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Mild thrombocytopenia and postpartum hemorrhage in pregnancies with placenta previa

Plasenta previa tanısı olan gebelerde hafif trombositopeni ile postpartum kanama ilişkisi

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ÖZ

Amaç: Doğum sonu kanama (PPK), maternal mortalite ve morbiditenin önemli bir nedenidir. Trombositopeni, doğum sonu kanama için bilinen risk faktörlerinden biri olmasına rağmen, hafif trombositopeninin doğum sonu kanama üzerindeki etkisi hakkında çok az şey bilinmektedir. Bu çalışma, plasenta previalı gebelerde doğum sonu kanama ile hafif trombositopeni arasındaki ilişkiyi araştırmayı amaçladı.

Metod: 1 Ekim 2019 ve 1 Mayıs 2022 tarihleri arasında plasenta previa ameliyatı geçirmiş gebelerde retrospektif bir kohort çalışması gerçekleştirdik. Çalışma grubunu hafif trombositopenisi (trombosit sayısı 100.000-149.999/ µl) olan kadınlar oluşturdu. Kontrol grubundaki kadınların trombosit sayıları normaldi (trombosit sayısı 150.000- 450.000 / µl). Sonuç, aşağıdakilerden birinin veya daha fazlasının bir kombinasyonu olan doğum sonu kanama insidansıydı: 1) intraoperatif veya doğum sonrası dönemde eritrosit süspansiyonu transfüzyonu gerekliliği; 2) Doğum öncesi döneme göre doğum sonrası hemoglobin düzeylerinde en az 3 gr/dL azalma.

Bulgular: Çalışmada 170 gebe mevcuttu; 30'u hafif trombositopenili grupta, 140'ı kontrol grubundaydı. Hafif trombositopeninin doğum sonu kanama ile ilişkili olduğu bulundu (düzeltilmiş olasılık oranı: 3.90 %95 GA: 1.56-9.72). Ayrıca hafif trombositopeni grubunda kan transfüzyonu alan ve hemoglobin düşüşü >3 g/dL olan hasta sayısı kontrol grubuna göre anlamlı olarak yüksekti (p<0,05).

Sonuç: Plasenta previa hastalarında, ameliyat öncesi hafif trombositopeni, doğum sonu kanama riskinin artmasıyla bağlantılıydı.

Anahtar Kelimeler: kan transfüzyonu, plasenta previa, plasenta akreata spektrumu, postpartum kanama, hafif trombositopeni

ABSTRACT

Objective: Postpartum hemorrhage (PPH) is a major cause of maternal mortality and morbidity. Although thrombocytopenia is one of the known risk factors for postpartum hemorrhage, little is known about the effect of mild thrombocytopenia on PPH. The current study aimed to investigate the relationship between postpartum hemorrhage and mild thrombocytopenia in pregnant women with placenta previa.

Materials and Methods: We conducted a retrospective cohort study of pregnant women who underwent placenta previa surgery between October 1, 2019 and May 1, 2022. Women with mild thrombocytopenia (platelet count 100,000-149,999/ µl) comprised the study group. The women in the control group had normal platelet counts (platelet count 150.000- 450.000 / µl). The outcome was the incidence of postpartum hemorrhage which is a combination of one or more of the following: 1) the requirement for a transfusion of pRBC during the intraoperative or postpartum period; 2) a decrease in Hb levels of at least 3 gr/dL postpartum compared to prepartum.

Results: There were 170 women in the study; 30 were in the group with mild thrombocytopenia and 140 were in the control group. Mild thrombocytopenia was found to be associated with postpartum hemorrhage (adjusted odds ratio: 3.90 95% CI: 1.56-9.72). Also in the mild thrombocytopenia group, the number of patients receiving blood transfusion and Hb decline >3 g/dL were significantly higher compared to the control group (p<0.05).

Conclusion: In placenta previa patients, preoperative mild thrombocytopenia was linked to an increased risk of postpartum hemorrhage.

