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## Фактори који су повезани са идиопатском адолесцентном сколиозом у женској популацији – прелиминарни резултати

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### САЖЕТАК

**Увод/Циљ** Идиопатска сколиоза (ИС) представља патолошки ентитет мултифакторијалног узрока.

Циљ рада је утврдити факторе који су повезани са ИС у женској популацији и факторе који су повезани са варикозним венама код испитаница са ИС.

**Метод** У ову ретроспективно-проспективну студију пресека укључено је 89 испитаница, док је у контролној групи било 87 испитаница. Анализирани су следећи параметри: телесна тежина, телесна висина, присуство и степен тежине (први, други и трећи степен) варикозних вена и године живота (група између 17 и 26, између 27 и 36 и између 37 и 46 година).

**Резултати** У студијској групи регистрована је значајно нижа телесна тежина ( $p = 0,046$ ), значајно већа учесталост варикозних вена ( $p < 0,001$ ) у поређењу са контролном, значајно нижа учесталост ових промена код болесника животне доби од 27 до 36 година ( $p = 0,014$ ) и значајно веће присуство ис-

тих код болесника старије животне доби од 37 до 46 година ( $p = 0,025$ ), у поређењу са контролном групом. У студијској групи је регистрована значајно већа учесталост болесника са проширеним венама првог степена ( $p = 0,007$ ). Утврђено је да постоји блага позитивна корелација између телесне тежине и висине у групи болесника без варикозних вена ( $p = 0,456$ ) и у групи болесника са варикозним венама другог степена ( $p = 0,291$ ), док је у групи болесника са варикозним венама првог степена утврђена умерена позитивна корелација ( $p = 0,543$ ).

**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 чешће проширене вене у односу на контролу.

**Кључне речи:** идиопатска сколиоза; проширене вене; године живота; телесна тежина; телесна висина

## ORIGINAL ARTICLE / ОРИГИНАЛНИ РАД

# Pre-pregnancy body mass index and the risk of gestational diabetes mellitus

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## SUMMARY

**Introduction/Objective** Not only do pre-pregnancy overweight or obesity increase the risk of adverse maternal and perinatal outcomes but they also lead to the development of gestational diabetes mellitus. The objective of this study was to estimate the prevalence of pre-pregnancy overweight and obesity in the Republic of Srpska and to investigate its association with hyperglycemia and risk of gestational diabetes mellitus.

**Methods** A cross-sectional study was carried out during the period from February to October 2012 among 555 pregnant women in gestational period from 24 to 28 weeks. The criterion for exclusion from the sample was previously diagnosed type 1 or type 2 diabetes.

**Results** Before pregnancy, 20.39% of participants had increased body mass index, while 4.04% [95% confidence interval (CI); 2.62–6.13] were obese. Gestational diabetes mellitus was diagnosed in 10.91% (95% CI, 8.44–13.98) of them. The increase in body mass index by 1 increased the risk of gestational diabetes mellitus by 1.09 times [odds ratio (OR) = 1.09; 95% CI; 1.02–1.16]. Pregnant women who were overweight had a 4.88 times greater risk (OR = 4.88; 95% CI, 1.23–29.41) of developing gestational diabetes.

**Conclusion** Every fifth pregnant woman in this study was overweight or obese before pregnancy. The increase in body mass index by 1 increased the risk of gestational diabetes by 1.09 times (OR = 1.09; 95% CI; 1.02–1.16). Counselling is necessary for overweight and obese women planning pregnancy.

**Keywords:** pre-pregnancy body mass index; hyperglycemia; gestational diabetes mellitus

## INTRODUCTION

Improvement of maternal, fetal and child health are key public health goals. Changes in public health trend have challenged the healthcare sector to provide optimal guidance to women before, during, and after pregnancy so that they can achieve healthy outcomes for both themselves and their newborns [1].

It has been shown that women being overweight or obese before pregnancy are at increased risk of adverse maternal and perinatal outcomes [2]. The Hyperglycemia Adverse Pregnancy Outcome (HAPO) study confirms that both obesity and maternal hyperglycemia alone are independently associated with adverse obstetrical outcomes, particularly abnormal fetal growth, newborn percent body fat and preeclampsia [3]. Pre-pregnancy overweight and obesity are also associated with gestational diabetes mellitus (GDM) development, as 65–75% of women with GDM are also overweight or obese [4].

