

## Thrombocytopenia in Pregnancy

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### Abstract

**Objective:** To study the proportion of thrombocytopenia in normal pregnancy, compare it with thrombocytopenia in pregnancy with associated complications. It was also to study maternal and fetal outcomes in pregnancies associated with thrombocytopenia.

**Materials and Methods:** In this study, 76 pregnant women were recruited from Department of Obstetrics and Gynecology, Gandhi hospital from August 2012 to October 2014. Antenatal women were enrolled in the study at first visit, irrespective of gestational age. Details were entered in the proforma. All women had platelet count estimation at the time of enrollment. Women with normal platelet count before 28 weeks had a repeat platelet count in third trimester to detect gestational thrombocytopenia. All the thrombocytopenic cases were followed up throughout the antenatal period till delivery to record any complications that developed due to low platelet counts. Later maternal and fetal outcomes were also recorded

**Results:** women were tabulated according to their demographic characteristics, gestational age at the time of first onset of thrombocytopenia, severity of thrombocytopenia and need for blood transfusion or requirement of any other intervention. The fetal and maternal outcomes were recorded.

**Conclusion:** GT is the most common cause of thrombocytopenia during pregnancy (70%). If no antecedent history of thrombocytopenia is present and platelet counts are above 70,000/mcL, the condition is more likely to be GT. If platelet counts fall below 50,000/mcL or if a preexisting history of thrombocytopenia is present, the condition is more likely to be ITP. Follow platelet counts every 1-2 months or more frequently if the patient is symptomatic. Cesarean deliveries should be reserved for obstetrical indications only. With ITP, obtain cord blood at delivery for platelet count. For GT, document normalization of maternal platelet counts after delivery.

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### Introduction

Thrombocytopenia affects 6% to 10% of all pregnant women and other than anemia is the most common hematologic disorder in pregnancy. Pregnancy is associated with numerous metabolic, immunologic, and other homeostatic changes that require careful consideration.

### Classification of Thrombocytopenia

Thrombocytopenia is defined as a platelet count of less than  $150 \times 10^9/l$ . Normal pregnancy generally thought not to affect the platelet count<sup>5</sup>, but it has been suggested that the normal range is lower in pregnancy, and that the count falls in the third trimester<sup>6,7,8</sup>.

Demand for folic acid rises to 300-400 ng/day in normal pregnancy, and dietary deficiency may cause thrombocytopenia, particularly where demand is increased by multiple pregnancy, or by an underlying hemolytic state<sup>9</sup>.

### Causes of thrombocytopenia in pregnancy

#### 1. Reduced production

Congenital  
Precursor deficiency  
Marrow failure  
Malignancy

#### 2. Increased consumption

Idiopathic (auto-immune) thrombocytopenia (M, F)  
Pre-eclampsia/eclampsia (M)  
Thrombotic thrombocytopenic purpura(M)  
Disseminated intravascular coagulopathy (M)  
Drugs including heparin (M)  
Alloimmune thrombocytopenia F (M)

M = disease process causes thrombocytopenia in mother;

F = disease process causes thrombocytopenia in fetus.

### Laboratory Evaluation of Platelet Number & Function

In patients suspected of a disorder of haemostasis, defects in platelet number or function, impaired coagulation or abnormalities in vascular function should be considered.

**Platelet count:** This screening test is performed routinely as a part of the complete blood count using automated particle counters. A typical reference range is 1, 50,000- 4, 40,000/mc 3.

**Bleeding time:** the length of time a small skin wound continues to bleed depends largely on the number and function of platelets. The bleeding time cannot predict bleeding, blood loss or transfusion requirements.

**Coagulation mechanism:**

There are three simple rapid in vitro tests of the integrity of the coagulation cascade.

1. Activated partial thromboplastin time (APTT) - intrinsic system.

2. Prothrombin time (PT) - extrinsic system.

3. Thrombin time (TT) - final common pathway

**Patients and Data:**

**Sources of Data:**

From the records of pregnant women admitted in the Department of Obstetrics and Gynaecology, Gandhi Hospital Secunderabad.

