Etiology and Fetomaternal Outcomes of Thrombocytopenia During Pregnancy

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Abstract

Background and Aim: Literature is scarce on thrombocytopenia during pregnancy; hence, this study was done to establish its etiology and the fetomaternal outcome.

Materials and Methods: This was a prospective observational study on 120 pregnant women with thrombocytopenia. Bleeding manifestations before delivery, intrapartum complications, and fetal outcomes were evaluated.

Results: At term, the platelet count was < 50,000/µL in 47.5% of the women; 50,000/µL to 1,00,000/µL in 48.3%; and > 1,00,000/µL in 4.2%. The etiologies were gestational thrombocytopenia (GT; 53.3%); syndrome of hemolysis, elevated liver enzyme levels and low platelet count (35%); abruption-induced disseminated intravascular coagulation (4.2%); malaria (3.3%); dengue (3.3%); and immune thrombocytopenic purpura (ITP, 0.8%). Overall, 3.2% of the women had bleeding manifestations before delivery; 15.8% had primary postpartum hemorrhage; and 24.5% had other intrapartum complications such as incision site ooze, wound hematoma, episiotomy hematoma, and placental abruption.

A weak positive correlation was observed between maternal and fetal platelet counts, and no significant association between maternal thrombocytopenia and neonatal complications was noted. A statistically significant association was found between maternal thrombocytopenia and stillbirths (P < .001). One neonate had intracranial hemorrhage. Platelet
Introduction
After anemia, thrombocytopenia is the second most common hematologic abnormality encountered during pregnancy and is found to complicate 7% to 8% of pregnancies in India, mostly in the third trimester.1 The major function of platelets is the initiation of hemostasis, and hence, thrombocytopenia can result in spontaneous bleeding from any part of the body. It may be associated with serious bleeding at delivery and may require emergent maternal and neonatal care.2

The causes can be exclusive to pregnancy, such as gestational thrombocytopenia (GT) and hypertensive disorders (preeclampsia; eclampsia; the hemolysis, elevated liver enzyme levels, low platelet count syndrome [HELLP syndrome]; and acute fatty liver of pregnancy). Other causes are disseminated intravascular coagulation (DIC), thrombotic thrombocytopenic purpura, hemolytic uremic syndrome, immune thrombocytopenic purpura (ITP), viral infections, autoimmune disorders, consumption of drugs, vitamin B₁₂ or folate deficiency, aplastic anemia, and myelophthisis. Pseudothrombocytopenia can result from ethylenediaminetetraacetic acid (EDTA)–induced clumping of platelets, in which case, a new sample should be analyzed using citrate as an anticoagulant.

Aim
This study was conducted in a tertiary care center in north India to elucidate the etiology and fetomaternal outcomes of thrombocytopenia during pregnancy.

Materials and Methods
Study design
This prospective observational study was conducted at the Government Medical College and Hospital (Chandigarh, India), which is a tertiary care center in north India. It was done over 18 months, after approval by the ethics committee. After obtaining informed consent, 120 pregnant women with thrombocytopenia who were undergoing antenatal consultation at term were investigated and followed up for analysis of complications and platelet counts; they were monitored till 6 weeks postpartum.

Inclusion and exclusion criteria
All antenatal women with platelet count < 1,50,000/µL were enrolled in the study, except those with congenital malformations of the fetus and those requiring termination of pregnancy.

Study procedure
Specialized tests such as autoantibodies, viral markers, serologies for tropical infections, and bone marrow examination were carried out wherever required. Platelet transfusions were given when indicated. Platelet counts were repeated 48 hours after delivery and at 6 weeks postpartum, and the fetomaternal outcomes were evaluated.
Statistical analysis

Descriptive statistics were obtained for all study variables. All categorical variables were compared using \( \chi^2 \) test and Fisher exact test, and continuous variables were compared using Student t test. All data were expressed as mean \( \pm \) SD. The strength and direction of linear relationship between 2 variables were measured using the correlation coefficient \( (r) \). For all statistical analysis, \( P < .05 \) was considered statistically significant.

