ASSESSMENT OF THE PLATELET COUNT IN THE PREGNANT WOMEN IN IGIMS, PATNA, BIHAR

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Abstract
The major risk associated with low platelet count in pregnancy is the increased risk of bleeding during the childbirth or post that. There is an increased blood supply to the uterus during pregnancy and the surgical procedure requires cutting of major blood vessels. Women with thrombocytopenia are at increased risk of losing excessive blood. The risk is more in case of caesarean delivery as compared to vaginal delivery. Hence based on above findings the present study was planned for Assessment of the Platelet Count in the Pregnant Women in IGIMS, Patna, Bihar.

The present study was planned in Department of Pathology, Indira Gandhi Institute of Medical Science, Patna, Bihar, India. The present study was planned from duration of January 2019 to June 2019. In the present study 200 pregnant females samples received for the platelet estimation were enrolled in the present study.

Clinically platelet indices can be a useful screening test for early identification of preeclampsia and eclampsia. Also platelet indices can assess the prognosis of this disease in pregnant women and can be used as an effective prognostic marker because it correlates with severity of the disease. Platelet count is a simple, low cost, and rapid routine screening test. Hence the data generated from the present study concludes that platelet count can be used as a simple and cost effective tool to monitor the progression of preeclampsia, thereby preventing complications to develop during the gestational period.

Keywords: Platelet Count, Pregnant Women, IGIMS, Patna, Bihar, etc.

Introduction
A pregnant woman may face various medical challenges during her pregnancy and one such challenge is a low platelet count or Thrombocytopenia. Pregnant women go through many physical and emotional changes during pregnancy and these severe pathological changes in the body may result in conditions such as thrombocytopenia.

Platelets are responsible for blood clotting and play a significant role during pregnancy as well. The average or normal platelet count of a non-pregnant woman may range between 150,000 and 400,000 per microlitre of blood. The platelet count of a woman may drop to 116,000 per microlitre of blood during pregnancy. However, if it is less than 116,000, the condition is known as thrombocytopenia.

Thrombocytopenia or low platelet count during pregnancy is the second most common blood disorder after anaemia. It is observed that nearly 5 to 8 percent women may get diagnosed with a low platelet count during their pregnancy. Not all cases of thrombocytopenia may cause serious complication in pregnancy or childbirth, but it is better to prepare to face any complications that may arise with this condition.

Thrombocytopenia, or a low blood platelet count, is encountered in 7-12% of all pregnancies. [1] Women are more commonly diagnosed with platelet disorders during pregnancy since screening is done as part of the initial clinic evaluation with automated blood counts. Thrombocytopenia can result from a wide range of conditions with several of them being pregnancy related. [2] Platelets are nonnucleated cells derived from megakaryocytes in the bone marrow and normally live in the peripheral circulation for as long as 10 days. Platelets play a critical initiating role in the hemostatic system.

Primary hemostasis begins when platelets adhere to the site of endothelial disruption, leading to platelet clumping. This is followed by platelet activation, which is characterized by release of granules containing von Willebrand factor, adenosine 5’-diphosphate (ADP), and serotonin. This serves to recruit other platelets into the growing platelet plug, which acts to stop the bleeding. Simultaneously, the synthesis of thromboxane A2 and release of serotonin leads to vasoconstriction to reduce blood loss at the site of vascular injury. The secondary hemostatic phase begins when the coagulation pathway is activated on the surface of the activated platelets to form a fibrin meshwork, which serves to reinforce the platelet plug.
A retrospective study by Shin et al indicated that in pregnant women with aplastic anemia, obstetric and disease complications are more prevalent in those with severe thrombocytopenia than in those with nonsevere thrombocytopenia. The study, which included 61 patients with aplastic anemia, found that in women with severe thrombocytopenia, the incidence of transfusion during pregnancy or the postpartum period (72.7% and 45%, respectively) was greater than in those with nonsevere thrombocytopenia (15.4% and 2.7%, respectively). It was also found that 25% of women with severe thrombocytopenia underwent bone marrow transplant after delivery, compared with 0% of those in the nonsevere thrombocytopenia group. [3]