Maternal overweight and obesity are the highest ranking modifiable risk factors. Raising of awareness and implementation of effective interventions for modifiable risk factors are priorities for stillbirth prevention [5]. Obesity

prevalence has continued to grow, particularly in lower and middle-income countries. According to World Health Organization (WHO), in 2014, more than 1.9 billion adults 18 years and older were overweight. Of these, over 600 million were obese [6]. The prevalence of overweight and obesity in women older than 20 increased between 1980 and 2013 from 29.8% (29.3–30.2) to 38.0% (37.5–38.5) [7]. According to the 2010 Household Health Survey in the Republic of Srpska, one of two entities in Bosnia and Herzegovina (BiH), the obesity prevalence in women older than 18 is 22.7% [8].

The objective of this study is to estimate the prevalence of pre-pregnancy overweight and obesity among women in the Republic of Srpska (BiH) and to investigate its association with hyperglycemia and increased risk of GDM.

## METHODS

### Study design

The research was carried out in the form of a cross-sectional study during the period from February to October 2012 among pregnant women who had regular appointments with

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their gynecologists. The total sample consisted of 555 pregnant women in gestation period from 24 to 28 weeks. Data were collected by trained gynecologists and nurses from outpatient clinics whose selection was based on the Statistical Office analysis to ensure the equal presentation of all regions of the Republic of Srpska.

Ethical approval for the study was obtained from the Ethics Committee for Clinical Research of the Clinical Center of Banja Luka, and written informed consent was obtained from all the participants. The informative consent contained the basic information about the research, the explanation about the confidentiality of the information and to what end the information obtained in the research will be used [9, 10].

The information about the body mass before pregnancy was taken from the pregnancy medical records, or if the information was missing, it was taken from the pregnant women. The anthropometric measurements included height (cm) and weight (kg). Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters [11]. Classification of the nutritional status before pregnancy was done according to the WHO criteria [12]. Between 24 and 28 weeks of pregnancy, all the women underwent a 75-g oral glucose tolerance test (OGTT) in the morning, after fasting for 8–14 hours, according to WHO criteria [13]. Plasma glucose levels were taken before and one and two hours after the consumption of 75 g of glucose. Weight gain from pre-pregnancy to OGTT was estimated as gain in body weight. Plasma glucose was measured by a glucose oxidase method. GDM is defined according to the criteria of the American Diabetes Association (ADA) and its diagnosis is confirmed by one measurement of plasma glucose expressing values greater than  $> 5.1$  mmol/l at start,  $> 10$  mmol/l 1 hour or  $> 8.5$  mmol/l two hours after the intake of 75 g of glucose [14].

### Statistical methods

All statistical analyses were conducted using SPSS Statistics for Windows, Version 17 (SPSS Inc., Chicago, IL, USA). Baseline demographic characteristics were summarized using frequencies and percentages for categorical characteristics, and mean  $\pm$  SD for continuous variables. Symmetric

95% confidence intervals (95% CI) were calculated for frequency. Spearman rank correlation was used for testing the association between an age group and a pre-pregnancy BMI. The evolution of glycemic levels was evaluated by the Friedman repeated measure test (one-way ANOVA test) in each group. The categorical variables were compared using Fisher's exact  $\chi^2$  test where appropriate, and for continuous variables using the Student's t-test. We used Mantel-Haenszel  $\chi^2$  test to test for association between an age group (ordinal categorical variable) and the diagnosis of GDM. Finally, we used binary logistic regression to analyze whether GDM could be predicted by both pre-pregnancy BMI and an age group, while controlling for the effect of other variables. P values lower than 0.05 in two-tailed tests were considered to be significant.

### RESULTS

The characteristics of the screened sample are shown in Table 1. The sample included 555 pregnant women from the Republic of Srpska in the gestation period from 24 to 28 weeks. The highest percentage of pregnant women, [36.27% (95% CI; 32.32–40.30)] was in the 25–29 years age group. A majority of participants (60%) resided in urban areas. For 6.49% of the participants there was no information related to the nutritional status before pregnancy. The highest percentage of pregnant women [70.96% (95% CI; 66.91–74.70)] were in normal BMI range before pregnancy, whereas 20.39% of the them had increased BMI, and 4.04% (CI 95%; 2.62–6.13) were obese, while 8.65% were underweight (Table 1).

Overall, age correlated positively with the BMI score  $r_s$  (520) = 0.188;  $p < 0.001$ , Table 2. In particular, it was obvious that obesity before pregnancy was more frequent among the older participants. Although we had only 10.44% of participants older than 35, they comprised almost a half of all obese participants in our sample (9/21, 42.85%).

