Bi BIOMEDICINSKA ISTRAŽIVANJA
2024;15(1):1–10

UDK: 618.3-06+616.12-008.331.1
DOI: 10.59137/BII202401373P

Original article

Preeclampsia and preterm delivery risk: the significance of obesity in pregnancy

Tamara Perić[1,2], Mirjana Bogavac[1,3], Zoran Belopavlović[1,3]

[1]University of Novi Sad, Faculty of Medicine, Novi Sad, Serbia

[2]PHI Hospital „Sveti Vračevi", Bijeljina, Republic of Srpska, Bosnia and Herzegovina

[3]Clinical Centre of Vojvodina, Department of Obstetrics and Gynecology, Novi Sad, Serbia

Primljen – Received: 12/02/2024
Prihvaćen – Accepted: 01/04/2024

Corresponding author:
Tamara Perić, MD
Hajduk Veljkova 3, 21000 Novi Sad
E-mail: tasa_93bn@hotmail.com

Summary

Introduction. A significant proportion of women globally, constituting 38%, are obese, among whom 24.5% reside in Europe. Obesity elevates the risk of premature birth due to associated maternal conditions, such as preeclampsia. The objectives were to assess: variations in demographic and clinical characteristics among pregnant women across groups; the impact of obesity on the incidence of preeclampsia and preterm delivery; and the influence of obesity on newborn characteristics.

Methods. One-year prospective study included 133 pregnant women gestational age 11-14 gestational week (GW), divided into two groups: OB (41.35%) and CG (58.65%). The data were analyzed using IBM SPSS version 23.

Results. There is statistically significant difference in average body mass index (BMI) (22.01 ± 1.83 vs. 30.26 ± 4.52; $p < 0.001$) and delivery time (37.94 ± 2.05 vs. 36.87 ± 2.45; $p = 0.003$) between CG and OB. Obese pregnant women developed preeclampsia significantly more often than normal weight (61.82% vs. 28.21%; $p < 0.001$). Body mass index has significant moderate predictive ability to predict preeclampsia (AUC 0.696 (95% CI: [0.601; 0.79]). Higher BMI (OR = 1.19, [1.09; 1.29], $p < 0.0001$) was associated with higher rates of preeclampsia. Overweight (OR = 2.41, [1.07; 5.43], $p = 0.0335$), obesity class I, II and III (OR = 20.36, [4.32; 95.99], $p = 0.0001$) were associated with higher rates of preeclampsia. A poor negative correlation was found between BMI and GW of pregnancy outcome ($\rho = -0.24$; $r2 = 0.104$; $p = 0.006$). Higher BMI ($\beta = -0.14$, [-0.21; -0.07], $p = 0.0002$) was associated with lower values of GW of pregnancy outcome.

Conclusions. Presence of obesity or overweightness in the first trimester of pregnancy poses a significant risk factor for preeclampsia and preterm delivery.

Keywords: obesity in pregnancy, preeclampsia, preterm delivery

Introduction

Obesity is acknowledged by the World Health Organization (WHO) as an independent disease. Obesity is a metabolic disorder in which weight gain is achieved at the expense of fatty tissue, so that body fat is greater than 30% in women. The World Health Organization (WHO) has stated that obesity is the predominant chronic health concern among adults worldwide, surpassing malnutrition and growing into a more severe issue. The incidence of obesity on a global scale has markedly risen over recent decades, prompting the World Health Organization (WHO) to characterize it as a "global epidemic." The most recent report from the World Health Organization (WHO) indicates that in the European region, more than half of adults are affected by these conditions. Although approximately 54% of women experience overweight, they are more frequently affected by obesity, with 24% of women affected compared to 22% of men [1].

Fat tissue is a great source of energy, but it is also an important endocrine organ in which numerous adipocins are secreted. In obesity, fat tissue produces significantly more adipocytes than in normal nutrition, with much more significant visceral fat tissue that is metabolically active. Adipocins in the liver trigger the generation of acute phase reactants like C-reactive protein (CRP) and inflammatory cytokines such as PAI-1, leptin, adiponectin, IL-6, TNF-α, among numerous others [2, 3].

