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Original Research Article

Pregnancy emerged thrombocytopenia: maternal and fetal outcome

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ABSTRACT

Background: A low platelet count is often an incidental finding in pregnancy. It can be an indicator of a severe systemic disorder requiring emergent maternal and fetal care or can just be unique to pregnancy with no harm to mother or fetus. Physiological decrease in platelet count is seen in pregnancy due to hemodilution and hypercoagulating state, though the exact pathophysiology is still unclear.
Methods: It is a prospective observational study done in a tertiary care centre.
Results: In about 11,258 cases screened 46 patients had thrombocytopenia (0.4%). The commonest etiology is found to be gestational thrombocytopenia (n=21, 45.6%) followed by preeclampsia/ eclampsia/ HELLP (haemolysis, elevated liver enzymes, low platelet count) syndrome (n=19, 41.3%). Only one patient had immune thrombocytopenic purpura (ITP) and 7 (15.3%) were associated with amplified fragment length polymorphism (AFLP). Maximum of them (n=19, 41.3%) underwent spontaneous vaginal delivery. 4 patients (8.6%) had postpartum haemorrhage, 6 (13.04%) had ceserean section wound infection, 4 (8.6%) had disseminated intravascular coagulation (DIC) and 4 (8.6%) had multiorgan failure. 13 patients (28.3%) had platelet count between 40 to 60 thousand per cumm, 11 (23.9%) had between 60 to 80 thousand per cumm, 10 (21.7%) had between 80,000 to 1 lakh and none had their platelet count less than 20,000 per cumm.
Conclusions: Gestational thrombocytopenia is not a preventable condition. It is an incidental finding in pregnancy. With strict vigilance during intrapartum and postpartum period, even without any treatment proper for the same, the maternal and fetal outcome is found to be good.

Keywords: DIC, HELLP, Multiorgan failure

INTRODUCTION

Megakaryocytes in bone marrow fragment to form thrombocytes also called as platelets. Circulating unactivated platelets are biconvex discoid structures, 2-3 micrometres in largest diameter. They remain in the peripheral circulation for eight to ten days and are cleared by macrophages. Platelets have a key role in primary hemostatic plug formation. Platelet count of less than 15*106 per cumm of blood is termed as thrombocytopenia. It is the second most common haematological abnormality seen in pregnancy next to anemia.[1] Although thrombocytopenia in pregnancy is not uncommon, it is not always severe. A low platelet count is often an incidental finding in pregnancy. Thrombocytopenia in pregnancy is easily detected as complete blood count is the initial evaluation done. It can be an indicator of a severe systemic disorder requiring emergent maternal and fetal care or can just be unique to pregnancy with no harm to mother or fetus.[2] Overall, around 75% of cases are due to gestational thrombocytopenia, 15-20% secondary to hypertensive disorders, 3-4% due to autoimmune process and 1-2% due to infections or malignancies.[3]

Gestational thrombocytopenia is a benign condition, seen in late second or third trimesters. Physiological decrease in platelet count is seen in pregnancy due to hemodilution and hypercoagulating state, though the exact pathophysiology is still unclear. This is of milder degree and has no significant maternal or fetal adverse outcomes. Gestational thrombocytopenia is usually a diagnosis of exclusion.[4] Immune thrombocytopenic purpura (ITP) is an autoimmune disorder characterized by destruction of circulating antibody bound platelets by reticuloendothelial system, particularly spleen. These antibodies cross the placenta placing the infant at a risk of thrombocytopenia. Thus ITP has potential risk to both mother and fetus in antenatal and postnatal period.[5] There is no pathological test to differentiate ITP from GT, hence, history of bleeding, bruising, low platelets prior to pregnancy can help us. Preeclampsia with thrombocytopenia can occur in late second, third trimester, also infrequently seen in first week of postpartum. HELLP (haemolysis, elevated liver enzymes, low platelet count), a variant of preeclampsia is more fulminant. Amplified fragment length polymorphism (AFLP) and HELLP have overlapping features. The approach towards AFLP and HELLP is medical stabilization and expeditious delivery (irrespective of fetal condition) in intensive care unit in collaboration with physician and anaesthetist. Psuedo-thrombocytopenia is seen when anticoagulants like ethylenediaminetetraacetic acid (EDTA) are used when collecting blood, as they induce platelet aggregation and give false low platelet counts. A peripheral smear will establish a diagnosis in such cases (the platelets are arranged in stacks).[6]

Drugs such as aspirin, acetaminophem, heparin, methyldopa, cyclosporine and antibiotics like penicillin may cause thrombocytopenia. Treatment of HIV with thrombocytopenia involves highly active antiretroviral therapy (HAART).[4]

This study is an effort to say, gestational thrombocytopenia is not a matter to panic, unless it is associated with certain pathological conditions where maternal and fetal, morbidity and mortality are high.

