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Original Research Article

Evaluation of Etiological Factors of Thrombocytopenia in Pregnancy and its Effects on Feto-Maternal Outcomes

Sujata Deo[1], Akancha Pandey[1], Pratibha Kumari[1*], Mohd. Kaleem Ahamad[2]

[1]Department of Obstetrics and Gynaecology, King George's Medical University, Uttar Pradesh Lucknow, India

[2]Department of Biochemistry, King George's Medical University, Uttar Pradesh Lucknow, India

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Corresponding author: Dr. Pratibha Kumari

Conflict of interest: Nil

Abstract:

Background: Thrombocytopenia is defined as a platelet count of less than 150×109/L, or the 2.5th lower percentile of the normal platelet count distribution. Aim of the study was to evaluate the etiological Factors of Thrombocytopenia in pregnancy and its effects on feto-maternal Outcomes.

Material and Methods: The prospective observational study was done from September 2020 to October 2021 on one hundred fifty-eight pregnant females with low platelet count or who were diagnosed as thrombocytopenia in second and third trimester at QMH, Department of Obstetrics and Gynaecology, King George's Medical University, Lucknow. The Chi-square test will be used to compare the categorical variables. The Unpaired t-test was used to compare the continuous variables. The p-value<0.05 was considered significant. All the analysis was carried out on SPSS-21.0 version.

Results: The mean age of all pregnant women was found to be 25.69 ± 3.78 years. With mean Manual Platelet Count (Lacs/cu.mm) 0.83 ± 0.37 lacs/cumm. Out of 158 subjects most common etiology of thrombocytopenia was obstetric causes 70(44.3%) which included 55(34.8%) had hypertensive cause, 8 (5%) subjects had DIC and 7 (4.4%) subjects had abruptio placentae. Out of 55 subjects having hypertensive causes of thrombocytopenia, 43 (27.2%) subjects had preclampsia, 8(5%) had eclampsia and 4(2.53%) subjects had HELLP syndrome etiology of thrombocytopenia of 21 subjects having medical thrombocytopenia, 6(3.79%) subjects had ITP as the cause of thrombocytopenia, 12(7.59%) subjects had dengue, 2(1.26%) subjects had infections like HIV, HCV. There was one subject having hypersplenism as the cause of thrombocytopenia contributing to 0.6 % of the entire causes. No subject had TTP, HUS or TMA as the cause of thrombocytopenia. Second most common cause was gestational thrombocytopenia 67(42.4%). Majority 123(77.8%) of neonates did not have thrombocytopenia at all, 20(12.65%) neonates had mild thrombocytopenia, 12(7.5%) neonates had moderate thrombocytopenia and 3(1.8%) neonates had severe thrombocytopenia. The association between maternal complication and severity of thrombocytopenia PPH, MOD and DIC (p value: 0.005,0.001,0.001 respectively) were significantly associated with thrombocytopenia. The association between perinatal complication with severity preterm birth, LBW, SNCU admission (p-value: 0.002, 0.001, <0.001, respectively) was significantly associated with thrombocytopenia.

Conclusion: Our findings suggest that evaluation of thrombocytopenia in pregnancy is important and a detailed workup with careful monitoring is required as early diagnosis and management may play a key role in decreasing the adverse outcomes. Special attention should be given to patients with thrombocytopenia due to preeclampsia and HELLP syndrome to establish the best moment for therapeutical intervention.

Keywords: Thrombocytopenia, Etiology, Hypertension, Maternal Outcome, Pregnancy.

Introduction

Thrombocytopenia is defined as a platelet count of less than 150×109/L, or the 2.5th lower percentile of the normal platelet count distribution [1]. It is a disorder that is under studied in Indian women and frequently remains under diagnosed. Along with anaemia, thrombocytopenia is most generally recognized haematological disorder that occurs during pregnancy and it has been found to complicate 7 % to 8% of pregnancies in India, primarily in the 3rd trimester [2] with just 1% of pregnant women suffering from severe thrombocytopenia [3] .

Platelets are megakaryocyte-derived non-nucleated cellular pieces. They are important in hemostasis. Platelet counts (1.5-4.5 lac cell/L) remain normal in most uncomplicated pregnancies. In uncomplicated

singleton pregnancies, the mean platelet count drops gradually throughout pregnancy and increases after birth. Because platelets' primary job is to initiate hemostasis, thrombocytopenia can result in spontaneous bleeding from any portion of the body. It is associated with severe bleeding during birth and might require urgent maternal and newborn care [4]. Platelet count may decline by approximately 6% to 10 % worldwide during the 3rd trimester due to hemodilution of plasma volume, however absolute platelet count stays within normal references range in most cases. [5,6] The severity of thrombocytopenia is classified as mild (100,000-150,000/μL), moderate (50,000-100,000/μL) and severe (less than 50,000/μL). The most prevalent cause of thrombocytopenia is an exclusion diagnosis accompanied with mild thrombocytopenia. A platelet count of 70,000/L rule out gestational thrombocytopenia [7].

10% of all pregnancies affected by thrombocytopenia complications. There are numerous probable causes, but three are responsible for nearly all cases: incidental gestational thrombocytopenia (IGT) 74%, preeclampsia and HELLP (hemolysis, high liver function test, low platelet count) syndrome (21%) and immune thrombocytopenic purpura (ITP) 4%. Although there is no risk of maternal or foetal haemorrhage with IGT, a benign disorder, preeclampsia, HELLP syndrome and ITP expose mother and child to potentially life threatening consequences. Other rare cause of serious consequences include thrombocytopenic purpura, hemolytic and uremic syndrome, disseminated intravascular coagulation and von willebrand disease type IIB [5,6].

