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Original Research Article

Etiological review and outcome of thrombocytopenia in pregnancy in the tertiary care centre

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ABSTRACT

Background: Objective of the study was to identify and analyse the etiology of thrombocytopenia in pregnancy and review the evaluation of thrombocytopenia and its outcome in pregnancy.

Methods: Retrospective study conducted at D. Y. Patil Hospital, Kolhapur, Maharashtra, India, from January 2021 to January 2023, in the Department of Obstetrics and Gynecology. All the antenatal women admitted in the ward of obstetrics and gynecology with platelet count less than 1 lakh/cubic cc were included in the study. Thorough evaluation for the cause of thrombocytopenia and outcome of the patient were collected and results were analyzed.

Results: Out of 3319 deliveries, 100 patients had platelet counts less than 1 lakh. Overall, in the present study, Gestational thrombocytopenia (38%) is the most common cause of low platelets in pregnancy, followed by pre-eclampsia (20%) and DIC (16%). The rest of the etiologies rarely cause thrombocytopenia in pregnancy (<10%).

Conclusions: Despite thrombocytopenia is a common abnormality in pregnancy, it seldom leads to life-threatening complications by itself. By contrast, a significant thrombocytopenia associated with medical conditions can have serious maternal-fetal consequences and requires appropriate management. The management of thrombocytopenia focuses on the underlying cause/etiology which is challenging because there are many potential causes, some directly related to the pregnancy and some unrelated. Cause directed therapies, if promptly administered, may significantly improve the maternal and fetal outcomes. Study intended to evaluate the wide spectrum of causes for thrombocytopenia in pregnancy and its outcome. Preeclampsia with or without HELLP syndrome is found to be very important cause of severe thrombocytopenia and attributed with maternal complications. while the perinatal outcome of gestational thrombocytopenia and immune thrombocytopenic purpura is basically favourable.

Keywords: Thrombocytopenia in pregnancy, Etiology of thrombocytopenia in pregnancy, Maternal mortality associated with thrombocytopenia, Outcome of thrombocytopenia in pregnancy

INTRODUCTION

Thrombocytopenia, defined as blood platelet count below 150,000/ μ l is the second leading cause of blood disorders in pregnancy after anemia. It complicates 7 to 10% of all pregnancies.¹ There is a physiological decrease in platelet count during normal pregnancy due to haemodilution, increased consumption in peripheral tissue and increased aggregation (higher levels of thromboxane A₂). The

physiological thrombocytopenia of pregnancy is mild and has no adverse effects for the mother and fetus. By contrast, a significant thrombocytopenia associated with medical conditions can have serious maternal-fetal consequences and requires specific monitoring and appropriate management. The International working group (IWG) adopted a lower threshold of platelets, $100 \times 10^9/l$, to define immune thrombocytopenia, which is observed in less than 1% of all pregnancies.²⁻⁴ Thrombocytopenia in

pregnancy occurs either due to obstetric conditions (like gestational thrombocytopenia, preeclampsia/eclampsia) or secondary to systemic disorders (like thrombocytopenic thrombotic purpura, immune thrombocytopenia).^{5,6} Even though thrombocytopenia is a common abnormality in pregnancy, it seldom leads to life-threatening complications by itself. The management of thrombocytopenia focuses on the underlying cause/etiology.

METHODS

This is a retrospective study conducted at D. Y. Patil Medical College, Hospital and Research Centre from January 2021 to January 2023.

Inclusion criteria

All the antenatal women admitted in the ward of obstetrics and gynecology with platelet count less than 1 lakh/cubic cc were included in the study.

Exclusion criteria

All the antenatal women admitted in the ward of obstetrics and gynecology with platelet count more than 1 lakh/cubic cc.

We present a retrospective analysis of series of antenatal patients with thrombocytopenia in a single teaching institution, with an objective of evaluation of the etiology and outcome of patients. This study helps to stimulate more research in our population and to develop institutional guidelines. Data was extracted from patients' medical records, hospital computerized databases. The sample was calculated on the basis of the Cochrane formula (4 pq/lit sq) on the basis that thrombocytopenia in pregnancy affects 7–11% of pregnancies.¹ Patients were selected by the convenient sampling method. Verification done that each woman was represented only once in the dataset. Data was entered in a systematic manner in Microsoft Office excel 2016 and results were analyzed with software Microsoft Office excel 2016. Among obstetric causes of thrombocytopenia, gestational thrombocytopenia is the leading cause. Among non-obstetric causes immune thrombocytopenic purpura and dengue were the leading causes.

