

A COMPARATIVE OBSERVATIONAL STUDY TO EVALUATE MATERNAL MORBIDITY IN PREGNANT FEMALES WITH AND WITHOUT THROMBOCYTOPENIA DURING DELIVERY OVER A PERIOD OF ONE YEAR IN A TERTIARY CARE HOSPITAL.



Gynaecology

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ABSTRACT

INTRODUCTION: W.H.O lists hemorrhage as the most common cause of maternal death. Thrombocytopenia though occurring in miniscule of the pregnant women, gives rise to serious maternal and neonatal complications if not detected or attended to.

OBJECTIVE: A comparative observational study to evaluate maternal morbidity in pregnant females with thrombocytopenia during delivery in comparison with pregnant females without thrombocytopenia over a period of one year in a Tertiary care hospital.

METHODS: Pregnant women with thrombocytopenia in labor were compared with the pregnant females without thrombocytopenia delivering consecutively, and evaluated for Mode of delivery, PPH, any need for blood and blood products, APH, DIC, MICU admission, maternal mortality, APGAR score, birth weight, meconium stained amniotic fluid, still birth, IUGR, NICU admission and neonatal mortality.

RESULTS: Association between qualitative variables was assessed by Chi-Square test, with Continuity Correction for all 2 X 2 tables and by Fisher's Exact test for all 2 X 2 tables where Chi-Square test was not valid due to small counts. Gestational thrombocytopenia was the most common cause of thrombocytopenia (48%). PPH was significantly higher in patients of thrombocytopenia when compared to patients of non-thrombocytopenia. (p-value 0.017). The rate of blood and blood products given to the pregnant patients with thrombocytopenia was high in the study as compared to the control group, and this was statistically significant.

CONCLUSIONS: Careful surveillance is required for pregnancies with thrombocytopenia for early detection and treatment of possible complications with multidisciplinary approach, in order to try to reduce maternal and neonatal morbidities.

KEYWORDS

Thrombocytopenia In Pregnancy, Gestational Thrombocytopenia.

INTRODUCTION

Thrombocytopenia, defined as platelet count less than $150,000 \mu\text{L}^{-1}$ is a common hematological disorder. It is second only to anaemia as the most common hematological abnormality in pregnancy⁽¹⁾. It usually results in bleeding into mucus membranes presenting as petechiae, echymoses, epistaxis, gingival bleeding etc. However, bruising, hematuria, gastrointestinal bleeding and rarely intracranial haemorrhage can also occur.

The incidence of thrombocytopenia in pregnancy is 6 - 8%.⁽²⁾ Thrombocytopenia in pregnant women may result from the effects of several diverse processes, which may be either physiological or pathological. Thrombocytopenia is divided according to severity into mild ($\geq 100,000$ to $< 150,000 \mu\text{L}^{-1}$), moderate ($\geq 50,000$ to $< 100,000 \mu\text{L}^{-1}$) and severe ($< 50,000 \mu\text{L}^{-1}$) thrombocytopenia.

The majority of thrombocytopenic pregnant women are healthy, and have no history of thrombocytopenia, and is incidentally diagnosed. This condition, called incidental or Gestational thrombocytopenia (GT), usually has no influence on pregnancy, labour & delivery or on the newborn. GT accounts for about 75% cases of thrombocytopenia during pregnancy. It is defined by a platelet count of $70 \times 10^9 / \text{L}$, especially during third trimester of pregnancy, and the count returns to normal within 12 weeks of delivery. There may not be a risk of severe haemorrhage in GT, but other causes such as pre eclampsia, HELLP syndrome and ITP (Immune Thrombocytopenic Purpura) expose mother and child to potentially life threatening complications. Other rare causes of thrombocytopenia like Thrombotic thrombocytopenic purpura (TTP), Haemolytic uremic syndrome (HUS), disseminated intravascular coagulopathy (DIC) and vonWillebrand disease IIB (vWD IIB), Infections like Dengue, are also associated with severe complications.

In the following study, we have compared pregnant women with and without thrombocytopenia during labour, in terms of maternal and neonatal morbidity and mortality, so that careful surveillance for these pregnancies can be taken up in high risk units for early detection and treatment of the possible complications.