On the other hand, some thrombocytopenia related diease may be linked to severe maternal and foetal morbidity and mortality or other significant medical conditions. Three uncommon conditions include thrombotic thonbocytopenic purpura (TTP), hemolytic uremic syndrome (HUS) and disseminated intravascular coagulopathy (DIC) [8,9]. Other potential cause of thrombocytopenia include nutrient deficiencies including dolic acid or vitamin B12 deficiency, viral disorder like leukemia, & aplastic anaemia, HIV/AIDS, malaria [10-13]. All the women's mean platelet counts fell during pregnancy, compared to other etiologies, GT is the most common cause of pregnancy related thrombocytopenia, linked to better fetometernal outcomes. Early interdisciplinary evaluation of thrombocytopenia during pregnancy can aid optimizing care as negative consequences and management rely on the etiology [14]. Since the management varied greatly, determining the cause is quite important. Thus, raising knowledge of the various reasons, establishing early diagnosis and implementations specialized treatment may enhance both maternal and newborn outcomes. There is a dearth of information from patients reaching term in the Indian population and the maternal that is currently accessible in this area is narrowly focused one etiology [14-16]

After the brief knowledge we planned this study, the aim of the study was to evaluate the etiological Factors of Thrombocytopenia in pregnancy and its effects on feto-maternal Outcomes.

Material and Methods:

The prospective observational study was conducted after taken the ethical clearance approval (ref code: 102nd ECM IIB Thesis/P69, vide no. 94/Ethics/2020 dated 05/09/2020) from institutional ethical committee of King George's Medical University (KGMU), Uttar Pradesh Lucknow, India. This study was done from September 2020 to October 2021 on one hundred fifty-eight pregnant females with low platelet count or who were diagnosed as thrombocytopenia in second and third trimester at QMH, Department of Obstetrics and Gynaecology, King George‟s Medical University, Lucknow. Participants who fulfilled the inclusion criteria were enrolled after taken informed consent. All the cases were enrolled according to following inclusion exclusion criteria:

Inclusion Criteria:

All admitted pregnant women in 2nd and 3rd trimester of pregnancy who were diagnosed as thrombocytopenia after complete blood count was done as a part of their routine workup.

All pregnant women who gave the informed consent and detailed history and met the inclusion criteria.

Exclusion Criteria:

All pregnant women with normal platelet count.

Patients not giving consent for participating in the study.

Sample collection and Assessment:

To confirm the diagnosis of thrombocytopenia 5 ml venous blood sample was taken in EDTA vial for manual platelet count and peripheral blood smear which was done in hematological laboratory, KGMU. Diagnosis of thrombocytopenia was established if platelet count is <150,000/μL in automated count as well as manual platelet count. After establishing the diagnosis, the patient was investigated for the etiopathogenesis of thrombocytopenia for which a panel of investigations was done in department of Pathology and department of Microbiology in KGMU which includes: Liver function test, Kidney function test, Antinuclear antibody, APLA profile, Bleeding time, Clotting time, Coagulation profile

(prothrombin time, APTT, FDP, D dimer), Serum folate, Serum Vit B12, CMV,EBV, Ns1 Ag for dengue, USG whole abdomen, Etiopathogenesis of thrombocytopenia was established, Patient was followed till delivery and 6 weeks post partum. Maternal outcome were assessed in thrombocytopenic patientslike: PPH, DIC, multiple organ failure, placental abruption, preterm delivery.

At the time of delivery 5 ml of cord blood was taken in EDTA vial to routine hematological test and complete blood count and manual platelet count was done. Correlation between maternal and cord blood platelet count was seen. Neonates of thrombocytopenic mothers were assessed based on the parameters: Live/stillbirth, APGAR score, Birth weight, Intra Ventricular hemorrhage (IVH) or other bleeding manifestation.

Statistical Analysis:

After data collection, results will be presented in frequencies, percentages and mean±SD. The Chi-square test will be used to compare the categorical variables. The Unpaired t-test was used to compare the continuous variables. The p-value<0.05 was considered significant. All the analysis was carried out on SPSS-21.0 version (Chicago, Inc., USA).

Results:

Distribution of subjects according to the age is shown in Table-1, Total 158 subjects were enrolled in the study who had thrombocytopenia in 2nd or 3rd trimester of pregnancy out of which, 82 (51.9%) were between 18-25 years, 64 (40.5%) were between 26-30 years, 7 (4.4%) were between 31-35 years, 5 (3.2%)were above 36 years. The mean age was found to be 25.69 ± 3.78 years.

Table 1: Distribution of Subjects according to Age (n=158)

Age Group	N	%
18-25 Year	82	51.9%
26-30 Year	64	40.5%
31-35 Year	7	4.4%
>36 Year	5	3.2%
Total	**158**	**100**
Mean age	**25.69 ± 3.78 years**	

Distribution of subjects according to severity of thrombocytopenia is shown in figure 1, we found that out of 158 subjects, 67 (42.4%) had Mild Thrombocytopenia (platelet count 1,50,000/cumm-1,00,000 cumm), 61(38.6%) had moderate thrombocytopenia (platelet count 1,00,000/cumm-50,000 cumm)and 30(19.0%) had severe thrombocytopenia (platelet count <50,000 cumm).The mean Manual Platelet Count (Lacs/cu.mm) was 0.83 ± 0.37 lacs/cumm.

