

The association between obesity and hematologic inflammatory markers in the first trimester pregnancies

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Abstract

Objective: Obesity is the defined as the abnormal or excessive accumulation of the fat which is harmful for the health, and its prevalence has been increasing. Many studies have shown that obesity alone leads to inflammation and causes poor gestational outcomes. In our study, we aimed to investigate the association between basic hematologic markers and obesity in the first trimester pregnancies.

Methods: A total of 321 pregnant women who admitted to the clinic of gynecology and obstetrics in a tertiary state hospital were included in the study. The patients were separated into three groups, which were normal weight (BMI: 18–24.9 kg/m²), overweight (BMI: 25–29.9 kg/m²), and obese (BMI>30 kg/m²). Of the patients, the demographic data (age, gravida, and parity) and the parameters of hemoglobin, hematocrit, white blood cell, neutrophil, lymphocyte, platelet (PLT), eosinophil, basophil, mean platelet volume (MPV), platelet distribution width (PDW), neutrophil/lymphocyte ratio (NLR), red blood cell distribution width (RDW), plateletcrit (PCT) and platelet/lymphocyte ratio (PLR) measured in the complete blood count which was checked in the first trimester routinely during the pregnancy follow-up were analyzed. The three groups were compared in terms of inflammatory markers.

Results: The patients were evaluated in three groups: 108 patients with normal weight (Group 1), 109 overweight patients (Group 2) and 104 obese patients (Group 3). No significant difference was found in terms of age, parity and gravida when the demographic data were analyzed among the groups (p>0.05). When the groups were compared in terms of hematologic markers, similar values were found in the markers other than white blood cell, neutrophil, lymphocyte, PLT and PCT values. The difference among white blood cell, neutrophil, lymphocyte, PLT and PCT values were between the patients with normal weight and obese patients, and the values of these markers were found higher in overweight / normal weight patient groups than the normal group (p<0.05).

Conclusion: The values of white blood cell, neutrophil, lymphocyte, PLT and PCT which were shown to be associated with inflammation were higher in the obese patients.

Keywords: Obesity, platelet, inflammation, hemoglobin.

Özet: İlk trimester gebeliklerde obezite ve hematolojik inflamasyon belirteçleri arasındaki ilişki

Amaç: Obezite, sağlığa zarar veren anormal ya da aşırı yağ birikimi olarak tanımlanmakta olup sıklığı giderek artmaktadır. Obezitenin tek başına inflamasyona sebep olup olumsuz gebelik sonuçlarına sebep olduğu birçok çalışmada gösterilmiştir. Bu çalışmamızda basit hematolojik belirteçler ile ilk trimester gebeliklerde obezite durumunun araştırılması amaçlanmıştır.

Yöntem: Üçüncü basamak bir devlet hastanesinin kadın hastalıkları ve doğum polikliniğine başvuran 321 gebe çalışmaya dâhil edildi. Hastalar normal kilolu (VKİ: 18–24.9 kg/m²), fazla kilolu (VKİ: 25–29.9 kg/m²) ve obez (VKİs30 kg/m²) olarak gruplandrıldı. Hastaların demografik verilerine (yaş, gravida, parite) ve rutin olarak gebe takibinde ilk trimesterde bakılan, tam kan sayımında ölçülen hemoglobin, hematokrit, beyaz küre, nötrofil, lenfosit, trombosit, eozinofil, bazofil, ortalama trombosit hacmi (MPV), trombosit dağılım genişliği (RDW), nötrofil-lenfosit oranı (NLR), eritrosit dağılım genişliği (RDW), plateletkrit (PCT) ve trombosit-lenfosit oranı (PLR) parametrelerine bakıldı. Bu üç grup inflamasyon belirteçleri açısından karşılaştırıldı.

