Thrombocytopenia in Pregnancy and Associated Maternal and Fetal Outcomes in A Tertiary Care Centre

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Abstract

Background and Objectives: Thrombocytopenia is the second most common hematological abnormality in pregnancy. This research study was undertaken to evaluate the etiology of thrombocytopenia in third trimester of pregnancy & to analyze maternal and fetal outcomes of thrombocytopenia.

Methodology: In this observational study 210 females who presented to department of Obstetrics and Gynaecology, Gandhi medical college, Bhopal with thrombocytopenia in their third trimester of pregnancy were enrolled. In all patients history was taken, routine lab tests (Complete blood count, Platelet Count, Liver function test, Renal function test, Coagulation Profile) were done. General and Obsteric examination were done, obstetrical intervention was done when needed.

Results: This observational study had 210 participants. Most common cause of thrombocytopenia was found to be gestational thrombocytopenia (69%) followed by pre-eclampsia (14.2%) and dengue (8.1%). Most commonly affected females were multigravida in 20-25 age group. The most common clinical feature seen among the study participants was edema. When comparing the severity of thrombocytopenia, 64.8% of participants had mild thrombocytopenia, 27.6% had moderate thrombocytopenia and 7.6% had severe thrombocytopenia. Out of 201 newborns, 41 of them needed NICU monitoring with Low birth weight and Respiratory Distress syndrome being notable contributors. Maternal mortality was seen in 8 out of 210 cases, most common cause of mortality was HELLP [Hemolysis, Elevated liver enzymes and Low platelets].

Conclusions: The study found that with increasing severity of thrombocytopenia, the percentage of maternal ICU admissions and maternal death increases. Severity of thrombocytopenia is associated with increasing rates of

IUFD (Intrauterine Fetal Death), preterm deliveries and NICU admission. Although the incidence of low birth weight and neonatal death increases as the severity of thrombocytopenia in mother increases but association between them is not statistically significant. Thrombocytopenia during pregnancy is an underexplored condition in Indian women and there is an imperative need of more extensive studies in the field.

Keywords: Thrombocytopenia, HELLP Syndrome, Gestational thrombocytopenia, Severe Pre eclempsia

Introduction

Thrombocytopenia is the 2nd most common hematological abnormality encountered during pregnancy after anemia affecting 7-11% of all pregnancies worldwide [1]. Thrombocytopenia is defined as platelet count less than 150 x 10^3/µL. It can be categorized into mild (100 x 10^3/µL to 149 x 10^3/µL), moderate (50 x 10^3/µL - 99 x 10^3/µL) and severe (<50x 10^3/µL) [2]. Most of the decrease in platelet count occurs during the 3rd trimester. The cause for decreased platelet count is multifactorial and is related to increased platelet consumption, hemodilution and increase in platelet aggregation mediated by increased level of thromboxane A2 (TXA2) [1]. But pregnant woman with thrombocytopenia have lower bleeding complications when compared to non-pregnant women because of procoagulant state induced by increased levels of factor VIII, fibrinogen, VWF suppressed fibrinolysis as well as reduced protein S activity.

Thrombocytopenia in pregnancy can result from conditions such as Gestational Thrombocytopenia (GT),hypertensive disorders of pregnancy [pre-eclampsia, eclampsia and its complications such as HELLP Syndrome], Amniotic Fluid Embolism, Disseminated Intravascular Coagulopathy (DIC), medical causes like Hemolytic Uremic Syndrome (HUS), Thrombotic Thrombocytopenic Purpura (TTP), autoimmune disorders such as Systemic Lupus Erythematosus (SLE), Idiopathic Thrombocytopenic Purpura (ITP) and Antiphospholipid Syndrome, Infections, Sepsis, Hypersplenism and Primary bone marrow dysfunction. Other reasons could be spurious/pseudo-thrombocytopenia or drug induced thrombocytopenia.[3] Gestational or incidental thrombocytopenia accounts for 75% of pregnancy-associated thrombocytopenia and considered as the most common cause of thrombocytopenia during pregnancy. [4] .Platelet counts normalize within 2-12 weeks after delivery.[1].