METHODS

The study is conducted in a tertiary care centre, in Department of Obstetrics and Gynaecology, from April 2019 to April 2020 being a prospective observational study.

All the patients attending the out-patient department and admitted in in-patient department after valid consent are investigated with their complete blood picture in automated blood counter. If thrombocytopenia is seen detailed history, clinical examination, peripheral smear and other related tests such as dengue, coagulation profile, renal and liver functions are done. Further, thrombocytopenia is classified as (1) mild = 1 lakh to 1.5 lakhs per cumm, moderate = 50,000 to 1 lakh per cumm and severe ≤50,000 per cumm.

Inclusion criteria

All pregnant women giving consent to be a part of our study.

Exclusion criteria

All pregnant women who are not giving consent. All pregnant women with mild thrombocytopenia.

A platelet count of less than 1 lakh is defined as thrombocytopenia by the international working group.[7]

Statistical analysis

MS excel were used in analyses of the data.

RESULTS

Around 11,258 pregnant women screened, 46 patients were identified to have thrombocytopenia due to various causes. The patients with 19-35 years of age were encountered in our study (mean±SD=23.80±3.46) with a median of hospital stay being median (Q1-Q3)=4 (3-7) days. 24 cases (52.2%) were primigravida and 22 cases (47.8%) were multigravida.

Table 1: Cause of thrombocytopenia.

Cause	No. of patients	Percentage (%)
Gestational thrombocytopenia (GT)	20	43.4
Preeclampsia/eclampsia/ HELLP	12	26.1
Chronic hypertension	01	2.2
AFLP (acute fatty liver of pregnancy)	07	15.3
Fever	05	10.8
Idiopathic thrombocytopenic purpura (ITP)	01	2.2
Total	46	100

The most common etiology found in our study is gestational thrombocytopenia (n=21, 45.6%) (Table 1). Preeclampsia/ eclampsia/ HELLP syndrome had second position (n=19, 41.3%). 5 patients (10.8%) had fever, of which 3 had dengue IgM reactive and 2 had widal positive. 7 patients (15.3%) had acute fatty liver of pregnancy (AFLP), all the 7 succumbed due to hepatic encephalopathy and not due to obstetrical causes. Another death was due to acute respiratory distress syndrome (ARDS) who was a patient of HELLP syndrome. 30 patients (65.2%) were successfully discharged whereas 8 patients (17.4%) went against

medical advice. In the 19 patients (41.3%) who were associated with preeclampsia/ eclampsia/ HELLP syndrome, 14 had HELLP syndrome, 3 had mild preeclampsia and 2 had eclampsia .1 more patient (2.17%) had chronic hypertension. There is an overlapping of AFLP and HELLP syndrome patients. Only 2 patients (4.3%) of second trimester were found in our study, rest all (n= 44, 95.7%) were of third trimester. One of the second trimester patient was 20 weeks with chronic hypertension underwent termination of pregnancy for fetal indication while the other was 24 weeks with idiopathic thrombocytopenic purpura who went against medical advice.

Maximum of our patients (n=13, 28.3%) had platelet count between 40,000 to 60,000 at admission. 11 patients (23.9%) had platelet count 60,000 to 80,000 and 10 patients (21.7%) had 80,000 to 1 lakh counts. 7 patients (15.3%) had 20,000 to 40,000 whereas none had counts less than 20,000 in our study population (Table 2).

Table 2: Platelet count (on admission).

Platelet count	No. of patients	Percentage (%)
80,000 – 1 lakh	10	21.7
60,000- 79,999	11	23.9
40,000 – 59,999	13	28.3
20,000 – 39,999	7	15.3
<20,000	0	0
Total	46	100

19 patients (41.3%) had spontaneous vaginal delivery, 8 (17.4%) had induced vaginal delivery, 11 (23.9%) underwent LSCS for obstetrical indications only and not merely for thrombocytopenia. 7 (15.3%) patients remained undelivered of which 1 expired due to hepatic encephalopathy before delivering, 4 cases of gestational thrombocytopenia were discharged and had regular follow up, one patient each of ITP and GT went against medical advice and missed their follow ups too (Table 3).

Table 3: Mode of delivery.

Mode of delivery	No of patients	Percentage (%)
Spontaneous vaginal delivery	19	41.3
Induced vaginal delivery	08	17.4
LSCS	11	23.9
Abortion	01	2.1
Instrumental vaginal delivery	00	0
Undelivered	07	15.3
Total	46	100

Table 4: Maternal complications.