Preeclampsia is characterized by the onset of high blood pressure (≥140 and/or ≥90 mmHg) occurring for the first time after the 20th week of pregnancy, with measurements taken at least twice within a span of four to six hours, accompanied by proteinuria exceeding 300 mg in a 24-hour urine sample [4–6]. The exact mechanisms underlying preeclampsia are still not fully understood, but it is believed to result from a combination of factors including stress on syncytiotrophoblasts, dysfunction of the maternal endothelium, oxidative stress, and systemic inflammation in the pregnant woman [7]. In obese participants who later develop preeclampsia, pro-inflammatory markers (including IL-1α, IL-1β, IL-6, IFN-α, IFN-γ, GM-CSF, IL-12p70, IL-17α, TNF-α, and IL-8) as well as anti-inflammatory markers (such as IL-4, IL-10, and IL-13) are elevated during the first and second trimesters compared to those who do not develop preeclampsia [8]. Furthermore, there exists a robust correlation between maternal obesity and preeclampsia, characterized by a similar pattern of heightened cytokine expression [9]. The broadening of the preeclampsia definition by the International Society for the Study of Hypertension in Pregnancy (ISSHP) in 2018 has resulted in a greater number of women being diagnosed with the condition. Consequently, studies similar to those referenced above would likely reveal an even more pronounced correlation between maternal obesity and preeclampsia [10]. Consequently, there has been a rise in the prevalence of maternal obesity, emerging as the paramount concern in pregnancy-related health. Obesity exerts profound effects on both the mother and her offspring, leading to a spectrum of complications such as gestational hypertension, diabetes, preeclampsia, premature delivery, and spontaneous abortions. Moreover, it is linked with short- and long-term repercussions for both maternal and offspring health [11]. The results of numerous studies indicate a link between obesity and complications in mothers and fetuses (gestational diabetes, gestational hypertension, premature labor, preeclampsia, eclampsia, fetal macrosomy, stillbirth, etc.). Obesity of mothers doubles the risk of perinatal death. Obesity, through epigenetic alterations, also influences future generations. Exposure to an obesogenic environment in utero triggers developmental programming, heightening the likelihood of obesity in offspring. Furthermore, as these offspring encounter environmental factors conducive to obesity, particularly high-calorie diets and sedentary lifestyles, their susceptibility to becoming overweight or obese as adults amplifies, thereby escalating the risk of developing diabetes and cardiovascular disease later in life [12, 13].

Research conducted in Sweden revealed that elevated maternal pre-pregnancy body mass index (BMI), a gauge of weight relative to height, was linked to heightened odds of adverse pregnancy outcomes [14]. Obesity elevates the likelihood of a medically indicated premature birth [15, 16]. Both obese and overweight women faced an elevated risk of delivering at or before 32 weeks gestation and showed a slightly increased likelihood of delivering prior to 37 weeks [17]. A recent meta-analysis indicates that the occurrence of preterm prelabor rupture of membranes and extreme preterm birth (< 28 weeks gestation) rises with escalating BMI. Given that overweight and obese (OWO) pregnant women are more prone to pregnancy complications such as preeclampsia and gestational diabetes, the incidence of medically-indicated preterm birth is also elevated [18]. The United States Institute of Medicine (IOM) has provided guidelines concerning ideal gestational weight gain (GWG) during pregnancy to enhance outcomes for both mother and infant. The IOM recommends a total GWG range of 11 to 20 pounds (5 to 9 kg) for obese women and 15 to 25 pounds (6.8 to 11.3 kg) for women classified as overweight [19]. Medical societies universally advocate for prompt screening for gestational diabetes mellitus and early anesthesia evaluation in obese women. They also propose administering aspirin to prevent preeclampsia in the presence of additional risk factors. As a means to enhance pregnancy outcomes, aspirin initiation in the first trimester is recommended for all patients with a BMI exceeding 35 kg/m^2 [20, 21].

The aims of this study were to determine: differences in demographic and clinical characteristic of pregnant women between groups OB (obesity in pregnancy) and CG (control group with normal weight); the effect of obesity on the occurrence of preeclampsia in pregnancy; the effect of obesity on the occurrence of preterm delivery; the effect of obesity on the characteristics of the newborn (weight, length and Apgar score).

Methods

The research spanned the one-year period and was conducted prospectively at the Clinic for Gynecology and Obstetrics, Clinical Center of Vojvodina. It involved 133 pregnant patients aged over 18 years with singleton pregnancies between 11+0 and 13+6 weeks of gestation. Respondents were divided into two groups: OB - pregnancy with obesity (N = 55); and CG - control group without obesity (N = 78). The study included an analysis of data collected through a questionnaire containing demographic data, clinical data, and pregnancy completion data. Research instruments were specially constructed questionnaires.

