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## Factors associated with idiopathic adolescent scoliosis in female population - preliminary results

Фактори повезани са идиопатском адолесцентном сколиозом у женској популацији - прелиминарни резултати

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# Factors associated with idiopathic adolescent scoliosis in female population – preliminary results

Фактори повезани са идиопатском адолесцентном сколиозом у женској популацији - прелиминарни резултати

#### **SUMMARY**

**Introduction/Objective** Idiopathic scoliosis (IS) is an orthopedic condition of multifactorial origin.

**Objective** The aim of our study was to evaluate the factors that are associated with IS in female population and factors associated with varicose veins in females with IS.

**Methods** This retrospective-prospective cross-section study included 89 patients (study group) and 87 controls. Further parameters were analyzed: body weight, body height, presence and degree of varicose veins (first, second and third degree) and age (groups between 17-26 years, between 27-36 years and between 37-46 years).

Results The study group has significantly lower body weight (p=0.046), significantly higher proportion of varicose veins (p<0.001) compared to controls, significantly lower proportion of patients aged 27-36 years (p=0.014) and significantly higher proportion of patients aged 37-46 years (p=0.025) compared to controls. There is significantly higher proportion of patients in study group with first degree of varicose veins (p=0.007). There is weak positive correlation between body weight and body height in group of patients without varicose veins (R=0.456) and group with second degree of varicose veins (R=0.291), while for the group with first degree of varicose veins there is moderate positive correlation (R=0.543).

**Conclusion** Our preliminary findings pointed out that the lower body weight and presence of varicose veins are significantly associated with IS. Group of patients with IS above 37 years of age tend to have significantly higher proportion of varicose veins.

**Keywords:** Idiopathic scoliosis; varicose veins; age; body weight; body height

#### Сажетак

Увод/Циљ Идиопатска сколиоза (ИС) представља патолошки ентитет мултифакторијалног узрока. Циљ Утврдити факторе који су повезани са ИС у женској популацији и факторе који су повезани са варикозним венама код испитаница са ИС. Методе У ову ретроспективно-проспективну студију пресека укључено је 89 испитаница, а у контролној групи је било 87 испитаница. Анализирани су следећи параметри: телесна тежина, телесна висина, присуство и степен (први, други и трећи степен) варикозних вена, и године живота (група17-26, 27-36 и 37-46 година). Резултати У студијској групи регистрована је сигнификантно нижа телесна тежина (p=0.046), сигнификантно већа учесталост варикозних вена (p<0.001) у поређењу са контролом, сигнификантно нижа учесталост ових промена код пацијената животне доби од 27-6 година (p=0,014) и сигнификантно веће присуство код старије животне доби од 37–46 година (p=0,025), у поређењу са контролном групом. У студијској групи је регистрована сигнификантно већа учесталост пацијената са проширеним венама првог степена (р =0,007). Утврђено је да постоји блага позитивна корелација између телесне тежине и висине у групи без варикозних вена (Р=0,456), и у групи пацијената са варикозним венама другог степена (Р=0,291), док је у групи пацијената са варикозним венама првог стпена утврђена умерена позитивна корелација (Р=0,543).

Закључак Прелиминарни резултати ове студије показали су да су нижа телесна тежина и присуство проширених вена значајно повезани са ИС. Група испитаница са ИС преко 37 година је имала значајно чеће проширене вене у односу на контролу. Кључне речи: идиопатска сколиоза; проширене вене; године живота; телесна тежина; телесна висина

#### INTRODUCTION

Idiopathic scoliosis (IS) is an orthopedic condition that is defined as pathologic state of multifactorial origin, with a major relevance of those genetic and biomechanical factors that have impacts on the central nervous system, growth and metabolism [1, 2, 3]. The diagnosis is established on the base of clinical examination, radiographic imaging and stereophotogrametry. Assessment of the patients with scoliosis includes medical history, clinical, physiatrist and neurological examination, and diagnostic tests [4]. Treatment of IS can be conservative and/or surgical.

Previous studies stressed out that in certain hereditary pathological conditions, such as IS, the loss of integrity of the matrix proteins in the skin affects the blood vessels, so that one is followed by the high incidence of varicose veins [5, 6]. Conditions such as varicose veins and bone fragility are associated with changes in the strength of collagen and changes in its metabolism [7]. In previous reports, there is insufficient information on the incidence of complications such as varicose veins in women affected with IS, although the theory of the defect in the synthesis of collagen and connective tissue suggests a higher incidence of these complications in a population of women treated for IS. It is unknown to what extent these complications are represented in the aforementioned population in relation to the population of women who are not treated for IS, and if it can even be promptly diagnosed and treated.

