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# Primary autoimmune thrombocytopenia in pregnancy: maternal and neonatal outcomes

## *Gebelikte primer otoimmun trombositopeni: maternal ve fetal sonuçlar*

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**ABSTRACT**

**Aim:** To evaluate clinical characteristics, maternal and neonatal outcomes among pregnant women with primary autoimmune thrombocytopenia (ITP).

**Materials and methods:** All pregnant women with ITP who had undergone antenatal follow-up and delivery at the Department of Obstetrics and Gynecology at a referral center, between 2011 and 2021, were retrospectively investigated. Patients were evaluated in three groups according to antenatal treatment modality.

**Results:** 42 pregnant women with ITP were included in the study. A total of 29 (%69) pregnant women had been diagnosed with ITP before pregnancy and 13(%31) were diagnosed during pregnancy. 17 (%41) pregnant women did not receive any antenatal treatment, and 25 (%59) pregnant women receieved treatment. Postpartum haemorrhage (%50) was reported more frequently in the steroids+IVIG group. A total of 42 pregnancies, 43 babies (one twin pregnancy, 41 singletons) were liveborn. Three neonates (%7) had thrombocytopenia and one of them had intracranial haemorrhage.

**Conclusions:** In pregnancies complicated with ITP, the platelet count is moderately or severely low, which can have adverse maternal and neonatal outcomes. Postpartum haemorrhage is a significant cause of maternal morbidity in cases with ITP. Therefore, pregnant women with ITP should be delivered in facilities that can adequately manage postpartum haemorrhage.

**Keywords:** Primary autoimmune thrombocytopenia, neonatal thrombocytopenia, pregnancy, antenatal treatment.

***ÖZ***

***Amaç****: Primer otoimmün trombositopenili (ITP) gebelerde klinik özellikler, maternal ve yenidoğan sonuçlarını değerlendirmek.*

***Gereç ve Yöntem****: 2011 ve 2021 yılları arasında referans bir merkezde, Kadın Hastalıkları ve Doğum Bölümünde antenatal takip ve doğumları gerçekleştirilen tüm ITP' li gebe kadınlar retrospektif olarak incelendi. Hastalar antenatal tedavi modalitelerine göre üç grupta değerlendirildi.*

***Bulgular:*** *Çalışmaya ITP' li 42 gebe kadın dahil edildi. Gebe kadınların 29' u (%69) gebelik öncesi, 13' ü (%31) gebelik sırasında ITP tanısı aldı. Gebe kadınların 17' si (%41) antenatal dönemde tedavi almaz iken, 25' i (%59) antenatal tedavi aldı.*

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*Postpartum hemoraji steroid+İVİG grubunda daha sık görüldü (%50). 42 gebelikten 43 (bir ikiz gebelik, 41 tekil gebelik) canlı doğum gerçekleşdi. Üç yenidoğanda (%7) trombositopeni görülürken, bunlardan birinde intrakranial kanama izlendi.*

***Sonuç:*** *ITP ile komplike gebeliklerde platelet sayısı orta veya ciddi derecede düşüktür, olumsuz maternal ve neonatal sonuçlara neden olabilir. İTP' li olgularda postpartum hemoraji önemli bir maternal morbidite nedenidir. Bu nedenle İTP 'li gebeler, postpartum hemorajiyi etkin bir şekilde yöneten merkezlerde doğurtulmalıdır.*

***Anahtar Sözcükler:*** *Primer otoimmün trombositopeni, neonatal trombositopeni, gebelik, antenatal tedavi.*

## INTRODUCTION

Primary immune thrombocytopenia (ITP) is an acquired autoimmune disease that develops due to autoantibodies formed against platelet membrane glycoproteins shortening the life expectancy of platelets and is progressing with thrombocytopenia (1). Immune thrombocytopenia is ten times more common in pregnant women than in the general population, with 1 to 3 cases per 10,000 (2, 3). It is known that pregnancy affects the course of autoimmune diseases. The disease may recur in patients who have previously been treated for ITP, the platelet count in patients with chronic ITP may drop even further, or the initial attack may occur in any trimester of pregnancy (4).