Moreover, the odds ratios for composite disease complications and composite obstetric complications were higher in the women with severe thrombocytopenia than in the nonsevere thrombocytopenia patients. In addition, among patients in the severe thrombocytopenia group, gestational age at the platelet count’s nadir and at delivery was lower than in the women with nonsevere thrombocytopenia. [3]

Lescale evaluated 8 different platelet antibodies in 250 gravidas with thrombocytopenia (160 with presumed GT, 90 with ITP) to determine if any antibodies could distinguish the 2 conditions. Platelet-associated IgG was comparably elevated in most women with GT (69.5%) and ITP (64.6%), P=0.24. A significantly higher proportion of patients with ITP had indirect IgG compared with patients with GT (85.9% vs 60.3%, P<0.001), but significant overlap existed, limiting its clinical value. Antiplatelet antibody tests, either alone or in combination, cannot be used to distinguish ITP from GT. [4]

Preeclampsia occurs in 3 to 4% of pregnancies and accounts for 5 to 21% of cases of maternal thrombocytopenia. [1] Thrombocytopenia is usually moderate and platelet count rarely decreases to <20,000/μL. Thrombocytopenia in patients with preeclampsia always correlates with the severity of the disease. A platelet count of <100,000/μL is diagnostic for preeclampsia. It is considered a sign of worsening disease and is an indication for delivery.

In Burrows’ 1993 study of women with thrombocytopenia, 216 had preeclampsia and HELLP and 4 gave birth to infants with severe thrombocytopenia. Among 1198 women with preeclampsia but no thrombocytopenia, 1 infant had severe thrombocytopenia. Of the 5 infants with severe thrombocytopenia, all were preterm, 3 were small-for-gestational age, and all were delivered by cesarean delivery. Two infants experienced intracranial hemorrhages, despite being born by cesarean delivery. [5]

Maternal sensitization to antigens on the surface of the fetal platelets results in alloantibodies, which can cross the placenta and bind to fetal platelets, resulting in their destruction. Involved human platelet antigens (HPA) now uniformly described with numbers that identify a specific antigen group with alleles marked as "a" or "b." There are currently >15 recognized platelet-specific antigens.

[1] The most common is HPA-1a (formerly known as P1A1 and Zwa). Unlike Rh disease, alloimmune thrombocytopenia can affect the first pregnancy. Half of all cases occur in the first pregnancy and are not preventable.

Risks include petechiae, ecchymosis, and intracranial hemorrhage (10-20%). Intracranial hemorrhage can occur in utero, resulting in parenchymal damage, porencephalic cysts, and obstructive hydrocephalus. About 52% can be detected by ultrasound before labor starts. [1]

In Burrows' study, 19 pregnancies were complicated by alloimmune thrombocytopenia. Nine infants were born with severe thrombocytopenia. Intracranial hemorrhage was observed in 3 fetuses, one with a fetal demise; no new cases occurred in neonates. Alloimmune thrombocytopenia accounted for all the thrombocytopenia-related fetal morbidity and mortality in this large study.

Gestational thrombocytopenia is the most common cause of thrombocytopenia during pregnancy (70%), but other underlying causes must be considered as well. A thorough history and physical examination is important to rule out most other causes. Look at the remainder of the CBC and smear to rule out pancytopenia and platelet clumping associated with pseudothrombocytopenia.

If no antecedent history of thrombocytopenia is present and platelet counts are >70,000/μL, the condition is more likely to be GT. If platelet counts fall to <50,000/μL or if a preexisting history of thrombocytopenia is present, the condition is more likely to be ITP.