Bulgular: Hastalar 108 normal kilolu (Grup 1), 109 fazla kilolu (Grup 2) ve 104 obez (Grup 3) olmak üzere 3 grupta incelendi. Gruplar arasında demografik veriler incelendiğinde; yaş, parite ve gravida açısından anlamlı fark gözlenmedi (p>0.05). Hematolojik belirteçlere bakıldığında beyaz küre, nötrofil, lenfosit, PLT, PCT değerleri dışında diğer belirteçler gruplar arasında benzer bulundu. Beyaz küre, nötrofil, lenfosit, PLT, PCT değerleri arasındaki farklılık normal kilolu ile obez hastalar arasında olup, bu belirteçlerin değerleri fazla kilolu / obez hasta grubunda normal gruba göre daha yüksek bulundu (p<0.05).

Sonuç: Obez hastalarda inflamasyonla ilişkisi gösterilmiş beyaz küre, nötrofil, lenfosit, PLT, PCT değerleri daha yüksek olarak bulunmuştur.

Anahtar sözcükler: Obezite, trombosit, inflamasyon, hemoglobin.

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Introduction

Obesity is the defined as the abnormal or excessive accumulation of the fat which is harmful for the health. Since 1975, its rate increased three times all over the world.^[1] According to the data of the World Health Organization (WHO) in 2016, 40% of adult women and 39% of adult men are overweight while 15% of adult women and 11% of adult men are obese.^[2] According to the data of Public Health Agency of Turkey in 2010, 20.5% of men, 41% of women and 30.3% of the society are obese.^[3] Clinically most appropriate marker for the classification of obesity is body mass index (BMI). BMI is found by dividing weight in kilograms by height in meters squared (kg/m²). WHO classified obesity in 6 groups according to BMI values: Underweight BMI<18.5 kg/m², normal weight BMI: 18-24.9 kg/m², overweight BMI: 25-29.9 kg/m², obese class 1 BMI: 30-34.9 kg/m², obese class 2 BMI: 35-39.9 kg/m², and obese class 3 BMI>40 kg/m².^[1] Obesity a significant public health problem with many potential risks in the long term; cardiovascular disease, diabetes, osteoarthritis and cancer (breast, endometrium, ovary, liver, colon, prostate etc.) are among these risks. Maternal obesity is important in terms of the complications before, during and after pregnancy. Subfertility during preconceptional period, spontaneous abortion, gestational hypertension, preeclampsia, gestational diabetes, surmaturity, macrosomia, dystocia and intrauterine death during antenatal period, and increased risks of hemorrhage, infection and thromboembolism during postnatal period are associated with maternal obesity.^[4] It is known that fat tissue is associated with inflammation and infection.^[5] It is considered that obesity leads to inflammation and therefore causes poor obstetric outcomes (preeclampsia, gestational diabetes) and neonatal complications.^[6] It is known that fat tissues in non-pregnant obese women call macrophage and initiate inflammatory process, and that they secrete high levels of proinflammatory cytokines such as tumor necrosis factor (TNF-α), IL 6, monocyte chemoattractant protein 1 (MCP 1), and transforming growth factor β (TGF- β).^[5] The levels of high sensitivity C-reactive protein (HsCRP), leptin and MCP-1 were correlated with the increase of BMI in obese pregnant women.^[6]

Complete blood count is a cheap and simple laboratory examination used routinely in pregnancy. When hematologic parameters are evaluated, it is known that NLR (neutrophil/lymphocyte ratio), PLR (platelet/lymphocyte ratio), RDW (red blood cell distribution width) and PCT (plateletcrit) have prognostic and predictive features in various diseases such as coronary artery disease, autoimmune diseases, inflammatory diseases, and gynecological and gastrointestinal cancers.^[7,8] It was found that the levels of these markers increased in the inflammatory processes of pregnancy such as gestational diabetes, acute appendicitis, preeclampsia, etc.^[9-11] In this study, we aimed to investigate the change of inflammatory markers according to BMI values in the first trimester pregnancies.

Methods

A total of 321 pregnant women during first trimester who admitted to the Clinic of Gynecology and Obstetrics of a tertiary state hospital between January 2019 and June 2019 were included in the study. The approval of the local ethics committee was obtained for this study. The patient data were accessed retrospectively from the hospital records.