In this study we analyzed: the age of pregnant women, BMI of pregnant women, the number of pregnancies, gestational week of pregnancy outcome, birth length and birth weight of the newborn, Apgar score in the first and fifth minute, presence of preeclampsia in pregnancy.

Maternal demographics, medical, and obstetric history were gathered through a self-report questionnaire, while body mass index was assessed during the initial hospital visit. Gestational age at the time of serum collection (between 11+0 and 13+6 weeks) was determined using ultrasound measurements and the first day of the last menstrual period. Information regarding pregnancy outcomes was extracted from the hospital maternal records.

Statistical analysis

The data were processed in the IBM SPSS Statistical Statistics Program, version 23 (SPSS Inc., Chicago, IL) and MedCalc for PC (MedCalc Software, Mariakerke, Belgium). Numeric variables were expressed as mean (±SD), while discrete outcomes were shown as absolute and relative (%) frequencies. Participants were categorized into two groups based on the obesity status. Normality and heteroskedasticity of continuous data were evaluated using the Shapiro-Wilk and Levene's tests, respectively. Continuous variables were compared using the unpaired Student t-test, Welch t-test, or Mann-Whitney U test depending on the data distribution. Categorical variables were compared using chi-squared test or Fisher's exact test as appropriate. Sensitivity, specificity, positive predictive value and negative predictive value for PE were determined with 2-by-2 contingency tables. We used Receiver-Operating-Characteristic curves to assess the ability to predict PE according to BMI (kg/m^2). The area under the curve and 95% confidence intervals were calculated. A multivariate logistic regression was performed to assess the relation between PE and the explanatory variables: Type of OB and BMI (kg/m^2); and Gestational week of pregnancy outcome with BMI (kg/m^2). Data were checked for multicollinearity and heteroskedasticity Spearman's coefficient was used to assess the correlation between BMI (kg/m^2) and gestational week of pregnancy outcome. The difference between gestational weeks of pregnancy outcome according to modalities of Type of OB was assessed with the Kruskal-Wallis. The existence of a statistically significant difference was taken at p <0.05. Sampling weights (except for sample description) were used during statistical analysis of data. The results were presented in tables and figures.

Results

The study included 133 pregnant women in the first trimester of pregnancy, among whom 41.35% were obese pregnant women, and 58.65% were of normal weight. Table 1 shows the results of the examined data between the groups. A statistically significant difference in average BMI (22.01 ± 1.83 vs. 30.26 ± 4.52; p < 0.001) and delivery time (37.94 ± 2.05 vs. 36.87 ± 2.45; p = 0.003) between control group and obese pregnant women was shown. The characteristics of the newborn differed significantly among the studied groups. Pregnant women who were obese developed PE significantly more often than the control group (61.82% vs. 28.21%; p < 0.001). The diagnostic performance of examined groups (obese

Table 1. Comparison according to group (control group vs obesity group)

Variable	CG N = 78	OB N = 55	p-Value
Age	30.67 (± 5.44) 95% CI: [29.44; 31.89] Range: (18.0; 42.0) N = 78	31.96 (± 5.55) 95% CI: [30.46 ; 33.47] Range: (21.0; 43.0) N = 55	0.182
BMI (kg/m^2)	22.01 (± 1.83) Range: (16.9; 24.9) N = 78	30.26 (± 4.52) Range: (25.0; 41.0) N = 55	<0.001
Number of pregnancies	2.29 (± 1.48) Range: (1.0; 7.0) N = 78	2.58 (± 1.52) Range: (1.0; 9.0) N = 55	0.131
Gestational week of pregnancy outcome	37.94 (± 2.05) Range: (28.0; 41.0) N = 78	36.87 (± 2.45) Range: (32.0; 41.0) N = 55	0.003
Body weight of child	3182.69 (± 600.63) 95% CI: [3047.27; 3318.11] Range: (1150.0; 4510.0) N = 78	2952.55 (± 621.25) 95% CI: [2784.6; 3120.49] Range: (1850.0; 4080.0) N = 55	0.034
Body length of child	49.47 (± 2.54) Range: (40.0; 56.0) N = 78	48.2 (± 2.27) Range: (45.0; 52.0) N = 55	0.002
Apgar score in 1st minute	8.77 (± 1.18) Range: (6.0; 10.0) N = 78	8.31 (± 1.2) Range: (6.0; 10.0) N = 55	0.017
Apgar score in 5th minute	9.41 (± 0.829) Range: (7.0; 10.0) N = 78	9.0 (± 0.923) Range: (7.0; 10.0) N = 55	0.006
PE Yes No	22 (28.21%) 56 (71.79%) N = 78	34 (61.82%) 21 (38.18%) N = 55	<0.001

