# A Comparison of Maternal and Fetal Outcomes of Pregnancies Complicated by Moderate to Severe Thrombocytopenia Caused by Gestational Thrombocytopenia Preeclampsia / HELLP Syndrome and Immune Thrombocytopenic Purpura

**Suna ÖZDEMİR[1], Hüseyin GÖRKEMLİ[1], Ali ACAR[1], Çetin ÇELİK[1], Erkan KAYIKÇIOĞLU[2]**

*Konya, Turkey*

**OBJECTIVE:** Aim of this study was to compare obstetric risk factors and complications, and outcomes of pregnancies associated with moderate to severe thrombocytopenia caused by gestational thrombocytopenia (GT), preeclampsia/HELLP syndrome, and immune thrombocytopenic purpura (ITP).
**STUDY DESIGN:** The study was composed of 135 women with a platelet count below 100.000/mm$^3$. The characteristics and clinical details of all women and neonatal were recorded during their hospital course.
**RESULTS:** The ratio of severe thrombocytopenia was observed significantly lower in GT group compared with preeclampsia / HELLP syndrome and ITP groups. Higher rates of oligohydroamnios, IUGR, and placental abruption were found among patients in preeclampsia+HELLP syndrome group. The rates of Apgar scores (<7) at 1 and 5 min, pH values (<7,2), and amniotic fluid with meconium were higher in preeclampsia / HELLP syndrome group. Neonatal thrombocytopenia was recorded in a total of 5 infants.
**CONCLUSION:** The thrombocytopenia with preeclampsia/HELLP syndrome had less favorable obstetric and fetal outcomes.

**Key Words:** Gestational thrombocytopenia, Preeclampsia/HELLP syndrome, Immune thrombocytopenic purpura, Fetal outcomes

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## Introduction

Thrombocytopenia, defined as a platelet count below 150.000 /ul complicates up to 10% of all pregnancies.[1] It is caused by accelerated destruction or decreased production and classified as mild with a platelet count of 100-150.000 /ul, moderate at 50-100.000/ul and severe with less than 50.000 /ul.[2] Thrombocytopenia in pregnancy may result from a variety of causes. Gestational thrombocytopenia (GT), preeclampsia/HELLP (Hemolysis, elevated liver enzymes and low platelet count) syndrome, and immune thrombocytopenic purpura (ITP) are most common causes of thrombocytopenia in pregnancy. In these thrombocytopenias, there was an increased destruction or utilization in thrombocytes. In addition to these causes, thrombotic thrombocytopenic purpura (TTP), hemolytic uremic syndrome (HUS), disseminated intravascular coagulation (DIC), anti-phospholipid antibodies syndrome (APLA), or systemic lupus erythematosus (SLE) are rarer causes of thrombocytopenia during pregnancy.

The decrease in platelet count in pregnancy occurs during the third trimester and identified with a shift in the histogram of platelet count distribution.[3,4] Although some of these causes are not associated with adverse pregnancy outcomes, others are associated with considerable maternal and neonatal morbidity and mortality. Mild thrombocytopenia with a platelet count of 100-150.000 /ul is generally caused by gestational thrombocytopenia, and it has a good prognosis with no major complications. Most of adverse pregnancy outcomes are observed in patients with moderate to severe thrombocytopenia. In the literature, there are a few data comparing pregnancy outcomes in different etiologies of thrombocytopenia during pregnancy.

In this study, we investigated obstetric risk factors and complications, and outcomes of pregnancies associated with moderate to severe thrombocytopenia caused by GT, preeclampsia and HELLP, and ITP. The findings of three groups were compared statistically.