STUDY DESIGN: A Comparative observational study.

SAMPLE SIZE: 100.

DURATION OF STUDY: 1 year.

STUDY POPULATION:

Pregnant women with thrombocytopenia delivering during the study period were be the study population and pregnant women without thrombocytopenia delivering consecutively will be the control group.

INCLUSION CRITERIA:

- Pregnant women with thrombocytopenia during delivery.

EXCLUSION CRITERIA:

- Maternal cardiac diseases, Twins, fetal malformations.

ETHICAL COMMITTEE APPROVAL TAKEN.

METHODOLOGY

Pregnant women with thrombocytopenia delivering during the study period of one year in a tertiary care hospital were compared with the pregnant females without thrombocytopenia delivering consecutively, The following factors were evaluated -

- Mode of delivery, postpartum hemorrhage, any need for blood and blood products, placental abruption, DIC, Medical intensive care unit admission, maternal mortality.
- Maternal age, parity, gestational age and cause of thrombocytopenia.
- APGAR score at 1 and 5 minutes, birth weight, meconium stained amniotic fluid, still birth, IUGR, NICU admission and neonatal mortality.

RESULT AND ANALYSIS

Qualitative data was represented in form of frequency and percentage. Nominal type of Qualitative data included group category (Mothers With thrombocytopenia & Without thrombocytopenia), Religion of mothers, Gestation of Delivery, Mode of Delivery, MICU Admission, Neonatal Mortality, Blood Transfusion, etc.

Association between qualitative variables was assessed by Chi-Square test, with Continuity Correction for all 2 X 2 tables and by Fisher's Exact test for all 2 X 2 tables where Chi-Square test was not valid due

to small counts. In presence of small counts, in tables with more than two rows and/or columns, adjacent row &/or Column data was pooled & Chi-Square Test reapplied. Continuity Correction was applied for all 2 X 2 tables after pooling of data. Fisher's Exact test was applied for all 2 X 2 tables where p-value of Chi-Square test was not valid due to small counts, in spite of pooling of data (**E.g. Association between Neonatal Mortality & group category (Mothers With thrombocytopenia & Without thrombocytopenia)**).

Quantitative data was represented using mean $\pm$ sd and Median & IQR (Interquartile range).

Quantitative data included Age of the mothers, weight of the baby, day 1 Platelet Count & day 3 Platelet Count.

Analysis of Quantitative data between the two groups (Mothers with thrombocytopenia & without thrombocytopenia) was done using unpaired t-test if the data passed 'Normality test' or by Mann-Whitney Test if data failed 'Normality test'. (E.g. Comparison of age between Mothers with thrombocytopenia & without thrombocytopenia).

Results were graphically represented where deemed necessary.

Appropriate statistical software, including but not restricted to MS Excel, PSPP version 0.8.5 was used for statistical analysis. Graphical representation was done in MS Excel 2010.

Table 1 : Etiology Of Thrombocytopenia

Etiology of Thrombocytopenia	No.	Percentage
Gestational	24	48.0%
Preeclampsia	15	25.0%
ITP	5	10.0%
Dengue	3	6.0%
Apla positive	1	2.0%
Dilutional	1	2.0%
Jaundice	1	2.0%
Total	50	100.0%

ITP: immune thrombocytopenic purpura, **DIC:** disseminated intravascular coagulation, **TTP:** thrombotic thrombocytopenic purpura, **APLA:** antiphospholipid antibodies

In our study there were 100 pregnant women in labour, 50 of them were diagnosed with thrombocytopenia and remaining 50 were without thrombocytopenia.

