. gastrocnemius.

In patient with hemiplegia we noticed almost continual contraction of m. tibialis anterior (co-contraction) during all gait cycles, and similar contraction of m. gastrocnemius. Results of this contractions was good organisation of support phase of gait. From this results we could conclude that we don't need some intervention on m. gastrocnemius, but the co-contraction of m. tibialis anterior we could control using some orthoses.

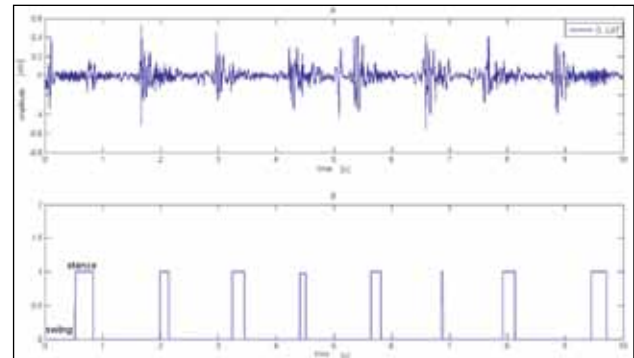


Figure 4. Contraction of m. gastrocnemius lat. dex. in patient with diplegia before the application of botulinum toxine type A

In patient with diplegia we noticed strong and prolonged contraction of m. gastrocnemius especially during the stance phase and as a. results of this contractions are very short support phase of gait. From this results we could preliminary conclude that some intervention on m. gastrocnemius should be applied in order to improve support phase of gait.

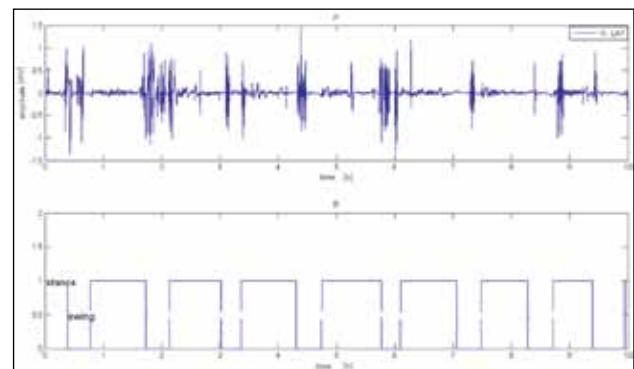


Figure 5. Contraction of m. gastrocnemius lat. dex. in patient with diplegia after one months of application botulinum toxine type A

In patient with diplegia after one month of application botulinum toxine type A we noticed lower and shorten contraction of m. gastrocnemius most time during the swing phase, and as a. results of this is longer support phase of gait.

## Discussion

Dynamic electromyography gait assessment following a complete clinical evaluation of a patient provides a great variety of valuable information.

The relevant information are thus obtained, enabling to determine the contraction intensity, beginning, end and duration of the examined muscles' contraction, as well as clinically relevant evaluation of the contraction quality and quantity of agonists and antagonists in the course of a specific movement, detection of muscle co contraction, respective muscles' weakness, and other information. All these information are exceptionally important for an evaluation of both the patients' functional status, and effects of the applied therapy modes (9,10).

The selection of the muscles for EMG screening varies and depends on a physician's appraisal and a type of the disorder to be examined. It is essential the selected muscle is suitable for screening by surface electrodes. A special attention has been paid to the analysis of two muscles in the patients with cerebral palsy: *m.gastrocnemius (caput laterale)* in the posterior lodge of lower leg and *m. tibialis anterior* (in the anterior lodge of lower leg) (9).

Once the signals are recorded, they are processed in order to be adequately presented and the gait parameters obtained. EMG signal processing includes: 1) filtration, and 2) detection of gait phases. In our study, filtration was performed by the Butervort's filter drain of the second-line frequency range (12). Good results are obtained by the filter of the lower and upper limit frequency of 20Hz and 200Hz respectively. The filter adjusted in this way efficiently eliminates variations of the signal base line due to the movement artifact (movement-induced trans location of the electrodes on the patient's skin), and the signal rumor is significantly reduced. If needed, on the basis of the obtained EMG signals, applying the algorithms based on the „rule of three sigmas“, determine the moment of the muscle activation and deactivation (13). The time of 20 ms is sufficient to determine the muscle activation and deactivation thresholds (14).

After dynamic EMG screening, additional processing can provide a great number of space and time parameters: step length – longitudinal distance between the two feet, stride length, step width (the distance between the two feet), support base width,

number of steps, walking speed, moment and sequence of activation of certain muscle groups, intensity and duration of the activity of one or several muscles in certain phases of the gait cycle (2,7,9).

Dynamic EMG screening may be repeated within the course of habilitation and rehabilitation treatment, correlating the obtained results, revising the therapeutic goals, planning drug injections (e.g. botulinum toxin type A) into selected muscle groups, correcting gait patterns by an aiding device (e.g., orthoses, walkers or sticks) (15), assessing whether the most suitable orthoses has been selected for a particular patient, (16), or planning a potential surgery (17). Dynamic electromyography should be included in the clinical treatment follow-up protocols of the patients with cerebral palsy (18). Electromyography may also be used to assess the activity of certain muscle groups in sportsmen when evaluating training plans (19).

Gait assessment by dynamic EMG contributes to better understanding of the normal gait and detection of deviation in certain diseases and damages of the locomotor system, peripheral or central motor neuron. For example, in patients with paresis, the dynamic EMG finding is clearly different from the one in normal subjects “imitating” the hemiparetic gait pattern (20).

When applied for the gait assessment, dynamic EMG can provide valuable information about patients' functional status, which might be useful in evaluating the patients themselves, in selecting the therapy mode to be applied, as well as in monitoring and assessing its effects. The apparatus for dynamic electromyography designed at the Faculty of Technical Sciences in Novi Sad represents one possible technical solution suitable for a wider clinical use. For all these reasons, dynamic EMG should be obligatory included in the functional examination of all patients with any type of gait disorders.

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# System for Femoral tunnel position determination based on the X - ray

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## Abstract

Verification of the post-operative results of the human knee anterior cruciate ligament reconstruction depends, mostly, on the angle and position (o'clock) of the graft (screw) which is built into the human femur (tunnel position). This verification has very significant influence on the patient's recovery and estimation of the success of the knee anterior cruciate ligament reconstruction. Usual method for the screw angle and position determination is CT (Computed Tomography), which exposes patient to significant radiation and is very expensive. To avoid this, basic idea, which is discussed in this paper, is to generate screw angle in the third orthographic view based on the two orthographic views obtained by the X-ray images. Generated screw angle third orthographic view is most interesting for post-operative patient recovery and estimation of the success of the knee anterior cruciate ligament reconstruction, according to medical standpoint. The program system is developed by using VTK (Visualisation ToolKit) library and Visual C++ environment. System, based on the JPG input image, which represents scanned x-ray images, generates third screw view with appropriate screw angle – graft position.

**Key words:** Anterior cruciate ligament (ACL) reconstruction, femur, tunnel position, marching cubes algorithm, VTK

## 1. Introduction

Static and dynamic stability of the knee is provided by the ligamentous structures and optimal anatomical reconstruction of the broken anterior cruciate ligament (ACL) is essential for achie-

ving knee functional stability [1]. In that sense, a different methods for X-ray control for localizing a correct position of the graft placement (femoral tunnel, screw) have been proposed [2,3].

Reconstruction of the ACL (Anterior Cruciate Ligament) presents "quality life" surgery, which enables young people to return to their professional and sport activities and protects the knee of dangerous degenerative changes which appear in the subsequent patient life. This operation is a most frequent activity in the human knee surgery nowadays.

Frequency and difficulty of the knee and ligaments injury, in the last couple of decades, are permanently increased. At the same time, a need for stability restoring and complete functional recovery of the injured knee increases.

Correct tunnel placement, in which will be built graft, is a critical and very important step for final outcome in anterior cruciate ligament reconstruction surgery [5,2]. Some authors believe improper femoral tunnel placement is a common reason for failure of an ACL reconstruction [6]. Locations of the femoral and tibial tunnels have significant effects on the knee function and longevity of the new ligament. If the graft is incorrectly positioned, then it will undergo abnormal stresses and may impinge on adjacent structures and fail to control the combined rotational and translational abnormalities of ACL deficiency. A graft that is significantly anisometric will stretch out and cause laxity or be an excessive constraint and cause loss of motion [12]. Also, it should be investigated the influence of ACL reconstruction, using different tunnel placement strategies, on the resulting knee kinematics [4].

There have been various studies reporting of the assessment of femoral tunnel position in relation to biomechanical stability and clinical outcome of the ACL reconstruction [8,9]. General

agreement on the method of measurement, more exactly determination of the graft position, however, has never been reached.

Biomedical engineering, nowadays, is of great significance in the up-to-date medical research [10,11]. The medical aspects of the ACL reconstruction are not discussed in this paper. Attention is aimed, exclusively, at the possibilities of the technical realization of the mentioned reconstruction postoperative results verification. Postoperative results estimation has very significant influence on the estimation of the necessary rehabilitation process and the quality of patient's life [7]. Mentioned verification will be carried out by determination of the tunnel position, more exactly by determination of the position and angle of the screw which is built into human knee.

From the technical point of view, verification of the postoperative results of the ACL reconstruction presents a geometric problem. This problem could be solved by determination of the space position (o'clock) and angle of the screw which is built in the knee. One of the ways of the very efficient verification is CT (Computed Tomography) method. However, CT is not used in everyday practice, because this method is expensive, work with contrast means is unavoidable and the patient is exposed to the considerable radiation dose. More accessible and cheaper method is X ray images utilization.

In the paper will be presented first step in the graft position determination – determination of the tunnel – screw angle, which will enable estimation of the different tunnel placement methods on the final knee kinematic capability.

## 2. Method

X ray images of the knee (with screw built in it), from the geometric point of view, present views (of the knee with the screw built in it) from above - top (ZX plane) and side - profile (ZY plane), because the X ray head is directed exactly in the mentioned directions. Based on the previous fact, there are three steps in this work:

1. Set up of the scanned knee (with the screw) X ray images (JPG format) into appropriate coordinate planes.

2. Picking the characteristic screw points on both views using a touch screen.
3. Automated front view (XY plane) generation of the screw, and real screw angle determination.

Mentioned steps have been a starting point for the software system development, which enables determination of the screw position and the angle which is built into human knee.

## 3. Developed software system

Software system is developed in C++ program language supported by VTK (Visualization Toolkit) library – [13]. As mentioned above, software system should, based on the knee X ray images (above and side view), determine screw angle in the femur's front view. This is very important for the patient's rehabilitation analysis after the ACL surgery and prediction of functional outcome. Previous methodology is proposed and appropriate software system is developed because of the facts that CT image is very expensive, patients are exposed to much more radiation. and front knee X ray, immediately after operation, is impossible.

Environment of the developed software system contains following options:

- X ray reading
- Leg (right/left) defining
- Picking of starting and end screw point in the top/above view
- Picking of starting and end screw point in the side/profile view
- Coordinates recording
- Views drawing

On the Figure 1 software system environment with left leg X ray is shown. To show difference between left and right leg, X ray is given on Figure 2. After the X ray (JPG format) reading, system has to conclude which leg is shown on the X ray – a right or a left. In the present version of the software system, user should define whether leg is left or right. This information follows every X ray image, while experts (doctors) can conclude this based on the location of the other bones on the X ray. In the next version of the software, system



will be able, based on the coordinates of the screw starting and end points, in the automatic cycle, to define which leg is on the X ray.

After that, a picking of starting and end points of the screw in the top (Pt1 and Pt2) and profile (Ps1 and Ps2) views should be done.

For picking the screw points, in the top and profile views, user does not have to have any skill or experience. In the presently developed system, for this task, touch screen is provided. This task could also be done by mouse, but in our opinion touch screen enables more accuracy of the picked point coordinates.

Obtained points' coordinates are presented in the window coordinate system (x - y), which is shown on Figure 2. Within the software system a separate environment for the X ray images review is developed (Figure 1 and Figure 2).

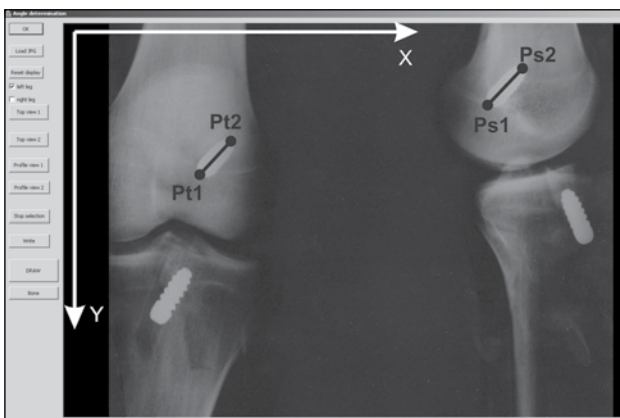


Figure 1. Developed software system environment with left leg X ray

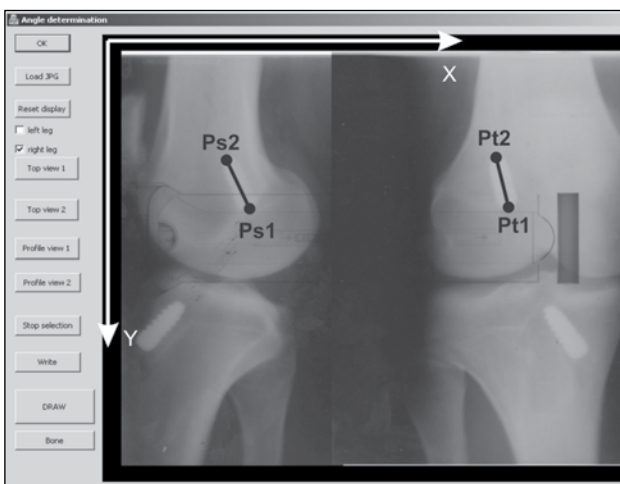


Figure 2. Developed software system environment with right leg X ray

After the screw angle determination, software system draws all screw views, which could be used for later analysis. Determined screw angle is recorded into patient data base.

To establish the desired screw angle, relative distances of the points' ( $dx$  and  $dz$ ) are needed (Figure 3):

$$dx = Pt2(x) - Pt1(x)$$

$$dz = Ps1(x) - Ps2(x)$$

Desired screw angle in the front view is then determined by:

$$\alpha = atan(dz/dx)$$

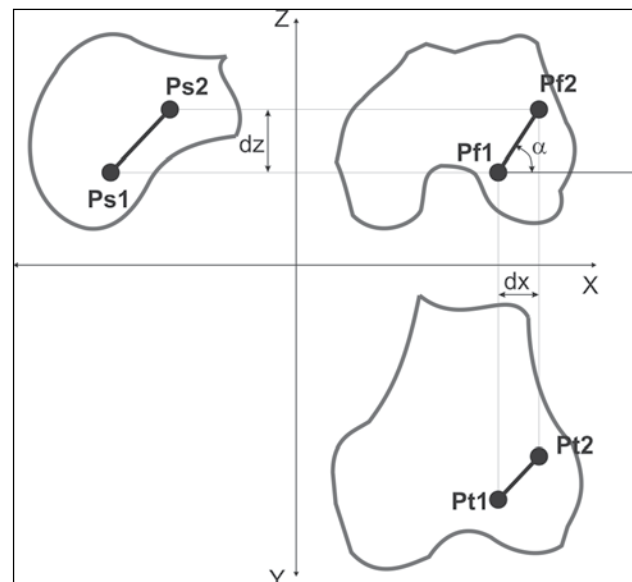


Figure 3. Screw angle in the front view determination

#### 4. Results verification

Verification of the obtained results has been carried out on several patients, by comparison to CT description [18], but in this paper only results of two patients are shown. For the verification process a separate software system, supported by VTK library, is developed [14]. Patient's knee CT descriptions have been made with a series of images (JPG format), in the axial direction, at the distance of 1mm. Based on the mentioned series of images, supported by Marching Cubes algorithm [15] a 3D knee models with screws built in them have been generated. Procedure of the 3D model

generation based on the series of images is presented on Figure 4.

System input data are, as mentioned above, series of images of the knee axial cross section. Software system takes these images through `vtkVolume16Reader` class. After that, through `vtkContourFilter` class, when a contour surface for each section is isolated.

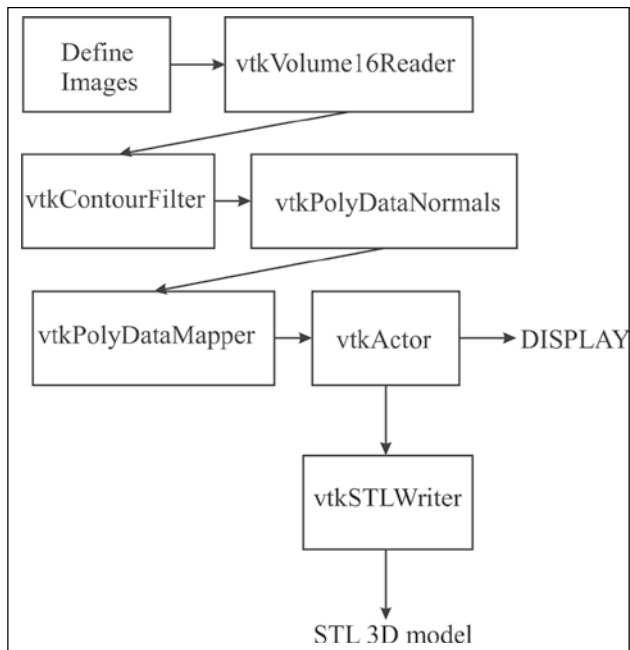


Figure 4. Procedure of the 3D model generation

Next step is verticals determination through `vtkPolyDataNormals`, and, at the end, mapping, i.e. 3D model generation through `vtkPolyDataMapper` class. Final class of 3D models presents `vtkActor` class, which is possible to display on the graphic window of the developed software system. For additional manipulation of the generated 3D models, class `vtkSTLWriter` is used. This class records generated model in STL format, which is a possible export in some of the CAD systems and could be used for additional analysis afterwards.

Series of images which are input in the system with their parameters, are shown on Figure 5.

Parameter  $n$ , represents a number of images and for first patient is 129; for second patient is 137. As mentioned above, distance between images is  $d=1$  mm. Number of images' pixels in x and y directions ( $px$  and  $py$ ) are 512. These parameters are important for `vtkVolume16Reader` class [15].

For isolated contour surfaces of bone and screw, by `vtkContourFilter` class, different contour

values are used for tested patients' series of images. For the first patient isosurface contour value of 1200 is used for bone surface extraction, and contour value of 2800 is used for screw surface extraction. For the second patient, these values were 1450 and 2700 respectively.

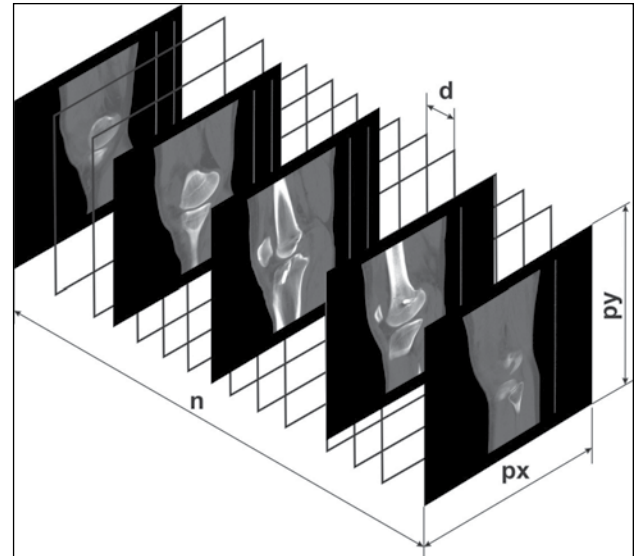


Figure 5. Series of input images in the system with their parameters

Femur's natural position is shown on the Figure 6. It could be seen that femur, in the front view, is rotated by angle  $\Delta\alpha$ . Analysis of large number of human femurs shows that this angle is approximately  $17^\circ$  [16].

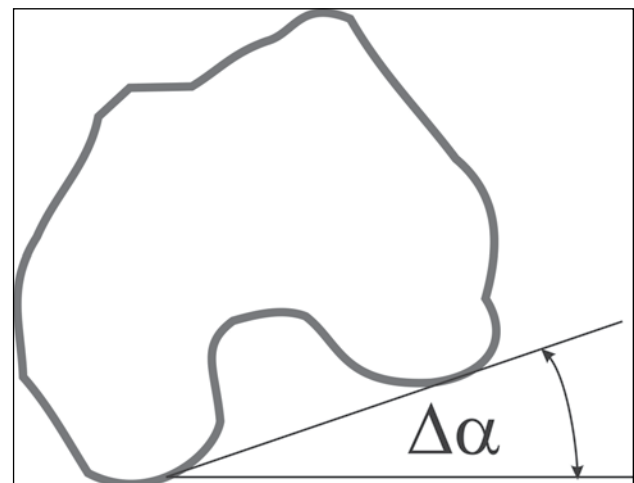


Figure 6. Femur natural position

During the generation of the CT images, patient is kept in natural position and femur has been in the position as shown on Figure 6. Patient is prepared for X ray so that femur position is as shown

on the Figure 3. Such obtained images are more suitable for analysis, because some of the characteristic femur surfaces are more visible [16].

Based on the previous facts, it can be concluded that the determined screw angle, obtained by the developed software system, will be less by angle  $\Delta\alpha$  as compared to an angle in 3D knee model generated by CT images.

Comparison of the screw angle values obtained by the developed software system and generated 3D knee model should confirm that screw angle, obtained by the developed software system enlarged by  $\Delta\alpha$ , should be equal to angle obtained by 3D knee model generation.

As formerly emphasized, verification of the obtained results has been carried out on two patients. Generated 3D models (knee with the crew) based on the CT images, for both patients, are shown in Figure 7.

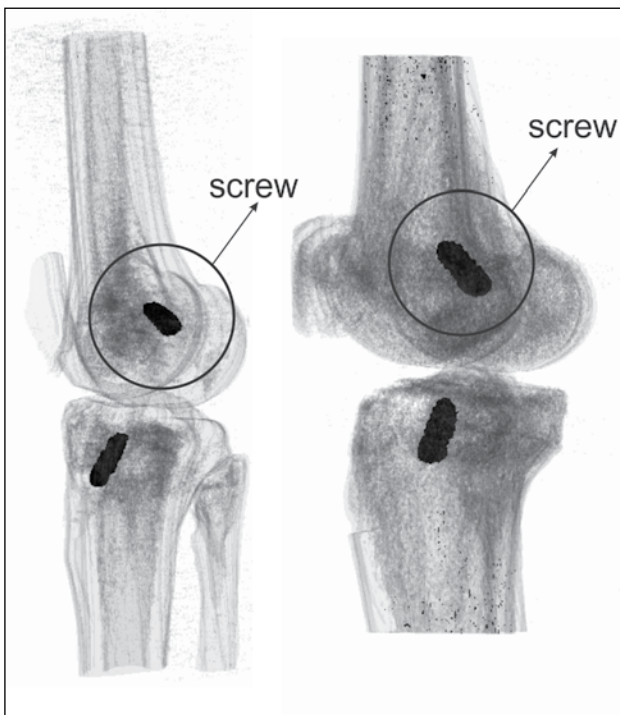


Figure 7. Generated 3D knee models for both patients

For the first patient, on Figure 8 screw angle value obtained by the developed software system, in the front view, is  $46^\circ$ , while angle value obtained by 3D model, based on the CT images, generation (Figure 8) is  $62^\circ$ . For the second patient (Figure 9) respective angle values are  $34^\circ$  and  $52^\circ$ . Difference in the first case is  $16^\circ$  while in the second case is

$18^\circ$ . Having in mind that natural femur position has an angle greater for approximately  $17^\circ$  (Figure 6), it can be concluded that obtained results are absolutely satisfactory.

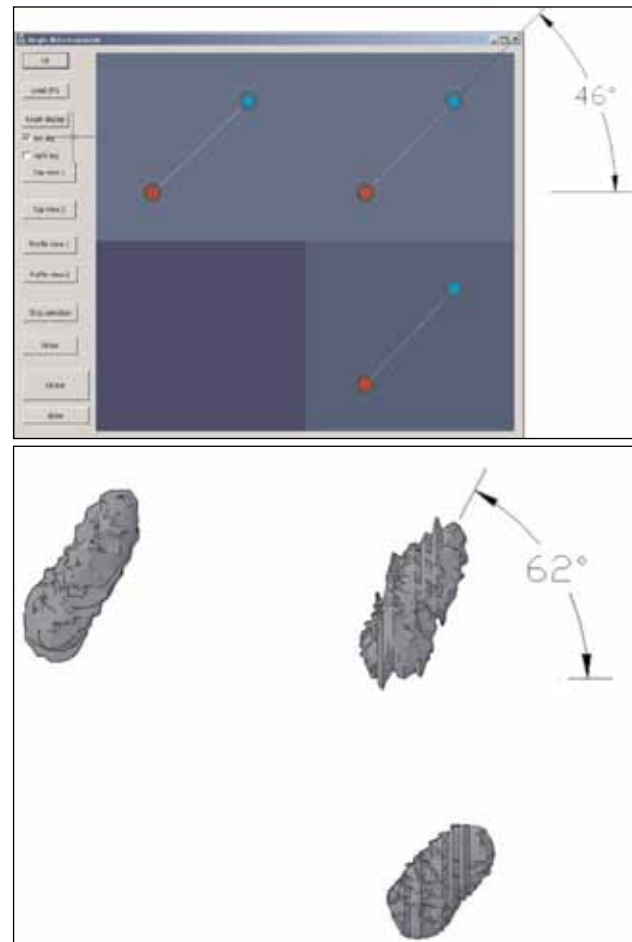


Figure 8. Screw angle obtained values for first patient

On Figures 8 and 9 (right part), all screw views and appropriate screw angle obtained by 3D model based on the CT images generation, are given to enable comparison with views obtained by the developed software system (left part).

## 5. Future research

In the future, research will be aimed at development of the femur 3D model generated from X ray. Because of the complex shape of the femur, femur will be approximated, as accurately as possible, via 3D geometrical primitives – spheres and cylinders, similarly to the methodology presented in the [17]. Mentioned approximate femur 3D mo-

del will be used for determination of the starting point of the tunnel – screw (o'clock). In that way exact tunnel position will be determined.

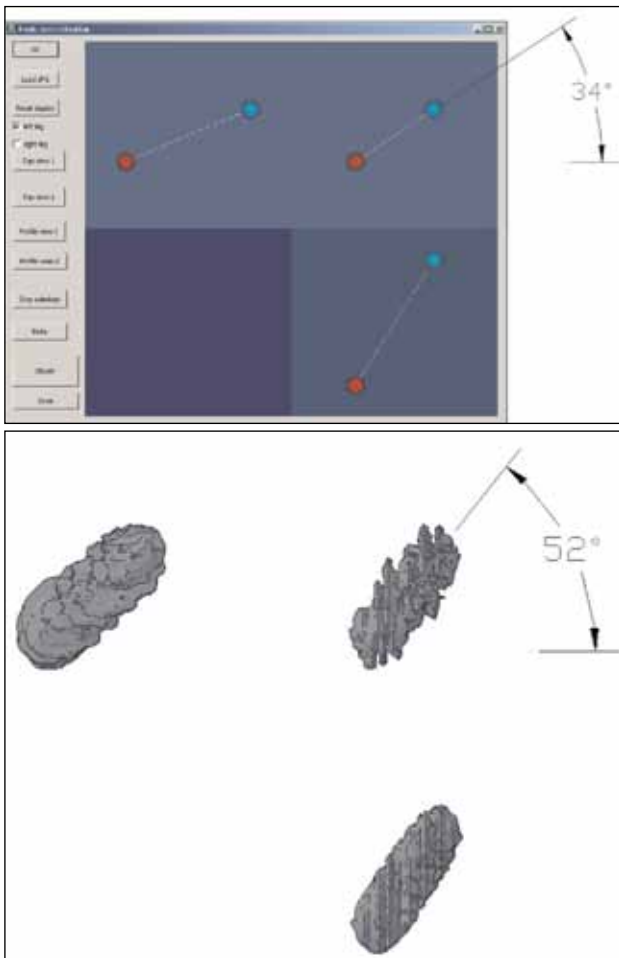


Figure 9. Screw angle obtained values for second patient

## 6. Conclusion

Results, presented in this article, confirm hypothesis that it is possible to determine the value of the screw angle, which is built into human femur, using the knee X ray. For that purpose an appropriate software system is developed. This system enables avoidance of expensive and, for human, negative influence of CT devices. Obtained results could be very useful in the prediction of the patient's rehabilitation process.

In general, research results of the reconstruction of the human knee LCA, presented in this paper, could be classified into several conclusions:

A software system, which is capable to generate third (front) screw view, based on the two vi-

ews obtained by knee X ray, is developed. System, based on the generated third view, determines the screw (built into human knee) angle, and, based on it, indirectly ACL graft position.

Developed system enables simply, fast and accurate verification of the ACL reconstruction post-operative results verification.

A software system for 3D knee model generation, based on the CT (Computed Tomography) images, is developed.

Both systems have been tested on real cases – patients.

Comparison of the results, a coincidence, with satisfactory accuracy, of the screw angle values, obtained by both systems, has been proved.

Obtained results and acquired experience could be a good basis for the development of the mathematical model for 3D knee model generation based on the X ray.

## 7. Acknowledgement

In the paper some results of the project: “Development of the Software/Hardware System for Verification of Post-operative results of the Reconstruction of Anterior Cruciate Ligament of the Human Knee”, carried out by the Faculty of Technical Sciences and Medical Faculty, University of Novi Sad, Serbia, are presented. The project is supported by the Provincial Secretariat for Science and Technological Development of Vojvodina, Serbia.

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# Antioxidant capacity in women with Preeclampsia

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## Abstract

**Aim:** Preeclampsia (PE) remains a frequent and potentially dangerous complication of pregnancy. Free radical damage has been implicated in the pathophysiology of this condition. In this study, we aimed to measure the antioxidant capacity in plasma samples from normotensive and pregnant women to evaluate their antioxidant status using three different measurement methods.

**Methods:** the study was conducted on the sample of 28 women with PE and 29 women with normotensive pregnancies. The levels of superoxide dismutase, hydroxyl and peroxy radical antioxidant capacity were measured in the two groups.

**Results:** statistically significant differences (determined using Mann-Whitney's test) were noted between the normotensive and the PE groups in the levels of hydroxyl radical antioxidant capacity ( $p < 0.001$ ). There was a negative correlation between the levels of systemic blood pressure and the hydroxyl radical antioxidant capacity values. Also, the mean levels of superoxide dismutase were impressively higher in the PE group.

**Conclusions:** we found significant increase in antioxidant capacity levels in two out of three methods used in the case of women with PE. We suggest that there is a mobilization of endogenous antioxidants during PE but it might happen just to a certain extent as the levels of antioxidant power diminish with the severity of PE.

**Key words:** preeclampsia, antioxidants, oxidative stress, superoxide dismutase

## Introduction

Preeclampsia is a pregnancy-specific disorder characterised by hypertension and proteinuria occurring after the 20th week of gestation. Oxidative stress is regarded as a key element in the pathogenesis of preeclampsia, although its precise role has not been fully elucidated (1-4). There are differing views as to how oxidative stress arises but most probably it is secondary to reduced uteroplacental arterial flow due to inadequate remodelling of the spiral arteries during placentation (5,6).

In preeclamptic pregnancies the remodelling of spiral arteries causes maternal blood to enter the intervillous space at a higher pressure and a faster rate, in a pulsatile manner, exposing placental villi to fluctuating oxygen concentrations (7-9). This leads to the ischaemia-reperfusion (I/R) type injury of the placenta and increased production of free radicals in the ischaemic tissue (10, 11).

Cells, tissues, and body fluids are equipped with powerful defense systems that help counteract oxidative challenge. Matching the diversity of prooxidants, the antioxidant armamentarium comprises a widespread array of systems (antioxidant network). Foremost, this system ranges from the classical enzymes, like superoxide dismutases (SOD), to ancillary enzymes and backup systems required to maintain a steady-state. Regulation of the capacities of these antioxidant enzymes in response to changing levels of oxidative stress is a prerequisite for efficient defense (12). These defences are not perfect and when the balance between oxidants and anti-oxidants is disturbed

and oxidation prevails, a cell or organism is considered to be in a state of oxidative stress (13,14).

There are several ways to assess antioxidant status in women with preeclampsia: measuring total antioxidant capacity, individual antioxidant levels or the levels and enzyme activity of antioxidant enzymes (15).

SOD is one of the best studied enzymatic antioxidants in preeclampsia and other oxidative stress induced disorders. It converts the most commonly produced superoxide into less reactive, more stable hydrogen peroxide. Superoxide generation could be one of the factors initiating or maintaining oxidative stress in the maternal circulation in preeclampsia (15,16).

There is an array of methods developed to assess the total antioxidant capacity of human serum/plasma measuring each antioxidant component separately or the interactions among different antioxidant components in the serum/plasma (17). It is very appealing to researchers to have a convenient method for the quick quantitation of antioxidant effectiveness in preventing diseases (18). In the case of preeclampsia several measuring methods of total antioxidant capacity have been used so far with conflicting results.

## Material and Methods

The study population, treated in the Department for Gynecology and Obstetrics, Clinical Center of Vojvodina, consisted of 28 women with preeclampsia and 29 women with normal, normotensive pregnancies. The diagnosis of preeclampsia was established in accordance with the American College of Obstetrics and Gynecology definition (19). The women were age and gestational week matched. Both the cases and controls were primiparas having more than 24 weeks of gestation. None of the patients had pre-existing hypertensive disorders or any renal, hepatic, or hematologic diseases and had received no medication or vitamin supplementation. None of them were smokers. The normotensive women had no signs of any complications of pregnancy, and all gave birth to healthy infants. All women gave informed consent to participate in the study, which had been approved by the local Ethics Committee.

History and examination findings of both cases and control were noted. Fasting blood samples were collected; the plasma was separated and analyzed for SOD, hydroxyl radical antioxidant capacity (HORAC) and peroxy radical antioxidant capacity (ORAC).

SOD was measured using Cell Biolabs OxiSelect™ Superoxide Dismutase (SOD) Activity Assay which uses a xanthine/xanthine oxidase system to generate superoxide anions. The included chromagen produces a water-soluble formazan dye upon reduction by superoxide anions. The activity of SOD is determined as the inhibition of chromagen reduction. The results are expressed both as SOD concentrations (SODc) and SOD activity (SOD%).

Hydroxyl radical antioxidant capacity was measured by Cell Biolabs' OxiSelect™ HORAC Activity Assay and peroxy radical antioxidant capacity by Cell Biolabs' OxiSelect™ ORAC Activity Assay. These assays are based on the oxidation of a fluorescent probe by peroxy (ORAC)/hydroxyl (HORAC) radicals by way of a hydrogen atom transfer process. The sample antioxidant capacity correlates to the fluorescence decay curve, which is represented as the area under the curve (AUC). The AUC is used to quantify the total hydroxyl/peroxy radical antioxidant activity in a sample and is compared to of the water soluble vitamin E analog Trolox™ (ORAC) or a gallic acid antioxidant standard curve (HORAC). The results are expressed both as netAUC and as  $\mu\text{Mole Trolox}^{\text{TM}}$  Equivalents per liter ( $\mu\text{Mole TE/L}$ ) (ORAC) or  $\mu\text{Mole Gallic Acid}$  Equivalents per liter ( $\mu\text{Mole GAE/L}$ ).

Data were analyzed using SPSS 8.0 software. Differences between the two groups were assessed by Chi-Square Tests, the Mann-Whitney test and ANOVA for several groups. The relationship between the various parameters was assessed by correlation. Data were expressed as mean (95% confidence interval for mean) and two-tailed p-values less than 0.05 were considered statistically significant.

## Results

The results of antioxidant markers are shown in Table 1.

Table 1. Groups' structure and markers of antioxidant capacity in both groups of pregnant women

	Preeclamptic pregnancy (n=28)	Normal pregnancy (n=29)	p value
Maternal age (years)	30,43 ± 6,24	27,90 ± 5,70	NS*
Gestational age (weeks)	31,54 ± 3,92	31,9 ± 3,66	NS
SOD concentration	666 ± 2286	379 ± 1851	NS
SOD activity (SOD%)	24 ± 19,2	17,7 ± 17,6	NS
ORAC (net AUC)	3,91 ± 0,340	3,9 ± 0,467	NS
ORAC (µMoleTE/L)	679 ± 50,0	671 ± 81,7	NS
HORAC (net AUC)	0,785 ± 0,389	0,687 ± 1,96	<0,001
HORAC (µMole GAE/L)	3360 ± 1495	2020 ± 2160	0,002

Results are mean ± SD; NS\*, not significant according to Mann-Whitney's

The significant difference between the two groups was found only in HORAC values expressed as both netAUC and µMole Gallic Acid Equivalents per liter.

Although there is no statistical significance, SOD concentration and activity is much greater in the preeclamptic group than in the normal pregnancy group.

A negative correlation was found between the systolic blood pressure (SBP) and SOD concentration ( $r=-0,378$ ,  $p=0,047$ ), and between SBP and SOD activity ( $r=-0,392$ ,  $p=0,039$ ). Similarly, a negative correlation was also found between SBP and HORAC, expressed both as HORACnetAUC ( $r=-0,577$ ,  $p=0,001$ ), and as HORACGAE/l ( $r=-0,582$ ,  $p=0,001$ ).

## Discussion

Most studies so far have confirmed increased oxidative stress during pregnancy. Although there is a definite physiological role of oxidative stress (2,20) and although local oxidative stress within the placenta may be important for placental development (21,22), at the same time there might be detrimental effect on maternal health. Most authors believe that if there is an exaggeration of imbalance between the increased reactive oxygen species ROS and maternal antioxidant defense mechanisms, systemic oxidative damage occurs which then leads to complications such as preeclampsia.

In preeclampsia, antioxidant activity is generally, but not uniformly low. Most studies found low levels of individual antioxidants and/or total antioxidant capacity (23). Certainly measurement

of a single antioxidant in a particular biological fluid or tissue at a given point in pregnancy may not adequately reflect the balance between prooxidant and antioxidant forces. We investigated three different levels of antioxidant defense system in two groups of patients. The two groups were gestational age matched which was important since levels of oxidative stress increase longitudinally antepartum (21). Other causes of oxidative stress were excluded and the women did not take any antioxidants.

No agreed "golden standard" exists for routine analysis of antioxidant capacity in the human circulation. We chose to use three different markers of antioxidant activity. Besides determining levels of well known oxidative marker SOD, we used less known ORAC and never before used HORAC assays. Our goal was to look at the different levels of antioxidant defense system and maybe offer an indication of the antioxidant status of these patients.

Enzyme SOD represents first line of defense against detrimental effect of ROS and can be rapidly induced in some conditions when cells or organisms are exposed to an oxidative stress (24). The same accounts for oxidative stress in preeclampsia (15).

In this study we found that the levels of SOD were not significantly different between the non preeclamptic and preeclamptic group, but the mean value was much higher in the preeclamptic group. A possible cause of the lack of statistical significance was a SOD value of over 10000 found in one sample in the control group. Although this is probably a false positive result, it affected the analysis.

There is no consensus about the SOD levels in preeclampsia. Aydina et al. found decreased SOD



and NO concentrations and increased markers of inflammation and lipid peroxidation in patients with preeclampsia (25). Dordevic and his group also found a lower SOD activity in preeclamptic group of women compared to healthy controls (26). Mahadik et al. found low levels of SOD in preeclamptic subjects and even determined a cut off value of serum SOD (0.52 U/mL) that might be important in deciding the time of intervention such as termination of pregnancy (27).

Our results are similar to those found by Kaur and associates. This group found high SOD concentrations in normal pregnancy and mild preeclampsia compared to non-pregnant women (28). Krishna and Ventmataramana also found significant increase in SOD activities in women with preeclampsia (29). In these two studies the increase in antioxidant enzymes activity was accompanied by a rise in lipid peroxidation products. Both groups concluded that increased activities of antioxidant enzymes may be a compensatory regulation in response to increased oxidative stress. In an in-depth analysis Llurba et al. found significantly enhanced antioxidant enzyme SOD activities in erythrocytes of women with preeclampsia together with significantly increased alpha-tocopherol/lipids and elevated plasma total lipid hydroperoxides levels (30).