Even though most individuals with ITP are asymptomatic, the risk of maternal haemorrhage necessitates close follow-up and treatment throughout pregnancy. Rather than normalizing platelet values, the main goal of treatment is to achieve a safe platelet range that will prevent major bleeding and maternal and fetal complications (5). In these cases, platelet-specific IgG antibodies may also cause neonatal thrombocytopenia by crossing the placenta, increasing the risk of neonatal intracranial haemorrhage during delivery (6). Maternal mortality due to ITP has been reported to be <1%, and neonatal mortality has been reported to be 1.5% with close follow-up and treatment of patients with ITP during pregnancy (7). The number of studies in the literature that examine maternal and neonatal outcomes of pregnant women with ITP, determine their treatment needs, and provide information about delivery time and mode is limited.

In our study, we aimed to evaluate the obstetric, maternal, and neonatal outcomes achieved with current treatment strategies by collecting the data of pregnant women with ITP retrospectively in a single center.

## MATERIALS and METHODS

The data of pregnant women and neonates with ITP who had antenatal follow-up and delivery at the Department of Obstetrics and Gynecology in Ege University School of Medicine Hospital, between 2011 and 2021 were retrospectively analyzed in the study group. This study was approved by the Local Ethics Committee of the Ege University School of Medicine (22-6T/45-09.06.2022).

The cases were initially identified by a computerized search for the diagnosis of "Primary autoimmune thrombocytopenia" (International Classification of Diseases 10th Revision, Codes D69.3), and subsequently, all cases were selected during pregnancy. Gestational thrombocytopenia, preeclampsia, haemolysis, elevated liver enzymes, low platelets syndrome (HELLP), acute fatty liver in pregnancy, systemic lupus erythematosus (SLE), cytomegalovirus (CMV), hepatitis C, human immunodeficiency virus (HIV), thrombocytopenia secondary to drug use and other hereditary thrombocytopenias were excluded from the study.

Information about the demographic characteristics, age, parity, diagnosis time, pre-pregnancy platelet count, first-trimester platelet count, platelet count at delivery, the cord blood platelet count, treatment during pregnancy, need for blood transfusion, route of delivery, delivery week, birth weight, Apgar scores, the indication for cesarean section, type of anesthesia, obstetric, maternal and fetal complications were were obtained from the antenatal follow-up files of the patients.

The Statistical Package for the Social Sciences (SPSS) version 25.0 was used for the statistical analysis. Descriptive statistics were presented. The numerical variables were given in mean, standard deviation, or median (min-max). The categorical variables were given in numbers and

percentages. The statistical and multivariate analysis could not be performed due to the nature of the study and asmall number of critical outcomes.

## RESULTS

42 patients with ITP during pregnancy were identified during the study period. ITP was detected in almost two-thirds of the patients before pregnancy. While 6 of the cases had a history of splenectomy before pregnancy, none of the patients required splenectomy during the pregnancy. Demographic data and obstetric characteristics of the patients are shown in Table-1 in detail.

Although most cases of ITP are asymptomatic, 59% of patients (n: 25/42) received prophylactic treatment during the antenatal period to avoid major haemorrhage and achieve the target platelet count at birth. Antenatal treatment typically consisted of three different protocols: steroids (40%), IVIG (20%), steroids+IVIG (40%). Maternal complications that may occur due to ITP during pregnancy were evaluated in detail in Table-2, according to the treatment protocols. The classic definition of postpartum haemorrhage (PPH) is an estimated blood loss of >500 mL in vaginal delivery and >1000 mL in the cesarean section within the first 24 hours following delivery (8). Using these criteria the rate of PPH in this cohort is 33% (n: 14/42). The group receiving steroids+IVIG treatment had the highest PPH rate of 50% when evaluated according to treatment protocols. The median platelet count at delivery for women with PPH was $62\times10^9$/L. No patients required a hysterectomy due to PPH, and there was no maternal mortality. The postpartum haematoma was observed only in two patients. In one case, a 90*75 mm perineal haematoma occurred on the right lateral wall of the vagina after vaginal delivery, which was treated with haematoma evacuation, suture, and platelet transfusion. In the other case, cesarean section wound haematoma was detected and follow-up was sufficient.

