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A PROSPECTIVE STUDY ON THROMBOCYTOPENIA: COMMON CAUSES, ITS MATERNAL AND FETAL OUTCOME IN A TERTIARY CARE CENTRE.

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ABSTRACT **Aim:** To identify the various causes of thrombocytopenia in pregnant women and to analyze the maternal and fetal outcome of pregnancy with thrombocytopenia. **Method:** This is a prospective study and was conducted over a period of 1 year from December 2019 to December 2020. It included all pregnant women with Thrombocytopenia detected after 28 weeks of gestation. All the mothers were followed up throughout the antenatal period till delivery for any complications that developed due to low platelet count. Maternal outcome and neonatal outcome were documented. **Result:** The commonest cause for thrombocytopenia among mothers was gestational thrombocytopenia 68.75% with least impact on feto-maternal outcome. In our study Antepartum hemorrhage was encountered in 5%.and PPH in 23.75%. There were 2 neonatal deaths. **Conclusion:** Patients with GT and ITP have better maternal and perinatal outcomes as compared to preeclampsia and HELLP syndrome, which are associated with adverse feto-maternal outcome. Favorable feto-maternal outcome is possible with early diagnosis, proper evaluation and careful surveillance.

KEYWORDS : Thrombocytopenia, Platelet Count, Feto-maternal Outcome.

INTRODUCTION

Platelets are non-nucleated cellular fragments of megakaryocytes responsible for maintaing hemostasis. . The normal reference range of platelets in non- pregnant women is 150 -400x 109/L. Due to hemodilution , platelet count may drop during 3rd trimester,though absolute platelet count remains within normal reference range in most patients. Decrease in the platelet count is usually caused by accelerated platelet destruction or decreased production. The normal increased splenic mass characteristic of pregnancy may also have a contributory effect . Most of the evidence shows that the life span of platelets remain unchanged in normal pregnancy.

Thrombocytopenia, defined as a platelet count of less than 150 × 10/L, is common and occurs in 7-12% of pregnancies at the time of delivery.1 Thrombocytopenia can be classified as mild with a platelet count of 100–150x 109/L, moderate at 50–100 x 109/L, and severe with less than 50 x 109/L.

Thrombocytopenia in pregnancy can be isolated or associated with systemic disorders like severe preeclampsia, HELLP syndrome (hemolysis, elevated liver enzymes, low platelets), or AFLP (acute fatty liver of pregnancy). Furthermore, autoimmune diseases, including systemic lupus erythematosus, anti-phospholipid syndrome, thrombotic thrombocytopenic purpura, hemolytic uremic syndrome, and immune thrombocytopenia (ITP) may relapse or be first detected during pregnancy.

Gestational thrombocytopenia is considered as the most common cause of thrombocytopenia , accounting for about 75% of cases . It is characterised by incidental identification of mild to moderate reduction in platelet count during pregnancy in healthy women with no previous history of thrombocytopenia or conditions known to be associated with thrombocytopenia. There is no significant fetal or maternal morbidity in this entity and platelet count reaches a value within normal range postpartum in vast majority of patients.

Rest of the 25% of cases include other causes like Pre-eclampsia/ HELLP syndrome , immune thrombocytopenic purpura , infections like malaria , dengue ,obstetric DIVC , hemolytic anaemia ,thrombotic angiopathies (TTP), SLE . Confirmation of normal platelet count prior to pregnancy decreases the probability of underlying immune thrombocytopenia purpura. ITP has to be differentiated from gestational thrombocytopenia in women with pregnancy. The latter usually develops in the late second or third trimester of pregnancy and the platelet counts rarely fall below 70 X 109/L. ITP on the other hand is a diagnosis of exclusion. In the presence of a previous history of thrombocytopenia, an underlying autoimmune condition, and platelet count < 50 X 109/ L, ITP is the most probable cause of thrombocytopenia.2

We carried out the present study to see the causes of thrombocytopenia during pregnancy, and its effect on feto-maternal outcome.

MATERIALS AND METHODS

The objective of our study was to identify the various causes of thrombocytopenia in pregnant women and to analyze the maternal and fetaloutcome of pregnancy with thrombocytopenia .

