Original Article

# Frequency of Thrombocytopenia in Pregnancy and Its Causes in Pregnant Women

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## Abstract

Objective: To determine the frequency of thrombocytopenia in pregnancy and its causes at tertiary care hospital. Settings Pathology department Diagnostic and Research laboratory LUMHS Jamshoro/Hyderabad.
Methodology: This Cross-Sectional study was conducted at Pathology department Diagnostic and Research laboratory LUMHS Jamshoro/Hyderabad. There were 242 pregnant women presenting at any gestational age were included in this research. Following a thorough clinical evaluation, every patient had a full blood count using the Sysmex XN1000. Performa was filled out with all the details about the thrombocytopenia and its cause.
Results: The average age of the women was 25.99±4.49 years. Frequency of thrombocytopenia in pregnant women was 9.09% (22/242). Out of 22 women with thrombocytopenia, gestational thrombocytopenia was the common cases that was observed in 72.7% (16/22) followed by preeclampsia 9.1% (2/22), HELLP syndrome 9.1% (2/22), and ITP was seen in 9.1% (2/22).
Conclusion: Thrombocytopenia during pregnancy increases the risk of complications for both the mother and the baby. Obstetricians, neonatologists, and primary care physicians must work together in a multidisciplinary fashion to manage pregnant women with platelet problems.
Key Words: Thrombocytopenia, HELLP syndrome, gestational thrombocytopenia.

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## Introduction

A platelet count below 150,000/uL is referred to as thrombocytopenia.[1] A mild depression is indicated by counts between 100,000 and 150,000/uL, a moderate depression by counts between 50,000 and 100,000/uL, and a severe depression by counts below 50,000/uL.[2] One of the most frequent hematologic abnormalities that can occur during pregnancy is thrombocytopenia.[3]

The platelet count often drops throughout pregnancy, particularly as the pregnancy progresses. The dilutional effect, caused by an increase in plasma volume and a quickening of platelet breakdown across the placenta, is primarily responsible for this.[4, 5] It is recommended to evaluate the peripheral blood film to rule out factitious thrombocytopenia before classifying the patient as thrombocytopenic.[6] Although low platelet counts are usually unrelated, they can be an indicator of a gestational or systemic disease that the mother may be experiencing, which could lead to a therapy or intervention that is harmful to the unborn child.[7]

Thrombocytopenia during pregnancy is the leading cause, accounting for about 75% of all cases.[1] GT usually goes away on its own within a month or two after the baby is born.[8] Thrombocytopenia is caused by hypertensive diseases in 21% of instances.[1] People

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with eclampsia are more likely to have thrombocytopenia (30%) compared to people with mild or severe preeclampsia (15%-18%).[3] Between four percent and twelve percent of patients with severe preeclampsia will show signs of HELLP syndrome, which includes hemolysis, high liver enzymes, and low platelet counts.[3] About 4.1% of instances are caused by immune-mediated thrombocytopenia, which includes conditions like newborn alloimmune thrombocytopenia and idiopathic thrombocytopenia purpura.[1] Despite the generally moderate course of pregnancy-related thrombocytopenia, there is some evidence that it increases the risk of preterm delivery and placental premature separation.[9] A patient's risk of developing thrombocytopenia and the severity of their illness are both affected by the course of their illness.[10] Eight percent of pregnant women get thrombocytopenia.[3] In pregnant women who are generally healthy, thrombocytopenia is most noticeable in the third trimester,[2] when the platelet count typically stays around 110×109 /L and rarely drops below 70×109 /L.

There is a risk of neonatal thrombocytopenia, making the differential diagnosis between ITP and gestational thrombocytopenia clinically essential for the fetus. Nevertheless, making this type of differential diagnosis when pregnant is extremely challenging.[11] In Pakistan, the primary population of pregnant women with severe thrombocytopenia has a history of immune thrombocytopenia, making management of these pregnancies difficult.[12] Safe and effective management is possible with a complete medical history, physical exam, targeted laboratory testing, and collaboration with obstetricians and hematologists as needed for these individuals.[13]

The purpose of this research is to identify the reasons of thrombocytopenia and the frequency with which it occurs during pregnancy. In light of the foregoing, this investigation is intended to determine the extent of the condition. The correct care and prevention of this disease may be planned once the burden of this disease is known. In addition, this study aimed to determine the various causes of low platelet counts in pregnant women, which will aid clinicians in treating patients appropriately and avoiding transfusion-related complications by reducing the need for platelet transfusions.