Direct or circulating antiplatelet antibodies has no value in the workup of thrombocytopenia in pregnancy because they usually are nonspecific and will not distinguish GT from ITP. Cesarean deliveries for ITP or GT should be reserved for obstetrical indications only because vaginal delivery itself has not been demonstrated to be a cause for intracranial hemorrhage.
Invasive procedures to determine fetal platelet counts (scalp sampling, PUBS) are no longer considered necessary for ITP, because an infant who is thrombocytopenic may be delivered vaginally. However, PUBS may still be of value in alloimmune thrombocytopenia to assess the severity of the condition and therapeutic response.

With ITP, obtain cord blood at delivery (if possible) for platelet count and notify the pediatricians to assess neonatal platelet counts due to the risk for continued quantitative platelet decline and postnatal hemorrhage. For GT, document normalization of maternal platelet counts after delivery.

Normal pregnancy is characterized by physiological fall in platelet count. Platelet count decreases by an average of 10% during pregnancy. [6] Physiological fall in the platelet count occurs as a result of hemodilution and because of rise in physiological strain on endothelium resulting in platelet aggregation in blood vessels and thus decrease in number of platelets in circulation. [7] Thrombocytopenia is defined as the subnormal number of platelets in the circulating blood, usually less than 150,000/cu mm. [8] It is classified as mild with platelet count 100-150 x 10^9/l, moderate at 50-100 x 10^9/l, and severe with less than 50 x 10^9/l. [9] Thrombocytopenia complicates up to 10% of all pregnancies [10] and is second most common haematological abnormality during pregnancy following anemia. [8] Gestational thrombocytopenia is considered as the most common cause of thrombocytopenia in pregnancy and about 75% cases of pregnancy associated thrombocytopenia are due to gestational thrombocytopenia. [8] The etiology is unknown, but is thought to be physiological. It is considered as mild form thrombocytopenia with no risk to the mother or infant.

The major risk associated with low platelet count in pregnancy is the increased risk of bleeding during the childbirth or post that. There is an increased blood supply to the uterus during pregnancy and the surgical procedure requires cutting of major blood vessels. Women with thrombocytopenia are at increased risk of losing excessive blood. The risk is more in case of caesarean delivery as compared to vaginal delivery. Hence based on above findings the present study was planned for Assessment of the Platelet Count in the Pregnant Women Referred to IGIMS, Patna, Bihar.

Methodology:

The present study was planned in Department of Pathology, Indira Gandhi Institute of Medical Science, Patna, Bihar, India. The present study was planned from duration of January 2019 to June 2019. In the present study 200 pregnant females samples received for the platelet estimation were enrolled in the present study.

Relevant data were obtained from case files and compiled by a common proforma that included socio-demographic characteristics of mothers, obstetric history, signs and symptoms in mother at presentation, laboratory data, and maternal and perinatal outcomes. The data collection was followed by analysis of the collected data.

Clinical details of all cases were documented. Those cases with pre-existing hypertension, having associated co morbid diseases such as diabetes mellitus, auto immune disorders, ITP, neoplastic diseases, heart diseases and cases on anticoagulants were excluded from the study.

All the patients were informed consents. The aim and the objective of the present study were conveyed to them. Approval of the institutional ethical committee was taken prior to conduct of this study.

Following was the inclusion and exclusion criteria for the present study.

Inclusion Criteria: The records of pregnant women with proved platelet abnormalities Normal pregnancy at 2nd-3rd trimester.

Exclusion criteria: All cases with pre-existing hypertension other than PIH. Patients having co morbid conditions such as Severe anaemia, Diabetes mellitus, History of auto immune disorder, History of Idiopathic Thrombocytopenic Purpura, History of receiving drugs like aspirin, anti-coagulants etc.

