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RESEARCH ARTICLE

MATERNAL AND FOETAL OUTCOMES IN PREGNANCY WITH GESTATIONAL THROMBOCYTOPENIA: A PROSPECTIVE OBSERVATIONAL STUDY

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Abstract

Thrombo cytopeniais second to anaemia as the most common hematological abnormality during pregnancy. Accurate etiological diagnosis is essential for optimal therapeutic management and thus can prevent maternal and fetal morbidity and mortality.

Aim &Objective: To study the clinical profile, maternal and perinatal outcomes in thrombocytopenic antenatal patients.

Design: This Prospective observational study design was carried out in the department of obstetrics and gynecology at Chalmeda Anand Rao Institute of Medical sciences Karimnagar, over a period of 18 months from October 2020 to April 2022.

Materials And Methods: All the pregnant women who attended antenatal OPD at Chalmeda Anand Rao Institute of Medical Sciences were tested for thrombocytopenia. 70 pregnant women with thrombocytopenia, platelet count lessthan 150x 10^9 /L and 70 pregnant women with normal platelet count were recruited into the study and the maternal & Fetal outcomes of both groups were studied and compared.

Results: Gestational thrombocytopenia is the most common etiology (57.1%). Incidence of thrombocytopenia due to severe preeclampsia and Hemolysis, Elevated Liver enzymes, Low Platelet (HELLP) syndrome in the study group was 28.5% and 8.5% of them had medical cause like malarial or dengue fever. Major causes were gestational thrombocytopenia (GT), Idiopathic Thrombocytopenic Purpura (ITP), Preeclampsia, HELLP syndrome, Malaria, and Dengue. Maternal complications due to bleeding tendencies like placental abruption, Postpartumhemorrhage were evident in the study population. Fetal complications were significantly higher in the study group. Early neonatal thrombocytopenia depended on etiology rather than severity of maternal thrombocytopenia.

Conclusions: Outcome of pregnancy with moderate to severe thrombocytopenia dependsmainly on the etiology of thrombocytopenia. Adverse outcomes are especially seen with pregnancy complicated by preeclampsia and HELLP syndrome. Fetomaternal outcome is favorable in gestational thrombocytopenia. Thus, accurate etiological diagnosis is essential for optimal therapeutic management.

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Introduction:-

Thrombocytopenia is second to anaemia as the most common hematological abnormality during pregnancy. Thrombocytopenia is defined as a platelet count below $150x10^{9L}$, caused by accelerated platelet destruction or decreased production. It is classified as mild with a platelet count of $100\text{-}150x\ 10^{9L}$, moderate at $50\text{-}100 \times 10^9$/L and severe with less than $50x\ 10^9$/L. The prevalence of platelet count of less than $150x\ 10^9$ /L in the third trimester of pregnancy is 6.6 to 11.6% [1-3]. A platelet count of less than 100×10^9/L is defined as thrombocytopenia by the international working group is observed in only 1% of pregnant women [6]. The normal range of platelets in non pregnant women is 150×10^9- $400\ x10^9$/L.

Causes of thrombocytopenia during pregnancy can be :
1. Pre existing to pregnancy most common Idiopathic Thrombocytopenic Purpura (ITP).
2. Decreased platelet count or newly discovered thrombocytopenia in pregnancy which may or may not be related to pregnancy.
3. Acute onset of thrombocytopenia in cases of severe preeclampsia, Hemolysis, Elevated Liver enzymes, Low Platelet (HELLP) syndrome or Acute Fatty Liver of Pregnancy (AFLP)[2].

Pregnancy is associated with a physiological fall in platelet count with leftward shift in distribution [11]. It can result from various mechanisms like hemodilution and accelerated clearance. Incidental or gestational thrombocytopenia occurs in approximately 8% of all pregnancies and is the reason for 70 to 80% of cases of thrombocytopenia of pregnancy [5]. Although, the pathophysiology is not clear it may be because of increased activation, increased peripheral consumption and increased platelet aggregation driven by increase levels of thromboxane A_2[4]. No confirmatory diagnostic test is available and it is the diagnosis of exclusion and occurs in mid second to third trimester.