Maternal complications	Gestational thrombocytopenia	Preeclampsia/eclampsia/ HELLP	AFLP	Fever
Vaginal hematoma	0	1	0	0
Postpartum hemorrhage	0	1	3	0
LSCS wound gape	2	2	0	2
DIC	0	0	4	0
Multiorgan dysfunction syndrome	0	0	4	0
Acute kidney injury	0	0	2	0
Repiratory failure	0	1	1	0
Paralytic ileus	1	1	0	0
ARDS	0	1	0	0

ARDS- acute respiratory distress syndrome. DIC- disseminated intravascular coagulation.

Table 5: Fetal outcome.

Fetal outcome	Gestational thrombocytopenia	Preeclampsia/eclampisa/ HELLP	AFLP	Fever
Preterm live	2	2	0	2
Preterm still	1	1	5	0
Term live	11	10	0	1
Term still	0	2	0	1

Table 6: Birth weight.

Birth weight	No. of babies	Percentage (%)
Normal weight	16	34.7
Low birth weight	18	39.2
Very low birth weight	3	6.5
Extremely low birth weight	2	4.3
Undelivered	7	15.3
Total	46	100

Focussing on maternal complications (Table 4) 1 patient of HELLP syndrome had vaginal hematoma and underwent vaginal exploration. Postpartum haemorrhage was seen in 3 patients of AFLP and 1 patient of HELLP syndrome, all of the 4 patients (8.7%) underwent intrauterine tamponade to successfully arrest bleeding. 6 patients (13.04%) had caesarean section wound gape of which 2 had gestational thrombocytopenia, 2 were associated with typhoid fever, 1 had HELLP syndrome and last had mild preeclampsia. The patient with mild preeclampsia underwent exploratory laparotomy for puerperal sepsis, intraoperatively showed to have bladder injury. 4 patients (8.7%) of AFLP landed up in disseminated intravascular coagulation (DIC) and 4 (8.7%) in (MODS) multiorgan dysfunction syndrome. 2 patients (4.3%) of AFLP had acute kidney injury (AKI). All the patients with MODS and AKI succumbed due to hepatitis. One patient of gestational thrombocytopenia and one with HELLP with DIC had paralytic ileus with hypokalaemia. If one patient of HELLP syndrome had ARDS, one more had respiratory failure. 8 patients (17.4%) had mild ascites and 1 patient had mild splenomegaly noted in ultrasound of abdomen. One patient with antepartum eclampsia with HELLP syndrome and one more with hepatic encephalopathy had their CT report showing posterior reversible encephalopathy syndrome (PRES). One patient with hepatic encephalopathy with MODS had CT showing venous thrombosis.

Gestational thrombocytopenia and preeclampsia/ eclampsia favoured term live births (n=11 and 10 respectively) whereas AFLP has more (n=5) preterm still births (Table 5). 18 babies (39.1%) had low birth weight, 3 (6.5%) had very low birth weight and 2 (4.3%) had extremely low birth weight (Table 6).

DISCUSSION

The prevalence of thrombocytopenia in our study is 0.45% i.e. 46 cases in 11,258 cases which is much higher than the prevalence of 2-3 cases per 10,000 in studies like Nisaratanaporn.[8] The mean age in our study is 23.80±3.46 years (19-35 years), a maximum case were seen between 21-24 years age group which is similar to the study by Sumathy et al.[9] 52.2% of primi and 47.8% of multigravida were seen in our study, comparable to 55.6% primi and 44.4% multi in the same study by Sumathy et al.[9] The most common etiology found in our study is gestational thrombocytopenia (45.6%), similar results are found in study by Begum et al (49%), Vyas et al (44.6%) and Pallavi et al.[4,10,11] 41.3% of cases had hypertensive disorder of which 14 had HELLP syndrome and 1 had chronic hypertension, comparable to study by Begum A et al where 36.5% cases of hypertension with 2 cases of chronic hypertension and 7 cases of HELLP were seen.[4] 7 cases (15.3%) of AFLP are seen in our study similar to that by Zahida Parveen et al (n=7, 35%).[5] 3 cases of dengue and 2 cases of typhoid of which one had sepsis and no cases of malaria are seen in our study. Sumathy et al study reported 10 patients of dengue, 5 patients of typhoid, 2 cases of intrauterine sepsis and 13 patients of malaria.[9] Only one case of ITP is found in our study who went against medical advice, follow up was not available.

