RESEARCH ARTICLE

Clinical Study of Thrombocytopenia in Pregnancy

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Abstract

Aim: To enumerate the causes of thrombocytopenia in pregnancy according to etiology and to study the maternal and fetal outcomes.

Materials and methods: It is a longitudinal study and included antenatal women from the out-patient department who were admitted to the hospital with thrombocytopenia, from the year September 2016 to August 2017 and data were analyzed by statistical package for social sciences (SPSS), version 15.

Results: A total of 238 cases of thrombocytopenia were studied. Most of the patients are referred to cases with thrombocytopenia detected in the third trimester. Gestational thrombocytopenia was found to be the most common (78.5%) etiology. Hypertensive disorders of pregnancy were found to be more common in obstetric causes. Maternal morbidity was mainly due to medical causes. Neonatal thrombocytopenia is found in 3.3% of cases.

Conclusion: Gestational thrombocytopenia is the most common cause of thrombocytopenia in pregnancy, with most cases detected in the third trimester being either mild or moderate thrombocytopenia. Since maternal morbidity and neonatal thrombocytopenia are common medical causes, the distinction between gestational thrombocytopenia and pregnancies with immune thrombocytopenic (ITP) purpura have severe neonatal thrombocytopenia with the risk of neonatal intracranial hemorrhage.

Clinical significance: Mild or moderate thrombocytopenia cases are mostly detected in the third trimester. Risking in complications such as maternal morbidities or neonatal thrombocytopenia. As pregnancy with procured thrombocytopenia is a critical matter of worry as both the mother and the babies are possibly at risk of bleeding, it should be early detected and treated to diminish the fetomaternal morbidities

Keywords: Hypertension, Idiopathic, Neonatal thrombocytopenia, Pregnancy, Prenatal care, Pregnancy induced, Purpura, Severe preeclampsia, Thrombocytopenia.

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Introduction

Thrombocytopenia is the second most common problem during pregnancy which goes undetected and hence results in inappropriate management.[1,2] It is added to the significant public health concern because thrombocytopenia during pregnancy has the risk of significant bleeding at the time of delivery.[1] It is a hematological disorder where platelet count is less than 1,50,000 μL^{-1} and after anemia, thrombocytopenia is the most common hematological abnormality in pregnancy.[2] It is found that it can occur during pregnancy due to preexisting conditions which are very common in women of reproductive age group such as immune thrombocytopenia (ITP), systemic lupus erythematosus (SLE), or gestational thrombocytopenia or hemolysis, elevated liver enzymes, low platelets (HELLP) syndrome.[3] Clinically it represents bleeding of mucous membranes presenting as petechiae, ecchymoses, epistaxis, gingival bleeding, etc. However, bruising, hematuria, gastrointestinal bleeding, and rarely intracranial hemorrhage can also occur.[2]

Thrombocytopenia can be differentiated into three types, mild (platelet count of 1,00,000–1,50,000 $\times$ 10^9/L), moderate (platelet count of 50,000–1,00,000 $\times$ 10^9/L), or severe (platelet count less than 50,000 $\times$ 10^9/L), according to platelet range.[1] Thrombocytopenia affects 6–10% of all pregnant women across the globe. When this condition is associated with medical disorders hemostatic complications become life-threatening during delivery and in the postpartum period, risking maternal and perinatal morbidity and mortality.[4] Gestational thrombocytopenia is the most common seen during pregnancy and is not associated with any adverse events for either mother or baby generally causes only mild thrombocytopenia, and occurs in the latter half of pregnancy, from the mid-second or third trimester.[5] However primary ITP occurs in the first and second trimesters and is found in 1/1,000–1/10,000 pregnancies, contributing 3% of women thrombocytopenic at delivery.[5]

Accuracy in diagnosing etiology ensures therapeutic management. Hence, this study is designed to review the magnitude of the condition, address the diagnostic challenge, predict maternal and neonatal complications for preparedness, and if any hemorrhagic catastrophe is to occur. With the increase in the incidence of neonatal complications with severe thrombocytopenia, ITP has to be differentiated from severe