It is well known that the overexpression of the antioxidant complex enzyme SOD has been one of the major mechanisms by which cells counteract the deleterious effects of ROS and protect themselves from oxidative damage. In preeclampsia this upregulation could play a protective role against initial peroxidation processes. (31,32).

Because the protection against free radical injury is achieved by a wide spectrum of antioxidants with synergic action, measuring total antioxidant capacity might be a better way to assess antioxidant status. Many investigations have evaluated total antioxidant capacity in preeclampsia. The results have been usually, but not uniformly low; however, the different methods used are not always comparable and also do not necessarily provide a reliable overview of antioxidant status (23,33,34).

We know that during uncomplicated pregnancy, an increase in total antioxidant power accompanies a rise in lipid peroxides (35). A recent study showed alterations in plasma oxidants and antioxidants with overt preeclampsia, including total

antioxidant power, which was reduced, and the concentration of malondialdehyde, which was increased (36). High concentrations of prooxidants and low total antioxidant power were shown in placental and decidual tissue from women whose preeclampsia was complicated by the hemolysis, elevated liver enzymes, and low platelets syndrome, but not in the tissue from other gravidae with preeclampsia (33,37).

We decided to use ORAC assay because they are superior to some prior methods used for estimating antioxidant capacity. Firstly, ORAC assay uses inhibition methods: a sample is added to a free radical-generating system; the inhibition of the free radical action is measured and this inhibition is related to the antioxidant capacity of the sample. This method makes these kinds of assays highly specific because they measure the capacities of antioxidants to directly quench free radicals. Also, the area under-curve technique combines both inhibition percentage and the length of inhibition time of free radical action by an antioxidant into a single quantity, which makes it superior to similar methods that use either an inhibition percentage at a fixed time or a length of inhibition time at a fixed inhibition percentage (17,18,38). The ORAC assay has been used in a great number of studies in different biological systems and for assessing antioxidant defense systems in several different conditions associated with oxidative stress. To the best of our knowledge, only one group so far has used ORAC to assess antioxidant capacity in women with preeclampsia. This was a study conducted on a rather small number of patients (16 preeclamptic, 18 noneventful pregnancies) and they found that lower ORAC values appear in both uterine and umbilical venous plasma of women with preeclampsia (39). We investigated systemic venous plasma and found no difference in ORAC values between the two groups. On the other hand, we found a significant difference between HORAC values.

HORAC assay has been introduced by Ou B et al. in 2002 (40) assay for measuring antioxidant scavenging capacity of hydroxyl radicals. The assay was introduced as a complimentary test to ORAC. ORAC and HORAC values did not correlate.

As ROS in general have a very short life time, only consequences of their action or the antioxi-

dant response can be observed. Hydroxyl radical is directly liable for lipid peroxidation and it is well known that MDA and TBARS levels are raised in preeclampsia (23). The impressive contrast in HORAC values between the two groups can be explained by mobilization of antioxidant systems in response to a rise in hydroxyl radical during preeclampsia. Similarly to raised SOD levels, high HORAC values can be interpreted as an upregulation of anti-hydroxyl elements as compensatory response to events preceding preeclampsia. Why no such raise is seen in ORAC values remains unclear and calls for further investigations. The negative correlations found between SBP and both SOD and HORAC might indicate that the compensation mechanisms might depend on the severity of preeclampsia and that in the more severe cases these mechanisms might not be as efficient, which in turn leads to eclampsia.

There is no doubt that pregnancy leads to the generation of an increased oxidative burden, but whether this overwhelms the anti-oxidant capacity within the placenta and/or the peripheral circulation remains a point of conjecture. We used a novel method for determining antioxidant capacity in preeclamptic women and found some interesting results that need confirmation. However, there are indications of up regulation of endogenous antioxidant system and adaptive response to oxidative stress. We believe that there might be a potential for an early intervention with exogenous antioxidants in order to mobilize the intricate defensive mechanism of natural antioxidant system of the body.

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# The systematic review of head and neck Paragangliomas: clinical presentation, classification, multimodalities imaging findings, differential diagnosis and treatment outcomes

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## Abstract

Head and neck paragangliomas are rare neoplasms originating from paraganglionic tissue, located at four typical locations: the carotid bifurcation, along the vagus nerve, in the jugular fossa and tympanic cavity. Knowledge of the characteristic sonography, MDCT, MRI and DSA appearances of head and neck paragangliomas is mandatory in establishing diagnosis. Special emphasis is given on specificities of carotid, vagal, tympanic and jugular paragangliomas regarding their clinical presentation, localisation, extension and relationship with surrounding structures demonstrated by imaging. Knowledge about differential diagnosis of neoplasms of the carotid space, jugular foramen and middle ear can help in avoiding misinterpreted diagnosis of paragangliomas. Imaging based classifications are necessary for treatment planning, widely used are Shamblin classification for carotid body tumors and Fisch and Glasscock-Jackson classifications for glomus jugulotympanicum tumors. For safe and accurate diagnosis and treatment planning of head and neck paraganglioma it is necessary to be familiar with clinical presentation, classification, multimodalities imaging findings, differential diagnosis and treatment outcomes.

**Key words:** paraganglioma, head, neck

## Background

Paragangliomas account for 0,6% of all neoplasms of the head and neck and 0,03% of all neoplasms (1).

Head and neck paragangliomas (also commonly referred to as glomus tumors or chemodectoma) are highly vascular lesions originating from paraganglionic tissue, located at four typical locations: the carotid bifurcation (carotid body tumors), along the vagus nerve (vagal paragangliomas), and in the jugular fossa and tympanic cavity (jugular and tympanic paragangliomas) (2,3,4). These lesions are histologically similar to the pheochromocytomas that may develop in the adrenal medulla, but unlike pheochromocytomas, head and neck paragangliomas rarely secrete catecholamines (5).

In most cases they are benign neoplasms; overall less than 10% of all paragangliomas have been cited to be malignant (1).

## I Clinical presentation

The clinical symptoms vary according to size and location of the paraganglioma (6). Cervical paragangliomas generally present in mid-adult life as asymptomatic, nonfunctional lateral neck masses (7).

**1. Carotid body paraganglioma** represents the most common form of cervical paraganglioma that accounts for 60% (7).

A carotid body tumor often presents as a painless, slowly enlarging mass in the lateral neck (8) at the level of the carotid bifurcation. The lesion is more freely movable horizontally than vertically because of adherence to the carotid artery („Fontaine’s sign“) (8, 9).

Physical examination of a patient with a carotid body tumor typically reveals a rubbery, nontender mass along the anterior border of the sternocleidomastoid muscle (8). As carotid bruit or tumor pulsations as the VIIth, IXth, Xth, XIth and XIIth cranial nerves deficits can be present in a carotid body tumor, careful neurological examination for cranial nerve palsy is necessary.

**2. Vagal paraganglioma:** A painless neck mass is also the most frequent symptom in patients with vagal paragangliomas (10). Those tumors most commonly arise from the inferior (nodose) ganglion of the vagus nerve, but it has been demonstrated that they might actually arise at any point along the course of the vagus nerve, most commonly located behind the angle of the mandible (4,10). They are most frequently associated with progressive dysphagia and hoarseness with increasing tumor size (7). Horner’s syndrome (ptosis, myosis, anhidrosis, enophthalmos) may result from cervical sympathetic chain invasion and syncope can occur after carotid sinus compression (4,6,7). The more superiorly extending vagal paragangliomas can also cause the jugular foramen syndrome by compressing the IXth, Xth and XIIth cranial nerves (7). Vagal paragangliomas can even extend into the posterior fossa through the jugular foramen, causing the same symptoms as a jugular paraganglioma (11, 12).

**3. Jugular paraganglioma** originates from the jugular bulb near the skull base and extends both inferiorly in the parapharyngeal space and intracranially. It is not usually accompanied by a palpable neck mass (7).

The most common symptoms in patients with jugular paragangliomas are pulsatile tinnitus and hearing loss (9, 13, 14). Audiologic examination reveals significant conductive hearing loss or mixed conductive and sensorineural hearing loss (13,14). Involvement of the inner ear produces vertigo and

sensorineural hearing loss (13,15). Less common aural signs and symptoms included fullness, bleeding, pain, otorrhea, bruit. Otoscopic examination reveals a characteristic pulsatile, reddish-blue tumor behind the tympanic membrane (13). Cranial nerve deficits in jugular paragangliomas usually present with a Vernet i.e. jugular foramen syndrome which includes paralysis of cranial nerves IX–XI (16). This syndrome is pathognomonic for glomus jugulare and includes : hoarseness due to vocal cord paralysis (X), difficulty in swallowing (IX) and weakness and atrophy of the trapezius and sternocleidomastoid muscles (XI)(6,13). Collet Sicard syndrome is present in larger tumors with the XIIth cranial nerve involvement. Collet Sicard syndrome includes Vernet syndrome with involvement of the XII cranial nerve) causing ipsilateral atrophy of the tongue (6,17). Less commonly, larger glomus tumors produce facial nerve palsy (due to VII cranial nerve involvement) or Horner syndrome (13).

**4. Tympanic paraganglioma** is usually relatively small at diagnosis, since symptoms are produced at an early stage. As they originate in the middle-ear cavity they usually become symptomatic as a pulsatile tinnitus that might be accompanied by a conductive hearing loss (18). Tympanic and jugular paragangliomas often present otoscopically as a reddish-blue, pulsating mass behind the tympanic membrane.

## II Imaging Findings:

Evaluation by an imaging procedure is absolutely necessary to establish the diagnosis of a head and neck paraganglioma and for treatment planning (19).

Diagnostic imaging can be considered in patients who present with clinical symptoms suggestive of a paraganglioma, and in patients from families with hereditary paragangliomas. Patients with a positive family history are at a higher risk of having multicentric disease (6).

Imaging includes 4 diagnostic modalities such as:

1. B-mode sonography with color and power Doppler sonography
2. Multidetector computed tomography (MDCT)
3. Magnetic resonance imaging (MRI)
4. Digital subtraction angiography (DSA)

**1. B-mode sonography in combination with color-coded Doppler sonography** is an inexpensive, non-invasive, readily available diagnostic tool that is frequently used as first-line diagnostic procedure for cervical paragangliomas (7,19). Some authors report that the role of color Doppler ultrasound in the diagnostic work-up of paragangliomas is limited because only a limited area of the neck can be investigated, but on the other hand some of them report that ultrasound is the best in detection and follow-up of cervical paragangliomas and in detection of small paragangliomas (4,20). Ultrasound study is performed with 5-10MHz transducer with color and power Doppler options. It is necessary to detect tumor localisation, borders, extension and relationship with surrounding structures, as well as its vascularity. In general, evaluation of skull base paragangliomas (jugular and tympanic) is not possible by ultrasound.

**Carotid body tumors** are most accessible of all paraganglioma to sonography examination. They usually present as solid, ovoid, hypoechoic tumors with sharp margins in B-mode sonography (Fig.1.). By using high-resolution transducer, small vessel flow can be demonstrated within the tumor matrix (4). Typically, there is a splaying of the carotid bifurcation such as the external carotid artery is usually displaced anteriorly and the internal carotid artery and internal jugular vein are displaced posteriorly. Using B-mode sonography only, finding can be suggestive, but it is sometimes difficult to differentiate a carotid body tumors from other solid masses in this region (19). Using color and power Doppler sonography glomus caroticum tumors demonstrate the very strong hypervascularity (Fig 1.). The typical location and hypervascularisation on sonography can establish the diagnosis of carotid body tumors almost certainly.

Carotid body tumors are classified according to imaging into 3 classes by Shamblin et al (21), (Table1):

Table 1. Classification for carotid body tumors by Shamblin

I	Localized tumor
II	Adherent to and partially surrounding carotid arteries
III	Large tumor adherent to and totally enveloping carotid arteries

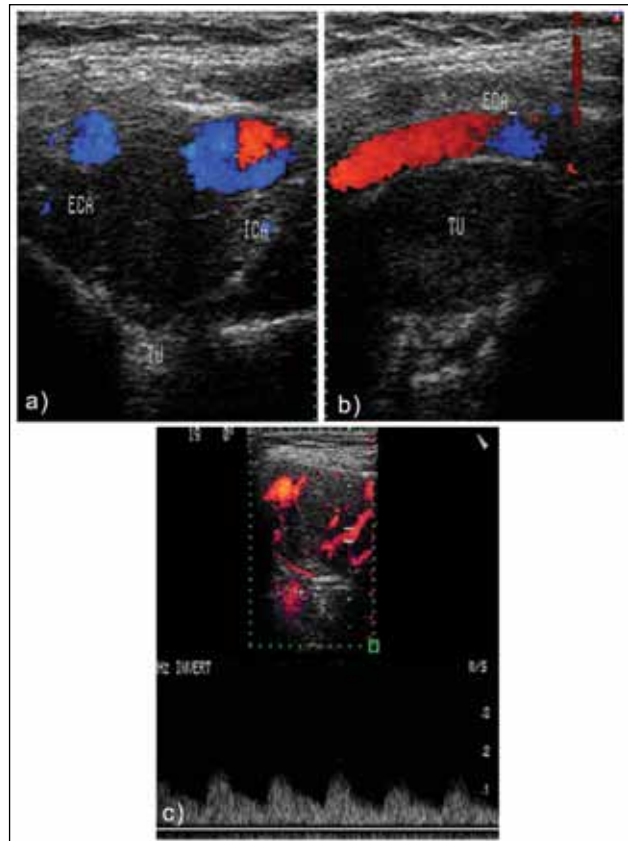


Fig. 1. Left sided carotid body tumor in 64 year-old woman: a) color doppler sonography shows solid, well-defined, hypoechoic tumoral mass with splaying of carotid bifurcation. b) power doppler sonography demonstrates tumoral hypervascularity

**Vagal paragangliomas** often cannot be examined in their full extension by B-mode sonography and color Doppler sonography. Large vagal paragangliomas may also cause splaying of the carotid bifurcation and might be misinterpreted as a carotid body tumors.

Delineation of high cervical vagal and jugular paragangliomas is cumbersome and concomitant lesions in the skull base region remain undetected, while such lesions are important in future treatment planning (20).

**2. MDCT scanning** with thin sections are superior at demonstrating the extent of bone destruction (13) in **jugular and tympanic paragangliomas** (Fig 3,6.). The patterns of spread of the glomus jugulare paragangliomas tumors are predictable and follow the paths of least resistance (4). High resolution CT of the temporal bone will show expansion and a moth eaten pattern of erosion of the jugular foramen in case of jugular paragangliomas (Fig. 3.). Tumor expansion will occur superiorly

and subsequently into the tympanic cavity, causing destruction of the ossicular chain (4). Further extension laterally will destroy the bony canal of the facial nerve with infiltration of the nerve itself. Finally, intracranial posterior fossa extension can occur (4), (Fig. 3). The tympanic paragangliomas present usually like a small mass at the cochlear promontory (Fig. 6.). Ossicular destruction is not common (Fig. 6.) and is especially present in larger lesions (6).

The extension of temporal bone destruction is important to classify those tumors. The two established classifications of temporal bone paraganglioma are based mainly on tumor size with special emphasis on intracranial extension as a decisive factor for resectability. Paragangliomas of the temporal bone are usually staged according to the classification by Fisch (22), (Table 2) and Glasscock and Jackson (23), (Table 3).

The preoperative classification of jugular and tympanic paragangliomas is essential, since the operative approach will be chosen depending on the tumor stage (15). All these classifications distinguish a group of complex tumors that present challenges to treatment and are associated with adverse outcomes (24).

The CT appearance reflects the hypervascular nature of the head and neck paragangliomas resulting in homogeneous and intense enhancement after administration of intravenous contrast material (4), (Fig.2,3.). In addition, the typical localization of each type of paraganglioma contributes to the specific diagnosis. MDCT angiography allows visualization of feeding vessels in cases of large paragangliomas (6).

Table 2. Fisch classification of paragangliomas of the temporal bone

A	Tumors arising along the tympanic plexus on the promontory; confined to the middle ear	
B	Tumors arise in the canalis tympanicus and invade the hypotympanum and mastoid	
C	Tumors originate from the dome of the jugular bulb and invade the petrous bone and pyramid; subgrouping C1-4 is based on the degree of erosion of carotid canal from the carotid foramen to the cavernous sinus	
D	Tumors with intracranial extension (posterior fossa); subdivided according to depth of invasion	
De:	extradural	
	De1	- displacement of the dura less than 2 cm
Di:	De2	- displacement of the dura more than 2 cm
	intradural	
	Di1	- intradural invasion less than 2 cm
	Di2	- intradural invasion more than 2 cm
	Di3	- inoperable

Table 3. Glasscock-Jackson classification of Glomus Jugulotympanicum Tumors  
*Glomus Tympanicum*

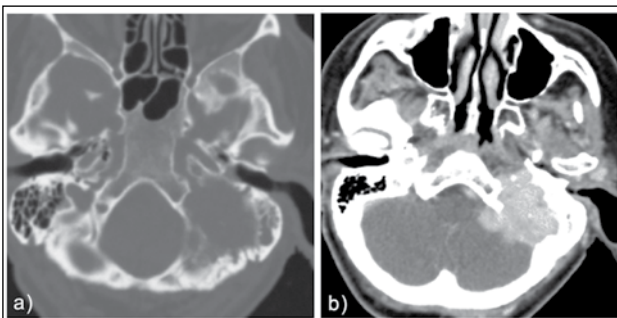
1	Small mass is limited to the cochlear promontory
2	Mass completely fills the tympanic cavity
3	Mass fills the tympanic cavity and the mastoid
4	Mass fills the tympanic cavity, extending into the mastoid, the external auditory canal, or anterior to the carotid

*Glomus Jugulare*

1	Mass is confined to the jugular bulb, middle ear and mastoid
2	Mass extends below to the internal auditory canal (with or without intracranial extension)
3	Mass involves the petrous apex (with or without intracranial extension)
4	Mass extends into the infratemporal fossa and clivus with intracranial extension



*Fig. 2. Left sided carotid body tumor in 52 year-old woman -MDCT postcontrast imaging: a) axial b) coronal and c) sagittal maximum intensity projection images demonstrate strong postcontrast tumoral enhancement d) volume rendering reconstruction image show multiple tumoral blood vessels*



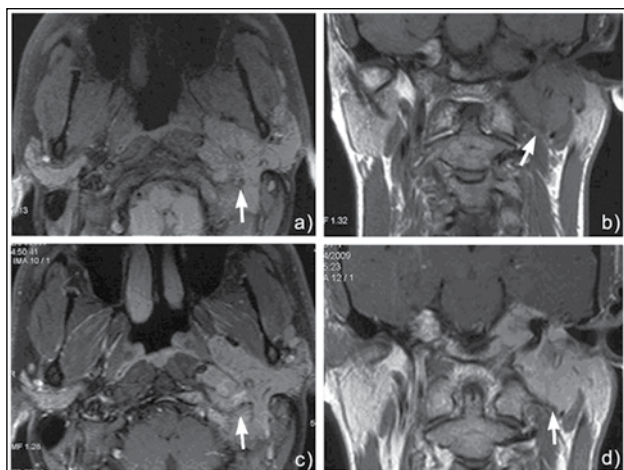
*Fig. 3. Left sided glomus jugulare paraganglioma in 58 year-old man: a) axial skull base MDCT image (bone window) demonstrate destruction and enlargement of the jugular foramen and b) axial postcontrast MDCT show strong tumoral enhancement with skull base destruction and extension in posterior cranial fossa*

**3. MRI** plays an important role in evaluation of head and neck paragangliomas. The recommended MR pulse sequences should include: a T1 weighted spin echo and a T2 weighted turbo spin echo sequence. T2 weighted fat suppressed and contrast-en-

hanced fat-suppressed T1-weighted sequences can offer additional diagnostic information for improved depiction of paragangliomas in the skullbase region but have not proven to be as effective as a pre- and post-contrast enhanced 3D Time of Flight (TOF) MR angiography sequence (25).

The MR appearance of a lesion exhibiting low signal intensity on T1 and a high signal intensity on T2 weighted images(6), (Fig. 4, 7). Multiple serpentine and punctate areas of signal void characterize the typical paraganglioma with all MRI sequences; these areas are variably distributed throughout the mass and represent flow voids in the larger intratumoral vessels (26, 27). Multiple areas of high and low signal intensity, the so-called “salt and pepper appearance”, originally described by Olsen and al. (26) can be seen within the lesion on T1w and T2w images (Fig. 7) . The “pepper” component represents the multiple areas of signal void interspersed with the “salt” seen as hyperintense foci (due to slow flow or hemorrhage) on both T1w and T2w images (26, 28); (Fig. 7). This feature is especially seen in larger paragangliomas. On a 3D TOF MR angiographic sequence these areas of high flow are seen as areas of high signal intensity within the tumor. 3D TOF MR angiography is more susceptible in showing these high flow areas within the tumor than are conventional spin echo MR sequences (25). The combination of imaging features with the typical localization, typical vessel displacement, enlarged feeding vessels, and intra tumoral flow signal makes the diagnosis paragangliomas highly likely, and the combination of these features almost rules out other causes. When paragangliomas are localized in the region of the skull base, coronal MR images will give information on the extension of the tumor in and around the jugular foramen, but even the coronal and sagittal reconstructions of a 3D TOF MRA sequence can provide this information, contrast enhanced MR angiography has been used to study the tumor hemodynamics of paragangliomas. Paragangliomas show a rapid and intense homogeneous enhancement following the intravenous administration of contrast material (Fig. 4). These features could be established in tumors as small as 10 mm in diameter (29).





*Fig. 4. Left sided glomus jugulare paraganglioma in 34 year-old man: different tumoral presentations on MRI sequences a) T1w axial fat suppressed image shows isointense tumor b) T1w coronal image demonstrates hypointense tumor c) T1w axial postcontrast fat suppressed and d) T1w coronal postcontrast images show strong tumoral enhancement*

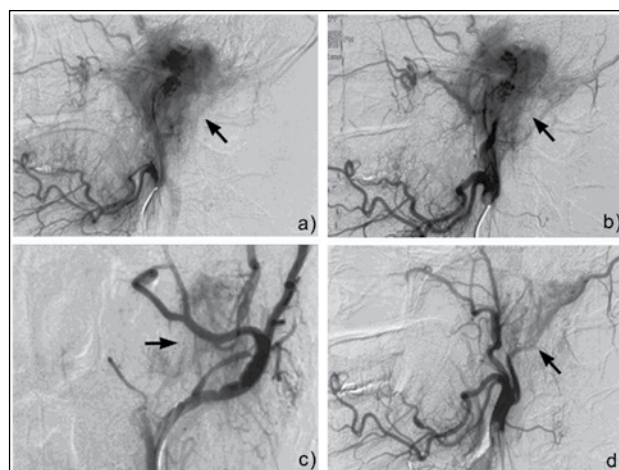
**4. The digital subtraction angiography** is definitive imaging procedure to confirm the diagnosis of a head and neck paraganglioma and some authors report that it is still the gold standard in detection of small paragangliomas (8,25, 26). Angiography shows the specific vascular supply of the paraganglioma (30).

For carotid body tumor evaluation by carotid angiography provides more information about the tumor (the location with respect to the mandibular ramus and the skull base, size of the tumor and evaluation of possible bilateralism), which may help in preoperative planning. Sometimes the carotid body tumors are large at the time of diagnosis, and then preoperative embolization is useful for decreasing of surgical blood loss.

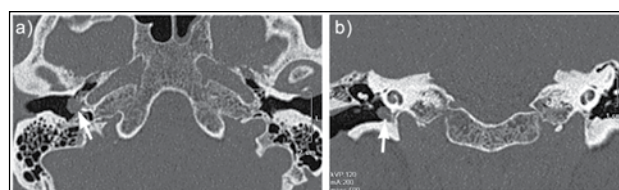
The arteriographic findings of glomus tumors are typically a hypervascular mass with an intense characteristic tumor “blush” (4); (Fig. 5 a, b). Large feeding vessels and early draining veins are commonly encountered, constituting an early arterovenous shunting (31). Glomus jugulare tumors are predominantly supplied by the external carotid artery system, including mainly the ascending pharyngeal artery. The ascending pharyngeal artery can be considered “the artery of the paraganglioma”, because its branches can supply tympanic, jugular, vagal, carotid, and even laryngeal paragangliomas (32).

In addition, the supply of paragangliomas is derived from the occipital artery, posterior auricular artery, muscular branches of the vertebral artery and deep cervical artery and thyrocervical trunk can also contribute to the vascularization (6). The highly vascular nature of the tumor is reflected in enlargement of the feeding arteries, the intense staining of the tumor and a rapid venous drainage. If a lesion does not answer the angiographic criteria, other causes must be considered (6).

Embolization can be performed with DSA for preoperative devascularization of the tumor (Fig. 5 c, d). The primary aim of preoperative embolization is to reduce tumor vascularity which can lead in a decreased intraoperative blood loss. This fact obviously provides a better operative field for the surgeon, thus reducing the possibility of a nerve or vessel injury (7).



*Fig. 5. Left sided glomus jugulare in 34 year-old man: DSA- sagittal view a,b) DSA imaging before embolization demonstrates characteristic intense tumor “blush” and intratumoral shunts c,d) DSA imaging after selective embolization- significant reduction in vascular “blush” indicative of reduced arterial supply to the tumor*



*Fig. 6. Left sided tympanic paraganglioma in 63 year-old man - MDCT of the skull base (bone window) a) axial and b) coronal images demonstrate small, oval mass at right cochlear promontory without ossicle chain destruction*

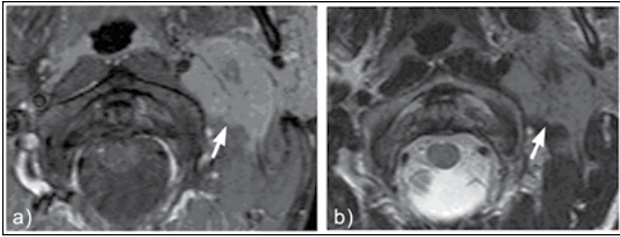


Fig. 7. Left sided glomus vagale paraganglioma in 52 year-old man: MRI a) T1w axial postcontrast fat suppressed image - tumoral enhancement (arrow) b) T2w axial image - "salt and pepper" appearance (arrow)

### III Differential diagnosis

**A) Masses of the carotid space:** other masses beside paragangliomas may arise in the carotid space. These include nerve sheath tumors, nodal metastases, abscess and venous thrombosis as the most common considerations. Much rarer possibilities as lipoma, liposarcomas and hibernoma may also occur. At MRI schwannoma appear isointense relative to soft tissue on T1-weighted sequences and hyperintense on T2-weighted images. On both contrast-enhanced CT and MR images they enhance intensely and homogeneously. Metastases from renal and thyroid malignancies may mimic paragangliomas in their CT and MR appearances. This uncommon lesions infiltrate more into the surrounding soft tissues and do not follow the typical routes of spread of paragangliomas (27).

**B) Tumors involving the jugular foramen** are infrequent. In descending order of frequency, glomus jugulare tumors, schwannomas and meningiomas are the three most common primary tumors in this region (33).

Jugular foramen tumors may be classified as primary and secondary lesions according to their origin. Careful and meticulous analysis of some differentiating imaging findings may lead to a correct preoperative diagnosis, which allows adequate patient counseling and surgical planning. In the group of primary tumors, glomus jugulare tumors may contain flow voids on T1-weighted images, "salt-and-pepper" appearance and are arteriographic hypervascular lesions with large feeding vessels and early draining veins. Meningiomas present with a "dural tail", while neurinomas are well-delimited lesions

with smoothly margined enlargement and non-invaded marrow space of the jugular foramen on CT scans. Some cases may present with cystic degeneration. In the group of secondary tumors, chordomas and chondrosarcomas are hypointense on T1-weighted sequences and very hyperintense on T2-weighted images with accentuate bony destruction on CT scans. Chordomas usually originate from the midline, while chondrosarcomas predominately arise laterally. Chondroblastomas may present similar radiological features to chordomas and chondrosarcomas, although intense calcification may be encountered in some of these lesions. Cholesterol granulomas and giant cholesterol cysts are well-delimited lesions, which are hyperintense on T1- and T2-weighted images. Endolymphatic sac tumors may also have high signal intensity on both T1- and T2-weighted images. However, their heterogeneity, less well-defined limits and hypervascularity seen on arteriography differentiate these tumors from cholesterol granulomas and cholesterol cysts. Reactive myofibroblastic tumors occur in young patients (neonates, infants and during the childhood) and are isointense masses on T1-weighted sequences and hypointense masses on T2-weighted sequences, with gadolinium enhancement. Lytic skull base lesions or other bone or organ metastases are present in most patients with jugular foramen metastases (33).

**C) Masses in the middle ear:** The differential diagnosis considerations for the middle ear mass include benign neoplasms (adenoma, endolymphatic sac tumors, choristoma, cholesteatoma, cholesterol granulomas) and malignant neoplasms (squamous cell carcinoma, adenocarcinoma, sarcoma). Adenomatous tumors (mixed patterns type) of the middle ear manifest as soft-tissue masses in the tympanic cavity, usually without destruction of surrounding osseous structures. These tumors may enhance intensely following the intravenous administration of contrast material (34). Endolymphatic sac tumors of the temporal bone arise from the region of vestibular aqueduct. Although they may closely resemble glomus jugulare tumors, their origin from the vestibular aqueduct is a useful discriminative characteristic. They are frequently quite large at the time of presentation, demonstrate lytic changes in the temporal bone and characteristically have regions of T1-weighted sequences on MRI (35).

#### IV Therapy

Therapy options for paragangliomas is still controversial in literature. Despite extensive work on the development of surgical and radiation treatment strategies, considerable controversy still exists regarding the optimal management of these lesions, specially in complex paragangliomas (i.e. giant size, multiple paragangliomas, malignancy, catecholamine secretion, association with other lesions, previous treatment with adverse outcome, radiation therapy, or adverse effects from embolization)(23). Surgery is the treatment of choice for most patients with head and neck paragangliomas. A major advancement in the surgical treatment of glomus jugulare tumors occurred with the development of preoperative superselective embolization. Preoperative embolization is necessary in patients with jugular paragangliomas, carotid body and vagal paragangliomas with a diameter larger than 3 cm for reducing intraoperative blood loss, specially in extensive jugulare paraganglioma (15). In addition, embolization led to a higher rate of complete resection. Nevertheless, there did not appear to be a reduction in the risk of injury to the lower cranial nerves. As for the morbidity associated with the embolization procedure, the current state of technology and expertise in interventional radiology has significantly reduced the incidence of stroke and cranial nerve injury.

Whenever surgical extirpation is too risky, stereotactic radiosurgery and conventional radiotherapy are alternative treatment options. The role of tumor irradiation in the management of paragangliomas remains controversial. To date, there is no conclusive data establishing radiation as the optimal primary treatment for all glomus jugulare neoplasms. External tumor irradiation may reduce tumor growth and may provide symptomatic relief in a selected subpopulation of patients. The principal indications for the use of radiotherapy as a primary treatment include larger tumors where after careful staging resection may result insignificant morbidity, patients in poor health status with concomitant medical conditions, or as an adjunct to incompletely excised tumors with skull base or intracranial invasion (7).

#### V Complications after preoperative embolisation, radiotherapy and surgical extirpation

Complications of preoperative embolisation include cerebral ischemia and cranial nerve palsies. Stroke may occur with accidental introduction of embolic material into the vertebrobasilar system via ECA or through the anastomoses between the ECA and ICA. Cranial nerve palsies are possible with accidental introduction of embolic material into ascending pharyngeal artery, the middle meningeal and stylomastoid arteries which supply the VIIth and cranial nerve IX-XII (36). Other major risk of preoperative embolisation include transient aphasia, carotid sinus syndrome and the sequela of catecholamine secretion.

Frequent side effects of irradiation include acute dermatitis, alopecia, external otitis, serous otitis media, altered taste and xerostomia. Serious complications such as radionecrosis of the temporal bone, brain necrosis and radiation-induced malignant disease have been reported (37).

Potential complications associated with surgical resection of carotid body tumors include cranial nerve deficits, perioperative mortality and stroke (38).

The surgical removal of glomus jugulare tumors include cranial nerve palsies, cerebrospinal fluid leak and ICA damage (32).

#### VI Conclusion

Head and neck paragangliomas are rare neoplasms. A proposed diagnostic algorithm in management of head and neck paragangliomas includes B-mode sonography with color-coded Doppler sonography, computed tomography, magnetic resonance imaging and digital subtraction angiography. Paragangliomas of the head and neck have different clinical symptoms, most important is low cranial nerve deficit, which may suggest the diagnosis. In general, paragangliomas of head and neck are highly vascular lesions and their hypervascularity is demonstrated on each diagnostic modalities. Imaging studies depict the location and extent of tumor involvement, help determine the type of head and neck paraganglioma and their classification. Each

imaging modality has its own role in establishing diagnosis. Color Doppler sonography is first imaging step and it is useful in diagnostics of carotid body tumors and paragangliomas which extended to the neck. MDCT is sensitive in evaluation of bony destructions which demonstrate jugular, sometimes vagal and tympanic paragangliomas. MRI is the important imaging technique for tissue characterisation and it shows the typical “salt and pepper” appearance of paragangliomas. Magnetic resonance angiography provides information concerning the vascular supply of the lesion and displacement of adjacent vessels. Knowledge about differential diagnosis of neoplasms of the carotid space, jugular foramen and middle ear can help in avoiding misinterpreted diagnosis of paragangliomas. Imaging based classifications are necessary for treatment planning, widely used are Shamblin classification for carotid body tumors and Fisch and Glasscock-Jackson classifications for glomus jugulotympanicum tumors. The definitive imaging procedure to confirm the diagnosis of a head and neck paraganglioma represents the DSA, which is the gold standard in detection of small paragangliomas. Angiography shows the specific vascular supply of the paraganglioma and it is required preoperatively in larger paragangliomas for surgical planning and preoperative embolisation. For safe and accurate diagnosis and treatment planning of head and neck paraganglioma it is necessary to be familiar with clinical presentation, classification, multimodalities imaging findings, differential diagnosis and treatment outcomes.

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# Endoscopic correction of vesicoureteral reflux with Deflux – lessons learned

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## Abstract

**Background:** Vesicoureteral reflux is diagnosed in one third of children who present with a urinary tract infection. There is no general agreement as to what constitutes the optimum management of children with vesicoureteral reflux, even-though there have been a number of studies prospectively comparing medical and surgical management of reflux. The aim of this study is to evaluate a single center experience with Deflux<sup>®</sup> procedure and assess its effectiveness.

**Material and Method:** 67 patients treated endoscopically over the period of three years (2005-2008) were included in the study. We analyzed the effectiveness of the therapy, the average volume of Deflux<sup>®</sup> used per ureter, and the presence of complications. The follow-up ranged from 4-26 months (median 11 months).

**Results:** The overall success rate of endoscopic treatment was 94.4%, with an average 0,95ml of Deflux<sup>®</sup> used per ureter. Reflux was absent in 88.9% of the ureters and 5.5% of the ureters had downgraded reflux. Ultrasound examination at discharge showed transitory occlusion of the ureteric orifice (i.e. dilatation of the pyelocalyceal system) in 5 patients. Dilatation resolved in 7 days in 4 patients, and one patient had decreasing but still persistent dilatation for 4 weeks. An IVP was performed 4 weeks after the procedure. It showed adequate transition of contrast from the ureter to the bladder.

**Conclusion:** The submucosal injection of Deflux<sup>®</sup> is an alternative to open surgery or conservative treatment with antibiotics. In order to achieve good results an over-correction is some-

times necessary. Consequential dilatation of the pyelocalyceal system resolves spontaneously in most of the patients without any derivation.

**Key words:** vesicoureteral reflux, Deflux procedure, children

## Sažetak

**Uvod:** Vezikoureteralni refluks se dijagnosticuje kod trećine djece sa urinarnom infekcijom. Ne postoji konsenzus oko optimalnog vida liječenja, iako postoji veliki broj studija koje su prospektivno komparirale konzervativni i hirurški tretman refluksa. Cilj ove studije je da se evalui- ra iskustvo sa endoskopskim liječenjem refluksa Defluks<sup>®</sup> procedurom i utvrdi njegova efektivnost.

**Materijal i metode:** 67 pacijenata tretiranih endoskopski tokom perioda od 3 godine (2005-2008) je uključeno u studiju. Analizirali smo efektivnost terapije, prosječna količina potrošene Defluks<sup>®</sup> paste po ureteru, i prisustvo komplikacija. Pacijeti su praćeni od 4-26 mjeseci (median 11 mjeseci).

**Rezultati:** Sveukupna stopa uspješnosti endoskopskog tretmana iznosi 94.4%, sa prosječnom potrošenom količinom od 0,95ml Deflux<sup>®</sup> paste po ureteru. Refluks je bio odsutan kod 88.9% uretera i 5.5% uretera je imalo niži stepen refluksa. Ultrazvučni pregled na otpustu je ukazivao na tranzitornu okluziju ureteralnog ušća (dilataciju pijelokaliksnog sistema) kod 5 pacijenata. Dilatacija je spontano regresirala kod 4 pacijenta za 7 dana, dok je jedan pacijent imao nešto manju, ali ipak prisutnu dilataciju tokom 4 nedelje. Intravenska pijelografija je načinjena 4 sedmice nakon

procedure koja je pokazala adekvatnu tranziciju kontrasta od uretera do mokraćne bešike.

**Zaključak:** Submukozna injekcija Deflux® paste predstavlja alternative otvorenoj hirurgiji ili konzervativnom tretmanu antibioticima. Da bi se postigli dobri rezultati neophodna je nekad aplikacija veće količina Defluks® paste. Posljedična dilatacija pijelokaliksnog sistema nakon aplikacije Defluks® paste prolazi spontano bez ikakve derivacije.

**Ključne riječi:** vezikoureteralni refluks, defluks procedura, djeca

## Introduction

Vesicoureteric reflux (VUR) allows the retrograde flow of urine from the urinary bladder into the upper parts of the urinary tract. Combined with urinary infection and pyelonephritic scarring, it represents a well known triad in pediatric practice that can lead to severe changes of the kidneys and to the development of the so-called reflux nephropathy [1].

The possibility of spontaneous regression of reflux has enabled medical therapy to find a place in the treatment of VUR, especially of the mild forms [2]. Severe reflux is treated surgically. With the availability of bulking agents that is well tolerated, and have demonstrated long-term efficacy as a single injection procedure in the treatment of VUR, endoscopic injection has become an important intermediary option between conservative management and major surgery [3].

The most popular bulking agent in the past, used by many surgeons was Teflon. However, there have been concerns regarding the distant particle migration to parenchymatous organs, both in experimental animals [4] and in humans [5].

Stabilized, non-animal hyaluronic acid/dextranomer, Nasha™/Dx (Deflux®, Q-Med, Uppsala, Sweden) gel is a biocompatible bulking agent with a large particle size that reduces the risk of particle migration [6]. Deflux® has been shown to be well tolerated and to have long-term efficacy in the endoscopic treatment of VUR [7]. Furthermore, this gel is currently the only material approved by the Food and Drug Administration for endoscopic injection in the treatment of VUR.

## Material and Methods

Over the period of three years (November 2005 – November 2008) 79 patients were referred to the Pediatric Surgery Clinic for treatment of VUR. All of the patients had a VCUG confirming the presence of VUR. Twelve patients were treated surgically, because of the presence of ureterocele in 5 patients, posterior urethral valves in 3 patients and 4 patients with double ureters and afunctional upper pole of the kidney. Sixty-seven patients were treated endoscopically. The study included 50 girls and 17 boys, aged 1-9 years. Twenty-three patients (34,3%) had bilateral VUR, and 44 (65,7%) patients had unilateral reflux. A total of 90 ureters were treated. Reflux ranged from grade I to grade V; grade I refluxing ureters were treated only if they were associated with a higher grade reflux on the other side.

Under general anesthesia, routine cystoscopy was performed. The bladder was filled to half to three-fourths volume to permit visualization of the ureter and to avoid tension within the submucosal layer of the ureter, secondary to over distension. A Storz cystoscope (Storz, Tuttlingen, Germany) Ch 9 and 14,5 Fr with a 0° optic lens was used. Deflux® was injected through a needle provided by the producer of the substance itself (polytetrafluoroethylene coated, 25 cm long, 3,5 Fr Needle, Q-Med, Uppsala, Sweden). The needle was inserted a few millimeters below the ureteric orifice and the material was injected in the terminal, subureteral space of the intramural ureter. In cases of higher grade of reflux, the needle was inserted into the ureter and the substance was injected there.