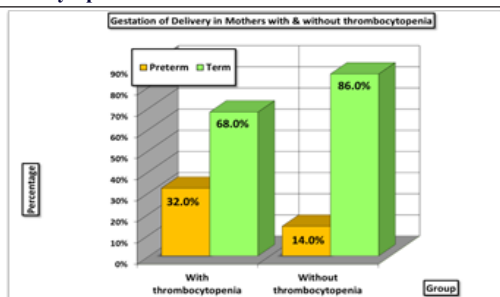
The etiology of thrombocytopenia in the study included: 24 (48%) women with Gestational thrombocytopenia, 15(25%) were with preeclampsia, 05 (10%) patients had ITP, 03(6%) had Dengue fever, 01 (2%) with Jaundice, 01(2%) with APLA syndrome, and 01(2%) with dilutional thrombocytopenia

Table 2 : Grades Of Thrombocytopenia

Grade of Thrombocytopenia	No.	Percentage
Mild	4	8.0%
Moderate	40	80.0%
Severe	6	12.0%
Total	50	100.0%

In the study 80% of the cases had moderate thrombocytopenia, 12% had severe thrombocytopenia and 8% had mild thrombocytopenia.

Chart 1: Gestation of Delivery in mothers with and without thrombocytopenia



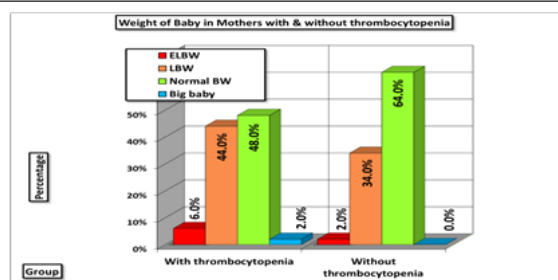
In the study 16 patients (68%) with thrombocytopenia had preterm delivery as compared to 7 patients in control group, the association being significant (p-value-0.047). Since the management of preeclampsia and HELLP syndrome includes early delivery of fetus, hence in patients with thrombocytopenia had preterm delivery.

Table 3 : Gravida Status

GRAVIDA STATUS	WITH THROMBOCYTOPENIA	PERCENTAGE	WITHOUT THROMBOCYTOPENIA	PERCENTAGE
PRIMIGRAVIDA	23	46%	21	42%
MULTIGRAVIDA	27	54%	29	56%

23(46%) patients in thrombocytopenia group were primigravida as compared to 21(42%) in control group and 27(54%) were multigravida in cases as compared to 29(56%) in the control group, with no significant association (p-value 0.840).

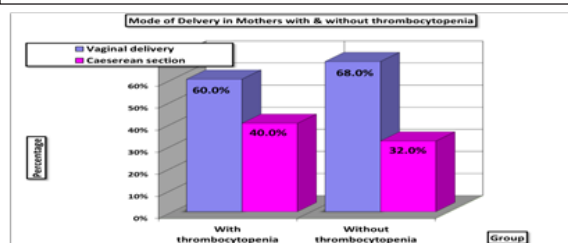
Chart No 2: Weight of Baby in mothers with and without thrombocytopenia



The number of cases with ELBW (<1kg), LBW (<2.5kg), Normal Bwt (above 2.5 kg) were 3, 22 and 14 respectively. There being no significant association between the cases and control group (p-value 0.226)

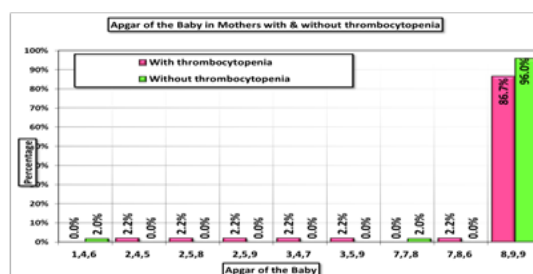
Women with thrombocytopenia were more likely to deliver preterm (< 0.001) as compared to non thrombocytopenic patients. Thrombocytopenia was significantly associated with preterm deliveries (weighted OR = 3.14, 95% CI = 1.7–6.03, p < 0.001). Gravida status of the mother and birth weight of the baby were not affected by thrombocytopenia.

Chart No 3: Mode of delivery



In the study, rate of vaginal delivery was 60 % in women with thrombocytopenia and 68 % in women without thrombocytopenia, whereas rates of caesarean section were 40 % and 32 %.

