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Original Article

Does Gestational Thrombocytopenia and Immune Thrombocytopenic Purpura Warrant Hospital Admission?

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ABSTRACT

Objective: To determine the severity of thrombocytopenia in pregnancy and manage gestational thrombocytopenia patients in the outpatient department in order to reduce the economic burden on hospitals.

Study Design: Cross-sectional study.

Place and Duration of Study: Department of Haematology, Pakistan Railway Hospital, Rawalpindi, in collaboration with the Departments of Obstetrics and Gynaecology of Combined Military Hospital and Fauji Foundation Hospital, Rawalpindi, Pakistan from Oct 2018 to Oct 2019.

Methodology: The sample population included ninety pregnant females with platelet count <150x10^9/l. Blood samples were analyzed for complete blood count, peripheral blood smear, manual count by improved Neubauer chamber, serum uric acid, urinary proteins, liver function tests (bilirubin and aspartate aminotransferase), lactate dehydrogenase, coagulation profile and viral serology (hepatitis B & C).

***Results*:** Out of 90 thrombocytopenic pregnant females, gestational thrombocytopenia was most common, 86 (95.5%), while immune thrombocytopenic purpura was detected in 4 (4.5%) patients. Mild thrombocytopenia was frequently observed in patients of gestational thrombocytopenia 59 (68.6%), and severe thrombocytopenia was mostly detected in patients of immune thrombocytopenic purpura 3 (75%). About 58 (64.4%) of these patients were hospitalized, irrespective of the cause of thrombocytopenia.

Conclusion: Mild thrombocytopenia was commonly observed in gestational thrombocytopenia, and severe thrombocytopenia was usually diagnosed in patients with immune thrombocytopenic purpura. Gestational thrombocytopenia is frequent in pregnancy and does not require hospitalization. In contrast, patients with immune thrombocytopenic purpura require rational hospitalization for appropriate and judicious management for the safety of the mother and fetus.

Keywords: Gestational thrombocytopenia, Hospitalization, Immune thrombocytopenic purpura, Thrombocytopenia.

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INTRODUCTION

Thrombocytopenia is a platelet count of <150x10^9/l, frequently observed in 7–10% of pregnant females. It is the most frequent haematological condition encountered during pregnancy after anaemia. Thrombocytopenia is graded as mild (platelet count 100–150 x10^9/l), moderate (platelet count 50–100 x 10^9 /l), and severe (platelet count < 50 x 10^9/l).1,2 Gestational thrombocytopenia (GT) is described as a self-limiting benign disorder which does not cause any harm to the fetus or mother, and it does not necessitate any additional evaluation or intervention. GT is the most common cause of thrombocytopenia occurring in about 70-80% of all pregnancies with low platelet count. It is asymptomatic, mild thrombocytopenia, usually with a platelet count of >70 x 109/l. It is not associated with fetal thrombocytopenia, and platelet count returns to normal after delivery. There is no preceding history of thrombocytopenia in GT. 3

According to the American Society of Hematology, ITP is described as isolated thrombocytopenia that occurs with the lack of identifiable and specific causative factors.6 Based on international consensus, diagnosis of ITP requires a constant platelet count of less than 100x 109/l. 4 ITP is diagnosed by precise analysis of peripheral blood smear and assessment of patient's history and physical examination with some further tests including viral serology and coagulation profile.5 ITP is a diagnosis of exclusion. Consequently, ITP diagnosis takes place by eliminating several supplementary causes of thrombocytopenia, such as infections, haematological malignancies, medications, DIC, and autoimmune

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disorders.6 Bone marrow examination is not required for the diagnosis of ITP in pregnancy.8Spontaneous bleeding in ITP, though occasional, is the main maternal risk, especially when the platelet count falls below 20x109/l.9 Likewise, treatment is indicated when there is bleeding or platelet count falls below 20x 109/l. 7 First line treatment for ITP include oral steroids or IV immunoglobulins.8 Patients who are refractory to single therapy should be given combination of therapies such as steroids + IVIg and/or IV anti-D. 8