The patients were classified as normal weight (BMI: 18–24.9 kg/m²), overweight (BMI: 25–29.9 kg/m²) and obese (BMI>30 kg/m²). Of the patients, the demographic data such as age, gravida and parity, and the levels of hemoglobin, hematocrit, white blood cell, neutrophil, lymphocyte, platelet, eosinophil, basophil, MPV, platelet distribution width (PDW), NLR, RDW, PCT and PLR measured in the complete blood count which was checked in the routine pregnancy follow-up were analyzed.

The patients on medications for those except pregestational diabetes, folic acid and infection which may cause chronic and acute inflammation were excluded from the study.

Statistical analysis

The data were analyzed by using Statistical Package Social Sciences (SPSS), version 22.0 (SPSS Inc., Chicago, IL, USA). The descriptive statistics were presented as standard deviations and mean values for numerical variables. In order to determine the normal distribution of the variables, Histogram and Kolmogorov-Smirnov test were used. Where applicable, Mann-Whitney U test and Student's t-test were used for the comparisons of two groups. For multiple group comparisons, one-way ANOVA and Kruskal-Wallis H test were used. In the values with significant multiple group results, Tukey test was

Table 1. The comparison of demographic data and hematologic markers between the patients with normal weight, and overweight and obese patients.

	Patients with normal weight (n=108)	Overweight patients (n=109)	Obese patients (n=104)	p-value
Age	26.5 (18–40)	29 (18–40)	26 (18–40)	0.178
Gravida	4 (1–7)	4 (1–7)	4 (1–7)	0.583
Parity	3 (0–6)	3 (0–6)	3 (0–6)	0.558
Hgb	12.7 (10.1–15.1)	13.0 (10.2–15.0)	12.6 (10.1–14.7)	0.286
Htc	37.4±2.94	37.9±2.8	38.0±2.9	0.200
WBC	8.4±2.2*	8.6±2.3 c	9.4±2.0*, [†]	0.001
Neutrophil	5.4 (2.3–10.6)*,†	5.3 (2.5–13.2)	6.34 (2.8–10.2)*,†	<0.001
Lymphocyte	2.0 (0.05–5.01)*,†	2.0 (0.97–5.6)	2.3 (1.1–5.9)* ^{,†}	0.023
PLT	263 (134–464)*,†	266 (155–529)	295 (122-462)* ^{,†}	<0.001
PCT	0.28 (0.17–0.45)*,†	0.28 (0.15-0.51)	0.31 (0.15–0.51)*,†	<0.001
PDW	12.4 (8.8–19.4)	12.7 (8.1–24.9)	12.7 (9.6–46.4)	0.170
MPV	10.6 (8.6–42.5)	10.7 (6.6–81)	10.6 (6.6–12.4)	0.886
RDW	40.7 (32.3–62.2)	39.8 (13.1-63.2)	40.5 (33.9–48.5)	0.119
NLR	2.6 (0.9–18.4)	2.6 (0.009–5.57)	2.7 (0.8–7.7)	0.775
PLR	133 (58.2–6880)	130 (<0.001–282)	134 (45–238)	0.630

Hgb: hemoglobin; Htc: hematocrit; MPV: mean platelet volume; NLR: neutrophil/lymphocyte ratio; PCT: plateletcrit; PDW: platelet distribution width; PLR: platelet/lymphocyte ratio; PLT: platelet; RDW-SD: red blood cell distribution width; WBC: white blood cell. *Between the patients with normal weight and obese patients; [†]Between the overweight patients and obese patients. Median value (min–max) has been given for those underwent Kruskal-Wallis test. Mean (±SD) value has been given for those underwent one-way ANOVA test.

used for those with homogeneous variance and Mann-Whitney U test when non-parametric test was used. The value of p<0.05 was considered statistically significant.

the groups. White blood cell, neutrophil, lymphocyte, PLT and PCT levels were higher overweight/obese patient groups than the normal group (p<0.05).

