Original article

Relationship between Maternal Pregestational Body Mass Index and Neonatal Oxidative Stress

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Summary. *Introduction.* Obesity represents a public health problem and within women in labor, it affects not only the mother and the pregnancy but also the health of the fetus. Maternal overweight and obesity in pregnancy are factors that cause metabolic changes in the newborn, including elevated levels of oxidative stress (OS). The aim of the study was to determine the association between maternal body mass index (BMI) and oxidative stress marker levels in their newborns. *Methods.* A prospective study included 150 mothers and their healthy newborns who were divided into three groups according to progestational BMI. Maternal and umbilical cord blood samples were collected immediately after delivery. Triglycerides and Thiobarbituric Acid Reactive Substances (TBARS) levels were quantified. *Results.* Triglyceride levels were significantly higher in obese mothers and their newborns compared to overweight and normal weight mothers. Significantly elevated levels of TBARS have been observed in obese mothers and their newborns. Maternal BMI was significantly positively correlated with TBARS in mothers ($r = 0.290$; $P = 0.000$) and in newborns ($r = 0.387$; $P = 0.000$). Maternal ($r = 0.540$; $P = 0.000$) and neonatal triglycerides levels ($r = 0.483$; $P = 0.000$) were significantly positively associated with BMI. *Conclusion.* The values of oxidative stress markers TBARS and triglycerides in mothers and newborns immediately after birth were significantly higher in the obese mothers group.

Key words: Pre-pregnancy body mass index, oxidative stress, newborn

Introduction

Obesity is a public health problem in both developed and developing countries (1). Endogenous and exogenous factors have a significant influence on the increase in the prevalence of obesity. Of the exogenous factors, the most common are inadequate diet, decreased physical activity, and sedentary lifestyle (2). In recent decades, the prevalence of overweight in women, including women in the reproductive period, has increased worldwide and is around 38% (3). Research on women in the Republic of Serbia (4) and Vojvodina (5) has shown that overweight is present in 29.1% and 31.9% and obesity in 17.8% and 22.2% respectively.

Maternal obesity not only affects the mother and pregnancy, but also the health of the fetus. Maternal overweight and obesity in pregnancy are factors that cause metabolic changes in the newborn, including elevated levels of oxidative stress (OS). Numerous studies indicate that obesity in pregnancy is associated with OS (6-9). OS is defined as an imbalance between the formation of free radicals and the antioxidant capacity of an organism (10). It is cited as a significant risk factor for the development of numerous neonatal diseases such as necrotizing enterocolitis, retinopathy of prematurity, bronchopulmonary dysplasia, respiratory distress syndrome, periventricular leukomalacia, intraventricular hemorrhage and congenital malformation

(11,12). Obesity can also be a risk factor for the developing diseases later in life, such as metabolic, cardiovascular, and neurodegenerative diseases (13).

A good biomarker of oxidative stress, which is often used in clinical researches and represents the end product of lipid peroxidation, is malondialdehyde (MDA) (11,14). MDA is determined indirectly, by measuring a substance that reacts with thiobarbituric acid (TBARS) in plasma. It is a highly toxic molecule, and its interaction with DNA and proteins can be mutagenic and atherogenic (15-17).

Numerous studies have shown increased levels of lipid peroxidation products in the plasma of obese women and newborns during childbirth (6-8). Despite data on the impact of obesity on the oxidative/antioxidant status of mothers and newborns, there are still insufficient data on the mechanisms that explain these changes. The levels of OS should be monitored before, during, and after gestation in obese mothers. Therefore, the aim of this study was to determine the association between maternal pregestation BMI and TBARS oxidative stress marker levels in their neonates.