Differentiating between GT and ITP is a diagnostic challenge mainly because of the absence of specific symptoms. Occurrence of thrombocytopenia prior to pregnancy or presence of moderate or severe thrombocytopenia is frequently identified as ITP.9 Presence of thrombocytopenia in the first trimester of pregnancy is not associated with gestational thrombocytopenia and favours an alternate diagnosis of ITP. 10 There is a difference of opinion regarding the management of GT and ITP, as much less work is done in this field. Gestational thrombocytopenia is most common in pregnancy, and it does not cause any risk of bleeding, and there is no harm to the mother and fetus. Hence, these patients can be safely treated in outpatient departments. Patients diagnosed with ITP require hospitalization due to the risk of bleeding, and there is a consequent risk to the mother and fetus as well. It is the need of the hour to accurately diagnose and wisely differentiate between GT and ITP haematologists and gynaecologists promptly and hospitalize patients accordingly, which needs learning at the national and global levels. This will reduce the workforce, human resources, and economic burden on the healthcare budget. This study aims to determine the severity of thrombocytopenia in GT and ITP and decrease the economic burden on hospitals by managing GT patients outdoors.

METHODOLOGY

The cross-sectional study was conducted at the Department of Haematology of Pakistan Railway Hospital Rawalpindi in collaboration with the Departments of Obstetrics and Gynaecology of Pak-Emirates Military Hospital and Fauji Foundation Hospital Rawalpindi, Pakistan after approval from Ethics Review Committee (Riphah/ERC/18/0311), from October 2018 to October 2019.

Inclusion Criteria: Pregnant females aged 18-38 years with a platelet count of <150 x109/l were included.

Exclusion Criteria: Patients having pseudo thrombocytopenia, microangiopathies e.g., HELLP syndrome, haemolytic uraemic syndrome, thrombotic thrombocytopenic purpura (TTP), preeclampsia, chronic diseases (diabetes mellitus, known hypertension, heart disease, renal disease, connective tissue disorders & chronic liver disease), infections, drugs (anti-inflammatory drugs, antibiotics, anti-epileptic, heparin, methyldopa, digitalis & cyclosporine), megaloblastic anaemia and lymphoproliferative disorders.

A detailed history was obtained, and maternal particulars like age, parity, gestational age and blood pressure recordings were noted. A complete blood count (CBC), including platelet count, was done. A manual count on the improved Neubauer chamber confirmed thrombocytopenia. A peripheral blood smear was made and examined to see giant platelets in patients with immune thrombocytopenic purpura. Peripheral smear was also analyzed to exclude patients having platelet clumps (seen in pseudo thrombocytopenia), schistocytes (seen in HELLP syndrome and TTP), macrocytes and hypersegmented neutrophils (seen in megaloblastic anaemia) & smudge cells and increased lymphocytes (seen in lymphoproliferative disorders). The blood pressure of all the study patients was taken, and hypertensive patients (preeclampsia/HELLP syndrome) with increased urine proteins, serum uric acid, serum bilirubin, serum aspartate transferase and reticulocyte count were excluded from the study population. After excluding all other causes of thrombocytopenia. Venous blood (5ml) was obtained using a 21G syringe after taking informed consent from all the pregnant patients. About 3 ml of venous blood was transferred to EDTA vacutainers for complete blood count, peripheral blood smear analysis, manual count on improved Neubauer chamber, and reticulocyte count (performed only in patients of HELLP syndrome). Platelet count was done using a three-dimensional, haematology auto analyzer SYSMEX XP-100i, which was analyzed by running haematology cell controls. A peripheral blood smear was prepared by staining it with Leishman stain, and at least ten fields were counted for platelet estimation under an oil immersion lens. The improved Neubauer chamber was charged by making a 1:20 dilution of the whole blood sample (1% ammonium oxalate used as diluting fluid, which causes RBC lysis). Platelets were counted in the large central square, of which one central and four corner

squares were taken and calculated using the following formula.

Approximately 2 ml of venous blood was transferred to a plain tube (containing trisodium citrate) for biochemical tests and a coagulation profile (done in ITP to exclude DIC) using a Cobas C 111 semi-automated analyzer. The serum was separated by centrifugation at 5000 rpm for 5 min for biochemical analysis.