According to the methodology applied in the research, plasma glucose values were assessed between the 24th and 28th week of gestation [14]. Fasting plasma glucose values and OGTT were measured in 89.2% of participants. Women with higher BMI scores before pregnancy tend-

**Table 1.** Baseline characteristics of the study population screened for gestational diabetes mellitus

Characteristics	Number (n)	Percentage (%)	95% CI
Age group (years)	< 25	165	29.73
	25–29	201	36.27
	30–34	130	23.42
	35–39	50	9.01
	> 40	9	1.62
Body mass index (kg/m <sup>2</sup> ) category*	< 18.50	45	8.65
	18.50–24.99	368	70.96
	25–29.99	85	16.35
	> 30	21	4.04
Place of living	Rural area	222	40
	Urban area	333	60

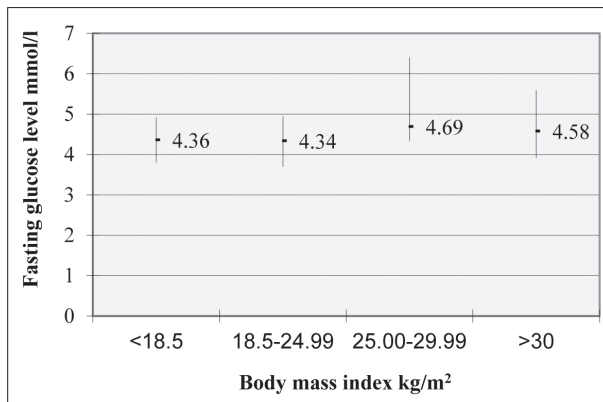
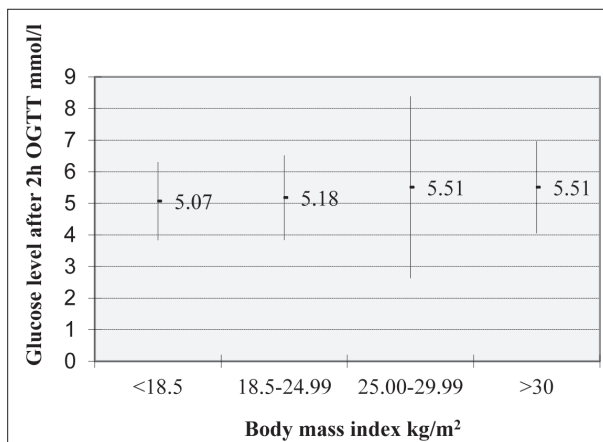
\*Note: information about pre-pregnancy nutritional status for 36 examinees was missing

**Table 2.** Nutritional status related to age category in women screened for gestational diabetes mellitus

Prepregnancy BMI group* (kg/m <sup>2</sup> )	Total		Age group (years)									
			< 25		25–29		30–34		35–39		> 40	
	n	%	n	%	n	%	n	%	n	%	n	%
< 18.5	45	8.65	22	48.89	16	35.56	5	11.11	2	4.44	0	0
18.5–24.99	368	70.96	106	28.73	141	38.48	92	24.93	25	6.78	4	1.09
25–29.99	85	16.35	22	25.88	25	29.41	20	23.53	14	16.47	4	4.71
> 30	21	4.04	5	23.81	4	19.05	3	14.29	8	38.09	1	4.76
Total	519	93.69	155	27.92	187	33.69	120	21.62	49	8.82	9	1.62

Note: information about pre-pregnancy BMI for 36 examinees was missing;

\*p < 0.001, value derived from Spearman range of correlation

**Figure 1.** Distribution of fasting glucose level related to the prepregnancy BMI in women screened for gestational diabetes mellitus**Figure 2.** Distribution of postload glycemia values two hours after OGTT compared to BMI before pregnancy, in women screened for gestational diabetes mellitus

ed to have higher plasma glucose values both at fasting [ $r_s(446) = 0.14, p = 0.002$ ] and two hours after OGTT ( $r_s(462) = 0.11, p = 0.014$ ). Figure 1 illustrates that plasma glucose levels were higher in pregnant women which were overweight or obese before pregnancy [ $F(3.461) = 3.221, p = 0.023$ ].