This is a prospective study and was conducted over a period of 1 year from December 2019 to December 2020 .It included all pregnant women with Thrombocytopenia detected after 28 weeks of gestation ,attending the outpatient clinic and admitted as inpatients in the Department of Obstetrics and Gynaecology, Government thoothukudi medical college hospital after approval from Institutional human ethical committee and obtaining informed consent from the pregnant women . Patients on certain drugs like steroid, NSAIDS , antibiotics like cephalosporins, sulfonamides , vancomycin , antiepileptic drugs , aspirin and anticoagulants were excluded from the study.

Antenatal mothers were enrolled in this study at the first visit , when low platelet count was detected. All women had a platelet count estimation at the time of enrollment. Detailed workup of all cases of thrombocytopenia was done to ascertain the causative factor .History of gum bleeding, easy bruising, petechiae, viral infection, drug usage, thrombocytopenia in previous pregnancy elicited in detail. General,systemic and obstetric examination done to find out signs of thrombocytopenia and its effects if any .All women were subjected to blood tests for Complete blood count including hemoglobin, TLC, DLC, peripheral smear with manual platelet count, blood sugar, urea, creatinine, LFT, coagulation profile, HIV, VDRL ,HBsAg and urine analysis.Women with fever were tested for Dengue IgM.

All the mothers were followed up throughout the antenatal period till delivery for any complications that developed due to low platelet count. Intra partum events (mode of delivery, APH, associated GHT, fever) and post partum events (PPH, wound infection ,subinvolution of uterus) were documented . The neonatal characteristics such as gestational age at birth, viability of baby, APGAR score, birth weight at birth, IUGR, neonatal thrombocytopenia and bleeding tendencies in neonates were documented.

RESULTS

Table – 1 Causes Of Thrombocytopenia

CAUSES	NO OF CASES	PERCENTAGE
GESTATIONAL	55	68.75%
PET	7	8.75%
HELLP	5	6.25%
PARTIAL HELLP	5	1.25%
ITP	2	2.50%
DIC	1	1.25%

DENGUE	3	3.75%
OTHERS	2	2.5%

Of the 4485 deliveries in the period from December 2019 to December 2020, 80 cases of thrombocytopenia were analyzed in our study totally.out of the 90 cases enrolled in our study, 6 cases had a normal platelet count in manual platelet count. Hence taken out of the study. 2 had platelet clumps in peripheral smear. They were labelled pseudo thrombocytopenia and they were removed too.2 cases were lost for follow up after COVID outbreak. In this study , out of 80 cases of thrombocytopenia in the study, 55 cases belonged to gestational thrombocytopenia (68.75%) and the rest were due to pre-eclampsia and its complications , ITP,DIC and dengue. ITP is the second most common cause of thrombocytopenia in pregnancy after gestational thrombocytopenia and affects 1–2 cases per 10,000 pregnancies in our country There are very few studies on the outcome of pregnancy in Indian women with ITP2.

Table -2 Maternal Thrombocytopenia And Its Outcome

MATERNAL OUTCOME	NO OF CASES	PERCENTAGE
MODE OF DELIVERY		
NORMAL DELIVERY	27	33.75%
LSCS	52	65%
INSTRUMENTAL DELIVERY	1	1.25%
ANAESTHESIA USED		
REGIONAL	43	83%
GENERAL	9	17%
OTHERS		
ANTEPARTUM HAEMORRHAGE	4	5%
PRIMARY PPH	15	18.75%
SECONDARY PPH	3	3.75%
PRIMARY AND SECONDARY PPH	1	1.25%
PLATELET TRANSFUSION	21	26.25%
WOUND INFECTION	4	5%
> 7 DAYS HOSPITAL STAY	53	66.25%
MATERNAL MORTALITY	0	0

The above table summerises the maternal charecteristics such as mode of delivery , bleeding manifestations , blood and component transfusions, maternal morbidity and mortality.

In our study, 65% of pregnant mothers with thrombocytopenia were delivered by LSCS (maternal indication – 35 cases and fetal indication – 17 cases). 17 % of LSCS mothers required general anaesthesia considering the severity of thrombocytopenia.

Bleeding manifestations like antepartum hemorrhage and post-partum hemorrhage were studied. Antepartum hemorrhage was encountered in 4 mothers (5%). The incidence of APH in our study is in agreement with a study by Arora et al (6.6%).2

One of them had DIC for which she required blood and component therapy. In our study 23.75 % (19 cases) of thrombocytopenia mothers had PPH .15 mothers had primary PPH and 3 mothers had secondary PPH. A mother who was a case of twin gestation complicated by HELLP syndrome, had both primary PPH in the immediate post-partum period and secondary PPH at 19 th postpartum day and was treated with blood and component therapy. Out of the 80 mothers, almost 71 of them required steroids in one form or the other. 21 mothers (26.25%) required transfusion of platelet concentrates.5 cases required FFP and 2 of them needed all the blood components in our study.