## Material and Method

This prospective study included 135 consecutive pregnant women with GT, preeclampsia/HELLP syndrome and ITP

*[1]Department of Gynecology and Obstetric and [2]Hematology Selçuk University Meram Medical Faculty, Konya*

*Address of Correspondence: Suna Özdemir*
*Selçuk University Meram Medical Faculty*
*Department of Gynecology and Obstetric*
*Meram, Konya*
*snmstf@yahoo.com*

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complicated by moderate to severe thrombocytopenia delivered in our clinic between February 2005 and August 2007 at the Meram Medical Faculty of Selcuk University, which is the sole tertiary center of Konya, the southern part of the middle Anatolia. All of the diagnoses of thrombocytopenia (platelet count below 100.000 /ul) were identified by the computerized hematology laboratory report of the hospital. We diagnosed the etiologies of thrombocytopenia together with a hematologist. The complete blood count and peripheral smear were done for all patients. Visualizing the smear was essential to rule out spurious thrombocytopenia because clumping of platelets could artificially lower the platelet count. Women with no history of thrombocytopenia during preconception period, a normal early-gestation platelet count, mild thrombocytopenia (usually above 70.000/ul), and asymptomatic with no history of bleeding was diagnosed as GT. The diagnosis of ITP was based upon very simple clinical criteria according to the guidelines of the British Society for Hematology.[5] Preeclampsia was diagnosed from the presence of blood pressure >140/90 mm Hg and proteinuria >0,3 gr in a 24-hour urine specimen that occurred after 20 weeks of gestation, according to the American Collage of Obstetricians and Gynecologist.[6] HELLP syndrome was diagnosed in accordance with the following laboratory findings: hemolysis (lactic dehydrogenase >600 IU/L, serum bilurubin >1,2 mg/dl); increased aminotransferase concentrations (>70IU/L); and thrombocytopenia (platelet count<100.000/ul).[7] DIC was defined as platelet count <100.000/ul, plasma fibrinogen <3 gr/L, and fibrin degradation products>40 mg/dL.[7]

The characteristics and clinical details of all women were recorded during their hospital course. Neonatal outcomes were evaluated by our neonatology clinic. The following clinical characteristics were evaluated: maternal age, previous gestations, parity, gestational age, and birth weight, cause of thrombocytopenia, and platelet count. The following obstetrical risk factors were assessed: Diabetes mellitus including pregestational and gestational diabetes, previous cesarean section (CS), maternal anemia, hydroamnios, oligohydroamnios, multiple pregnancies (twin/triplets), and intrauterine growth restriction (IUGR). Blood and platelet transfusions, placental abruption, placenta previa, labor induction, mode of delivery, Apgar scores at 1 and 5 min less than 7, umbilical cord artery pH less than 7,2 DIC, meconium-stained amniotic fluid, stillbirth and post-partum neonatal death were examined as labor complications and birth outcomes. The protocol was approved by the institutional ethics committee, and all subjects signed an informed consent form.

Statistical analysis was performed using the SPSS package program. Statistical significance was calculated using the x2-test for categorical variables. One-way ANOWA and Tamhane test were used for continuous variables. P<0,05 was considered statistically significant.

## Results

The study was composed of 135 women with a platelet count below 100.000/mm$^3$. There were 48 women with GT (35,5%), 32 with ITP (23,7%), 28 with HELLP syndrome (20,7%), and 18 with severe preeclampsia (13,3%) and 9 women with other rare causes (6,6%). These women in the study group delivered 147 infants during the study period; there were 8 twins and two triplets. Systemic steroid treatment was used in the patients with ITP or HELLP syndrome. Blood products were transfused to the patients due to severe anemia and increasing the platelet values in operative deliveries.

Clinical characteristics of the pregnant women were shown in Table 1. The mean age in the groups was significantly lower for ITP group when compared with GT and preeclampsia/HELLP syndrome group (p<0,01). The lower numbers of previous gestation and parity were observed in GT group. Higher rates of gestations and parity (5+) were recorded in ITP groups. The higher rate of preterm delivery with lower gestation week was found among patients in preeclampsia/HELLP syndrome group compared with patients in GT and ITP groups (p<0,0001). Birth weight was also lower in preeclampsia/HELLP syndrome group than other two groups (p<0,0001). The ratio of severe thrombocytopenia was observed significantly lower in GT group compared with preeclampsia/HELLP syndrome and ITP groups (p<0,0001).