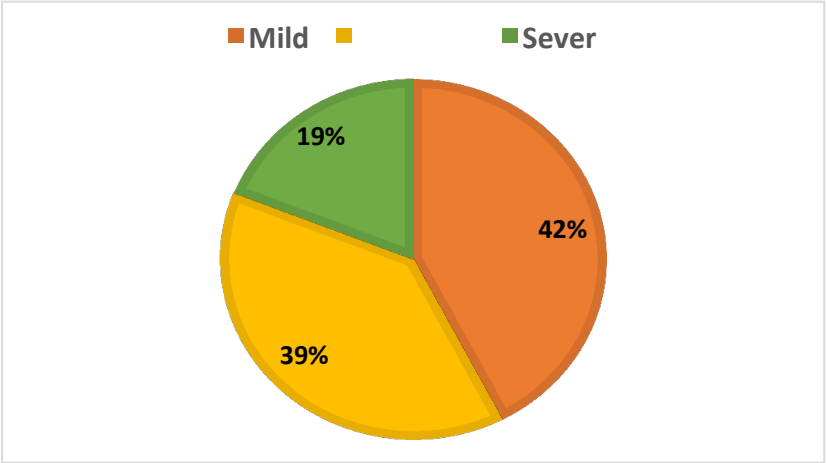


Figure 1: Distribution of Subjects according to severity of thrombocytopenia (n=158)

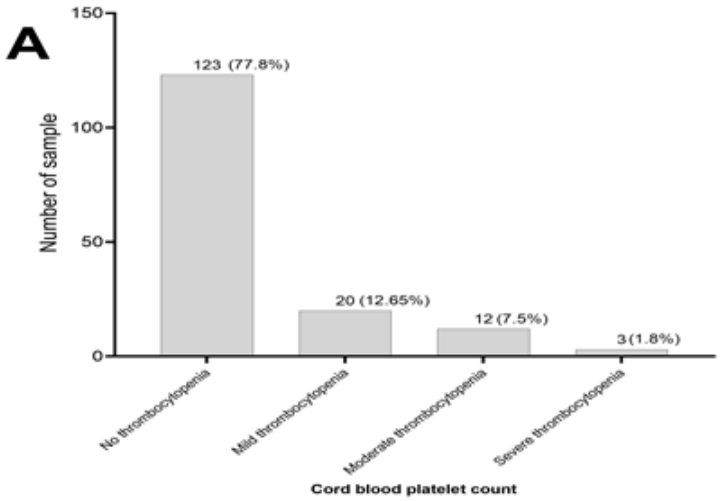
In the present study, in table 2, it was found that out of 158 subjects enrolled, 67 (42.4%) of subjects had gestational thrombocytopenia, 70 (44.3%) had obstetric causes of thrombocytopenia and 21 (13.2%) had medical causes of thrombocytopenia. Out of 70 subjects having obstetric causes of thrombocytopenia, 55(34.8%) had hypertensive cause, 8 (5%) subjects had DIC and 7 (4.4%) subjects had abruptio placentae. Out of 55 subjects having hypertensive causes of thrombocytopenia, 43 (27.2%) subjects had preclampsia, 8 (5%) had eclampsia and 4 (2.53%) subjects had HELLP syndrome etiology of thrombocytopenia of 21 subjects having medical thrombocytopenia, 6 (3.79%) subjects had ITP as the cause of thrombocytopenia, 12 (7.59%) subjects had dengue, 2 (1.26%) subjects had infections like HIV, HCV. There was one subject having hypersplenism as the cause of thrombocytopenia contributing to 0.6 % of the entire causes. No subject had TTP, HUS or TMA as

the cause of thrombocytopenia in our study.

Table 2 : Distribution of cases according to the Etiology ofThrombocytopenia (n=158)

Etiology	N	%
1) Gestational	67	42.4
2) Obstetric	70	44.3
a) Hypertensive	55	34.8
PET	43	27.2
Eclampsia	8	5
HELLP	4	2.53
DIC	8	5
b) Abruptio placentae	7	4.4
3) Medical	21	13.2
ITP	6	3.79
Dengue	12	7.59
Infections (HIV, HCV)	2	1.26
TTP/HUS/TMA	0	0
Hypersplenism	1	0.6
Total	**158**	**100**

Figure-2 shows distribution of neonates according to the severity of cord blood platelet count. We found that out of 158 neonates born to thrombocytopenic pregnant females enrolled in our study, 123 (77.8%) of them did not have thrombocytopenia at all, 20(12.65%) neonates had mild thrombocytopenia, 12 (7.5%) neonates had moderate thrombocytopenia and 3 (1.8%) neonates had severe thrombocytopenia. We found that there was significant association between cause of maternal thrombocytopenia and presence of neonatal thrombocytopenia. Medical cause of maternal thrombocytopenia was highly associated with presence of neonatal thrombocytopenia. There is no association between cause of maternal thrombocytopenia and severity of neonatal thrombocytopenia.