The highest mean value of plasma glucose two hours after OGTT with 75 g of glucose (5.51 mmol/l) was established in pregnant women who were overweight or obese before pregnancy. However, no significant statistical correlation of plasma glucose values with the nutritional status was established [ $F(3.461) = 1.102, p = 0.348$ ]. The greatest

**Table 3.** Maternal characteristics stratified by gestational diabetes mellitus diagnosed by the American Diabetes Association criteria

Characteristics	Non-GDM 441 (89.1)	GDM 54 (10.9)	p-value	
Age group, year	< 25	143 (32.4)	7 (13)	< 0.001*
	25–29	164 (37.2)	16 (29.6)	
	30–34	98 (22.2)	16 (29.6)	
	35–39	31 (7.0)	11 (20.4)	
	> 40	5 (1.1)	4 (7.4)	
Pre-pregnancy BMI Group (kg/m <sup>2</sup> )	< 18.50	39 (8.8)	2 (3.7)	0.056†
	18.50–24.99	297 (67.3)	33 (61.1)	
	25–29.99	66 (15)	10 (18.5)	
	> 30	16 (3.6)	4 (7.4)	
Pre-pregnancy BMI (kg/m <sup>2</sup> )	22.51 ± 3.67	24.10 ± 4.97	0.006§	
Weight gain	8.22 ± 4.49	8.27 ± 4.27	0.949§	

GDM – gestational diabetes mellitus;

Note: information about the nutritional state before pregnancy was missing for 28 examinees;

\* $\chi^2$ -test, †Fisher's exact test, §Student's t-test

dispersion of measured glycemia values two hours after OGTT was established in pregnant women who were overweight ( $M = 5.51 \pm 2.88$  mmol/l), as shown in Figure 2.

GDM was diagnosed in 10.91% (95% CI; 8.44–13.98) of participants according to the ADA criteria for diagnosing gestational diabetes mellitus. We observed that with the increase of pregnant woman's age, the frequency of GDM increased as well: ( $\chi^2(1) = 24.81, p < 0.001$ ), as shown in Table 3. By applying the ADA criteria for diagnosing gestational diabetes for the measured values of glycemia and by analyzing the prevalence of GDM related to the pre-pregnancy BMI group for the participants who had information about their nutritional status before pregnancy, we found a positive trend of GDM with increasing BMI scores (Wald  $z = 7.07, p = 0.001$ ).

The increase of BMI by 1 increased the risk of GDM occurrence by 1.09 times [odds ratio (OR) = 1.09; 95% CI; 1.02–1.16]. Nevertheless, the effect of BMI became slightly smaller and statistically insignificant (Wald  $z = 2.28, p = 0.131, OR = 1.06$ ) when it was controlled for age in a multiple logistic regression. In contrast, the effect of age remained significant (Wald  $z = 19.98, p = 0.001$ ). For instance, compared to women younger than 25, the women who were between 35 and 39 years of age had 8.32 times greater risk of developing diabetes, while the risk increased up to 18.67 times for those who were older than 40. Pregnant women who were overweight had a 4.88 times greater risk (OR = 4.88; 95% CI, 1.23–29.41) of developing GDM.



## DISCUSSION

The results of our research showed a statistically significant correlation between the increased pre-pregnancy BMI and the presence of GDM and a significant positive association between age and the presence of GDM. According to the ADA criteria for diagnosing gestational diabetes, the prevalence of GDM was 10.91% [14].

Pre-pregnancy overweight and obesity have many adverse pregnancy outcomes, including those related to hyperglycemia and the risk of developing GDM [3]. According to the results of our research, 16.35% of pregnant women were overweight, while 4.04% of the participants were obese before pregnancy. Hence, every fifth pregnant woman in the Republic of Srpska was overweight or obese before pregnancy. Statistically significant linear increase of pre-pregnancy BMI was evident in women over the age of 35. According to the WHO, the prevalence of overweight and obesity has been increasing in middle income countries to which Bosnia and Herzegovina also belongs [6, 15]. The prevalence of obesity is increasing, especially in women at the generative age. In France, the obesity prevalence increased from 5.2% to 11% over the period from 1997 to 2006 in women aging between 20 and 39 [16]. In America, according to the data from Pregnancy Risk Assessment Monitoring System (PRAMS), one in five women was obese when they became pregnant, which presents the increase of the obesity prevalence by 70% compared to the previous decade [17].