Thrombocytopenia is typically asymptomatic, mild to moderate with twothird women have platelet count 130 - 150 $x10^9$L and never less than 70 $x10^9$L [3]. There is usually no past history of thrombocytopenia (except during previous pregnancy), resolves spontaneously within 1 -2 months of delivery and does not lead to thrombocytopenia in newborn but may recur in subsequent pregnancy. The main competing diagnosis to gestational thrombocytopenia is ITP.

Pre-pregnancy thrombocytopenia and response to immune modulation with steroids and immunoglobulin favors ITP. Unfortunately, there are no laboratory tests to differentiate between the two conditions[6]. ITP seen in 5% of cases of thrombocytopenia in pregnancy is characterized by a moderate to severe decrease in the platelet count, due to platelet auto-antibodies. ITP patients with severe thrombocytopenia require treatment due to risk of maternal hemorrhage and also risk of neonatal thrombocytopenia.

Preeclampsia and HELL syndrome is the second most frequent cause ofthrombocytopenia in late second and third trimester, accounting for 21% of cases of thrombocytopenia at the time of delivery [9].

It affects 5 to 8% of pregnant women and is defined withhypertension BP> 140/90 mm Hg, proteinuria (20.3g in 24 hrs) after 20 weeks of gestation [8]. Coagulation abnormalities are rare if platelet count is more than 100×10^9/ L. Maternal platelet count return to normal within 3 to 5 days of delivery, it is responsible for maternal mortality and still birth as a result of placental abruption and preterm delivery.

AFLP is a rare but life threatening complication of third trimester of pregnancy (1 in 20,000 pregnancies) characterized by elevated liver enzymes, conjugated bilirubin > 5mg/di and coagulopathy. AFLP with thrombocytopenia has overlapping features with HELLP.

Other etiologies of thrombocytopenia are rare, e.g.ThromboticThrombocytopenic purpura (TTP), Hemolytic Uremic Syndrome (HUS), Disseminated Intravascular Coagulopathy (DIC), Systemic Lupus Erythematosus (SLE), Anti PhospholipidsAntibody (APLA) and drug induced [9].

Basic laboratory evaluation of thrombocytopenia of pregnancy recommended is Complete Blood Count (CBC), reticulocyte count, blood smear, liver function test, viral screening (HIV, HCV, and HBV) [10]. Tests to be considered if clinically indicated are anti phospholipid antibodies, antinuclear antibodies, thyroid function test, H. pylori testing, DIC testing, VWB type testing, Direct Coombs test. Present study was carried out to determine

various etiologies of maternal thrombocytopenia, their complications and fetomaternal outcome compared with normal pregnancy.

Materials And Methods:-

Detail history including maternal age, obstetric history, menstruation history, previous major illness, any medication history, past and present medical and surgical history wasnoted.General and systemic examination was done.

Pregnancy and labor complications if any, were noted as maturity of thefetus and mode of delivery, post partum hemorrhage, need for blood transfusion and platelet transfusion or operative intervention, and neonatal details in form of any morbidity and mortality was noted.

The detailed investigation in the form of blood test forHb, TLC, DLC, bleeding time, clotting time, RFT, LFT, HBsAg and HIV were done in all cases of thrombocytopenia to ascertain the cause. Women with fever were tested for Dengue IgM, IgG and Malaria antigen.Coagulation tests (PT, APTT, FDP and fibrinogen) were done in those with signs or symptoms of DIC.Antiphospholipid antibodies were tested after ruling out all other etiologies.

Women with moderate thrombocytopenia without any other etiology were classified as gestational thrombocytopenia.

Women with normal platelet count before 28 weeks had a repeat platelet countin the third trimester to detect gestational thrombocytopenia. All thrombocytopenic cases were followed up till delivery. Platelet counts were repeated once in the postpartum period at 8weeks. Neonates were screened for thrombocytopenia and any complications.

Ethical Issues:-

Informed consent was taken verbally from all women, the study was approved by ethics committee CAIMS, Karimnagar. These findings were recorded on a standardized proforma.

Results:-

There was a statistically significant falling the mean platelet count of the control group members from first trimester to third trimesterwhich may be due to physiological causes as none of them had thrombocytopenia. And no such change in the mean platelet count was seen with increasing period of gestation among thrombocytopenia cases.

Distribution of the cases according to their etiology is presented in following Table 1.