Results

The results of demographic and hematologic comparisons according to BMI values are summarized in **Table 1**. The patients were evaluated in three groups, which were normal weight with 108 patients (Group 1), overweight with 109 patients (Group 2) and obese with 104 patients (Group 3). When the demographic data were evaluated among the groups, no significant difference was observed in terms of age, parity and gravida (p>0.05). In terms of hematological markers, all markers except white blood cell, neutrophil, lymphocyte, PLT and PCT levels were similar among the groups. The difference among white blood cell, neutrophil, lymphocyte, PLT and PCT values were between the patients with normal weight and obese patients.

The patients were also compared by separating them into two groups as the patients with normal weight and overweight/obese patients. The results of this comparison are shown in **Table 2**. The demographic data were similar between two groups (p>0.05). For the hematological markers, all markers except white blood cell, neutrophil, lymphocyte, PLT and PCT levels were similar among

Table 2.	The cor	mparison (of de	emograpł	nic da	ita and	hematol	logic
	markers	between	the	patients	with	normal	weight	and
	overwei	ight/obese	patie	ents				

	Patients with normal weight (n=108)	Overweight and obese patients (n=213)	p-value
Age	26.5 (18–40)	27 (18–40)	0.376
Gravida	4 (1–7)	4 (1–7)	0.805
Parity	3 (0–6)	3 (0–6)	0.677
Hgb	12.7 (10.1–15.1)	12.8 (10.1–15)	0.096
Htc	37.4±2.94	37.9±2.8	0.097
WBC	8.4±2.2	9.0±2.2	0.017
Neutrophil	5.4 (2.3–10.6)	5.8 (2.5–13.2)	0.013
Lymphocyte	2.0 (0.05-5.01)	2.2 (0.9–5.9)	0.042
PLT	263 (134–464)	285 (122–529)	0.013
PCT	0.28 (0.17–0.45)	0.30 (0.15–0.51)	0.010
PDW	12.4 (8.8–19.4)	12.7 (8.1–46.4)	0.060
MPV	10.6 (8.6–42.5)	10.7 (6.6–81)	0.704
RDW	40.7 (32.3–62.2)	40.2 (13.1–63.2)	0.108
NLR	2.6 (0.9–18.4)	2.7 (0.009–7.7)	0.580
PLR	133 (58.2–6880)	132 (<0.001–282)	0.886

Hgb: hemoglobin; Htc: hematocrit; MPV: mean platelet volume; NLR: neutrophil/lymphocyte ratio; PCT: plateletrit; PDW: platelet distribution width; PLR: platelet/lymphocyte ratio; PLT: platelet; RDW-SD: red blood cell distribution width; WBC: white blood cell. Median value (min-max) has been given for those underwent Mann-Whitney U test. Mean (±SD) value has been given for those underwent Student's t-test.

Discussion

Due to the rapid increase of obesity rates in the world, WHO has considered obesity as one of the most serious global health problems of the 21st century. The obesity prevalence in pregnancy has been reported between 1.8% and 25.3%.^[4,12] The Centers for Disease Control and Prevention (CDC) reported that the obesity prevalence among the pregnant women completely reflects the obesity among women in fertility ages, 25% of the women at fertility ages in the USA were overweight and 25% of them were obese, and that maternal obesity is a major risk factor for maternal and perinatal mortality.^[13]

The obesity has many adverse impacts on pregnancy. In Lashen et al. showed in their study that spontaneous abortion risk increases 1.2 times and recurring abortion risk increases 3.5 times in the first trimester of the pregnant women whose BMI was over 30 kg/m².^[14] There are also studies reporting that the obesity increases the incidences of gestational diabetes, preeclampsia and macrosomia,^[15,16] and that it increases the rates of shoulder dystocia during delivery and cesarean section.^[17] Pregestational maternal obesity is accounted for the most common reason of unexplained intrauterine fetal deaths.^[18]

Chronic inflammatory conditions such as obesity causes elevated white blood cell (WBC) levels by increasing granulocyte production. It is known that the impaired glucose metabolism of WBC is associated with insulin resistance and type 2 diabetes.^[19] It was reported that elevated WBC caused gestational diabetes during early pregnancy.^[20] In our study, we found that WBC, neutrophil and lymphocyte levels which are directly associated with inflammation were significantly high in the obese group. This supports our hypothesis.