The preterm birth rate was 19%, and no decision was made regarding iatrogenic preterm birth (induced by severe ITP). The causes of preterm birth were obstetric (50%), fetal (37.5%) and maternal (12.5%), respectively. 19 of the cases (45.3%) had undergone vaginal delivery; 23(54.7%) cesarean section. Due to the risk of neonatal intracranial haemorrhage, operative vaginal deliveries such as forceps or vacuum were avoided. The decision for the cesarean section is made on the fetal, maternal, and obstetric indications. (26% fetal, 17% maternal, 57% obstetric, respectively). The neuraxial blockade was not applied in vaginal deliveries. 69.6% of cesarean deliveries were performed with general anesthesia and 26% with spinal anesthesia. The mean platelet value in patients who performed neuraxial blockade was $114\pm37\times10^9$/L.

A total of 42 pregnancies, 43 babies (one twin pregnancy, 41 singletons) were liveborn. Thrombocytopenia was observed in three of the infants in the neonatal period. There was only one case of neonatal intracranial haemorrhage (ICH). The case with ICH was delivered cesarean section at the 38th gestational week with the indication of acute fetal distress. This case did not receive antenatal treatment during pregnancy, and the maternal platelet count was $79\times10^9$/L, the umbilical cord platelet count was $18\times10^9$/L, and the Apgar score was 7/8 at the time of delivery. The baby was followed up in the neonatal intensive care unit and received immunoglobulin infusion and platelet transfusion in the first 24 hours. Twenty-four hours later, cranial ultrasonography revealed echogenic lesions in the left parieto-occipital region, with computer tomography confirming the haemorrhagic nature of the lesions. The baby was discharged after the platelet count was increased to $85\times10^9$/L on the 14th day of life. There were no cases of neonatal deaths. Neonatal outcomes were evaluated in detail in Table-3 according to treatment protocols.

**Table-1.** Demographic and clinical characteristics of the patients.

| Parameters | Results |
|---|---|
| Maternal age,years | 28±5.4 (18-39) |
| Parity n (%) | |
| Nulliparous | 20 (%47.6) |
| Parous | 22 (%52.4) |
| Age at ITP diagnosis, years | 23±6.1 (15-34) |
| Date of diagnosis ITP *, n% | |
| Before pregnancy | 29 (%69) |
| During pregnancy | 13 (%31) |
| Platelet count | |
| Prior to pregnancy $\times 10^9$/L | 102±58 (8-246) |
| at first trimester $\times 10^9$/L | 80±52 (5-201) |
| at delivery $\times 10^9$/L | 99±20 (5-164) |
| Mode of delivery | |
| Cesarean section, n% | 23 (54.7) |
| Vaginal delivery, n% | 19 (45.3) |
| GA at delivery (weeks) | 38± 1.5 (34-40) |
| Term delivery, n% | 34 (%81) |
| Preterm delivery, n% | 8 (%19) |
| Birthweight, g | 3178±563 (2170-4410) |
| Anesthesia for cesarean section | |
| General, n% | 16 (%69,6) |
| Spinal, n% | 6 (%26) |
| Not known, n% | 1 (4.4) |