Obstetric risk factors and labor complications were shown in Table 2 and 3. Higher rates of oligohydroamnios (p<0,001), IUGR (p<0,001), and placental abruption (p<0,01) were found among patients in preeclampsia+HELLP syndrome group compared with GT and ITP groups. Labor induction, placenta previa, and transfusion need were also higher in patients of preeclampsia/HELLP syndrome group, but difference was not statistically significant. The vaginal delivery was observed most commonly in GT group, and the ratio of C/S operation was higher in preeclampsia/HELLP syndrome group compared other two groups (p<0,001). The other risk factors and labor complications were not different for each groups (p>0,05).

Perinatal outcomes were presented in Table 4. The rates of Apgar scores (<7) at 1 and 5 min, pH values (<7,2) and amniotic fluid with meconium were higher in preeclampsia/ HELLP syndrome group compared with GT and ITP groups (p>0,001). Intrauterine fetal death and postpartum deaths were also higher in preeclampsia/HELLP syndrome group, but difference did not reach to statistical significant. Neonatal thrombocytopenia was recorded in a total of 5 infants, three born to mothers with ITP, two to mothers with preeclampsia+HELLP syndrome. No major bleeding was observed among these infants.

*Table 1. Clinical charecteristics of pregnant women with GT, preeclampsia + HELLP and ITP*

| Charecteristic | GT (n: 48) | Preeclampsia + HELLP (n: 46) | ITP (n:32) | p |
|---|---|---|---|---|
| **Maternal age** | 29,1+5,2 | 29,3+6,4 | 25,4+5,3 | 0,006 |
| **Previous gestation** | | | | |
| 1 | 14,6 % | 30,4% | 40,6% | |
| 2-4 | 79,2% | 56,3% | 43,5% | |
| 5+ | 6,3% | 26,1% | 3,1% | 0,001 |
| **Parity** | | | | |
| 1 | 16,7% | 39,1% | 40,6% | |
| 2-4 | 79,2% | 50% | 56,3% | |
| 5+ | 4,2% | 10,9% | 3,1% | 0,027 |
| **Gestational age** | | | | |
| <37 weeks | 10,4% | 87,4% | 6,3% | |
| 37-39 weeks | 68,8% | 13% | 78,1% | |
| >40 weeks | 20,8% | - | 15,6% | 0,001 |
| **Birth weight** | | | | |
| <2500 g | 4,2% | 87% | 15,6% | |
| 2500-4000 g | 93,8% | 13% | 84,4% | |
| >4000 g | 2,1% | - | - | 0,001 |
| **Platelet count** | | | | |
| Moderate | 87,5% | 43,5% | 43,8% | |
| Severe | 12,5% | 56,5% | 56,3% | 0,001 |

*Table 2: Obstetric risk factors in the study population*

| Characteristics | GT (n=48) | Preeclampsia + HELLP (n= 46) | ITP (n=32) | p |
|---|---|---|---|---|
| Previous CS | 27,1% | 15,2% | 15,6% | 0,27 |
| Diabetes Mellitus | 10,4% | - | 9,4% | 0,08 |
| Anemia | 16,7% | 21,7% | 18,8% | 0,82 |
| Hydramnios | 4,2% | 0 | 9,4% | 0,11 |
| Oligohydramnios | 14,6 | 41,3% | 3,1% | 0,001 |
| Multiple pregnancy | 10,4% | 8,7% | 3,1% | 0,48 |
| IUGR | 4,2% | 43,5% | 9,4% | 0,001 |