The aim of our study was to determine the factors that are associated with IS in female population and factors associated with varicose veins in females with IS.

#### **METHODS**

This study was designed as a retrospective-prospective cross-section study that investigated the incidence of varicose veins in the population of women with idiopathic scoliosis, treated at the Department of Physical Medicine and Rehabilitation "Dr Miroslav Zotović" in Banja Luka. The study group included 89 patients, while the control group comprised of 87 participants. The inclusion criteria were: female gender and signed informed consent of participation to the study. The exclusion criteria were: secondary scoliosis and pregnancies. Patients from the control group were subjected to the same questions, tests and exams.

This study was approved by the relevant ethical committee (Ethics Committee of the Institute of Physical Medicine and Rehabilitation "Dr Miroslav Zotović" Banja Luka) and followed by the adoption of the necessary documentation: "The notification for respondents of the study" and "Informed Consent". Prior inclusion in the study all participants were informed about study protocol and informed consent was obtained.

Further parameters were analyzed: body weight, body height, presence and degree of varicose veins and age (groups between 17-26 years, between 27-36 years and between 37-46 years).

The examination of the physical medicine specialist comprised of the examination of the clinical and ultrasound examination of the state of the venous system and was presented as follows: normal state of the venous system (without any observed changes); medium stage expression of the venous disease (varicose veins confirmed by clinical inspection, but without trophic changes; the ultrasonic examination verified obstruction in the superficial system or in the perforated veins (C2-3 according to CEAP Classification)); and severe venous disease (trophic changes observed by inspection and ultrasonic examination verified obstruction of the deep venous system (C4-C6 according to CEAP Classification)).

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#### Statistical analysis

Categorical data were presented as whole numbers and percents, while continuous variables as median values with standard deviation and analyzed by SPSS statistical program (version 17). Chi squared test was used for statistical analysis of categorical data, while Mann Whitney U test and Student t-test for independent samples for analysis of continuous variable. Pearson's correlation was performed to assess correlation between body height and body weight in group of patients with IS regarding the presence and degree of varicose veins. For statistically significant values were taken those values where p<0.05. The minimal, statistically valid sample size was determined to be 86 subjects according to the Cohen tables.

#### **RESULTS**

In table 1, we presented distribution of evaluated parameters in evaluated groups of participants. The study group has significantly lower body weight (p=0.046), and significantly higher

Table 1. Distribution of evaluated parameters in study group and

controls.

(p<0.001)compared controls (Table 1). The study group had significantly lower proportion of patients aged 27-36 years (p=0.014) and significantly higher proportion of patients aged 37-46 years (p=0.025)compared

proportion of varicose veins

**Control group** Study group **p** -**Evaluated parameters** (n=89)(n=87)value 30.9±7.9 Age (years)  $29.9\pm6.7$ 0.367\* Body weight (kg)  $\bar{x}\pm SD$ 0.046\*  $63.6 \pm 9.6$ 67.0±12.7 Body height (cm) 168.6±6.5 169.0±6.2 0677\* Varicose veins 23 (25.8) 7 (8.0)  $0.001^{\dagger}$ 17 - 26 $0.710^{\dagger}$ 28 (32.2) 31 (34.8) years 27 - 36n (%) 26 (29.2) 41 (47.1)  $0.014^{\dagger}$ Age vears 37 - 4632 (36.0) 18 (20.7)  $0.025^{\dagger}$ years

Table 2. Distribution of varicose veins regarding severity degree and participants age between evaluated groups of participants.

Varicose veins		Study group	Control group	ur trerpunts	
n (%)		(n=89)	(n=87)	<i>p</i> -value	
None		66 (74.1)	80 (92.0)	0.001*	
First degree		17 (19.1)	5 (5.7)	0.007*	
Second degree		6 (6.8)	2 (2.3)	0.157*	
Third degree		0 (0)	0 (0)	-	
Participants with varicose veins					
Age	17–26 years	2 (8.7)	0 (0)	0.419*	
	27–36 years	7 (30.4)	4 (57.0)	0.199*	
	37–46 years	14 (60.9)	3 (43.0)	0.400*	
*Chi sau	ared test				

Chi squared test

There is significantly higher proportion of participants in control without group varicose veins (p<0.001), and significantly higher proportion of patients in study group with first degree of varicose veins (p=0.007) (Table 2).

