

Thrombocytopenia in pregnancy; cause evaluation and follow-up

Aysha Khan¹, Shagufta Yousaf², Maliha Saad², Syed Rehan Asghar Naqvi², Saba Rizwan²

¹Combined Military Hospital, Malir Pakistan / Armed Forces Institute of Pathology, Rawalpindi

²Combined Military Hospital, Malir Pakistan

ABSTRACT

Objective: To determine the various causes of thrombocytopenia in pregnancy and its outcome.

Material and Methods: This quasi-experimental study was conducted at the tertiary care setup Combined Military Hospital Malir, Karachi, over three years. Pregnant women with a platelet count $<150 \times 10^9/L$ were enrolled, evaluated for the cause of thrombocytopenia, and followed until delivery and the postpartum period. Clinical history, including gestational age, age, comorbidities, and drug use, were recorded. Peripheral blood smears and relevant laboratory investigations (including Coombs test, liver and renal function tests, urine protein, HBsAg, and anti-HCV) were performed to determine the etiology.

Results: A total of 160 females were recruited in study. Thrombocytopenia in pregnancy is most commonly caused by gestational thrombocytopenia, seen in 120 cases (75.0%), and is usually mild and harmless. Pre-eclampsia and HELLP syndrome account for 16 cases (10.0%) and are serious conditions requiring close monitoring. DIC (disseminated intravascular coagulation), a life-threatening clotting disorder, was found in 4 cases (2.5%). Hepatic diseases, such as liver dysfunction, contributed to 2 cases (1.2%). Infections like malaria and dengue were responsible for 7 cases (4.4%). Autoimmune causes included ITP 4 cases (2.5%), TTP 3 cases (1.9%), and APLA 1 case (0.6%). Other causes were seen in 3 cases (1.9%).

Conclusions: Maternal outcome can be improved if exact cause is diagnosed during pregnancy. For most of the cases only reassurance is required.

Keywords: Gestational thrombocytopenia, Pregnancy, Thrombocytopenia

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INTRODUCTION

One of the most frequent disorder which is encountered in pregnancy is thrombocytopenia which is defined as platelet count of $<150 \times 10^9/L$. Most cases are benign and need only reassurance, but moderate to severe cases require careful evaluation and proper follow up [1,2]. Distinguishing gestational thrombocytopenia from life threatening conditions is essential for safety of both mother and baby [3].

The time of onset of thrombocytopenia is crucial. Its incidence in the first trimester is very low, and when present, it is usually unrelated to pregnancy itself and may result from conditions such as immune thrombocytopenia, type II von Willebrand disease, or viral infections [4].

Gestational thrombocytopenia and other pregnancy-related causes typically appear in the late second or

third trimester.

The Gestational thrombocytopenia is the most common cause and does not pose any harm to the mother and baby. This is the diagnosis of exclusion and platelet count usually returns to the normal within four weeks after delivery. [5]

Second most important cause of thrombocytopenia is pre-eclampsia, eclampsia and HELLP syndrome (haemolysis, elevated liver enzymes, and low platelet count) presents after 20 weeks of gestation and most commonly between 30-34 weeks of gestation [6]. History of hypertension, proteinuria, and deranged liver function test is very important in diagnosis of these patients.

Although rare, some patients may present with TTP/HUS (thrombotic thrombocytopenic purpura/haemolytic uremic syndrome) for the first-time during pregnancy. Despite its rarity, this condition is potentially life threatening and must be recognized early. History of altered conscious level, presence of schistocytes in peripheral blood and raised LDH should raise the suspicion [7].

Other causes include DIC, antiphospholipid antibody syndrome, fatty liver of pregnancy and infectious diseases such as malaria, dengue and hepatitis are also rare.

Correspondence: Dr. Aysha Khan, Consultant Haematologist, Department of Haematology, Armed Forces Institute of Pathology, Rawalpindi Pakistan

Email: aysharao@yahoo.com

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A platelet count of more than $30 \times 10^9/L$ is safe during pregnancy and prevent spontaneous bleeding and miscarriages. According to the latest guidelines, vaginal delivery is considered safe with a platelet count above $30 \times 10^9/L$. For cesarean sections, a platelet count of $50 \times 10^9/L$ is deemed adequate, while a count of $80 \times 10^9/L$ is recommended for epidural injections and anaesthesia. [8]

This study is undertaken to analyze the causes and emphasize the importance of systematic assessment in guiding safe management.