Methods

The research has been conducted as a randomized prospective study of the clinical type at the Clinic for Gynecology and Obstetrics of the Clinical Center of Vojvodina, Novi Sad, Serbia. Inclusion criteria were: maternal health, regularly monitored, normal course of pregnancy, gestational age of 37 - 41 weeks, healthy newborns, without congenital anomalies and complications during childbirth. Exclusion criteria were: pregnant women with chronic disease (asthma, diabetes, heart disease, autoimmune and other diseases), anemia (Hgb<105 g/L), pregnant women taking certain therapy during pregnancy, and twin pregnancy.

Body weight before pregnancy was obtained from medical record. At admission, body height was measured with a stadiometer in cm and body weight with a medical scale in kg. Pregestational BMI was calculated as the ratio of body weight in kg to the square of body height in meters. Based on BMI, mothers and their newborns were classified into three groups: normal weight - NW (BMI = 18.5-24.9 kg / m2), overweight - OW (BMI = 25-29.9 kg / m2), and obese - OB (BMI ≥ 30 kg / m2) according to WHO criteria (18).

In the examined mothers, 4 ml of venous blood was taken from the peripheral vein, and in newborns, 4 ml of venous blood was taken from the umbilical vein at the time of umbilical cord clamping from the part that is later cut off. The samples were collected using violet-topped evacuated tubes with ethylenediaminetetraacetic acid dipotassium salt dehydrate (K_2EDTA) as a blood clotting inhibitor (Becton Dickinson, USA). Enzymatic determination of triglycerides in blood plasma was performed immediately after the blood collection on the chemistry analyzer AU 480 (Beckman Coulter, Switzerland) at the Clinic for Gynecology and Obstetrics of the Clinical Center of Vojvodina in Novi Sad, Serbia. The remaining aliquots were stored at -20 °C in the period not longer than three months up until biochemical analysis of the oxidative stress biomarkers. TBARS levels were analyzed by Agilent 8453 ultraviolet-visible spectrophotometry system (Agilent Technologies, USA) in the Department of Pharmacy, Faculty of Medicine, University of Novi Sad, Serbia. The assay was performed, as previously described by Buege et al. (19). The results were expressed in nmol/mg protein.

Written informed consent was obtained from all participants, i.e. mothers. The study has been approved by the Ethics committee of the Clinical Center of Vojvodina.

StatisticalAnalysis

Data are presented as average value and standard deviation for continuous variables, and number and corresponding percentage for categorical variables. The Shapiro-Wilks test was used to assess the normality of the distribution. The difference between the groups was determined using One-Way ANOVA with the post-hoc Bonferroni test. The Chi-square test was used for comparing categorical variables. The association between TBARS and triglycerides with maternal BMI was determined by Pearson correlation analysis and estimated linear regression line. Statistical analyzes were carried out using the IBM SPSS Statistics 20. Results were considered significant at $P < 0.05$.

Results

Maternal age, maternal body height, and gestational age (Table 1) did not differ in the study groups ($P>0.05$). The largest increase in maternal body weight was in the NW group (9.1 ± 2.0 kg), and the smallest in the OB group (7.8 ± 1.2 kg). Newborns of obese mothers had a statistically significantly higher birth weight than newborns of mothers with normal weight ($P<0.01$).

Table 1.The triglyceride values of obese mothers and their newborns were significantly higher than the values of overweight and normal-weight mothers (Table 2).

Table 2.The concentration of TBARS is significantly higher in obese mothers. Newborns of obese mothers had statistically significantly higher values of TBARS than newborns of mothers of normal weight (Table 3). Newborns of obese mothers had statistically significantly higher TBARS values than newborns of normal-weight mothers (Table 3).