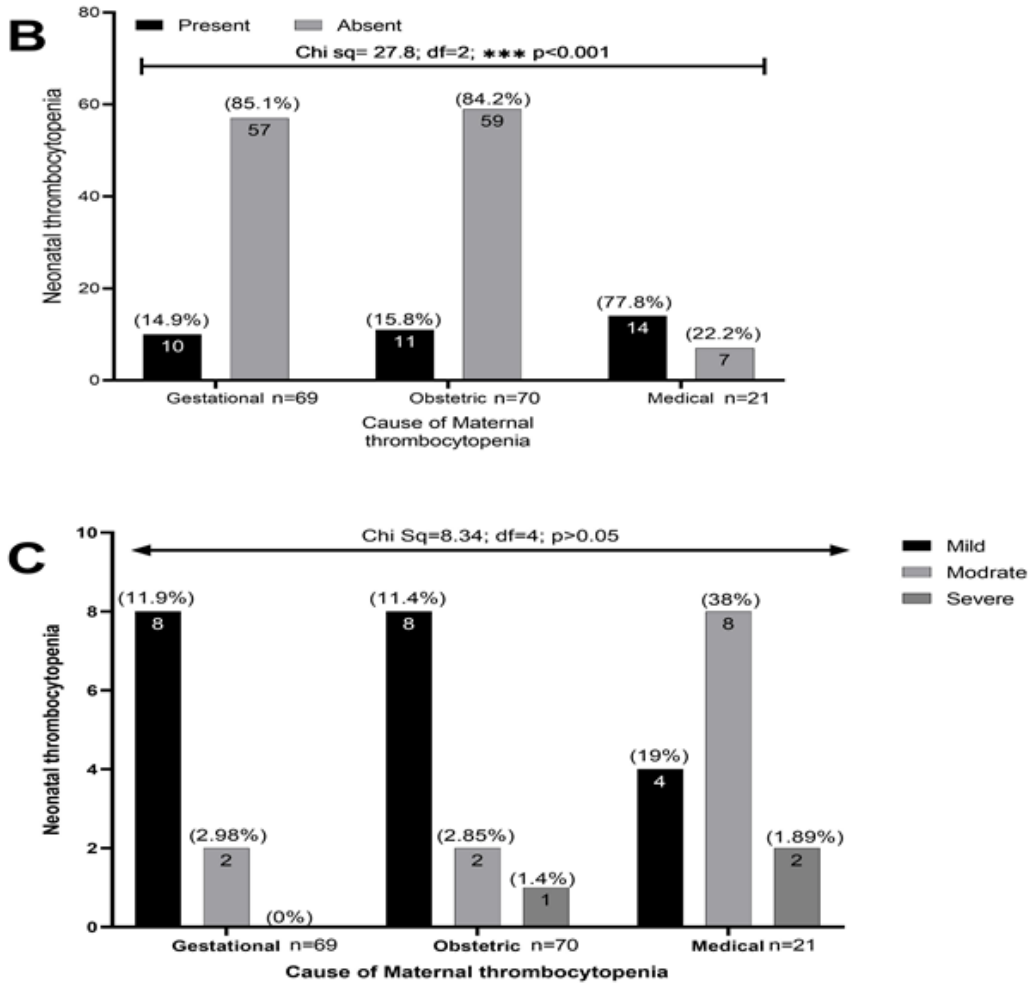


Figure 2: A: Distribution of neonates according to Cord blood platelet count (n=158); B: Association between maternal thrombocytopenia with neonatal Thrombocytopenia; C: maternal thrombocytopenia with severity of neonatal Thrombocytopenia.

Table-3 shows Perinatal outcomes in subjects of thrombocytopenia, on analyzing 158 thrombocytopenic subjects, 67 (42.44%) subjects who had gestational thrombocytopenia delivered 19 (12%) preterm and 43 (30.37%) term neonates. 12 (7.59%) neonates were low birth weight (birth weight <2500 gms) while 55 (34.8%) neonates were of birth weight >2500 gms. 8 (5%) babies were SGA. 4 (2.5%) required SNCU admission. There were no NICU admission/neonatal deaths in neonates of mothers with gestational thrombocytopenia.

Out of 158 subjects, 70 (44.3%) subjects who had obstetric causes of thrombocytopenia delivered 26 (16.4%) preterm and 44 (27.8%)term neonates. 18 (11.39%) neonates were low birth weight (birth weight <2500 gms) while 52 (32.9%) neonates were of birth weight >2500 gms. 10 (6.3%) babies were SGA. 8 (5%) required SNCU admission. 2 (1.26%) required NICU admission and there was 1 (0.6%) neonatal death.

Out of 158 subjects, 21 (13.29%) subjects who had medical causes of thrombocytopenia delivered 3 (1.89%) preterm and 18 (11.39%)term neonates. 3 (1.89%%) neonates were low birth weight (birth weight <2500 gms) while 18 (11.39%) neonates were of birthweight >2500 gms. 1 (0.6%) baby was SGA who got admitted in SNCU. There was no neonatal death in any neonate.

Thus we found that out of 158 neonates of thrombocytopenic mothers observed for complication, total 48/158 (30.37%) were preterm neonates, 110/158 (69.62%) were term neonates. 33/158 (20.88%) were LBW neonates while 125/158 (79.11%) were birth weight >2500 gms. 19/158 (12.05%) were SGA babies. 13/158 (8.2%) required SNCU admission, 2/158 (1.26%) required NICU admission. 1/158 (0.6%) neonate died. There was no bleeding complication in any neonate. The association between perinatal outcomes and causes of thrombocytopenia was not statistically significant.

Table 3: Perinatal outcomes in subjects of thrombocytopenia (n=158)

Perinatal Outcomes N=158	Causes of maternal thrombocytopenia			Total n=158 (Percentage)	p value
	Gestational (n=67)	Obstetrics (n=70)	Medical (n=21)		
Fetal maturity					
a) Preterm(<37weeks)	19 (12%)	26 (16.4%)	3 (1.89%)	48(30.37%)	0.122
b) Term(>37weeks)	48 (30.37%)	44 (27.8%)	18(11.39%)	110(69.62%)	
Birth weight					
<2500 gm	12(7.59%)	18(11.39%)	3(1.89%)	33(20.88%)	0.387
>= 2500 gm	55(34.8%)	52(32.9%)	18(11.39%)	125(79.11%)	
SGA	8 (5%)	10 (6.3%)	1 (0.6%)	19 (12.05%)	0.5
Bleeding complication	0	0	0	0	-
SNCU admission	4 (2.5%)	8 (5%)	1 (0.6%)	13 (8.2%)	0.4
NICU admission	0	2 (1.26%)	0	2 (1.2%)	0.2
Neonatal death	0	1 (0.6%)	0	1 (0.6%)	0.5