Thrombocytopenia carries a risk for both the mother as well as developing fetus and is associated with substantial maternal or neonatal morbidity and mortality. Diagnosis and management of individual cases of thrombocytopenia in pregnant women focuses on excluding important underlying causes as well as weighing the risks of bleeding in both mother and baby against hazards of diagnostic and therapeutic interventions. In advent of same, the present study was conducted to determine the etiological factors of maternal thrombocytopenia in pregnancy and to evaluate feto-maternal outcome in relation to severity and different causes of thrombocytopenia.

Materials and Methods

After approval from the institutional ethical committee, the present observational study entitled "Thrombocytopenia in Pregnancy" was undertaken for a period of 18 months at department of obstetrics and gynecology, Gandhi Medical College, Bhopal, Madhya Pradesh. Patients who qualified the inclusion criteria were enrolled for the study after taking written informed consent.

Inclusion Criteria

1. All pregnant women admitted in the hospital with thrombocytopenia in 3rd trimester of pregnancy.

2. Patients who consented to participate in the study.

Exclusion Criteria

1. All pregnant women in first and second trimester of pregnancy.

2. All pregnant women with Chronic liver diseases.

3. All pregnant women with drug induced thrombocytopenia.

4. Patients not willing to give written & informed consent.

Methodology

This study included 210 pregnant women with thrombocytopenia in 3rd trimester of pregnancy after taking a written and informed consent.

Thrombocytopenia was classified based on the severity:

(i) Mild: Platelet count $(100 - 150 \times 10^3 \text{ cells}/\mu L)$

(ii) Moderate: Platelet count $(50 - 100 \times 10^3 \text{ cells}/\mu L)$

(iii) Severe: Platelet count $(<50 \times 10^3 \text{ cells}/\mu L)$

A predesigned structured proforma was used for collecting the information about patient's demography, socio-economic status, menstrual history as well as complete obstetrical history including previous antenatal record if available. Presenting complaints if any, general examination findings, systemic and obstetric examination findings and routine lab tests (CBC, Platelet Count, LFT, RFT, Coagulation Profile) of all the patients were recorded in an approved proforma.

Platelet count estimation was done through automated hemato-analyzer with routine antenatal hematological evaluation of the patient. Gestational age was derived from menstrual history and clinical examination which was confirmed by USG. A diagnosis was inferred from the above investigations.

Patients with complications such as pre-eclempsia and eclempsia or those with DIC were managed with supportive care in the intensive care unit in collaboration with the Department of Medicine and Hematology. All the patients were observed to record any complications like preterm labor, abruption, postpartum hemorrhage or any other morbidities. Gestational age at the time of delivery, indication for induction and method (if required) and mode of delivery including indication for instrumental delivery or lower section caesarean section were recorded. Progress of labor was monitored with partograph.

All neonates were looked up for birth weight, NICU admission, its causes and neonatal death.

Statistical Analysis

The data was coded and entered into Microsoft excel 2010 (Microsoft corp.), analyzed using excel 2010 and SPSS 20.0 for Windows (SPSS inc). Prevalence of an outcome variable along with 95% confidence limits was calculated.

Descriptive statistics was used and percentages were calculated for qualitative variables like cause of thrombocytopenia complications, maternal and fetal outcome. Appropriate statistical analysis was done to assess the result by using parametric and non-parametric test of significance i.e. Chi square, T-Test, Z-Test, U Test for deciding level of significance. A p value less than 0.05 was considered statistically significant.

Results

Majority of the study participants were in the age group of 20-25 year followed by 25-30-year age group. A higher percentage of participants with thrombocytopenia were multigravidas making up 60.5% of the cases. The most common clinical feature seen among the study participants was edema which was followed by abdominal pain. Other clinical features include

hematuria, headache, blurring of vision, petechiae and joint swelling.