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gestational thrombocytopenia. This paper will highlight the identification of different causes, and management options and also to know maternal and fetal outcomes. Awareness of the complex disorders in which thrombocytopenia occurs ensures prompt diagnosis and referral into healthcare centers with expertise in these rare conditions, to optimize the outcome for mother and fetus.[5]

Methodology

It is a longitudinal study conducted for one year (September 2016 to August 2017) in Govt Lady Goschen Hospital and Kasturba Medical College, Attavar, Mangaluru, Karnataka, India. The study population was antenatal women from the outpatient department who were admitted to Govt Lady Goschen Hospital and Kasturba Medical College, Attavar, Mangaluru, Karnataka, India thrombocytopenia were enrolled in the study. Approval was taken by the ethics committee of Kasturba Medical College and Kasturba Hospital, Institutional Ethics Committee at the beginning of the study. For the data collection tool used, a pre-tested, semi-structured proforma was used. A total of 238 cases of thrombocytopenia were noted. Inclusion criteria for the study were antenatal women with platelet count below or equal to 1,50,000/µL, irrespective of gestational age were considered.

The patient was asked about the history of thrombocytopenia in a previous pregnancy, complications during the present and past pregnancy, medical history, and family history. A general examination to look for petechiae, bruises, and purpura was done. A systemic examination for hepatic causes was done. Platelet count estimation was done as a routine at the time of enrollment for all outpatient department patients in Lady Goshen Hospital and Kasturba Medical College and Hospital, Attavar, Mangaluru, Karnataka, India.

Platelet counts were repeated every trimester and followed throughout the antenatal period till delivery. Platelet counts were repeated twice a week in case of gestational thrombocytopenia and ITP. Platelet counts were repeated daily in case of HELLP syndrome, severe preeclampsia, complicated malaria, and dengue. In all cases, platelet counts were repeated during labor and 48 hours following delivery. Investigations such as hemoglobin, total leucocyte count, differential leukocyte count, peripheral smear, bleeding time, clotting time, renal function tests, liver function tests, serology [HIV and hepatitis B surface antigen (HbsAg)], and coagulation tests (prothrombin time, activated partial thromboplastin time) were documented.

The period of gestation at the time of delivery, whether induced or spontaneous, was noted. Any intrapartum or postpartum complications (abruption, hemorrhage, and hematoma at the episiotomy site) were recorded. Indication for cesarean section, and intraoperative or postoperative complications (hemorrhage, hemoperitoneum, and wound hematoma) were observed. Transfusion of blood or blood products was noted. Fetal outcomes in the form of low birth weight, meconium-stained liquor, appearance, pulse, grimace, activity, and respiration (APGAR) score at 1 and 5 minutes, asphyxia, neonatal intensive care unit (NICU) admission, any stillbirths were noted. Neonatal platelet counts were also documented.

The collected data was coded and entered on to statistical package for social sciences (SPSS), version 15. For comparisons across groups, the Chi-square test was used, and a p-value of < 0.05 is considered statistically significant.

Table 1: Severity of thrombocytopenia

Severity of thrombocytopenia			
	Mild	*Moderate*	*Severe*
Primigravida	83	21	08
Multigravida	89	25	12
Total	172	46	20
The severity of thrombocytopenia among each group			
Gestational thrombocytopenia	156	20	07
Obstetric causes	10	17	07
Medical causes	06	09	06

Table 2: Causes of thrombocytopenia

Causes	*Number of cases*
Obstetric causes	
Hypertensive disorders	28
Severe preeclampsia	8
Imminent eclampsia	2
Eclampsia	3
HELLP with DIC	7
Abruption with severe preeclampsia	2
Abruption placenta	6
Medical causes of thrombocytopenia	
Medical causes	23
Malaria	9
Dengue	8
ITP	6
Other risk factors	
Anemia	9
Gestational diabetes	5
Deep venous thrombosis	1
Chronic hypertension	1
Fetal growth restriction	1
Hypothyroid	1
Heart disease	1
Placenta previa	1