## Methodology

This cross-sectional study was conducted in the Pathology Department at the Diagnostic and Research Laboratory, LUMHS Jamshoro/Hyderabad, from September 2022 to February 2023, using a non-probability consecutive sampling method. Sample size calculation was performed with a 95% confidence interval and a 2.5% margin of error, the calculated sample size was 242. The prevalence of immune thrombocytopenia was 4.1%.[1]

All pregnant women, regardless of gestational age, with a positive pregnancy test or ultrasound, and between the ages of 17 and 45, were included in the study. Individuals with nutritional deficiencies, thrombotic thrombocytopenic purpura (TTP), disseminated intravascular coagulation (DIC), chronic liver disease, drug-induced thrombocytopenia, hemolytic uremic syndrome (HUS), or chronic liver disease were excluded.

Written informed consent was obtained before the study commenced, and ethical approval was granted by the Institutional Ethics Review Board and CPSP. A random sample of pregnant women was selected from the gynecology outpatient department and ward. Each patient underwent a clinical evaluation, and a complete blood count was conducted using the Sysmex XN1000 after collecting medical history, demographic data, and other relevant information. Patients diagnosed with thrombocytopenia (platelet count < 150,000/uL) were further investigated for underlying causes by performing liver function tests (LFTs), a urine detailed report, PT/APTT, serum vitamin B12, and red cell folate levels.

The exclusion criteria included histories of non-alcoholic hepatitis, drug-induced thrombocytopenia, nutritional deficiencies, DIC, TTP, or HUS. Data was recorded using the Performa application.

Data entry and analysis were performed using SPSS version 20.0. Quantitative variables such as complete blood count, PT, APTT, LFTs, vitamin B12, serum and red cell folate levels, age, parity, body mass index (BMI), and standard deviation were calculated. Qualitative variables such as residential status (urban/rural), socioeconomic status (upper, middle, or lower class), educational level, and causes of thrombocytopenia were analyzed using frequencies and percentages.

Stratification was applied to control for effect modifiers such as gestational age, age, parity, BMI, residence, education level, and socioeconomic status. To account for potential confounders, restrictions and stratifications were implemented, followed by the Chi-square test. A

p-value of < 0.05 was considered statistically significant.

## Results

There were 242 pregnant women presenting at any gestational age were included in this research. The average age of the women was 25.99±4.49 years. Similarly mean gestational age, weight, height and BMI of the women are also reported in table I.

**Table I: Descriptive statistics of the cases.**

| Variables | Mean ± SD | Median(IQR) |
|---|---|---|
| Age (Years) | 25.99±4.49 | 25(5) |
| Gestational age (Weeks) | 37.03±1.96 | 37(2) |
| Weight (kg) | 74.42±16.32 | 75(22) |
| Height (cm) | 162.21±8.54 | 165(10) |
| BMI (kg/m$^2$) | 28.257±5.94 | 27.46(6.5) |

Almost 66% of the women had primiparous and 34% had multiparous. (figure 1) Residential status of the women are approximate same.

Out of 242 cases, 30% were illiterate, 29.34% were primary/secondary educated, 30.6% were matric /intermediate while only 9.92% were graduate or above as shown in figure 2.

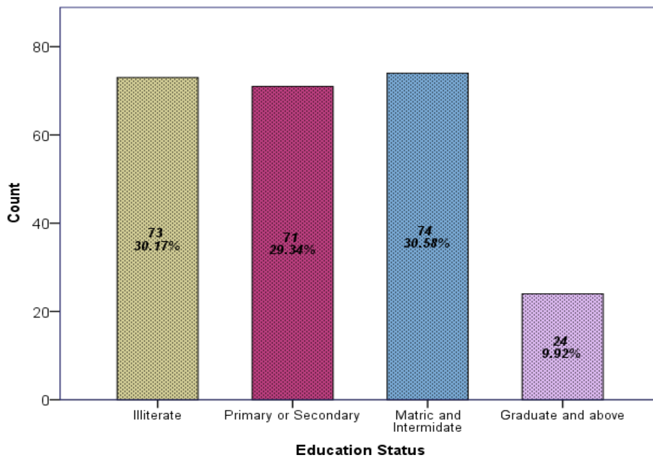


**Figure 2. Educational status. (n=242)**

**Table II: Clinical Investigation.**

| Variables | Mean | SD | Median | IQR |
|---|---|---|---|---|
| Vitamin B12 levels | 460.14 | 174.34 | 369 | 228 |
| serum and red cell folate levels | 13.25 | 3.25 | 14.5 | 3.5 |
| Serum Bilirubin | 0.68 | 0.63 | 0.6 | 0.10 |
| Direct | 0.35 | 0.76 | 0.20 | 0.30 |
| Indirect | 0.68 | 0.23 | 0.70 | 0.25 |
| SGPT | 37.41 | 5.18 | 38 | 5.0 |
| Phosphate | 117.17 | 21.56 | 123 | 10.0 |
| Gamma | 25.80 | 17.06 | 15 | 28.0 |
| HB | 10.85 | 1.34 | 10.80 | 1.6 |
| WBC | 6.45 | 1.86 | 6 | 3.0 |
| Neutrophil | 54.79 | 8.16 | 56 | 10.3 |
| Lymptrophils | 34.13 | 5.29 | 35 | 2.0 |
| Monoyctes | 5.47 | 1.57 | 5 | 1.0 |
| Eosinophil | 4.79 | 1.26 | 5 | 2.0 |
| Basophile | 0.50 | .14 | 0.5 | 0.1 |
| ESR | 18.65 | 5.01 | 20 | 9.0 |
| Platelet | 241.33 | 90.58 | 240 | 77.0 |