Table 1:- Etiology of Thrombocytopenia in the Study Group.

ETIOLOGY	n = 70
GESTATIONAL THROMBOCYTOPENIA	40 (57.1%)
PRE ECLAMPSIA AND HELLP SYNDROME	20 (28.5%)
DISSEMINATED INTRAVASCULAR COAGULATION	2 (2.8%)
HEPATIC DISEASES	0
MALARIAL AND DENGUE FEVER	6 (8.5%)
MEGALOBLASTIC ANAEMIA	0
IMMUNO THROMBOCYTOPENIC PURPURA	1 (1.4%)
APLA SYNDROME	1 (1.4%)

Gestational thrombocytopenia (57.1%)was the commonest etiology.

The prevalence of thrombocytopenia due to severe preeclampsia and HELLP syndrome in the study group was 20% and 6% of them had medical cause like malarial or dengue fever.

Both the cases of study and control group were followed till their delivery. The duration of pregnancy in both these group is represented in Table 2.

Table 2:- Duration of Pregnancy in study and control Groups.

DURATION OF PREGNANCY	STUDY GROUP (n = 70)	CONTROL GROUP (n = 70)

PRETERM	18 (25.7%)	17 (24.2%)
TERM	52 (74.3%)	53 (75.8%)

Of the study group of 70 cases delivered during the study period, 74.3% delivered at term whereas 25.7% delivered preterm whereas in the control group the incidence of preterm delivery was only 24.2% of 17 patients who delivered preterm, 53 had induction of labor for maternal safety indication.

Thrombocytopenia per se do not affect mode of delivery. In the study group out of 70 cases 50% had vaginal delivery, 30% had Cesarean Section (CS) and 20% had instrumental delivery. All the cesarean sections were performed for obstetric/medical causes and none for thrombocytopenia. Whereas, in the control group 54% had normal vaginal delivery, 41% had CS and 5% had instrumental delivery as presented in Table 3.

Table 3:- Mode of Delivery in study and Control Groups.

MODE OF DELIVERY	STUDY GROUP (n=70)	CONTROL GROUP (n=70)
VAGINAL DELIVERY	35 (50%)	34 (49%)
CAESAREAN DELIVERY	21 (30%)	25 (36%)
INSTRUMENTAL DELIVERY	14 (20%)	11 (15%)

Maternal complications seen in study group with thrombocytopenia like placental abruption (9.4%). postpartum hemorrhage (5.3%), episiotomy hematoma (2.5%), rectus sheath hematoma (1%) were more than in control group as only 3% cases had placental abruption and 1.3% had postpartum hemorrhage where as no one had episiotomy or rectus sheath hematoma. Also fetal complications were more in study group as represented in Table 4.

Table 4:- Maternal Complications and Fetal Outcome.

	CONTROL GROUP (n=70)	STUDY GROUP (n =70)
MATERNAL COMPLICATIONS		
PLACENTAL ABRUPTION	3%	9.4%
POSTPARTUM HEMORRHAGE	1.3%	5.3%
EPISIOTOMY HEMATOMA	0%	2.5%
CS INCISION SITE OOZING (RECTUS SHEATH HEMATOMA)	0%	1%
FETAL COMPLICATIONS		
STILLBIRTH	1%	6%
INTRAUTERINE GROWTH RESTRICTION	8%	19%
MECONIUM STAINED LIQUOR	4%	8%
BIRTH ASPHYXIA	6%	13%
NEONATAL THROMBOCYTOPENIA	0%	7%

Out of 70 cases of thrombocytopenia 4 needed platelet transfusion for bleeding 5 with

HELLP syndrome and 2 with DIC. A total of 15 (25%) women received blood transfusion in thrombocytopenia group versus 40 (20%) in non thrombocytopenia group.

A total of 9 newborn had thrombocytopenia, out of which 5were born to mothers with preeclampsia and HELLP syndrome, 1 to a mother with ITP, and2 to mother with malaria and dengue fever. 1 neonate received platelet transfusion for Gastrointestinal (GI) bleeding.

Table 5:- Adverse Pregnancy outcomes according to etiology of thrombocytopenia in study group.