Results

A total of 238 cases of thrombocytopenia were noted during 1 year study period. Mild thrombocytopenia was found in 72.2% of cases, with moderate and severe thrombocytopenia cases being 19.3 and 8.4%, respectively. Thrombocytopenia was seen more in multigravidas 53%, accounting for a p-value of 0.71, which was not significant. The majority of the cases are seen in the third trimester 75% (Table 1).

Gestational thrombocytopenia was seen in 78.5% of cases, while obstetric and medical causes accounted for 11.7 and 9.8% of cases. Mild thrombocytopenia was seen in 85.2% of cases in the gestational thrombocytopenia group, and 65% of severe thrombocytopenia cases were due to medical and obstetric causes. Hypertensive disorders of pregnancy contributed to the majority of obstetric causes of thrombocytopenia. Dengue, hemorrhagic fever, ITP, and malaria were the medical causes of thrombocytopenia (Table 2).

Table 3: Maternal outcomes and perinatal outcomes

Maternal outcomes	*Cases*
ICU admissions	05
Atonic postpartum hemorrhage	05
Peripartum hysterectomy	02
Hysterotomy (eclampsia with HELLP syndrome)	01
Perinatal outcomes	
Severe preeclampsia	03
ITP	05

Table 4: The ICU and NICU admissions

Causes	*Cases*
HELLP with DIC	02
ITP	02
Severe anemia with cardiac failure with deep venous thrombosis	01
NICU admission	
ITP	05
Preterm with sepsis	03
Low birth weight	01
Neonatal birth weight	
Low birth weight	49 cases
Preterm low birth weight	44.8% cases
Term with gestational thrombocytopenia in	36.7% cases
Term with hypertensive disorders of pregnancy	18.3% cases

Gestational age at delivery was more than 37 weeks in 61.4% of cases. Gestational thrombocytopenia cases had no history of thrombocytopenia in a previous pregnancy. No significance was found in the mode of delivery. All cesarean deliveries, 48.3%, were done in view of obstetric indications. One patient of ITP with severe thrombocytopenia underwent emergency LSCS given fetal distress. Severe thrombocytopenia was found in 20 patients, and only six patients required platelet transfusion. Packed RBC transfusion was done in 7 patients with anemia and three patients with atonic PPH. Platelet counts returned to normal within 48 hours following delivery in all the cases except in cases of ITP (Table 3). There were no maternal deaths in our study.

Neonatal thrombocytopenia was found in 8 cases of maternal ITP and severe preeclampsia with severe thrombocytopenia. No case of neonatal thrombocytopenia was found among the mild gestational thrombocytopenia group. Birth weight less than 2.5 kg was found in 20.9% of cases. Among six cases of maternal ITP, neonatal thrombocytopenia was found in five cases, which was found to be statistically significant with a *p*-value of 0.003. One neonatal death is noted in one maternal severe thrombocytopenia case with severe preeclampsia, and the cause of death is preterm with sepsis. Birth weight less than 2.5 kg was found in 20.9% of cases (Table 4).

Discussion

This study was conducted to evaluate the causes of thrombocytopenia and its effects on maternal and perinatal outcomes. As thrombocytopenia is one of the common hematological problems seen in pregnancy, accurate diagnosis helps in proper management. A total of 238 cases of thrombocytopenia were diagnosed in this study.

Thrombocytopenia was found to be more frequent in multigravida (55%) as compared to the study done by Huparikar et al. in 2016 it was 53%.[6] Parity and age were not found to be significantly associated with thrombocytopenia. The majority of the cases were detected in the third trimester. Cases found in the first trimester are only 1% in this study. Whereas, in a study conducted by Nisha et al., cases enrolled in the first trimester were found to be significantly higher (4.2%) and they included ITP cases detected before pregnancy which were referred in the first trimester.[2] Cases found in the second and third trimester were 24 and 75%, respectively.