Patients were followed by the ultrasound examination the day after the procedure, and if there were no signs of dilatation of the upper urinary tract, patients were discharged. All the patients were treated with antibiotics 7 days after the procedure. Prophylaxis (uroantiseptic) lasted 3 months until the follow-up VCUG. In cases of repeated urinary infection antibiotic treatment was administered according to the biogram.

Patients which had dilatation of the upper urinary tract visible on ultrasound the day after the procedure were followed by ultrasonography every 7 days until the resolution of the dilatation.

The follow-up ranged from 4-26 months (median 11 months).

**Results**

During the study period 67 patients were treated endoscopically, with a total of 90 ureters. Endoscopic treatment was performed bilaterally in 23 patients (34,3%). Most of the ureters (49) had a reflux grade III (54,4%). Twenty-three ureters (25,5%) had a reflux grade IV, and 14 ureters (15,6%) had reflux grade II. There was one ureter treated endoscopically with grade I reflux, and it was done in a case of bilateral reflux, where the contralateral ureter had reflux grade IV. Three ureters (3,3%) were treated endoscopically for the V grade reflux (Table 1).

Results of the endoscopic treatment are presented in Table 2 and Figure 1. The resolution rate for reflux grade I and II was 100%. Reflux grade III was absent after endoscopic treatment in 93.9% of the ureters, while in another 4.1% the reflux was downgraded. Nineteen ureters with reflux grade IV (82.6%) were without any reflux after endoscopy, and in another 3 ureters (13.0%) reflux was downgraded. We were unable to resolve reflux endoscopically in one patient with IV grade reflux, as well as in all the patients (3) with the reflux of the fifth grade.

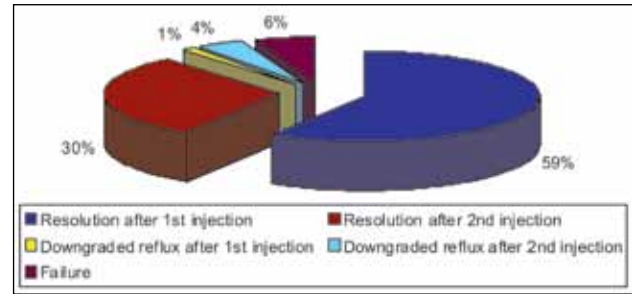


Figure 1. Overall success rate of endoscopic treatment.

The overall success rate of endoscopic treatment was 94.4%. Reflux was completely absent in 88.9% of the ureters and 5.5% of the ureters had downgraded reflux.

The average amount of Deflux<sup>®</sup> used per ureter was 0,95ml.

All the patients were discharged the day after the procedure. Ultrasound examination at the discharge showed transitory occlusion of the ureteric orifice (i.e. dilatation of the pyelocalyceal system) in 5 patients. They were all asymptomatic and were discharged despite the presence of dilated pyelocalyceal systems. They were followed by ultrasound every 7 days. Dilatation resolved in 7 days in 4 patients, and one patient had decreasing but still persistent dilatation for 4 weeks. An

Table 1. The number of treated ureters classified according to the grade of the reflux and the side of the body

Grade of reflux	Unilateral reflux				Bilateral reflux				Total	
	Left		Right		Left		Right			
	n	%	n	%	n	%	n	%	n	%
I	0	0	0	0	1	1.1	0	0	1	1.1
II	2	2.2	3	3.3	3	3.3	6	6.7	14	15,6
III	6	6,7	14	15,6	16	17,8	13	14,4	49	54,4
IV	11	12,2	7	7,7	2	2,2	3	3,3	23	25,5
V	0	0	1	1,1	1	1,1	1	1,1	3	3,3
Total	19	21.1	25	27.8	23	25.6	23	25.6	90	100

Table 2. Results of the endoscopic treatment with Deflux

Grade of reflux	Absent reflux		Downgraded reflux		Failed treatment		Total	
	n	%	n	%	n	%	n	%
I	1	100	0	0	0	0	1	100
II	14	100	0	0	0	0	14	100
III	46	93.9	2	4.1	1	2.0	49	100
IV	19	82.6	3	13.0	1	4.3	23	100
V	0	0	0	0	3	100	3	100
Total	80	88.9	5	5.5	5	5.5	90	100



IVP was performed 4 weeks after the procedure. It showed adequate transition of contrast from the ureter to the bladder, and since the patient was all the time asymptomatic, we did not do anything further.

We have encountered only minor complications. Microhematuria was present in 3 patients (3.3%), it lasted on average 7 days and resolved spontaneously in all of the patients. Four patients had break-through infections, despite prophylaxis, and they have all been treated with antibiotics according to the biogram. Only one patient developed pyelonephritis with fever up to 38°C.

## Discussion

VUR is a heterogenous disease and remains one of the most controversial problems in pediatrics. It is diagnosed in one third of children who present with a urinary tract infection. There is no general agreement as to what constitutes the optimum management of children with VUR, even-though there have been a number of studies prospectively comparing medical and surgical management of reflux [8].

Medical therapy of reflux is based on possible spontaneous resolution. The overall spontaneous resolution rate is approximately 15% and the median time to resolution is 5 years [2]. For reflux grade I and II, long-term antibiotic prophylaxis to prevent UTIs is generally recommended as initial therapy while awaiting spontaneous resolution. This practice may require several years of antibiotic use [9]. Although the dosage used is low (1/2 or 1/3 of the daily therapeutic dose), over time the amount of antibiotics ingested is pretty high, and antibiotic-related adverse events are well known [10]. In addition, antibiotic prophylaxis requires annual imaging that is expensive, invasive and uncomfortable for the patient.

Surgical treatment offers instantaneous disappearance of reflux in most patients. It is very effective but not without complications [11]. Another drawback of this kind of treatment is the prolonged hospital stay (5-7 days). There is also a matter of parental preference with respect to choice of treatment. It has been shown that 80% of parents would choose endoscopic treatment over

reimplantation and antibiotic prophylaxis when given a free choice after detailed information about all three treatment options [12].

The success rate of endoscopic treatment of VUR with Deflux® have varied from 63-100% [13,7]. In our study the overall success rate was 94.4%. This result is better than the result we previously published (85.0%). We have even then suggested that endoscopic correction of VUR requires a long learning curve. We were at that time proud that the amount of Deflux® that we were using was decreasing year by year. However, in the present study we have applied on average 0,15 ml of Deflux® more compared to the previous study. It has resulted in an increased incidence of transitory occlusion of vesicoureteral orifice (5,5% compared to 0), but it has also resulted in better overall success rate.

Early failure of the procedure is usually due to an incorrect technique, in general due to an injection that was too deep, with secondary migration of the material along the Waldeyer's sheath. In patients who underwent a second injection this was usually confirmed: the implant was either not found at all, or it was displaced medially or distally to the ureteric orifice.

Deflux® (dextranomer/hyaluronic acid copolymer) is composed of microspheres of dextranomer (80-250µm in diameter) and sodium-hyaluronan [7]. These constituents form a viscous solution that is biodegradable, non-allergenic, non-mutagenic and non-immunogenic. The volume decreases slightly, and ingrowth of fibroblasts and generation of collagen between the microspheres may account for the endogenous tissue augmentation and a smaller loss of volume than expected [14]. However, the consistency of the Deflux® paste, once under the ureteric orifice seems to be unable to complete occlusion of the orifice, i.e. allowing the overcorrection.

Our own experience suggests that endoscopic correction should be performed in all patients with grade II, III and IV reflux. Grade one should be treated conservatively and grade V reflux should be treated surgically. There are authors who have reported very good results with endoscopic treatment of V grade reflux [15], but we were unable to repeat their success.

## Conclusion

Endoscopic correction of vesicoureteral reflux is an easy, simple, fast and safe procedure that, in most cases prevents the regurgitation of urine from bladder to the upper parts of the urinary system. In order to achieve good results, an over-correction is sometimes necessary. Consequential dilatation of the pyelocalyceal system resolves spontaneously in most of the patients without any intervention.

## Abbreviations

**VUR** - vesicoureteral reflux

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# Use of Botulinum toxin type a in children with Spastic Cerebral Palsy

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## Abstract

**Background:** Cerebral palsy (CP) is one of the most common causes of activity limitation in children. Botulinum toxin (BoNT-A) is relatively recent addition to the available medical interventions for children with cerebral palsy.

**Objective:** to determine possible effects of injections of BoNT-A on muscle tone, passive range of motion in lower extremity and gross motor function in children with spastic CP.

**Methods:** Forty one children with spastic CP were included in this prospective study. They received for the first time treatment with botulinum toxin type A in the period 2003-2008. Before and after the treatment with BoNT-A they were evaluated: passive range of joint motion (PROM) of low extremity, spasticity using Modified Ashworth Scale (MAS) and individualized therapeutic goals were planned using the Goal Attainment Scale (GAS).

**Results:** PROM-abduction in hips was significantly improved two weeks, one and half, three and five months after the treatment. Knee-popliteal angle unilateral and popliteal angle bilateral were significantly improved two weeks, one and half, three and five months after the treatment. PROM-dorsiflexion of ankle with extended knee left was significantly higher after 2 weeks and 3 months compared with pretreatment. PROM- dorsiflexion of ankle with knee flexion at 90 ° was significantly higher after 3 months (right) and after 1.5 and 3 months (left) compared with pretreatment. MAS of adductors was significantly decreased

two weeks, one and half and three months after the treatment. After the treatment all mean values of MAS were lower compared with baseline values. Approximately 85% of patients achieved the expecting therapeutic goals according to GAS after the 5 months of treatment with BoNT-A.

**Conclusions:** BoNT-A injections should always be used as an adjunctive treatment to physiotherapy, occupational therapy and orthotic management. In combination with post-injection physiotherapy this treatment could provide long-term benefits.

**Key words:** Cerebral Palsy, Children, Botulinum-Toxin Type A

## Introduction

Cerebral palsy (CP) is one of the most common causes of activity limitation in children. The central nervous system (CNS) lesion causing the disorder of posture and movement is no progressive, but manifestations of the lesion may change over time (1,2).

Spasticity is a complex phenomenon and has been defined as "a motor disorder characterized by a velocity-dependent increase in tonic stretch reflexes (muscle tone) with exaggerated tendon jerks, resulting from hyper excitability of the stretch reflex, as one component of the upper motoneuron syndrome". Spasticity can be associated with co-contraction, clonus and hyperreflexia. Children with spastic cerebral palsy generally have a typical pattern of muscle weakness, impairment in selective motor control and sensory impairment (1,3,4).

Botulinum toxin is relatively recent addition to the available medical interventions for children with cerebral palsy (1,4). Significant improvements in tone and range of joint motion (ROM) with botulinum toxin type A (BoNT-A) alone suggest that BoNT-A injection may be effective in treating a spastic equinus foot in children with CP (5). Lindera et al.(2001) recorded a significant improvement in joint mobility and a reduction in spasticity compared to pretreatment values as well as significant functional benefit after 1 year of treatment in the patient group (6).

Some results suggest that BoNT-A can be effective in reducing muscle tone over a longer period, but not in preventing development of contractures in spastic muscles (7). Mechanical and functional alterations can arise from the muscle tissue itself even though the nervous system is the site of the primary lesion. The gross mechanical changes occur in skeletal muscle secondary to spasticity and during development of contracture (8). Muscle stiffness can change for a variety of structural reasons, only one of which is altered fiber length (9). There is currently no evidence in the literature that muscle fiber length is shortened in contracture or in spastic skeletal muscle. Contracture formation results from inappropriate architectural adaptation of extremity muscles in response to upper motor neuron lesion (8).

The aim of the present study was to determine possible effects of injections of BoNT-A on muscle tone, passive range of motion in lower extremity and gross motor function in children with spastic CP.

### Material and methods

Forty one children with spastic CP were included in this prospective study. They received for the first time treatment with botulinum toxin type A in the period 2003-2008. Records were excluded for patients with spasticity predominantly in upper extremities, fixed contractures and hip, knee and ankle deformities, or history of previous surgery in the past year. A deficit in cognitive function was not a criterion for exclusions.

Patients with CP were admitted to the Clinic for Child Habilitation and Rehabilitation, and before

the treatment with BoNT-A they were evaluated by physiotherapist passive range of joint motion (PROM) of low extremity, spasticity using Modified Ashworth Scale (MAS)(10). Also, they were examined by Physical Medicine and Rehabilitation specialist and individualized therapeutic goals were planned together with parents and physiotherapist using the Goal Attainment Scale (GAS)(11,12).

Functional status was classified by Gross Motor Functional Classification System (GMFCS) level I-V. GMFCS for CP is based on self-initiated movement, which represents the child's present abilities and limitations in motor function (13).

The injection were administered using multi-level approach at single injection session if were indication for this type of treatment. The various muscle groups that were injected in each session were the gastrocnemius, hamstring muscles and the adductors.

A standard concentration of BoNT-A (Dysport® 500U/ml) was used. The dosage for BoNT-A ranged from 10-20 U/kg. If only one side was injected the dose was 10 U/kg. The total maximum dose was 1000 U/kg. The total muscle dose was divided between 2 and more injection sites, depending on muscle size. The injections were administered using palpation of the muscle in identification of target muscles and motor points. Local anesthetic (Lidocain®) was used 10-15 minutes before administration of the injection.

An intensive physiotherapy program was started 2 days after the administration. The first two weeks the treatments were 3-5 days per week, and after was decreased to 1-2 days per week next five months. The physiotherapy sessions were planned to achieve an individualized therapeutic goals which were established for every patients. We recommended application of ankle foot orthoses.

The patients were assessed at baseline and at two weeks, one and half, three and five months after the treatment with BoNT-A.

### Results

Data from 41 patients who were followed for two weeks, one and half, three and five months were evaluated. The characteristics of patients are presented in Table 1.

**Table 1. Characteristics of the Patients**

Age (mean, SD, yrs)	5.48±3.79
Sex (F/M, %)	41.5/58.5
Type of CP (diplegia, quadriplegia, hemiplegia, paraplegia,%)	46.3/26.8/19.5/7.3
GMFCS (I/II/III/IV/V,%)	24.4/12.2/19.5/29.3/14.6

The distribution of treated muscles (%) and mean dose for each muscle (U/kg) are presented in Table 2.

**Table 2. The distribution of treated muscles (%) and mean dose for each muscle (U/kg)**

Treated muscles	%	U/kg
m. gastrocnemius	63.4	12.42±4.30
m. add. femoris magnus	48.8	12.70±3.88
m. semitendinosus	41.5	10.29±2.99
m. add. femoris longus	34.1	12.07±3.91

Passive range of joint motion (PROM) -abduction in hips was significantly improved two weeks, one and half, three and five months after the treatment (Table 3).

Knee-popliteal angle unilateral (PAU) and popliteal angle bilateral (PAB) were significantly improved two weeks, one and half, three and five months after the treatment. Also, the mean values after the five months were higher compared with baseline (Table 4).

Passive range of joint motion (PROM)- dorsiflexion of ankle with extended knee left was significantly higher after 2 weeks and 3 months compared with pretreatment. PROM dorsiflexion of ankle with knee flexion at 90° right was significantly higher after 3 months compared with pretreatment. PROM dorsiflexion of ankle with knee flexion at 90° left was significantly higher after 1.5 and 3 months compared with pretreatment (Table 5).

**Table 3. Passive range of joint motion (PROM) (abduction) in hips, mean±SD (number of patients)**

Period	with ext knee, right	with ext knee, left	with knee flex 90°, right	with knee flex 90°, left
Pretreatment	30.73±10.81 (41)	27.43±11.07 (41)	33.07±13.20 (39)	33.33±10.21 (39)
After 2 weeks	35±9.31 (39)	34.48±9.37** (39)	38.91±10.41* (37)	38.37±10.80* (37)
After 1.5 months	35±9.80 (40)	35.37±9.29*** (40)	39.1±11.69* (39)	39.35±10.883* (39)
After 3 months	35.41±11.17 (36)	35±10.95** (36)	40.42±13.30* (35)	38.77±11.81* (35)
After 5 months	34.83±12 (31)	33.87±12.69* (31)	39.33±10.56* (30)	39.16±11.67* (30)

\* $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$

**Table 4. Knee-popliteal angle unilateral (PAU) and popliteal angle bilateral (PAB), mean±SD (number of patients)**

Period	PAU, right	PAU left	PAB right	PAB left
Pretreatment	140±18.74 (41)	138.53±16.52 (41)	150.73±17.15 (41)	148.68±17.71 (41)
After 2 weeks	149.35±16.86* (39)	148.20±15.36** (39)	157.69±17.30 (39)	157.56±16.61* (39)
After 1.5 months	150.12±17.63* (40)	147.87±20.15* (40)	160.25±16.63* (40)	158.75±16.70* (40)
After 3 months	148.61±18.92* (36)	148.47±17.55* (36)	155.69±19.38 (36)	159.86±16.66** (36)
After 5 months	147.41±18.02 (31)	149.83±15.08** (31)	157.74±16.16 (31)	154.35±18.29 (31)

\* $p < 0.05$ , \*\* $p < 0.01$

**Table 5. Passive range of joint motion (PROM)- dorsiflexion of ankle, mean±SD (number of patients)**

Period	with ext knee, right	with ext knee, left	with knee flex 90°, right	with knee flex 90°, left
Pretreatment	93.29±14.34 (41)	91.82±15.56 (41)	102.80±19.17 (41)	101.21±19.51 (41)
After 2 weeks	97.43±14.27 (39)	99.1±13.41* (39)	106.79±14.30 (39)	108.20±12.74 (39)
After 1.5 months	96.50±16.10 (40)	97.25±15.84 (40)	109±14.37 (40)	109±12.91* (40)
After 3 months	98.75±16.36 (36)	99.16±13.91* (36)	111.25±13.16* (36)	110.41±13.05* (36)
After 5 months	98.06±15.63 (31)	96.93±14.06 (31)	110±13.16 (31)	110±13.10* (31)

\* $p < 0.05$

Table 6. Modified Ashworth Scale (MAS)-adductors, mean±SD (number of patients)

Period	with ext knee, right	with ext knee, left	with knee flex 90°, right	with knee flex 90°, left
Pretreatment	0.92±0.75 (41)	0.95±0.74 (41)	0.73±0.67 (41)	0.80±0.71 (41)
After 2 weeks	0.53±0.55** (39)	0.64±0.58* (39)	0.43±0.55* (39)	0.46±0.55* (39)
After 1.5 months	0.60±0.54* (40)	0.60±0.54* (40)	0.47±0.50 (40)	0.42±0.50** (40)
After 3 months	0.55±0.55* (36)	0.58±0.55* (36)	0.38±0.49* (36)	0.36±0.48** (36)
After 5 months	0.67±0.47 (31)	0.74±0.44 (31)	0.48±0.50 (31)	0.54±0.50 (31)

\* $p < 0.05$ , \*\* $p < 0.01$ 

Table 7. Modified Ashworth Scale (MAS)-hamstrings and plantar flexors of ankle, mean±SD (number of patients)

Period	Hamstrings, right	Hamstrings, left	Plantar flex. with ext knee, right	Plantar flex. with ext knee, left	Plantar flex. with knee flex 90°, right
Pretreatment	0.85±0.65 (41)	0.97±0.79 (41)	1±0.86 (41)	1.19±0.87 (41)	0.73±0.67 (41)
After 2 weeks	0.69±0.76 (39)	0.64±0.66* (39)	0.71±0.64 (39)	0.74±0.59 (39)	0.43±0.55 (39)
After 1.5 months	0.72±0.55 (40)	0.70±0.64 (40)	0.87±0.64 (40)	0.82±0.63 (40)	0.47±0.50 (40)
After 3 months	0.66±0.58 (36)	0.75±0.55 (36)	0.77±0.63 (36)	0.77±0.68 (36)	0.38±0.49 (36)
After 5 months	0.67±0.47 (31)	0.67±0.47 (31)	0.74±0.66 (31)	0.83±0.82 (31)	0.48±0.50 (31)

\* $p < 0.05$ 

Modified Ashworth Scale (MAS) of adductors- MAS values were significantly decreased two weeks, one and half and three months after the treatment, but mean values after five month were lower compared with baseline (Table 6).

Modified Ashworth Scale (MAS) of hamstrings and plantar flexors of ankle -after the treatment all mean values of MAS were lower compared with baseline values. MAS values of hamstrings and plantar flexors were not significantly decreased compared with pretreatment, except of left hamstrings after two weeks (Table 7).

Table 8. Goal Attainment Scale (GAS) after 5 months of treatment with BoNT-A

GAS	Number of patients	%
-2	0	0
-1	6	14.6
0	22	53.7
+1	8	19.5
+2	5	12.2
Total	41	100

Goal Attainment Scale (GAS) after 5 months of treatment with BoNT-A -approximately 85% of patients achieved the expecting therapeutic goals according to GAS after the treatment with BoNT-

A. Only 15 % didn't achieved expecting goals, but all patients with CP had improvement in individual habilitation treatment after the injection of BoNT-A (Table 8).

## Discussion

Our study evaluated the effect of BoNT-A injection and physiotherapy on motor function and spasticity in children with CP. After the injection of BoNT-A into the muscle, muscle weakness appears as a result of blocking the release of acetylcholine at the neuromuscular junction (3). The effect of toxin is reversible but it is useful to help children to learn control their movements and improve function (3,14).

In our study mean patient age was 5,5 years. It is believed that better results may be obtained in patients who are treated at younger ages. As children grow, the risk of fixed contractures and bony deformities increases. Also, we notice decreased of spasticity after the treatment with BoNT-A which allow better stretching of the agonist muscles, increases the range of motion of the joint and strengthens the antagonist muscles. Our results showed that injections of BoNT-A of the musc-

les of the lower extremities decreased muscle tone and increased range of joint motion which is resulted in improvement in patients motor function.

In some studies it is found a significant positive correlation between the child's age and degree of muscle tone at 18 month after the last session. It is noticed a differential effect of BoNT-A on children above and below age 7. The age effect may be because of a change in the child's problems from dynamic to a fixed deformity over time as contracture develop. Also, this correlation may be explained by nervous system plasticity and an ability to learn new functions, especially in young children (3). Younger children with moderate involvement appear to derive the greatest benefit from the use of BoNT-A (1). The recent 11-year follow-up indicates an association between immobility and hip contractures/dislocation rather than a relation between muscle tone and contracture development (15).

In our study spasticity wasn't too high at the beginning according to Ashworth scale, but passive range of joint motion showed initial contractures. The Modified Ashworth Scale lacks the support of convincing pediatric reliability studies. However, it has been found to be valid compared with other muscle-tone assessment methods and it is widely used clinical tool for assessing spasticity and muscle tone in children. Therefore, experienced physiotherapists with high interrater agreements performed the testing (7).

A common model for the development of contractures suggests that increased muscle tone shortens muscles, which leads to reduced growth of sarcomeres (7). The contracture progression involves a progressive decrease in serial sarcomere number (8). On the other side, the progressive stretching of the muscle, in addition to sarcomere growth, could increased collagen deposition and muscle stiffness, results in a reduced range of joint motion (16,17). The dissociation between the effects on muscle tone and ROM indicates that development of contractures is not coupled to increase muscle tone only, but might be caused by other mechanisms (7). Although the primary lesion of upper motor neuron leading to spasticity, there is no doubt that the peripheral musculature has become abnormal. The following alterations occur in spastic muscle: 1. Altered muscle fiber size and fiber type distribution, 2. Proliferation of

extracellular matrix material, 3. Increased stiffness of spastic muscle cell (9). Details of the structural changes that occur in spastic muscle, as well as mechanistic explanations for how these changes occur, are lacking.

Tedroff et al. (2009) in their study try to explain theory of contracture development, because contractures appear to continue developing despite the reduction in muscle tone (7). Obviously, contracture development is not solely attributable to increased muscle tone, but depends on processes that the BoNT-A injections do not affect favorably. Molecular changes (8,9) including deposition of collagen (18) have been described in spastic muscle and during contracture development.

Multilevel BoNT-A injections for the treatment of spasticity in CP have been widely accepted by many researchers for more than 15 years (19,20). They have been shown to achieve better results than single-level treatments in children with CP. In our study the injections were administered using multilevel approach at single injection session always when we have indication for this type of treatment. Our results shows that the improvement in the clinical parameters decreased after 5 month but not to the baseline. One of possible explanations could be multilevel treatment in high percent of all cases. Also, BoNT-A treatment has a long-term effect on motor function even though the effect on muscle tone had disappeared (14,21). The effect of BoNT-A appears to last longer in physically more active patients (3). Unlu et al. (2010) noticed in their study that muscle tone increased between the three and six month evaluation (2).

Peker et al. (2006) in their study noticed that most of treated patients had functional improvement according to the gross motor function classification system and did not change at 6 month (22). The improvement in the clinical parameters decreased after 6 month but not to the baseline. In our study, approximately 85% of patients achieved the expecting therapeutic goals according to GAS after the treatment with BoNT-A. Only 15 % didn't achieved expecting goals, but all patients with CP had improvement in individual habilitation treatment after the injection of BoNT-A.

There are several limitations to this study. One is the lack of control group. Instead, data were compared with baseline values obtained before the

first injection. This might mask an injection-induced effect, because children with CP experience a progressive decrease in ROM cannot be detected by comparisons with baseline values, only significant changes can be registered.

We believe that our results support the idea that younger children may receive more benefit from multilevel BoNT-A injections, intensive physiotherapy and appropriate orthotic management compared to older children. Younger children might have been able to maintain the functional gains because the motor pattern of very young children provides greater scope for better development and recovery. A younger child has greater potential than older child for increasing the plasticity of the central nervous system (4). BoNT-A injections should always be used as an adjunctive treatment to physiotherapy, occupational therapy and orthotic management. In combination with post-injection physiotherapy this treatment could provide long-term benefits.

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# Chronic and acute complications in diabetic patients in Canton Sarajevo

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## Abstract

**Introduction:** Diabetes mellitus (DM) is the most frequent metabolic disorder and is one of the most common endocrine diseases. Chronic complications of diabetes are caused by prolonged poorly regulated diabetes, the duration of diabetes, and other risk factors of atherosclerosis (obesity, hyperlipidemia, hypertension, smoking, lack of physical inactivity, blood hypercoagulability, immunological factors, inflammatory factors and genetic predisposition).

**Aim of the study:** Aim of this study was to determine the incidence of diabetic patients compared to nondiabetics in the Department of Emergency Medical Service. We have monitored the incidence of diabetic patients due to acute and chronic complications of diabetes, compared to nondiabetics and cardiovascular disease.

**Patients and methods:** We monitored the diabetic and nondiabetic patients over the period of two years based on the protocol of disease, the reasons for reporting to the Department of Emergency Medical Services, and sorted them by age, sex, cardiovascular disease, height, blood sugar level, blood pressure level and ECG findings, and verified the diabetics with late macroangiopathic complications. Results: in 2008. there was significant difference in the incidence of diabetic patients in the Department of Emergency Medical Services as compared to nondiabetics followed for all diagnoses, except for heart failure. In 2009. there was significant difference in the appearance of diabetic patients in Department of Emergency Medical Services compared to nondiabetics except for hypertension and heart failure.

**Conclusion:** This study demonstrated that diabetics are more likely to report due to the acutisation of late complications, as opposed to the acute complications of diabetes. Also, we showed

that diabetics often require medical check-up for cardiovascular disease compared to nondiabetics.

**Key words:** diabetic patients, non diabetic patients, late diabetic complications, acute diabetic complications

## Introduction

Complications of diabetes are divided into acute and late (chronic) complications. Acute complications include: a.) Diabetic ketoacidosis and coma, caused by a deficiency of insulin, increased concentrations of glucagon, decrease of peripheral glucose utilization, which leads to hyperglycemia and osmotic diuresis, dehydration and reduction of volume, and the activation process of ketogenesis. b.) Hypersomolar non-ketotic state and coma are the syndromes of severe dehydration, which occurs due to persistent hyperglycaemic diuresis in the state when the patient is unable to take sufficient fluids, c.) Lactic acidosis occurs as a result of increased production or decreased utilization of lactate associated with tissue hypoxemia in patients with reduced blood oxygenation in the respiratory disease, myocardial infarction or cerebrovascular insult, which affects respiratory center, d.) Hypoglycaemic crisis and coma are caused by the fall in blood glucose which is a result of the challenging dose of insulin, excessive physical activity, failure to comply with the recommended diet or omitting meals. (1). Late (chronic) complications are divided into: Microangiopathic: diabetic retinopathy, nephropathy, neuropathy, diabetic foot (microangiopathy and neuropathy) and Macroangiopathic: myocardial infarction, cerebrovascular disease, peripheral angiopathy. The emergence of macroangiopathic changes is caused by not only hyperglycaemia, but also by number of other factors, such as hypertension,

hyperlipidemia, obesity, smoking, physical inactivity, genetic predisposition, immunological factors and other diabetogenic factors: microalbuminuria, macroalbuminuria, increased serum creatinine, increased platelet function, insulin resistance. All of these risk factors of cardiovascular disease in diabetic patients lead to accelerated atherosclerosis. The most significant factor for microangiopathic changes is permanent hyperglycemia. Macrovascular complications are the biggest problem in treating diabetes, because they lead to mortality (fatal myocardial infarction, fatal cerebrovascular insult), in contrast to the microvascular complications that lead to disability (blindness, renal failure, diabetic foot and amputation of feet or lower leg). (2).

**Aim of the study:** The aim of our study was to determine the incidence of diabetes patients compared to nondiabetics coming to the Department of Emergency Medical Services, for acute coronary syndrome, cerebrovascular insult, hypertension, changes in the lower extremities, as well as for acute diabetic complications, ketoacidosis, hyperglycemia and hypoglycemia in the course of two years.

**Patients and methods:** Based on data from all protocols from 1. January 2008. to 31. December 2009., we have verified all patients who have reported to the Department of Emergency Medical Services for any reason. Patients were classified as diabetics and nondiabetics, and the reason for reporting to the Department of Emergency Medical Services due to acute complications of diabetes or due to the actualisation of late complications.

**Methodology:** The study was retrospective in character, because the data used was for 2008. and 2009. Descriptive, analytical methods, functional tests, blood tests were used in the study. Technique of the study is as follows:

1. Medical history data:
  - a) information about diabetes,
  - b) evidence of the existence of long term complications of diabetes (after myocardial infarction, cerebrovascular insult, hypertension, phlegmona or amputation of part of lower extremity),
  - c) a reason to report to the Department of Emergency Medical Services,
2. Measurement blood glucose,
3. Measurement of blood pressure by sphygmomanometer,

4. ECG recording by the ECG apparatus in patients with symptoms of acute coronary syndrome,
5. Examination of lower extremities in patients with amputated parts of limbs: a. inspection of the skin and b. palpation of the skin and arterial pulsations,
6. The first and second diagnosis were made on the basis of examination: Based on the first diagnosis, patients were classified as:
  - a) acute coronary syndrome (myocardial infarction, angina pectoris),
  - b) hypertension,
  - c) cerebrovascular ischemia (TIA and acute insult),
  - d.) cardiomyopathy,
  - e.) acute diabetic complications (hypoglycemia, diabetic ketoacidosis). On the basis of second diagnosis, the patients were classified as diabetics and nondiabetics.

### Results of research

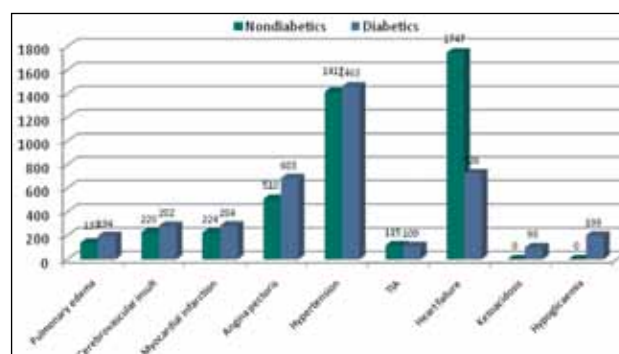


Figure 1. Reasons for the arrival of diabetics and nondiabetics in the central and field emergency medical service in 2008

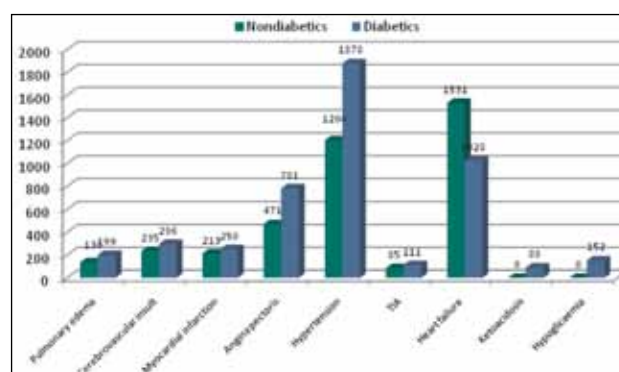


Figure 2. Reasons for the arrival of diabetics and nondiabetics in the central and field emergency medical service in 2009

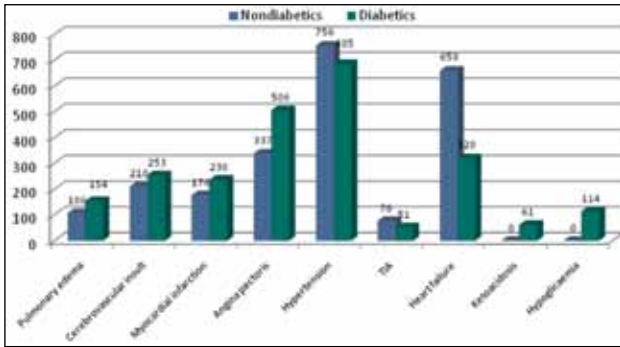


Figure 3. Reasons for the Emergency team to go to the field for non diabetics and diabetics in 2008

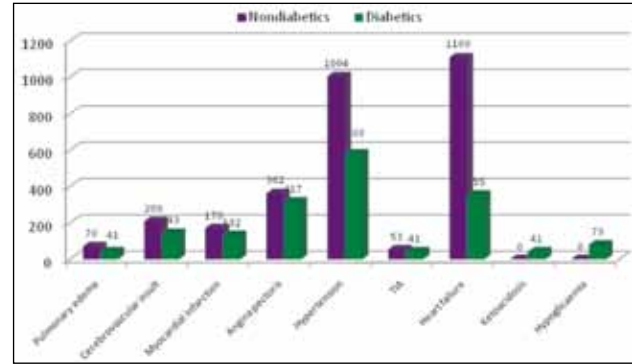


Figure 4. Reasons for the Emergency team to go to the field for non diabetics and diabetics in 2009

Table 1. Statistical significance for 2008. – ambulance

Reasons for arrival	DM total number for 2008.	%	Nondiabetics total number for 2008.	%	Diff	95% CI	Chi square	DF	Level of significance
Pulmonary edema	194	5,19	137	3,13	2,06	1,191%-2,955%	21,355	1	P<0,0001
Cerebrovascular insult	282	7,54	228	5,21	2,33	1,266%-3,415%	18,204	1	P<0,0001
Myocardial infarction	284	7,59	224	5,12	2,47	1,407%-3,554%	20,560	1	P<0,0001
Angina pectoris	683	18,26	510	11,65	6,61	5,054%-8,177%	69,781	1	P<0,0001
Hypertension	1463	39,11	1417	32,37	6,74	4,649%-8,827%	39,740	1	P<0,0001
TIA	109	2,91	115	2,63	0,28	-0,434%-1,012%	0,49	1	P=0,4840
Heart failure	726	19,41	1747	39,90	20,49	18,55%-22,402%	398,87	1	P<0,0001
TOTAL	3741	100	4378	100,0					

Table 2. Statistical significance for 2009. – ambulance

Reasons for arrival	DM total number for 2009.	%	Nondiabetics total number for 2009.	%	Diff	95% CI	Chi square	DF	Level of significance
Pulmonary edema	199	4,38	136	3,51	0,87	0,031%-1,7%	3,918	1	P<0,0478
Cerebrovascular insult	296	6,52	235	6,06	0,46	-0,588%-1,496%	0,673	1	P<0,4120
Myocardial infarction	250	5,50	213	5,50	0,00	-0,97%-0,99%	0,002	1	P=0,9617
Angina pectoris	781	17,19	471	12,15	5,04	3,53%-6,539%	41,566	1	P<0,0001
Hypertension	1878	41,34	1204	31,07	10,27	8,22%-12,304%	94,600	1	P<0,0001
TIA	111	2,44	85	2,19	0,25	-0,405%-0,893%	0,471	1	P<0,4926
Heart failure	1028	22,63	1531	39,51	16,88	14,912%-18,835%	280,824	1	P<0,0001
TOTAL	4543	100	3875	100,0					

Table 3. Statistical significance for 2008. – field

Reasons for arrival	DM total number for 2008.	%	Nondiabetics total number for 2008.	%	Diff	95% CI	Chi square	DF	Level of significance
Pulmonary edema	154	6,98	106	4,57	2,41	1,053%-3,79%	11,686	1	P<0,0006
Cerebrovascular insult	253	11,47	210	9,05	2,42	0,652%-4,199%	6,949	1	P<0,0084
Myocardial infarction	236	10,70	176	7,59	3,11	1,432%-4,803%	12,839	1	P<0,0003
Angina pectoris	506	22,95	337	14,53	8,42	6,152%-10,686%	52,311	1	P<0,0001
Hypertension	685	31,07	756	32,59	1,52	1,196%-4,23%	1,134	1	P<0,2868
TIA	51	2,31	76	3,28	0,97	0,003%-1,945%	3,551	1	P=0,0595
Heart failure	320	14,51	659	28,41	13,9	11,538%-16,241%	128,008	1	P<0,0001
TOTAL	2205	100,00	2320	100,0					

Table 4. Statistical significance for 2009. – field

Reasons for arrival	DM total number for 2009.	%	Nondiabetics total number for 2009.	%	Diff	95% CI	Chi square	DF	Level of significance
Pulmonary edema	41	2,55	70	2,35	0,20	-0,701%-1,215%	0,102	1	P<0,7490
Cerebrovascular insult	143	8,89	209	7,02	1,87	0,25%-3,592%	4,893	1	P<0,0270
Myocardial infarction	132	8,20	170	5,71	2,49	0,96%-4,129%	10,129	1	P<0,0015
Angina pectoris	317	19,70	362	12,16	7,54	5,305%-9,848%	46,481	1	P<0,0001
Hypertension	580	36,05	1004	33,73	2,32	-0,559%-5,229%	2,385	1	P<0,1225
TIA	41	2,55	53	1,78	0,77	-0,087%-1,753%	2,712	1	P<0,0996
Heart failure	355	22,06	1109	37,25	15,19	12,483%-17,818%	110,20	1	p<0,0001
TOTAL	1609	100,0	2977	100,0					

Table 5. Data for both years, the ambulance and field, diabetics and nondiabetics

Reasons for arrival	DM total number for two years	%	Nondiabetics total number for two years	%	Diff	95% CI	Chi square	DF	Level of significance
Pulmonary edema	588	4,86	449	3,31	1,55	1,063-2,037	39,199	1	P<0,0001
Cerebrovascular insult	974	8,05	882	6,51	1,54	0,902-2,178	22,352	1	P<0,0001
Myocardial infarction	902	7,46	783	5,78	1,68	1,069-2,291	29,105	1	P<0,0001
Angina pectoris	2287	18,90	1680	12,40	6,50	5,61-7,39	206,049	1	P<0,0001
Hypertension	4606	38,07	4381	32,33	5,74	4,57-6,91	92,266	1	P<0,0001
TIA	312	2,58	329	2,43	0,15	-0,233-0,533	0,53	1	P=0,4667
Heart failure	2429	20,08	5046	37,24	17,16	16,077-18,243	910,535	1	P<0,0001
TOTAL	12098	100	13550	100					

### Statistical significance of results

In Table 5., all results are presented relating to both study years (2008. and 2009.) for field and the ambulance. All parameters except TIA / no statistical significance for both groups / and heart failure / more nondiabetics / recorded a statistically significant difference between diabetics and nondiabetics, in favour of diabetics.