**Table III: Causes of thrombocytopenia.**

| Causes of thrombocytopenia | N | % |
|---|---|---|
| Gestational thrombocytopenia | 16 | 72.7% |
| ITP | 2 | 9.1% |
| Preeclampsia | 2 | 9.1% |
| HELLP syndrome | 2 | 9.1% |

Descriptive statistics of the clinical investigation of the women are reported in table II. Frequency of thrombocytopenia in pregnant women was 9.09% (22/242).

Out of 22 women with thrombocytopenia, gestational thrombocytopenia was the common cases that was observed in 72.7% (16/22) followed by preeclampsia 9.1% (2/22), HELLP syndrome 9.1% (2/22), and ITP was seen in 9.1% (2/22), as shown in table III.

Frequency of thrombocytopenia in pregnant women with respect to age groups, gestational age, BMI, parity status was also reviewed and only frequency of thrombocytopenia was significantly high in ≤37 gestational age (p=0.0005) as shown in table IV.

**Table IV: Frequency of thrombocytopenia with pregnancy demographics.**

| Variables | | THROMBOCYTOPENIA | | | | Total | P-Value |
|---|---|---|---|---|---|---|---|
| | | Yes (n=22) | | No (n=220) | | | |
| | | N | % | N | % | | |
| *Age Groups (Years) | <= 20 | 2 | 8.7 | 21 | 91.3 | 23 | 0.139 |
| | 21 to 25 | 10 | 9.7 | 93 | 90.3 | 103 | |
| | 26 to 30 | 10 | 12.3 | 71 | 87.7 | 81 | |
| | >30 | 0 | 0.0 | 35 | 100.0 | 35 | |
| Gestational Age (Weeks) | ≤37 | 18 | 20.9 | 68 | 79.1 | 86 | 0.0005 |
| | >37 | 4 | 2.6 | 152 | 97.4 | 156 | |
| BMI (kg/m2) | <30 | 12 | 7.3 | 152 | 92.7 | 164 | 0.164 |
| | >=30 | 10 | 12.8 | 68 | 87.2 | 78 | |
| Parity | Primi parous | 13 | 8.2 | 146 | 91.8 | 159 | 0.493 |
| | Multiparo us | 9 | 10.8 | 74 | 89.2 | 83 | |

**Table V: Frequency of thrombocytopenia with demographics.**

| Variables | | THROMBOCYTOPENIA | | | | Total | P-Value |
|---|---|---|---|---|---|---|---|
| | | Yes (n=22) | | No (n=220) | | | |
| | | Count | % | Count | % | | |
| Residential Status | Rural | 10 | 8.6% | 106 | 91.4% | 116 | 0.807 |
| | Urban | 12 | 9.5% | 114 | 90.5% | 126 | |
| *Education Status | Illiterate | 5 | 6.8% | 68 | 93.2% | 73 | 0.749 |
| | Primary or Secondary | 6 | 8.5% | 65 | 91.5% | 71 | |
| | Matric and Intermediate | 9 | 12.2% | 65 | 87.8% | 74 | |
| | Graduate and above | 2 | 8.3% | 22 | 91.7% | 24 | |
| *Occupation | House Wife | 21 | 9.4% | 203 | 90.6% | 224 | 1.000 |
| | On Job | 1 | 5.6% | 17 | 94.4% | 18 | |
| *Socio economic status | Upper Class | 2 | 8.3% | 22 | 91.7% | 24 | 0.533 |
| | Middle Class | 20 | 10% | 181 | 90% | 201 | |
| | Lower Class | 0 | 0% | 17 | 100% | 17 | |

Rate of thrombocytopenia was not statistically significant with residential status, education status, occupation and socio-economic status as shown in table V.