Gestational age at diagnosis was found to be 37–38 weeks period of gestation, similar to 36–37 weeks found in a study done by Vyas et al. in the year 2014.[7] This is explained by the decreasing platelet count as gestational age advances. However, the survey done by Huparikar et al. found the gestational age at diagnosis to be 28 weeks.[6] The difference in the time of diagnosis between studies is due to the increased number of referred cases to tertiary care hospitals at term or when the complications arise in this study.

According to Philipp et al., a statistically significant fall in platelet count was seen from 32 weeks onward.[8] Patients diagnosed in the first trimester with thrombocytopenia were found to be known cases of ITP and were referred. Myers described pregnancy as a state of subclinical coagulopathy, and the most considerable physiological decline was seen in the third trimester leading to mild and moderate thrombocytopenia in the study.[9]

Mild thrombocytopenia cases were found in 72.2% of cases in the present study, similar to 74.7% as in Huparikar et al.[6] Gestational thrombocytopenia was found to be the most common cause of thrombocytopenia, and it usually presents in a mild form of thrombocytopenia. Severe thrombocytopenia was found in 8.4% of cases which is slightly more than that of Elveđi-Gašparović et al. (6.6%), and Huparikar et al. (7.4%) as malaria and ITP are found to be more in our study compared to other studies.[3,6] ITP was found to contribute to 30% of cases of severe thrombocytopenia in our study.

Gestational thrombocytopenia was found in 78.5% of cases similar to Elveđi-Gašparović et al. (75%) and slightly more than that of Nisha et al. (64.2%) and Huparikar et al. (64.2%).[2,3,6] However, in studies done by in Vyas et al. and Parnas et al., gestational thrombocytopenia accounted by 44 and 53%, respectively, much less than this study as the upper limit for inclusion in these studies were platelet count of 1,00,000/μL. About 85% of gestational thrombocytopenia cases were found to be cases of mild thrombocytopenia; hence, labeled as just a laboratory diagnosis without much therapeutic significance.[7,10]

Obstetric causes of thrombocytopenia were found to be the second most common causes accounting for 11.7% of cases against 22% in Huparikar et al. as cases of severe preeclampsia are admitted at diagnosis early in pregnancy.[6] Medical causes accounted for about 9.8% which is less than Huparikar et al. (13.6%), and Parnas et al. (10%) studies.[6,10] A most common cause in medical cases was found to be ITP. Women with medical causes of thrombocytopenia were found to have significantly ($p = 0.03$) low levels of platelet count as most of the cases are of malaria and ITP.

The preterm delivery rate is 38.6% similar to that in the study by Nisha et al. (31.8%) due to associated indications for preterm delivery like obstetric and medical complications.[2] Labor was induced in 81.9% of thrombocytopenia cases due to obstetric indications such

as term gestation, and severe preeclampsia. The minimum platelet count prior to induction in gestational thrombocytopenia, obstetric, and medical causes was found to be 1,13,000, 1,05,000, and 53,850, respectively.[6] Patients who delivered at term were 61.4% similar to 60% in a study done by Huparikar et al.[6] However, in this study, the minimum platelet count prior to induction was 63,000. Patients with low platelet counts were given transfusions prior to delivery.