### Discussion

In the study we did in Sarajevo Canton area in 2008. and 2009. year, we found that in the Department of Emergency Medical Services Canton Sarajevo, diabetics report more frequently because of late complications, macroangiopathic changes (acute coronary syndrome, cerebrovascular insult, TIA, heart failure, hypertension, changes in the lower extremities) compared to nondiabetics, and in relation to acute complications, hypoglycemia and ketoacidosis.

During the two years of monitoring of all services in the Department of Emergency Medical Services Canton Sarajevo, we singled out medical interventions that are related to: pulmonary edema, myocardial infarction, angina pectoris, cerebrovascular insult, transient ischemic attacks, hypertension, cardiomyopathy, and medical examinations related to acute complications of diabetes- hypoglycemia and ketoacidosis. We separated the above mentioned diagnoses into interventions in the central ambulance and interventions in the field, conducted in a home visit. Patients were classified as diabetics and nondiabetics.

Based on the number of inhabitants in the Canton of Sarajevo in 2008. and 2009., and the number of diabetic patients registered in Canton in 2008. and 2009. it is statistically proven, that the number of medical examinations of diabetics is more frequent due to the acutisation of macroangiopathic late complications of diabetes than to the acute complications of diabetes - ketoacidosis and hypoglycemia, and also occur more frequently compared to nondiabetics.

When comparing the total population, and the number and percentage of diabetics: 2.43% in

2008. and 2.58% in 2009., the significance is even greater (3).

We note that the Department of Emergency Medical Services Canton Sarajevo, in ambulances, and on the field, examined the same patients several times due to the same or different diagnosis, so that the number of medical interventions is not an indicator of the number of patients.

In 1996., the results of the MICRO-HOPE study as well as the HOPE substudy were published, that showed the high risk of diabetes in cardiovascular death and chronic renal disease, where it was concluded that microalbuminuria, a marker of atherosclerosis, from 20-200 mg/min is a predictor of cardiovascular death and chronic renal disease, but also that ACE inhibitors can improve microalbuminuria (4).

In 2003., the results of PREVEND IT study were published, that show that ACE inhibitor treatment of patients with microalbuminuria without hypertension and hypercholesterolemia reduces cardiovascular and renal events by 44%, followed over 4 year period (5).

Logstrup Pulsen and associates published in 2003. the results of the risk of mortality in Type 1 diabetes. 272 diabetic patients were monitored during 25 year-period, who in 1977. were older than 15 years of age, with duration of diabetes over 5 years, with albuminuria, hypertension and late complications. They concluded that long-term albuminuria, hypertension, poor glycemic control and smoking are potentially modifying factors that can change, and are an important predictor of mortality in Type 1 Diabetes (6).

UK Prospective Diabetes Study Group published in 1998. the results of UKPDS study, which monitored and treated blood pressure, and proved that good control of blood pressure reduces the microvascular and macrovascular complications of diabetes. Reduction of risk due to good control of blood pressure decreases cerebrovascular insult by 44%, microvascular complications by 37%, risk of diabetes as an endpoint by 24%, and the risk of death due to diabetes by 32%. They had 3 groups of diabetics with different values of blood pressure and treated them with ACE inhibitors. Diabetics who had lower values of diastolic blood pressure by 60%, also had reduced cardiovascular death, and major cardiovascular events were reduced by 51%. (7).

EDIC group (Epidemiology of diabetes interventions and complications) in 2003. published the results of monitoring the patients from the DCCT study, 7-9 years after the completion in 28 Clinics, wanting to show the progression of atherosclerosis in type 1 diabetes. CT of the coronary arteries was made in 1150 patients, aged 43 yr., with diabetes duration of 21 years, of whom 52% were male and 48% female. They looked at the calcification of the coronary arteries and graded them into three stages, monitoring HbA1C, hypertension treated with antihypertensive medications, hyperlipidemia, cigarette smoking. The worst stage of calcification in coronary arteries was in diabetics with hypertension, hyperlipidemia, smokers, and those that had poor glycoregulation.(8).

In the Framingham study, which lasted 35 years and monitored 5209 patients, aged 30-62 yr., which have already had identified risk factors for developing coronary artery disease, showed that diabetics are two times more likely to suffer from cardiovascular disease compared to nondiabetics. (9).

In the MRFIT study (Multiple Risk Factor Intervention) during the period of 12 years, 5000 men with diabetes Type 2 were monitored, who apart from diabetes, had another risk factor, hypertension or hyperlipidemia or smoking, and came to the conclusion that those with diabetes with one risk factor had three times greater mortality compared to the nondiabetic group with multiple risk factors. (10).

Haffner and associates a study on 1373 nondiabetic patients and 1059 diabetic patients, monitoring them for seven years. They declared that diabetics have a much higher risk for myocardial infarction, compared to nondiabetics (11).

CHD Equivalent prospective study, which lasted for eighteen years in Finland, where the risk of coronary heart disease was followed in diabetic and nondiabetic patients, had proved that diabetes is a major risk for coronary disease, particularly among women (12).

## Conclusions

Based on our research, we reached the following conclusions:

1. There is an increase in the total number of medical interventions in the ambulance and on the field in 2009. compared to 2008.
2. There is an increase in the number of medical interventions related to "the target diagnoses": pulmonary edema, myocardial infarction, cerebrovascular insult, hypertension, angina pectoris, TIA, in ambulances and on the ground in 2009. compared to 2008.
3. The frequency of medical interventions for the late complications of diabetes is higher than that due to acute complications.
4. Pulmonary edema, angina pectoris, myocardial infarction, cerebrovascular insult, TIA, hypertension were more common in diabetics than in nondiabetics, and heart failure was more common diagnosis in nondiabetics.

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# Analysis of risk factors in patients treated by stroke in Clinical Hospital Mostar

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## Abstract

**Objective:** To examine risk factors in patients diagnosed with stroke and the association of these factors with the diagnosis, complications and outcome.

**Subjects and methods:** The study was structured as a study intersection. The sample includes 347 patients with stroke hospitalized in the period from 01 January 2006 till 31 December 2006 at the Neurology Clinic, Clinical Hospital Mostar.

**Results:** The mean age of patients was  $73 \pm 12$ . Cerebrovascular insult (CVI) is more common in patients older than 65. There was no significant difference in the representation of both sexes. Hypertension is the most common risk factor ( $P < 0.001$ ). Affiliation CVI with diabetes was not found ( $P = 0.485$ ). Most patients have elevated lipid concentration in serum ( $P < 0.001$ ). Most patients are smokers who have not consumed alcohol ( $P < 0.001$ ). Form of ischemic stroke was more common ( $P < 0.001$ ). CVI is more common in people with a positive family history ( $P < 0.001$ ). The most common complication was urinary tract infections ( $P < 0.001$ ).

There was no association of certain risk factors with complications ( $P = 0.218$ ) or outcome ( $P > 0.984$ ). The most important risk factor for ischemic stroke and hemorrhagic type is high blood pressure ( $P < 0.001$ ).

**Conclusion:** The risk for stroke is significantly increased with age. A large number of patients have multiple risk factors simultaneously, and most were older age, high blood pressure, smoking and family history.

**Key words:** stroke, ischemic stroke, urinary tract infections, cardiovascular risk factors.

## Introduction

According to World Health Organisation (WHO), cerebrovascular accident (CVA), stroke or stroke manifest abrupt development of clinical signs of focal or global disturbance of cerebral function with symptoms lasting 24 hours or longer and lead to death, with no other apparent cause other than vascular damage (1 - 3). According to WHO estimates, from stroke die 5.54 million people worldwide annually (4). In Europe, every tenth German above the 50 years of age die from stroke. Mortality increases with age and stroke in the seventh decade of life, the second most common cause of death. Mortality in hemorrhagic stroke is greatest in the first three days and by the end of the first month when is expected 80% of patient to dies, and ischemic stroke was 15% (5-8). It is noticed the increasing incidence in younger age groups - today is 50% of patients with CVI under the age of 60 years (2).

CVI, the coronary heart disease and cancer are the most common single causes of death in developed countries worldwide as well as in our country. In Croatia, the year 15 000 new cases of stroke are noticed annually, in the United States 700 000 new cases; every minute someone has stroke (9-11). The rate of death from stroke at the age above 55 is rapidly increasing, and most survivors suffer significant disability. In our country tendency of developing morbidity and mortality from stroke are increasing, while in developed countries it is reduced (9,13). CVI is divided into ischemic and hemorrhagic stroke (incidence ratio is 83%: 17%) (11). Ischemic stroke may occur due to thrombosis, embolism, or hemodynamic disturbance in the extracranial or intracranial blood vein.

Atherothrombosis infarction caused by atherosclerotic plaque that narrows or closes the blood vessel or thrombus superimposed on plaque. In clinical practice has been accepted classification

that takes into account the pathological-anatomical and pathophysiological parameters and different ischemic and hemorrhagic stroke (34)

1. Hemorrhagic stroke:
  - a) Intracerebral haemorrhage
  - b) subarachnoid hemorrhage (SAH)
2. Stroke:
  - a) thrombotic
  - b) embolic
  - c) hemodynamic (34).

Division based on disease stage so called clinical images of patients:

- First TIA (transient ischemic attack) - transient symptoms that last longer than 60 minutes (14)
- Second RIND (reversible ischemic neurological deficit) - characterized by symptoms lasting 24-72 hours, with no lasting brain damage (15)

### How to diagnose?

By Computed tomography (CT), cerebral infarction is shown as an area of reduced tissue density in the supply area of one or more arteries. Signs of early ischemia is usually determined 12-24 hours after the insult (5). Magnetic resonance imaging (MRI) is useful in the differential diagnosis of spontaneous hemorrhage and hemorrhage occurred as a result of bleeding from an aneurysm or vascular malformation, because the blood that flows differs from the stationary blood hematoma. Thus reducing the need for angiography (12).

Lumbar puncture and CSF analysis are needed in doubtful CT findings in patients with vasculitis, subarachnoid hemorrhage in distinguishing between infection and diagnosis of subarachnoid hemorrhage, in a case of negative CT findings (17). All the patients with CVI needs to record an ECG because of the high incidence of heart disease. Stroke and acute myocardial infarction can occur simultaneously. Hemispherical disrhythmia accident can cause and heart failure, and cardiac rhythm disturbances are a common cause of embolic stroke (18). The diagnosis of cerebral circulation is Doppler sonography useful method.

Extracranial and transcranial color Doppler ultrasonography allow rapid assessment of cere-

brovascular status in patients and display a variety of pathological conditions in blood vessels. New generation of ultrasonic detection devices allow embolic signal and Identification of patients with increased risk of recurrence or stroke (19).

### Treatment

Meta analysis of ten o'clock randomized study showed that the mortality rate in the first four months after the stroke was reduced by 28% in patients who were treated in specialized units (U.S. stroke units) and the favorable effect persisted after 12 months (20). It is necessary to ensure adequate oxygenation to maintain metabolic penumbra using 2-4 L of oxygen (2). Specific treatment is thrombolysis for recanalization attempt the circulation of the affected territories, and preservation of temporarily damaged neurons in the penumbra zone (2). Today it is used as a thrombolytic agent recombinant tissue plasminogen activator (r-TPA) after previous angiography

Local intraarterial application of trombolitic findings reduces the risk of systemic bleeding and allows opening of the blocked blood vessels in 67% of cases in the application of prourokinase (21-22). Acetyl-salicylic acid (aspirin) may prevent the distal and proximal propagation of arterial thromb in microcirculation and reembolisation because it prevents platelet aggregation (23-27). 100-300 mg of aspirin administered within 48 hours minimum reduces mortality and recurrent stroke (2).

In the case of atypical intraparenhimal hematoma or subarachnoid hemorrhage treatment include cerebral panangiography and neurosurgical care possible vascular or aneurysm formation (28-31).

### Risk Factors

Two groups of risk factors, of which first can not be affected while the other variable (3). Fixed factors (U.S. non-modifiable): older age, gender, race, heritage, diabetes and previous stroke and / or previous transient ischemic attacks. Variable factors (U.S. modifiable): smoking, alcohol, adiposity, physical inactivity, unhealthy diet, stress, oral contraceptives, hypertension, dyslipidemia and atrial fibrillation

(35). At the state level is difficult to conduct research on risk factors, because we do not know population characteristics (number, structure), for past events, and not conducted a census since 1991 (40).

### Methods

At the Neurology Clinic, Clinical Hospital Mostar (Mostar KB) we conducted a retrospective study on a sample of patients suffering from stroke who were treated in the period from 1 January to 31 December, 2006. The research was structured as a study intersection.

In research were involved subjects of all ages diagnosed with cerebrovascular accident in the period from 01 January 2006 till 31 December 2006. at the Neurology Clinic, Mostar. Data were collected and processed on the basis of insight into the history of the disease found in the archives of the Department. The sample included a total of 347 patients. Stroke was analyzed as ischemic or hemorrhagic type, and whether or relapse occurs first. Input indicators included age, sex, diabetes, blood pressure, total cholesterol, triglycerides, smoking, alcohol, family history, type of stroke (ischemic / hemorrhagic), appearing for the first time or in the form of recurrence. In history there were no data on body weight and obesity as they were not analyzed as risk factor. New indicator of family history is taken. Output indicators included diagnosis, complications and outcome (recovered, died, moved).

To display the mean and dispersion measures using the median and interquartile range because of the asymmetrical distribution of continuous data. For comparison of nominal and ordinal variables used  $\chi^2$  test, and the lack of the expected frequencies Fisher's exact test.

### Results

The average age of patients was  $73 \pm 12$ . CVI was more common in patientes older than 65. There was no significant difference in the representation of both sexes. Hypertension is the most common risk factor ( $P < 0.001$ ). Affiliation CVI with diabetes was not found ( $P = 0.485$ ). Most patients have elevated lipid concentration in serum ( $P < 0.001$ ).

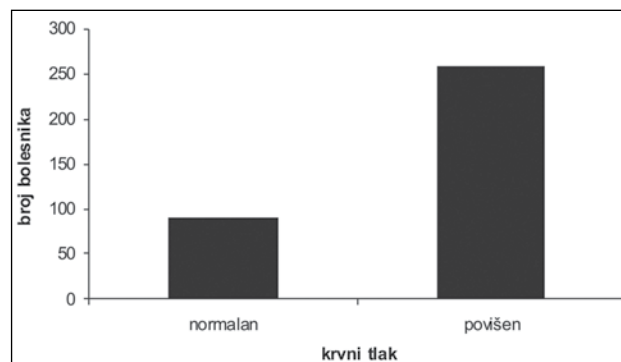


Figure 1. Blood pressure in patients with treated stroke

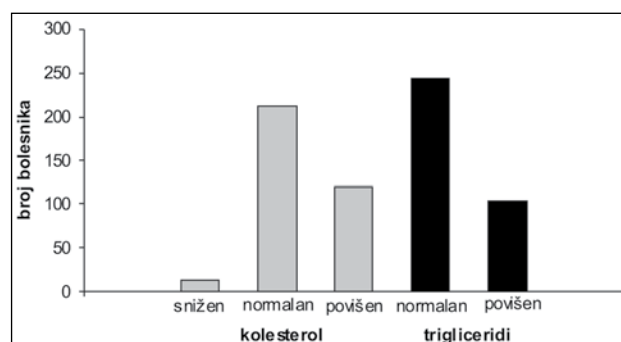


Figure 2. Cholesterol and triglycerides in patients with stroke

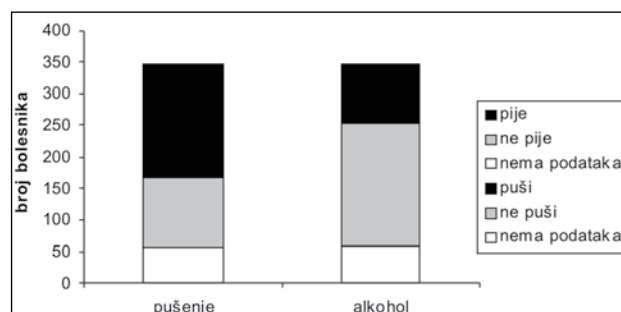


Figure 3. Smoking and alcohol consumption in patients with treated stroke

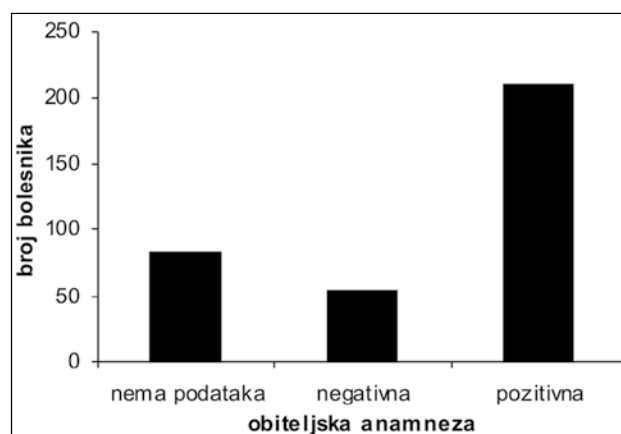


Figure 4. Family history in patients with stroke

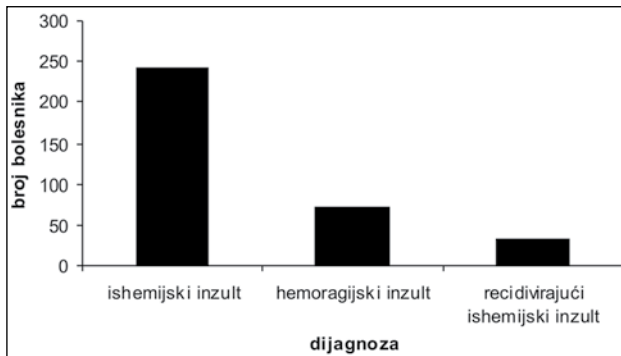


Figure 5. Diagnosis of patients with stroke

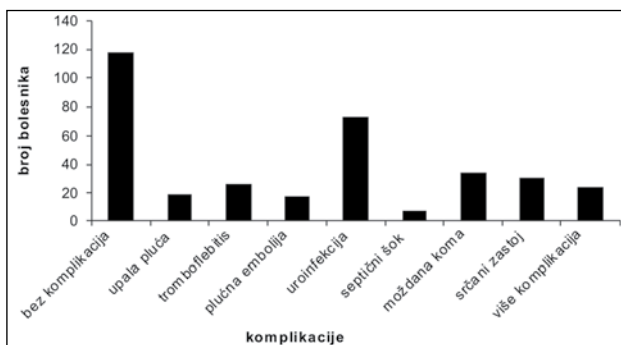


Figure 6. Complications of the disease in patients with stroke

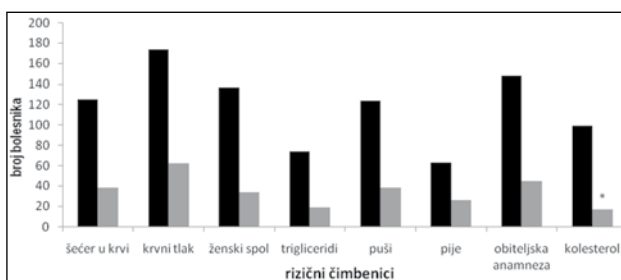


Figure 7. Risk Factors for Ischemic and hemorrhagic cerebral stroke

## Discussion

In the contemporary world cerebrovascular diseases are the third leading cause of death, behind cardiovascular disease and cancer, and they rank among the biggest health problems. The fact is that the CVI could significantly prevent the removal of major risk factors. A significant reduction in the incidence of stroke by 40% was reported in a large population study Oxfordshire Community Stroke Project conducted in the UK over the past 20 years (35). The study results showed that the application of preventive measures significantly reduced premorbid risk factors, reducing serum

cholesterol and high blood pressure and reducing the number of smokers with the application of preventive antiplatelet therapy and lipid-lowering drugs and blood pressure. High blood pressure, the most important and most common risk factor, set times increases the risk of stroke (12)

In recent years the population of Bosnia and Herzegovina was highly exposed to risks that could affect the chronic non-communicable diseases, especially cardiovascular. (41) In our study, elevated blood pressure had 74.4% patients with CVI, which corroborated the results of published studies. In the study, Systolic Hypertension in the Elderly Program (SHEP) has shown that treating isolated systolic hypertension in persons older than 60 reduces the incidence of stroke by 36%. (30). Aging increases the risk of stroke. According to the results of our study age is predisposing factor for stroke, which is corresponding to data shown in the literature (5-8).

Dyer and colleagues reported, in the epidemiological study conducted in West County in the period 1998 - 2002. that the greatest mortality of stroke in patients older than 65 years, was regardless of gender (36,37). Heredity is one of the leading risk factors for the 60.4% indicating the importance of genetic predisposition. Similar results showing a meta analysis of 76 research studies on various genes responsible for the development of ischemic stroke in Chinese population (39). Elevated levels of cholesterol were significantly found in 34.9% of cases and triglycerides in 29.7% of cases.

The results are consistent with the results of the U.S. cohort study which has been shown that elevated levels of serum lipids in asymptomatic patients increases the risk of ischemic stroke (38). Meta-analysis of 32 studies showed that smoking increases the risk of stroke for 50% and the risk for stroke increases with the number of cigarettes smoked (27). In our sample the most common type of stroke was ischemic stroke in 69.7% cases, which corresponds to data from the literature (11)

Lethal outcome of stroke is often caused by complications of which are usually deep venous thrombosis and pulmonary embolism, bronchopneumonia, urinary infection, septicemia, aspiration, cardiac arrhythmias and sudden death. Our results showed that 34% of patients had no complications and these complications are the most common urinary tract infections (21%).

## Conclusion

There is no significant difference among patients with CVI between the percentage of diabetics and nondiabetics ( $P = 0.485$ ). High blood pressure often presented a risk factor for stroke in our patients ( $P < 0.001$ ). In patients with stroke a significant increase of cholesterol and triglycerides has been found ( $P < 0.001$ ). Stroke was significantly more common in people with a positive family history ( $P < 0.001$ ). Significantly more often in the form of ischemic stroke ( $P < 0.001$ ). The most common complication in stroke patients is urinary tract infections ( $P < 0.001$ ).

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# Structure of the ontogeny of the morphological indicators of boy aged from 11 to 14

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## Abstract

The paper presents an insight into the structure of the ontogenetic morphological indicators of primary school children. Results of conducted research are related to children aged 11-14 years. The sample of respondents is 333 by year of birth, meaning total number of 1332 boys. The main problem of the research was identification of the latent structure, ontogenetic morphological indicators of primary school age boys. The aim of the research was to identify and define the latent structures of morphological ontogenetic indicators for primary school pupils.

A set of ten variables that reflect the specific morphological characteristics in the best way, has been used in the research. To determine the structure of ontogenetic morphological indicators in boys aged 11-14 years, we used factor analysis. By applying Bartlett test the possibility of being subjected to sets of morphological variables of any type of factorization has been tested. The results confirmed that the matrix of variables applied in this study may undergo the factorization. Obtained results show that sig. on the .01 level. Based on the calculated characteristic equation using the Guttman-Kaiser criteria, we obtained the characteristic roots for generations. Characteristically roots tell the explained joint variac. Inspecting the table we can conclude that the boy isolated components of morphological features and characteristic roots, which explain the high degree of common variance. With children of eleven and fourteen we have two isolated factors out of a possible ten, and with twelve and thirteen years old children three factors has been isolated. Numbers

of significant factors are also determined by Cattell screening test. Information about the cause - effect relationships of factors and variables we obtained through the complex matrix or matrices of factor patterns that contain the value of the parallel projection of the coordinates of a vector of variables on factors. Matrix assembly is of the utmost importance when interpreting isolated latent dimensions, and in this analysis we interpreted them out for these reasons. The analysis of the tables that determine the matrix assembly in boys shows voluminous factors, subcutaneous fat, growth and development and longitudinal dimensionality.

**Key words:** ontogeny, morphology, factor, boys

## Introduction

Morphological characteristics present the most obvious area in the bio-psycho-sociological status of the human population. Morphology is defined by a set of characteristics such as constitution, body composition, structure, or a set as organized and relatively constant characteristics in the mutual relationship. Period of development of the child from 11-14 years we call the period of sexual maturation.

If we look at the period with respect to the phase of schooling this age is in, we can call it the period of primary school age children that belong to the later grades of elementary school, from class V to VIII. Differences in the developmental characteristics of boys and girls in this period are more pronounced compared to previous periods of development. The increase in height, which in the previous period was slower and more evenly,

it is now intense. Characteristic of this period of growth and development is that it leads to more intensive growth of the extremities so that the changing relationship between the head - torso to the lower extremities is in favor of the lower extremities. With boys the population growth ranges between 13 and 15.5 cm. Increment of body mass is proportional to the increment of body height (1). Muscle development undergoes rapid development and the diameter of muscle fibers increases. Musculature represents 32.6% of total body weight. Particularly intensive is the development of back muscles and upper limbs (2).

The development is a continuous process that occurs with conception and takes place at a settled pace until death. Human development does not take place equally, but in phases of rapid progress interrupted by periods of inaction. Process of the human development takes place in cefalocaudal direction, head movement precede to the hand movements, and those precede leg movements. Development of limbs occurs in the proximodistal direction: willing to arm and leg movements, preceded by voluntary movements of the wrists, fingers, feet and toes. Onward, the development takes place from general to specific.

### **Aim of the research**

Aim of the research shows the definition of the latent structure of morphological traits in pupils of primary age children. The aim of the research shows a way verifying the results achieved by applying the scientific method, critical questioning and correcting any eventual weaknesses.

### **Method**

By applying the scientific method chosen in this study, the active task were represented by activities such as sampling of research, techniques and instruments in the process of data collection, techniques and procedures for data processing, design of research results and its presentation.

These activities were performed using the following methods: in the process of selecting and defining the problem, studying the sources, the

project design, sample selection and testing instruments, method of theoretical analysis has been used. The documents study and survey research methods, in the process of collecting empirical material we used survey research method and methods of documentation study. When we collected the relevant material we performed a statistical analysis of data, where we used analysis and synthesis, abstraction and generalization, in order to establish the facts, formulate laws and create a possible theory, in the process of verification of research results, we used methods of theoretical analysis and survey method.

The study was carried out in primary schools of the Herzegovina-Neretva Canton. Number of respondents by age is 333 for each year. Meaning 1332 boys aged 11-14. In selecting variables, we used variables that are appropriate to the age category, defined problems and research objectives. The variables selected in this study hypothetical cover a space of morphological characteristics (10 variables). Among measured are the anthropometrical characteristics that reflect in the best possible way the specific morphological characteristics, where we followed recommendations of the International Biological Program (IBP) and within it selected the most relevant measures for our research.

### **Longitudinal dimensionality of the skeleton**

- body height-ATVIS
- Length of the leg-ADNOG
- arm length-ADRUK

### **Weight and volume**

- volume of upper arm-AONL
- the middle volume of the thorax-AOPK
- the scope of leg-AOPK
- body weight-ATTEZ

### **Skin folds of the body**

- upper arm skin fold-AKNN
- skin fold of the back AKNL
- abdominal skin fold-AKNT

Basic methods for processing the results were determined by characteristics and size of the sample, just as the set aim of the research.

For the analysis of data we used statistical program SPSS 15.0. Determination of the structure of



the ontogenetic morphological indicators treated in this study were subjected to the procedure of factor analysis, by the component model of factor analysis, according to Harold Hotteling (1993). For Hotteling's model it is characteristic that from the set of manifest variables, linearly independent components are determined and which are based on the unreduced correlation matrix. The number of significant factors is determined by Guttman – Kaiser criterion, and system of orthogonal principal components has been transformed into normalized varimax orthogonal solution. According to the GK criterion, a significant number of components is determined by their variance, or through the eigenvalues of correlation matrices. Significant are considered those components where the characteristic values are equal or greater than 1 (one).

## Results and discussion

Applying the Bartlett test, the possibility of subjecting this set of morphological variables to any kind of sample, as well as the set of objectives has

been tested. Results in Table 1, confirms that this data matrix can be subjected to factorization. The results show that the sig. is on the level of .01.

Based on the calculated characteristic equation (Table 2) using the Guttman-Kaiser criteria, we obtained the characteristic roots by age, from 11 to 14 years old. Characteristic roots tell us the total explained common variance. With the 11 years old two characteristic roots isolated, which explains 83.05% of the common variance. From the above it can be concluded that this is a high proportion of common variability explained. Individual contributions to explaining the common variance (% of Variance) carries the first latent dimension of 62.29%. For the second latent dimension of 20.76% of the explained common variability. With the twelve years old children three characteristic roots were isolated, and which carry 92.59% of explained common variability. The first principal component carries a 59.04% of explained common variability, the second 22.33% and the third 11.21% of the explained variables. For boys aged 13 three characteristic roots, that carry the total 90.48 of the explained variables, isolated. First principal component carries

Table 1. KMO and Bartlett's Test – boys 11-14 years

		11 yrs.	12 yrs.	13 yrs.	14 yrs.
Kaiser-Meyer-Olkin Measure of Sampling Adequacy.		,883	,860	,833	,849
Bartlett's Test of Sphericity	Approx. Chi-Square	4215,496	4499,865	3886,011	2901,433
	Df	45	45	45	45
	Sig.	,000	,000	,000	,000

Table 2. Isolated components of morphological characteristics with boys aged 11-14

Age	Component	Initial Eigenvalues			Extraction Sums of Squared Loadings		
		Total	% of Variance	Cumulative %	Total	% of Variance	Cumulative %
11 god.	1	6,229	62,292	62,292	6,229	62,292	62,292
	2	2,076	20,761	83,053	2,076	20,761	83,053
Age							
12 god.	1	5,905	59,048	59,048	5,905	59,048	59,048
	2	2,233	22,333	81,381	2,233	22,333	81,381
	3	1,121	11,211	92,592	1,121	11,211	92,592
Age							
13 god.	1	5,254	52,536	52,536	5,254	52,536	52,536
	2	2,500	24,999	77,535	2,500	24,999	77,535
	3	1,295	12,946	90,481	1,295	12,946	90,481
Age							
14 god.	1	5,030	50,297	50,297	5,030	50,297	50,297
	2	2,561	25,613	75,910	2,561	25,613	75,910

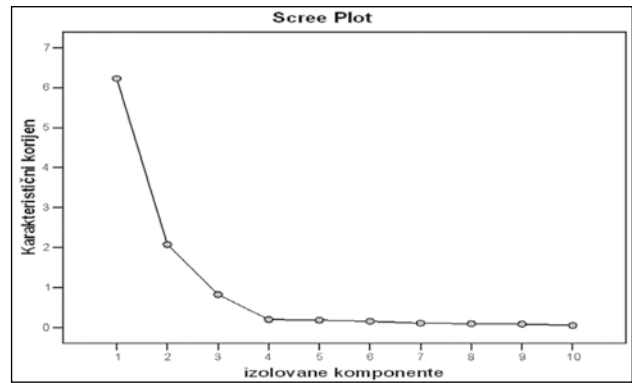
a 52.53% common variance, the second characteristic root has 24.99% of the explained variables and the third characteristic root has 12.94% of common variance. With the fourteen years old two characteristic roots have isolated, which have 75.91% of the explained variables. The first component defects 50.29% of the common variance and the second 25.61 %.

The number of significant factors (morphological indicators) we determined using the Cattell scree test, which is shown Graph 1 - Scree Plot. The ordinate show the size of the characteristic roots of the equation matrix of inter correlation, and on the X-axis are the numbers of characteristic vectors and equation.

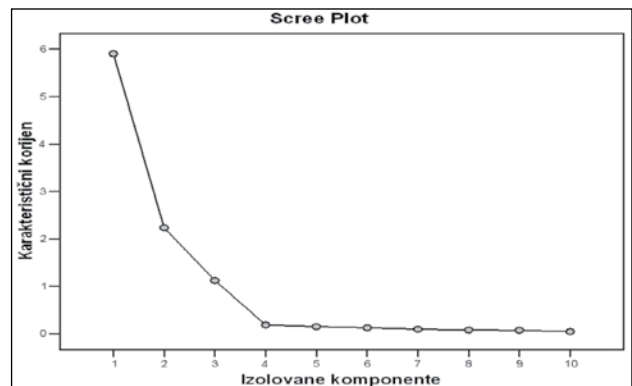
As it is known that number is equal to the number of manifest variables and vectors are of different linear combinations of all these variables. In Graph 1 seen that in the second and third characteristic roots, where the point of inflection in the obtained curve, a monotone decreasing values of characteristic roots occurs, what indicates that they are not relevant for this analysis. Based on that, we retained characteristic roots whose value exceeds 1, as indicators that it is a about significant morphological factors.

Matrix circuit (Table 3) or matrix of factor models contains the values of parallel projection of coordinates of a vector of variables on factors. Matrix circuit gives us information about the cause - effect relationship of factors and manifest variables. Matrix circuit is of the utmost importance when interpreting the isolated latent dimensions, and in this analysis out for these reasons we did interpret them. With the 11 years old the first general factor can be called as a factor of volume (puffiness) and subcutaneous adipose tissue.

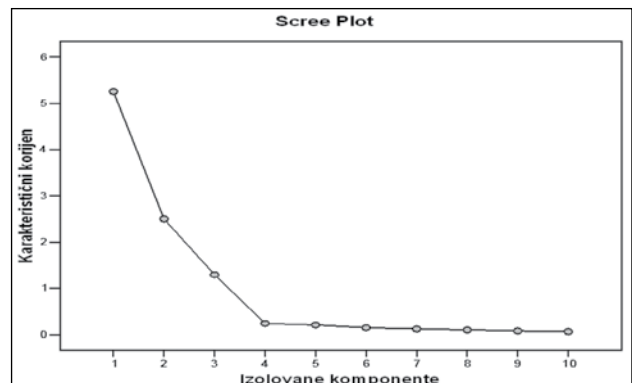
Another major component of the fifth-grade boys indicates specificity in relation to the anthropometric characteristics of the body height. This variable as variables for the assessment of the leg and arm length have the highest correlation with the other main component in boys and can be defined as a pure factor of longitudinal skeleton dimensionality, this factor can be defined as the General growth factor.



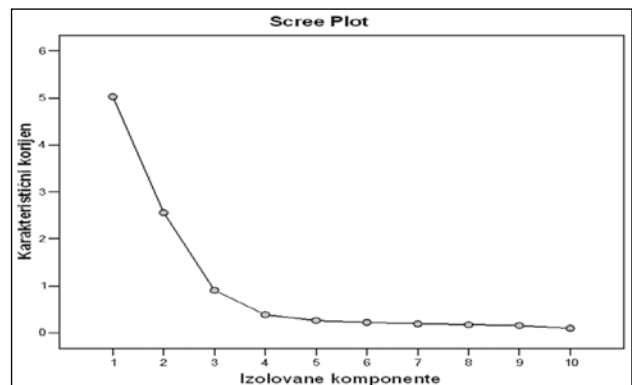
scrin plot 11 years



scrin plot 12 years



scrin plot 13 years



scrin plot 14 years

Figure 1. Scrin plot of isolated factors of morphological characteristics in boys 11-14

The first factor can be called the factor of body fat and mass. The second factor has the highest correlation longitudinal skeleton dimensionality, and the mass, this factor is called the growth factor. The third factor has a maximum projection with voluminous variables, and this factor is clear and it can be called a factor of voluminosity.

The analysis of the matrix circuit of children aged thirteen; we see that compared to the twelve years old children, the highest correlations with the first general factor achieved the variables that represent the subcutaneous adipose tissue. The first major factor is the clear factor and we can call it the factor of subcutaneous adipose tissue.

The second factor with the biggest projection, respectively correlation has with the variables of the longitudinal dimensionality, and the body mass. This factor can be called factor of longitudinal dimensionality and mass. The third factor as with the children in the sixth grade has the highest correlation with variables of voluminous, and this factor we call the factor of voluminosity.

Inspecting the results of the eighth grade children, we see that there has been regrouping of isolated factors. So the first isolated factor has the highest correlation with the variables of body weight, voluminous and subcutaneous adipose tissue. This factor can be called factor of voluminous and subcutaneous adipose tissue.

Inspecting the results of the analysis of the matrix of inter correlations of the isolated factors (Table 4) we can see the connection between isolated

factors within the space of morphological indicators. Based on the results obtained within this matrix, we see that the 11 year old children achieved a statistically significant coefficient of correlation where the first isolated factor correlates with factor two (.37), the twelve year old children the highest factor of correlation has the first and third factor (.51). Other factors have low correlation. The obtained highest correlation of the first factor with the third can be defined as they belong to and determine the general factor of development.

Table 4. Matrix of inter correlation of the isolated factors of morphological characteristics of boys aged 11-14 years

AGE	Component	1	2	
11 god.	1	1,000	,375	X
	2	,375	1,000	
AGE	Component	1	2	3
12 god.	1	1,000	,273	-,511
	2	,273	1,000	-,397
	3	-,511	-,397	1,000
AGE	Component	1	2	3
13 god.	1	1,000	,176	-,446
	2	,176	1,000	-,330
	3	-,446	-,330	1,000
AGE	Component	1	2	
14 god.	1	1,000	,190	X
	2	,190	1,000	

Table 3. Matrix of isolated factors of the morphological characteristics in boys V-VIII grade

Varijable	Component									
	11 years		12 years			13 years			14 years	
	1	2	1	2	3	1	2	3	1	2
ATVIS	,048	,946	,006	,984	,015	-,016	,970	-,002	,034	,932
ATTEZ	,734	,396	,605	,501	-,123	,341	,569	-,166	,732	,461
ADNOG	-,032	,951	-,019	,988	,056	,038	,986	,096	-,041	,926
ADRUK	-,005	,942	-,072	,945	-,070	-,158	,931	-,078	-,010	,908
AONL	,902	-,152	-,042	-,086	-,970	-,055	-,099	-,956	,757	,059
AOGK	,900	,085	,411	,197	-,571	,304	,198	-,665	,739	,266
AOPK	,835	,001	-,013	,055	-,960	-,024	,029	-,974	,774	,111
AKNN	,890	,010	,967	-,058	,015	,944	-,090	,012	,872	-,240
AKNL	,863	-,008	,964	-,034	,017	,940	-,007	-,009	,900	-,070
AKNT	,926	-,008	,956	-,027	-,032	,952	-,016	-,022	,858	-,170

## Conclusion

In its essence, physical development is a natural process, because it takes place on the basis that they are conveyed by heritage and which is subordinated to the laws of the nature. Physical development is not only natural, but socially conditioned process, which basically means that it can be affected from outside as well. In the science it is known that childhood and the young hood is the period of life in which by proper process of exercise we can significantly influence the development and changes of a large number of anthropological features and capabilities of the young man. The main task of kinesiology as a science is to find methods and models that will allow us to determine the factors, or dimensions of personality that are responsible for achieving success in sport.

In our study the longitudinal skeleton dimensionality grows continuously elongating the skeleton, especially the long bones, turbulent processes of ossification occur on their pineal gland, they elongate to the cephalo caudal directions columnae vertebrales, pelvic bone femur tibia fibula, to the final parts of our body, bones tarsus metatarsus on the upper limbs lengthened the long bone humerus radius and Ulna bones till the carpus and metacarpus bones having the point of inflection at age of 14.

In all of them, the longitudinal skeleton dimensionality variability grows around the age of 13, what was the case with our sample as well. As a result of sexual maturation in terms of longitudinal skeleton dimensionality, age of 13-14 years is very inhomogeneous in which the inhomogeneity is especially noticeable at age of 13. The variability of body fat in boys is reduced in the examined period of development but the relative variance remains unchanged due to the parallel reduction of subcutaneous adipose tissue.

The amount of subcutaneous fat in the extremities decreases in the examined period of development, but the fall in subcutaneous adipose tissue, on the lower leg, starts after the age of 13, as it was the case in our study. All voluminous variables systematically grow till the age of 14, and that justifies the isolation of voluminous factors in all ages. The stages of puberty the body volume is under strong influence of the longitudinal dimensionality of the

skeleton and by its end it decreases while the factor of the subcutaneous adipose tissue is clearly differentiated as separate anthropometric dimensions. The large relative variability of weight in the first stages of this period is a consequence of occurrence of unequal development of the intense development of the morphological characteristics. Later, when the individual morphological characteristics approach the upper limit of the homogeneity of the individual is smaller and consequently the relative variability as well, in accordance with this a lack of general growth factor occurs at the age of 13 and 14, respectively until its isolation at age of 11 and 12.