Keywords: blood transfusion, mild thrombocytopenia, postpartum hemorrhage, placenta previa, the spectrum of placenta accreta

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INTRODUCTION

Postpartum hemorrhage (PPH) is a major cause of maternal morbidity and mortality (1). Prior to delivery, identifying the risk factors for PPH enables the team to prepare the required supplies and blood products (2). Although thrombocytopenia is one of the definite risk factors of hemorrhage, it has not been adequately studied.

Thrombocytopenia is defined as a platelet count less than 150,000/microliter (µl) (3,4). The platelet threshold, which poses a risk for postpartum bleeding, has been reported as 70-100,000 / µl in different studies (5,6). While platelet count <100.000 / µl is seen 1%, mild thrombocytopenia (defined as platelet count between 100.000-149.999 / µl) is seen 10% in pregnant women (7), and the relationship of mild thrombocytopenia with PPH remains unclear.

Recently, the relationship between mild thrombocytopenia and PPH has been studied in the uncomplicated pregnant population (7-11) and there have been studies that found its relationship with increased blood loss and blood transfusion (7,9,11). However, none of these studies investigated the relationship between mild thrombocytopenia and PPH in a group with a high risk of bleeding such as placenta previa.

Placenta previa (PP) is characterized by the abnormal placenta overlying the endocervical os. PP is often complicated by the spectrum of placenta accreta (PAS), which is caused by the invasion of the placental villi below the decidua basalis. PAS may unexpectedly cause catastrophic blood loss, multiple complications, and even maternal death (12). The incidence of PPH has increased in PP due to the inability of the uterine segment with abnormal implantation to contract as effectively as a normal uterine segment. The increased number of PAS and the risk of the cesarean incision passing through the placenta also increase PPH in PP cases (13).

The aim of the present study was to determine the relationship between mild thrombocytopenia and PPH in the pregnant women with PP.

MATERIALS AND METHOD

We performed a retrospective cohort study with pregnant women who were operated for PP in a single tertiary center between 01 October 2019 and 01 May 2022. This study was approved by Ankara City Hospital Ethics Committee (E2-22-2201). All patients included in the study underwent a cesarean delivery with the indication of PP and had platelet and hemoglobin levels within 24 hours before delivery. The study group included women with mild thrombocytopenia (platelet count 100.000-149.999/ µl). The control group included women with normal platelet count (platelet count 150.000- 450.000 / µl). Women with severe thrombocytopenia (<100.000), thrombocytosis (>450.000), multiple gestations, abruption, and coagulopathy were excluded. Cases with missing information also were excluded.

Maternal age, gestational age, gravida, parity, preoperative and postoperative hemoglobin (Hb) levels, preoperative platelet levels, patients receiving packed red blood cells transfusion (pRBC), length of stay in the intensive care unit (ICU) were obtained from patient medical files and electronic recording media. Patients who were diagnosed with PAS, underwent a hysterectomy after cesarean section (C/S), required uterine balloon tamponade and pRBC transfusion were recorded.

The outcome was the incidence of PPH, which is a combination of one or more of the following: 1) the requirement for a transfusion of pRBC during the intraoperative or postpartum period; 2) a decrease in Hb levels of at least 3 gr/dL postpartum compared to prepartum. The postpartum Hb value was used as the hemoglobin level at postoperative 24 hours. The criteria for the transfusion of pRBC are any of the following: 1) visually estimated excess intraoperative blood loss; 2) clinically severe uncontrollable ongoing hemorrhage; 3) symptomatic anemia (maternal tachycardia>100/minutes, dizziness, syncope, orthostatic hypotension) in the presence of Hb 7–8 g/dL; or (3) intraoperative or postpartum Hb level<7 g/dL regardless of symptoms (11). Due to the method's stated inaccuracy, we did not use 'clinical estimation of blood loss as an outcome measure (14).

Statistical analysis

Statistical analysis was enforced using IBM SPSS Statistics Version 25.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were given as mean ± standard deviation for numerical data with normal distribution or median and minimum–maximum values for numerical data that do not follow a normal distribution. The normality of the variables was tested with both Shapiro–Wilk and Kolmogorov–Smirnov tests. Groups were compared with the Student t-test and Mann–Whitney U-test. A type-1 error less than 0.05 was considered statistically significant. Univariable analysis was performed to assess candidate variables as risk factors for PPH. The associations between potential risk factors and the outcome were quantified by the OR and 95% confidence interval (CI). Multivariable logistic regression was performed to assess the relationship between patient characteristics and PPH.