Mode of delivery was not influenced by platelet count 51.48% of patients had a normal delivery, and the remaining patients had cesarean delivery for obstetric indications. In a study conducted by Elveđi–Gašparović et al., cesarean delivery rates were found to be higher among gestational thrombocytopenia cases as the study excluded all cases of thrombocytopenia due to obstetric or medical causes.[3]

Platelet transfusions prior to delivery were done in six cases of severe thrombocytopenia to maintain minimal platelet counts and prevent postpartum hemorrhage. Platelet transfusions are done in two cases of ITP, two patients of HELLP syndrome, and two patients of gestational thrombocytopenia among 20 cases of severe thrombocytopenia. Transfusions are given in cases of ITP prior to induction to raise platelet counts to 50,000/μL in cases of normal delivery and 70,000/μL in cesarean deliveries.[11]

Postpartum hemorrhage was the most common complication found in 2.9% of cases similar to Elveđi–Gašparović et al. (2%) and less than the studies of Rupa et al. (5.3%), Dwivedi et al. (4.2%).[3,6,12] Cases complicated by postpartum hemorrhage were found to be mild thrombocytopenia cases. A higher incidence of 9.89% was seen in Huparikar et al. as this study reported many cases of postpartum hemorrhage in patients complicated by medical disorders like liver diseases and multisystemic disorders.[7] Abruptio placentae were seen in 1.2% of cases lesser than 2% in Elveđi–Gašparović et al., 2.4% in Dwivedi et al. as these cases were associated with severe preeclampsia in other studies.[3,12]

Peripartum hysterectomy was done in two cases of atonic postpartum hemorrhage. The two cases were presented with mild thrombocytopenia and no obstetric or medical causes. Thrombocytopenia in these cases was not statistically significant. Neonatal thrombocytopenia was found only in 3.3% of the cases similar results were obtained in other studies too.[6,10] Dwivedi et al. reported the incidence of neonatal thrombocytopenia of 17.02% as only cases of severe thrombocytopenia are included in the study.[12] The rate of neonatal thrombocytopenia in mild gestational thrombocytopenia cases is similar to that in the healthy population.[5]

Severe neonatal thrombocytopenia is found in 5 cases. All five cases of severe neonatal thrombocytopenia were found in maternal ITP cases with a *p*-value of 0.003, making it statistically significant. Except in cases of ITP, no correlation was found between maternal thrombocytopenia and the incidence of neonatal thrombocytopenia. Stavrou et al. also suggested that maternal thrombocytopenia is not a predictor of neonatal thrombocytopenia though it is an important but not a significant risk factor.[13]

Neonatal moderate thrombocytopenia was found in 2 cases among 22 cases complicated by hypertensive disorders of pregnancy. Elveđi–Gašparović et al. reported that 11.6% of cases of hypertensive disorders had neonatal thrombocytopenia as only moderate, and severe maternal thrombocytopenia cases were included in the study.[3]

Neonates of patients with thrombocytopenia did not have any bleeding complications in the study. No significance was found concerning neonatal acidosis or APGAR scores in neonatal thrombocytopenia cases. In a multicenter trial conducted by Noris et al., severe thrombocytopenia cases had very early preterm deliveries, low birth weight, and low APGAR scores as only maternal ITP cases with severe thrombocytopenia were studied.[14]

Birth weight less than 2.5 kg was found in 20.9% of cases among which term low birth weight was found to be 11.7%. Neonatal hemorrhagic complications like intracranial hemorrhage are not found in neonatal thrombocytopenia cases in this study similar to Nisha et al. study suggesting good perinatal outcomes even with severe maternal thrombocytopenia.[2]

Conclusion

There are an enormous number of causes of thrombocytopenia in pregnancy. The most widely known reasons are mild, however regular monitoring and surveillance are required in these high-risk patients for earlier detection and treatment of complications to diminish the fetomaternal morbidities. Pregnancy with acquired thrombocytopenia is a significant matter of concern as both the mother and the infants are conceivably at risk of bleeding.

Clinical Significance

Mild or moderate thrombocytopenia cases are mostly detected in the third trimester. Risking complications such as maternal morbidities or neonatal thrombocytopenia. As pregnancy with procured thrombocytopenia is a critical matter of worry as both the mother and the babies are possibly at risk of bleeding, it should be early detected and treated to diminish the fetomaternal morbidities.

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