**Table 1: Showing etiology of thrombocytopenia**

Pregnancy-specific	Not pregnancy-specific
Gestational thrombocytopenia	Primary immune thrombocytopenia
Preeclampsia/Eclampsia	Secondary immune thrombocytopenia
HELLP syndrome	Viral infection (HIV, Hep C, CMV, EBV, ot hers)
Acute fatty liver	Autoimmune disorders (SLE, others)
	Antiphospholipid antibodies
	Thrombotic microangiopathies
	<i>Thrombotic thrombocytopenic purpura*</i>
	<i>Hemolytic-uremic syndrome*</i>
	Disseminated intravascular coagulation (DIC)
	Bone marrow (MDS, myelofibrosis)
	Nutritional deficiencies
	Drugs
	<i>Type IIB vWD induced thrombocytopenia*</i>
	Inherited thrombocytopenia (May-Hegglin, etc)
	Hypersplenism

**Methodology**

In this study, 76 pregnant women, recruited from Department of Obstetrics and Gynecology, Gandhi hospital after approval from institutional Ethical Clearance Committee from august 2012 to October 2014. Written informed consent was taken from them. Antenatal women were enrolled in the study at first visit, irrespective of gestational age. Details were entered in the proforma regarding the detailed history of period of gestation, high risk factors, past history, complications- during present and past pregnancy. History of petechiae, bruising, drug usage, viral infection, thrombocytopenia in previous pregnancy was taken. General, systemic and obstetric examination was done.

All women had platelet count estimation at the time of enrollment. Platelet count assessment was done through automated blood count analyzer with routine

antenatal hematological evaluation of the patient. The detailed work up of all cases of thrombocytopenia was done to ascertain the cause of thrombocytopenia.

All women were subjected to blood test for Hb, TLC, DLC, bleeding time, clotting time, RFT, LFT, HBsAg & HIV. Women with fever were tested for Dengue IgM. Coagulation tests (PT, APTT, FDP and fibrinogen) were done in those with signs or symptoms of DIC. Women with normal platelet count before 28 weeks had a repeat platelet count in third trimester to detect gestational thrombocytopenia. All the thrombocytopenic cases were followed up throughout the antenatal period till delivery to record any complications that developed due to low platelet counts. Women with HIV status and on drugs causing thrombocytopenia were excluded from the study.

Maternal outcome regarding mode of delivery, complications occurring during delivery, postpartum period were observed.

Fetal outcome regarding birth weight, NICU admission, early neonatal outcome noted and were followed up for any complications.

**Sample Collection:** Blood specimen was withdrawn with minimal stasis from the ante-cubital vein using a dry sterile disposable syringe and needle. 3mm of blood is dispensed into EDTA anticoagulant tubes. The specimens were labeled with subject's age, sex and identification number. The EDTA samples were kept at room temperature until processed within 4 hrs of collection.

**Laboratory Analysis:** Platelet count was performed using manual method and automated hematology method.

### Study Area

All pregnant women who attended OPD at the Department of Obstetrics and Gynecology, Gandhi Hospital, for antenatal checkups.

**STUDY DESIGN:** Hospital based observational and Prospective study.

**STUDY DURATION:** November 2012 –October 2014.

**ESTIMATION OF SAMPLE SIZE:** 76

### Statistical Analysis

The data were registered in the computer by creating a spreadsheet. We received statistical advice from the Statistician from Department of SPM in our hospital. The statistical analyses were used to examine differences concerning the analyzed parameters.

All the quantitative variables like age, platelet count, etc. Will be expressed in terms of descriptive statistics like mean and standard deviation. All the qualitative variables will be expressed in terms of proportion.

The tests used for statistical calculations were as follows:

- 1) Chi-Square Test for use in the analysis of the difference between two proportions.
- 2) T-test to test the significance of the difference between two proportions or percentages.

For the parameters age, BMI, gestational age, hospital stay and hemoglobin an average value was obtained and a calculation of standard deviation was done. A p value less than 0.05 was considered to be statistically significant.

### Observation and Analysis

Total numbers of cases studied are 76, selected according to platelet count at admission. Presenting complaints were noted, the cases followed up for any changes in platelet count and associated complaints. Any complications during delivery, maternal and fetal outcome were noted.

For testing the equality of means among the groups, student's t test is carried out for those characteristics of continuous nature. In all the cases, the p value is noted.

### Discussion

#### 1. Patient demographic characteristic's

50 cases fall in age group of 20 to 25 years, thrombocytopenia is most common among age group 20 to 25 years. 34 cases are primigravida, 28 cases 2<sup>nd</sup> gravida and 14 cases are 3<sup>rd</sup> gravida.