Data was analyzed using the Statistical Package for Social Sciences (SPSS) 22.00. Quantitative data was represented as mean ± standard. Qualitative data was represented as frequency and percentage. Chi-square test was used for inferential statistics , the *p*-value of ≤ 0.05 was considered statistically significant.

RESULTS

A total of 90 patients were included in the study. There were 86(95.5%) patients of GT and 4(4.5%) patients of ITP. Peripheral blood film was completely normal in 87 patients, and giant platelets were seen in the peripheral blood film of only three patients (ITP). All patients of gestational thrombocytopenia presented in the third trimester of pregnancy, while three patients of ITP presented in the first trimester and one patient of ITP presented in the second trimester of pregnancy. The mean platelet count in GT was 102.70±22.56, while the mean platelet count in ITP was 49 x10^9/l. This data is presented in Table -I.

Table-I: Difference of Age, Platelet Count and Manual Platelet Count between Gestational Thrombocytopenia and Immune Thrombocytopenic Purpura Patients (n=90)

Parameters	Gestational Thrombocytopenia (mean±SD)	Immune Thrombocytopenic Purpura (mean±SD)
Age (years)	30.00±3.89	26.00±2.94
Platelet Count (10^9/L)	99.50±23.90	36.00±31.70
Manual Platelet Count (10^9/L)	99.20±22.04	47.20±24.90

Among 86 patients of GT, 59(68.6%) patients had mild thrombocytopenia, while 27(31.4%) patients had moderate thrombocytopenia. No patient had severe thrombocytopenia in GT. A significant amount of data was obtained, showing a substantial association of GT with thrombocytopenia. About four patients had ITP. Of 4 patients, 1(25.0%) had moderate throm-bocyto-penia, while 3 (75.0%) had severe thrombocytopenia. None had mild thrombocytopenia in this group. There was a significant association of ITP with thrombocytopenia (*p*-value = 0.01), as shown in Figure-1.

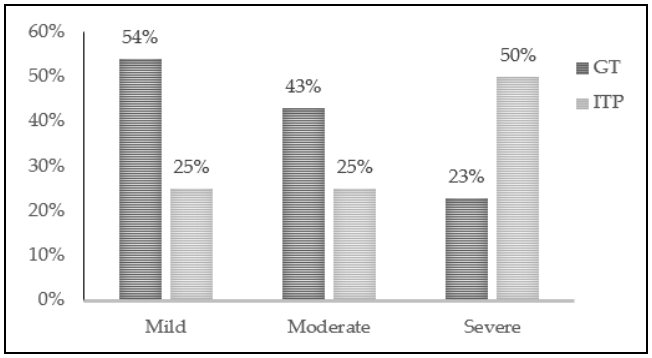

Figure-1: Severity of thrombocytopenia in GT & ITP
GT; Gestational thrombocytopenia, ITP; Immune thrombocytopenic purpura

Among the 90 patients, 58(64.4%) were hospitalized. In GT, 54(62.7%) patients were hospitalized, and 32 (37.5%) were treated as outdoor patients. In ITP, all 4(100%) patients were hospitalized, as shown in Table-II.

DISCUSSION

Thrombocytopenia in pregnancy is an incidental finding, but it might also provide a useful indicator of co-existing gestational disorder, which may cause harm to the mother or fetus. Prompt diagnosis and accurate management of GT and ITP are highly recommended to save the mother and child and

Table-II: Difference of Parity, Initial diagnosis of Thrombocytopenia and Hospitalized Patients between and Immune Thrombocytopenic Purpura (n=90)