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# Amperometric Determination of hydrogen peroxide with FeO Bulk-Modified Screen-Printed Carbon Ink Sensor

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## Abstract

Sensor for hydrogen peroxide determination was constructed by bulk-modification of carbon ink with iron (II) – oxide FeO as a mediator. The sensor could be operated at a working potential of -200 mV *versus* the Ag/AgCl, flow rate of 0.5 mL min<sup>-1</sup> and carrier medium (0.1 mol L<sup>-1</sup> phosphate buffer pH 7.5) and exhibited good reproducibility and stability. It has a detection limit for hydrogen peroxide of 40.2 µg L<sup>-1</sup> (3σ) and a dynamic range of 5 – 2000 mg L<sup>-1</sup> H<sub>2</sub>O<sub>2</sub> ( $i$  [µA] = 0.0176  $c$  [mg L<sup>-1</sup>] + 0.5066,  $r^2=0.998$ ).

**Key words:** Screen-printed electrode, iron(II) oxide, hydrogen peroxide, Flow-injection analyses, FIA, Amperometric determination.

## Sažetak

Razvijen je senzor za određivanje vodik peroksida modifikacijom karbon elektrode sa FeO kao medijatorom. Radni potencijal senzora je -200 mV *vs* Ag/AgCl, brzina protoka 0.5 mL min<sup>-1</sup> i noseći fluid (0.1 mol L<sup>-1</sup> fosfatni puffer, pH 7.5) uz dobru reproducibilnost i stabilnost. Senzor pokazuje limit detekcije za vodik peroksid od 40.2 µg L<sup>-1</sup> (3σ) i dinamičko područje linearnosti od 5 – 2000 mg L<sup>-1</sup> H<sub>2</sub>O<sub>2</sub> ( $i$  [µA] = 0.0176  $c$  [mg L<sup>-1</sup>] + 0.5066,  $r^2=0.998$ ).

**Ključne riječi:** štampana elektroda, željezo(II) oksid, vodik peroksid, protočno-injekciona analiza, amperometrijsko određivanje.

## 1. Introduction

Heterogeneous carbon materials have been used as electrochemical sensors and biosensors because of their availability and a variety of forms, low costs, broad exploitable potential window, low background current, chemical inertness, easiness of chemical derivatization and modification, and suitability for various applications [1-3].

One of the analytes detected oftentimes with modified heterogeneous carbon electrode in Kalcher's group was hydrogen peroxide. That group were developed different carbon-paste and carbon-ink-based MnO<sub>2</sub>-film modified amperometric sensors for H<sub>2</sub>O<sub>2</sub> that could be operated in ammonia and phosphate buffers with vary low detection limit (<1 µg L<sup>-1</sup>) and remarkably wide linear range of concentration [4-7].

The group was mainly involved in the development of amperometric sensors and enzyme biosensors, which are often based on the oxidation of the target analyte with the corresponding oxidase enzymes, and the formation of hydrogen peroxide was measured. Glucose oxidase represents one of the most exploited enzymes of the oxidases group [8]. Recently, Kalcher's group was developed several biosensors based on different mediators and oxidases enzymes [11-17]. It is known that the amperometric biosensors based on detection of hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) on the classic metal or carbon electrodes require high operating potential (> 600 mV) which causes the interference of a number of electroactive components in complex samples [9].

A common way to avoid such interference is to modify the electrode with substances which can specifically mediate the electron transfer between  $\text{H}_2\text{O}_2$  and the electrode at reduced over-voltage. For the purpose of this work iron (II) oxide (FeO) is used as a mediator to reduce the overvoltage on the electrode. The reaction mechanism of hydrogen peroxide at FeO bulk modified sensor is shown in Fig. 1. [10].

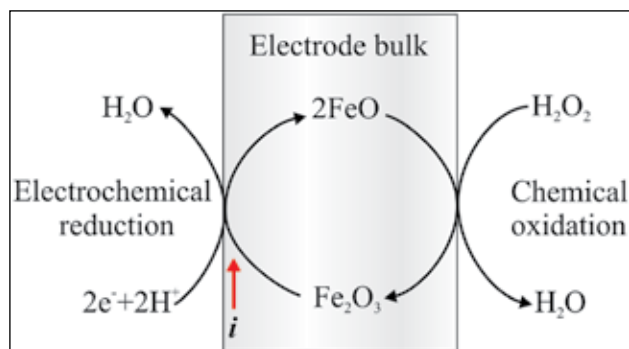


Figure 1. Reduction of hydrogen peroxide by iron(II) oxide

## 2. Experimental

### 2.1. Apparatus

Measurements were done at workstation BAS 100B using the corresponding software, chronoamperometrically by flow injection system and voltammetrically by cyclic voltammetry. The flow injection system consisted of a Multisolvent Delivery System (Waters 600 E), a 4-way rotary valve injection port (Rheodyne, model 5041; 0,8 mm i.d. PTFE tubing) with an injection loop of 100  $\mu\text{L}$  and a thin-layer electrochemical flow cell (CC5, BAS). An Ag/AgCl electrode (3 mol  $\text{L}^{-1}$  KCl, BAS RE-4, Part # MF-2021) served as the reference. The counter electrode (CE) was the stainless-steel back-plate of the cell. A screen printed carbon electrode as a working electrode (SPCE) was fixed via the polyester gasket (RS 770-771, RS components Handelsges m.b.H) with an oval opening directly to the thin-layer cell with a PTFE laboratory-made working electrode block as a holder. Silver conductive paint (Electrolube Ltd, Wargrave Berkshire, UK) was applied on one end of the SPCE, to which a crocodile clamp was attached for electrical contact. The surface area of

the working electrode was  $49.5 (\pm 3.1) \text{ mm}^2$ . The currents were recorded with the electrochemical workstation BAS 100B using the corresponding software (BAS 100W, version 2). The responses were evaluated by using the peak heights (difference between background and absolute current).

The pH values were measured by using a portable pH Meter (Thermo Orion, model 210 A+; Orion, Model SA 720) with corresponding pH electrode (SenTix 22 plus (A043019007).

### Reference Method

Reference determinations were performed with indirect iodometric titration.

### 2.2. Chemicals, Reagents and Solutions

Analytical-reagent grade chemicals were used. Disodium hydrogenphosphate, ascorbic acid ( $\geq 99.0\%$ ), citric acid monohydrate ( $\geq 99.5\%$ ), hypoxanthine ( $\geq 99\%$ ), xanthine, sodium chloride (99.5%), sodium fluoride ( $\geq 99.0\%$ ), potassium persulfate ( $> 99.0\%$ ) and ammonium vanadate were purchased from Fluka, iron(II) oxide (99.9%) and potassium perchlorate from Aldrich. Uric acid, D(-) fructose, D(+) glucose monohydrate, and lactose were of biochemical or bacteriological grade, and originated from Merck.  $\text{H}_2\text{O}_2$  (30%), oxalic acid, sodium dihydrogenphosphate monohydrate, potassium nitrate were also from Merck. Others include sodium dihydrogenphosphate monohydrate (Sigma-Aldrich), tartaric acid (Mallinckrodt), sodium thiosulfate solution (0.1 mol  $\text{L}^{-1}$  Roth), potassium iodate and potassium iodide (Pliva Zagreb), and starch (Kemika Zagreb). Argon ( $> 99.999\%$  (vol.), MESSER, Austria).

Water was distilled twice in quartz distiller and de-ionized with an ion exchange system (Nanopure, Barnstead). Hydrogen peroxide standard solutions: 1.00% (m/v)  $\text{H}_2\text{O}_2$  aqueous stock solutions were prepared freshly, each day, by mixing 1.00 mL of 30%  $\text{H}_2\text{O}_2$  with 29.00 mL of buffer and stored at  $+4^\circ\text{C}$ . Hydrogen peroxide was prepared just before use by dilution in the appropriate buffer. The FIA carrier was sonicated (with sonicator or ultra sonic bath Transsonic 700/H, Elma<sup>®</sup>) under reduced pressure before its use in the flow system to remove dissolved gasses. Phosphate buffers

( $0.1 \text{ mol L}^{-1}$ ) were prepared by mixing aqueous solutions ( $0.1 \text{ mol L}^{-1}$ ) of sodium dihydrogenphosphate and disodium hydrogenphosphate to produce solutions of the required pH. The pH values were measured by using a portable pH Meter (Thermo Orion, model 210 A+; Orion, Model SA 720).

### 2.3. Fabrication of the working electrodes

#### *Printing Methods*

The working electrodes were screen printed onto inert laser pre-etched ceramic supports (Colors Ceramics GmbH, 113x166x0.635 mm alumina plate, No.CLS 641000396R). Printing was done by applying thick layers of the ink onto the substrates through an etched stencil with the aid of a semi automatic screen printer (SP-200, MPM, Franklin, Ma; USA). The resulting plates (30 sensors per plate) were air-dried at room temperature overnight.

#### *Electrodes preparation*

Sensor electrode: Iron (II) oxide (FeO; 40,086-6; Aldrich) was mixed (5% m/m) with the conducting carbon thick film printing (TFP) ink (Electrodag 421 SS, Acheson). The modified ink was stirred for 20 minutes in a glass vial with a glass-rod and immediately printed with the printer.

### 2.4. Procedures

#### *2.4.1. Cyclic voltammetry*

Cyclic voltammetry experiments were handled by using the electrochemical workstation BAS 100B and the corresponding software (BAS 100W, version 2). Cyclic voltammograms were recorded by setting the initial potential at 0 mV and initially scanning towards the minus direction. The scan rates were  $25 \text{ mVs}^{-1}$ . The working electrode was screen printed carbon electrode, SPCE, with surface area of  $\sim (3.0 \times 21) \text{ mm}$ . Electrical connection was made at silver-ink spots via stainless-steel clips. The reference electrode (RE) was Ag/AgCl,  $3 \text{ mol L}^{-1}$  (RE-5B, BAS). The counter electrode (CE) was platinum wire. The supporting electrolyte (volume 10 mL in glass beaker, C-2,

BAS) was always de-aerated for at least 5 min by bubbling Ar.

#### *2.4.2. FIA with an amperometric detection*

Flow injection analysis (FIA) for SP(FeO)CE was performed with an applied potential of -200 mV. The typical flow rate for sensors was  $0.5 \text{ mL min}^{-1}$  with an injection volume of  $100 \mu\text{L}$ . Evaluation was done by their peak heights. The height was enumerated by adjusting a tangent (identical to the baseline) to the base of the peak and determining the distance to the peak maximum.

Figure 2. shows a FI amperogram obtained using the FeO modified SPE on Hydrogen peroxide.

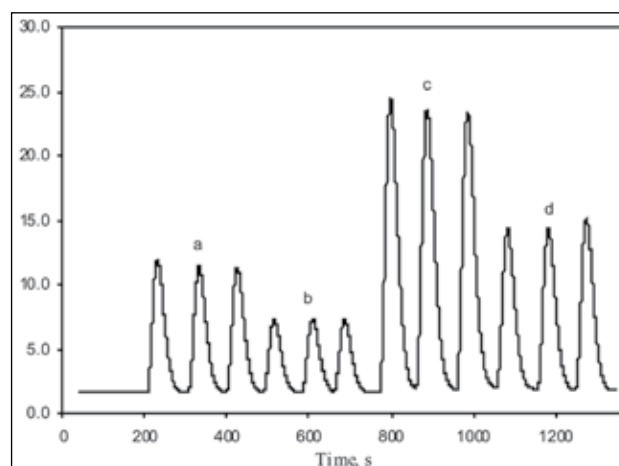


Figure 2. Current response FeO modified SPE on hydrogen peroxide. Concentration of a) 500, b) 300, c) 1000 and d)  $750 \text{ mg L}^{-1} \text{ H}_2\text{O}_2$ . Working conditions: Applied potential -200 mV vs. Ag/AgCl, flow rate  $0.5 \text{ mL min}^{-1}$ , injection volume 100 mL, and carrier phosphate buffer ( $0.1 \text{ mol L}^{-1}$ , pH 7.5).

### 2.5. Analysis of commercial sample

A medical solution containing hydrogen peroxide ("verdünnte Wasserstoffperoxidlösung, 3%", EAB) was bought in a pharmacy (Kaiser-Joseph-Apotheke, Graz) and stored at  $4^\circ\text{C}$  in a refrigerator. The solutions were analyzed with the new sensors based on FeO modified electrode. Before the FIA amperometric determination of the hydrogen peroxide content, appropriate volumes of the samples were diluted 1:1000, 1:500 and 1:400 (v/v) with phosphate buffer ( $0.1 \text{ mol L}^{-1}$ ,



pH=7.5) immediately before analysis. Quantitative determinations were made by injecting sample solutions directly into the FIA-system. Reference determinations were performed with indirect iodometric titration.

### 3. Results and discussion

#### 3.1. Amperometric determination of $H_2O_2$

According to preliminary investigations, carbon paste electrodes modified with iron(II) oxide showed very promising results as a mediator for the amperometric determination of hydrogen peroxide.

#### 3.2. Voltammetric behavior of hydrogen peroxide

Cyclic voltammetric behavior of hydrogen peroxide at FeO-modified carbon electrodes is showed on Figure 3. As can be seen, the current of reduction of  $H_2O_2$  has been several times higher in the presence of FeO as a mediator in relation to the unmodified electrode.

#### 3.3. Operational parameters

##### 3.3.1. Working potential

The sensor electrode is modified with 5% FeO (m:m). In previous investigations of FeO-bulk modified electrodes an operation potential of -200 mV was chosen as the working potential. Figure 4. shows the dependence of the current response and the background current on the applied potential, when the biosensor with glucose as an analyte has been used. When the applied potential drops below -200 mV the background current becomes higher than the signal. The reason for that is the increasing oxidation rate of the modifier FeO. A working potential of -175 mV was chosen for subsequent measurements although the background current was notably high. This potential is acceptable with respect to interferences in real sample. Electrochemical preactivation of the electrode helped to decrease the background current and to increase the current signal.

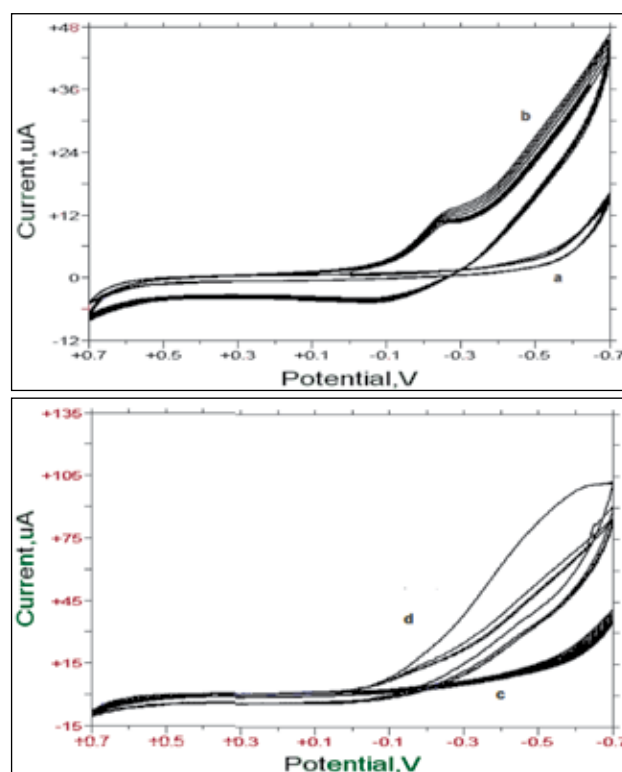


Figure 3. Cyclic voltammograms in the absence (a, b) and in the presence of hydrogen peroxide (c, d) at an unmodified (a, c) and at an FeO-modified SPCE (b, d). Batch experiment: cell volume 10 mL, unstirred solution, initial potential 0 mV, low vertex potential -700 mV, high vertex potential +700 mV vs Ag/AgCl, scan rate  $25 \text{ mV s}^{-1}$ , supporting electrolyte phosphate buffer (0.1M, pH 6.0),  $H_2O_2$  concentration 0 and  $100 \text{ mg L}^{-1}$ . Reduction currents have a positive sign. Electrode surface area  $\sim 3.0 \text{ mm} \times 21 \text{ mm}$  CE.

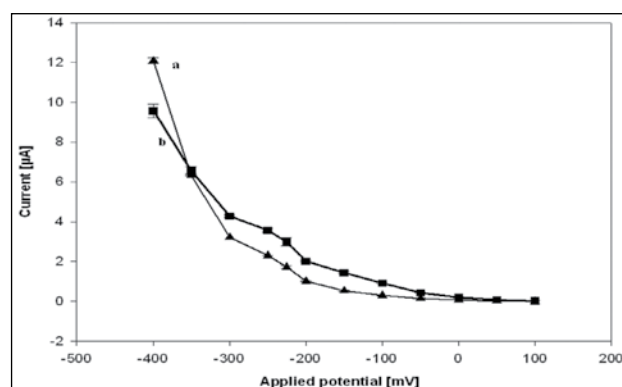


Figure 4. Dependence of the FIA peak current response of iron (II) oxide bulk-modified screen printed electrode on the applied potential. Working conditions: flow rate  $0.5 \text{ mL min}^{-1}$ , carrier phosphate buffer ( $0.1 \text{ mol L}^{-1}$ , pH 7.5), injection volume  $100 \text{ µL}$ ,  $H_2O_2$  concentration  $100 \text{ mg L}^{-1}$ , (a) background current, (b) peak height of the current response

### 3.3.2. Flow rate

The dependence of the current response of hydrogen peroxide on the flow rate is shown in Figure 5. with a concentration of  $100 \text{ mg L}^{-1} \text{ H}_2\text{O}_2$  at pH 6.0 and 7.5. The behavior of the signal was practically the same in both cases apart from the absolute difference of the current. According to these results a flow rate of  $0.5 \text{ mL min}^{-1}$  was chosen for subsequent measurements.

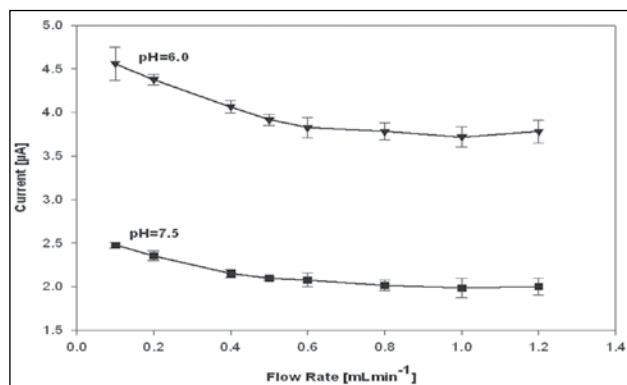


Figure 5. Dependence of the current response of hydrogen peroxide on the flow rate. Electrode: SP(FeO)CE. Working conditions: operating potential  $-200 \text{ mV}$  vs Ag/AgCl, injection volume  $100 \text{ µL}$ , carrier phosphate buffer ( $0.1 \text{ mol L}^{-1}$ , pH 6.0 and 7.5),  $\text{H}_2\text{O}_2$  concentration  $100 \text{ mg L}^{-1}$

### 3.3.3. Effect of pH

Preliminary investigation with carbon paste electrode modified with iron(II)oxide showed very promising results for the amperometric determination of hydrogen peroxide.

The dependence of the current response of  $100 \text{ mg L}^{-1}$  of  $\text{H}_2\text{O}_2$  of the pH of carrier was investigated with corresponding SPCEs in FIA using phosphate buffer (pH, 5.0 – 9.5) as a carrier. The results are shown in Figure 6. The best current response was obtained with pH 6.0 (b). Comparison of the background current (a) with the signal (b) demonstrates that the background current decreases from pH 5 up to pH 8, whereas it increases slightly beyond pH 8. For further investigation two different pH values were chosen, pH 6.0 and 7.5, since the current response has a maximum at pH 6.0, whereas pH 7.5, that correspond to the biological fluids, seems to be best suitable for amperometric biosensors.

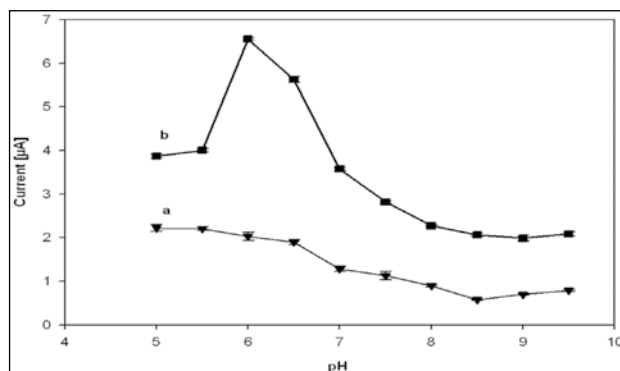


Figure 6. Dependence of the current response on the pH of carrier ( $0.1 \text{ mol L}^{-1}$  phosphate buffer). Electrode: FeO bulk modified SPCE. Working conditions: operating potential  $-200 \text{ mV}$ , flow rate  $0.5 \text{ mL min}^{-1}$ , injection volume  $100 \text{ µL}$ , (a) background current, (b) current response of  $\text{H}_2\text{O}_2$  concentration  $100 \text{ mg L}^{-1}$ .

### 3.4. Linear range, detection limit and reproducibility

Linear relation between the amperometric peak current and the concentration was found in concentration interval of  $5\text{--}2000 \text{ mg L}^{-1}$  hydrogen peroxide in  $0.1 \text{ mol L}^{-1}$  phosphate buffer (pH 7.5):  $i [\text{µA}] = 0.0176c [\text{mg L}^{-1}] + 0.5066$ ,  $r^2 = 0.998$ . For the concentrations higher than  $2000 \text{ mg L}^{-1}$ , a slight deviation from linearity was observed. The detection limit (given as  $3\sigma$  value calculated from 10 injections of  $100 \text{ µL}$  hydrogen peroxide at the concentration of  $10 \text{ mg L}^{-1}$ ) was found to be  $40.2 \text{ µg L}^{-1}$  (Figure 7). The reproducibility was determined as 3.6 % relative standard deviation (10 injections,  $50 \text{ mg L}^{-1}$  hydrogen peroxide).

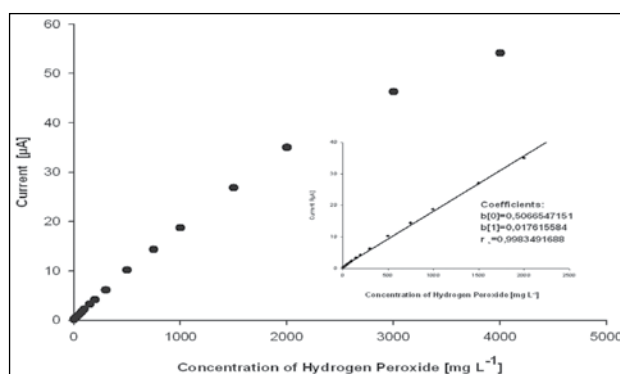


Figure 7. Calibration curve for different concentrations of hydrogen peroxide ( $n=3$ ). Electrode: SP(FeO)CE. Working conditions: operating potential  $-200 \text{ mV}$  vs Ag/AgCl, flow rate  $0.5 \text{ mL min}^{-1}$ , injection volume  $100 \text{ µL}$ , carrier phosphate buffer ( $0.1 \text{ mol L}^{-1}$ , pH 7).

### 3.5. Interferences study for FeO modified SPE sensor

According to specific requirements of the practical samples, some inorganic and organic interferences at pH 6.0 were investigated (Table 1): Electrode: SP(FeO)CE. Working conditions: operating potential -200 mV vs Ag/AgCl, flow rate 0.5 mL min<sup>-1</sup>, injection of 100 µL of an aqueous solution of H<sub>2</sub>O<sub>2</sub> containing the interferent, carrier phosphate buffer pH 6.0 (0.1 mol L<sup>-1</sup>).

Table 1. Relative changes of the current response of H<sub>2</sub>O<sub>2</sub> in FIA in the presence of interferents.

Interference	Change in current (%)			
	In the presence of 100 mg L <sup>-1</sup> H <sub>2</sub> O <sub>2</sub>			Interference 100 mg L <sup>-1</sup>
	10	100	1000	
Ascorbic acid	+6	+19	+86	+5
Citric acid	0	0	0	0
Oxalic acid	0	-2	-3	0
Tartaric acid	+1	+1	+11	0
D(-) Fructose	-1	-1	0	0
D(+) Glucose	+1	+2	-3	0
Lactose	0	0	+1	0
Hypoxanthin	-6	-12	-7	+5
Xanthine	+2	+5	-	+1
Uric acid	-4	-13	-	+3
Fluoride (NaF)	-1	-2	-4	0
Nitrate (NaNO <sub>3</sub> )	-1	+2	+5	0
Perchlorate (KClO <sub>4</sub> )	0	+1	+1	0
Persulfate (K <sub>2</sub> S <sub>2</sub> O <sub>8</sub> )	0	+1	+7	0

### 3.6. Testing of the FeO modified SPE sensor for hydrogen peroxide

Testing of the modified FeO SPE sensor was performed by determining the medical solution of H<sub>2</sub>O<sub>2</sub> (verdünnte Wasserstoffperoxidlösung, 3% EAB, pharmacy Kaiser-Joseph-Apotheke, Graz) at pH 7.5 and flow rate of a 0.5 mL min<sup>-1</sup>. Results

Table 2. Analysis of a medical solution containing hydrogen peroxide

Electrode	Operating Potential mV	H <sub>2</sub> O <sub>2</sub> %	Reference method H <sub>2</sub> O <sub>2</sub> %	Recovery value %
SP(FeO)CE	-200	2.84 ± 0.09	2.84 ± 0.11	100

of determination of this sample, on the basis of calibration curve, are presented in Table 2.

## 4. Conclusion

This work shows that FeO modified carbon electrode may be used as a mediator in amperometric sensor for hydrogen peroxide. FeO modified heterogeneous carbon electrodes, described in this paper, are very simple to prepare, showing a promising analytical performance and applicability to analysis of practical samples, such as hydrogen peroxide solutions.

Further investigations will be focused on the development of glucose biosensor modified with FeO as mediator and enzyme *glucose oxidase* as biocomponent.

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# Nuchal translucency screening for fetal Down's syndrome

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## Abstract

**Introduction:** Down's syndrome is the most common cause and best known chromosome disarrangement in humans (the incidence is about 1/600-2.000 pregnancies). A subcutaneous collection of fluid behind the neck, at 11-13 weeks + 6 days of gestation, can be visualized by ultrasound as nuchal translucency (NT). Increased fetal NT is associated with increased risk for chromosomal abnormalities, many different fetal anomalies and genetic syndromes.

**Aims:** To evaluate the NT screening, for fetal Down's syndrome, in the first trimester of pregnancy in relation with maternal age.

**Materials and methods:** This prospective study of screening was conducted among 105 pregnant women between 11-13 weeks + 6 days of gestation, at the Department of Obstetrics and Gynecology, Clinical Centre University of Sarajevo over a period May to September 2010. Gestational age was calculated from the last menstrual period and confirmed by measuring the Crown rump length (CRL) of fetuses which was 45-84 mm. NT measurement was performed by two ultrasonographers according to Fetal Medicine Foundation (FMF) guideline, following strict methodological criteria. Scans were performed using transabdominal ultrasound in mid-sagittal plane, with the fetus occupying at least 75% of the image. Fetal karyotyping was performed in cases of advanced maternal age (women who are 35 years old or older), positive family history of aneuploidy, and when the measured NT was over 3 mm.

**Results:** The median of maternal age was 33.0 years (IQR=15), and 54 (51.4%) women were 35 years old or older. In the group of women who were 35 years old or older, NT was over 2.5 mm in six fetuses, where NT was 2.6 mm in four fe-

tuses and the consecutive values of NT measurement in two fetuses were 3.6 mm and 4.5 mm. The age of pregnant women related to the last two mentioned fetuses were 35 years and 37 years. One Down's syndrome was confirmed genetically (NT-4.5 mm), one karyotype was found to be normal (NT-3.6 mm). In the group of pregnant women who were < 35 years, NT measurement was normal. There is statistically significant difference ( $p=0.027$ ), in the frequency of values of NT measurement over 2.5 mm for maternal age  $\geq 35$  compared with maternal age < 35 years.

**Conclusion:** The use of a single test is extremely valuable screening method in circumstances with no biochemical laboratories. If the conditions allow so, combined screening is recommended, which beside the ultrasound NT measurement includes biochemical detection of hormones (double test (fb-hCG i PAPP-A) or triple test (AFP, HCG and uE3)).

**Key words:** Ultrasound, Nuchal translucency, Chromosome Disorders, Down's syndrome

## Introduction

Down's syndrome is the most common cause and the best known chromosome disarrangement in humans. Mental retardation, dysmorphic facial features, and other distinctive phenotypic expressions characterize the syndrome. The incidence of this genetic disorder is about 1/ 600-2.000 pregnancies and it is in direct correlation with the age of a mother. The risk of appearance of this trisomy increases linearly and moderately up in mothers who are >35 years old, and then it exhibits abrupt exponential growth. Diagnosis of the syndrome may be presented by analysis of fetal karyotype. For karyotype analysis, fetal cells obtained by bi-

opsy of chorionic cups, amniocentesis and cordocentesis may be used. Recent method of molecular biology, fluorescent in situ hybridization (FISH), has enabled the utilization of fetal erythrocytes which are found in a small number in mothers blood flow for analysis of karyotype ploidy.

The nuchal translucency (NT) is formed by a layer of fluid beneath the nuchal skin extending for a variable distance over the head and neck (1). This layer of fluid is presented in all fetuses between 11-13 weeks + 6 days of gestation. It has been shown that as the amount of this fluid increases, there is an increasing chance of the fetus being affected by some type of a disorder. However, as it is the case with every true marker, even a very significant increase in NT thickness does not confirm the diagnosis of a fetal problem. This can be determined only by the appropriate diagnostic test such as chorionic villus sampling or amniocentesis. The sonographic detection of a fetal NT is regarded as the leading screening test for Down's syndrome in the first trimester of pregnancy. It may identify up to 75% of affected pregnancies, with a 5% false-positive rate (2,3). The Fetal Medicine Foundation (FMF) introduced guidelines, training and quality-control programs for sonographers who are certified to perform the 11-14 week scan.

The main guidelines are:

1. The fetal crown-rump length (CRL) should be in the range 45-84 mm;
2. The gestational age should be in the range 11-14 weeks;
3. A good sagittal section of the fetus should be obtained, preferably with the fetal spine at the bottom of the image;
4. The fetus should be in a neutral position, with the head in line with the spine, not hyper-extended or flexed;
5. Care must be taken to distinguish between fetal skin and amnion;
6. The maximum thickness of the subcutaneous translucency between the skin and the soft tissue overlying the cervical spine should be measured;
7. The magnification should be such that each increment in the distance between calipers should be only 0.1 mm;

An increased nuchal translucency may also be a marker for other chromosomal anomalies such as trisomy 13, trisomy 18 and Turner syndrome, as well as structural defects of the heart, great arteries and different skeletal dysplasias (2,3,4,5). The prevalence of chromosomal defects increases with increasing NT thickness (2,6). Most cases, about 92.5 % are caused by meiotic non-disjunction resulting in triplication of 21<sup>st</sup> chromosome, and recurrence of this type of disorder is about one to two percent. Three to four percent of all cases of trisomy 21 are due to Robertsonian translocation.

The extra chromosome 21 is the most often translocated with another acrocentric chromosome and recurrence of the problem might occur in 5-15% for t(Dq;21q) and t(21q;22q) and in 100% for t(21q;21q) of cases, depending on the type of translocation. The remainder of cases of trisomy 21 are due to mosaicism. In this case recurrence is sporadic. The majority of pregnancies with trisomy of chromosome 21 results in miscarriage in the first trimester, but some of these pregnancies are successful.

### Materials and methods

This prospective study of screening was conducted among 105 pregnant women between 11-13 weeks + 6 days of gestation, at the Department of Obstetrics and Gynecology, Clinical Centre University of Sarajevo over a period May to September 2010. Gestational age was calculated from the last menstrual period and confirmed by measuring the CRL. It is important to obtain an accurate CRL as the calculation of fetal risk must be based on the correct gestational age. A midline longitudinal view of the fetus is obtained and the image is magnified so that the fetus fills most of the image. The fetus is measured from the top of the head to the rump. The measurement should be done with the fetus in a neutral position, i.e. not hyperflexed or extended. CRL of fetuses was 45-84 mm. Nuchal translucency measurement was performed by five ultrasonographers according to Fetal Medicine Foundation (FMF) guideline, following strict methodological criteria. Scans were performed using transabdominal ultrasound in mid-sagittal plane, with the fetus occupying at least 75% of the

image. Calliper measurements were corrected to 0,1 mm. Care was taken to visualize clearly the fetal skin and amniotic membrane. The maximum thickness of subcutaneous translucency between the skin and soft tissue overlying the cervical spine was measured for several times, and the largest measurement was taken into the account. Fetal karyotyping was performed in cases of advanced maternal age (women who are 35 years old or older), positive family history of aneuploidy, and when the measured NT was over 3 mm. Results are expressed as median and interquartile range (IQR) in case of non-normal distributed continued variables. The Kolmogorov–Smirnov test with a Lilliefors significance level was used for testing normality. The Fisher's Exact Test was used to analyze categorical variables. A p-value <0.05 was considered significant. The SPSS software (SPSS Release 16.0; SPSS Inc., Chicago, Illinois, United States of America) was used.

## Results

The median of maternal age was 33.0 years (IQR=15), and 54 (51.4%) women were 35 years old or older. In the group of women who were 35 years old or older, NT was over 2.5 mm in six fetuses, where NT was 2.6 mm in four fetuses and the consecutive values of NT measurement in two fetuses were 3.6 mm and 4.5 mm. The age of pregnant women related to the last two mentioned fetuses were 35 years and 37 years. One Down's syndrome was confirmed genetically (NT-4.5 mm), one karyotype was found to be normal (NT-3.6 mm). In the group of pregnant women who were < 35 years, NT measurement was normal. There is statistically significant difference ( $p=0.027$ ), in the frequency of values of NT measurement over 2.5 mm for maternal age  $\geq 35$  compared with maternal age < 35 years.

## Discussion

Trisomy 21 is the sequelae of abnormal spermatozoid or egg cell, or the result of genetic error during early embryonal stage. The cause of the increasing incidence of Down's syndrome with the

older age lies probably in a long latent period of egg cell at the level of primary follicles with arrested process in diplogenetic subphase of meiosis, I prophase. Longer period of egg cell held up in a latent state may bring out the cellular metabolic disorders which will interfere with normal cell division and regular arrangement of chromosomes (formation of haploid and polyploid number of chromosomes).

In our study, 51.4% of pregnant women were 35 years old and older. There is statistically significant difference ( $p=0.027$ ), in the frequency of values of NT measurement over 2.5 mm for maternal age  $\geq 35$  compared with maternal age < 35 years.

Prospective studies in a total of 200.868 pregnancies, including 871 fetuses with trisomy 21, have demonstrated that increased nuchal translucency can identify 76.8% of fetuses with trisomy 21, which represents a false-positive rate of 4.2% (7).

In 1.015 fetuses undergoing first-trimester karyotyping because of the increased nuchal translucency thickness, the incidence of chromosomal abnormalities increases with both maternal age and nuchal translucency thickness. The observed numbers of trisomies 21, 18 and 13 in fetuses with nuchal translucency thicknesses of 3 mm, 4 mm, 5 mm and  $\geq 6$  mm were approximately 3 times, 18 times, 28 times and 36 times higher than the respective numbers expected on the basis of maternal age (8).

## Conclusion

Ultrasound screening in the first trimester of pregnancy increases the effectiveness of detection of fetal chromosomal diseases. It is worthwhile to use nuchal translucency measurement as a marker of fetal chromosomal diseases in ultrasound screening of general population.

In screening for chromosomal abnormalities, an approach which combines maternal age and NT is effective and increases the detection rate compared to the use of any single test. In fetuses with normal karyotype, the finding of increased NT demands a continuous sonographic follow up.

The use of a single test is extremely valuable screening method in circumstances with no biochemical laboratories. If the conditions allow

so, combined screening is recommended, which beside the ultrasound NT measurement includes biochemical detection of hormones (double test (fb-hCG i PAPP-A) or triple test (AFP, HCG and uE3)).

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# Importance of hemoglobin content in reticulocytes in the evaluation of iron status in hemodialysis patients

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## Abstract

**Introduction:** Monitoring of iron is required in HD patients and is based on an assessment of three main factors: the determination of serum ferritin, transferrin saturation, and percentage of hypochromic erythrocytes. Recent research highlights the importance of hemoglobin content in reticulocytes (CHR) as a sensitive and specific marker of iron deficiency in HD (HD) patients.

**Objective:** To determine the value of CHR in chronic HD patients receiving erythropoietin and those who are on HD and continuous peritoneal dialysis, and who do not receive erythropoietin. The study included 53 patients at the Department of Nephrology, HD and Transplantation UKC in Tuzla.

**Results:** The mean CHR in our study amounted to  $33.92 \pm 3.52$  pg for patients receiving erythropoietin and  $32.32 \pm 4.66$  pg for the group not receiving erythropoietin. Total 8/53 (15.1%) patients had CHR below 28 pg. Using the data obtained by ROC curve, a value of CHR with the best diagnostic performances, was 31.1 pg.

**Conclusion:** Determination of CHR could be a reliable parameter of functional iron deficiency in patients on HD. So, the diagnosis of iron status would be more accurate, as well as the use of iron and erythropoietin.

**Key words:** iron status, ferritin, transferrin saturation, CHR, HD

## Introduction

Monitoring of iron is required in HD patients and is based on an assessment of three main factors: determination of serum ferritin, transferrin saturation (TSAT), and percentage of hypochromic erythrocytes. Iron deficiency may be absolute, in which all body reserves are exhausted, or functional, where insufficient or even excessive amount of iron is present in the body that can not be activated quickly enough to meet the needs of the bone marrow.

The National Kidney Foundation-Dialysis Outcomes Quality Initiative (NKF-DOQI) guidelines recommended maintaining serum ferritin at or less than 100 ng/mL, or TSAT at or less than 20% to manage iron deficiency (1). Recent researches emphasize the importance of hemoglobin content in reticulocytes as sensitive and specific markers of functional iron deficiency in HD patients (2, 3, 4, 5, 6, 7, 8, 9, 10).

Serum ferritin is increased in the states of inflammation, infection, malignancy and liver diseases (11). Low values of TSAT can mean either iron deficiency or intense erythropoiesis, when disequilibrium occurs between iron stores and its distribution in the circulation and in the bone marrow. Assessment of the iron status is easier if the value of TSAT and serum ferritin is low or high.

However, if these values diverge, this restricts sensitivity of these parameters in assessing the iron

status, and then has a greater diagnostic importance of determining the CHr (12, 13). Hemoglobin content in reticulocytes may be a reliable indicator of response to i.v. iron therapy in the patients on HD (14, 15, 16, 17, 18, 19).

The dilemma exists around the cutoff values of this parameter. The value of mean hemoglobin content in reticulocytes of  $27.5 \pm 2.8$  pg, and value of less than 26 pg is a good indicator of functional iron deficiency (4). The study of Mittua et al (1997), which included 1364 patients on HD, determined the concentration of CHr of 28.3 pg. In patients who had a value of CHr of less than 26 pg, a correlation with changes in erythrocyte count, hemoglobin and hematocrit was established. After i.v. given iron, CHr shows the following dynamics: growth in the first 48 hours, reaches a peak at 96 hours after which it falls on the basal value.

Some authors prove the cutoff values for CHr of 27.2 pg (11) but the others show the cutoff value of CHr  $<32.4$  pg (17) and  $32.3 \pm 2.2$  pg (20) for detecting iron deficit.

There are still controversies about the most reliable indicators of iron status in HD patients.

The aim of this study was to determine the value of CHr in chronic HD patients and compare CHr with conventional tests.

## Patients and methods

The study included 53 patients who were dialyzed on HD machines 4008S and 5008S, which have the option of online monitoring of achieved dialysis dose (Kt/V), with dialyzers sterilized by steam or gamma radiation. Most patients received i.v. iron replacement therapy, or p.o. in order to maintain ferritin between 300 ug/l and transferrin saturation over 20%. The patients were of both sexes, randomly selected. At the moment of inclusion in the study, the patients had stable hemoglobin (9-11g/dl) at least two consecutive measurements. The study included 32 chronic HD patients who were on HD and receiving the rHuEPO and 21 patients on HD and continuous ambulatory peritoneal dialysis for more than three months without therapy by erythropoietin. The patients were older than 18 years. The study did not include patients who had malignant disease.