Table -4 shows association between the various etiologies of thrombocytopenia and severity of thrombocytopenia. We observed that 67/158 (42.4%) subjects diagnosed as gestational thrombocytopenia, 51/67 (76.11%) had mild thrombocytopenia and 16/67 (23.8%) had moderate thrombocytopenia. Subjects having severe thrombocytopenia were not diagnosed as GT 70/158 (44.3%) subjects diagnosed as obstetric thrombocytopenia, 55/70 (23.6%) had hypertensive cause, 8/70 (11.4%) had DIC as cause of thrombocytopenia, 7/70 (10%) had abruptio placentae as cause of thrombocytopenia. Out of 55 (23.6%) subjects who had hypertensive causes of thrombocytopenia, 43/55 (78.18%) had PET, 8/55 (14.54%) had eclampsia, 4/55 (7.27%) had HELLP syndrome as cause of thrombocytopenia. Of 43 PET subjects,13/43 (30.23%) had mild thrombocytopenia, 26/43 (60.46%) had moderate thrombocytopenia and 4/43 (9.3%) had severe thrombocytopenia. The results were statistically significant (p value-0.002). out of 8 eclamptic subjects, 4/8 (50%) had moderate and 4/8 (50%) had severe thrombocytopenia which was statistically significant (p value-0.017). Of 4 HELLP syndrome subjects, 1/4 (25%) had moderate thrombocytopenia and 3/4 (75%) had severe thrombocytopenia which was statistically significant (p value-0.017).

Out of 70/158(44.3%) obstetric causes, 8/70 (11.42%) had DIC and all subjects had severe thrombocytopenia which was statistically significant (p value-0.001). Out of 70/158(44.3%) obstetric causes, 7/70 (10%) had abruptio placentae. 1/7(14.2%) subjects had mild thrombocytopenia, 4/7 (57.14%) had moderate thrombocytopenia and 2/7 (28.5%) had severe thrombocytopenia which was statistically non-significant (p value-0.3). 21/158 (13.2%) were medical causes of thrombocytopenia out of which 6/21 (3.7%) were due to ITP, 12/21 (57.14%) had dengue infection, 2/21 (9.5%) had other infections like HIV/HCV and 1/21(4.7%) subject had hypersplenism. There were no subjects of TTP/TMA/HUS.

Out of 6 subjects who had ITP, 2/6 (33.33%) had moderate thrombocytopenia, 4/6 (66.66%) had severe thrombocytopenia and this result was statistically significant (p value-0.006). out of 12 dengue subjects, 7/12 (58.33%) had moderate thrombocytopenia, 5/12 (71.42%) had severe thrombocytopenia and this result was statistically significant (p value-0.005). 2 subjects who had HIV/HCV infection as a cause of thrombocytopenia had mild thrombocytopenia. One subject who had hypersplenism as cause of thrombocytopenia had moderate thrombocytopenia.

Table 4: Association between Severity and Etiology of thrombocytopenia.

Etiology	Severity of thrombocytopenia			P value (chi square value)
	Mild (n=67)	Moderate (n=61)	Severe (n=30)	
Gestational (n=67)	51 (76.11%)	16 (23.8 %)	0	0.001(36.5)
Obstetric (n=70)	14 (20%)	35 (50%)	21 (30%)	0.001 (27.13)
Hypertensive (n=55)	13 (23.6%)	31 (56.36)	11 (20%)	0.001(20.75)
PET (n=43)	13 (30.23%)	26 (60.46%)	4(9.3%)	0.002 (12.29)
Eclampsia (n=8)	0	4(50%)	4 (50%)	0.017 (8.1)
HELLP (n=4)	0	1 (25%)	3 (75%)	0.01(8.7)
DIC (n=8)	0	0	8 (100%)	0.001(35.9)
Abruptio placentae (n=7)	1 (14.2%)	4 (57.14%)	2 (28.57%)	0.3
Medical (n=21)	2 (9.5%)	10 (47.6%)	9 (42.85%)	0.001(43.6)
ITP (n=6)	0	2(33.33%)	4 (66.66%)	0.006(10.15)
Dengue (n=12)	0	7 (58.33%)	5 (71.42%)	0.005(10.3)
Infections (n=2)	2 (100%)	0	0	0.25
TTP/HUS/TMA (n=0)	0	0	0	0
Hypersplenism (n=1)	0	1(100%)	0	0.11

The association between maternal complications and severity of thrombocytopenia shown in table-5, in which we found that out of 45 subjects who had post-partum hemorrhage, 29 (64.44%) had mild thrombocytopenia, 14 (31.11%) had moderate thrombocytopenia and 2 (4.44%) had severe thrombocytopenia. Association between PPH as a complication in thrombocytopenic subjects and severity of thrombocytopenia was statistically significant (p value-0.005). Out of 7 subjects who had abruptio placentae, 1 (14.28%) had mild thrombocytopenia, 4 (57.14%) had moderate thrombocytopenia and 2 (28.57%) had severe thrombocytopenia. Association between abruptio placentae as a complication in thrombocytopenic subjects and severity of thrombocytopenia was statistically non-significant (p value-0.36). Out of 158, 3 subjects suffered from surgical site infection i.e LSCS wound gape and all of them had mild thrombocytopenia (p value-0.12).Out of 158, 3 subjects developed vaginal hematoma, out of which 1(33.3%) had moderate thrombocytopenia and 2 (66.66%) had severe thrombocytopenia (p value-0.08). 8 subjects out of 158 had DIC and all of them had severe thrombocytopenia. 13 subjects out of 158 had MODS out of which 3 (23.07%) had moderate thrombocytopenia and 10 (76.9%) had severe thrombocytopenia. The association between DIC and MODS as complication of thrombocytopenic subjects with severity of thrombocytopenia was found to be statistically significant (p value< 0.001).