Chart No 4: Apgar of baby in mothers with & without thrombocytopenia

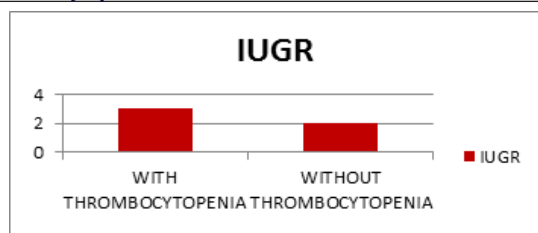


In the thrombocytopenia group, 6 patients had APGAR less than 8,9,9 as compared to 2 in non thrombocytopenia group, the association being not significant (p-value 0.144).

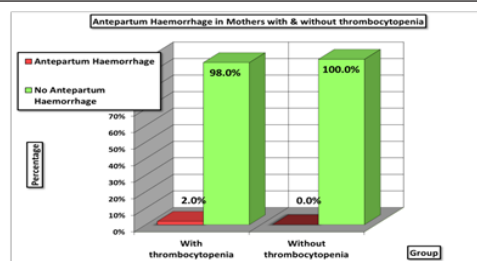
Table 4: Stillbirth In Patients With And Without Thrombocytopenia

	STILLBIRTH	PERCENTAGE
WITH THROMBOCYTOPENIA	5	10%
WITHOUT THROMBOCYTOPENIA	0	0%

5 cases of still birth were seen among the cases as compared to none in the control group, association being not significant.(p value-0.056). 4 of which were seen in patients with preeclampsia and HELLP.

Chart No 5 : IUGR in babies of patients with and without thrombocytopenia

3 cases had IUGR babies as compared to 2 among the control group, association was not significant (p value- 1). One out of the 3 was seen in preeclampsia and 2 were seen in ITP mothers.

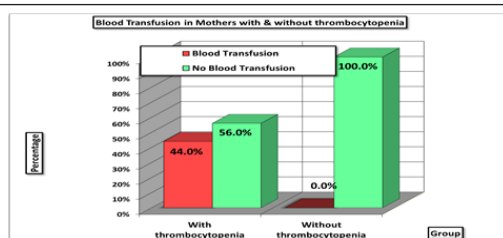
Chart No 6 : Antepartum haemorrhage

In our study, one patient among the cases had APH as compared to none in control group, association being not statistically significant. (p value 1).

Table 5: Post Partum Haemorrhage

	PPH	PERCENTAGE
WITH THROMBOCYTOPENIA	7	14%
WITHOUT THROMBOCYTOPENIA	0	0%

There were 7 patients in the thrombocytopenia group who had postpartum haemorrhage, as compared to none in non thrombocytopenic patients. The association was statistically significant (p value 0.012).

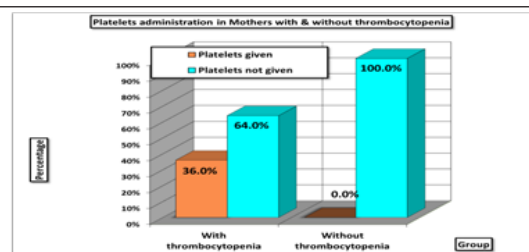
Chart No 7: Blood Transfusion in mothers with and without thrombocytopenia

22 cases required blood transfusion, as compared to none in controls. The difference being statistically significant (p value 3.99E-07).

Table 6: Ffp Transfusion

FFP TRANSFUSION	FFP TRANSFUSION	
WITH THROMBOCYTOPENIA	16	32%
WITHOUT THROMBOCYTOPENIA	1	2%

16 patients in the thrombocytopenia group required FFPs as compared to 1 in the non thrombocytopenic group. The association being statistically significant (p value – 0.00019).

Chart No 8 : Platelets transfusion

Platelet transfusion was given to 18 patients among the cases as compared to none in the controls, being statistically significant (p value 9.65E-06)

These data showed that requirement of transfusion of blood and blood products was significantly higher in thrombocytopenic group as compared to non- thrombocytopenic group.