Total number of deliveries in the study period were 3319.

Number of patients included in the study were 100.

RESULTS

Incidence of thrombocytopenia in pregnancy irrespective of the cause is found to be 3%. Out of 3319 deliveries, 100 patients had platelets count less than 1 lakh cubic mm. While 44 patients delivered vaginally, 56 patients required caesarean section delivery (Table 1).

Table 1: Mode of delivery in patients with thrombocytopenia in pregnancy.

Mode of delivery	Number of patients
LSCS	56
Vaginal delivery	44

With thorough and integrated evaluation for the cause of thrombocytopenia, 80 patients were related with one of the various obstetric causes of thrombocytopenia and 20 patients related with one of the various non-obstetric causes of thrombocytopenia (Figure 1).

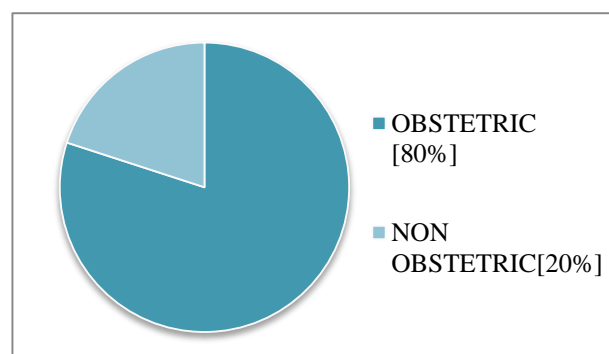


Figure 1: Etiology of thrombocytopenia in pregnancy.

Under obstetric causes, gestational thrombocytopenia (38%) accounts to be the major cause overall followed by pre-eclampsia (20%), DIC (12%), eclampsia (8%), and AFLP (2%) (Table 2).

Table 2: Distribution of patients with thrombocytopenia for obstetric causes

Obstetric causes	Number of patients	Percentage
Gestational thrombocytopenia	38	38
Pre-eclampsia (HELLP-5)	20	20
Eclampsia	8	8
DIC (atonic PPH/ abruptio placenta)	12	12
Acute fatty liver of pregnancy	2	2

Under non obstetric causes, immune thrombocytopenic purpura (8%), dengue (8%), DIC (4%) shared the etiology of thrombocytopenia (Table 3).

Outcome of the patients with Thrombocytopenia of various causes concluded with discharge (96%), maternal mortality (2%), and DAMA (2%) (Table 4).

Causes of maternal mortality summed up to be disseminated intravascular coagulation due to severe anemia and eclampsia.

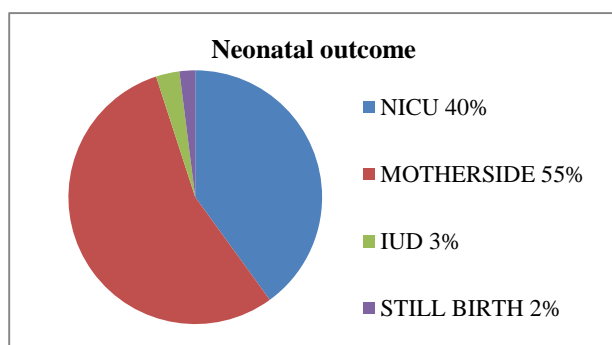
Table 3: Distribution of patients with thrombocytopenia for non-obstetric causes (20 out of 100 patients).

Non-obstetric causes	Number of patients	Percentage
Immune thrombocytopenia	8	8
Dengue	8	8
DIC (severe anemia)	4	4

Table 4: Outcome of the patients with thrombocytopenia.

Outcome of patients	Number of patients
Discharge	96
Death	02
DAMA	02

Neonatal outcome revealed 40% required NICU management, 55% managed in general ward (motherside), 3% were IUD by the time of admission, 2% were still births (Figure 2).