Results

The study included 120 antenatal women with thrombocytopenia (mean age = 25.63 \( \pm \) 3.89 y), 70% of whom were multiparous.

The initial platelet count at term ranged from 7000/\( \mu \)L to 140,000/\( \mu \)L, with the distribution as shown in Table 1. At 6 weeks postpartum, the platelet counts normalized (> 150,000/\( \mu \)L) in all except 1 woman.

The severity of thrombocytopenia could not be attributed to the etiology \( (P = .819) \). Bleeding manifestations before delivery, in the form of petechia, purpura, epistaxis, gum bleeding, and gastrointestinal bleeding, were seen only in 3 women with GT and in 1 woman with malaria (Table 2). Statistical significance could not be established \( (P = .157) \). Of the 4 women with bleeding, only 1, who had gastrointestinal bleeding, had platelet count < 50,000/\( \mu \)L. A statistically significant association was found between maternal thrombocytopenia and stillbirths \( (P < .001) \).

Overall, 19 women had primary postpartum hemorrhage (PPH), 11 of whom had platelet count < 50,000/\( \mu \)L; 1 woman had secondary PPH. No statistical significance was noted between PPH and maternal thrombocytopenia, as mentioned in Table 3 \( (P = .55) \).

The incidence of other intrapartum complications is as shown in Table 4.

Of the 120 women, 64 (53.3%) delivered low-birthweight neonates weighing < 2.5 kg and 56 (46.7%) delivered neonates weighing \( \geq \) 2.5 kg. Complications developed in 23 neonates born to these mothers with thrombocytopenia. Of the 120 deliveries, 20 (16.7%) were stillborn, 2 (1.6%) had early-onset sepsis (EOS), and 1 (0.8%) had intracranial hemorrhage (ICH). The mother of the fetus with ICH had a platelet count of 82,000/\( \mu \)L due to HELLP syndrome.

A weak positive correlation was found between maternal platelet count (initial) and neonatal platelet count \( (r = 0.02; \text{Figure}) \).

<table>
<thead>
<tr>
<th>Platelet Count At Term, ( \mu )L</th>
<th>At Term, ( n ) (%)</th>
<th>48 h Postpartum, ( n ) (%)</th>
<th>6 wk Postpartum, ( n ) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 50,000</td>
<td>57 (47.5%)</td>
<td>24 (20%)</td>
<td>1 (0.8%)</td>
</tr>
<tr>
<td>50,000–1,00,000</td>
<td>58 (48.3%)</td>
<td>63 (52.5%)</td>
<td>—</td>
</tr>
<tr>
<td>&gt; 1,00,000</td>
<td>5 (4.2%)</td>
<td>33 (27.5%)</td>
<td>119 (99.2%)</td>
</tr>
</tbody>
</table>

Table 2. Association Between Etiology and Platelet Count \( (N = 120) \)

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Platelet Count At Term, ( \mu )L</th>
<th>No. of Women, ( n ) (%)</th>
<th>Occurrence of Bleeding Manifestations, ( n ) (%)</th>
<th>Stillbirths, ( n ) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational Thrombocytopenia, ( n ) (%)</td>
<td>29 (24.2) 33 (27.5) 2 (1.7)</td>
<td>64 (53.3)</td>
<td>3 (2.5)</td>
<td>7 (5.8)</td>
</tr>
<tr>
<td>HELLP Syndrome, ( n ) (%)</td>
<td>19 (15.8) 20 (16.7) 3 (2.5)</td>
<td>42 (35)</td>
<td>—</td>
<td>7 (5.8)</td>
</tr>
<tr>
<td>Abruption-Induced DIC, ( n ) (%)</td>
<td>4 (3.3) 1 (0.8) —</td>
<td>5 (4.2)</td>
<td>—</td>
<td>5 (4.2)</td>
</tr>
<tr>
<td>Dengue, ( n ) (%)</td>
<td>3 (2.5) 1 (0.8) —</td>
<td>4 (3.3)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Malaria, ( n ) (%)</td>
<td>2 (1.7) 2 (1.7) —</td>
<td>4 (3.3) 1 (0.8%)</td>
<td>1 (0.8)</td>
<td></td>
</tr>
<tr>
<td>ITP, ( n ) (%)</td>
<td>— 1 (0.8) —</td>
<td>1 (0.8)</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