For each patient ten days prior to the measurement of biochemical and hematological parameters, i.v. or p.o. iron therapy was suspended.

Profile of iron includes the following parameters: serum iron, ferritin, TIBC (total transferrin), UIBC (free transferrin), TSAT, CHr and hemoglobin. These parameters were determined on the apparatus Sysmex XE 2100 at the Polyclinic for Laboratory Diagnostics at the Medical Biochemistry Department. A copy of these findings is stored in histories of patients at the Department of Nephrology, Dialysis and Kidney Transplantation UKC Tuzla.

## Statistical analysis

Statistical analysis was done by SPSS 15.0 (Chicago, IL, USA). The basic tests of descriptive statistics were made, showing a measure of central tendency and dispersion. Testing of each variable for affiliation to the normal distribution was done using Kolmogorov-Smirnoff test, and the histogram display. Quantitative variables were compared by t-test with correction for unequal variance where this has been arranged by a normal distribution. For quantitative variables that were not distributed according to normal distribution, Mann-Whitney U test was used. Categorical variables were analyzed by X<sup>2</sup>-test. To test the diagnostic accuracy of reticulocyte hemoglobin we used ROC (Receiver Operating Characteristics) curve, as well as the calculation of other values in the Bayes's analysis (sensitivity, specificity, positive and negative predictive value). All the statistical tests were carried out with the level of statistical probability of 95% ( $p < 0.05$ ).

## Results

The average age of patients was uniform and was  $53 \pm 9$  years with a minimum of 22 and maximum of 70 years and there were no significant differences between the tested ( $53 \pm 11$  years) and the control group ( $53 \pm 7$  years).

The values of transferrin saturation and serum ferritin were significantly higher in the tested group while the values of TIBC, UIBC and transferrin were significantly higher in the control group (Table 1).

Table 1. Comparative study on the average values of parameters related to iron deficiency between patients and control groups

Parameter	Group	Arithmetic mean	SD	p-value
Serum iron	Patients	16.84	9.81	0,42
	Controls	14.70	8.71	
TIBC	Patients	37.95	9.81	<b>0,005</b>
	Controls	47.29	13.22	
UIBC	Patients	21.12	11.30	<b>0,002</b>
	Controls	32.53	13.84	
Transferrin	Patients	1.58	0.42	<b>0,001</b>
	Controls	2.07	0.60	
Transferrin saturation	Patients	44.64	23.90	<b>0,04</b>
	Controls	32.06	17.37	
Ferritin	Patients	715.41	41.95	<b>0,02</b>
	Controls	403.03	56.39	
Reticulocyte hemoglobin	Patients	33.92	3.52	0,16
	Controls	32.32	4.66	
Hemoglobin	Patients	105.75	15.77	0,06
	Controls	115.24	18.64	

Total 8/53 (15.1%) of patients had CHr below 28 pg. Although there were more patients with lower CHr within the control group, this difference was not statistically significant ( $X^2 = 3.34$ ,  $df = 1$ ,  $p = 0.07$ ), but it was on the verge of statistical significance (Table 2).

Table 2. Comparative study of patients with hemoglobin content in reticulocyte below 28 pg within the tested and control groups

		Reticulocyte Hb		
			<28 pg	≥28 pg
Group	Patients	N	2	30
		%	6.3%	93.8%
	Controls	N	6	15
		%	28.6%	71.4%
Total		N	8	45
		%	15.1%	84.9%

The area under the ROC (AUROC) curve for reticulocyte Hb was 0.73 (95% CI = 0.59 to 0.84) and was statistically significant ( $p = 0.001$ ). ROC curve is given in the Figure 1. Using the data obtained by means of ROC curve, a value of CHr with the best diagnostic performances was 31.1 pg. This value had a sensitivity of 50%, specificity of 96%, and positive predictive value of 93% and negative predictive value of 68%.

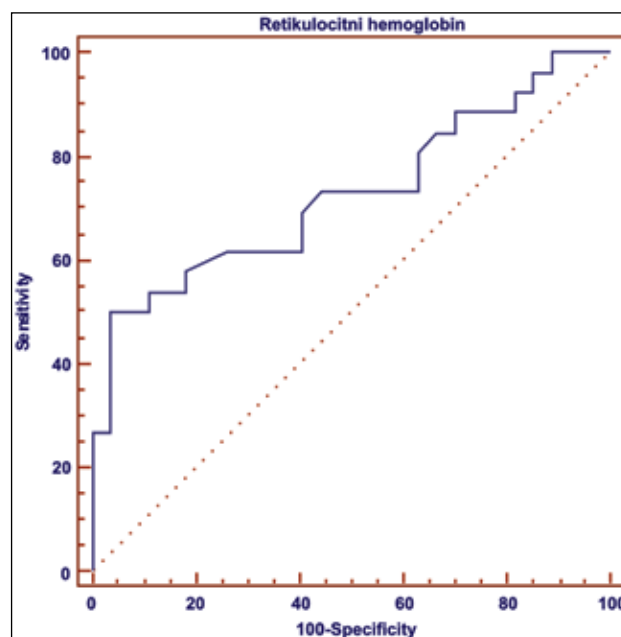


Figure 1. Receiver Operating Characteristics (ROC) curve of diagnostic accuracy of reticulocyte hemoglobin compared to common criteria for the deficit in serum iron in HD patients

### Discussion

Today there is no ideal test for monitoring of iron status in patients who do not have enough iron, and receive therapy of rHuEPO. Tests that are ava-

ilable, are used for measuring only specific part of the metabolic pathway of iron, which makes a comprehensive analysis. The most frequently are used the tests to measure serum ferritin, transferrin saturation and hypochromic erythrocyte. Hemoglobin content in reticulocytes was suggested as a new marker of iron deficiency in HD patients. Initial studies done on neuremic populations show more of the average value of CHr ( $28.6 \pm 1.6$  pg) than in HD patients tested by other authors. Different values of CHr were suggested: 26 pg (4),  $27.5 \pm 2.8$  pg (6), 30.6 pg (21),  $31.1 \pm 1.8$  (2).

The obtained mean values of CHr in our study amounted to  $33.92 \pm 3.52$  pg for the patients who received erythropoietin, and  $32.32 \pm 4.66$  pg for the group not receiving erythropoietin. Some authors considered that 32 pg is appropriate for the CHr cutoff value (22).

Our results are similar to the results of some authors (18, 20, 21). We compared the values of associated parameters related to iron deficiency. There was no significant difference in serum iron, hemoglobin and CHr between the patients and the control groups. Transferrin saturation values ( $44.64 \pm 23.9$ ) and the value of ferritin ( $715.41 \pm 41.95$ ) were significantly higher in the tested group than in controls ( $32.06 \pm 17.37$ ).

The area under the ROC (AUROC) curve for reticulocyte Hb was 0.73 (95% CI = 0.59 to 0.84) and was statistically significant ( $p = 0.001$ ). Using the data obtained by means of ROC curve, a value of CHr with the best diagnostic performances was 31.1 pg. This value had a sensitivity of 50%, specificity of 96%, and positive predictive value of 93% and negative predictive value of 68%.

Receiver operator characteristic (ROC) curve analysis revealed values of the area under the curve for CHr of 0.913 ( $P < 0.0001$ ). With a CHr cutoff level of 27.2 pg, iron deficiency could be diagnosed with a sensitivity of 93.3%, and a specificity of 83.2% (10).

## Conclusions

Patients who received rHuEpo have increased demands for iron and can lead to reduced iron incorporation into hemoglobin. The biggest challenge for clinicians is to maintain a balance between

the need for iron and supplementary therapy. There is a need for the use of new markers for assessing iron status in HD patients. Determination of CHr could be a reliable parameter of functional iron deficiency in patients on HD.

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# Effects of static and dynamic training on the cardiovascular system

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## Abstract

**Introduction:** Adaptation of the cardiovascular system to a standard work or the work of a certain intensity, in the physiology of sport, represents a criterion of cardiovascular capacity, and physical ability of an individual in a broader sense of the word.

**Aims:** The aim of this study was to determine whether the values of hemodynamic parameters, heart rate and blood pressure measured at rest and during exercise, significantly differ between the trained persons and the average value of the general population.

**Materials and methods:** A retrospective study was conducted, and as a source of data we used medical records of ergometric test on a bicycle, made in "Atrium" clinic, for the period 2006-2009 years. The sample consists of 52 subjects, members of the Police Unit for Special Purposes, who were chosen by random sampling.

**Results:** The mean age of examinees was 31.4±0.7 years. There is a statistically significant difference between the mean values of heart rate of examinees and the population at rest ( $p<0.0001$ ), and the workload of 50W ( $p<0.0001$ ), 75W ( $p<0.01$ ), 100W ( $p<0.0001$ ), 125W ( $p<0.0001$ ), and 150W ( $p<0.0001$ ). There is a statistically significant difference in median values of systolic pressure (mmHg) of the examinees and the population at the workload of 50W ( $p<0.0001$ ), 75W ( $p<0.0001$ ) and 100W ( $p<0.0001$ ) and the mean

values of examinees and the populations at workload of 125W ( $p<0.0001$ ) and 150W ( $p<0.0001$ ). There is a statistically significant difference in median values of diastolic blood pressure (mmHg) of the examinees and the population at a workload of 50 W ( $p<0.0001$ ), 75W ( $p<0.0001$ ) and 100W ( $p<0.0001$ ), 125W ( $p<0.0001$ ), and 150W ( $p<0.0001$ ).

**Conclusion:** Training has an effective impact on the cardiovascular system in terms of reducing the value of heart rate, and reduction of systolic and diastolic blood pressure at different workloads.

**Key words:** Cardiovascular system, Adaptation, Workload, Police Unit for Special Purposes

## Introduction

World Health Organization (WHO) in its annual report in 2002. emphasized that the mortality, morbidity and disability associated to chronic non-infectious diseases, are responsible for more than 60% of mortality in the world, and that an unhealthy diet and lack of physical activity are the main risk factors for these diseases. The study of the mechanisms which are in the fond of heart and blood vessels diseases is of a great importance, above all, because cardiovascular abnormalities, to a large extent, reflect the functioning of all tissues, organs and systems in our body. On the other hand, diseases of the heart and blood vessels belong to the group of diseases of modern civiliza-

tion, which greatly threaten the health of population of our country. Modern life is full of stressful situations that lead to not only physical, but primarily to the affective and emotional tension, which again through various psychosomatic mechanisms have very adverse impact on particular functions of the heart and blood vessels. Extraordinarily high percentage of disability, partial or absolute loss of working capacity, which results from heart and vascular disease of the cardiovascular system, gives to the mentioned diseases the character of a very important social diseases.

Adaptation of the cardiovascular system to a standard work or the work of a certain intensity, in the physiology of sport, represents a criterion of cardiovascular capacity, and physical ability of an individual in a broader sense of the word. Exercises can generally be divided into dynamic (resistance) or static (strength) exercise (1). In dynamic exercise there is a linear relationship between oxygen consumption and exercise intensity up to a maximum amount of oxygen an individual can consume (2). Factors affecting oxygen consumption ( $VO_2$ max) are being best represented by Fick's equation  $VO_2 = CO \times a-VO_2$ , where CO is cardiac output and  $a-VO_2$  is arteriovenous oxygen difference. Increase either CO, or further  $VO_2$  may increase oxygen consumption and improve performance. Maximal dynamic exercise result in four to six times increase of cardiac output, threefold increase in heart rate and double increase in stroke volume (3).

As mentioned above, cardiac output will increase with the increase in heart rate or stroke volume. A linear relationship exists between cardiac output / cardiac output and oxygen uptake. Cardiac output during exercise is largely associated with an increase of heart rate (4). The initial reaction of central nervous system (CNS) with the first exercise, results in reduction of vagal tone, and causes rapid increase in heart rate. These centrally mediated changes are associated with cerebral mechanisms and reflex changes are caused by the activation of mechanical receptors in skeletal muscle that are activated (5). As the exercise continues, sympathetic nervous system increases the level of activity, allowing a further increase in heart rate. In the early stages of exercise, cardiac output is increased secondary to the increase in

stroke volume. This is caused by increased venous inflow from activated skeletal muscle. The main cause of increased cardiac output during exercise in humans is the increased contractility of heart muscle and increased venous flow to the heart (2).

Overall increase in stroke volume from resting period to maximum exercise is usually 30% to 40% (6,7). During dynamic exercise, there is an increase in venous inflow, with redistribution of blood flow and venous volume from organs to active skeletal muscles (2). Relative blood flow remains constant in the brain, reduced to half in kidneys and intestinal organs, and increased in heart and skeletal muscles used for exercise up to 4-10 times, respectively (3,8,9). Increase of blood flow in heart and skeletal muscles caused by exercise is called exercise induced hyperemia (2).

Vasodilation and reduction of vascular resistance in active muscle causes a reduction in total peripheral resistance. An increase in systolic and mean arterial pressure and small reduction of diastolic blood pressure has been noticed (3). Changes in blood pressure are not linearly related to workload, because blood pressure is influenced by the magnitude of muscle mass changes (10). For example, dynamic exercise that is performed with the arms will cause a greater increase in blood pressure compared to those carried out by feet, because there is little reduction in total systemic vascular conductance, based on differences in muscle mass. Although we saw a big drop in systemic vascular resistance during dynamic exercise, mean arterial blood pressure actually increases, due to the greater effect of increased cardiac output.

## Materials and methods

A retrospective study has been conducted, and as a source of data the existing medical records of the Department of occupational health and safety of police officers of Sarajevo Canton were used, for the period 2006-2009 year. The study included 52 subjects, members of the police unit for special-purposes, who underwent ergometric exercise testing on a bicycle by WHO ramping protocol with electrodes in the Mason Likar positions using CardioSoft V4.2 program. Exercise testing was performed in the "Atrium" clinic in the morning.

Before the test, electrodes were placed to subjects in the Mason Likar positions.

Along with ergometric parameters the data on the subjective assessment of the load were monitored (SAO) under the modified Borg's scale (1973). To adapt the device for dosed load, examinees who had never been on the, had a chance to practice on cycle ergometer in 15-20 minutes, before the measurement. Schiebe (1986) stated that 10-15 minutes of exercise on cycle is enough of practice in order to adjust to the device. After the break, and 10 minutes of stretching, a multiphase exercise testing on a bicycle by WHO ramping protocol was conducted. The test is performed in a closed and ventilated room, with constant microclimatic conditions (18-21 ° C and 40-60% humidity).

Apparatus with a computer allows data to be displayed during the test numerically and graphically in real time on the computer screen and automatically stored in computer memory for later analysis. The above mentioned parameters can be monitored for each QRS cycle, but due to large amounts of data in this case, the same are divided over time intervals of 30 seconds, and maximum values of the parameters are related to the maximum value at a particular interval of 30 seconds. SAO is applicable in every sport, based on a scale from 6 (00)-20 (13). Values 6 (00) and 20 (13) were taken as the initial and final value of the scale due to the analogy with Rejeski Feeling Scale (FS) at rest (60) and at maximum load (200).

During the test, in addition to continuous monitoring of cardiofunctional parameters on the computer screen, monitor, a subjective sense of load of examinees using a modified Borg scale was monitored. Follow-up of the subjective overload feelings during the test provides important information about the tolerance of effort, and it turned out that the subjective sense of overload correlates with high energy consumption, heart rate and other physiological variables. The Borg scale has 15 categories of perception of intensity, and the same is located in a visible place in front of the subjects. Examinee at each stage of loading, on examiner's request, points by hand on the scale number that corresponds to his perception of the load. Before the test subjects are given written instructions for determining the subjective feelings of stress using a modified Borg's table. Measurement of

morphological characteristics of the examinees was conducted in accordance with the guidelines of the International Biological Program (IBP, Weiner and Lourie, 1969; Mišigoj-Duraković et al., 1996). Morphological measures that were used in the survey were measures of body height (cm) and body weight (kg).

Results are expressed as mean value and standard deviation in case of normal distributed continue variables, as median and IQR in case of non-normal distributed continue variables. The Kolmogorov-Smirnov statistic with a Lilliefors significance level was used for testing normality. In case of categorical variables, counts and percentages were reported. Statistical analysis comparing average values of the observed parameters to average population values was performed with One-Sample t-Test for continue normal distributed variables, with One-Sample Wilcoxon Signed Rank Test for continue non-normal distributed variables. A p-value <0.05 was considered as significant. Statistical analysis was performed by using the Statistical Package for the Social Sciences (SPSS Release 16.0; SPSS Inc., Chicago, Illinois, United States of America) software.

## Results

The mean age of examinees was 31.4±0.7 years. The mean body height of examinees was 183.3±0.8 cm, and the mean body weight of examinees was 86.7±1.5 kg. Out of the total number of examinees (n=52), 32 of them (61.5%) were overweight (BMI=25.0-29.9 kg/m<sup>2</sup>). Examinees had a significantly smaller mean of heart rate at rest [-4.9 bpm; 95% CI (-7.49; -2.35)] than the population (p<0.0001). Consisted with the workload of 50W, the examinees had a significantly higher mean of heart rate [10.6 bpm; 95% CI (6.91; 14.24)] higher value of heart rate than the population (p<0.0001).

Consisted with the workload of 75W, the examinees had significantly smaller mean of heart rate [-4.6 bpm; 95% CI (-7.78; -1.45)] than the population (p<0.01). At a workload of 100W, the examinees had significantly smaller mean of heart rate [-8.9 bpm; 95% CI (-11.71; -6.10)] than the population (p<0.0001). At a workload of 125W,



the examinees had significantly smaller mean of heart rate [-11.7 bpm; 95% CI (-14.43; -8.96)] than the population ( $p < 0.0001$ ). At a workload of 150W, the examinees had significantly smaller mean of heart rate [-12.9 bpm; 95% CI (-16.04; -9.77)] than the population ( $p < 0.0001$ ) (Figure 1).

At resting period, there is no statistically significant difference in median values of systolic pressure (mmHg) between the examinees (median=130; IQR=15) and the population ( $p > 0.05$ ). Consisted with the workload of 50W, there is a statistically significant difference in median values of systolic pressure (mmHg), between examinees (median=130; IQR=10) and the population ( $p < 0.0001$ ). At the workload of 75W, there is a statistically significant difference in median values of systolic pressure (mmHg), between examinees (median=137; IQR=11,3) and the population ( $p < 0.0001$ ) (Figure 2).

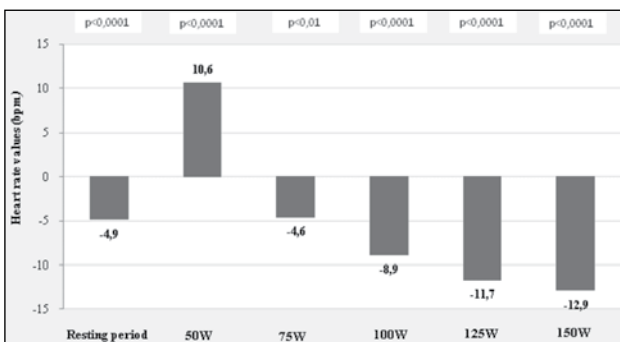


Figure 1. The difference of heart rate values (beats per minute) between examinees and the population

At a workload of 100W, there is a statistically significant difference in median values of systolic pressure (mmHg), between examinees (median=140; IQR=14,5) and the population ( $p < 0.0001$ ). Examinees had significantly smaller mean of systolic blood pressure [-24.3 mmHg; 95% CI (-27.57; -20.97)] than the population at a workload of 125 W ( $p < 0.0001$ ). Examinees had significantly smaller mean of systolic blood pressure [-27.9 mmHg; 95%CI (-31.57; -24.20)] than the population at a workload of 150W ( $p < 0.0001$ ).

At resting period, there is no statistically significant difference in the median value of diastolic blood pressure (mmHg), between examinees (median=75, IQR=10.0) and the population ( $p > 0.05$ ). At the workload of 50W, there is a statistically

significant difference in median values of diastolic blood pressure (mmHg), between examinees (median=78.5, IQR=5.0) and the population ( $p < 0.0001$ ). At the workload of 75W, there is a statistically significant difference in the median value of diastolic blood pressure (mmHg), between examinees (median=80.0, IQR=5.0) and the population ( $p < 0.0001$ ).

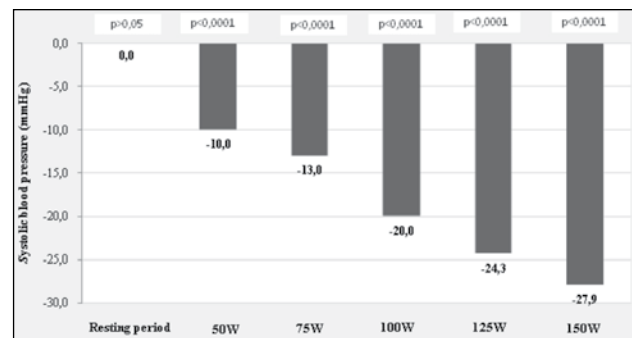


Figure 2. The difference of systolic blood pressure values between examinees and the population

At a workload of 100W, there is a statistically significant difference in the median value of diastolic blood pressure (mmHg), between examinees (median=80.0, IQR=0.0) and the population ( $p < 0.0001$ ). At a workload of 125W, there is a statistically significant difference in the median value of diastolic blood pressure (mmHg), between examinees (median=80.0, IQR=0.0) and the population ( $p < 0.0001$ ). At a workload of 150W, there is a statistically significant difference in the median value of diastolic blood pressure (mmHg), between examinees (median=80.0, IQR=3.8) and the population ( $p < 0.0001$ ) (Figure 3).

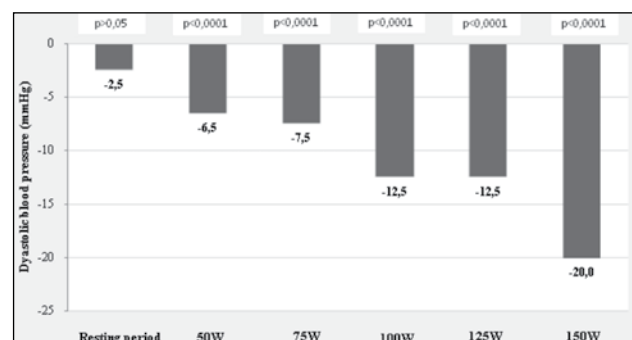


Figure 3. The difference of diastolic blood pressure values between examinees and the population

Out of the total number of subjects ( $n=52$ ), 35 examinees (67.3%) had a value of 19 on Borg sca-

le, 12 subjects or 23.1% had a value of 17, while only 5 subjects or 9.6% had a value 19 on the Borg scale (Figure 4).

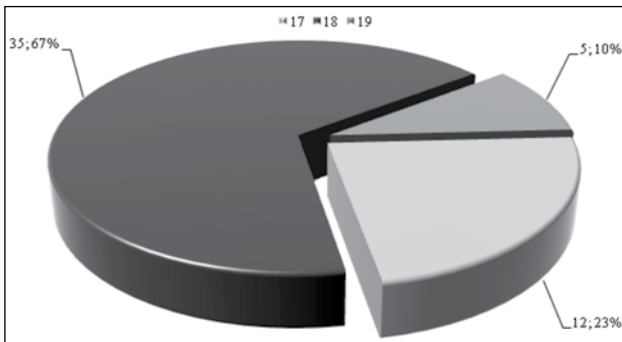


Figure 4. Structure of examinees according to the values on Borg's scale (n=52)

## Discussion

The data in our study indicate that with the level of significance  $\alpha=0.05$ , there is no significant difference in median values of systolic blood pressure at rest (mmHg) between the examinees and the population ( $p=0.964$ ). However, there is a statistically significant difference in median values of systolic blood pressure (mmHg) between the examinees and the population, with the load of 50W (-10.0 mmHg), 75W (-13.0 mmHg), 100W (-20.0 mmHg), and the difference between the mean values of the examinees and the population at workload of 125W (-24.3 mmHg) and 150W (-27.9 mmHg). There was no statistically significant difference in median values of diastolic blood pressure at rest (mmHg) between the examinees and the population ( $p=0.168$ ). However, there is a high significant difference in median values of diastolic blood pressure (mmHg) between the examinees and the population with the workload of 50 W (-6.5 mmHg), 75W (-7.5 mmHg), 100W (-12,5 mmHg), 125W (-12.5 mmHg) and 150W (-20.5 mmHg).

Studies on the influence of dynamic exercise on blood pressure have shown mixed results with respect to changes in systolic and diastolic blood pressure levels. Kelley and colleagues did a meta-analysis of the year 1995 to examine the effects of aerobic exercise on resting values of systolic and diastolic blood pressure in normotensive adults (11). In all other studies (randomized

controlled study, control cases and nontrained controls), systolic blood pressure was reduced by 4.4 mmHg, a diastolic blood pressure was reduced by 3.2 mmHg. These practicing groups also showed slight decrease in body weight, fat mass, and changes of 14% in peak oxygen consumption and 8% in heart rate at rest. The effect that these parameters had on blood pressure at rest was not a subject of debate.

Fagard in 1993. reported that aerobic exercise training caused a continuous drop in blood pressure, systolic blood pressure (SBP) and diastolic blood pressure (DBP) were decreased by an average of 3 mmHg in normotensive subjects, 6-7 mmHg in subjects with high normal blood pressure and 8-10 mmHg in subjects with documented hypertension (12). Although it is generally believed that dynamic exercise reduces blood pressure, studies that do not support this finding are common (13). Pescatello LS, JM Kulikowich in 2001. made an analysis to determine the subsequent effect of dynamic exercise on ambulatory blood pressure (14). Musso et al. believe that ambulatory blood pressure accurately reflects the blood pressure of persons held during daily activities (15). Meta-analysis of studies has raised concerns about several experimental insufficiencies within the various experimental studies and called on stricter way of investigation. However, the final conclusion of the study is that dynamic exercise shows that day, night, and 24-hour ambulatory blood pressure was reduced after exercise between the average white middle-aged men and women who are obese, and not taking medications. The reductions are most visible in hypertensive individuals and less visible in the normotensive population.

## Conclusion

Adaptation of the cardiovascular system to a standard work or the work of a certain intensity in the physiology of effort, a criterion of cardiovascular capabilities in a narrow sense and physical abilities of a person in a broader sense of the word. Data on kardivaskularnoj ability of a person are obtained from the load tests. Some tests are used to assess reactions of examinees to a given load intensity; the ability is even greater, if the re-

actions are less. Other tests are used to determine the intensity of cardiovascular adaptations during maximal performance; the ability is even greater if the relevant parameters may reach higher values.

The size of energetic capacities and the level of their use is quite different for different individuals. The knowledge about these characteristics is the basis for planning and implementing such forms of physical activity that will enable an increase in the optimal utilization of energetic capacity of the organism, which is of particular interest in the possibilities of improving the sport and business results.

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# Professionalism of the deaf persons in Bosnia and Herzegovina

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## Abstract

The paper analyzes the attitudes of deaf people on an apprenticeship. Applied to a sample of 122 deaf and hard of hearing tend to patients older than 20 years, with space in BiH. For the study questionnaire was used to examine attitudes regarding the choice of occupations. The aim was to determine the frequency of interest for people with hearing problems, work in the profession, years of service, and satisfaction with the choice of their own professions. The results showed that the prevailing unskilled workers, then, craft professions: tailor, cobbler, a locksmith, and autolimar Autolakirer, that most respondents have an average of up to 5 years of service. Values of chi-square test showed that there was a statistically significant difference between the obtained and expected results of test of attitudes on occupations of persons with hearing, that choice is limited to certain occupations and that most of these people are not satisfied with the choice of their own professions. Based on these results, it is necessary to thoroughly investigate the whole process of occupational rehabilitation of people with hearing problems in BiH, in order to determine possible causes of these attitudes and take action to resolve existing problems.

**Key words:** deaf people, professions.

## Introduction

Vocation Guidance of the Deaf is directing them as individuals to, according to their own preferences and capabilities, on the one hand, and social needs on the other hand, choose a profession where they have the most chance for success. In a study of the World Health Organization, UN, UNESCO, International Labor Organization on

children with hearing impairment, 1955. vol. emphasizes the "Aim of professional orientation (Vocation Guidance) of deaf young people is to ensure maximum opportunity for a satisfactory choice of one among the many occupations that come to mind, wherever possible, so that they can use their abilities to the highest level, but also keeping in mind market demand. Professional conversation or series of conversations with the candidate and his or hers parents should remain central activity. It is necessary to examine and take a look at their desires, in order to achieve the best plan of choice of occupation. First, assessment should be made for each individual about: habits, interests, preschool education, health, intelligence, general psychological status, etc." (Masovic, 1964).

The mentioned activities should be directed towards the primary goal, which is to make the most appropriate choice of profession, which will help as much as possible to reduce the differences between deaf and hearing people. (Hasanbegović, 2006). This is important, especially since today's scientific knowledge contribute to the better considering the influence of hearing loss on individuals, making it possible to deny the assertion that states Mašović (1964), the proverb "Man is what he does", in his opinion, due to difficulty in communications, deaf persons have no chance expressing themselves in the field of science, art, sports, etc., deaf person is left with only chance to experience affirmation through work, to which he/she has the same right. Good choice of profession should be most pronounced in children with hearing impairment, who really want to get information on specific occupations, and that is from a professional point of view, in accordance with their mental and physical abilities and other characteristics, which is determined by adequate monitoring and evaluation. Although

students with hearing loss have a desire for a profession, they are, at this age (end of primary school), often willing to accept occupation to which they are advised.

Based on the research conducted by Ivanovic (1987, according to Ivanovic, 1995), the largest number of 124 participants, have chosen their profession on their own (50%). About 30% of respondents relayed on parent's advice, while 15% have requested the assistance of the Association of the Deaf.

Counseling, as part of a professional orientation, according to Jakulić (1986), should deliver the following results: To alleviate the frustration that are common in deaf children; to solve professional status, through mitigation, or overcoming obstacles, realistic look at your own handicap, opportunities and requirements and to develop responsibility job that is to be performed.

Therefore, through consultation we try to avoid scenario in which the choice of future career is only influenced by current mood and interests of candidates, or, as is often the case, under the influence of parents' ambitions and the influence of a friend or someone else.

**Objectives:** To determine the frequency of interest for people with hearing disability in Bosnia and Herzegovina, working in the profession, years of service, and satisfaction with the choice of their own profession.

**Hypothesis:** It is assumed that there was no statistically significant difference between the obtained and expected results of a survey of attitudes about the occupations of persons with hearing disability, that career is not limited to certain professions, and that most of these people were satisfied with the choice of their own profession.

## Methods

### The sample of respondents

The research was performed on a sample of  $N = 122$  subjects who have hard of hearing condition and deaf persons, aged 20 years and older, from all over Bosnia and Herzegovina, randomly selected based on internal database run by associations of persons with hearing impairments. Given the age

of the respondents, that it is a working age and capable people, the chosen subjects are relevant for the respective test sample.

### Measuring instrument and method of conducting research

For this study used a questionnaire to investigate the relationship between educational and social status of the Deaf (Hasanbegović, Ahmetović 2009), with two systems of variables, where the first system, which consists of moderator variables of the basic characteristics of respondents, given the problem, were deemed important and used: age of participants, profession, position, years of service, and the second, which consists of 15 variables, which examines the educational and social status, we used three relevant variables.

These variables are modified according to the same direction, so that the respondents had the opportunity to answer the following statements: In the course of vocational rehabilitation hard of hearing and deaf person selection of profession is done adequately. Hard on hearing and deaf persons are not focused in a small number of occupations. I am satisfied with the very choice of my profession. For each statement three answers were offered: I cannot decide, yes and no. The study was conducted through the whole of Bosnia and Herzegovina, with the direct interviews method and during the interview assistance was provided by a professional sign language interpreter, by secretaries of associations of persons with hearing impairments and other professionals.

### Data processing methods

Survey data obtained were analyzed using parametric and nonparametric statistics. Descriptive analysis was used, calculated as frequencies and percentages, and performed in tabular and graphical display. To test the hypotheses is calculated chi-square test. The statistical analysis used by a computer statistical program SPSS for Windows 13.0.

**Results and discussion**

Table 1 shows the frequency of interest in the applied sample, from which it is evident that the sample was structured to largely dominated by unskilled workers (16 subjects), and then craft occupation: tailor (15 patients), cobbler (8 subjects), machinist (7 respondents), body mechanic and car painter (by 6 respondents).

In comparison to these results, research by Ivanovic (1987, according to Ivanovic, 1995) have shown that, in professions, the jobs are available in metal industry (35,55%), followed by textile industry with 30.67%, while all other professions fall under one third of the respondents.

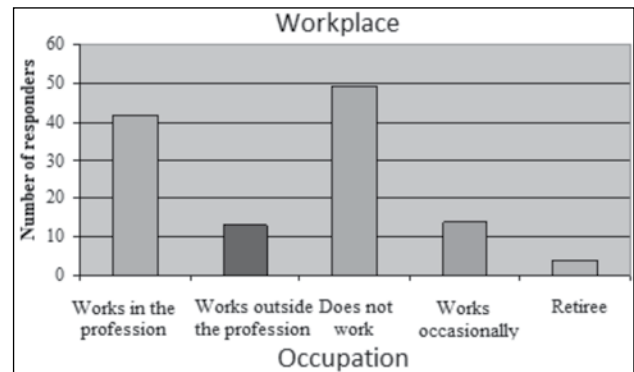
Characteristics of the sample hard of hearing and deaf subjects, when it comes to the workplace, and general work activities, shows that most respondents in relation to vocational training, do not working or working in some other profession (altogether 62.4%). Based on the total sample (N = 122), the profession is, or was 34.4% of responders is or was working in its profession, while only 3.3% has managed to earn a pension in its profession. This situation of working status raises questions of successful vocational guidance, employment and improving the social position of these individuals (Table 2 and Chart 1).

In relation to this research, in the research Ivanovic (1987, according to Ivanovic, 1995), points out that most respondents did not change job on which basis we conclude that most of them are absolutely

or relatively satisfied with their jobs, or did not have conditions and opportunities to change job.

*Table 2. The structure of the hard of hearing and deaf subjects in relation to the workplace*

	Workplace	Frequency	%
1.	Works in the profession	42	34,4
2.	Works outside the profession	13	10,7
3.	Does not work	49	40,2
4.	Works occasionally	14	11,5
5.	Retiree	4	3,3
	TOTAL	122	100,0



*Chart 1. Structure subsample hard of hearing and deaf subjects in relation to the workplace*

By looking at Table 3 and Chart 2 can be observed that the largest number of respondents had up to 5 years of service, which is considering the average age in relation to the total number of subjects, very unfavorable, but also indicative for further research in order to determine the causes of such poor employment.

*Table 1. The structure of the hard of hearing and deaf subjects in relation to interest*

Occupation	Number of respondents by occupation
Unskilled workforce (PS, etc.)	16
Tailor	15
Shoemaker	8
Locksmith	7
Body mechanic, Car painter	6
Sign painter, Tailor, Trader, Car mechanic	4
Painter, Plumber, Textile technician, Carpenter, Cook, Electrician	3
Hairdresser, Economist, Draftsman, Graphic artist, Typographer, Precision mechanic	2
Mechanical Engineer, Goldsmith, Watchmaker, Traffic Technician, Driver, Mason, Beautician, Photographer, Leathersmith, Graduated economist, Economics Technician, Administrative Technician, Bookbinder, Butcher, Optician, Special education teacher, Biology teacher, Soldier	1

Table 3. Structure subsample harder hard of hearing and deaf subjects compared to the years of service

Years of service		Frequency	%
1.	From 1 to 5 god.	36	29,5
2.	From 6 to 10 god.	20	16,4
3.	From 11 to 15 god.	9	7,4
4.	From 16 to 20 god.	16	13,1
5.	from 20 and more	8	6,6
6.	No working experience	33	27,0
TOTAL		122	100,0

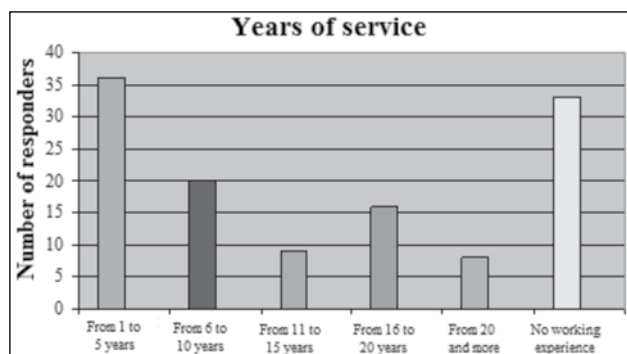


Chart 2. Structure subsample hard of hearing and deaf subjects in relation to the years of service

In order to assess the attitudes of hard of hearing and deaf persons towards their occupations, were applied three variables that intentionally indicate educational and social status. Based on these results we can conclude that their views were unfavorable, and that 70.5% of respondents believe that in the course of vocational rehabilitation of hard of hearing and deaf person does not perform an adequate choice of occupation, 78.7% of respondents believe that these persons are directed to small number of occupations, and 51.6% are not satisfied with the choice of occupations (Table 4, Chart 3).

The results of this study are compatible with studies of attitudes of deaf and hearing respondents, according Iličković (1999), which show that both subsamples stated that deaf persons are unjustly directed at a small number of occupations.

Table 4. Attitudes of hard of hearing and deaf responders about subjects on the occupations of people with hearing impairment

Num.	Variables	Undecided		Affirmative		Negative	
		f	%	f	%	f	%
1.	Adequate choice of occupation	18	14,8	18	14,8	86	70,5
2.	No guidance in a small number of occupations	17	13,9	9	7,4	96	78,7
3.	Satisfaction with career choice	26	21,3	33	27,0	63	51,6

However, these research is contradictory research conducted by Ivanovic (1987, according to Ivanovic, 1995), stating that the majority of hearing impaired individuals would again chose the same profession, indicating that most of them satisfied with their jobs, or that he or she got that job for which he or she was preparing and have chosen in the professional orientation. This assertion is confirmed by the research results of Majsec-Sobota (2005).

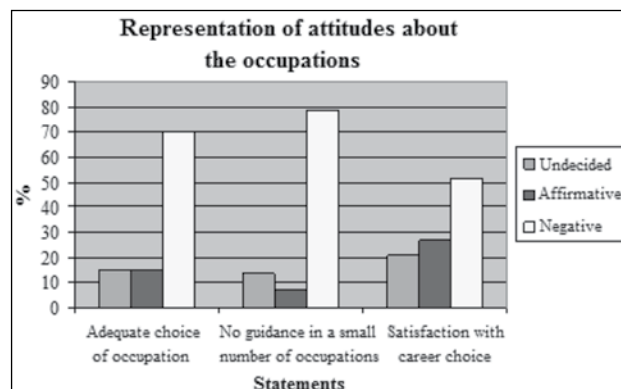


Chart 3. Percentage representation of attitudes of hard of hearing and deaf subjects about the occupations of persons with hearing impairments

On the basis of the frequencies on the assessment of attitudes of hard of hearing and deaf persons about their interests and expectations that the properties are normally distributed among subjects, we calculated the chi-square test for each variable individually. The values of  $X^2 = 20.49$ , for the first,  $X^2 = 48.16$ , for a second and  $X^2 = 190.95$  for the third variable are larger than the limit, with the level of significance of  $P = 0.01$ . Based on these results, the hypothesis that there was no statistically significant difference between the obtained and expected results of examination of attitudes about the occupation of a person with hearing impairment, i.e. that most respondents considered that the choice of occupation for severe hearing-

impaired and deaf persons in BiH is conducted in an appropriate way, that choice is not restricted to certain professions and most of these persons were satisfied with the choice of their own interest can be rejected.

### Conclusion

Descriptive statistics showed that the hard of hearing and deaf persons, are mostly unskilled and trade workers. Regardless of education level and type of occupation most of them do not work, or work outside their profession. Also, most of them have up to 5 years of service, and only a small number qualify for a pension. The results of Chi-square test showed hard of hearing and deaf persons feel that the career choice for people with hearing problems in BiH is not perform adequately, it is limited to certain professions and most of these persons are not satisfied with the selection of occupations. The causes of these results and opinions may be different. Current socio-economic reality in BiH, post-war transitional period can be one of these causes, but for the accurate determination of reasons, it is necessary to conduct comprehensive multi-disciplinary scientific research, in particular, to inspect and analyze the entire process of vocational rehabilitation of deaf persons.