MATERIAL AND METHODS

This quasi-experimental study was carried out in the department of pathology (Haematology), Combined Military Hospital CMH Malir from October 2019 to September 2022 after approval from ethical review committee (91/22/105/ERC).

Sample size was calculated using the WHO calculator, keeping the confidence interval of 95%, prevalence of thrombocytopenia as 10.0 % and margin of error as 5%, sample size calculated was 138[9]. We included 160 females in this study.

All the pregnant females who were referred from obstetric department to haematology department for evaluation of thrombocytopenia were recruited in this study using non-probability convenient sampling. Serious pregnant females who were admitted in obstetric ward or intensive care unit were also included in this study. A detailed clinical history was taken along with physical examination.

History of onset of thrombocytopenia, duration of pregnancy, age of the patient, past medical and surgical history, history of thrombocytopenia before pregnancy or in previous pregnancies was taken. Any co-morbid conditions and drug history related or not related to thrombocytopenia was also taken.

For the confirmation of thrombocytopenia, blood sample was taken in EDTA vial and were processed on Sysmex XP 100 and slides were made to verify platelet count microscopically. Samples having platelet clumps and clots on slides were repeated. Slides were also examined for red Blood Cells (RBC) fragmentation, malarial parasite and abnormal white blood cells.

Thrombocytopenia was defined as mild, when platelet count was between $100-150 \times 10^9/L$, moderate as $50-100 \times 10^9/L$ and severe if platelet count was less than $50 \times 10^9/L$. [10]

Relevant other laboratory investigations were also carried out to evaluate the cause of thrombocytopenia such as Coombs test, prothrombin time (PT), activated partial thromboplastin time

(aPTT), liver function tests, renal function tests, urine for protein, etc. Patients who presented with fever were also tested for dengue (NS1 and IgM) and malaria (Malarial antigen and slide verification). Selected cases also had ultrasound abdomen to rule out visceromegaly.

Data was analyzed by using Statistical Package for Social Sciences (SPSS) 22.00. Normality of data was checked by Shapiro-Wilk test that showed that age was non-normal distributed represented using median (IQR). Qualitative data (Etiological Factors, weeks of pregnancy, Thrombocytopenia Severity, Proteinuria, Elevated Liver Enzymes and Positive coombs Test) was represented by using percentage and frequency. Chi square test/fisher exact test was used to find out the association of clinical characteristics and trimester of study participants. The p value ≤ 0.05 was considered as significant.

RESULTS

A total of 160 pregnant females, who had platelet count less than $150 \times 10^9/L$ were recruited in the study. Median age of the patients was 27.5 (33.0 – 22.0) years range from 18 to 39 years.

Majority of females, once thrombocytopenia was first detected were in third trimester ($n=86$, 53.75%), followed by second ($n=54$, 33.75%) and then third ($n=20$, 15.5%). Mild thrombocytopenia was reported in 89 females (55.6%) followed by moderate ($n=54$, 33.8%) and severe thrombocytopenia was observed in 17 females (10.6%). Furthermore, 34 (21.3%) females had proteinuria, 23 (14.4%) females had elevated liver enzymes and only 1 case (0.7%) had positive coombs Test. The detail of demographic and clinical characteristics of the study is shown in Table-I.

Thrombocytopenia in pregnancy is most commonly caused by gestational thrombocytopenia, seen in 120 cases (75.0%), and is usually mild and harmless. Pre-eclampsia and HELLP syndrome account for 16 cases (10.0%) and are serious conditions requiring close monitoring. DIC (disseminated intravascular coagulation), a life-threatening clotting disorder, was found in 4 cases (2.5%). Hepatic diseases, such as liver dysfunction, contributed to 2 cases (1.2%). Infections like malaria and dengue were responsible for 7 cases (4.4%). Autoimmune causes included ITP (4 cases, 2.5%), TTP (3 cases, 1.9%), and APLA (1 case, 0.6%). Other causes seen in 3 cases (1.9%) shown in Table-II. Table-III represents trimester wise severity of thrombocytopenia and its association with laboratory tests; most of the cases with severe

thrombocytopenia and elevated liver enzyme plus proteinuria occurred in second-third trimester.