DIC, disseminated intravascular coagulation; ITP, immune thrombocytopenic purpura; HELLP, hemolysis, elevated liver enzymes, low platelet count.
The causes of thrombocytopenia at term in the study population were GT (53.3%), HELLP syndrome (35%), abruption-induced DIC (4.2%), malaria (3.3%), dengue (3.3%), and ITP (0.8%). GT has consistently been the most common cause of maternal thrombocytopenia in various other studies. It occurs in up to 11% of all pregnancies. It is followed by hypertensive disorders and ITP, although in South Asia and Africa, tropical infections can supersede them, depending on the local prevalence. In a case series by Vyas et al, the incidence of thrombocytopenia due to malaria was 14.28%. A large prospective study by Burrows et al reported that platelet count returned to normal by the seventh postpartum day in all women with GT, as was seen in our cohort. Only one patient (having ITP) remained thrombocytopenic at 6 weeks in our study.

Maternal outcomes

Bleeding manifestations in the form of petechia, gastrointestinal bleeding, gum bleeding, and epistaxis were seen in 3.2% of the women in our study, which was not statistically significant ($P = .70$). It has previously been established that GT is not associated with increased bleeding risk. In our study, 15.8% of the women had primary PPH, 24.5% had other intrapartum complications such as incision site ooze, wound hematoma or episiotomy hematoma, and placental abruption, which were not statistically significant ($P = .550$). The incidence of placental abruption was 7.5%. Dwivedi et al reported 4.2% PPH, 2.4% placental abruption, and 8.4% incision site ooze in their study population. The incidence of PPH may have diverged as the diagnosis and estimated blood loss are subjective and also depend on the clinical profile of patients.

Neonatal outcomes

GT had favorable maternal and neonatal outcomes in our study, which was in agreement with data from other studies. The mean maternal platelet count at term was 51,125/µL ± 27,257/µL, and the mean neonatal platelet count at birth was 1,80,077/µL ± 63,434/µL. The neonatal platelet count was significantly higher than the maternal platelet count ($P < .00$) but was not related to the severity of thrombocytopenia ($P = .49$). Burrows et al evaluated 1027 thrombocytopenic women, of whom 756 (73.6%) were diagnosed with GT, and only 1 neonate had thrombocytopenia.
The sole patient with ITP in our study had a good outcome, although the neonate had thrombocytopenia at 6 weeks. Rottenstreich et al.,8 in their study on 253 pregnant women with ITP, found that 9.5% of the neonates had thrombocytopenia and that pregnancy-onset ITP conferred a higher risk.

Neonatal thrombocytopenia occurs in 15% to 38% cases of maternal HELLP syndrome.9 This has been found to be the risk factor for ICH in neonates.10 In our study, 1 neonate (with platelet count of 67,000/µL) developed ICH, and the mother had HELLP syndrome with a platelet count of 82,000/µL.

Conclusion

GT is the most prevalent cause of pregnancy-related thrombocytopenia, with mild-to-moderate thrombocytopenia generally developing at term. HELLP syndrome, apart from causing maternal morbidity, is also associated with an increased risk of fetal ICH. Tropical infections are important differentials of maternal thrombocytopenia, especially in regions having high prevalence. Neonates born to mothers with ITP can have persistent thrombocytopenia and need to be managed accordingly.

References


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