Data are given as mean ± SD. The range is given in parentheses

ITP: Primer immün trombositopeni, GA: Gestational age

**Table-2.** Maternal outcomes with ITP in pregnancy.

| Parameter | No treatment (n=17) | Steroids (n=10) | IVIG (n=5) | Steroids + IVIG (n=10) | Total (n=42) |
|---|---|---|---|---|---|
| GA at delivery | 38 (34-40) | 38 (35-39) | 39 (37-40) | 38 (35-40) | 38 (34-40) |
| Mode of delivery | | | | | |
| Cesarean section, n% | 13 (%76.4) | 3 (%30) | 2 (%40) | 5 (%50) | 23 (%54.7) |
| Vaginal delivery, n% | 4 (%23.6) | 7 (%70) | 3 (%60) | 5 (%50) | 19 (%45.3) |
| Perineal haematoma, n% | 0 | 0 | 0 | 1 (%10) | 1 (%2.4) |
| Cesarean section wound haematoma, n% | 0 | 0 | 0 | 1 (%10) | 1 (%2.4) |
| Postpartum haemorrhage, n% | 4 (%23.5) | 3 (%30) | 2 (%40) | 5 (%50) | 14 (%33.3) |
| Need of transfusion with packed red cell and/or platelet, n% | 4 (%23.5) | 4 (%40) | 1 (%20) | 5 (%50) | 14 (%33.3) |
| Hysterectomy for PPH, n% | 0 | 0 | 0 | 0 | 0 |
| Death, n(%) | 0 | 0 | 0 | 0 | 0 |

Data are given as mean ± SD. The range is given in parentheses

GA: Gestational age, PPH: Postpartum haemorrhage

**Table-3.** Neonatal outcomes with İTP in pregnancy.

| Parameter | No treatment (n=17) | Steroids (n=10) | IVIG (n=5) | Steroids + IVIG (n=10) | Total (n=42) |
|---|---|---|---|---|---|
| Birthweight, g | 3077±614 (2270-4410) | 3314±622 (2400-4280) | 3262±186 (3130-3560) | 3174±572 (2285-4100) | 3178±563 (2170-4410) |
| Apgar scores (5 minutes) | 9± 0.8 (7-10) | 9.1± 0.9 (8-10) | 9.2± 0.8 (8-10) | 9.1± 0.9 (8-10) | 9.1±0.8 (7-10) |
| Cord platelet count $\times 10^9$/L | 209±94 (18-345) | 228±48 (142-280) | 204±112 | 201±134 | 211±92 |
| Recorded | 15 (%88) | 6 (%60) | (81-320) | (34-329) | (18-345) |
| Not taken/no result | 2 (%12) | 4 (%40) | 4 (%80) | 5 (%50) | 30 (%71.4) |
| Neonatal thrombocytopenia within first week, n% | | | 1 (%20) | 5 (%50) | 12 (%28.6) |
| Yes | 2 (%11.8) | 0 | 0 | 1 (%10) | 3 (%7.1) |
| No | 12 (%70.6) | 7 (%70) | 3 (%60) | 6 (%60) | 28 (%66.7) |
| Unknown/not recorded | 3 (%17.6) | 3 (%30) | 2 (%40) | 3 (%30) | 11 (%26.2) |
| Admissions to NICU, n% | 4 (%23.5) | 1 (%10) | 1 (%20) | 2 (%20) | 8 (%19) |
| Intracranial haemorrhage, n% | 1 (%6) | 0 | 0 | 0 | 1 (%2.3) |
| Death | 0 | 0 | 0 | 0 | 0 |

Data are given as mean ± SD. The range is given in parentheses

GA: Gestational age, NICU: Neonatal intensive care unit

## DISCUSSION

Thrombocytopenia is a common hematological disorder with a prevalence of 7% to 12% of all pregnant women. Only 1% to 4% of women with thrombocytopenia are caused by primary autoimmune thrombocytopenia (7, 9, 10). Unlike gestational thrombocytopenia, ITP causes a moderately or severely low platelet count, which can be devastating for the mother, fetus, and neonate. For this reason, pregnant women with ITP should be managed by a multidisciplinary team that includes a hematologist, perinatologist, neonatologist, and anesthesiologist in a health facility where neonatal and adult intensive care conditions are provided.

According to earlier studies, almost half of ITP was detected for the first time during pregnancy in women of reproductive age; in our study, this rate was 31% (2, 11). The management varies depending on the trimester in which ITP is diagnosed or the presence of symptoms (such as epistaxis, bruising, bleeding, petechial haemorrhages). In general, patients with mild to moderate thrombocytopenia (50-149$\times 10^9$/L) without symptoms do not require treatment, whereas patients with values below 50$\times 10^9$/L require treatment (12). In our study, 59% of the patients received treatment during the antenatal period. However, in the study of Webert et al, this rate was reported as 31% (13). We may be over-treating asymptomatic patients.