*CG - control group; OB - obesity group; BMI - body mass index; PE - preeclampsia vs. non obese), as a predictor for PE, was assessed. The results demonstrated a sensitivity of 60.7% and a specificity of 72.7%, while the positive predictive value (PPV) and negative predictive value (NPV) were 61.8% and 71.8%, respectively. The area under the curve was 0.696 (95% CI: [0.601; 0.79]) for BMI (kg/m²) to predict PE. BMI had significant, but moderate predictive ability to predict PE (Figure 1). In multivariate analysis, higher BMI (kg/m²) (OR=1.19, [1.09; 1.29], $p < 0.0001$) was associated with higher rates of PE. For every 1 increase in BMI, the chance of developing PE increased 1.19 times (Table 2). The PE

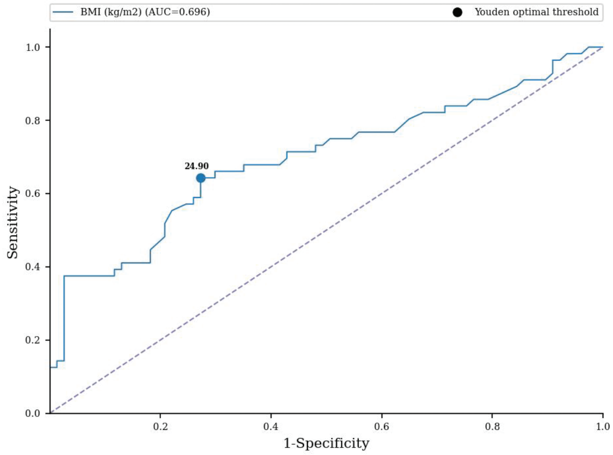

Figure 1. The area under the curve for BMI to predict PE

*BMI - body mass index; AUC - area under the curve

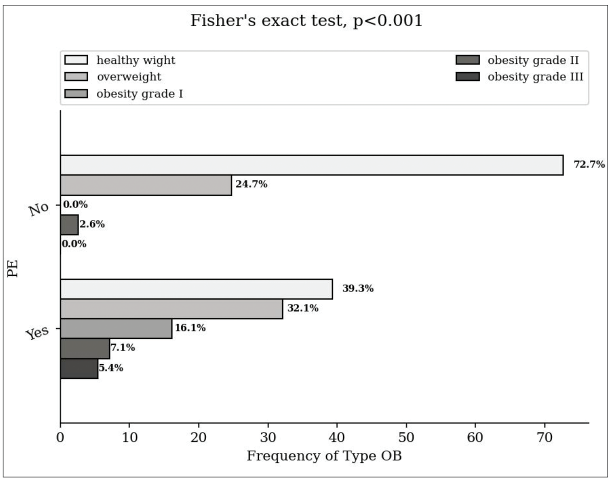

Figure 2. Frequency of type of obesity in the occurrence of PE

*PE - preeclampsia; OB - obesity

Table 2a. Prediction of BMI and type of OB in occurrence of PE

	Odds Ratio	p-Value
BMI (kg/m²)		
Risk for each 1-unit increase	1.19 [1.09; 1.29]	<0.001
Type OB		
Reference: normal weight change reference		
obesity I, II, III	20.36 [4.32; 95.99]	<0.001
overweight	2.41 [1.07; 5.43]	0.033