Gestational thrombocytopenia being the diagnosis of exclusion accounts for 69% of all cases. Severe preeclampsia and eclampsia contribute to 14.2% and 4.3% of the cases, respectively. Dengue accounts for 8.1%, while HELLP syndrome accounts for 1.9% cases. Pancytopenia, hypersplenism, SLE and PLHA [People living with HIV/AIDS] with MDR TB [Multidrug-resistant tuberculosis] are rare causes, each contributing less than 1% to the total cases.

When comparing the platelet count, it was observed that 64.8%, 27.6% and 7.6% of patients had mild, moderate and severe thrombocytopenia respectively. Of total, 69.0% patients underwent normal vaginal while 31.0% underwent cesarean section.

Among all, 21 mothers were admitted to the ICU with Maternal death in 8 cases. Out of all the maternal mortalities, 4 deaths (50%) were due to HELLP Syndrome,2 deaths (5%) were due to Eclampsia, 1 death was due to Pre Eclempsia with severe features and its complications and 1 death was in patient with PLHA with MDR TB. Intensive care monitoring was required in 3.70% cases of mild thrombocytopenia, 15.50% cases of moderate thrombocytopenia and 43.80% cases of severe thrombocytopenia. In patients with mild thrombocytopenia there were no maternal deaths, in

moderate thrombocytopenia there were 5 maternal deaths, out of 16 cases of severe thrombocytopenia there were 3 maternal deaths (18.80%).This suggests that with increasing severity of thrombocytopenia, the percentage of maternal ICU admissions and maternal death also increases (p value : 0).

In the present study, majority of the patients i.e. 155 patients (73.8%) patients had term delivery while rest of the patients 26.2% underwent preterm delivery. Of all the newborns born to mothers with thrombocytopenia, 112 (53.3%) had birth weight > 2500gms and 98 (46.7%) newborns had birth weight < 2500gms.Out of 201 newborns, 41 of them needed NICU monitoring. Among all the indications, low birth weight and respiratory distress syndrome were the notable contributors followed by Hyperbilirubinemia, Sepsis, Congenital Anomalies, Symptomatic Hypoglycemia and Congenital Heart Disease.

The analysis from our study indicates that there is a statistically significant association between preterm delivery, IUFD and rate of NICU admission and increasing severity of thrombocytopenia [p values = 0.033, 0.000 & 0.000 respectively].Although the incidence of low birth weight and neonatal death increases as the severity of thrombocytopenia in mother increases but association between them is not statistically significant.

Table 1: Distribution of Patients Based On Age Group

Age distribution	Frequency	Percentage
<20 years	23	11.0%
20-25 years	87	41.4%
25-30 years	67	31.9%
30-35 years	26	12.4%
35-40 years	7	3.3%
Total	210	100.0%

Table 2: Distribution of Patients Based On Signs and Symptoms

Signs And Symptoms	Frequency	Percentage
Edema	61	29.04
Asymptomatic	55	26.25
Abdominal Pain	23	11
Hematuria	22	10.50
Fever	20	9.5
Headache	14	6.6
Blurring Of Vision	7	3.3
Petechiae	6	2.86
Joint Swelling	2	0.95
Total	210	100

Table 3: Distribution of Patients Based On Etiology of Thrombocytopenia

Etiology	Frequency	Percentage
Gestational Thrombocytopenia	145	69
Severe Pre Eclempsia	30	14.2
Dengue	17	8.1
Eclempsia	9	4.3
Hellp	4	1.9
Pancytopenia	2	1
Hypersplenism	1	0.5
SLE	1	0.5
PLHA With MDR Tb	1	0.5
Total	210	100

Table 4 : Severity Of Thrombocytopenia

Severity	Frequency	Percentage
Mild	136	64.8
Moderate	58	27.6
Severe	16	7.6
Total	210	100