A positive relation was established between the nutritional status before pregnancy and the mean values of fasting and postload plasma glucose levels. The results showed an association between fasting and postload plasma glucose levels and adverse pregnancy outcomes, even in the range previously considered normal [18]. The Monash Medical Center (Clayton, Australia) research [19] also found the correlation between the increased BMI and glycemia during pregnancy. It was established that pre-pregnancy BMI higher than or equal to 35 kg/m<sup>2</sup> was the third independent risk factor in the development of gestational diabetes (after already diagnosed GDM registered in previous pregnancies and older age). The results of our study are in concordance with previous studies [19, 20, 21], meaning that the advance maternal age implies higher risk factor for GDM. Similarly to our research, French study of Pre and Early Post Natal Determinants of the Child's Development and Health (EDEN study) [22] also showed that BMI before pregnancy is independently associated

with increased plasma glucose level, i.e. gestational diabetes. The risk for the gestational diabetes in EDEN study increased with the increase of BMI before pregnancy [22]. Pregnant women from the research done in the Republic of Srpska, who were obese before pregnancy, had a 4.88 times higher risk of developing GDM. Results of meta-analysis of 20 studies show that the risk of developing GDM was about two, four, and eight times higher among overweight, obese or severely obese compared with normal-weight women at the beginning of their pregnancies, respectively [23].

Meta-analysis of the observation studies including several electronic databases and research published from 1977 to 2000 showed that the risk of gestational diabetes is positively associated with the pre-pregnancy BMI [22]. For every 1 kg/m<sup>2</sup> increase in BMI, the prevalence of GDM increased by 0.92% [24], which is similar to the results from the research done in the Republic of Srpska, where every 1 kg/m<sup>2</sup> increase in BMI increased the risk for developing GD by 1.09%. Our research did not establish any correlation between weight gain during pregnancy and the prevalence of gestational diabetes. Meta-analysis of the research done in England from 1990 to 2007 showed inconsistent results related to the maternal weight gain during pregnancy and the risk of GDM [25]. According to the EDEN study, the association between the risk of gestational diabetes and maternal gestational weight gain was positive and significant only when the pre pregnancy BMI was increased [20].

We are fully aware of the limitation of our study in that the information about pre-pregnancy BMI was taken from pregnancy medical records or during interviews with mother if the information was not in the medical record.

## CONCLUSION

Overweight and obesity are largely preventable. Based on the results of our research done in the Republic of Srpska, it can be concluded that it is necessary to counsel women on the importance of obtaining normal weight before pregnancy. It is necessary that the creators of healthcare policies and public healthcare institutions intervene with the aim of providing non-obesogenic environments, the education related to healthy diet before and during pregnancy, and the importance of physical activity. The abovementioned activities can result in the reduction of overweight and obesity prevalence and to reduced risk for developing gestational diabetes.

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## Индекс телесне масе пре трудноће као чинилац ризика за настанак гестацијског дијабетес мелитуса

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### САЖЕТАК

**Увод/Циљ** Повећана телесна маса и гојазност пре трудноће повећавају ризик за настанак компликација код мајке и плода у току трудноће, у току и после порођаја, а доводе се у везу са појавом гестацијског дијабетес мелитуса (ГДМ).

Циљ истраживања био је утврдити учесталост повећане телесне масе и гојазности пре трудноће код жена и њихову повезаност са појавом повећане хипергликемије и ГДМ-а.

**Метод** Студија пресека спроведена је од фебруара до октобра 2012. године са 555 трудница гестације 24–28 недеља. Критеријум за искључење из испитивања био је раније дијагностикован дијабетес мелитус тип 1 или тип 2.

**Резултати** Повећан индекс телесне масе (ИТМ) пре трудноће имало је 20,39% испитаница, од којих је 4,04% (CI 95%;

2,62–6,13) било гојазно. ГДМ је дијагностикован код 10,91% (CI 95%; 8,44–13,98) испитаница. Повећање ИТМ-а за један повећавало је ризик за појаву ГДМ-а 1,09 пута (OR = 1,09; CI 95%; 1,02–1,16). Труднице које су имале прекомерну телесну масу пре трудноће имале су 4,88 пута већи ризик (OR = 4,88; CI 95%; 1,23–29,41) за развој ГДМ-а.

**Закључак** Свака пета испитаница имала је прекомерну телесну масу или гојазност пре трудноће. Повећање ИТМ-а за један повећавало је ризик за појаву ГДМ-а 1,09 пута. Неопходно је саветовање жена са прекомерном телесном масом и гојазношћу које планирају трудноћу.

**Кључне речи:** индекс телесне масе пре трудноће; хипергликемија; гестацијски дијабетес мелитус