Table-5 also shows association between perinatal complications and severity of thrombocytopenia. We found that out of 48 preterm neonates, 34 (70.8%) neonates were born to mothers who had mild thrombocytopenia, 10 (20.8%) neonates were born to mothers who had moderate thrombocytopenia and 4 (8.3%) neonates were born to mothers who had severe thrombocytopenia. Association between preterm deliveries in thrombocytopenic subjects and severity of thrombocytopenia was statistically significant (p value =0.002). Out of 33 LBW neonates, 4 (12.1%) neonates were born to mothers who had mild thrombocytopenia, 19 (57.57%) neonates were born to mothers who had moderate thrombocytopenia and 10 (52.63%) neonates were born to mothers who had severe thrombocytopenia. Association between LBW as a complication in thrombocytopenic mothers and severity of thrombocytopenia was statistically significant (p value =0.004). Out of 158 neonates, there were 19 (12.05%) SGA (small for gestational age) neonates out of which 3 (15.78%) neonates were born to mothers who had mild thrombocytopenia 10 (57.57%) neonates were born to mothers who had moderate thrombocytopenia and 6 (31.57%) neonates were born to mothers who had severe thrombocytopenia. Association between SGA neonates as a complication in thrombocytopenic mothers and severity of thrombocytopenia was statistically significant (p value =0.038). Total 13 neonates got admitted in Special Newborn Care Unit(SNCU) out of which 7 (53.84%) were born to mothers with moderate thrombocytopenia while 6 (46.15%) were born to mothers with severe thrombocytopenia. No neonate born to mothers having mild thrombocytopenia got admitted to SNCU. Association between SNCU admission of a neonate and severity of maternal thrombocytopenia was statistically significant (p value- 0.002). Two neonates were admitted in NICU, each were born to moderately

and severely thrombocytopenic mothers and this was not statistically significant (p value-0.37). 1 neonate expired who was born to mother having severe thrombocytopenia (p value-0.11).

Table 5: Association between Maternal complications, Perinatal complication and Severity of thrombocytopenia.

Complications	Severity of thrombocytopenia			p value(Chi square)
	Mild N=67	Moderate N=61	Severe N=30	
Maternal complications				
1) PPH (n=45)	29 (64.44%)	14 (31.11%)	2 (4.44%)	0.005 (15.1)
2) Abruptio Placentae (n=7)	1(14.28%)	4(57.14%)	2(28.57%)	0.36
3) Surgical Site Infection (n=3)	3 (100%)	0	0	0.12
4) Vaginal Hematoma (n=3)	0	1 (33.33%)	2 (66.66%)	0.08
5) Multiorgan dysfunction (n=13)	0	3(23%)	10(76.9%)	<0.0001(31.9)
6) DIC (n=8)	0	0	8(100%)	<0.0001 (35.9)
Perinatal complications				
1) Preterm birth (n=48)	34(70.8%)	10 (20.8%)	4(8.3%)	0.002(17)
2) Low birth weight (n=33)	4 (12.1%)	19 (57.57%)	1(30.30%)	0.004 (15.7)
3) SGA (n=19)	3(15.78%)	10(52.63%)	6(31.57%)	0.038
4) SNCU admission (n=13)	0	7(53.84%)	6(46.15%)	0.002(11)
5) NICU admission (n=2)	0	1(50%)	1(50%)	0.37
6) Neonatal deaths (n=1)	0	0	1(100%)	0.11

Discussion

In the present study, the mean age group was found to be 25.69 ± 3.78 years. The maximum number of thrombocytopenic women belonged to 18-25 years (51.9%) and 26-30 years (40.5%). This was similar to the study conducted by Modi K. *et al* (2020) where 62.67% of thrombocytopenia occurred in 18-26 years age group, 33.33% of thrombocytopenia occurred in 26-35 years and4% in 36-46 years [17]. In a similar study conducted by Singh S. *et al* (2020) 47.8% of thrombocytopenia was found in age group 21- 25 years and 27.6 % occurred in 26-30 years [18]. In the present study, out of 158 subjects, 70 (44.3%) subjects had obstetric causes of thrombocytopenia which included hypertensive disorders 55/70 (34.8%), DIC 8/70 (5%), Abruptio placentae 7/70 (4.4%). Out of 70/158 (44.3%) obstetrics cases, 43/70 (27.2%) subjects had preeclamptic toxemia (PET), 8/70 (5%) had eclampsia, 4/70 (2.53%) had HELLP syndrome. Singh *et al* (2020) found that PIH contributes to 12.7% of all the causes of thrombocytopenia [18], Al husban *et al* (2020) found pre-eclamptic Toxemia (PET)/HELLP syndrome accounting for 7.41% of all causes of thrombocytopenia [19]. In a study conducted by Modi *et al* (2020), 13.33% of pregnant patients having thrombocytopenia were due to preclampsia, 8% due to eclampsia and 2.67% due to HELLP/DIC [17]. The results were similar to the rest of the literature.

Timely identification of high-risk cases and early diagnosis of HELLP syndrome patients from amongst the preclampsia group should be done. Management and delivery of HELLP syndrome mothers and care of newborns should be undertaken.

Disseminated Intravascular Coagulation may arise from a number of events in pregnant woman like placental abruption, uterine rupture and, amniotic fluid embolism. we found DIC in 5% of subjects of our study while it was 1.05% in study conducted by Nisha *et al (*2012) [7], 4.47% in an observational study by Pandey U. *et al* (2016) [20],

In a prospective study conducted by Madge *et al* (2019) on Maternal and perinatal outcome in patients of preeclampsia with and without HELLP syndrome, it was found that 11.6% maternal mortality was observed in HELLP syndrome group as compared to group having only preclampsia without HELLP [21].