**Figure 2: Neonatal outcome with maternal thrombocytopenia in pregnancy.**

DISCUSSION

Thrombocytopenia is the second most common hematologic abnormality in pregnancy after anaemia.² There is a physiological decrease in platelet count during pregnancy due to haemodilution, increased consumption in peripheral tissue and increased aggregation (raised levels of thromboxane A2). The physiological thrombocytopenia of pregnancy is mild and has no adverse effects for the mother and foetus. By contrast, a significant thrombocytopenia associated with medical conditions can have serious maternal-fetal consequences and requires specific monitoring and appropriate management.

In the authors' study 56.0% of patients underwent LSCS, 44.0% delivered vaginally. Gašparović et al and Ying-Hsuan et al, found that thrombocytopenic women had a significantly higher rate of cesarean delivery as compared to their healthy peers, as, the neonates with severe thrombocytopenia may experience bleeding

complications, especially intracranial hemorrhage, particularly as a consequence of head trauma during vaginal delivery.^{16,17} From a practical standpoint, the current guidelines consider that vaginal delivery is safe when platelet count is higher than 30.000/mcl. For operative vaginal or caesarean deliveries, the safe platelet count should be at least 50.000 platelets/mcl. The exact platelet number needed to achieve a safe epidural anaesthesia is debated, but in most guidelines, the reference value is around 75.000-80.000/mcl.⁷ There is a theoretical concern over the risk of epidural hematoma with lower platelet values. Spontaneous bleeding may occur with less than 20.000 platelets/mcl and the risk of internal bleeding is increased if the platelet count falls below 10.000/mcl.² Thrombocytopenia in pregnancy happens secondary to many aetiologies, differing in their pathophysiology and presentation. A summary of possible aetiologies is listed here.

Gestational thrombocytopenia

A study conducted by Parnas et al found that the main causes of TCP were gestational TCP (59.30%) while the results in the authors' study revealed to be 38%.¹³ It is diagnosed based on the following criteria.^{6,10} Onset in mid-second to the third trimester, no symptoms in the mother and no history of bleeding, no effect on the outcome of the pregnancy, no thrombocytopenia in the neonate, self-limited course and resolution in 4 to 8 weeks. A tendency to recur with the same degree in subsequent pregnancies. Gestational thrombocytopenia is a diagnosis of exclusion which is based on a thorough history and physical exam and ruling out of conflicting diagnosis with lab support.^{6,10} Rarely, the platelet count drops below $70 \times 10^9/l$, then the patient should be evaluated for a secondary cause like ITP.^{5,6}

Immune thrombocytopenia

Parnas et al found that the cause of TCP due to immune thrombocytopenic purpura is 11.05% while in the study of Sainio et al, the incidence ITP was 3% and in a study conducted by Wang et al, the incidence of ITP made up 11.8% while the results in the authors' study revealed to be 8%.¹³⁻¹⁵

Thrombotic microangiopathy

It divides into pregnancy-specific Thrombotic microangiopathy (TMA) and non-pregnancy specific TMA due to differences in management.

Table 5: Various causes of TMA.

Pregnancy specific TMA	TMA not specific to pregnancy
Pre-eclampsia (PEC), HELLP syndrome, acute fatty liver of pregnancy (AFLP)	Thrombotic thrombocytopenic purpura (TTP), typical haemolytic-uremic syndrome (HUS)

Pre-eclampsia

Patients present with severe hypertension after 20 weeks of gestation (defined as systolic pressure more than 160mmHg and diastolic pressure more than 110 mmHg on two separate occasions, at least 4 hours apart) or with severe persistent right upper quadrant epigastric pain which is unresponsive to medications. Eclampsia can present as a sequela to pre-eclampsia with seizures. In a study conducted by Wang et al, the incidence of hypertensive disorders was 28.2%, while the results in the authors' study revealed to be 28% which is comparable.¹⁴

HELLP syndrome

It correlates with generalized edema in more than 50% of patients who demonstrate hepatic and renal insufficiency in labs.^{5,6} A study conducted by Parnas et al, found that the causes of TCP due to HELLP syndrome observed in 12.06%, while the results of the authors' study revealed to be 5%.¹³

AFLP

Clinically, it is quite challenging to distinguish between AFLP and HELLP syndrome. However, encephalopathy, hypoglycemia, severe coagulopathy, along with TMA like hemolysis, are more frequently present in patients with AFLP.^{5,6}