We encountered 4 cases (8.6%) of PPH, all were atonic and intrauterine tamponade worked well in arresting bleeding. The studies by Sumathy et al had 8 cases of atonic PPH all managed medically; Pallavi et al showed 5.3% PPH, Arora et al showed 6 cases of PPH. 6 cases of caesarean section wound gape where one underwent exploratory laparotomy is seen in our study.[9,11,12] The study by Pallavi et al showed 1% cases and that of Sumathy et al shows that 0.5% case of incisional site oozing.[9,11] 1 case of vaginal hematoma (2.17%) is seen which is similar to study by Pallavi et al having 1 case (2.5%) of episiotomy hematoma and Arora et al reported 5 (3.6%) cases of wound hematoma.[11,12] Audibert et al says 15% had cerebral bleeding, whereas our study has one patient with intracranial venous thrombosis and two patients with PRES (posterior reversible encephalopathy syndrome).[13] 4 patients had DIC (8.6%) and 1 patient had ARDS in our study whereas 4 cases of DIC and 1 case of ARDS are showed by Sumathy et al and 13.6% cases of DIC showed by Sibai et al.[9,14] 5 cases (2.7%) of placental abruption and 9.4% cases of abruption was reported by Sumathy et al and Pallavi et al respectively, but no cases of abruption were seen in our study.[9,11] None of our patients had hemoperitoneum similar to study by Arora et al.[12]

According to the British committee for standards in hematology the mode of delivery in women with thrombocytopenia should be decided primarily by obstetrical indications. There is no evidence to support the routine use of caesarean section.[9] 27 underwent vaginal delivery i.e. 19 (41.3%) had spontaneous and 8 (17.4%) had induced vaginal labour, 11 cases (23.9%)

had caesarean section done for obstetrical indications only, and none underwent instrumental delivery in our study. 61.54% (n=80) had vaginal delivery and 36.26% (n=47) had caesarean section and 2.2% (n=3) had instrumental delivery in the study by Pallavi et al.[11] 7 patients were undelivered in our study of which 1 expired due to hepatic encephalopathy before delivering, 4 cases of gestational thrombocytopenia were discharged and had regular follow up, one patient each of ITP and GT went against medical advice and missed their follow ups too. One case of twin pregnancy was seen in our study. The study by Zahida Parveen et al had 12 cases undelivered, 5(41.6%) died due to hepatitis E, 7 (58.3%) had gestational thrombocytopenia treated conservatively. In our study, 16 patients out of 46 received platelets concentrations and 24 received blood transfusion.[5] 10 patients with HELLP syndrome, 3 with gestational thrombocytopenia, 2 with dengue fever and 1 with chronic hypertension with thrombocytopenia received platelets. Platelet transfusion was mostly done when platelet count was less than 50,000 per cumm. Due to the non- availability of platelets and unaffordability of the platelets, they were judiciously used to the critical patients. The current recommendation for safe vaginal delivery as reported by Provan et al is platelet count should be more than 30,000/cumm, for operative vaginal or caesarean section should be higher than 50,000/cumm and for epidural anaesthesia should be higher than 80,000/cumm.[15] Similarly, the study by Gernsheimer, spontaneous bleeding occurs when platelet count is less than 20,000/cumm and internal bleeding when less than 10,000/cumm.[16] No patients in our study received IvIg (Immunoglobulins), or underwent splenectomy or plasmapheresis.

13 neonates (28.2%) had preterm birth and 25 (54.3%) had term birth. 11 (23.9%) of these had 11 still birth (8- preterm still and 3- term still birth). 23 babies had low birth weight in our study. The study by Pallavi S V et al showed 6% still birth and 19% intrauterine growth restriction, Arora M et al showed 14 cases of low birth weight and 11 cases of still birth.[11,12] Though HELLP is a severe condition, the fetal outcome was found to be good, whereas AFLP had the worst fetal outcome.

The mortality rate in our study is found to be 17.4% (n=8). Mortality rate in study by Zaheda Parveen et al is 28.1% (n=20) and 3.8% (n= 7) by Sumathy et al.[5,9] Except for 8 deaths and 8 who went against medical advice, the rest had their platelet count in an increasing trend from day 3 onwards (few cases of HELLP had day 5 onwards). Their platelet count was monitored periodically. The study by Burrows et al showed normalizing platelet count by seventh postpartum day.[3]

CONCLUSION

Gestational thrombocytopenia is found to be the most common etiological factor for thrombocytopenia in pregnancy followed by preeclampsia/ HELLP syndrome. Though many studies say Gestational thrombocytopenia is not seen below 1 lakh platelet count, our study had platelet count upto but not less than 50,000/ cumm. The worst maternal and fetal outcome (mortality) in thrombocytopenia in pregnancy is seen in AFLP (acute fatty liver of pregnancy). Hence, further research is required to conquer this dark side of obstetrics.

Gestational thrombocytopenia is not a preventable condition. It is an incidental finding in pregnancy. With strict vigilance during intrapartum and postpartum period, even without any treatment proper for the same, the maternal and fetal outcome is found to be good.

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