Out of the total number of patients, 120 had a normal vaginal delivery, in contrast, 30 patients underwent a lower segment cesarean section (LSCS) and additionally, 10 patients experienced preterm

deliveries. Figure-I representing the distribution of outcomes and complications among the 160 maternal cases. Each segment reflects the percentage of patients experiencing specific outcomes or complications, providing a clear visual overview of the data.

Table-I: Demographic and clinical characteristics of study Participants (n=138).

Variables	Values
Age in Years	Median (IQR)
	27.5 (33.0 – 22.0)
Trimester	First
	20 (15.75%)
	Second
	54 (33.75%)
Thrombocytopenia Severity	Third
	86 (53.75%)
	Mild
	89 (55.6%)
Proteinuria	Moderate
	54 (33.8%)
	Severe
Elevated Liver Enzymes	Yes
	34 (21.3%)
	No
Positive coombs Test	126 (78.8%)
	Yes
	23 (14.4%)
	No
	137 (85.6%)
	yes
	1 (0.6%)
	No
	159 (99.4%)

Table-II: Distribution of etiological factors of thrombocytopenia among study participants (n=138).

Etiology	Frequency (%)
Gestational thrombocytopenia	120 (75.0%)
Pre-eclampsia and HELPP syndrome	16 (10.0%)
DIC	4 (2.5%)
Hepatic disease	2 (1.2%)
Malaria & Dengue	7 (4.4%)
TTP	3 (1.9%)
ITP	4 (2.5%)
APLA	1 (0.6%)
Others	3 (1.9%)

Table-III: Association of Clinical Characteristics and Trimester of study Participants (n=138)

Clinical Characteristics		Trimester			p-value
		First (n=20)	Second (n=54)	Third (n=86)	
Thrombocytopenia Severity	Mild	15 (75.0%)	28 (51.9%)	46 (53.5%)	0.354
	Moderate	03 (15.0%)	19 (35.2%)	32 (37.2%)	
	Severe	02 (10.0%)	07 (13.0%)	08 (9.3%)	
Proteinuria	Yes	0 (0%)	14 (25.9%)	18 (20.9%)	0.044
	No	20 (100.0%)	40 (74.1%)	68 (79.1%)	
Elevated Liver Enzymes	Yes	0 (0%)	7 (13.0%)	16 (18.6%)	0.096
	No	20 (100.0%)	47 (87.0%)	70 (81.4%)	
Positive coombs Test	Yes	0 (0%)	1 (1.9%)	0 (0%)	0.372
	No	20 (100.0%)	53 (98.1%)	86 (100.0%)	

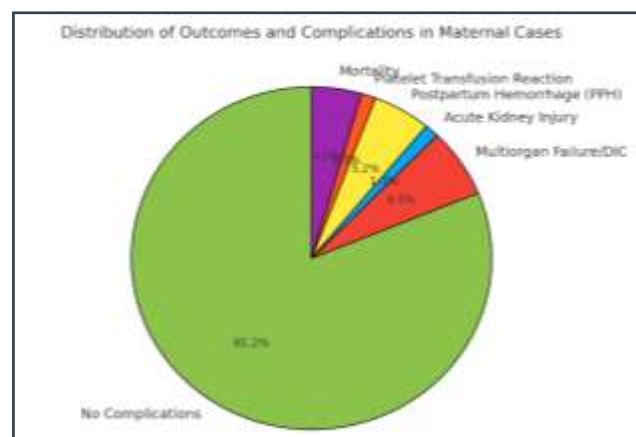


Figure-I: Distribution of outcomes and complications in maternal cases.

DISCUSSION

Thrombocytopenia is the second most important haematological condition, after anaemia that requires evaluation and follow up. Once the patient presents with thrombocytopenia in pregnancy, the decision for intervention depends upon the cause of thrombocytopenia [11]. The case must be thoroughly investigated, starting from pre-pregnancy status, previous platelet count, drug history, previous laboratory tests or any other cause of thrombocytopenia not related to pregnancy itself [12]. Gestational thrombocytopenia is the most common cause of low platelets in pregnancy, with incidence of 5-11% of all pregnancies.

In our study 120 patients (75.0%) had gestational thrombocytopenia which was similar to a study from India by Hooli [13], as compared to another study from India by Tanseem which showed an incidence of 45.6% (n=21) [14]. The diagnosis of gestational thrombocytopenia was confirmed as diagnosis of exclusion after doing all the relevant investigations. These patients were followed up till their safe delivery and no complication was observed in mother and baby. Similar findings were reported in study by Munera Burhany from Karachi, Pakistan which showed 78 (48%) patients with gestational thrombocytopenia [15].