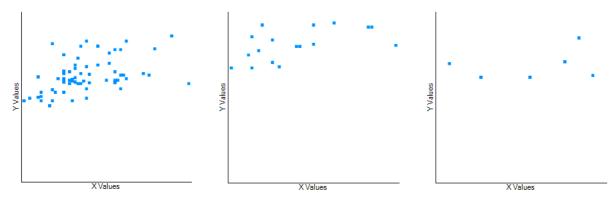
controls.

There is non significant difference for evaluated variables (age, body weight and body height) in both study and control groups with

regards to the degree of varicose veins (p>0.05) (Table 2).

In Figure 1 correlations between body height and body weight in patients with idiopathic scoliosis with regards to the presence and degree of varicose veins are presented. There is weak

<sup>\*</sup>Students t-test; \*Chi squared test.



A) Without varicoses\*

B) First degree<sup>†</sup>

C) Second degree<sup>‡</sup>

Figure 1. Correlations between body height and weight in group of patients due to the varicose veins presence and severity degree.

(X-Values – Body height; Y-Values – Body weight; \*R=0.456;  $^{\dagger}$ R=0.543;  $^{\ddagger}$ R=0.291)

Table 3. Distribution of evaluated parameters in group of participants with different degrees of varicose veins

Parameters	Study	p value*	
rarameters	1 <sup>st</sup> degree	2 <sup>nd</sup> degree	p value.
Age (years) (x±SD)	36.6±5.1	$34.3\pm6.0$	0.308
Body weight (kg) (x±SD)	$64.9 \pm 7.4$	$68.8 \pm 8.9$	0.646
Body height (cm) (x±SD)	$169.4 \pm 7.0$	$174.4\pm8.2$	0.219
Danamatana	Contro	l group	n valua <sup>†</sup>
Parameters	Contro 1 <sup>st</sup> degree	l group  2 <sup>nd</sup> degree	p value <sup>†</sup>
Parameters Age (years) (x±SD)			<i>p</i> value <sup>†</sup> 0.939
	1 <sup>st</sup> degree	2 <sup>nd</sup> degree	*

<sup>\*</sup>Mann Whitney U-test; †Students t test

positive correlation between those two variables in group of patients without varicose veins (R=0.456) and group with second degree of varicose veins (R=0.291), while for the group with first degree of varicose veins there is moderate positive correlation (R=0.543) (Table 3).

#### DISCUSSION

This research is based on the theory that bone fragility is associated with changes in the strength of collagen and changes in its metabolism, where one of the crucial factors could be the quality of connective tissue [8]. Disruption in the synthesis of collagen is typical of varicose veins. Smooth muscle cells from varicose veins synthesize more collagen I, less collagen III, and similar amounts of collagen V. This imbalance is a possible reason for the mechanical properties of the tissue, which, under these conditions, has a poorer quality [9, 10]. It should be stated, that in the current literature, there are reports stressing out defective synthesis of collagen and bad posture followed by the appearance of varicose veins, however well-designed studies are still missing.

From the clinical point of view we have noticed in the study that females with diagnosed IS had significantly lower weight. Even though there were non significant differences in the age between two studied populations, age distribution frequencies demonstrated that it could be considered as significant factor associated with IS. Our results stressed out that female above 37 years of age had more frequent IS, while those between 27 and 36 significantly lesser frequency of occurrence. Our findings are to the certain degree consistent with previous reports which stated that age is associated with a prevalence of idiopathic scoliosis [11]. Further, we have pointed out that varicose veins are shown to be significant factor associated with presence of IS, where almost one out of four females

with scoliosis had varicose veins, while less than one in ten in control group were with such condition. Bearing in mind that etiology of idiopathic adolescent scoliosis is multifactorial including genetic predisposition, abnormalities of connective musculoskeletal tissues, it could be assumed that these individuals are more prone to develop varicose veins [12, 13, 14]. The complexicity and multifactorial origin was underlined as well in the study of Burwell and Dangerfiled, where the epigenetics was introduced as a concept in the evaluation of adolescent idiopathic scoliosis [15]. They further stated that this type of scoliosis is associated with lower body mass index among other factors [15]. Therefore, patients with IS should be screened for the presence of varicose veins and included into regular follow-up. Considering the degree of varicose vein presence, this study pointed out that first degree was significantly more frequent in patients with IS, while second degree although frequent in the group of patients was not significant. This observation could be explained to the certain degree that other factors might influence in the pathology of second degree of varicose veins and thus influencing the frequency of occurrence in population.