DISCUSSION

Our study was aimed at investigating the maternal and fetal outcomes of pregnancies complicated by thrombocytopenia. Most cases of thrombocytopenia were caused by GT (48%). GT is known to be the most common cause of thrombocytopenia in pregnancy.

Other causes include ITP, Dengue, HELLP syndrome, jaundice, eclampsia, preeclampsia, and APLA syndrome, dilutional state (caused by blood transfusion). Similar results were also seen by Habas E et al⁽⁴⁾ And Keith R. McCrae et al⁽⁵⁾, these studies concluded that the Gestational thrombocytopenia (GT) is recognized as a major cause of thrombocytopenia in pregnant women. They recommended Careful follow up during and after pregnancy for these thrombocytopenic women.

Jefery A et al⁽⁶⁾ also concluded that, even if the so-called gestational thrombocytopenia is the most common etiology, a careful history and simple laboratory tests are needed in order not to miss a serious condition that may require specific and sometimes urgent treatment.

The major findings of our study were that thrombocytopenia points to a higher degree of severity of the primary disease (HELLP, preeclampsia, Dengue etc.), which is known to increase perinatal complications, both maternal and neonatal. Such complications include preterm deliveries, low birth weight, low Apgar scores ,still birth, NICU admissions, antepartum and post partum haemorrhage.

Higher rates of preterm deliveries (were observed among parturients with moderate to severe thrombocytopenia. Since the management of preeclampsia and HELLP syndrome includes early delivery of fetus, labour induction could be a confounder for this association. This might be the major cause of Foetal morbidity because of prematurity and low weight at delivery, similar to the study by Chaker A et al.⁽⁷⁾.

It is interesting that while dealing with thrombocytopenia, major bleeding requiring blood , FFP and platelet transfusion was significant, and occurred in 22,17,18 patients respectively. These patients had Preeclampsia, eclampsia or HELLP syndrome. It is probably the result of careful surveillance and treatment. Adverse perinatal outcome was mostly associated with preeclampsia, HELLP syndrome, and the group of rarer causes, including Dengue, APLA syndrome.

Our study stresses on the importance of screening all pregnant women routinely for thrombocytopenia to avoid excessive bleeding during or after childbirth. This could be managed properly if we are prepared of such complications because of routinely screening all pregnant women for thrombocytopenia. Similarly Ajibola SO et al⁽⁸⁾ concluded that although majority of the pregnant women had mild thrombocytopenia, healthcare providers should screen all pregnant women routinely for thrombocytopenia to avoid excessive bleeding during or after childbirth.

Habas et al⁽⁴⁾ concluded in his study that in pregnant patients with hypertension, thrombocytopenia is seen in the third trimester and careful surveillance is required. In our study total 15 cases had hypertension.

McCrae⁽⁹⁾ concluded that hypertensive disorders are associated with more severe cases of IUGR. The incidence of IUGR in pregnant women with HELLP syndrome compared with women without HELLP syndrome. Placental abruption, low Apgar scores, and stillbirth were found in the group of rarer causes.

Kunal et al⁽¹⁰⁾ suggested that APLA syndrome may be associated with recurrent neonatal losses, required blood and blood products and with strict vigilance had a favourable outcome, in our study we had one patient with APLA syndrome who had moderate thrombocytopenia and did not require blood or blood products to be given, nor had any postpartum complications. In general, non-thrombocytopenic group had a favourable pregnancy outcome in our analysis. In view of significantly low incidence of pre-term deliveries, PPH and Transfusion of blood and blood products

In our study we had 3 cases of thrombocytopenia seen in Dengue positive patients, all of them had moderate thrombocytopenia. 2 of them were admitted in MICU, 2 required FFPs, Platelets and blood transfusion, and one required platelets and blood transfusion. One Neonatal death was seen in view of ELBW and IVH (Intraventricular haemorrhage), other two babies were discharged without any complications. Carles G et al⁽¹¹⁾, in their study concluded that Dengue in pregnancy was associated with severe haemorrhagic complications, and preterm delivery. Chitra TV et al⁽¹²⁾ in their study observed that the patients with dengue could be managed conservatively in most of the cases.