Results & Discussion:

Platelet is formed primarily in the bone marrow. They are released into the blood stream in large number to maintain the vascular integrity. Platelet is formed primarily in the bone marrow megakaryocytic in both the pregnant and non pregnant states, mature platelets circulate for 8-9 days platelets act to repair defects in the vascular endothelium and reduce hemorrhage by promoting blood clot formation when activated, typically by vessel wall trauma. Platelets become adherent to themselves and all surfaces including glass. Hence the need to collect blood for platelet counts in bottles containing anticoagulant such as sodium, heparin or citrate. Endothelial damage promotes platelet aggregation and degranulation which is inturn stimulates the release of prostaglandin and thromboxane A2, amplifying the platelet clumping and vasoconstriction. The normal non-
pregnant platelet count is 150000-400000/mm³. During pregnancy the platelet count falls progressively but tends to remain in the normal range.

Pregnancy is associated with complex changes involving blood coagulation, a transient mild thrombocytopenia is seen due to increased platelet consumption. [11] Hypertension is one of the most common obstetric problems resulting in preeclampsia and eclampsia which in turn associated with thrombocytopenia. [12] The obstetrician nowadays rely increasingly on laboratory test for the management of pregnant women. [13] The most common cause of thrombocytopenia in pregnancy is preeclampsia and eclampsia and also found associated with increased risk of perinatal complications such as abruptio placenta, preterm delivery, low Apgar score and still birth. [14-16] The estimation of platelet indices is a reliable method. [17]

Preeclampsia is one of the commonest medical disorders during pregnancy and affects approximately 5–10% of all pregnancies mostly affecting the primigravida. It continues to be major causes of maternal and perinatal morbidity and mortality. [18] It is a multisystem disease and many theories are proposed for pathophysiology. So there is a constant search for better prognostic factors to predict the progression and severity of disease. Activation of coagulation, fibrinolysis, platelet and vascular endothelial function are believed to play an important role in pathogenesis of preeclampsia. The fall in platelet count is most frequently found in preeclampsia and is probably due to consumption during low grade intravascular coagulation. [19]

In normal pregnancy, platelet count may slightly fall, upto 15% of pre-pregnancy level due to haemodilution& increased platelet consumption. But it does not cause any complication. Thrombocytopenia is diagnosed when platelet count falls below 1,50,000/cumm. In mild to moderate preeclampsia, this platelet fall does not lead to much complications, but as the severity of the disease increases, as in severe preeclampsia &eclampsia, it leads to bleeding diathesis. Low platelet count is a component of HELLP syndrome, ultimately progressing to DIC & maternal death.

**Table 1:** Age groups and number of cases in two groups

<table>
<thead>
<tr>
<th>Age</th>
<th>Cases: with thrombocytopenia</th>
<th>Control: without thrombocytopenia</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;20 years</td>
<td>35</td>
<td>24</td>
<td>59</td>
</tr>
<tr>
<td>21-25 years</td>
<td>46</td>
<td>48</td>
<td>94</td>
</tr>
<tr>
<td>26-30 years</td>
<td>10</td>
<td>20</td>
<td>30</td>
</tr>
<tr>
<td>&gt;31 years</td>
<td>9</td>
<td>8</td>
<td>17</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100</td>
<td>200</td>
</tr>
</tbody>
</table>

The commonest age group in which thrombocytopenia seen was between 21 to 25 years. Table 1 shows that age was an important criterion and there was difference in the occurrence of thrombocytopenia in different age groups.

**Table 2:** Mean platelet count in cases and controls

<table>
<thead>
<tr>
<th>Conditions</th>
<th>No. of Cases</th>
<th>Platelet Count (x 10⁹/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>30</td>
<td>26-370</td>
</tr>
<tr>
<td>Mild Pre eclampsia</td>
<td>62</td>
<td>66-375</td>
</tr>
<tr>
<td>Severe Pre eclampsia</td>
<td>78</td>
<td>27-259</td>
</tr>
<tr>
<td>Controls</td>
<td>40</td>
<td></td>
</tr>
</tbody>
</table>

Various systems of classifications are noted in literature with modifications being made constantly[14] making comparison difficult. Bangal et al.[20] excluded gestational HTN and clubbed mild and severe PIH. While Mohammed et al.[21] have studied the variations of platelet indices in PIH in a fixed study group of 20 cases each under each category, whereby the incidence of each cannot be commented upon and Parmar et al.[22] have categorized PIH cases into mild, moderate and severe PIH. Wolde et al.’s[23] method to categorize cases with PIH based on the National High BP Education Working Group (2000) criteria has been done in this study owing to feasibility and simplicity of categorization into the five mentioned groups.