Table 2b. Prediction of BMI in occurrence of preterm delivery

BMI (kg/m²)		
Risk for each 1-unit increase	-0.141 [-0.213; -0.0698]	<0.001

*BMI - body mass index; OB - obesity; PE - preeclampsia

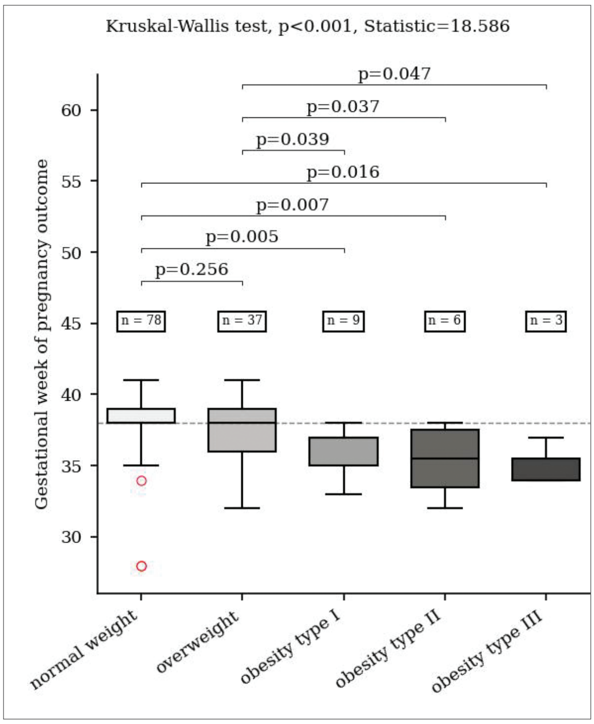

Figure 3. Median values of Gestational week of pregnancy outcome between obesity groups

rates were respectively 61.82% in obese patients and 28.21% in non-obese patients (OR = 4.12; CI [1.98 ; 8.59]; $p < 0.001$). Pregnant women who developed PE had a significantly ($p < 0.001$) higher percentage of overweight (32.1% vs. 24.7%), obesity degrees I (16.1% vs. 0%), II (7.1% vs 2.6%) and III (5.4% vs. 0%) compared to pregnant women who did not develop PE, where the highest percentage of pregnant women had a normal weight (72.7% vs. 39.3%) (Figure 2). In multivariate analysis, overweight (OR = 2.41, [1.07; 5.43], p = 0.0335), obesity I, II, III (OR = 20.36, [4.32; 95.99], p = 0.0001) were associated with higher rates of PE. Pregnant women who were overweight were 2.41 times more likely to develop PE than those with a normal weight. Pregnant women who were obese (grade I, II, III) had a 20.41 times greater chance of developing PE (Table 2). A significant difference in median GW was shown between all examined groups (38 (IQR 1.0) vs. 38 (IQR 3.0) vs. 37 (IQR 2.0) vs. 35,5 (IQR 4.0) vs. 34 (IQR 1.5); $p < 0.001$). A significant difference in GW between the group of normally nourished pregnant women and those with I (p = 0.005), II (p = 0.007) and III (p = 0.016) degrees of obesity was shown, as well as between GW in overweight and each of the obese groups (p = 0.039; p = 0.037; p = 0.047). There was no difference in GW between normally nourished and overweight pregnant women (p = 0.256) (Figure 3). A poor negative correlation was found between BMI (kg/m^2) and gestational week of pregnancy outcome (p = -0.24; r2 = 0.104; p = 0.006). The higher the pregnant woman's BMI, the earlier the delivery ended (Figure 4). In multivariate analysis, higher BMI (kg/m^2) (β = -0.14, [-0.21; -0.07], p = 0.0002) was associated with lower values of gestational week of pregnancy outcome. For every 1 increase in BMI, delivery ended 0.14 times earlier (Table 2).

