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Association between platelet indices and missed abortion

Missed abortus ile platelet indekslerinin ilişkisi

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Abstract

Aim: The incidence of missed abortion is around 15% of clinically diagnosed pregnancies, and the etiology is uncertain. Limited studies in the literature report increased platelet indices such as mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit (PCT). The number of cases in these studies is low and results are inconsistent. There is no study that investigates all platelet indices. This study has the largest series in the literature and investigates all platelet indices in missed abortion.

Methods: In this retrospective case-control study, the complete blood count parameters of patients who were diagnosed with missed abortion were examined. Among 500 cases, 228 women with missed abortion constituted the study group, and 272 healthy pregnant women constituted the control group. Women who were 18–45 years of age and 6–14 weeks of gestational age were included.

Results: In the missed abortion group, PDW value was higher (P=0.007), while platelet MPV and PCT values were lower (respectively P<0.001 and P=0.008) than the control group.

Conclusion: Platelet indices parameters in missed abortion are inconsistent.

Keywords: Missed abortion, Platelet indices, Mean platelet volume, Platelet distribution width

Öz

Amaç: Klinik olarak tanı almış gebeliklerin %15'i missed abortus ile sonuçlanmaktadır. Missed abortusun etyolojisi kesin olarak bilinmemektedir. Literatürde sınırlı sayıda çalışmada ortalama platelet hacmi (MPV), platelet dağılım genişliği (PDW), plateletrikt (PCT)'in missed abortusta arttığı bildirilmiştir. Çalışmalardaki olgu sayısı az ve sonuçları tutarsızdır. Literatürde, missed abortusta tüm platelet indekslerini değerlendiren bir çalışma bulunmamaktadır. Bu çalışma missed abortusta tüm platelet indekslerini değerlendiren literatürdeki en geniş seridir.

Yöntemler: Bu retrospektif olgu-kontrol çalışmasında, missed abortus tanısı alan hastaların tam kan sayımı parametreleri karşılaştırıldı. Çalışmada toplam 500 olgunun missed abortus tanısı alan 228'i çalışma grubu, 272 sağlıklı gebe olanı kontrol grubu belirlendi. Çalışmaya 18-45 yaş aralığında, 6-14 gebelik haftasındaki tekil gebeler dahil edildi.

Bulgular: Missed abortus grubunda PDW değeri kontrol grubuna göre yüksek bulunurken (P=0,007); MPV ve PCT değerleri düşük bulundu (sırasıyla P<0,001 ve P=0,008).

Sonuç: Missed abortusta platelet indeksi parametreleri tutarsızdır.

Anahtar kelimeler: Missed abortus, Platelet indeksleri, Ortalama platelet hacmi, Platelet dağılım genişliği

Introduction

The term "missed abortion" refers to a clinical abortion in which the products of conception are not spontaneously expelled from the uterus. The incidence of missed abortion is reported as around 15% of clinically diagnosed pregnancies [1].

Genetic, anatomic, endocrine factors and thrombophilia are responsible for the etiology of missed abortion. Several studies have demonstrated that thrombophilia may cause pregnancy loss and missed abortion [2-4]. The prevalence of thrombophilia in the etiology of missed abortion is not clearly understood.

In thrombophiles, the risk of thrombosis increases [5]. Some studies have shown that MPV was significantly increased in subjects with arterial thrombotic events, i.e. acute myocardial infarction (MI) [6]. Platelet Distribution Width (PDW) and plateletcrit (PCT) values were found high in MI patients [7].

In the literature, there are limited studies that investigate platelet indices such as MPV, PLT and PCT in missed abortion [8,9]. The number of cases in these studies is small and the results are inconsistent. Up to this day, there is no study which investigates all platelet indices regarding this subject. This study has the largest series and investigates all platelet indices in missed abortion.