RESULTS

The total number of patients that underwent C/S for PP was 227 during the study period. 57 patients were excluded for the reasons shown in Figure-1. There were 30 patients in the mild thrombocytopenia group and 140 patients in the control group. The total number of patients that underwent C/S for PP was 227 during the study period. 57 patients were excluded for the reasons shown in Figure-1. There were 30 patients in the mild thrombocytopenia group and 140 patients in the control group.

The baseline characteristics of the patients were listed in Table-1. There was no significant difference in terms of baseline characteristics between the two groups except preoperative platelet values.

The median preoperative platelet count was 136.000 in the mild thrombocytopenic group and 244.000 in the control group. Comparison of the groups in terms of obstetric outcomes was described in Table 2. There was no significant difference in gestational age at delivery, birth weight, PAS, underwent a hysterectomy, uterine balloon tamponade, and hospitalization in the ICU.

Figure-1 Selection of study groups

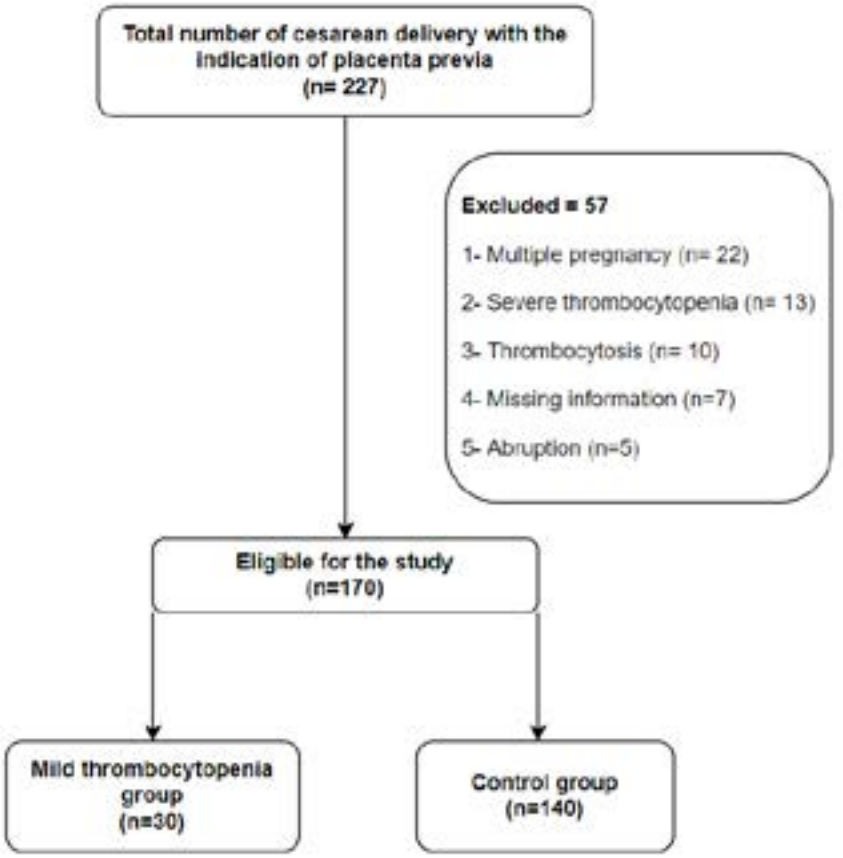

Table-1 Baseline Characteristics

	Mild thrombocytopenia group ***(platelet count 100.000-149.999/ µl)*** **(n= 30)**	**Control group** **(platelet count 150.000- 450.000 / µl)** **(n= 140)**	**p value**
Maternal age (years) (±SD)	31.5 (±4.8)	31.7 (±4.9)	0.908
Gravida, (median, IQR)	3 (2)	3 (2)	0.953
Primiparous, n (%)	6 (2)	28 (2)	1.000
Previous C/S, n (%)	22 (73.3)	83 (59.2)	0.151
Preoperative hemoglobin, g/dl (IQR)	11.9 (1.3)	11.5 (1.5)	0.061
Preoperative platelet count, 100.000/ µL (IQR)	136.000 (15.200)	244.000 (84.500)	**<0.001**