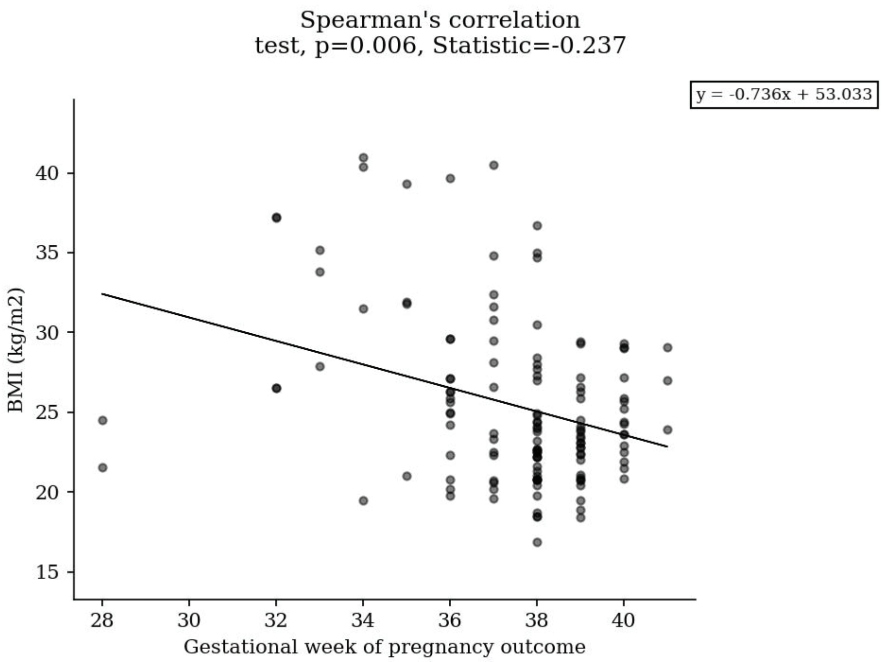

Figure 4. Correlation between BMI and GW
*BMI - body mass index; GW - gestational week of pregnancy outcome

Discussion

The findings from the study conducted by Baeten et al. reaffirmed that obesity significantly increased the risk of pregnancy complications and adverse outcomes [15]. Higher maternal pre-pregnancy BMI, a measure of weight for height, was associated with the increased risk of adverse pregnancy outcomes [14]. In our study preeclampsia was statistically significantly more frequent in the OB group and there were significant differences in type of obesity between group of pregnant women with and without preeclampsia. These results are consistent with many studies. Mohammadi et al. have shown that women who were overweight or obese were at increased risk of preeclampsia in comparison with women of normal weight [16]. Bornard's findings corroborate these results, indicating a remarkable escalation in the risk of preeclampsia from BMI of 15 to 30 kg/m². Relative to women with BMI of 21, the adjusted risk of preeclampsia doubled at BMI of 26 and nearly tripled at BMI of 30. Conversely, women with BMI of 17 exhibited a 57% decrease in the risk of preeclampsia compared to those with BMI of 21, while BMI of 19 was linked with a 33% reduction in risk [17]. The likelihood of developing preeclampsia was 1.4 times higher in overweight women and 1.8 times higher in obese women compared with women with a normal BMI. Furthermore, this relationship between BMI and preeclampsia is slightly more pronounced among mothers delivering at term than among those delivering preterm [18]. In a cohort study conducted by Thelma et al., it was demonstrated that elevated pre-pregnancy BMI served as a robust and independent risk factor for preeclampsia [19].

In a nationwide cohort study led by Sven et al., encompassing over 1.5 million deliveries and including data on early pregnancy BMI, it was discovered that maternal overweight and obesity during pregnancy were linked to heightened risks of preterm delivery. Particularly elevated risks were noted for extremely preterm deliveries [20]. Several studies have indicated an elevated risk of preterm birth in overweight and obese women [21–23], while others have suggested a slight reduction in risk [24, 25]. In our study there were significant differences between the groups with respect to gestational week of pregnancy outcome, and we calculated medium negative correlation between mothers BMI and gestational week of pregnancy outcome. These results mean that pregnant women who have been overweight or obese have given birth in earlier gestational weeks. Women classified as obese or overweight faced heightened risks of delivering at or before 32 weeks gestation and exhibited a slightly elevated likelihood of delivering before 37 weeks [15]. Inadequate gestational weight gain in underweight pregnant women, excessive gestational weight gain in overweight/obese women, and excessive gestational weight gain in the third trimester emerged as significant predictors of preterm birth [26].

The findings from certain pooled cohort studies [6, 22] indicated that overweight and obese women experienced a reduced likelihood of delivering the infant with low birth weight, which contradicts our own results. Also, Mohammadi et al. showed that infants of obese women were more likely to be macrosomic [16]. The study by Lima et al. corroborated the notion that mothers with higher pre-pregnancy BMI typically deliver heavier babies. Furthermore, they found that greater gestational weight gain had a more pronounced impact on birth weight than pre-pregnancy BMI alone. Pregnant women with higher pre-pregnancy BMI and increased weight gain during pregnancy tended to have newborns with higher birth weights. However, it was observed that mothers with high pre-pregnancy BMI who gained less weight during pregnancy had children with lower birth weights [27]. We find low negative correlation between mothers' BMI and characteristics of newborn. The results of our research are in accordance with the study of Bawtwn et al. showing that higher BMI was inversely associated with delivery of the small-for-gestational-age infant [15]. In the study by Bogaerts et al., it was demonstrated that women with gestational weight gain (GWG) below the Institute of Medicine (IOM) guidelines had a higher likelihood of being diagnosed with gestational diabetes mellitus. Additionally, they were at increased risk for placental abruption, delivering small-for-gestational age infants, and having neonates with low birth weight [28]. Our results underscore the significance of enhancing healthcare for women of reproductive age by integrating them into family planning programs that incorporate nutritional monitoring and education. Furthermore, our findings reinforce existing recommendations to mitigate excessive weight gain during adolescence and early adulthood, preceding the first pregnancy. Maternal overweight stands out as one of few modifiable risk factors for adverse gestational outcomes prior to pregnancy, and this study provides additional support for weight management initiatives aimed at enhancing the overall health of our population.