Table 1. Demographic and anthropometric data of mothers and their newborns

	NW (n=83)	OW (n=36)	OB (n=31)	P-value*
Mother (Pre-pregnancy)				
Age (y)	30.4 ± 4.8	32.2±5.3	30.9±5.9	0.226
Height (cm)	165.5 ±6.5	166.1 ±5.0	165.2 ±5.8	0.829
Weight (kg)	61.5 ±5.9	73.3 ±4.6[a]	83.1 ±10.2[ab]	<0.001
BMI (kg/m^2)	23.6±2.0	27.6±1.2[a]	31.7±1.8[ab]	<0.001
Weight gain (kg)	9.1±2.0[c]	8.7±1.3	7.8±1.2	0.004
Newborn				
Gender M/F	40/43	22/14	15/16	0.744
Gestational age at delivery (wk)	38.8 ±1.0	38.8 ±0.8	39.1±1.16	0.667
Birth weight (g)	3372.3±362.4	3531.8±389.5	3583.2±471.5[a]	0.017

Data are presented as mean ± standard deviation. *One-Way ANOVA and χ^2 tests were used for continuous and categorical variables comparison, respectively. Post hoc comparisons using the Bonferroni test; a - statistical significance relative to Normal weight; b - statistical significance relative to Overweight; c - statistical significance relative to Obesity; NW = normal weight; OW = overweight; OB = obese; BMI = body mass index

Table 2. The triglyceride values of obese mothers and their newborns

	NW (n=83)	OW (n=36)	OB (n=31)	P-value*
The triglyceride of newborns	0.33±0.09	0.48±0.11 [a]	0.73±0.12 [ab]	<0.001
The triglyceride of mothers	2.60±0.79	3.32±0.87[a]	3.88±0.98[ab]	<0.001

Data are presented as mean ± standard deviation. *One-Way ANOVA. Post hoc comparisons using the Bonferroni test; a - statistical significance relative to Normal weight; b - statistical significance relative to Overweight; NW = normal weight; OW = overweight; OB = obese; BMI = body mass index

Table 3. The concentration of TBARS for newborns and theirmothers

	NW (n=83)	OW (n=36)	OB (n=31)	P-value*
TBARS of newborns	2.69±0.92	3.18±0.86	3.67±0.94[a]	<0.001
TBARS of mothers	2.18±0.80	2.61±0.76	3.70±0.98[ab]	<0.001

Data are presented as mean ± standard deviation. *One-Way ANOVA. Post hoc comparisons using the Bonferroni test; a - statistical significance relative to Normal weight; b - statistical significance relative to Overweight; NW = normal weight; OW = overweight; OB = obese; BMI = body mass index

Table 3.Graph 1 shows a significant positive correlation between BMI TBARS mothers (r = 0.290; P = 0.000) and their newborns (r = 0.387; P = 0.000).

Figure 1**.** The triglyceride values of mothers (r = 0.540; P = 0.000) and their newborns (r = 0.483; P = 0.127) are significantly positively correlated with pregestational BMI (Figure 2).

Discussion

The study aimed to establish a relationship between maternal pregestation BMI and oxidative stress in newborns. In this study, the birth weight of the newborns of obese mothers was significantly higher compared to the birth weight of the newborns of normal-weight