So our study stresses the importance of routine screening all pregnant women routinely for thrombocytopenia and its cause to reduce the fetal morbidity and mortality.

Pregnancy can be uncomplicated even in those with severe thrombocytopenia during pregnancy when under the strict care of a haematologist and gynaecologist.

For most women with ITP, pregnancy is uncomplicated, and even those with severe thrombocytopenia during pregnancy have good outcomes when under the strict care of a haematologist and gynaecologist.

Weber et al⁽¹³⁾ found that the median age of women with ITP at the time of delivery was 29 years. Hence, it commonly affects women in the childbearing age group. Indeed, the mean maternal age in our whole population including all causes of thrombocytopenia (taken in our study) was 28 which were very similar to that in the above study.

CONCLUSION

In conclusion, the common cause of moderate to severe thrombocytopenia in pregnancy is mainly GT, while ITP, preeclampsia, and HELLP syndrome are less common. Patients with thrombocytopenia are significantly associated with Careful surveillance is required for these pregnancies in high-risk units for early detection and treatment of possible complications, in order to try to reduce maternal and neonatal morbidities.

Further prospective studies among these populations with moderate to severe thrombocytopenia should investigate the efficacy of possible surveillance programs

References

- 1) Williams obstetrics 24th edition (2014): chapter 4, pg 57.
- 2) Sullivan CA, Martin JN., Jr Management of the obstetric patients with thrombocytopenia. Clin Obstet Gynecol. 1995;38:521-534. doi: 10.1097/00003081-199509000-00011.
- 3) Saino S, Keomaki R, et al. Maternal Thrombocytopenia: a population based study. Acta Obstet Gynecol Scand. 2000;79:744-9.
- 4) Habas E, Rayani A, Ganter R (2013). Thrombocytopenia in hypertensive disease of pregnancy. J Obstet Gynaecol India. 2013 Apr;63(2):96-100.
- 5) Parnas, Michal, et al. "Moderate to severe thrombocytopenia during pregnancy." European Journal of Obstetrics & Gynecology and Reproductive Biology 128.1 (2006): 163-168.
- 6) Levy JA, Murphy LD. Thrombocytopenia in pregnancy. J Am Board Fam Pract. 2002 Jul Aug;15(4):290-7.
- 7) Chaker A, Ferchiou M, Lahmar MM, Boubaker M, Zhioua F, Meriah S, Hafsia A. Management of severe thrombopenia in pregnancies and labor. Report of 14 cases and review of the literature. Tunis Med. 2004 Oct;82(10):941-6.
- 8) Ajibola SO, Akinbami A, Rabiu K, Adewunmi A, Dosunmu A, Adewumi A, Oskomaiya B, Ismail K (2014) Gestational thrombocytopaenia among pregnant women in Lagos, Nigeria. Niger Med J. 2014 Mar;55(2):139-43
- 9) McCrae KR Thrombocytopenia in pregnancy: differential diagnosis, pathogenesis, and management. (2003) Blood Reviews :Volume 17, Issue 1, Pages 7-14, doi.org/10.1016/S0268-960X(02)00056-5.
- 10) Kunal Mahajan, Virender Katyal, Suvrat Arya, and Meha Shrama, —Antiphospholipid

Syndrome in a Pregnant Female Presenting with Severe Thrombocytopenia and Bleeding. J Case Reports in Medicine, vol. 2015, Article ID 234878, 3 pages, 2015. doi:10.1155/2015/234878.

- 11) Carles G, Talarmin A, Peneau C, Bertsch M. Dengue fever and pregnancy. A study of 38 cases in French Guiana J Gynecol Obstet Biol Reprod (Paris). 2000 Dec;29(8):758-762.
- 12) Chitra TV, Panicker S. Maternal and fetal outcome of dengue fever in pregnancy. J Vector Borne Dis. 2011 Dec;48(4):210-3.
- 13) Weber KE, Mittal R, Sigouin C, Hedde NM, Kelton JG A retrospective 11-year analysis of obstetric patients with idiopathic thrombocytopenic purpura. Blood. 2003 Dec 15;102(13):4306-11. Epub 2003 Aug 28.