Conclusion

Presence of obesity or overweightness in the first trimester of pregnancy poses a significant risk factor for preeclampsia and preterm delivery.

Hence, establishing standardized international protocols for the efficient management of obese women is crucial to provide clear guidance for clinical practice and ultimately enhance pregnancy outcomes safely.

Funding source. The authors received no specific funding for this work.

Ethical approval. The Ethics Committee of the Clinical Center of Vojvodina, Novi Sad, Serbia, approved the study and informed consent was obtained from all individual respondents. Participation in the research was voluntary. The research was conducted according to the Declaration of Helsinki.

Conflicts of interest. The authors declare no conflict of interest.

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Preeklampsija i rizik od prevremenog porođaja: značaj gojaznosti u trudnoći

Tamara Perić[1,2], Mirjana Bogavac[1,3], Zoran Belopavlović[1,3]

[1]Univerzitet u Novom Sadu, Medicinski fakultet, Novi Sad, Srbija

[2]JZU Bolnica „Sveti Vračevi“, Bijeljina, Republika Srpska, Bosna i Hercegovina

[3]Klinički centar Vojvodine, Klinika za ginekologiju i akušerstvo, Novi Sad, Srbija

Uvod. U svetu ima 38% gojaznih trudnica, od toga 24,5% u Evropi. Gojaznost povećava rizik od prevremenog porođaja kroz poremećaje trudnice koji su povezani sa gojaznošću, uključujući preeklampsiju. Ciljevi su bili da se utvrde razlike u demografskim i kliničkim karakteristikama trudnica između grupa, uticaj gojaznosti na pojavu preeklampsije i prevremenog porođaja, uticaj gojaznosti na karakteristike novorođenčeta.

Metod. Jednogodišnja prospektivna studija obuhvatila je 133 trudnice gestacijske starosti 11–14 gestacionih nedelja (GN), podeljene u dve grupe: OB (41,35%) i CG (58,65%). Podaci su obrađeni u IBM SPSS verziji 23.

Rezultati. Dokazana je statistički značajna razlika u prosečnoj vrednosti BMI (22,01 ± 1,83 vs. 30,26 ± 4,52; $p < 0{,}001$) i vremena porođaja (37,94 ± 2,05 vs. 36,87 ± 2,45; $p = 0{,}003$) između CG i OB. Gojazne trudnice su češće razvijale preeklampsiju nego normalno uhranjene trudnice (61,82% vs. 28,21%; $p < 0{,}001$). BMI ima značajnu slabu prediktivnu sposobnost za preeklampsiju (AUC 0,696 (95% CI: [0,601; 0,79]). Više vrednosti BMI (OR = 1,19, [1,09; 1,29], $p < 0{,}0001$) su povezane sa većim stopama preeklampsije. Prekomerna težina (OR = 2,41, [1,07; 5,43], $p = 0{,}0335$), gojaznost I, II i III stepena (OR = 20,36, [4,32; 95,99], $p = 0{,}0001$) su povezani sa većim stopama preeklampsije. Dokazana je slaba negativna korelacija između BMI i GN porođaja ($p = -0{,}24$; $r2 = 0{,}104$; $p = 0{,}006$). Više vrednosti BMI ($\beta = -0{,}14$, [-0,21; -0,07], $p = 0{,}0002$) su povezane sa ranijim porođajem.

Zaključak. Trudnice prekomerne težine i gojazne trudnice u prvom trimestru značajno češće imaju preeklampsiju i prevremeni porođaj nego trudnice normalne uhranjenosti.

Ključne reči: gojaznost u trudnoći, preeklampsija, prevremeni porođaj