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# The serum homocysteine concentration at haemodialysis patients

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## Abstract

At present study we measured serum concentration of homocysteine (tHcy), active form of cobalamines (Holo TC), albumine and creatinine in haemodialysis patients (men 25 and women 27) before dialysis and tHcy after dialysis. The measurement of total L-homocysteine in human serum was done using AxSYM fluorescence polarisation immunoassay (Abbott). The active form of cobalamines (Holo TC) in human serum was measured using AxSYM microparticle enzyme immunoassay (Abbott). The reference interval for blood tHcy concentration was 3.36-20.44  $\mu\text{mol/L}$  and Holo TC concentration was 19.1-119  $\text{pmol/L}$ . The albumine and creatinine were measured using Automatic Analyser Dimension (Dade Behring). The mean serum concentration before dialysis was tHcy  $28.9 \pm 22.6 \mu\text{mol/L}$ , albumine  $36.5 \pm 4.2 \text{ g/L}$ , and creatinine  $993 \pm 10 \mu\text{mol/L}$  and after dialysis tHcy  $18.1 \pm 4.1 \mu\text{mol/L}$ . Dialysis induced a significant reduction in tHcy of  $35 \pm 10 \%$  ( $P < 0.05$ ). Before haemodialysis about 40 patients have hyperhomocysteinemia and after dialysis only 10. The main difference between tHcy before and after dialysis was statistically significant for  $P < 0.05$  using Student t test with correlation coefficient ( $r = 0.95$ ). We found significant correlation between tHcy and mean serum concentration of Holo TC  $64 \pm 26 \text{ pmol/L}$  ( $r = -0.0937$ ,  $P < 0.05$ ). The elimination of Hcy from serum was improved after haemodialysis. The haemodialysis probably removes uremic toxins that inhibit activities of one or more enzymes of remethylation pathway (methionine synthase) and/or the transsulphuration pathway (cystathionine  $\beta$ -synthase).

**Key words:** homocysteine, cobalamines (Holo TC) and haemodialysis patients

## Sažetak

Studija je obuhvatala pacijente na hemodijalizi (25 muškaraca i 27 žena) kojima su prije dijalize određene serumske koncentracije homocisteina (tHcy), zatim aktivne forme kobalamina (Holo TC), albumina i kreatinina, a nakon dijalize koncentracija tHcy. Ukupni L-homocistein u humanom serumu je određen pomoću aparata AxSYM (Abbott) mjerenjem fluorescentne polarizacije. Aktivna forma kobalamina (Holo TC) u humanom serumu je određena korištenjem aparata AxSYM (Abbott) pomoću mikročestičnog enzimskog imunoeseja. Referentna vrijednost homocisteina u krvi je 3.36-20.44  $\mu\text{mol/L}$ , a za Holo TC je 19.1-119  $\text{pmol/L}$ . Albumin i kreatinin su određeni korištenjem automatskog analizatora Dimension (Dade Behring). Prosječne vrijednosti serumskih koncentracija prije dijalize su iznosile: tHcy  $28 \pm 22.6 \mu\text{mol/L}$ , albumina  $36.5 \pm 4.2 \text{ g/L}$  i kreatinina  $993 \pm 10 \mu\text{mol/L}$ , a nakon dijalize tHcy  $18.1 \pm 4.1 \mu\text{mol/L}$ . Dijaliza uzrokuje značajno smanjenje serumske koncentracije tHcy za  $35 \pm 10 \%$  ( $P < 0.05$ ). Prije dijalize je oko 40 pacijenata imalo hiperhomocisteinemiju, a nakon dijalize samo 10. Osnovna razlika između tHcy prije i nakon dijalize je statistički značajna za  $P < 0.05$  koristeći Student t test sa koeficijentom korelacije ( $r = 0.95$ ). Postoji značajna korelacija između tHcy i prosječne serumske koncentracije Holo TC  $64 \pm 26 \text{ pmol/L}$  ( $r = -0.0937$ ,  $P < 0.05$ ). Izlučivanje tHcy iz seruma je poboljšano nakon hemodijalize jer se postojećim tretmanom mogu ukloniti uremični toksini koji inhibiraju aktivnost jednog ili više enzima remetilacijskog (metionin sintaza) ili trans-sulfuracijskog puta (cistation  $\beta$ -sintaza).

**Ključne riječi:** homocistein, kobalamin (Holo TC) i hemodijalizirani pacijenti.

## Introduction

The amino acid homocysteine, which occurs by demethylation of methionine, essential amino acids which in human body enters with food. At the plasma circulates mainly in the oxidized state (homocysteine or homocysteine-cysteine disulfide) and bound with proteins. Approximately 75% of homocysteine is bound with plasma proteins, primarily to albumin. It was found that the kidneys play an important role in the metabolism of amino acids. More than 99% of amino acids in the proximal renal tubule are reabsorbed while around 5 mmol / L excreted in urine. The kidneys filter and metabolize homocysteine and the glomerular filtration rate of 125 ml / min to approximately 6  $\mu$ mol / L, or 1% of homocysteine, excreted in urine. During kidney damage in the event of disease, progression and the occurrence of acute renal failure (end-stage renal disease ESRD), the value of homocysteine growth for about 85%. At patients on dialysis ultimately we are expecting mild to moderate hyperhomocysteinemia.

The hyperhomocysteinemia is main atherothrombotic factor by patients with end-stage of renal disease (1,3).

Abnormal concentrations of homocysteine leads to the occurrence of atherosclerosis in at least 3 ways:

1. directly toxic effect of homocysteine on endothelium of arteries,
2. interference with clotting factors and
3. oxidation of low-density lipoprotein (LDL).

Therefore patients with kidney disease have high concentrations of homocysteine, the risk for cardiovascular disease is higher by about 30 times compared to the healthy population (4,5). Although there are data on homocysteine metabolism, the pathogenesis hyperhomocysteinemia still not clear. Homocysteine exceeds to methionine by remethylation; methyl group donor in most tissues is 5-methyltetrahydrofolate in the liver, kidney and eye lens is betaine. The reaction is catalyzed by methionine-synthase (MS) with cofactor vitamin B12. Tetrahydrofolate incurred exceeds the 5,10-methyltetrahydrofolate with the enzyme methylene-tetrahydrofolate reductase (MTHFR) and then in 5-methyl-tetrahydrofolate. Another pathway of homocysteine

metabolising is transsulphuration pathway where homocysteine with serine exceeds to cystathionine under the action of enzymes cystathionine- $\beta$ -synthase (CBS) and cofactor vitamin B6. After that cystathionine goes in to cysteine under the influence of the enzyme  $\gamma$ -cystathionase (GCT) (6-8). Homocysteine metabolism is regulated by the concentration of methionine that is normally used for protein synthesis and synthesis of S-adenosyl-methionine. Homocysteine lies at an intersection two of metabolic pathways, transsulphuration pathway and remethylation cycle, let alone the current availability of methionine depends which way will be metabolising of homocysteine. Decrease of folic acid and vitamin B12 leads to increase of homocysteine and decrease remethylation of homocysteine (9,10). Today there is interest in measuring the biologically active form of cobalamin. The vitamin B 12 (cobalamin) in serum is bound to two proteins, transcobalamin (TC) and haptocorrin (HC). About 20% of cobalamin is related to transcobalamin and it is biologically active, while 80% is related to haptocorrin is biologically inactive. The transcobalamin-vitamin B-12 complex is called holotranscobalamin (Holo Tc) and it is used in vitro diagnostic assay for the quantitative determination of cobalamin. The reduced concentration of Holo Tc, it is an indicator of deficit vitamin B 12. Notably, low values have been reported in vegetarians and populations with low intake of vitamin B 12. The tests for measuring total vitamin B 12 are based on the measurement of active and inactive fractions, but very often do not correlate with existing symptoms of the deficit. The reference area of vitamin B 12 is difficult to determine because it is too close to "normal" samples. Holo Tc levels reflect vitamin B 12 status, independent of recent absorption of the vitamin (11-15). The values of free and bound homocysteine rise in kidney diseases. Free homocysteine is filtered through the glomerulus and it has lower concentration. Although uraemic patients has low levels of albumin, the concentration of protein bound homocysteine is increased. It is considering that uremic toxins play a role in binding of homocysteine. Decline in glomerular filtration rate leads to a reduction in homocysteine degradation and increasing its concentration in the serum. (1). The patients with impaired renal function, especially on dialysis, have increased concentration of creatinine,

which can be 8-15 times higher than the reference. The concentration of creatinine must be determined in the morning before dialysis (16). The current study attempted to find a correlation between serum homocysteine concentration with concentrations of albumin and creatinine. Therefore, the vitamin B12 is cofactor during remethylation pathway of homocysteine, we determined concentration of vitamin B12 on the basis of its active form holotranscobalamin (Holo Tc).

## Material and methods

The value of serum homocysteine concentration was determined using AxSYM (Abbott), based on measurements of fluorescence polarization immunoassay (FPIA) technology. The reaction principle is conversion of homocystine, mixed disulfide and protein-bound forms of homocysteine in the sample to form of free homocysteine by the use of dithiothreitol (DTT). After that free homocysteine is converted to S-adenosyl-L-homocysteine (SAH). Under physiological conditions, SAH - hydrolases converts SAH to homocysteine. Existing methods is to determine L-homocysteine in human serum. Normal concentration of homocysteine in serum of women is 3.36-20.44  $\mu\text{mol} / \text{L}$  and in men is 5.90-16  $\mu\text{mol} / \text{L}$ .

AxSYM Holo Tc is microparticle enzyme immunoassay (MEIA) for the quantitative determination of human holo TC in serum and determination deficit of vitamin B 12.

Microparticles are coated with an Anti-Holo Tc monoclonal antibodies in the presence of human antigens on the Holo Tc microparticles arises immune complex. On Anti-Holo Tc antibodies present a conjugate of alkaline phosphatase in the next reaction, which reacts with the substrate 4-methylumbelliferyl phosphate (MUP). The resulting fluorescent product is measured by MEIA optical system. The reference value for the healthy population Holo Tc is 19.1-119  $\text{pmol} / \text{L}$  (12). Method for determination of creatinine is a modification of the kinetic reaction of Jaffee. The reference value for serum creatinine concentration is 45-115  $\mu\text{mol} / \text{L}$ . Albumins were determined using automatic analyzer Dimension (Dade Behring). The reaction occurs albumin-bromocresol green

that has a maximum absorption at 620-630 nm. The reference value for the concentration of albumin in serum is 35-50  $\text{g} / \text{L}$  (18).

The patient samples of blood were collected in serum separation Vacutainer test tubes (Beckton Dickinson, Rutherford, NJ 07,070 U.S.) in volume of 3.5 mL. The anticoagulant sodium - heparin or EDTA was used. After collection, samples were placed in ice and, after 30 to 60 minutes. Serum samples were obtained by centrifugation at 3000 rpm using centrifuge (Sigma 4-10). After centrifuging, serum concentration of homocysteine, active form cobalamina (Holo Tc), albumin and creatinine were determined. The homocysteine concentration was determined before after dialysis.

The investigation was done respecting ethical standards in the Helsinki Declaration. The study completed 25 men and 27 women (age 45-55 years). The retrospective study included patients who were hospitalized at Ptuj Hospital, Ptuj Slovenia at period of 2003-2004 year. The study was not included the patients on treatment with methotrexat, carbamazepine, phenytoin, and theophylline.

The results were statistically analyzed using Microsoft Excel and NCSS. Determined by the average value ( $\bar{x}$ ), standard deviation (SD), Pearson correlation coefficient (r), equations of linear regression and Student t test with statistical significance level of 0.05 ( $P < 0.05$ ).

## Results

The results of serum concentrations homocysteine, Holo TC, albumin and creatinine before dialysis and concentration of homocysteine after dialysis patients (25 men and 27 women) are shown in Table 1.

The mean serum concentration of homocysteine after dialysis was lower for  $35 \pm 10\%$  than before dialysis. The hyperhomocysteinemia was presented at 40 patients before dialysis and after at only 10 dialysis patients. Comparing the concentration of homocysteine before and after dialysis the linear regression equation was  $y = 1,1973x - 14,023$  and coefficient of correlation  $r = 0.95$ . The results of comparison of serum concentrations of homocysteine are shown in Figure 1.

Table 1. Serum concentration of biochemical parameters at haemodialysis patients

Mean serum concentration of biochemical parameters before dialysis (n=52) ( $\bar{x} \pm SD$ )			
Homocysteine	Holo Tc	Albumin	Creatinine
( $\mu\text{mol/L}$ )	( $\text{pmol/L}$ )	( $\text{g/L}$ )	( $\mu\text{mol/L}$ )
28.9 $\pm$ 22.6	64 $\pm$ 26	36.5 $\pm$ 4.2	993 $\pm$ 10
Mean serum concentration of biochemical parameters after dialysis ( $\mu\text{mol/L}$ ), $\bar{x} \pm SD$		18.1 $\pm$ 14.1	

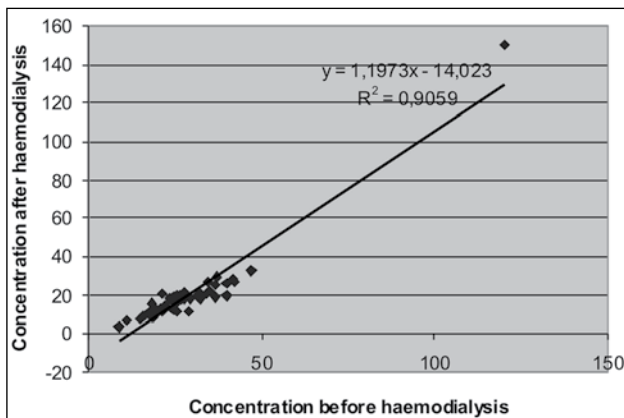


Figure 1. Comparison between homocysteine serum concentration ( $\mu\text{mol/L}$ ) before and after haemodialysis

Using Student t test, we get a statistically significant difference mean values of homocysteine before and after dialysis for  $P < 0.05$ . Found a significant correlation between the average values of homocysteine and Holo TC in serum before dialysis with the statistical significance of  $P < 0.05$  and correlation coefficient  $r = -0.0937$ . Established a significant correlation ( $r = 0.31$ ) between the mean values of homocysteine and serum albumin before dialysis. Correlation coefficient between the mean values of homocysteine and serum creatinine before dialysis was amounted  $r = 0.03$ .

## Discussion

Results of existing studies showed that hyperhomocysteinemia present in more than 90% of patients on haemodialysis. Hyperhomocysteinemia comprises 85-100% of patients on dialysis and is an independent cardiovascular risk factor uraemic patients. Cardiovascular disease causes 10-20 times higher mortality in patients with chronic renal insufficiency compared to patients with preserved renal function (19,20). When homocysteine con-

centration increase for 1  $\mu\text{mol/L}$  in patients with acute renal disease, increased risk for cardiovascular disease (1%) and mortality (3%) (21). The presence of vitamin B6, vitamin B12 and folic acid is necessary for maintain value of homocysteine in the reference area. The process of elimination of homocysteine is not explained deeply, and the enzymes necessary for homocysteine metabolism are mainly found in hepatocytes and cells of proximal tubules. Every day, kidneys is forming about 20 000  $\mu\text{mol}$  homocysteine, and about 1200  $\mu\text{mol/day}$  is excreted in the plasma. Possible explanation of origin hyperhomocysteinemia in uraemic patients with renal diseases is inhibition of enzymatic degradation of homocysteine. Specifically, uraemic toxins can lead to inhibition of one or more enzymes in the metabolism of homocysteine. Uremia reduces the elimination of amino acids by reduced glomerular filtration rate. This latter process tends to decrease the time of contact between amino acids and renal tubular cells, impairing the ability of these cells to take up and metabolize filtered amino acids. Increased tubular amino acid secretion may also theoretically contribute to the higher excretion rate of homocysteine (1,22).

Our results has showed that the average value of serum homocysteine concentration before dialysis was  $28.9 \pm 22.6 \mu\text{mol/L}$ , and after dialysis  $18.1 \pm 14.1 \mu\text{mol/L}$ . The value of homocysteine decreased for  $35 \pm 10\%$  after dialysis. According to some researchers the value of homocysteine before dialysis on average amounted to 22.5-26.3  $\mu\text{mol/L}$  after 15.6-19.4  $\mu\text{mol/L}$  (21,22). During dialysis the concentration of homocysteine is lowered for about 30-50% (1,18,23). Pearson correlation coefficient ( $r = 0.95$ ,  $P < 0.05$ ) indicates very good correlation of results for serum homocysteine before and after dialysis. Arnadottir and colleagues have found significant correlation between the value of homocysteine before and after dial-

ysis ( $r = 0.83$ ,  $P < 0.05$ ) (22). It is considered that dialysis can improve the clearance of homocysteine, a frequent dialysis can decrease serum homocysteine concentration and establishes a state of equilibrium (steady - state). Removing of uraemic inhibitory factors leads to the establishment of the normal metabolism of homocysteine (1). However, dialysis partially reduce homocysteine concentration, which gradually increases depending on the re-accumulation uraemic toxins (22). Other authors found a significant correlation (Pearson correlation coefficient) between serum concentrations of homocysteine, albumin and creatinine in patients on haemodialysis (24). Our results showed that the serum albumin concentration significantly correlated with the values of homocysteine ( $r = 0.31$ ,  $P < 0.05$ ), and similar outputs were confirmed by other research groups ( $r = 0.28-0.34$ ) (22). It is considered that albumin is the only variable that predicts the value of serum homocysteine with respect to individual differences of patients on hemodialysis, and depending on the diet. According to a given study, the correlation coefficient between the average values of homocysteine and serum creatinine before dialysis amounted to  $r = 0.03$ . Glomerular filtration rate is inversely proportionate to the concentration of homocysteine in the serum. Precursor in the synthesis of creatine is creatinine, and estimated that the creatine about 90% of the donor of methyl groups to S-adenosylmethionine. Furthermore, there is a close correlation between the concentration of S-adenosylmethionine and formation of homocysteine. Next study will show whether the reverse correlation with creatine homocysteine associated with glomerular filtration rate or biochemical metabolism (1). Holo Tc concentration in the existing study was in the reference area ( $64 \pm 26$  pmol / L), which excludes the presence of the deficit of vitamin B (12). Patients on haemodialysis take vitamins B therapy concentrations of cobalamin is in the reference area (22,25). However, due its significant role in the metabolism of homocysteine, it would be necessary to set it together with homocysteine.

## Conclusion

The current study showed a good correlation found homocysteine before and after dialysis. However, it would be possible to reduce the value could be predicted before completing dialysis. The elimination of homocysteine from serum is facilitated after haemodialysis, so such treatment may remove uraemic toxins with inhibitory activities against one or more enzymes of remethylation (methionine synthase) or transsulphuration pathway (cystathionine- $\beta$ -synthase). Although the values reduce serum homocysteine in hemodialysis, but after some time growth. More frequent dialysis, values of serum homocysteine may be possible to keep the reference area. In today's laboratory diagnostics of haemodialysis patients, in addition to albumin and creatinine, it is necessary the determining concentration of homocysteine and Holo Tc.

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# The efficiency of biologic therapy Infliximab in Rheumatoid Arthritis and Ankylosing Spondylitis - A case series

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## Abstract

**Background:** Infliximab is a chimeric anti-tumor necrosis factor (TNF- $\alpha$ ) (anti-TNF- $\alpha$ ) three-fourths human and one-fourth mouse protein, and is the only drug of that mechanism that is to be given intravenously. The main indications for infliximab therapy are rheumatoid arthritis, ankylosing spondylitis, psoriasis, psoriatic arthritis, colitis ulcerosa and Crohn's disease.

**Objective:** The purpose of this observational study was to examine the efficacy and safety of infliximab in ankylosing spondylitis (AS) and rheumatoid arthritis (RA).

**Methods:** Five patients with AS were treated with 5 mg infliximab infusion for 9 months in average and two patients with definite RA were treated with 3 mg infliximab infusion along with weekly 15 mg methotrexate injections for 17 months in average. Changes in CRP, ESR, adverse effects and clinical response were monitored in all patients. Disease severity in RA patients was measured using Disease Activity Score (DAS) and Health Assessment Questionnaire (HAQ).

**Results:** In AS patients, mean initial ESR of 104 mmHg and CRP of 71.8 mg/l were reduced to 27 mmHg and 3 mg/l respectively at the end of observation. In RA patients, the median initial DAS of 6.75 and HAQ of 1.75 was reduced to 4.21 and 0.93. No significant clinical adverse effect was attributed to this treatment in any patient.

**Conclusion:** Our case series supports results obtained from previous studies examining efficacy of infliximab in patients with RA and AS disease. Infliximab was effective in all patients with more prominent efficacy observed in patients

with AS than in RA. The authors did not observe any side effects. This small case series suggests that infliximab might be an optimal option for the treatment of AS and RA.

**Key words:** Infliximab, Rheumatoid arthritis, Spondylitis ankylosans

## Introduction

Infliximab is an anti-TNF- $\alpha$  antibody which is effective in certain autoimmune diseases (1). TNF- $\alpha$  is the main pro-inflammatory cytokine in RA, which stimulates the production of other pro-inflammatory cytokines. In combination with methotrexate, infliximab is approved for treatment in rheumatoid arthritis and in RA patients with reported ineffectiveness on one or more DMARDs (2). Its efficacy in RA was noted in reducing the disease activity, improvement of general physical function, reducing the further progression of joint damage and in prevention of deformities. In the treatment of ankylosing spondylitis, infliximab reduces non-specific inflammatory parameters with its beneficial effect on axial symptoms. Infliximab is not indicated in children under 17 years of age. This is the only anti-TNF- $\alpha$  which is given intravenously. The indications of infliximab are rheumatoid arthritis, ankylosing spondylitis, psoriasis, psoriatic arthritis, ulcerative colitis and Crohn's disease. Drug dosing for RA is 3 mg/kg body weight given by intravenous infusion for two hours followed by other administrations in a timely designed protocol. The dose for ankylosing spondylitis is 5 mg/kg/bw. The projected premedication with 200 mg of hydrocortisone, anti-histaminic and paracetamol was applied as well.

## Objective

The objective of this paper was to present our first experience in the application of biological medication Infliximab in inflammatory rheumatic disease, rheumatoid arthritis and ankylosing spondylitis.

## Methods

The combined retrospective- prospective clinical investigation and monitoring of patients suffering from inflammatory rheumatic diseases. There were 7 patients, 2 patients with rheumatoid arthritis and 5 patients with ankylosing spondylitis. All patients exhausted all possibility of conventional treatment including the cytotoxic drugs methotrexate. Subjects with RA using methotrexate continued to initiate therapy with Infliximab. In the group with RA, there were 2 female patients, mean age of 61 years old and average duration of disease of 12 years. The average dose of methotrexate was 15mg/weekly. The co-morbidity was present, (hypertension and insulin dependent diabetes mellitus), in one patient. In assessing disease severity of RA, we used DAS (4) score (number of painful joints, number of swollen joints, erythrocyte sedimentation rate and VAS scales for assessing the general status of the patient), and health assessment questionnaires (HAQ). In the group with ankylosing spondylitis, there were 5 patients in total with 4 males and 1 female included. The average age of patients was 34.6 years in total, of which 35.75 years for males and one female was 30 years old. The average duration of illness for all 5 patients amounted to AS was 12.4 years, with 14.25 years in the male group. The female patient's disease have been lasting for 5 years.

## Results

The total dose of Infliximab in 2 RA patients was 8 cycles. Disease activity score (DAS4 score) before treatment was 6.75 and the HAQ score of 1.75, corresponding to highly active disease. After therapy, the DAS score was 4.21, and 0.93 in HAQ.

The laboratory findings before treatment in the average value of ESR was 39, CRP 19.5, serum amyloid A 160, rheumatoid factor RF Latex 3860, and 1560 W. Rose. After therapy, the average sedimentation rate was 28mmHg. The observational therapy until now averages 34 months for both patients or almost 3 years in patient's years. In average 17 months each per patient were observed. In the group with ankylosing spondylitis, a total of 28 doses of Infliximab has been administered, with average 5.6 doses per patient. Total 44 months was observed so far with more than 3.5 years in observed patient years. The average duration amounted to 8.8 months per participant. Laboratory findings before treatment with infliximab averaged out red blood cells was 104mmHg and CRP 71.8 mg/l. After the therapy, the control sed rate was 27mmHg, and CRP 3mg/dl/l.

## Discussion

Our results, although on a small number of patients showed efficacy in all treated, while there has never been a side effect. This efficacy was higher in patients with AS compared to RA. Compared with results of other authors, the efficiency is about the same. As far as side effects, since we did not have any side effects so far, our results are encouraging because the other authors cited mild to moderate side effects. One possible explanation may be in adequate selection of patients for biological therapy. In the PROMPT study of Infliximab, the effect was detected after 48 hours and increased to 60-70% after 24 weeks in 558 patients. The average age of patients was 58 years with 78% of women involved RA in these patients lasted an average of 12 years (3). ASPIRE study on 1049 patients, average age 51 years with 72% of women showed a significant reduction of X-ray changes in Scharp's score.

In the group with MTX, Scharp's score was 4.53, while among MTX and infliximab Scharp's score was 1.25 (4). In the ASSERT study, Infliximab has proven to be effective in 201 patients with AS in the follow-up of 24 weeks, with mild to moderate side effects in 82.2% of cases (5). Significant improvement in enthesitis of AS have been recorded in the multicenter study (6). The increase



of transaminases in patients with RA was recorded in the treatment with infliximab, but there was no hepatitis (7). Cytokine TNF- $\alpha$  mRNA and protein were present in SI joints in AS (8). Infliximab in combination with methotrexate achieved the significant improvement in symptoms, functional status and quality of life in RA (9).

### Conclusion

Total time clearance accompanied by patients with rheumatoid arthritis and ankylosing spondylitis and is now 78 months or 6.5 patient years with an average of 11.14. Total 36 doses of Infliximab was administered.

The effectiveness of all patients reported the significance of improving in the subjective level, physical status, mobility, improved quality of life and in resuming work, as well as in the laboratory parameters reducing non-specific inflammatory parameters. The remission was achieved in all treated. No side effects were detected. In the comparison between the treatment of RA and AS, there is a greater efficacy in AS.

In conclusion, all patients who have received biologic drug infliximab, have recorded significant improvement in subjective and objective level as well as in the quality of life.

Given that, the therapy with NSAIDs, corticosteroids, DMARDs (methotrexate and sulphasalazine) was not adequately effective in non-responders, the only choice for these severe patients are biological agents (10, 11).

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# Analysis of projection of quantity medical waste generation in dependence on influencing factors

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## Abstract

Starting from the definition of statistics as a scientific discipline that deals with collection, analysis and interpretation of data mass occurrence and frequency of use of statistical methods in research and publications, and the need for studying the assessment amounts of medical waste generated in the period from 2010 - 2030. in health care facilities in the municipalities of Bijeljina, Ugljevik, Lopare and Zvornik, is created in this study.

In this study, you can find collected data on the generation of medical waste in health care facilities in these municipalities, in 2009. year. A survey is conducted, and then using simple linear regression models evaluating the effects of significant factors predicting the generation of medical waste in the period from 2010. 2030.

By calculating the Pearson correlation coefficient, determining and analyzing the function of the trend we have found that the number of individuals for each percent increases the total amount of medical waste generated for 145 tons per year, and the increase in GDP for each U.S. \$ 1,000 per capita, it increases the total amount of medical waste generated by 4 t / yr. Estimate of gross domestic product of 20,000 U.S. dollars per capita, a reduction in the total amount of medical waste generated, which can be explained by the presence of increasing trend of using modern technologies.

Based on these investigations, it can be concluded that a high increase in the generation of medical waste in most health facilities in the municipalities of Bijeljina, Brcko, Ugljevik, Lopare and Zvornik, due to the lack of recycling activities.

Management of health institutions need to make a decision on the performance of educational proce-

ss for staff at all levels in order to enable the separation and selection of medical waste on site.

**Key words:** Medical Waste Management, a linear regression model, estimate the amount of medical waste, the influencing factors.

## 1. Introduction

Medical Waste Management is a series of environmental challenges and it is getting more attention in most urban centers.

Medical waste includes all waste generated in health facilities, and a heterogeneous mixture of classic trash, infectious, pathological and laboratory waste, organic materials, packaging and other chemical waste. Between 75-90% of medical waste generated in health care activity is comparable to having solid waste (CCE) risk-free management, and the remaining 10-25% of the total amount of medical waste is considered potentially hazardous, which may be infectious, toxic or radioactive (1).

At the beginning of the XXI century in Bosnia a number of health facilities, at this time do not carry enough effort in managing medical waste in accordance with the recommendations of the World Health Organization (WHO) and EU Directives. Medical waste is not classified at source and in most cases it is collected along with CCE and ends without processing at the landfill, which poses a serious threat to environmental quality and public health.

The problems of medical waste management have been discussed in many studies. The main problems relate to lack of legal regulations for the medical separation of solid waste, lack of educational training of medical waste management in health institutions. (2)

Research in the Federation of Bosnia and Herzegovina (7) aimed to examine the manner of storage, transportation, disposal and control of infectious and laboratory waste in three major clinical centers: Sarajevo, Tuzla and Mostar. The results showed that 60% of infectious and laboratory waste is disposed together with household waste. In this way, this type of waste is a major epidemiological risk.

To establish a comprehensive system of healthcare waste management at the state level, the Federation, Canton and individual health institutions, it is first necessary to create legislation and regulations in order to accurately regulate the system of medical waste management. Studies report that the amount of medical waste generated varies in response to changes in legislation. (3,4,5,6) required the production of three-or five-year plan for disposal of infectious and other medical waste, as well as the development and application of detailed guidance on the principles of handling this type of waste at all levels of health care. (7)

In order to establish a proper model of medical waste management, it is necessary to define the relationships between the influencing factors: the economic status of the country, the annual population growth and the monetary allocation per capita.

In the municipalities of Bijeljina, Ugljevik, Lopare and Zvornik, conducted a survey to investigate and analyze the projected amount of medical waste, using selected factors. Thus, the projections showed increasing amounts of waste from 440 tons in 2010 to 470 tons of 2030.

## 2. Research Methodology

Starting from the definition of statistics as a scientific discipline that deals with the collection, analysis and interpretation of data mass phenomenon, given the frequent use of statistical methods in research and publications, research in this paper are based on collecting data through surveys in the municipality of Bijeljina, Brcko, Ugljevik, Lopare and Zvornik. In this territory is concentrated around 450,000 residents and 42 medical institutions, organized in primary and secondary levels of care, generating a greater amount of medical waste.

Some project team members are committed visits and interviews in each health institution in the

area above municipality from September to December 2009. year. The information referred to the waste management system, estimate the amount of waste, methods of collection and transport, reducing and recycling waste disposal methods and other operational requirements.

As a result of surveys conducted in 42 health facilities in these regions has led to the approximate amount of medical waste generated. The absence of monitoring the amount of generating leads to some inaccuracy of data, and should be taken with some reserve. Certain data obtained estimates were statistically reduced in these municipalities in order to improve estimation accuracy, and better impact on predicting the growth of the amount of waste generated.

The types and quantities of medical waste generated varies depending on the type of health facility. (8) Notice that most medical waste generated in the diagnosis, treatment and immunization of patients. Identified the following categories of waste: a pathological and infectious waste, sharps, pharmaceuticals, radioactive materials, pressure vessels, chemical waste and inert (general) waste. Table 1 summarizes the average total amount of medical waste per annum which is generated by the various medical facilities.

*Table 1. Summary of estimated average annual amount of medical waste*

Type of health facilities	Estimated total amount of medical waste (t / yr)
Health Centers	56,9
International dialysis center	71,4
Clinics	132,1
Hospitals	155,1
Ambulances	24,5
Total:	440,0

*Source: Research data 2009*

Many factors are involved in generating of medical waste, often build upon each other and require a comprehensive analysis. The aging population has no significant effect on the level of health expenditure to gross domestic product. (9)

In order to successfully budget projections of the amount of medical waste in the municipalities of Bijeljina, Brcko, Ugljevik, Lopare and Zvornik in the period from 2010 to 2030, it was incorpora-

ted into the budget impact of the most important factors for the generation of waste, particularly through the following parameters and values:

- Annual estimates of population trends
- The estimated current amount of waste per year (for 2010).

Estimates of population trends on an annual basis according to the Statistical Office of the Republic of Serbian in the period since 2000. by 2008. was shown in the diagram (Fig. 1).

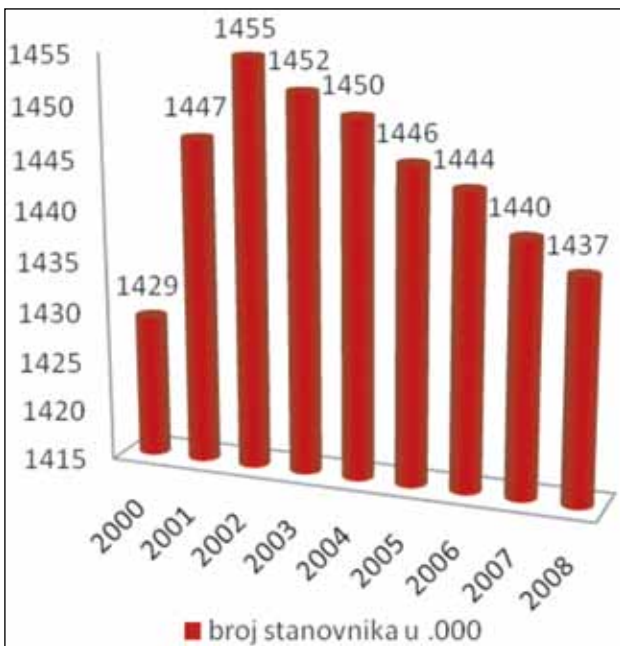


Figure 1. Population estimates of Serbian in the period since 2000. until 2008 is given in thousands (14)

Simple linear regression model can explain the impact of factors related to the estimated annual amount of medical waste growth, population growth, growth in gross domestic product per capita and spending per capita of gross domestic product, as important factors predicting.

Using simple regression models

$$Y = 330.5 + 145 X,$$

leads to the relationship to estimate parameters of the natural movement of population in the Republic of Serbian annually and the total amount of medical waste generated in the municipalities of Bijeljina, Brcko, Ugljevik, Lopare and Zvornik. From the raw input parameters can not be defined

properly dependence, and provides static further movement of this size. This value in the past nine years is extremely low for European and international standards. It is assumed that in the future lead to an increase of this parameter. The plan covers the period of the next 20 years and was divided into three groups according to the annual percentage growth in population:

- 2010th 2015. The population growth of 0.28% per annum,
- 2016th 2020. The population growth of 0.70% per annum,
- 2021st 2030. The population growth of 1.00% on annual level.

Based on the estimated amount of medical waste generated in 2010. year the amount of generated waste was calculated by 2030. year, using the annual percent population growth. It came to the data that the total amount of medical waste generated increased from 440 t / yr 2010th year to 470 tons per year 2030th year. (Fig. 2).

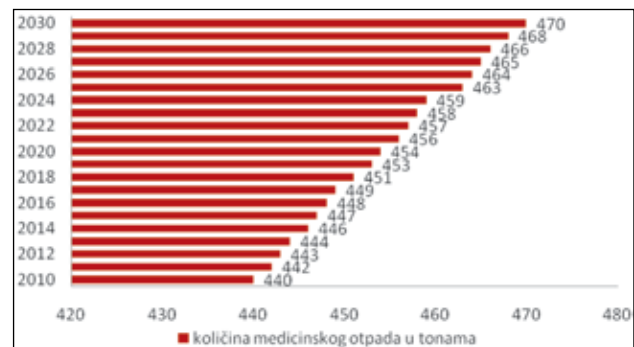


Figure 2. Growth projection of the total amount of medical waste generated in the period from 2010 to 2030

Research shows that the methods and analytical procedures, efficiency analysis, game theory, analysis of transaction costs, social costs, public choice econometric and statistical methods and others applied in health care, can provide new and interesting insights. (10)

### 3. Results

Generated amounts vary depending on the type of medical institutions and economic powers. The report published by WHO suggests that generate

medical waste directly proportional to the gross domestic product (GDP), ie. exclusion from gross domestic product per capita.

Budget projections for gross domestic product per capita should be incorporated into the estimated amount of medical waste generated in the model one-dimensional regression analysis.

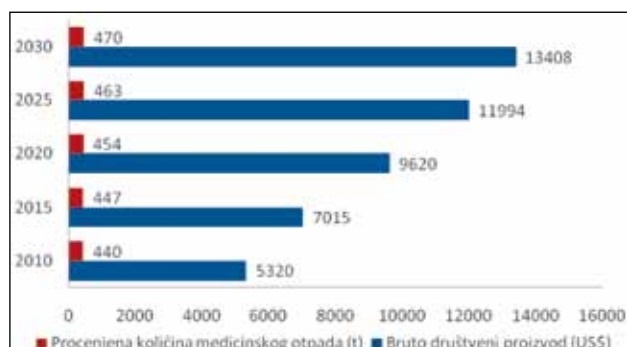


Figure 3. Estimates of gross domestic product per capita and the amount of medical waste generated in the period from 2010 to 2030

Table 2. Display gross domestic product and estimates of amounts of total medical waste generated from the projection to 2030.

Year	GDP per (U.S. \$) capita	The total quantity of waste generated (t/yr)
2010	5.320,00	440
2015	7.050,00	447
2020	9.620,00	454
2025	11.994,00	463
2030	13.408,00	470

Applying simple regression model

$$Y = 416.9 + 0.004 X,$$

leads to the relationship between the parameters of the gross domestic product per capita and the total amount of medical waste generated. If gross domestic product estimate, the amount of 20,000 U.S. dollars per capita, then the amount of medical waste generated by reducing the amount of 336.9 tons per year. Calculating the coefficient of determination-R2, it can be estimated depending on the amount of waste generated by the gross domestic product per capita. In this case the coefficient of determination was  $R^2 = 0.98$  and shows that the amount of medical waste generated depends on the gross domestic product in 98%, and that ot-

her factors affect from 2%. The model is representative, since the coefficient of determination is approximately one.

#### 4. Discussion

Although there are a number of different influencing factors on the generation of the total amount of medical waste in health care facilities in providing services, as the most influential factors are selected: the gross national product per capita and the annual population growth.

In the empirical part of the work is used the one-dimensional model of regression analysis, thus creating the preconditions for an explanation of the dependencies between these influencing factors.

By calculating the Pearson correlation coefficient, and determination and analysis of the trend function, we found that:

- Population growth for each percentage increases the total amount of medical waste generated for 145 t / yr.
- The increase in gross domestic product for each U.S. \$ 1,000 per capita, leads to an increase in the total amount of medical waste generated by 4 t / yr.
- Estimates of gross domestic product of 20,000 U.S. dollars per capita, a reduction in the total amount of medical waste generated, which can be explained by the presence of increasing trend of using modern technologies.

To achieve more efficient management of medical waste, it is proposed establishment of a database within the information system of health care institutions (11, 12). We also need education of human resources in order to adapt to learning in the modern digital environment (13).

#### 5. Conclusion

Based on these investigations, it can be concluded that there is a high increase in the generation of medical waste in most health facilities in the municipalities of Bijeljina, Brcko, Ugljevik, Lopare and Zvornik, due to the lack of recycling activities.

The share of potentially hazardous medical waste, which represents 10-25% of the total amount of medical waste, can be further reduced to 1-5% with the use of appropriate procedure of separation at source.

Health facilities do not have sufficient resources for the recycling of medical waste. There are not enough trained staff to manage medical waste.

It is essential that health facilities access to education of staff to the successful separation and selection of medical waste at source.

Given that health institutions are responsible for generating medical waste, it is necessary to make a serious effort to reduce the total amount and increase the degree of separation and segregation of medical waste.