In this study out of 70 subjects having obstetric causes of thrombocytopenia, 7 (4.4%) subjects had abruption and it was in accordance with 4% in a study conducted by Huparikar A. *et al.*(2016*)* [22]. In the present study out of 21 subjects having medical thrombocytopenia, 6 (3.79%) subjects had ITP as the cause ofthrombocytopenia. The results were similar to study by Huparkar A. *et al (*2016) where ITP as cause of thrombocytopenia was 1%. Nisha *et al* (2012) found ITP as a cause in 5.26% of thrombocytopenic cases [7]. Very high percentage (28.2%) of ITP cases as a cause of thrombocytopenia was found in a study by Wang *et al* (2017) [23]. Al Husban *et al* (2020) found ITP as a cause of

thrombocytopenia in 1.93% cases [19] and 6.67% cases had thrombocytopenia due to ITP in a study by Modi *et al* (2020) [17].

On this study out of 21 subjects having medical thrombocytopenia 7.59% subjects had dengue, 1.26% subjects had infections like HIV, HCV. There was one subject having hypersplenism as the cause of thrombocytopenia contributing to 0.6 % of all the causes. These results were similar to results of studies by Nisha et al (2012) where hypersplenism contributed to 2.11% as cause of thrombocytopenia [7]. There was no case of dengue and HIV/HCV infection in the same study. In a study by Modi et al (2020) contribution of dengue was found to be 2.67% towards causes of thrombocytopenia [17].

In the present study we find out whether maternal thrombocytopenia also manifests in neonate or not. We found that there was statistically significant association between cause of maternal thrombocytopenia and presence of neonatal thrombocytopenia (P value= <0.001). Medical cause of maternal thrombocytopenia was highly associated with presence of neonatal thrombocytopenia. Out of 21 neonates born to mothers having medical causes of thrombocytopenia (ITP, dengue, HIV, HCV,hypersplenism), 77.8% neonates had thrombocytopenia. This percentage was the maximum observed as compared to other causes of thrombocytopenia like gestational or obstetrics. 11/70 (15.8%) neonates born to mothers having thrombocytopenia due to obstetrics causes (hypertension, DIC, abruptio placentae

We also found that there was no association (P Value= 0.080) between maternal thrombocytopenia with severity of neonatal thrombocytopenia. Salnlo *et. al* (2000) found that there was no association between maternal and fetal platelet counts of the infants born to thrombocytopenic mothers, 2.1% had thrombocytopenia in the cord blood, which did not differ significantly from the 2.0% of thrombocytopenic infants born to non-thrombocytopenic mothers [24]. Onisai M. *et al* (2012) in their retrospective study on perinatal outcome for pregnancies complicated with thrombocytopenia concluded that thrombocytopenia in pregnancy was associated with perinatal morbidity with the strongest association for preeclampsia and HELLP syndrome for both prematurity and low-birth-weight, the lower the platelet count, the higher the risks for the fetus/newborn. Highest risk for severe thrombocytopenia (RR=8.69, p.value<0.01) in case of premature delivery and it is also a risk factor for low- birth-weight newborns, especially severe thrombocytopenia (p=0.02) [25]. Modi *et al* (2020) in their study found that 60% were term neonates and 40% were preterm neonates born to thrombocytopenic mothers [17]. So out of 158, we found that maximum 69.62% were term deliveries while 30.37% were preterm deliveries, 20.8% were LBW infants, 12.05% were SGA babies, 8.2% required SNCU admission, 1.2% required NICU admission for assisted ventilation and there was 0.6% neonatal death. There was no statistically significant difference in the perinatal outcomes and the causes of thrombocytopenia in our study. There was no bleeding complications like intracranial hemorrhage in any neonate in our study thus suggesting the rarity of bleeding manifestations even in neonates having thrombocytopenia. These results were similar to another study where mortality rate in a neonate (<1%) and chances of intracranial hemorrhage in a neonate range from 0-1.5% [30]. Madge et al [201] found that 54.5% babies in HELLP group had an abnormal perinatal outcome as opposed to 24.6% in non-HELLP group [21]. It suggests that adverse perinatal outcomes are more in hypertensive females as compared to gestational thrombocytopenia. These results were in accordance with our study where LBW and SGA infants requiring SNCU/NICU admission were more in obstetrics group as compared to gestational and medical thrombocytopenia group. One neonatal death seen in our study also belonged to obstetrics group.

These adverse perinatal outcomes were found in rare causes of thrombocytopenia such as disseminated intravascular coagulation (DIC), familial thrombotic thrombocytopenic purpura (TTP), anti-phospholipid antibodies (APLA) syndrome, and myeloproliferative disease, and not among patients with GT [31]. In our study we found that postpartum hemorhage was the most common complication (28.2%). Modi *et al* (2020) found that postpartum hemorrhage occurred in 22.67% of pregnant females having thrombocytopenia. In a similar study conducted by Nisha *et al* (2012), it was found that the percentage of PPH in cases of thrombocytopenia was 9.89% [7]. PPH was the most common complication in many studies like Huparikar A. *et al* (2016) [22]. In a study by Tasneem *et al* (2020), 8.6% cases with PPH were observed, all were atonic [26]. Sumathy et al found that atonic PPH occurred in 17.1.% patients [27]. PPH was observed in 4.3% cases by Arora *et al* (2019)[28]. We found that out of 45 subjects who had PPH, 16 8iig massage/ carboprostol or methergine. 28 (62%) subjects underwent balloon tamponade insertion to control bleeding and 1(2%) subject who had massive hemorrhage required hysterectomy. All were due to atonicity of uterus. These results were similar to other studies like Tasneem *et al* (2020) and Sumathy *et al* (2019) [26,27] In our study, 7 (4.4%) subjects had abruptio placentae, 8 (12.7%) had DIC and 13 (8.2%) had multiorgan dysfunction. Tasneem *et al* (2020) [26] observed 8.7% cases had DIC and 8.7% had MODS as complications due to thrombocytopenia, no case of placental abruption were

found. Sibai e*t al (1993)* [29] found 13.6% DIC and placental abruption in 16%, Sumathy *et al* (2019) [27] found DIC in 2.1% cases.