Pre-eclampsia or eclampsia was the second most frequent cause, observed in 34 cases (24.6%), reflecting the significant impact of hypertensive disorders on platelet levels in our study. All of these patients presented with hypertension and were diagnosed in third trimester. Comparatively, Munera et al. reported similar issue in 18 patients (11.9%). However, this contrast with the findings of Fasiha et al where 41.3% of cases involved hypertensive disorders. Among the 16 patients in our study, three developed DIC. All patients were managed effectively, with no recorded mortality. Supportive care, including red cell concentrate and platelet transfusions, was administered to five patients.

Infections were another common cause of thrombocytopenia in our study. All patients with high grade fever and thrombocytopenia were investigated for malaria, due to its endemic presence in this area and plus for dengue as seasonal outbreaks of dengue fever occur frequently. Three patients had malaria and four patients had dengue infection. Only one patient of dengue had platelet transfusions. She presented at 20 weeks of gestation with high grade fever with platelet count of $18 \times 10^9/l$. She developed petechial haemorrhages on lower limbs and also had hematuria. Platelets were transfused and supportive care was given. She recovered smoothly and no maternal or fetal complication was observed. Study of Munera (Jan 2017-Aug 2020) and Hooli (Jan 2021-Dec 2021) showed similar results. We had only two patients with hepatitis B and C infection as compared to study by Munera et al which showed 9 (6%) patients with hepatitis C. One of the reasons can be that most of the patients received in our set up were from army background where better health facilities are available. Platelet count of these patients were in the range from $40-50 \times 10^9/l$. No patient required platelet transfusion.

In our study no patient was diagnosed as fatty liver of pregnancy as compared to Munera (3.3%) and

Fasiha which showed high incidence of this disease (15.3%). No patient with thrombocytopenia had leptospirosis or Covid 19 as compared to the study by Hooli. Another important cause of thrombocytopenia not related to pregnancy was ITP. We had four patients (2.5%) of ITP. They were managed with steroids during pregnancy with an aim to keep their platelet count of more than $30 \times 10^9/l$. Mode of delivery was determined by gynaecologist. One patient received IVIG, a day before delivery, after which she delivered safely. No complication was noted in baby and mother after delivery. Our results were similar to the study of Fasiha (n=1, 2.2%) and bit lower than study by Ghafoor [16] but in contrast to the study by Muneera (n=30, 20%) and Sangeeta et al (n=8,8%) [17] who showed higher incidence of ITP. Three patients (1.87%) in our study had TTP/HUS. Diagnosis was made on the basis of history and laboratory findings of raised LDH and bicytopenia with schistocytes on peripheral blood film. ADAM-TS assay was not available. No patient with TTP/HUS is reported by Munira et al and Sangeeta. Plasma exchange was started as soon as positive diagnosis was suspected, but none of three could survive.

The distributions of outcomes and complications among 160 patients is presented in pie chart. Each segment reflects the percentage of patients experiencing specific outcomes or complications, providing a clear visual overview of the data. Regarding overall maternal outcome no complication occurred in 128 (80%) patients, 10 (6.25%) had multi-organ failure followed by DIC, out of these 10 patients, 6 patients unfortunately (3.75%) died. Two patients (1.25%) had acute kidney injury followed by dialysis and luckily, they survived. Whenever thrombocytopenia occurs in pregnancy, it should be investigated in detail, it may be representing a serious underlying medical condition [18].

CONCLUSION

Maternal outcome can be improved if exact cause is diagnosed during pregnancy. In developing countries, examination of peripheral blood films is very important, as it gives valuable information about the presence of schistocytes, pseudo thrombocytopenia and malaria parasite and other laboratory investigations like raised LDH and thrombocytopenia leads to prompts diagnosis of TTP/HUS.

CONFLICT OF INTEREST

Authors declare no conflict of interest.

GRANT SUPPORT & FINANCIAL DISCLOSURE

Declared none

AUTHORS CONTRIBUTION

Aysha Khan: Study design, conceptualization, data curation, data analysis and interpretation, final approval, accountable for all aspects of publication.

Maliha Saad: Data curation, statistical analysis, supervision, final approval, accountable for all aspects of publication.

Syed Rehan Asghar Naqvi, Saba Rizwan: Critical review, final approval, accountable for all aspects of publication.

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