Materials and methods

Bursa Yüksek Ihtisas Hospital ethics committee approval (2011-KAEK-25 2018/05-13) was obtained for this retrospective case-control study. The medical records of patients who underwent curettage with a diagnosis of missed abortion between January 2014 and January 2018 at Bursa Karacabey, Bursa Mustafakemalpaşa and Muş State Hospital, were reached. Among 500 cases, 228 women with missed abortion constituted the study group and 272 healthy pregnant women constituted the control group. The control group was selected among healthy pregnant women with no complicating conditions for pregnancy and no systemic illness that could affect a complete blood count. Missed abortion was defined as an absence of fetal heart tone that was detected between the 6^{th} and 20^{th} gestational weeks. Gestational age was determined according to the last menstrual period and was confirmed using ultrasonographic findings. If the last menstrual period date was unknown, gestational age estimation was based on ultrasonography. Age, gravida, parity, current age, currently living child, height and history of surgical operations and laboratory values, i.e. hemoglobin, hematocrit, platelet, mean corpuscular volume, mean platelet volume, platelet distribution width, and plateletcrit were recorded. Women who were 18–45 years of age and 6–14 weeks of gestational age were included. Exclusion criteria included conditions such as thyroid dysfunction, hematologic disease, history of thrombosis, SLE, multiple pregnancies, use of anticoagulants, smoking, and uterine anomalies. Blood samples were obtained from the antecubital vein. Ethylene diamine tetra acetic acid (K3EDTA) tubes were used and samples were examined within two hours at the latest. Missed abortion group blood samples were extracted immediately after diagnosis and complete blood count tests were performed with Cell-Dyn 3700 (Abbott, Abbott Park (USA)).

Statistical analysis

Continuous variables were expressed as either mean (standard deviation) or median values and categorical variables were expressed as n (%). Chi-square testing was used for comparing categorical variables between groups and independent T test was used for comparisons of continuous variables between groups. SPSS (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0, Armonk, NY: IBM Corp.) was used for statistical analysis and a value of $P<0.05$ was considered statistically significant.

According to the power analysis based on platelet count, a sample size of 386 patients (193 per group) was required for 80% power and %5 conventional two-sided type 1 error.

A receiver operating characteristic curve was constructed to determine PLT, MPV and plateletcrit cut-off values for the diagnosis of the missed abortion.

Results

The mean age was higher in the missed abortion group ((29.44 (5.80) years vs. 27.20 (5.80) years)) ($P<0.001$). Mean gestational ages of the missed abortion and control groups were 60.79 (15.14) days and 62.94 (14.22) days, respectively. In terms of gestational age, gravida, parity and currently living child derivatives, the differences between the two groups were not statistically significant ($P=0.103$, $P=0.058$, $P=0.442$ and $P=0.089$, respectively). Previous abortion curettage was more frequent in the missed abortion group ($P<0.001$); the history of surgical operations was more frequent in the control group ($P=0.006$), and height and weight were similar between the two groups ($P=0.828$ and $P=0.684$, respectively) (Table 1).

In the missed abortion group, hemoglobin (Hb), hematocrit (Hct), mean corpuscular volume (MCV), and platelet distribution width (PDW) were significantly higher ($P=0.005$, $P<0.001$, $P<0.001$ and $P=0.007$, respectively), whereas platelet count (PLT), mean platelet volume (MPV), plateletcrit (PCT) were significantly lower ($P=0.030$, $P<0.001$ and $P=0.008$, respectively) (Table 2).

Table 1: Comparison of groups regarding demographic data

	Missed abortion (n=228)	Control (n=272)	*P*-value
Age (year)	29.44 (5.80)	27.20 (5.80)	<0.001
GA (day)	60.79 (15.14)	62.94 (14.22)	0.103
Height (cm)	162.19 (6.05)	162.07 (6.18)	0.828
Weight (kg)	66.82 (11.82)	67.22 (10.10)	0.684

GA: Gestational age

Table 2: Comparison of groups regarding laboratory values

	Missed abortion (n=228)	Control (n=272)	Reference values	*P*-value
Hemoglobin (g/dL)	12.84 (0.97)	12.58 (1.06)	11-16	0.005
Hematocrite (%)	39.12 (2.50)	37.97 (2.81)	37-54	<0.001
Platelet (/mcL)	255956 (69735)	268875 (62548)	150000-400000	0.030
MCV (fl)	83.65 (6.55)	79.95 (6.16)	80-100	<0.001
MPV (fl)	9.01 (1.49)	9.46 (1.22)	6.5-12	<0.001
PCT (%)	0.237 (0.082)	0.255 (0061)	0.11-0.28	0.008
PDW (%)	17.77 (1.72)	17.36 (1.63)	9-17	0.007

MCV: Mean corpuscular volume, MPV: Mean platelet volume, PCT: Plateletcrit, PDW: Platelet distribution width

Independent variables included in multiple logistic regression analysis are adjusted according to age. Hemoglobin values between the two groups remained different when the age factor was kept constant.

Receiver operating characteristic analysis was performed to determine the diagnostic PLT, MPV and plateletcrit values for missed abortion.

PLT <252.000 predicted miscarriage with 58% sensitivity and 54% specificity. The sensitivity and specificity of MPV <9.05 in predicting miscarriage was 61% and 48%. The same values for PCT <0.205 were 77.2% and 55.3% (Figure 1).