There are evidences showing that platelets do not only play a role in the coagulation mechanisms in the body, but also are associated with the development of immune response, allergic reactions and inflammation.^[21] While the number of platelets decreases in order to provide hemostasis in the gestational thrombocytopenia, its functions and predispositions to aggression increase.^[22] However, there are controversial opinions in terms of PDW, PCT and MPV levels in the blood during pregnancy. While some studies claim that there are differences between the trimesters,^[23,24] there are also studies asserting that there is no difference between pregestational and post-gestational periods.^[25,26] MPV indicates mean platelet volume, and it ranges between 7.4 and 10.4 fl.^[10] Elevated MPV levels are correlated with the increased hemostasis and coagulation systems. This is explained with higher activity with the increase of platelet levels.^[23,27] Elevated MPV levels are also associated with diabetes and its complications.^[28] Bozkurt et al. reported elevated MPV levels in the pregnant women with gestational diabetes who are at the 3rd trimester.^[29] In our study, we did not find any difference among the BMI groups in the first trimester in terms of MPV levels.

PCT shows the volume of platelets by percentage in the blood, and it is calculated with the formula PLT × MPV / 10,000 and it is much more significant parameter than PLT and MPV.^[30] Its normal level in the blood is 0.22–0.24%.^[31] Many studies investigated PCT level for many diseases associated with pregnancy. For example, it was high in hyperemesis gravidarum,^[32] low in preeclamptic patients,^[33] and there was no difference in molar pregnancies.^[34] In our study, we found that PCT level was significantly higher in obese group than the normal weight group and in the obese/underweight groups than normal weight group.

PDW is a marker indicating the variations in the platelet volume. Its level varies according to the size and activation of platelets. Its normal reference range in the blood is between 8.3% and 56.6%.^[30] It is known that PDW decreases during pregnancy compared to the pregestational period. Some studies reported that it has a positive correlation with preeclampsia severity and ectopic pregnancy,^[33,35] while there is a negative correlation with ablatio placentae.^[22] In our study, we did not find any increase in PDW level by elevated BMI value.

NLR and PLR levels are the systemic inflammatory indices associated with platelet. There is a study showing that NLR is associated with metabolic syndrome.^[36] It is known that high NLR and PLR are associated with gestational diabetes and preterm labor.^[9,7] We did not find any difference between the groups in terms of NLR and PLR values in our study.

RDW shows the variation in the red blood cell volume called anisocytosis, and its reference value is 11.5–15.5%.^[10] While it is considered that high RDW levels indicate inflammation and oxidative stress, the mechanism is still unclear.^[38] There are studies asserting that it is associated with the impairment of iron metabolism and the suppression of erythropoietin.^[39] Many studies in the literature investigated the association of RDW level with the diseases in pregnant women. While there is no association with hyperemesis,^[40] its association with preeclampsia is controversial,^[8,11] and it is not associated with gestational diabetes.^[41] In our study, RDW level was similar among the groups.

The limitations of our study are being retrospective, single-centered, limited number of patients, and not checking other inflammatory markers except hematologic markers. In addition, we did not investigate gestational and neonatal outcomes of inflammatory markers. There are no studies in the literature investigating the association between obesity during pregnancy and inflammatory markers. Further clinical researches which are planned prospectively, randomized controlled and investigating the obstetric outcomes of maternal obesity and inflammation values are needed.

Conclusion

Hematologic inflammatory markers are simple and cheap markers which can be detected in the hemogram count easily. The association between inflammation and obesity during pregnancy has been proven, and it is considered that it is associated with the potential poor outcomes during pregnancy. We found that white blood cell, neutrophil, lymphocyte, platelet and PCT levels are associated with high BMI values during pregnancy. Further studies are needed to confirm the association between these markers and poor obstetric and neonatal outcomes.

Conflicts of Interest: No conflicts declared.

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