Maternal morbidity in the form of surgical site wound infection and secondary suturing was done in 4 cases(5%). Out of 80 mothers, 53 mothers had a hospital stay of > 7 days. 3 patients had a longer stay of > 28 days . They were cases of severe pre eclampsia with LSCS wound site hematoma, LSCS wound gaping and a mother who had both primary PPH and secondary PP. There were no maternal death in our study.

Table -3 Platelet Count At Delivery And PPH Incidence

PPH	1-1.5 L	50,000- 1 L	<50,000	P-VALUE
PRIMARY (15)	8(53%)	4(27%)	3(20%)	0.024
SECONDARY(3)	0	3(100%)	0	
NO PPH (41)	41 (67%)	18(29%)	2 (3%)	
BOTH (1)	0	1(100%)	0	
TOTAL	49	26	5	

Out of the PPH cases, 53 % of mothers had platelet count of 1 – 1.5 lakh. 27% of mothers had platelet count of 50000-1 lakh. 20 % had platelet count of less than 50000. Among the 17 hypertensive cases complicated by thrombocytopenia, 7 patients had PPH

Table 4 Maternal Thrombocytopenia And Fetal Outcome

NEONATAL OUTCOME	NO OF CASES	PERCENTAGE
GESTATIONAL AGE AT BIRTH		
TERM	64	73.6%
PRETERM	19	21.84%
LATE PRETERM	4	4.6%
VIABILITY		
ALIVE	84	97.7%
DEAD	3	3.4%
APGAR		
< 7	1	1.19%
>7	83	98.8%
BIRTH WEIGHT		
< 2.5 KG	12	13.8%
>2.5 KG	75	86.2%
OTHERS		
IUGR	15	17.2%
THROMBOCYTOPENIA	2	2.4%
BLEEDING TENDENCY	3	3.4%
COMPONENT TRANSFUSION	2	2.3%
PERINATAL MORTALITY	4	4.59%

N= 87

In our study population there were 7 sets of twins. Hence the total number of newborns in our study is 87. Of them , 1 was an intrauterine death and there were 2 cases of early neonatal deaths.

The neonatal characteristics such as gestational age at birth, viability of baby, APGAR score, birth weight at birth, IUGR, neonatal thrombocytopenia and bleeding tendencies are summarized in the table above.

In our study, 26.44% (23 neonates) of neonates were born preterm. Hence gestational age at delivery also has an influence on the neonatal outcome.

84 newborn required NICU admission. None stayed in NICU for more than1 month. There were 2 neonatal deaths. Newborns of mothers with HELLP and ITP were in NICU little longer. Neonates of hypertensive mothers were admitted for basic evaluation and were discharged on day 4. 10 % required NICU admission for more than 1 week.

There were 15 IUGR babies. Of them 13 were neonates of hypertensive mothers. There were 2 newborns with low platelet count at birth . of them one was < 1.5 lakh and the other was < 50,000. There were bleeding tendency in 3 babies (3.75%). Upper GI bleed in 2 babies and oral mucosa bleed in 1 baby.of them 2 babies required platelet transfusion. The number of neonates with thrombocytopenia is in agreement with study by Arora et al (4.3%).3

Our study had some limitations and potential biases, mainly because our hospital is tertiary care referral hospital and referral bias cannot be excluded. Also Gestational age at delivery acts as a confounding factor in our study in respect to the fetal outcome. A majority required timely termination for obstetric indication resulting in high preterrm birth. Maayan –Metzger et al conducted a retrospective study with 723 pegnant women and confirmed it4. The size of the present study is small, and a larger study is required to validate our findings.

CONCLUSIONS

The analysis in our study showed that the commonest cause for thrombocytopenia among mothers was gestational thrombocytopenia 68.75% with least impact on feto-maternal outcome. The second commonest cause was pre-eclampsia and its complications with guarded feto-maternal outcome.

26.43% of our study population had bleeding manifestations in the form of APH and PPH with most of them requiring platelet and other

component transfusion. Management of these patients is a challenge as it is associated with potential risks of maternal bleeding episodes and neonatal thrombocytopenia. Favorable feto-maternal outcome is possible with early diagnosis, proper evaluation and careful surveillance.

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