The platelet index (PCT, PDW, MPV) values remained different between the two groups when the age factor was corrected. When the platelet index data were compared with respect to abortion numbers in the missed abortion group, no significant difference was observed in MPV and PCT values. For every increasing number of abortions, PDW value decreased significantly by 0.693 units ([OR] -0,693, 95% CI -1,067- (-0,319)).

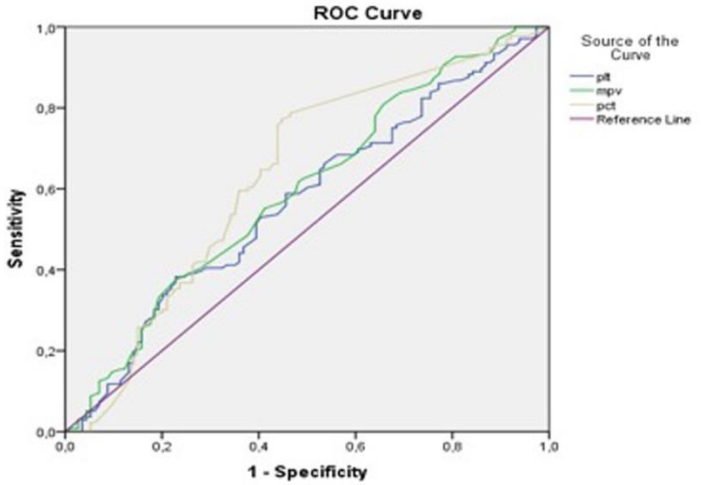

Figure 1: Receiver operating characteristic analysis performed to determine diagnostic mean platelet volume, platelet and plateletcrit values for missed abortion. PLT: platelet count, MPV: mean platelet volume, PCT: plateletcrit, ROC: receiver operating characteristic

Discussion

The etiology of missed abortion has been reported as maternal disease. Thrombophilia, which may be a maternal disease, increases susceptibility to clotting [10]. It is currently investigated whether a hypercoagulable state due to thrombophilia may predispose to immunological rejection or placental damage [11]. In a previous study, hysteroscopic biopsies obtained from the endometria of missed abortion patients were found to have increased thrombosis in the small endometrial vessels [12].

Platelets are primarily responsible for clotting, and their role has been of interest in thrombophiles and vascular pathologies. Platelet volume indices including MPV, PDW, PCT and platelet count are indicators of platelet activity, and these are routinely reported in automated full blood counts [13]. PDW represents the range of variability in platelet size, and it has been suggested that a large PDW may be an indicator of prothrombotic status. PCT, the product of MPV and platelet count, projects the number of platelets in a unit of blood volume and is a marker of total platelet mass [14].

The platelet parameters were investigated in various studies in cases of missed abortion. Kosus et al. [8] compared MPV and PLT values between 100 missed abortion cases and 100 normal pregnant women. MPV values were similar in missed abortion and control groups. Eroglu et al. [9] examined MPV and PDW values of 54 threatened, 46 missed abortion patients and 40 control subjects, both of which were found similar among all three groups.

In various studies on the loss of pregnancy, MPV was found to be higher than [15], lower than [16] or similar with the control group [17]. MPV, PCT, and PDW were significantly higher in studies that investigated platelet parameters in cases with recurrent pregnancy loss [18-21].

Past obstetrical history is an important predictor of subsequent pregnancy outcome. The risk of miscarriage in future pregnancies is approximately 20% after one miscarriage, 28% after two consecutive miscarriages, and 43% after three or more consecutive miscarriages [22]. In accordance with the literature, we found that the number of previous abortions in the missed abortion group was higher than the control group.

In our study, MPV value was lower in the missed abortion group. The results were different from studies which compared a control group with missed abortion patients. Unlike other studies, PDW value was higher in our missed abortion group. Although it has been suggested that microvascular pathology may be responsible for missed abortion, low MPV and high PDW drove us away from this hypothesis. We also found that Hb and Hct values were higher in the missed abortion group. An important part of the missed abortion patients consists of those with vaginal bleeding complaints, whose blood samples were taken upon hospital admission. It is our opinion that higher Hb and Hct values in the missed abortion group may be due to the relative hemoconcentration that occurs during the early stage of bleeding.

Limitations

Evaluation of the diagnostic accuracy of platelet indices in missed abortion would have been more accurate had we obtained the values before the incident and investigated changes in a sequential timeframe.

Conclusion

Our study is the largest series investigating platelet indices in patients with missed abortion. Although PDW value of the missed abortion group was higher than the control group, PLT, MPV and PCT were lower. The platelet indices parameters in missed abortion are inconsistent.

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