*Table 3: Labor complications in the study population*

| Characteristics | GT (n=48) | Preeclampsia + HELLP (n= 46) | ITP (n=32) | p |
|---|---|---|---|---|
| Placental abruption | 2,1% | 13% | - | 0,01 |
| Placenta previa | 6,3% | 13% | 3,1% | 0,24 |
| Labor induction | 12,5% | 19,6% | 9,4% | 0,40 |
| Mode of delivery | | | | |
| CS | 43,8% | 91,3% | 71,9% | 0,001 |
| Vaginal | 56,3% | 8,7% | 28,1% | 0,001 |
| Blood transfusion | 10,4% | 19,6% | 18,8% | 0,41 |
| DIC | 2,1% | 2,2% | - | 0,70 |

*Table 4: Birth outcomes in the study population*

| Characteristics | GT (n=48) | Preeclampsia + HELLP (n= 46) | ITP (n=32) | p |
|---|---|---|---|---|
| Apgar at 1 min <7 | 19,6% | 56,1% | 9,4% | 0,001 |
| Apgar at 5 min <7 | - | 24,4% | 3,1% | 0,001 |
| pH<7,2 | 2,1% | 30,4% | 3,1% | 0,001 |
| Amniotic fluid with meconium | 4,2% | 28,3% | 6,3% | 0,001 |
| IUMF | 2,1% | 8,7% | - | 0,10 |
| PPD | - | 8,7% | 3,1% | 0,09 |
| Neonatal trombocytopenia | - | 6,5% | 6,2% | 0,75 |

## Discussion

In the present study, we found that pregnancies with preeclampsia/HELLP complicated with moderate to severe thrombocytopenia had less favorable obstetric risk factors and outcomes of pregnancies. Pregnancies with GT complicated with severe thrombocytopenia and the mean age of women with ITP were lower than the other pregnancies. GT is known to be the most common cause of thrombocytopenia in pregnancy, affecting 5% of all pregnant women and accounting for more than 75% of cases of pregnancy-associated thrombocytopenia.[8,9] The platelet count of these patients is usually above 110.000/ul, but there are several cases in healthy pregnant women with no history of ITP and a platelet count as low as 70.000/ul.[10,11] Pathophysiology is unknown but is thought to represent accelerated consumption of platelets. Risk of fetal or neonatal thrombocytopenia is extremely low, with no fetal or neonatal bleeding complications reported.[12,13] A prospective cohort study by Burrows and Kelton of 756 women with a diagnosis of GT showed that none of the mothers and only one infant with bone marrow dysfunction.[12] In our cases, numbers of previous gestation and parity were lower in GT group than the other two groups and vaginal delivery was observed most commonly in GT group. Neonatal thrombocytopenia was not detected in GT group.

HELLP syndrome accounts for 21% of maternal thrombocytopenia in pregnancy and it complicates 10% of all women with preeclampsia. This syndrome has been reported primarily in multiparous women above the age of 25 years.[14] Similarly, our study revealed that the mean age of women with HELLP syndrome was above 25 years, and the higher parity (>5) was observed among these cases when compared the other cases. In the present study, the adverse perinatal outcomes were most commonly associated with preeclampsia/HELLP syndrome. Parnas et al. also found the higher rates of IUGR, placental abruption, still birth, and Apgar scores at 1 and 5 (<7) in patients with preeclampsia/HELLP syndrome.[15] In our study the incidences of IUGR, low Apgar scores (<7) at 1 and 5 min, and intrauterine fetal death were relatively higher compared with this report. This condition may be related to increased ratio of HELLP syndrome among with preeclampsia and HELLP syndrome

in our series. In a study, it has been reported that patients with HELLP syndrome had a significant increased incidence of IUGR when they were compared women without HELLP syndrome.[16] In the same manner, in a recent study from our country, the patients with HELLP syndrome had a significant increased incidence of IUGR when they were compared women without HELLP syndrome.[17] Another study from our country evaluated the pregnancies with HELLP syndrome and they reported that the incidence of serious maternal and fetal morbidities and mortalities are increased in HELLP syndrome.[18] In addition to these findings, the ratio of preterm deliveries, infants with low birth weight, and operative deliveries were also determined higher in patients with preeclampsia / HELLP syndrome than the other groups in our study. In preeclampsia /HELLP syndrome group, neonatal thrombocytopenia was noted in 2 infants. Any neonatal bleeding complications were not recorded in these infants.