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# Determination of total inorganic arsenic in ground water samples in Canton Sarajevo with a Field Spectrometric Device based on Gutzeit reaction

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## Abstract

There are several U.S. EPA approved methodologies for the determination of arsenic in ground water. Different determination methods of inorganic arsenic have been developed over 40 years providing timely and efficient risk assessments of inorganic arsenic contamination worldwide. The new  $10 \mu\text{g L}^{-1}$  (10 ppb) arsenic standard in drinking water according the WHO guideline value for arsenic in drinking water, has been a spur to the search for reliable routine analytical methods with a limit of detection at the  $1 \mu\text{g L}^{-1}$  level. This paper reports the results obtained with a simple procedure for determination of total arsenic in ground water samples using the spectrometric field device Supralab SD which was initially designed for the determination of arsenic in drinking water. The  $3\sigma$  detection limit of the developed method was  $0.1 \mu\text{g L}^{-1}$ . The time of As determination in the solution is about 5 min. To validate the results obtained with the field device, inductively coupled plasma mass spectrometry (ICPMS) was used as a reference method. Very good agreement between results was obtained.

**Key words:** Inorganic arsenic; ground water; toxicity of arsenic; arsenic pollution; arsenic test; As (V) /As (III); field device; SupraLab.

## Sažetak

Postoji nekoliko US EPA metodologija za određivanje arsena u podzemnim vodama. U toku

prethodnih 40 godina razvijene su širom svijeta različite metode određivanja anorganskog arsena zbog procjene rizika od anorganskog arsena. Novi standard prema smjernicama Svjetske Zdravstvene Organizacije (SZO) za vrijednosti arsena u vodi za piće od maksimalno  $10 \mu\text{g L}^{-1}$  (10 ppb) bio je poticaj za razvijanjem pouzdanih rutinskih analitičkih metoda s granicama detekcije na nivou  $1 \mu\text{g L}^{-1}$ . Ovaj rad izvještava o rezultatima jednostavnog postupka za određivanje ukupnog arsena u uzorcima voda pomoću terenskog uređaja Supralab SD spektrofotometrijskom metodom koji je prvobitno bio osmišljen za određivanje arsena u vodi za piće.  $3\sigma$  granica detekcije ove metode je  $0.1 \mu\text{g L}^{-1}$ , a vrijeme određivanja arsena u rastvoru je oko 5 min. Za validaciju dobijenih rezultata je kao referentna korištena ICPMS metoda. Dobijeno je vrlo dobro slaganje rezultata. **Ključne riječi:** Anorganski arsen, tekuće vode, toksičnost arsena, zagađenje arsenom; arsen test; As (V) /As (III); terenski SupraLab uređaj.

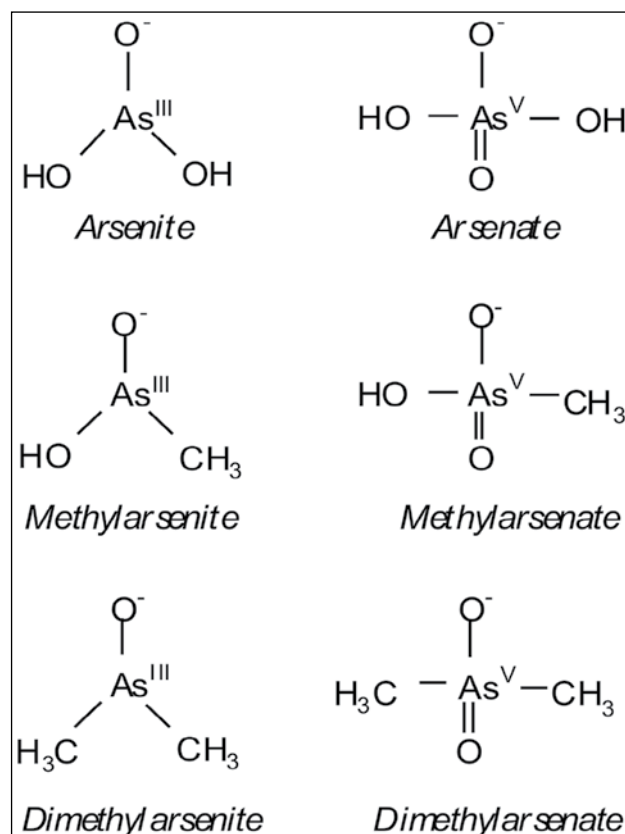
## 1. Introduction

The past decade is a period of eminent interest in a systematic monitoring of some areas polluted with highly toxic arsenic compounds [1]. Occurring of arsenic in subsurface aquifers and drinking water systems is a potentially serious human health hazard. The occurrence and biogeochemical cycling of arsenic in the environment is of continuing interest due to the world-wide consumption of arsenic

compounds from pesticides, including leather and wood treatments preservatives, glassware production, electronics industries, waste incineration and the amounts derived from volcanic emissions and fossil fuels have made arsenic be one of the abundant elements in pollution of environment [2,3,4]. Arsenic is a well-known toxic chemical that the Environmental Protection Agency (EPA) and the World Health Organization (WHO) list as a known carcinogen [5]. Arsenic is found in a wide variety of chemical forms throughout the environment that can be readily transformed by microbes, changes in geochemical conditions, and other environmental processes [6]. While arsenic occurs naturally, it also may be found as a result of a variety of industrial applications [7,8,9]. Man-made arsenic contamination results mainly from manufacturing metals and alloys, refining petroleum, and burning fossil fuels and wastes. These industrial activities have created a strong legacy of arsenic pollution around the world.

Living organisms are exposed to the toxic arsenic species primarily from food and water. Exposure to arsenic can cause many different health problems, including dermal changes, respiratory, cardiovascular, gastrointestinal, genotoxic, mutagenic and carcinogenic effects [10]. Some elements, even at trace levels, have negative or positive functions at various systems in human body [11–13]. Arsenic is known to cause negative effects in the human body even at a low intake level [14,15]. The toxicity of arsenic depends on its binding form. Inorganic forms of arsenic are more toxic than organic species, while arsenic (III) being more toxic than arsenic (V) [16,17]. Arsenates (V) are often isomorphic with phosphates; however, arsenates (V) are oxidants unlike phosphates. It is believed that toxicity of arsenates is caused by kinetic easiness of its reduction.  $\text{AsO}_4^{3-}$  can replace  $\text{PO}_4^{3-}$  in the cells where it is reduced to toxic As (III) compounds. Toxicity is the result of significant affinity of As (III) toward amino acids containing sulfur by inhibiting the activities of proteins [18]. In general, arsenates (V) are about 60 times less toxic than arsenates (III) [19]. Because of its toxicity and possible carcinogenicity, it is important to determine the species of inorganic arsenic (V) and arsenic (III), as well as organic arsenic in environmental samples including natural waters and biological fluids [20,21,22].

Arsenic occurs in the natural environment mostly in two oxidation states: As (V) and As (III). The mobility and toxicity of arsenic depend on its oxidation state, thus the behaviors of arsenic species would be changed depending on the biotic and abiotic conditions in water. In ground water, arsenic is predominantly present as As (III) and As (V) (Scheme 1), with a minor amount of methyl and dimethyl arsenic compounds being detected [23].



Scheme 1. Arsenic species found in water

In this work, we intend to make the initial monitoring of arsenic in some waters in the Canton of Sarajevo, in accordance with local and EU regulations related to water quality standards. Total inorganic arsenic in ground water samples was determined by the Field Spectrometric Device based on Gutzeit reaction [24].

## 2. Experimental

### 2.1. Arsine gas generation

Analytical method is based on the Gutzeit reaction, which means the conversion of inorganic ar-



senic (arsenate III and V) in the gaseous  $\text{AsH}_3$  and its reaction with mercuric bromide, immobilized in InMem membrane, to yellowish-brown product formulated as  $\text{As}(\text{HgBr})_n\text{H}_{3-n}$  which is detectable by spectrophotometrically. Reduction of arsenate (V) and arsenate (III) to arsine is accelerated by sodium tetrahydridoborate (Sodium Borohydride). Sulfide, which is often present in water, is eliminated by absorption through ReMem membrane.

## 2.2. Apparatus and methods

Field device Supralab SD (HELMOTEC, Kalsdorf, Austria) was used for measurements of As in water samples. Erlenmeyer flask (100 mL) as part of the instrument is used to generate the hydride. Sodium tetrahydroborate reagent is added to the sample solution in the form of tablets that simplifies the measurements on terrain. The main part of the device is a filter impregnated with mercuric bromide. Impregnated paper, LED (Light Emitting Diode) and a photodiode are arranged axially in the measuring cell which was placed on Erlenmeyer flask where Arsine is generated. Arsine enters the cell and passes through the filter impregnated with mercuric bromide, forming a yellowish-brown product, whose color intensity is measured with the LED and photodiode in transmittance mode.

As a comparative and a control method for the determination of arsenic in water samples, Inductively Coupled Plasma Mass Spectrometry ICP-MS (Hewlett Packard 4500) was used.

## 2.3. Reagents and Materials

Impregnated membranes (InMem, ReMem) and the Sodium tetrahydroborate tablets (HyGen) were obtained from Helmotec. Deionised water was purified with a cartridge system from NANO-pure BARNSTEAD.

Water samples were tested on the same day after collection, with no pretreatments. Testing has shown that there are no differences in the content of arsenic when the samples were stored in the refrigerator for several days

## 3. Results and discussion

### 3.1 Arsenic content in Sarajevo Canton Rivers

The ground water samples collected from the rivers in Canton Sarajevo are measured with arsenator Supralab. Three repeated measurements of each sample gave a standard deviation less than 0.3 ppb for concentrations up to 3.0 ppb, the standard deviation of 4.0 ppb for the concentration to 42 ppb and standard deviation of 65.25 ppb for concentrations up to 760 ppb in the thermal baths water.

The results of arsenic contents (Table 1.) in main ground waters in the Canton Sarajevo, that accumulate numerous smaller tributaries, showed generally low arsenic level by the criteria of local [25] as well as EU standards.

Unlike ground water with relatively low content of arsenic, the measurements extended to mineral, thermal and drinking fountain waters showed different, in some case, problematical levels of arsenic.

### 3.2 Arsenic content in Mineral water from the store

Table 2. shows the contents of arsenic in mineral water "Ilidža Diamant" is very close to 50 ppb, which is almost five times more than the permitted content in relation to the standards mentioned above. Clearly, in such cases, the treatment plant to remove excess of arsenic from water has to be installed.

### 3.3 Arsenic in Drinking fountain water

In the cases of some public "drinking fountain" it turned out that one of the tested has higher arsenic content than allowed in the appropriate standards (Table 3.) which also implies control of all public drinking water in arsenic content in BiH.

### 3.4 Arsenic in Thermal bath water

There are many reports describing the possible relationship between skin cancer and the water

Table 1. Arsenic content in Sarajevo Canton Rivers

As [ppb] in sampling points										
RIVER ŽELJEZNICA										
sample	1	2	3	4	5	6	7	8	9	
I	<0.20	<0.20	0.20	0.20	0.40	1.2	<0.20	<0.20	<0.20	
II	<0.20	<0.20	0.20	0.20	<0.20	1.1	<0.20	<0.20	<0.20	
III	<0.20	<0.20	0.20	0.20	0.30	1.3	<0.20	<0.20	<0.20	
St.dev.	Indef.	Indef.	0.00	0.00	Indef.	0.1	Indef.	Indef.	Indef.	
RIVER BOSNA										
I	<0.20	2.2	2.2	2.0	1.9	2.6	1.6	2.2	2.1	1.9
II	<0.20	1.9	2.3	2.2	1.5	2.0	1.8	1.8	1.7	1.9
III	<0.20	1.8	1.8	1.9	1.9	2.4	1.8	1.6	1.8	1.8
St.dev.	Indef.	0.208	0.264	0.152	0.230	0.305	0.115	0.305	0.208	0.057
RIVER MILJACKA										
I	0.4	0.3	0.9	0.3	0.4	0.8	0.2			
II	0.5	0.4	0.8	0.3	0.4	0.8	<0.2			
III	0.4	0.3	0.7	0.3	0.5	0.9	<0.2			
St. dev.	0.057	0.057	0.100	0.000	0.057	0.057	Indefinite			
RIVER DOBRINJA										
I	0.4	0.5	0.5	0.3	0.3	0.4				
II	0.4	0.3	0.4	0.4	0.3	0.3				
III	0.3	0.4	0.5	0.3	0.5	0.3				
St. dev.	0.057	0.100	0.057	0.057	0.115	0.057				
RIVER LJUBINA										
I	<0.2	<0.2	0.3							
II	<0.2	<0.2	0.2							
III	<0.2	<0.2	0.2							
St. dev.	Indef.	Indef.	0.057							
RIVER VOGOŠĆA										
			Radića potok							
I	<0.2	0.3	<0.2							
II	<0.2	0.2	<0.2							
III	<0.2	0.2	<0.2							
St. dev.	Indef.	0.057	Indef.							
RIVER ZUJEVINA										
						Žunovačka rijeka				
I	0.2	0.2	1.2	0.2	0.5	0.2				
II	<0.2	<0.2	1.0	<0.2	0.4	0.2				
III	<0.2	<0.2	1.1	<0.2	0.4	<0.2				
St. dev.	Indef.	Indef.	0.100	Indef.	0.058	Indef.				

Table 2. As content in Mineral water from the store [ppb]

Mineral water from the store As [ppb]						
Sample	Olimpija	Ilidža's diamant (2011)	Ilidža's diamant (2010)	Ilidža's diamant (2009)	Tešanj's diamant (2010)	Sarajevo's „Natural spring water“ (2010)
I	1.9	48.6	34.4	28.1	0.4	7.4
II	1.9	49.7	39.3	29.8	0.3	7.9
III	1.9	50.0	42.4	28.7	0.3	8.2
St. dev.	0.00	0.74	4.03	0.86	0.05	0.40

Table 3. Drinking fountain

Drinking fountain As [ppb]						
Sample	Srednje	Trnovo	Ozimine	Begova džamija	Brestovac Vogošća	Česma Barice
I	13.9	<0.2	<0.2	1,4	<0,2	<0,2
II	13.1	<0.2	<0.2	1,4	<0,2	<0,2
III	12.6	<0.2	<0.2	1,3	<0,2	<0,2
IV	11.4	<0.2	<0.2	-	-	-
St. dev.	1.04	Indef.	Indef.	0.06	Indef.	Indef.

Table 4. Thermal bath

THERMAL BATH - As [ppb]						
Sample	ILIDŽA			FOJNICA	OLOVO	KAKANJ
	1 2009	2 2010	3 2011	1 2010	1 2010	1 2010
I	670	760	640	61	1.2	40.4
II	595	630	625	53	0.9	40.2
III	630	685	625	60	1.1	41.9
St.dev.	37.52	65.25	8.67	4.35	0.15	0.93

Table 5. Comparative measurements

Water sample	METHOD	
	Supralab SD field device	ICP-MS
Drinking water	1.53 ± 0.06 ppb	2.30 ppb
Ilidžanski dijamant	49.43 ± 0.74 ppb	52.00 ppb
Terme Ilidža	630.0 ± 8.66 ppb	630.00 ppb

containing arsenic especially thermal baths which have an increased content of arsenic. However, there is little explicit evidence about the relationship of skin cancer and dermal absorption of arsenic. According to the DES Environmental Health Program, the concentration of arsenic in water used for bathing, laundry, dishwashing, and other non-consumptive uses should be less than 0.500 mg / L (500 ppb) [26]. In this sense, thermal water in Ilidža bath has significantly increased content of arsenic (about 50% above, according DES Environmental Health Program) which would certainly have been the subject of serious investigation on possible effect of arsenic for people health.

### 3.5 Comparative measurements

As a comparative method for the determination of arsenic, ICP-MS method was used. Table 5. shows the good agreement of results, unlike

expected difference due to close values of detection limit and the measured contents of arsenic in the case of drinking water.

## 4. Conclusion

Spectrometric field device Supralab SD, used in this work for determination arsenic in ground water samples, has shown vary good reproducibility, sensitivity and good  $3\sigma$  detection limit of  $0.1 \mu\text{g L}^{-1}$ . As the results with real samples have demonstrated, the Arsenator method is reliable, accurate and precise although it is primarily field method. Compared to other determination methods of inorganic arsenic in water samples, the method presented here appears to offer some advantages. It is mobile, simple to use, inexpensive. This is important to control the levels of arsenic in water from region because of man-made arsenic contamination have growing tendency. The

contents of arsenic in drinking water, measured here, are acceptable under EU standards, but the concentration of arsenic in some drinking mineral and thermal water are not. The results presented in this paper imply further measurements of arsenic in water extended to all publicly accessible drinking water and thermal water. Increased content of arsenic presented here requires further studies of effects of arsenic-contaminated thermal bath and other water on human health. Our results should initiate urgent actions on water treatments according to standards and health risks.

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# Antimicrobial susceptibility of *E. coli* and *Klebsiella pneumoniae* strains isolated from urine samples

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## Abstract

Urinary tract infections, along with respiratory tract infections, are the most frequent bacterial infections and they are a reason for empirical prescription of large quantities of antimicrobial medications. About 50% of women suffer from urinary tract infections at least once in their lifetime and 40-60% of all hospital infections refer to urinary infections. This paper presents the results of microbiological examination of urine at the Microbiological Laboratory of the Cantonal Hospital in Zenica, in the period 2005 – 2007. Urine samples of 164 patients treated in and out of the hospital were microbiologically examined, as well as urine samples of 382 individuals treated out of hospital, in the period of 2009. The isolated strains of *E. coli* in hospital-treated patients (2005-2007) are the most resistant to ampicillin, amoxicillin and trimethoprim/sulfamethoxazole, in the range of 79.4 to 51.3%, while the percentage of resistance to other tested antibiotics ranged between 37.5 and 10.5%. *E. coli* still has not developed resistance to nitrofurantoin and imipenem. Isolated strains of *K. pneumoniae* in the same patients are significantly resistant to all tested antibiotics, except the resistance of 30.8% to amoxiclav and the lack of resistance to imipenem. The isolated strains of *E. coli* in ambulance-treated individuals are the most resistant to ampicillin, amoxicillin and trimethoprim/sulfamethoxazole, in the range of 69.0 to 51.1%, while the percentage of resistance to other tested antibiotics ranged between 16.6 and 2.5%. *E. coli* still has not developed resistance

to imipenem. Isolated strains of *K. pneumoniae* are resistant to ampicillin in 60.0% of cases, and the results of testing other antibiotics refer to resistance in the range between 40 and 10%. *K. pneumoniae* is completely susceptible to imipenem. The isolated strains of *E. coli* in the period of 2009 were the most resistant to amoxicillin (68.4%) and trimethoprim/sulfamethoxazole (47.4%), while the percentage of resistance to other tested antibiotics ranged between 17.4 and 1.3%. Isolated strains of *K. pneumoniae* are significantly resistant to amoxicillin (70.6%) and trimethoprim/sulfamethoxazole (35.3%), while the percentage of resistance to other antibiotics ranged between 20.6 and 11.4%.

**Key words:** *Escherichia coli*, *Klebsiella pneumoniae*, urinary tract infections, antibiotic resistance

## 1. Introduction

Urinary tract infections (UTI), along with respiratory tract infections, are the most frequent bacterial infections and they are a reason for empirical prescription of large quantities of antimicrobial medications. About 50% of women suffer from urinary tract infections at least once in their lifetime and 40-60% of all hospital infections refer to urinary infections. These infections are localized in any part of urinary tract and include a number of clinical syndromes and diseases, which defer depending on disorder severity, general symptoms, recurrence tendency, complication risks, re-

sult and prognosis. Urinary tract infection can be symptomatic or asymptomatic, uncomplicated or complicated. The most frequent infections occur in healthy population of women, during their reproductive age. Etiological agents of UTI include the bacteria from *Enterobacteriaceae* family that are a constituent part of intestinal physiological flora. *E. coli* causes about 80% of nonhospital urinary infection cases, both in uncomplicated (50-90%) and complicated infections, as well as 40% of hospital-acquired UTI. Beside the mentioned bacterium, UTI can also be caused by *Klebsiella spp*, *Proteus spp*, *Enterobacter spp* and other enterobacteria, as well as *Pseudomonas spp* or certain representatives of Gram-positive bacteria (*Staphylococcus saprophyticus*, enterococci, etc.). *Chlamydia trachomatis*, *Ureaplasma urealyticum* or some fungi species are also potential causal agents of the infections. All mentioned infections need to be treated. Goal of the therapy is to eliminate clinical symptoms, to eradicate the causal agent and to prevent complications and recurrence. While prescribing a medication, it is important to know the infected individual, causal agent of the infection, type of empirical therapy, as well as features of the medication itself. This implies the range of antimicrobial effects of a medication, possible combinations with other medications, adverse effects, side-effects and contraindications for its application. At the beginning of UTI treatment, doctors often decide to apply empirical therapy that would be corrected, continued or completely cancelled, depending on results of microbiological analysis. Therefore, it is necessary to follow-up on bacterial resistance to certain antimicrobics, those that are currently applied in empirical therapy of UTI, all in order to prescribe the medications rationally and efficiently (1, 2, 3, 4, 5, 6, 7).

Confirmation of the urinary tract infection implies microbiological detection of bacterium in biological material by examination of urine, i.e. by performing urinoculture. Follow-up on susceptibility/resistance of isolated strains of certain bacterial species is performed using the Kirby-Bauer disk-diffusion method and adequate laboratory recommendations (8, 9).

## 2. Goals of the study

Microbiological examination of urine of the patients with corresponding clinical suspicion of urinary infection, in order to identify the most frequent causal agents of UTI, as well as evaluation of their antimicrobial susceptibility to the antimicrobics tested.

## 3. Material and methods

This paper presents the results of microbiological examination of urine at the Microbiological Laboratory of the Cantonal Hospital in Zenica, in the period 2005 – 2007. Urine samples Of 164 patients treated in and out of the hospital were microbiologically examined, as well as urine samples of 382 individuals treated out of hospital, in the period of 2009. Medium urine stream was collected by the act of urination for microbiological examination. After being transported to the laboratory, the urine samples were microscopically and culturally examined. Result of the examination of microscopic preparation of urine provides an insight into possible presence of bacteria, approximate number in 1 ml of urine, as well as the presence of inflammation elements or other microorganisms. In accordance with the WHO recommendations, Geneva, 1991, filter paper strip method of Leigh and Williams was applied for determination of the overall number of bacteria in 1 ml of urine. A filter strip moistened by urine is pressed against the adequate medium of nutrient blood agar for 2-3 seconds. Inoculated agar is then incubated at 35-37°C for 24 h and the number of grown bacterial colonies is read in accordance with the scheme provided. Urine samples, in which significant number of bacteria is confirmed, are cultivated on Endo agar and incubated at 35-37°C for 24 h. After the incubation, the grown colonies are identified based on biochemical-physiological features, relation towards free oxygen, growth temperature, concentration of hydrogen ions, etc. For every isolated bacterial strain, their susceptibility/resistance to corresponding representatives of antimicrobial medication groups was tested by disk-diffusion method. Isolated bacterial strains were tested to some of the antibiotics: amoxicillin, ampicillin, gentamycin, trimethoprim/sulfamethoxazole,

nitrofurantoin, cefalexin, ciprofloxacin, pefloxacin, cefuroxim, imipenem, amoxiclav. Result of the test is presented as R (resistant), S (susceptible) and I (moderately susceptible) (8, 9).

#### 4. Results

In the period 2005 – 2007, results of positive isolation of bacteria from 164 urine samples of the patients treated in and out of the hospital were analyzed. Non-microbial infection was found in 104 or 93.6% of the patients treated in hospital and polymicrobial infection was found in 7 patients. Gram-negative bacteria were isolated in over 98% of cases, in the overall number of isolated bacterial species. The highest percentage of isolated strains in 104 patients treated in hospital referred to *E. coli* (38.5%), while *Klebsiella pneumoniae* was isolated in 12.5% of cases (Table 1).

Table 1. Percentage of individual causal agents of urinary infections in hospital-treated patients with non-microbial infection in the period 2005 – 2007

Species of isolated causal agents	Number of samples	%
<i>Escherichia coli</i>	40	38.5
<i>Proteus spp.</i>	20	19.3
<i>Pseudomonas spp.</i>	14	13.6
<i>Klebsiella pneumoniae</i>	13	12.5
<i>Enterobacter spp.</i>	7	6.8
<i>Citrobacter spp.</i>	5	4.8
<i>Morganella morganii</i>	1	0.9
<i>Acinetobacter spp.</i>	1	0.9
<i>Alcaligenes faecalis</i>	1	0.9
<i>Enterococcus faecalis</i>	1	0.9
<i>Staphylococcus aureus</i>	1	0.9
<b>Total:</b>	<b>104</b>	<b>100.0</b>

In the study period (2005 – 2007) that involved 53 ambulance-treated individuals, *E. coli* was isolated in 81.1% and *Klebsiella pneumoniae* in 18.9% of the individuals (Table 2).

In 2009, 382 individuals were tested at the same medical center, with the corresponding number of urine samples with confirmed UTI. *E. coli* was isolated in 80.1% of individuals, while *Klebsiella pneumoniae* was isolated in 9.1% of individuals, out of the overall number of isolated bacterial strains (Table 3). Comparing the results of percentage

of *E. coli* and *K. pneumoniae* in ambulance-treated individuals in the period 2005 – 2007 and hospital- and ambulance-treated patients in the period of 2009, it is evident that *E. coli* was present in 81.1% in the first group and 89.8% in the second group, while *K. pneumoniae* was present in 18.9% in the first group and 10.2% in the second group.

Table 2. Percentage of individual causal agents of urinary infections in ambulance-treated individuals in the period 2005 – 2007

Species of isolated causal agents	Number	%
<i>Escherichia coli</i>	43	81.1
<i>Klebsiella pneumoniae</i>	10	18.9
<b>Total:</b>	<b>53</b>	<b>100.0</b>

Table 3. Percentage of individual causal agents of urinary infections in 382 hospital- and ambulance-treated patients with non-microbial infection in the period of 2009

Species of isolated causal agents	Number	%
<i>Escherichia coli</i>	306	80.1
<i>Klebsiella pneumoniae</i>	35	9.1
<i>Proteus spp.</i>	29	7.6
<i>Pseudomonas spp.</i>	12	3.1
<b>Total:</b>	<b>382</b>	<b>100.0</b>

In the period 2005 – 2007, susceptibility/resistance of isolated strains of *E. coli* and *Klebsiella pneumoniae* in hospital- and ambulance-treated patients was tested to some of the antibiotics using the disk-diffusion method (Table 4, Table 5, Table 6, Table 7).

In the period of 2009, susceptibility/resistance of isolated strains of *E. coli* and *Klebsiella pneumoniae* to antibiotics applied in testing of enterobacteria was tested using the disk-diffusion method (Table 8, Table 9).

Tables 4 and 5 suggest that the isolated strains of *E. coli* in hospital-treated patients in the period of 2005 – 2007 are the most resistant to ampicillin, amoxicillin and trimethoprim/sulfamethoxazole, in the range of 79.4 to 51.3%, while the percentage of resistance to other tested antibiotics ranged between 37.5 and 10.5%. *E. coli* still has not developed resistance to nitrofurantoin and imipenem. Isolated strains of *K. pneumoniae* in the same patients are significantly resistant to all tested antibiotics, except the resistance of 30.8% to amoxiclav and the lack of resistance to imipenem.

Table 4. Results of the test of antimicrobial susceptibility of isolated strains of *Escherichia coli* in hospital-treated patients in the period 2005 - 2007

Antibiotic	R	%	S	%	I	%
	Number		Number		Number	
Amoxicillin	27/38	71.1	11/38	28.9	0/38	0
Ampicillin	27/34	79.4	7/34	20.6	0/34	0
Gentamycin	10/38	26.4	24/38	63.1	4/38	10.5
Trimethoprim/sulfamethoxazole	20/39	51.3	19/39	48.7	0/39	0
Nitrofurantoin	0/10	0	10/10	100	0/10	0
Cefalexin	10/39	25.6	24/39	61.5	5/39	12.9
Ciprofloxacin	13/39	33.4	24/39	61.5	2/39	5.1
Pefloxacin	12/32	37.5	18/32	56.3	2/32	6.2
Cefuroxim	6/37	16.2	28/37	75.7	3/37	8.1
Imipenem	0/36	0	36/36	100	0/36	0
Amoxiclav	4/38	10.5	27/38	71.1	7/38	18.4

Table 5. Results of the test of antimicrobial susceptibility of isolated strains of *Klebsiella pneumoniae* in hospital-treated patients in the period 2005 - 2007

Antibiotic	R	%	S	%	I	%
	Number		Number		Number	
Amoxicillin	12/13	92.3	0/13	0	1/13	7.7
Ampicillin	10/11	90.9	0/11	0	1/11	9.1
Gentamycin	9/12	75.0	2/12	16.7	1/12	8.3
Trimethoprim/sulfamethoxazole	9/13	69.2	4/13	30.8	0/13	0
Nitrofurantoin	½	50.0	½	50.0	0/2	0
Cefalexin	10/13	76.9	2/13	15.4	1/13	7.7
Ciprofloxacin	9/13	69.2	3/13	23.1	1/13	7.7
Pefloxacin	7/11	63.6	4/11	36.4	0/11	0
Cefuroxim	9/12	75.0	3/12	25.0	0/12	0
Imipenem	0/13	0	13/13	100	0/13	0
Amoxiclav	4/13	30.8	4/13	30.8	5/13	38.4

Table 6. Results of the test of antimicrobial susceptibility of isolated strains of *Escherichia coli* in ambulance-treated patients in the period 2005 - 2007

Antibiotic	R	%	S	%	I	%
	Number		Number		Number	
Amoxicillin	29/42	69.0	11/42	26.2	2/42	4.8
Ampicillin	22/33	66.6	9/33	27.2	2/33	6.2
Gentamycin	7/42	16.6	30/42	71.4	5/42	12.0
Trimethoprim/sulfamethoxazole	22/43	51.1	19/43	44.2	2/43	4.7
Cefalexin	2/43	4.6	35/43	81.4	6/43	14.0
Ciprofloxacin	4/43	9.3	38/43	88.4	1/43	2.3
Pefloxacin	7/43	16.3	35/43	81.4	1/43	2.3
Cefuroxim	1/40	2.5	37/40	92.5	2/40	5.0
Imipenem	0/43	0	43/43	100	0/43	0
Amoxiclav	2/24	8.3	18/24	75.0	4/24	16.7



Table 7. Results of the test of antimicrobial susceptibility of isolated strains of *Klebsiella pneumoniae* in ambulance-treated patients in the period 2005 - 2007

Antibiotic	R	%	S	%	I	%
	Number		Number		Number	
Amoxicillin	4/10	40.0	6/10	60.0	0/10	0
Ampicillin	6/10	60.0	2/10	20.0	2/10	20.0
Gentamycin	1/10	10.0	7/10	70.0	2/10	20.0
Trimethoprim/sulfamethoxazole	3/10	30.0	7/10	70.0	0/10	0
Cefalexin	3/10	30.0	7/10	70.0	0/10	0
Ciprofloxacin	2/10	20.0	6/10	60.0	2/10	20.0
Pefloxacin	2/10	20.0	8/10	80.0	0/10	0
Cefuroxim	3/10	30.0	7/10	70.0	0/10	0
Imipenem	0/10	0	10/10	100	0/10	0
Amoxiclav	3/10	30.0	6/10	60.0	1/10	10.0

Table 8. Results of the test of antimicrobial susceptibility of isolated strains of *Escherichia coli* in the period of 2009

Antibiotic	R	%	S	%	I	%
	Number		Number		Number	
Amoxicillin	93	68.4	40	29.4	3	2.2
Amoxiclav	13	3.9	280	92.2	13	3.9
Ceftriaxon	4	1.3	298	98.7	0	0
Gentamycin	39	12.7	249	81.4	18	5.9
Ciprofloxacin	53	17.4	242	79.6	9	3
Trimethoprim/sulfamethoxazole	145	47.4	156	51.0	5	1.6

Table 9. Results of the test of antimicrobial susceptibility of isolated strains of *Klebsiella pneumoniae* in the period of 2009

Antibiotic	R	%	S	%	I	%
	Number		Number		Number	
Amoxicillin	12	70.6	5	29.4	0	0
Amoxiclav	7	20.6	27	76.5	1	2.9
Ceftriaxon	4	11.4	31	88.6	0	0
Gentamycin	6	17.1	28	80	1	2.9
Ciprofloxacin	7	20	27	77.1	1	2.9
Trimethoprim/sulfamethoxazole	12	35.3	23	64.7	0	0

Tables 6 and 7 suggest that the isolated strains of *E. coli* in ambulance-treated individuals in the period 2005 – 2007 are the most resistant to ampicillin, amoxicillin and trimethoprim/sulfamethoxazole, in the range of 69.0 to 51.1%, while the percentage of resistance to other tested antibiotics ranged between 16.6 and 2.5%. *E. coli* still has not developed resi-

stance to imipenem. Isolated strains of *K. pneumoniae* are resistant to ampicillin in 60.0% of cases, and the results of testing other antibiotics refer to resistance in the range between 40 and 10%. *K. pneumoniae* is completely susceptible to imipenem.

Tables 8 and 9 suggest that the isolated strains of *E. coli* in the period of 2009 were the most re-

sistant to amoxicillin (68.4%) and trimethoprim/sulfamethoxazole (47.4%), while the percentage of resistance to other tested antibiotics ranged between 17.4 and 1.3%. Isolated strains of *K. pneumoniae* are significantly resistant to amoxicillin (70.6%) and trimethoprim/sulfamethoxazole (35.3%), while the percentage of resistance to other antibiotics ranged between 20.6 and 11.4%.

## 5. Discussion

*E. coli* and *Klebsiella pneumoniae* are a constituent part of normal microflora of certain parts of human organism, but if they are found in other parts of human organism in certain circumstances, they become potential pathogens (5, 10, 11).

Uncomplicated urinary tract infections require initiation of the treatment by empirical therapy, which depends on a number of factors, including continuous follow-up on the species of causal agents of the disease, as well as their antimicrobial susceptibility to adequate antimicrobics. Therefore, the problem of bacterial resistance to certain antimicrobics occurs as a consequence of inadequate application of antimicrobics or their application in inadequate concentrations, i.e. inadequate duration of ordination. Bacterial resistance to antimicrobics has greatly compromised the treatment of infectious diseases, since causal agent of the infection is unknown in the acute phase of the disease, and antibiotics are applied based on empirical knowledge. Empirical therapy is directed towards expected causal agents; however, not only should the expected bacterial species be taken into account nowadays, but also the distribution of bacterial resistance to well-known antimicrobics in local environment. It is important to control the occurrence of resistance of isolated bacterial species from *Enterobacteriaceae* family to certain representatives of antimicrobial groups, such as ampicillin, amoxicillin, amoxiclav, aminoglycosides, fluorokinolons and the combination trimethoprim/sulfamethoxazole, etc.

In the study of antimicrobial susceptibility of bacteria, the results presented for the period 2005 – 2007, as well as for 2009, suggest that the isolated strains of *E. coli* are the most resistant to ampicillin, amoxicillin and trimethoprim/sulfamethoxazole. Results of the test of antimicrobial susceptibility

of *E. coli* in 2001 in Croatia suggest that, in case of UTI, sepsis and all other infections, the isolated strains are resistant to amoxicillin in 48% of cases (range 41 – 69%), co-trimoxazole in 23% (range 15 – 39%), piperacillin in 21% (range 8 – 45%) and ampicillin-sulbaktam in 14% of cases (range 2 – 34%). According to the same report, results of the test of isolated strains of *Klebsiella pneumoniae* in urinary infections suggest that, during the year of 2001, this bacterium was resistant to amoxicillin-clavulanic acid in 22% of cases, to gentamycin in 17% of cases, netilmycin in 9% and to amikacin in 7% of cases. There was no resistance of isolated strains of *Klebsiella pneumoniae* to carbapenem (12, 13). The 2008 report on the study period 2003 – 2007 in Primorsko-Goranska County, Croatia, suggests that the isolates of *E. coli* are resistant to aminopenicilins in about 40% of cases and that the percentage is somewhat lower in relation to the overall results for the entire country. Resistance of isolated strains of *K. pneumoniae* to ampicillin ranged between 60.0 and 70.6% and to trimethoprim/sulfamethoxazole between 30.0 and 35.3%, in the same study period (14). It is important to underline that trimethoprim/sulfamethoxazole was the first-choice medication in empirical therapy of uncomplicated acute urinary infections for a long time. Since it was widely applied, the most frequent causal agents of UTI were able develop resistance after certain period of time. Reports of other countries suggest that bacterial resistance to similar groups of antibiotics is similar to our results. Follow-up on the resistance of *E. coli* to certain representatives of antibiotic groups in Spain suggested that the isolates developed resistance to ampicillin in 57.3% of cases, to co-trimoxazole in 25% and to other antibiotics in lower percentage (15). Testing of antimicrobial resistance of isolated strains of *E. coli*, as a causal agent of urinary and nosocomial infections in London (England) in the period 2005 – 2006, suggests that the isolates were resistant to ampicillin in 55% of cases and to trimethoprim in 40% of cases (16). Testing of susceptibility of *E. coli* isolates in the population of female students at the University of North Carolina, USA, in the period 2005 – 2007, suggests that the isolates were resistant to trimethoprim/sulfamethoxazole in 29.6% of cases, to ampicillin in 37% of cases, and none of them was resistant to furantoin (17).

## 6. Conclusions

*E. coli* was proven to be the bacterium that is the most frequently isolated from urine samples of hospital- and ambulance-treated patients, while *Klebsiella pneumoniae* is present in much lower percentage. Besides the isolation of *E. coli*, other uropathogenic bacteria are also isolated in hospital-treated patients, while only two bacterial species, *E. coli* and *Klebsiella pneumoniae* are isolated in ambulance-treated individuals. Optimal treatment of uncomplicated urinary infections caused by these bacteria, both in hospital- and ambulance-treated patients, should be based on the application of optimal medications. High degree of resistance of *E. coli* and *Klebsiella pneumoniae* to ampicillin and trimethoprim/sulfamethoxazole leads to the conclusion that these medications cannot be used in empirical therapy and it is necessary to check on the condition of bacterial resistance to antimicrobics on a daily basis and to modify the first-choice therapy of urinary tract infections.

Antibiotic resistance is a lasting problem that must be controlled, slowed down or stopped. Continuous follow-up on antibiotic resistance is of great importance for prevention of its spreading, with expected improvement of empirical therapy. Hospital and nonhospital isolates should be separated, in order to be able to determine optimal treatment of urinary tract infections.

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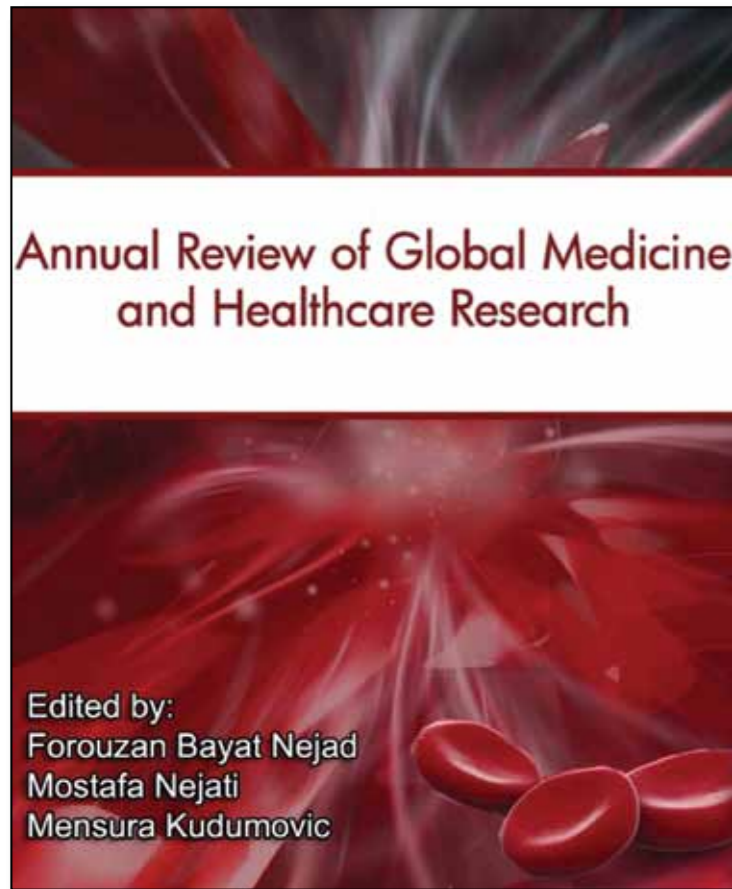
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Upotrebu kratica treba svesti na minimum. Konvencionalne SI jedinice mogu se koristiti i bez njihovih definicija.

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