Table 5: Causes of Maternal Death

Causes Of Maternal Death	Number	Frequency
Hellp	4	50
Eclempsia	2	25
Pre Eclempsia	1	12.5
PLHA With MDR Tb	1	12.5
Total	4	100

Table 6: Causes of Nicu Admission

Indications Of Nicu Admission	Frequency	Percentage
Low Birth Weight	14	34.3
Respriratory Distress Syndrome	10	24.4
Neonatal Hyperbilirubinemia	08	19.5
Neonatal Sepsis	04	9.7
Congenital Anomalities	02	4.8
Symptomatic Hypoglycemia	02	4.8
Congenital Heart Disease	01	2.5
Total	41	100

Discussion

Thrombocytopenia is second most diagnosed hematological disorder of pregnancy. Despite being encountered in 10% of pregnant women, it is often missed and commonly mismanaged especially in third world countries. Thrombocytopenia usually occurs in the latter half of pregnancy i.e., from mid-second or third trimester (65%), which could also be a socioeconomic influence, as most pregnant women in our population seek medical advice in late pregnancy or only when they develop complications.[5]

In the present study, we observed that majority of the study participants were in the age group of 20-25 years (41.4%) followed by 25-30 years of age (31.9%). Singh et al (2023) [6] from India studied 155 thrombocytopenic pregnant women (At > 37 weeks of gestation) and supported our finding by reporting that maximum number of subjects (65.8%) were in the age group of < 25 years. However, another Indian study, Nair et al. (2023)[7] , who studied 164 patients in the third trimester with thrombocytopenia, reported maximum patients in the age group of 26-30 years of age (37.2%).Hanif et al. (2023)[8], a study from Pakistan, noted majority of patients in the age group of 18-30 years (73.3%). This could be because of the higher pregnancy rate in younger age group, especially ≤ 30 years thus giving higher prevalence of thrombocytopenia in pregnancy in these age groups. We observed that maximum patients (60.5%) were multi gravida while rest were primigravida. However, Singh et al. (2023)[6] and Nair et al. (2023)[7] reported that majority of their patients were primigravida i.e. 43.2% and 45.7%, respectively. Most common

clinical presentation was edema (39.3%) followed by abdominal pain (14.8%). Abro et al. (2023)[5] however found most of the patients were asymptomatic (74.1%) followed by vaginal bleeding (11.4%), in their study of 35 thrombocytopenic pregnant women of all the gestational age. In our study, Gestational thrombocytopenia was found in 69% of patients. Similarly, various studies done previously showed gestational thrombocytopenia as the most common etiological cause i.e. 56.8% [6], 75.6% [7] and 73.75% [9]. Hanif et al. (2023)[8] also differed to our finding by reporting gestational thrombocytopenia as the most common etiological cause. We found that majority of the subjects had mild thrombocytopenic (64.8%) followed by moderate (27.6%) and severe (7.6%) thrombocytopenia. Nair et al. (2023)[7] supported us by documenting majority of their patients to be mildly thrombocytopenic (72.6%) followed by moderate (23.8%) and severe (3.7%) thrombocytopenia. However, Singh et al. (2023)[6] in contrast to our findings, reported majority of the patients with moderate thrombocytopenia (48.4%) followed by mild (45.2%) and severe (6.4%).

The most common mode of delivery was Vaginal Delivery (VD) (69%) while 31% were undergone Lower Segment Cesarean Section (LSCS). Singh et al. (2023) [6] also observed Vaginal Delivery (51.6%) as the most common mode of delivery. However, Sumathi et al. (2023)[9] reported LSCS in maximum patients (61.25%) followed by NVD (37.5%) and instrumental delivery (1.25%), which differs with our finding. In the present study 26.2% of the patients were noted to have preterm delivery. Similarly, Sumathi et al., (2023)[9] also observed preterm delivery in 21.84% and late preterm delivery in 4.6% of the total patients. Low birth weight (LBW) was noted in 46.7% of the newborns. Singh et al. (2023)[6] also observed LBW in majority (76.1%) of the newborns. In

contrast, Sumathi et al., (2023)[9] documented LBW only in 13.8% of the newborns. Only 19.5% of the newborns required NICU admission. Singh et al. (2023)[6] reported 31% neonates required NICU admission. Low birth weight was the most common cause for NICU admission in our study as supported by other previous studies.[6,9]