Data are presented as mean (± standard deviation), median (interquartile range) or number (percentage)
SD, standard deviation, *IQR*, interquartile range, *C/S*, cesarean section

Table-2 Comparison of the groups in terms of obstetric outcomes

	Mild thrombocytopenia group *(platelet count 100.000-149.999/ µl)* (n= 30)	Control group (platelet count 150.000- 450.000 / µl) (n= 140)	p value
Gestational age at delivery (week) (IQR)	35 (2.2)	36 (3)	0.572
Birth weight (gram) (±SD)	2586 (571)	2579 (647)	0.817
Placenta Accreata Sprectrum, n (%)	15 (50)	55 (39.2)	0.084
Hysterectomy, n (%)	9 (30)	38 (27.1)	0.137
Uterine balloon tamponade, n (%)	10 (33.3)	44 (31.4)	0.839
Hospitalization in the ICU, n (%)	7 (23.3)	24 (17.1)	0.426

Data are presented as mean (± standard deviation), median (interquartile range) or number (percentage)

IQR, interquartile range, *SD*, standard deviation, *ICU*, intensive care unit

As compared to the control group, PPH, the number of patients receiving pRCB, and Hb decline >3 g/dL were significantly higher in the mild thrombocytopenia group (Table-3).

Table-3 Outcomes of the study

	Mild thrombocytopenia group *(platelet count 100.000-149.999/ µl)* (n= 30)	Control group (platelet count 150.000- 450.000 / µl) (n= 140)	p value
PPH, n (%)	19 (63.3)	43 (30.7)	**0.001**
Patients received pRBC transfusion, n (%)	15 (50)	35 (25)	**0.006**
Hb decline >3 g/dL, n (%)	13 (43.3)	24 (17.1)	**0.002**

Data are presented as number (percentage).

PPH, postpartum hemorrhage, p*RBC*, packed red blood cell, *Hb*, Hemoglobin

In a multivariate logistic regression model, mild trombocytopenia was associated with PPH with an adjusted odds ratio (aOR) of 3.29 (95% CI 1.12-9.62 p=0.02) after adjusting for maternal age, gestational age at delivery, birth weight, preoperative anemia. PAS (aOR of 13.68, 95% CI 5.54-35.78), hysterectomy (aOR of 102.84, 95% CI 12.66-835.16), and previous C/S (aOR of 4.14, 95% CI 1.89-9.09) were also independent risk factors for the PPH (Table-4).

Table-4 Results of univariable analysis and multivariable logistic regression regarding the risk of postpartum hemorrhage

	OR (95% CI)	p value
Univariable analysis		
Maternal age	1.06 (1.00- 1.13)	0.44
Gestational age at delivery	1.03 (0.92-1.16)	0.52
Birth weight	1.00 (1.00-1.01)	0.37
Primiparous	3.26 (1.26-8.40)	**0.01**
Previous C/S	0.21 (0.10-0.45)	**<0.001**
Placenta Accreata Sprectrum	16.61 (7.24-38.11)	**<0.001**
Hysterectomy	107.00 (14.03-815.57)	**<0.001**
Mild thrombocytopenia	3.89 (1.7-8.89)	**<0.001**
Preoperative anemia	0.77 (0.39-4.52)	0.45
Multivariable analysis		
Mild thrombocytopenia	3.90 (1.56-9.72)	**0.003**
Placenta Accreata Sprectrum	13.68 (5.54-35.78)	**<0.001**
Hysterectomy	102.84 (12.66-835.162)	**<0.001**
Primiparous	0.37 (0.13-1.01)	0.06
Previous C/S	4.14 (1.89-9.09)	**<0.001**

OR, odds ratio, *CI*, confidence interval, *C/S*, cesarean section

DISCUSSION

In the present study, we aimed to investigate the relationship between mild thrombocytopenia and PPH in patients with PP. Our results are as follows: 1) Mild thrombocytopenia is associated with a higher rate of PPH, a significant decline in postoperative Hb, and a higher rate of blood transfusion in PP patients; 2) PAS, hysterectomy, and previous C/S were also found to be independent risk factors for PPH in PP patients.