According to study conducted by Singh Nisha, Dhakad Amita, Singh Uma, K. Tripathi, Sankhwar Pushplata (Prevalence and Characterization of Thrombocytopenia in Pregnancy in Indian Women) There was no significant difference in the distribution of cases and controls according to age (P = 0.923), religion (P = 0.947) and parity (P = 0.068). According to Genovese study The mean age was 30 ± 2 years and Average gestational age diagnosis was 28+3 weeks

**Table 3 - Gestational age at diagnosis**

First onset GT	History of previous GT
28 ±3 weeks	12±3 weeks

The mean platelet counts in gestational, obstetric and medical thrombocytopenia were 113,000, 105,000 and 53,850 ll-1, respectively. Women with medical thrombocytopenia had significantly (P<0.001) lower mean platelet count as compared to other causes of thrombocytopenia.

#### 2. Platelet Count and Transfusions:

Fresh frozen plasma infusion can be used for reversal of anticoagulant effects. Platelet transfusion is indicated to prevent hemorrhage in patients with thrombocytopenia or platelet function defects. Cryoprecipitate is used in cases of hypofibrinogenemia, which most often occurs in the setting of massive hemorrhage or consumptive coagulopathy.

#### Out of 76 patients 41 required transfusions

	Transfusions+ (n=41)	Transfusions- (n=34)
Mean platelet count	86,439mm <sup>3</sup>	1,13,352mm <sup>3</sup>
Standard deviation	33,261	25,150

Z is 3.99 and P value is < 0.05

As P value is <0.05 which means it is significant, so there is significant relationship between thrombocytopenia and transfusion.

According to Singh, Nisha study conducted in 2012, Out of 13 cases of medical thrombocytopenia, 8 were treated with steroids, blood transfusion and platelet transfusions. These eight included ITP, megaloblastic anemia and malaria cases. One case of DIC (obstetric thrombocytopenia) was also managed with transfusion of blood, platelets and FFP but no medical or surgical intervention was required in any case of GT.

**3. Thrombocytopenia And Maternal Outcome:**

Thrombocytopenia itself causes complications and thrombocytopenia is a complication of other disorders, PPH is the most common complication. Other complications include DIC, multiple organ failure, maternal death etc.

	Good maternal outcome	Bad maternal outcome
Mean platelet count	91,411mm <sup>3</sup>	1,02,482
Standard deviation of platelet count	37,240	2,8754

According to this study 16 cases had complications which included PPH, Liver failure, CCF, psychosis, renal failure, sepsis, DIC, 4 maternal deaths. Maternal deaths were 4 which come up to 5.33%. The mean platelet count for maternal complications is 1, 02, 482mm<sup>3</sup>, standard deviation 28,754. Z is 1.13 and p value is >0.05 which means it is not significant, So according to this study, thrombocytopenia is not directly related to maternal outcome, there are also other factors which influence the maternal outcome like anemia, preeclampsia, sepsis etc. thrombocytopenia is an additional factor and not independent factor.

According to study conducted by Dhakad Amita (2011) Incidence of PPH was 9.89% among cases. PPH was seen in 30% of medical, 15% of obstetric and only 4.92% of gestational thrombocytopenia. Incidence was significantly higher in medical thrombocytopenia (P = 0.008). Three cases of obstetric and two of medical thrombocytopenia died during the study giving a mortality rate of 5.26%. Significantly higher mortality (P = 0.009) was seen in these cases as compared to GT that showed nil mortality.

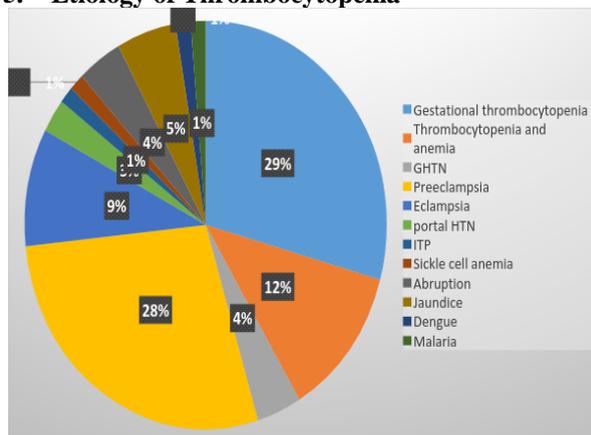
**4. Thrombocytopenia and Fetal Outcome:**

Neonatal complications are not directly related to maternal platelet count. The fetal complications occur in cases of preterm delivery, abruption, thrombocytopenia associated with anemia, sepsis.