In this study we found 3/158 (1.89%) subjects had surgical site infection and vaginal hematoma was also found in 3/158 (1.89%). Arora *et al* (2019) got 3.6% wound gape [28], Sumathy *et al* got 1% incision site oozing [27], Tasneem *et al* (2020) got 2.7% vaginal hematoma [26]. There was no cerebral bleeding as seen in studies like Audibert *et al* (1996) [32] where 15% cerebral bleeding was seen in thrombocytopenic subjects and Tasneem *et al* (2020) where 1 case (2.1%) was seen ofintracranial venous thrombosis [26]

We found that 79/158 (50%) subjects did not have any kind of complication in our study. We found that 3/158 (1.8%) subjects expired. All three subjects delivered normally and required platelet transfusion in the peripartum period. 2/3(66.66%) mortalities were from obstetric group (1 was diagnosed as HELLP and 1 suffered from disseminated intravascular coagulation). 1/3 (33.33%) mortality was from medical group diagnosed with dengue infection. All three subjects who expired had severe thrombocytopenia suggesting high percentage of severity of thrombocytopenia with maternal mortality. There was no mortality in subjects of gestational thrombocytopenia. In a similar study by Madge et al (2019) found that 11.6% maternal mortality was observed in HELLP syndrome group as compared to group having only preclampsia without HELLP [21]. Nisha et al (2012) found 5.26% mortality rate in thrombocytopenic cases out of which, 14.29% were due to obstetric causes and 15.38% were due to medical causes [7]. It can be inferred that mortality in thrombocytopenia may be due to associated complications like DIC, MODS, massive hemorrhage, associated anemia, etc.

We aimed to establish a correlation between the severity of thrombocytopenia and etiological factors contributing to it and found that in gestational thrombocytopenia, 51/67 (76.11%) had mild and 16/67 (23.8 %) had moderate thrombocytopenia and the results were statistically significant (p value 0.001). In cases of obstetric thrombocytopenia 35/70 (50%) subjects had moderate thrombocytopenia while 20% and 30% were from mild and severe thrombocytopenic groups and the results were statistically significant (p value 0.001). statistically significant results were obtained in subjects of medical causes of thrombocytopenia where 10/21 (47.6%) had moderate thrombocytopenia while 9/21 (42.85%) had severe thrombocytopenia (p value 0.001). Discussing about the severity of thrombocytopenia and adverse maternal outcomes, statistically significant (p value <0.05) results were obtained in outcomes like PPH, MODS and DIC. Subjects who suffered fromcomplications like DIC and MODS did not have mild thrombocytopenia at all suggesting a positive association between severity of thrombocytopenia and outcomes like PPH, MODS and DIC. Similar results were found in a study by Vyas *et al* (2014), where it was found that maternal bleeding complications are higher in cases of moderate to severe thrombocytopenia [33]. When we analysed perinatal outcomes according to severity of maternal thrombocytopenia, we found statistically significant association between severity and outcomes like preterm birth, LBW, SGA infant and SNCU admission of neonates. 34/48 (70.8%) preterm neonates had mild maternal thrombocytopenia, 10/48 (20.8%) preterm neonates had moderate maternal thrombocytopenia and 4/48 (8.3%) preterm neonates had severe maternal thrombocytopenia (p value 0.002). 19/33 (57.57%) LBW neonates had moderate maternal thrombocytopenia, 10/33 (30.30%) had severe maternal thrombocytopenia while 4/33 (12.1%) had mild maternal thrombocytopenia (p value0.004) 10/19 (52.63%) SGA neonates had moderate maternal thrombocytopenia, 6/19 (31.50%) had severe maternal thrombocytopenia while 3/19 (15.78%) had mild maternal thrombocytopenia (p value 0.038). 7/13 (53.84%) neonates who required SNCU admission had severe maternal thrombocytopenia and 6/13 (46.15%) had severe thrombocytopenia. Neonates of mothers having mild thrombocytopenia did not require SNCU admission. (p value 0.002). Similar results were found in a study conducted by Vyas *et al* (2014) who compared mild thrombocytopenia versus moderate to severe thrombocytopenia and concluded that fetal complications were higher in cases of moderate to severe thrombocytopenia. He also found that gestational thrombocytopenia and ITP had favorable outcomes for newborns [33].

For prompt diagnosis and to ensure a positive fetomaternal outcome during gestation and delivery, platelet count should be performed as a routine laboratory test during antenatal care visits. Women with severe thrombocytopenia should receive the appropriate attention during childbirth in order to avoid bleeding problems [34]

Conclusions

In our study there was significant association between cause of maternal thrombocytopenia and presence of neonatal thrombocytopenia. Medical cause of maternal thrombocytopenia was highly associated with presence of neonatal thrombocytopenia. No association between cause of maternal thrombocytopenia and severity of neonatal thrombocytopenia. There were no NICU admission/neonatal deaths in neonates of mothers with gestational thrombocytopenia The association between perinatal outcomes and causes of thrombocytopenia was not statistically significant.

Our findings suggest that evaluation of thrombocytopenia in pregnancy is important and a detailed

workup with careful monitoring is required as early diagnosis and management may play a key role in decreasing the adverse outcomes. Special attention should be given to patients with thrombocytopenia due to preeclampsia and HELLP syndrome to establish the best moment for therapeutical intervention.

Conflict of Interest: No conflict of interest

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