In the study being discussed 10% of the total subjects required ICU admission while the proportion was 25.7% of total subjects in the study done by Abro et al. (2023) [5]. We observed maternal mortality in 3.8% of the subjects. Kuna et al. (2023) [10] studied 384 pregnant women of all gestational age and documented that 10.9% of the subjects required ICU admission while maternal mortality in 4.97% of the subjects. However, Sumathi et al. (2023)[9] reported no maternal deaths. It was observed that higher severity of thrombocytopenia was significantly associated with the higher rate of maternal ICU admission (p value < 0.05).Abro et al. (2023)[5] also supported our finding by stating that severity of thrombocytopenia was significantly linked to the adverse feto-maternal outcome, requiring ICU admission for monitoring of the patients (p value = 0.001). Harde et al. (2019)[11] studied 150 pregnant patients admitted to labour ward with thrombocytopenia and stated that moderate to severe thrombocytopenia was observed mainly in Pre-eclampsia,

Thrombocytopenia due to HELLP syndrome was associated with maximum number of ICU admissions. We observed that higher degree of thrombocytopenia was significantly associated with the higher rate of maternal mortality (p value < 0.05). Abro et al. (2023)[5] showed similar finding and stated that severity of thrombocytopenia was significantly linked to the maternal deaths (p value = 0.001). Harde et al. (2019) [11]

also documented higher mortality in the pregnant women with moderate and severe thrombocytopenia.

Incidence of low birth weight and neonatal death was found to be higher in pregnant women with lower platelet count without any significant association. However, we observed that NICU admission, preterm delivery and IUFD are significantly linked to the higher severity of thrombocytopenia.

Abro et al. (2023)[5] showed that the severity of thrombocytopenia was considerably linked to IUFD, preterm birth, neonatal sepsis as well as death. Harde et al. (2019)[11] observed that all the complications like NICU admissions, IUFD etc in moderate to severe thrombocytopenia cases. Singh et al. (2023)[6] observed higher incidence of low birth weight in patients with higher severity of thrombocytopenia, without any significant association.

Conclusion

This study highlights that thrombocytopenia in the third trimester of pregnancy, particularly when severe was significantly associated with adverse outcomes like maternal ICU admission, maternal death, neonatal ICU admission, preterm delivery and IUFD. Low birth weight and neonatal death was observed to be considerably linked with higher severity of thrombocytopenia, however, without any significant association. These observations emphasize the importance of vigilant management and comprehensive care for these high-risk pregnancies. Early detection of thrombocytopenia in pregnancy and careful calculation of risks and presumptive management can be done in order to reduce the feto-maternal morbidity as well as mortality of the patients.

Limitations

The lack of assessment of platelet count of newborn in our study is one of its major drawbacks, as a result of which it is difficult to draw a direct association between severity of thrombocytopenia and unfavourable fetal outcomes. Being a single center study conducted on a relatively small sample size, the generalisation of our finding over the population could be in doubt. We included only women in third trimester of pregnancy which limited our view of overall effect of thrombocytopenia and its outcome and also prevented us from studying the outcome of early diagnosis and prevention on mother and fetus. However, the present study is unique of its sort and thus it could serve as a foundation for future studies given the dearth of evidence on the same subject in this region of the country.

Recommendations

Our findings should further be verified in further multicentric large trials including all gestational periods and should be prospectively observed in detail for the impact and outcomes of thrombocytopenia. Also, additional studies including laboratory assessment of thrombocytopenia in neonates and its correlation to perinatal morbidity and mortality will help in better understanding of the pathology and in preventing difficulties related to its management.

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