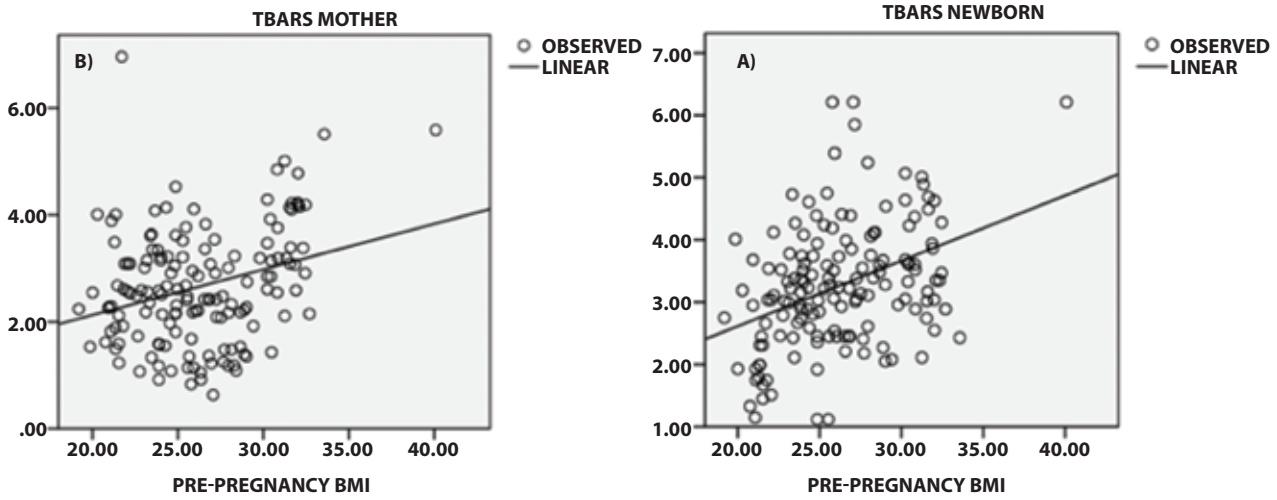

Figure 1. Correlation between BMI and A) TBARS Newborn (r=0.387; P=0.000); B) TBARS Mother (r=0.290; P=0.000)

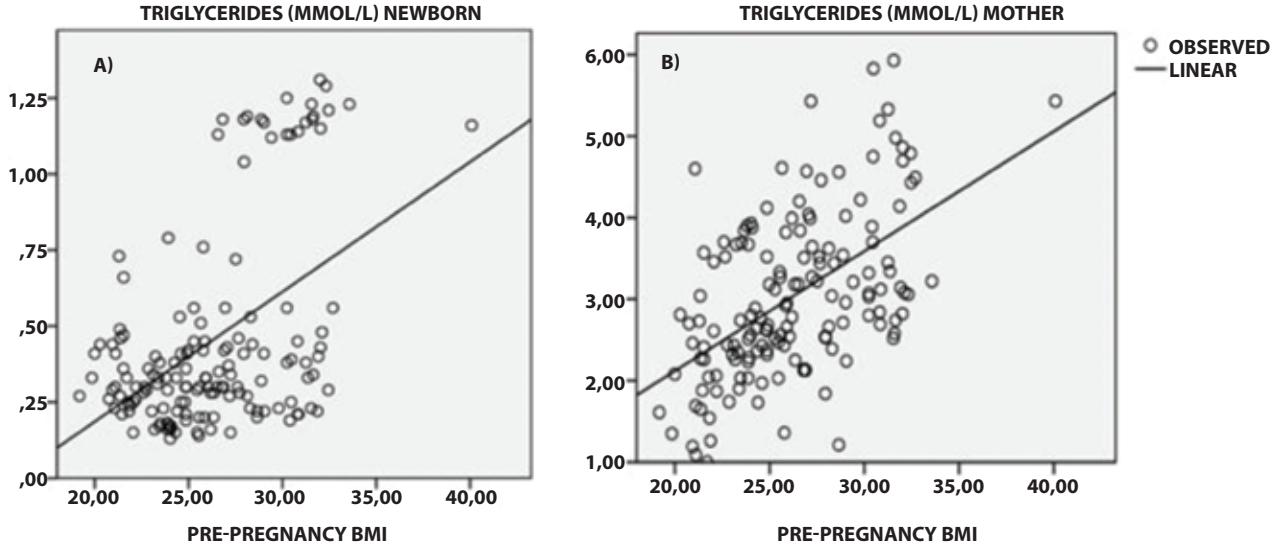

Figure 2. Correlation between BMI and A) Triglycerides (mmol/L) Newborn (r=0.483; P=0.000); B) Triglycerides (mmol/L) Mother (r=0.540; P=0.000)

mothers. These results are consistent with those obtained by Cnattingius et al. (20). However, there are studies in which no significant association was found between maternal BMI and the weight of newborns (7).