In the present study, similar to the study of Attali et al. performed with elective C/S pregnancies, there were a higher rate of blood transfusion and a more significant decrease in postoperative Hb levels in the mild thrombocytopenia group (11). Carlson et al. also observed more PPH in the mild thrombocytopenia group in the study of 54597 pregnant women who underwent C/S or vaginal delivery after C/S (5). In a recent study with 1085 twin pregnancies, a group in which mild thrombocytopenia is prevalent, a significant relationship was found between mild thrombocytopenia and PPH (15). In our study, the rate of receiving blood transfusion was 50% in the mild thrombocytopenia group and much higher than in these three studies (in other studies the rate was 4.7%, 3.7%, and 5.7%, respectively. We consider that the difference is caused by a cohort with high bleeding frequency and amount such as placenta previa.

Govindappari et al. found that there was a 2-fold increase for the risk of PPH in the mild thrombocytopenia group among nulliparous women with term, singleton, vertex pregnancies. In this study, the need for blood transfusion did not increase. However, uterotonic usage was significantly higher in the mild thrombocytopenia group. This may have reduced the need for blood transfusions (7).

In the study of Işıkalan et al., although estimated blood loss was significantly higher in the mild thrombocytopenia group, there was no significant difference with regard to the blood transfusion rate between groups. However, this study was carried out only with healthy pregnant women who underwent elective C/S. In our study, there were both elective C/S and emergency C/S deliveries due to PP. Işıkalan et al. attributed the lack of difference in blood transfusion despite more bleeding to less preoperative anemia in the mild thrombocytopenia group. In our study, there was no difference between the preoperative Hb values of the groups (9).

Contrary to these findings, there are two studies in the literature that did not find a relationship between PPH and thrombocytopenia. Xu et al. performed their studies only with low-risk C/S deliveries (10). Alison DiSciullo et al. used unclear criteria for blood transfusion and more strict criteria for the diagnosis of PPH (Hb decrease by >4 g/dL) (8).

In order to reduce maternal morbidity and mortality, it is important to identify PPH risk factors before delivery. Plt <100.000 (according to some sources 70.000) is stated in the guidelines as a risk factor for PPH (2,5,6). In the group with a platelet value between 100,000-150,000, the PPH risk is uncertain. As shown by previous studies mild thrombocytopenia is seen much more frequently than severe thrombocytopenia, it is also important to take precautions in this group before delivery.

PP and PAS are obstetric conditions with a high risk of PPH. In this group, it is also important to determine the platelet threshold that can cause PPH. Our study identifies mild thrombocytopenia as a risk factor for PPH and blood transfusion for pregnant women with PP. Therefore, cautious hemostasis during the procedure, liberal use of uterotonic medicines, close monitoring for the identification of any deterioration, preparation of blood products before the delivery, and the use of multiple large IV cannulas could be advised in the group of PP with mild thrombocytopenia.

The strength of our study are having a large cohort for PP. While other studies about mild thrombocytopenia have used ICD criteria with high sensitivity but low specificity (16), we have used more certain criteria for PPH. Additionally, we minimized the effect of potential co-founders such as preoperative anemia by using two homogeneous groups. Besides, we excluded the effects of serious diseases such as ITP, HELLP, SLE on PPH by not including severe thrombocytopenia. Our study is limited by the fact that it was planned retrospectively and a single-center study. In addition, the lack of information about how much and how often these patients bleed during their pregnancy limits our study.

CONCLUSION

In conclusion, our study identifies mild thrombocytopenia as a risk factor for PPH and blood transfusion for pregnant women with PP. To define mild trombocypenia as a risk factor for PPH and blood transfusion in the general pregnant population, prospective observational studies with larger sample sizes and randomized controlled trials are required.

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