In the first-line treatment at ITP, steroids are the first drugs of choice. IVIG treatment is recommended if first-line treatment fails to produce a response within 4-14 days or if a clinically urgent platelet response is necessary. If there is no response to steroids or IVIG, steroids+IVIG combination therapy or splenectomy is usually the next step (1, 14, 15). In our study, the treatments used during the antenatal period received a response, and splenectomy was not required during pregnancy. However, platelet transfusion is required in some cases. These cases are; those with clinical symptoms (specifically abruption or other spontaneous bleeding), a reduction in the platelet count below 10$\times 10^9$/L, or those with platelet count less than 50$\times 10^9$/L and requiring a surgical procedure (15). Platelet transfusion was required in 33% of our patients, with the largest requirement in the group receiving steroids+IVIG combined therapy.

ITP has been associated with higher rates of preterm birth, particularly when diagnosed before

pregnancy. Preterm birth was recorded at 8.5% in the cohort defined by Wyszynski et al., whereas it was reported at 11.2% in the subgroup diagnosed with ITP before pregnancy (16). In our study, the rate of preterm delivery was 19%, and 20.6% in those diagnosed with ITP before pregnancy. Vaginal delivery is the safest option for both mother and fetus in pregnant women with ITP, according to the American College of Obstetricians and Gynaecologists' recommendations. The decision for cesarean delivery is taken within routine obstetric indications (14). Cesarean section was the dominant type of delivery in our study, with a rate of 54.7%. However, this rate was reported as 25% in the multicentre study of Loustau et al (17). We believe this high rate was related to the increasing number of cesarean sections in our country. Instrumental deliveries such as vacuum or forceps should be avoided because there is a risk of intracranial haemorrhage secondary to neonatal thrombocytopenia in infants born to mothers with ITP. Therefore, vacuum or forceps was not applied in vaginal deliveries in our study. Although the minimum platelet count required for safe neuraxial anesthesia is not known, most anesthesiologists consider platelet counts above $80\times10^9$/L to be sufficient for neuraxial anesthesia (18). In our study, neuraxial anesthesia was used in 26% of cesarean deliveries, and the mean platelet count in the patients who underwent the procedure was $114\times10^9$/L.

Postpartum haemorrhage is observed at a higher rate in cases with ITP and is among the leading causes of maternal morbidity. PPH was identified in 33% of our cases, with the prevalence being highest in the group that received combined steroids+IVIG therapy. In a national cohort study by Care et al., the rate of PPH in pregnant women with ITP was reported as 52% (2).

The incidence of adverse fetal and neonatal outcomes, including intrauterine fetal loss and congenital anomalies, increases in pregnancies with ITP (16). The immunoglobulin G antibodies pass the placenta and cause platelet destruction in the fetus and neonate. Neonatal thrombocytopenia occurs in 8.9% to 14.7% of pregnant women with ITP (19). Although IVIG and steroids can cross the placenta, it has been shown that antenatal treatment does not reduce neonatal thrombocytopenia (20). In our study, the rate of neonatal thrombocytopenia was 7.1%, which is similar to the literature. On the other hand, intracranial haemorrhage is seen in 1.5% of infants born to mothers, with ITP (19, 21). Neonatal death was not recorded in our study, ICH was only seen in a newborn born to a mother with ITP who did not receive antenatal therapy and was discharged on the 14th day of life.

The small sample size, the retrospective nature of the study and insufficient neonatal data due to the postnatal follow-up of some newborns in different facilities were all limitations of our study.

## CONCLUSION

ITP in pregnancy is a hematological disorder that poses a significant concern for both obstetricians and patients. Pregnancies with ITP generally have a favorable outcome with proper antenatal treatment and follow-up. Vaginal delivery appears to be safe for both mother and fetus, and cesarean delivery should be reserved for the usual obstetric indications. Since pregnant women with ITP have a significant risk of postpartum haemorrhage, these patients should be managed by a multidisciplinary team in facilities with intensive care and well-equipped blood centers.

**Conflict of interest:** The authors have no conflict of interest.

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