Other etiologies are: disseminated intravascular coagulation (DIC); and hereditary thrombocytopenia (HT) - further classify according to the size of the platelet, genetic defect and inheritance pattern (WAS gene, HOXA 11 gene, and MYH9 disorders).⁸

Others

Bone marrow failure syndromes [aplastic anemia myelodysplastic syndrome (MDS), myeloproliferative neoplasms (MPN), and leukemia/lymphoma marrow infiltrative disorders].^{5,9}

Paroxysmal nocturnal hemoglobinuria (PNH) - patients usually present with hemolytic anemia, pancytopenia, and thrombosis; however, the characteristic finding of hemoglobinuria is almost never seen.¹¹ Although thrombosis is a rare presenting feature, it usually occurs in atypical sites, like the portal vein or the cerebral vein.¹¹

Drug-induced thrombocytopenia, type IIB von Willebrand disease (VWD), heparin-induced thrombocytopenia (HIT) - a history of recent exposure to heparin is quintessential to the diagnosis of HIT. The thrombocytopenia usually develops within 5 to 10 days of exposure to heparin but can occur sooner if the previous exposure was relatively recent. The presence of skin necrosis and/or venous thromboembolism should prompt a workup towards HIT. The clinical 4-T score also aids in the diagnosis of HIT.¹²

It is also worthwhile to distribute the etiology of thrombocytopenia according to the trimester and the platelet count.⁴

First trimester

Immune thrombocytopenia (ITP) (most common), hereditary thrombocytopenia (HT), others (above detailed list), and thrombotic microangiopathy (TMA).

Second trimester

It is described in Table 6.

Table 6: Platelet count based etiology.

Platelet count greater than 100×10/L	Platelet count under 100×10/L
Gestational thrombocytopenia, ITP, pre-eclampsia/ HELLP, HT/others/TMA	ITP (most common), HT, pre-eclampsia/HELLP, others, gestational thrombocytopenia, TMA

Third trimester

It is described in Table 7.

Table 7: Platelet count based etiology.

Platelet count more than 100×10/L	Platelet count less than 50×10/L
Gestational thrombocytopenia (most common), pre-eclampsia/HELLP (second most common), others/TMA/ITP/HT	Pre-eclampsia/ HELLP (most common), ITP, others, TMA, gestational thrombocytopenia/HT

In any patient with thrombocytopenia, a thorough history and physical exam help in establishing the etiology behind the low platelet count.³

Incidence of maternal mortality due to various causes in the authors study is 2%. Cause end up to be disseminated intravascular coagulation due to severe anemia and eclampsia.

In authors study neonatal outcome revealed 40% required NICU management, 55% managed in general ward [motherside], 3% were IUD by the time of admission, 2% were still births, this is in contrast to the studies by Gašparović et al, Chauhan et al, and Dwivedi et al, where no such complications were seen.^{16,18,19}

Limitations

The most important limitation to our study is missing data of the efficacy of the treatment and its effect on long term

outcome due to loss of follow up of the patients. Prevalence of the problem could not be addressed as the study was conducted in the tertiary care centre where the relative high risk patients of the region exists. Despite of it, this study offers a glimpse of practical approach and outcome of thrombocytopenia in pregnancy.

CONCLUSION

Despite thrombocytopenia is a common abnormality in pregnancy, it seldom leads to life-threatening complications by itself. By contrast, a significant thrombocytopenia associated with medical conditions can have serious maternal-fetal consequences and requires appropriate management. The management of thrombocytopenia is challenging because there are many potential causes, some directly related to the pregnancy and some unrelated. Thus, the working knowledge of the management of pregnant women with thrombocytopenia due to different etiological factors is important for effective management. Cause directed therapies, if promptly administered, may significantly improve the maternal and fetal outcomes. Study intended to evaluate the wide spectrum of the causes for thrombocytopenia in pregnancy and its outcome. Preeclampsia with or without HELLP syndrome is found to be very important cause of severe thrombocytopenia and attributed with maternal complications. While the perinatal outcome of gestational thrombocytopenia and immune thrombocytopenic purpura is basically favorable. Special attention should be given to patients with thrombocytopenia due to preeclampsia, HELLP syndrome, and rarer causes during pregnancy.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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