The recommended weight increase for obese women during pregnancy is up to 6.8 kg, overweight from 6.8 to 11.2 kg, and for normal-weight between 11.2 and 15.9 kg (21). In this study, body weight increase during pregnancy in normal-weight mothers was lower than recommended (9.1 kg), in obese mothers higher (7.8 kg), while in overweight mothers the increase was within the recommended values (8.7 kg). Similar results were reported by Gallardo et al. (7), while Soliman et al. (22) observed an increase in body weight in obese mothers over 20 kg.

Maternal obesity is known to lead to placental dysfunction (22-25). Saben et al. were examining changes in the placenta in obese women. They observed the presence of inflammation, increased lipid concentrations, and increased oxidative stress. Increased lipid concentration and lipid peroxidation levels in the placenta of obese women lead to increased production of free radicals and OS (26). Significant changes in oxidative/antioxidant balance also exist during a normal pregnancy due to increased metabolic activity and the need for oxygen in the placenta, which is a significant source of prooxidants in both mother and fetus. Obesity is considered to be a chronic inflammatory condition that can disrupt the placental barrier and allow the passage of prooxidant substances (27, 28). Obesity during pregnancy leads to an imbalance in the proantioxidant status of the mother and can additionally affect the increase of oxidative stress levels in both mothers and newborns. In previous studies, the association of maternal obesity with increased oxidative stress was observed (24).

In our study, TBARS values were significantly elevated in obese mothers compared with normal-weight mothers. Similar results were obtained in a previous study (6). The observed significant positive correlation between BMI and TBARS of mothers ($r = 290$; $P = 0.000$) is contrary to the results of Ballesteros-Guzman et al. (9).

The results of the study showed significantly elevated values of TBARS in newborns of obese mothers. Elevated levels of TBARS in newborns whose mothers were overweight or obese are a consequence of the mothers' oxidative stress. The obtained results are in accordance with the results of previous studies, where an increased concentration of OS markers was observed in newborns of obese mothers (6-8). The observed positive correlation between maternal BMI and newborns' TBARS ($r = 387$; $P = 0.000$) indicates that an increase in maternal BMI significantly increased TBARS in newborns, as shown in a previous study (6).

Oxidative stress associated with obesity during pregnancy can be a factor that contributes to the postnatal consequences of the newborn. MDA is thought to be potentially atherogenic. Increased concentrations of MDA in adults are associated with an increased risk of coronary artery disease (CAD). Descendants of mothers with overweight and obesity in pregnancy show elevated levels of MDA which can lead to greater susceptibility to the development of CAD in later stages of life (29, 30). Newborns of obese mothers also have an increased risk of neurodevelopmental disorders (motor and cognitive problems and attention deficit hyperactivity), obesity, insulin resistance and diabetes mellitus in adulthood (13, 31).

In our study, mothers with overweight and obesity had significantly higher triglyceride values compared to those with normal weight. These results are consistent with the findings of other authors, who observed elevated triglyceride levels in obese women (32, 33). Increased estrogen levels and insulin resistance during pregnancy are considered to be responsible for this hypertriglyceridemia (34). The level of triglycerides in newborns of obese mothers in our study was significantly higher than the level of values in newborns with normal-weight mothers, which is in line with previous research (35).

The advantages of this study are standardized measurement procedures and a sufficiently large number of patients included in the study, which enabled more accurate estimates between the examined groups. Limitations of the study are the lack of data on diet and habits (sedentary lifestyle, smoking, alcohol) before and during pregnancy.

Conclusion

The results of this study suggest that maternal overweight and obesity before pregnancy are

significantly associated with an increase in OS in their newborns. Since maternal obesity, in addition to affecting their health, also affects the health of their newborns, it is necessary to pay attention to educating women about the nutritional status before pregnancy and to newborns after birth and in later life. Newborns with high levels of oxidative stress should be identified early to avoid exposure to other risk factors, such as obesity, unhealthy diet, and sedentary lifestyle, which increase the risk of developing metabolic cardiovascular and neurodegenerative disorders in later life.

Conflict of Interest disclosure: The authors declare no conflicts of interest.

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