Fetal platelet count was done in 2 cases of ITP out of which one case had thrombocytopenia. None of the babies had bleeding complications

In this study fetal deaths were 13, NICU admissions were 21. According to study conducted by Nisha Singh in 2011 Out of the 91 newborns, platelet count assessment could be done in 75 (81.4%). All had normal platelet counts at birth except the one born to mother with ITP. Neonatal thrombocytopenia of 65,000 cumm on day-1 returned to normal on day eight. None of the babies had any bleeding complications.

**5. Etiology of Thrombocytopenia**



According to study conducted in Gandhi hospital hypertensive disorders causing thrombocytopenia is the most common etiology which included 42% of cases, next common is gestational thrombocytopenia which included 29% of cases. According to study conducted by Singh Nisha et al the etiology of thrombocytopenia was Distribution of thrombocytopenia cases according to etiology

S. no.	Cause	No. of cases	%
1.	Gestational	61	64.21
2.	Obstetric	21	22.11
	(a) Hypertensive disorders	20	21.05
	PET	19	20.0
	Eclampsia	1	1.05
	(b) DIC	1	1.05
3.	Medical	13	13.68
	(a) Hypersplenism	2	2.11
	(b) Hepatic diseases	3	3.17
	(c) Malarial	2	2.11
	(d) Megaloblastic anemia	1	1.05
	(e) ITP	5	5.26

As the referral cases are more in Gandhi hospital and most cases of gestational thrombocytopenia were undetected, no major complications were observed in gestational thrombocytopenia.

## 6. Severity of Thrombocytopenia:

According to the study

<50,000/mm<sup>3</sup> = 10 cases (severe)

50,000/mm<sup>3</sup> to 1,00,000/mm<sup>3</sup> = 26 cases (moderate)

1,00,000/mm<sup>3</sup> to 1,50,000/mm<sup>3</sup> = 40 cases

According to study conducted by Singh Nisha, Dhakad Amita, Singh Uma, K. Tripathi, Sankhwar Pushplata (Prevalence and Characterization of Thrombocytopenia in Pregnancy in Indian Women) 2012, prevalence of thrombocytopenia was 8.8%. There were 74.7% cases of mild thrombocytopenia, 17.9% of moderate thrombocytopenia and 7.4% with severe thrombocytopenia.

## 7. Thrombocytopenia, Mode of Delivery and Gestational Age at Delivery:

According to study 15 cases delivered between 28 to 32 weeks 16 cases delivered between 32 to 36 weeks and 45 cases delivered at term.

60 % of cases delivered at term, those delivered before term were mostly due to abruption or pregnancy was terminated for obstetric indications like severe preeclampsia, ante partum eclampsia, abruption or medical causes.

Mode of delivery is not influenced by platelet count. 60 % cases delivered by LSCS and 40% by SPVD. LSCS was done for obstetric and medical conditions like previous LSCS, fetal distress, failed induction etc.,

According to study conducted in 2011 in Kolkata, 91 cases delivered during the study. 68.1% delivered at term whereas 31.9% delivered preterm. 61.54% had normal vaginal delivery, 36.26% had CS and 2.2% had instrumental delivery. All the cesarean sections were performed for obstetric/medical causes and none for thrombocytopenia.

## Conclusion and Summary

GT is the most common cause of thrombocytopenia during pregnancy (70%), but other underlying causes must be considered as well. A thorough history and physical examination will rule out most causes. Look at the remainder of CBC and smear to rule out pancytopenia and platelet clumping associated with pseudo thrombocytopenia.

If no antecedent history of thrombocytopenia is present and platelet counts are above 70,000/mcL, the condition is more likely to be GT. If platelet counts fall below 50,000/mcL or if a preexisting history of thrombocytopenia is present, the condition is more likely to be ITP. Direct or circulating antiplatelet antibodies have no utility in the workup of thrombocytopenia in pregnancy because they usually are nonspecific and will not distinguish GT from ITP.

Follow platelet counts every 1-2 months or more frequently if the patient is symptomatic. Cesarean deliveries should be reserved for obstetrical indications only, because abdominal delivery itself has not been

demonstrated to be a cause for intracranial hemorrhage. Invasive procedures to determine fetal platelet counts (scalp sampling, PUBS) no longer are considered necessary because an infant who is thrombocytopenic may be delivered abdominally.

With ITP, obtain cord blood at delivery for platelet count and notify the pediatricians to assess neonatal platelet counts due to the risk for continued quantitative platelet decline and postnatal hemorrhage. For GT, document normalization of maternal platelet counts after delivery.

**Conflict of Interest: None**

**Source of Support: Nil**

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