ITP accounts for 3% of all thrombocytopenic gravidas. It is usually known that ITP affects women in childbearing age group. In the present study, the mean age of patients with ITP was significantly lower than women with GT and preeclampsia+HEELP syndrome. Similarly, a study by Lee et al which investigated the pregnancies of women with ITP reported that ITP tends to occur in younger women.[19] Type of the delivery in women with ITP is another controversial issue. A retrospective study evaluating 11-year analysis of patients with ITP in pregnancy found tha rate of C/S operation as 17.6%.[20] We detected that the rate of C/S operation in the present study was 71.9%. The ITP cases with a platelet count less than 20.000/ul can cause serious morbidity and mortality to the mother and neonate such as spontaneous hemorrhage in mother, thrombocytopenia, purpura, ecchymosis, even intracranial hemorrhage in neonatal period.[21,22] A retrospective case series showed that 12% to 15% of infants born to women with ITP develop platelet counts of less than 50.000/ul, with 3% having major bleeding complications and less than 1% having intraventricular hemorrhage.[19] In another study investigated the deliveries with ITP and the ratio of vaginal delivery was found higher in these cases. They showed that 15,38% of infants born to women with ITP develop platelet counts of less than 50.000/ul, with no major bleeding complications and intraventricular hemorrhage.[23] Women with ITP had no major bleeding complications in our study population. We recorded neonatal thrombocytopenia in 3 infants (9,3%) of ITP group. There was no major bleeding in this neonate.

In conclusion, severe thrombocytopenia is usually detected in pregnant women with preeclampsia/HELLP syndrome and ITP. While the pregnants with GT and ITP had favorable pregnancy outcomes, the patients with preeclampsia or HELLP syndrome associated with IUGR, placental abruption, still birth, and low Apgar scores (<7) at 1 and 5 min. Moderate to severe thrombocytopenia caused by preeclampsia/HELLP syndrome is required careful surveillance for decrease possible maternal and neonatal complications.

## Gestasyonel Trombositopeni Preeklampsi/HELLP Sendromu ve İmmün Trombositopenik Purpuranın Neden Olduğu Orta ve Şiddetli Trombositopenilerde Maternal ve Fetal Sonuçların Karşılaştırılması

Bu çalışmada gestasyonel trombositopeni (GT), preeklampsi/HELLP sendromu ve immün trombositopenik purpuranın neden olduğu orta ve şiddetli trombositopenilerde obstetrik risk faktörlerini, komplikasyonlarını ve gebelik sonuçlarının karşılaştırılması amaçlandı.

Çalışmaya trombosit sayısı 100.000/mm$^3$'den düşük olan 135 kadın alındı. Tanılar Hematoloji laboratuvarı tarafından konuldu. Olguların ve yeni doğanların hastane seyirlerindeki klinik özellikleri kaydedildi.

Şiddetli trombositopeni GT grubunda diğer iki gruba göre daha düşük gözlendi. Preeklampsi/HELLP sendromlularda oligohidramnios, intrauterin gelişme geriliği ve ablatio plasenta yüksek oranlarda saptandı. Bir ve 5. dakikada Apgar skor oranları (<7), pH değerleri (<7,2) ve mekonyumlu amniyotik sıvı oranları preeklampsi/HELLP sendromlularda daha yüksekti. Neonatal trombositopeni 5 yeni doğanda tespit edildi.

Sonuç olarak preeklampsi/HELLP sendromunun eşlik ettiği trombositopenili olgular, obstetrik ve fetal sonuçlar açısından en olumsuz grup olarak saptandı.

**Anahtar Kelimeler:** Gestasyonel trombositopeni, Preeklampsi /HELLP sendromu, İmmün trombositopenik purpura, Fetal sonuçlar

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