## Discussion

In eight percent of pregnant women, thrombocytopenia occurs; gestational thrombocytopenia is the underlying cause in over 70% of these cases. Thrombocytopenia becomes more apparent in otherwise healthy pregnant women during the third trimester, when the platelet count usually remains above 110×109 /L and rarely falls below 70Î109 /L. Hypertensive disorders, including HELLP syndrome and preeclampsia, affect 21% of cases.[14] A mother's platelet count usually recovers to normal within three to five days following delivering birth. The sentence is a Low platelet are a known cause of placental abruption, preterm birth, and maternal death.[15,16] The Systemic lupus erythromatosis, DIC, fatty liver, anti-phospholipid syndrome, thrombotic thrombocytopenia purpura, HIV infection, and certain medications are a few more, less common causes. The specific etiology of pregnant thrombocytopenia is unknown, while increased plasma volume may play a role, in autoimmune diseases, the spleen is crucial.[17]

Idiopathic thrombocytopenic purpura (ITP) is characterized by the tubuloendothelial system's clearance of antibody-linked circulating platelets. Unborn children may experience thrombocytopenia if the antibody crosses the placenta.[18] Because of the risk of maternal and foetal bleeding throughout the prenatal and peripartum phases, treating ITP during pregnancy is a difficult problem.[19,20] An average age of 25.99±4.49 years was recorded for the females involved in this study. Mothers who were having their first child made up the majority of our patient population. Brohi et al. found that the average age of the patients was 30.8 (±5.594) years.[21] The parity statuses of these occurrences were multigravida (53.5%), primigravida (40.8%), and grand multipara (5.6%). In their study, Bai et al. [22] found that the average age of the women was 26.91±5.28 years. Women who were moms for the first time made up the majority of the study's participants.

The majority of cases (72.7%) in this investigation were thrombocytopenia caused by pregnancy. Finding that 59.3% of all instances of thrombocytopenia occurred during gestation, another study reached a similar conclusion.[23] Among pregnancy-related thrombocytopenia, gestational thrombocytopenia is by far the most frequent in Pakistan, affecting around 6% of pregnancies and constituting 75% of all cases. During the third trimester, you may notice a 10% drop in platelet count; by the sixth week after giving birth, the impact has worn off. The incidence of immune thrombocytopenia during pregnancy ranges from 0.01% to 0.05%.[24,25] Although the specific reason behind gestational thrombocytopenia remains unknown, it is thought to be related to peripheral consumption and increased activation.

The second most common reason for low platelet counts was preeclampsia. Something along similar lines was also discovered in a previous study. Thrombocytopenia is usually moderate, and the platelet count seldom falls below 20,000/μl. The degree of thrombocytopenia in a person is proportional to the severity of preeclampsia. It impacts 0.5-0.9% of all pregnancies and occurs in 10% of preeclampsia patients. Our data shows that this happens to 40.9% of patients. The findings were consistent with one previous study (12.06%) as well.[26] The Hemolysis, elevated liver enzymes, and a drop in platelets are the symptoms. Endothelial damage, tissue factor release, and coagulation activation are components of the

pathophysiology that are similar to preeclampsia. A recent research discovered mutations in genes that regulate the alternative complement system; these findings suggest that excessive complement activation may play a role in the pathogenesis of atypical hemolytic uremic syndrome (atypical HUS).[27] About 3% of pregnant women with thrombocytopenia will have immunological thrombocytopenia, which affects 1% to 10% of all pregnant women.[28,29] It causes thrombocytopenia more often than any other factor in the first two trimesters of pregnancy. Autoantibodies against different platelet glycoproteins (IgG) cause autoimmune illness ITP, which impacts 18.2% of the population.[30] Attaching to specific antibody receptors on macrophages—which are mostly found in the liver and spleen—rapidly removes platelets that are associated to antibodies from the mother's circulation. An unborn child may get thrombocytopenia if IgG antibodies are able to cross the placenta.[31] With 24 cases (or 33.8% of the total), gestational thrombocytopenia was the most common cause of thrombocytopenia in the study conducted by by Brohi et al. [32] 10(16.3%) of the total, had hepatitis E, while nineteen patients, or 26.7%, had HELLP syndrome. Platelet counts varied between 20,000 and 50,000 in eleven cases, between 50,000 and 100,000 in eighteen cases, and between 50,000 and 100,000 in nineteen cases.[33] There are a few potential causes of thrombocytopenia during pregnancy, including antiplatelet antibodies, increased platelet consumption, or haemodilution. The presence or absence of these antibodies, however, does not aid in diagnosis or differentiate it from immune thrombocytopenic purpura.[34] It can be difficult to tell the difference between gestational thrombocytopenia, which goes away after delivery, and immunological thrombocytopenia, which stays after birth, until after the postpartum period has gone.[35] Up to the third trimester of pregnancy, gestational thrombocytopenia—the most common kind of thrombocytopenia in our study—is linked to a favorable pregnancy outcome.

## Conclusion

Thrombocytopenia during pregnancy increases the risk of complications for both the mother and the baby. Thus, it is crucial to closely monitor these moms and their newborns with thrombocytopenic symptoms in order to determine the cause and administer the necessary treatment promptly. Obstetricians, neonatologists, and primary care physicians must work together in a multidisciplinary fashion to manage pregnant women with platelet problems.

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