ADVERSE OUTCOME	GT	ITP	PRE-ECLAMPSIA HELLP	MALARIA
IUGR	9	0	12	4
PLACENTAL ABRUPTION	1	0	8	1
STILLBIRTH	0	0	4	1
BIRTH ASPHYXIA	2	0	3	0

Fetal Growth Restriction (FGR) was more common in the preeclampsia andHELLP syndrome group compared with the other etiologies. Also placental abruption, stillbirths, and birth asphyxia was more in preeclampsia and HELLP syndrome group.Out of 40 women with gestational thrombocytopenia20had normal platelet count at 8 weeks post delivery, 8 women had platelet count still below 150×10^9 /1 but had no complaints and 2women were lost to follow up.

Discussion:-

The present study was aimed at evaluating causes of thrombocytopenia in pregnancy and its fetomaternal effects.

Tejashwini et al. (2015) conducted a study which demonstrated that platelet count was significantly decreased during pregnancy as compared to puerperium in the same woman due to haemodilution and increased platelet destruction [9]. There was a physiologically increased fibrinolysis within the uteroplacental circulation in order to maintain blood flow.

Stirling et al. (1984), Wallenburg et al. (1978), Douglas er al. (1982), Fitzgerald et al.(1987) these studies demonstrated that, thrombocytopenia is the most common haemostatic abnormality observed in pregnancy, in many healthy women (around 10%) late pregnancy was associated with thrombocytopenia. At least in part this was due to haemodilution but the increase in mean platelet volume suggests that a compensated state of progressive platelet destruction occurs. Additional evidence of in vivo platelet activation in late pregnancy was the increased concentration of b-thromboglobulin42 and of thromboxaneA_2 derivatives.

Usha Perepu and Lori Rosenstein (2013) found that although thrombocytopenia during pregnancy was common, it was not frequently severe.

This was consistent with our study results.
Burrows and Kelton 1993 found thrombo-cytopenia in 6% and Sainio et al reported a 7.3% prevalence of thrombocytopenia in a population based surveillance study.

In the present study, incidence of thrombocytopenia during pregnancy was 8.78%. Thus, the prevalence of thrombocytopenia in Indian population is similar to world literature (5-12%).In our study most cases of thrombocytopenia were due to gestational thrombocytopenia followed by other causes as preeclampsia and HELLP syndrome [10]. Other causes were febrile conditions like malaria and dengue which are endemic in our area; some rare causes include DIC, IT and APLA syndrome.

The major findings of our study were that increase complications, both maternal and neonatal such as placental abruption, preterm deliveries, birth asphyxia, IUGR, and stillbirths were seen in thrombocytopenia group.

Higher rates of preterm deliveries (< 37 weeks) were observed among thrombocytopenia group,as management of preeclampsia and HELLP syndrome is early delivery of fetus. Labour induction could be a confounder for this association as 21 patients out of 35 with preterm delivery had to be induced for maternal indication. All fetal complications were significantly higher in study group like they were more due to maternal etiology like preeclampsia, HELLP syndrome and malaria (Table 4). Neonates may be at increased risk for thrombocytopenia. In Burrow (1993) study of women with thrombocytopenia, 216 had preeclampsia and HELLP and 4 gave birth to infants with severe thrombocytopenia.

Early neonatal thrombocytopenia was present in 7% of study group in present study, which is slightly higher than figure quoted by Parnas et al. (2006) 7/199 (3.51%) neonates had moderate to severe thrombocytopenia.

Conclusion:-

According to our findings in the study there is increase in complications, both maternal and neonatal such as placental abruption, preterm deliveries, birth asphyxia, FGR, and stillbirths were seen in thrombocytopenic group. we concluded that early interdisciplinary evaluation of thrombocytopenia in pregnancy is required for optimal care of mother and the neonate as risk varies greatly depending on cause of thrombocytopenia. The common causes of thrombocytopenia in pregnancy are gestational thrombocytopenia, preeclampsia, HELLP syndrome, malaria and

dengue. Gestational thrombocytopenia is associated with better maternal and perinatal outcome as compared to pre eclampsia, HELLP syndrome, ITP which expose them to life threatening complications as placental abruption, post partum hemorrhage, birth asphyxia and stillbirth. Thus, accurate etiological diagnosis is essential for optimal therapeutic management.

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