Maternal particulars		GT (n=86) Present	GT (n=4) Absent	p-value	ITP(n=4) Present	ITP (n=86) Absent	p-value
Parity	Primiparous	15(17.4%)	3(75.0%)	0.005*	3(75.0%)	15(17.4%)	0.005*
	Multiparous	71(82.6%)	1(25.0%)	0.005*	1(25.0%)	71(82.6%)	0.005*
Initial Diagnosis of Thrombocytopenia	1st trimester	0	3(75.0%)	0.001*	3(75.0%)	0	0.001*
	2nd trimester	0	1(25.0%)	0.001*	1(25.0%)	0	0.001*
	3rd trimester	86 (100.0%)	0	0.001*	0	86 (100.0%)	0.001*
Hospitalized Patients		53 (61.6%)	4 (100.0%)	0.12	4 (100.0%)	21 (24.4%)	0.12

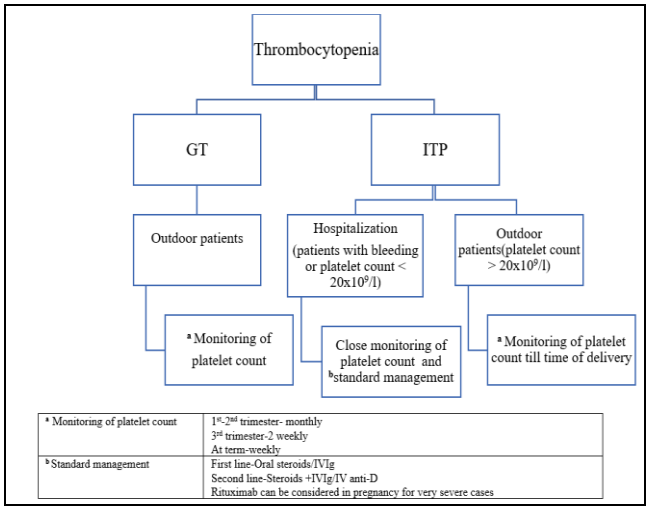

Figure-2: Management of thrombocytopenia in Gestational Thrombocytopenia and Immune Thrombocytopenic Purpura

reduce the patient burden on hospitals. Thrombocytopenia in GT is usually mild and can be managed by simple platelet count monitoring in the outpatient department.11 On the other hand, thrombocytopenia in ITP is mostly severe and requires early and prompt management, as shown in Figure-2.

In this study, GT is the most common cause of thrombocytopenia in pregnancy, with a prevalence of 95.5%. The results were similar to studies conducted in Sudan and India, which also stated that GT is the most frequent disorder encountered during pregnancy. [12,13] Mean platelet count in patients of GT was 102.7x 109/l. This was slightly lower than the mean platelet count in the mothers with GT (134 x10 9 /l), as documented by a study in the USA.[14] The lowest platelet count in GT was 70 x 109/l. Related results were reported by research approved in the USA. 15 This study reported that all patients of GT presented in the third trimester of pregnancy. Comparable findings were reported by a study in Japan.4 Out of these 86 patients of GT, 59 (68.6%) patients had mild thrombocytopenia, while 27 (31.4%) patients had moderate thrombocytopenia. This was comparable with the results of McIntosh et al., and Zutshi *et al*. also reported that most cases of GT were of mild thrombocytopenia. [16,17]

ITP is a relatively rare disorder, with only 4 (4.5%) patients presenting in pregnancy with low platelet count. The mean platelet count in ITP in the current study was 49 x 109/l. A much lower mean platelet count of 10x109/l was stated in a previous study. 18 This could be because patients with much lower platelet counts with bleeding manifestations or who are refractory to platelet transfusion were included in the study. [19] In this study, among four patients of ITP, one patient (25%) had moderate thrombocytopenia. In comparison, three patients (75%) had severe thrombocytopenia. None had mild thrombocytopenia in this group. This was consistent with the results of Kim *et al*.who reported that the most frequent cause of moderate to severe thrombocytopenia in pregnancy was ITP. [20]

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CONCLUSION

Diagnosing and discriminating between GT and ITP appropriately is imperative as their management is completely different. GT is a benign disorder mostly presenting with mild thrombocytopenia, and it can be managed outdoors with mere watchful platelet count and by educating primary /secondary health centres.

Conflict of Interest: None.

Authors Contribution

Following authors have made substantial contributions to the manuscript as under:

1,2: Conception, study design, drafting the manuscript, approval of the final version to be published.

3,4: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

5,6: Data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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