Our findings pointed to the fact that for patients with IS and first degree of varicose veins there is greater correlation between height and weight, while for those without varicose veins and second degree of varicose veins there is lower correlation. Such findings are to the certain degree in line with our previous statement that other factors might play certain role in severity degree of varicose veins for patients with IS.

Also, it should be underlined that there are several limitations to this study. First, the study included small proportion of participants in the group of varicose veins. Second limitation refers particularly to the actual age of female participants where increase of age along with other factors might influence the frequency of varicose veins occurrence and degree of such pathology. Therefore, further studies are needed on larger samples of patients and with longer follow-up observational periods.

#### **CONCLUSIONS**

Our findings demonstrated that lower body weight and presence of varicose veins are significantly associated with IS. Group of patients with IS above 37 years of age tend to have significantly higher proportion of varicose veins.

#### REFERENCES

- 1. Grivas TB, Burwell GR, Vasiliadis ES, Webb JK. A segmental radiological study of the spine and rib-cage in children with progressive Infantile Idiopathic Scoliosis. Scoliosis. 2006; 1: 1–17.
- 2. Grivas TB, Vasiliadis ES, Rodopoulos G, Bardakos N. The role of the intervertebral disc in correction of scoliotic curves. A theoretical model of idiopathic scoliosis pathogenesis. Stud Health Technol Inform. 2008; 140: 33–6.
- 3. Grivas TB, Vasiliadis ES, Rodopoulos G. Aetiology of Idiopathic Scoliosis. What have we learned from school screening? Stud Health Technol Inform. 2008; 140: 240-4.
- 4. Jandric S. Idiopathic scoliosis. Med Pregl. 2012; 65: 35–40.
- 5. Jackson SR, Avery NC, Tarlton JF, Eckford SD, Abrams P, Bailey AJ. Changes in metabolism of collagen in genitourinary prolapse. Lancet. 1996; 347: 1658–61.

- 6. Bouissou H, Pieraggi T, Jullian M, Douste Blazy L. Simultaneous degradation of elastin in dermis and in aorta. Front Matrix Biol. 1976; 3: 242–55.
- 7. Keane D, Sims T, Abrams P, Bailey A. Analysis of collagen status in premenopausal nulliparous women with genuine stress incontinence. Br J Obstet Gynaecol. 1997;104: 994–8.
- 8. Karin L, Sabrina LL, Marian AS, Leon CLTvK, Jan CMH, Mark EV, et al. Pelvic organ prolapse and collagen-associated disorders. Int Urogynecol J. 2012; 23: 313–9.
- 9. McIntosh LJ, Mallett VT, Frahm JD, Richardson DA, Evans MI. Gynecologic disorders in women with Ehlers-Danlos syndrome. J Soc Gynecol Investig. 1995; 2: 559–64.
- 10. Sansilvestri MP, Nonotte I, Fournet BP, Rupin A, Fabiani JN, Verbeuren TJ, et al. Abnormal deposition of extracellular matrix proteins by cultured smooth muscle cells from human varicose veins. J Vasc Res. 1998: 35: 115–23.
- 11. Soucacos PN, Zacharis K, Soultanis K, Gelalis J, Xenakis T, Beris AE. Risk factors for idiopathic scoliosis: review of a 6-year prospective study. Orthopedics. 2000; 23: 833–8.
- 12. Dickson RA, Lawton JO, Archer IA, Butt WP. The pathogenesis of idiopathic scoliosis. Biplanar spinala asymmetry. J Bone Joint Surg. 1984; 66: 8–15.
- 13. Murray DW, Bulstrode CJ. The development of adolescent idiopathic scoliosis. Eur Spine J. 1996; 5: 251–
- 14. Guo X, Chau WW, Chan YL, Cheng JC. Relative anterior spinal overgrowth in adolescent idiopathic scoliosis. Results of disproportionate endochondral-membranous bone growth. J Bone Joint Surg. 2003; 85: 1026–31.
- 15. Burwell RG, Dangerfield PH. Whither the etiopathogenesis (and scoliogeny) of adolescent idiopathic scoliosis? Stud Health Technol Inform. 2012; 176: 3–19.