In a study from Bhopal by Anand and Kirshnanand et al., [24] majority of the cases had preeclampsia (66.36%) and the rest eclampsia (33.64%). Wolde et al.’s[23] study showed preeclampsia as the most common hypertensive disorder of pregnancy (51.9%); followed by eclampsia (23.4%), HELLP syndrome (9.8%), mild preeclampsia (7.6%), and simple gestational HTN (5.1%). In our study, most cases belonged to the mild preeclampsia (56%) group followed by cases with severe preeclampsia (30%). The incidence of eclampsia however was much lower in our study (6%). These differences could be due to small sample size of our study and the social ethnic and cultural difference in group of population studied as noted by Wolde et al.[23] who has quoted black race as one of the risk factors for PIH.

Mohapatra S et al.15 (2007) in their study in S.C.B Medical College, Cuttack observed that there is an inverse relationship between the severity of PIH and platelet numbers. [25]

Vrunda JK et al.16 (2004) in their study on platelet count in PIH patients observed that thrombocytopenia is directly proportional to the severity of PIH. [26]

Shete AN et al.17 (2013), Government Medical College, Aurangabad, conducted a study to assess the Physiological stress during Pregnancy Induced
Hypertension and observed a significant decrease in platelet count. [27]

Thrombocytopenia is observed in 6 to 15% of pregnant women at the end of pregnancy, and is usually moderate. Its prevalence at the end of pregnancy is between 6.6% and 11.6% 2-4. Gestational thrombocytopenia is the most common cause of thrombocytopenia during pregnancy. Thrombocytopenia which need to be investigated are the following: thrombocytopenia known before pregnancy, thrombocytopenia occurring during the 1(st) and 2(nd) trimester, platelet count.

Gestational Thrombocytopenia is the most commonly observed during pregnancy (70%), but other underlying causes must be considered as well. A thorough history and physical examination will rule out most causes. Look at the remainder of CBC and smear to rule out pancytopenia and platelet clumping associated with pseudothrombocytopenia. If no antecedent history of thrombocytopenia is present and platelet counts are above 70,000/mcl, the condition is more likely to be GT. If platelet counts fall below 50,000/mcl or if a pre-existing history of thrombocytopenia is present, the condition is more likely to be ITP.

Because thrombocytopenia can be induced acutely by pre eclampsia – eclampsia, the platelet count is routinely measured in hypertensive pregnant women. The frequency and intensity of maternal thrombocytopenia varies and likely is dependent on the intensity of the disease process, duration of pre eclampsia, and the frequency with which platelet count are performed. Overt thrombocytopenia, defined by a platelet count less than 100,000/mm3 indicates severe disease. In most cases, delivery is indicated because the platelet count continues to decrease. After delivery, the platelet count increases progressively reach a normal level within 3 to 5 days.

Decrease in platelet count is proportional to severity of disease. Assessment of platelet count is a simple, cost effective & sensitive method to know the prognosis & fetomaternal outcome in preeclampsia & eclampsia.

Conclusion:

Clinically platelet indices can be a useful screening test for early identification of preeclampsia and eclampsia. Also platelet indices can assess the prognosis of this disease in pregnant women and can be used as an effective prognostic marker because it correlates with severity of the disease. Platelet count is a simple, low cost, and rapid routine screening test. Hence the data generated from the present study concludes that platelet count can be used as a simple and cost effective tool to monitor the progression of preeclampsia, thereby preventing complications to develop during the gestational period.

References: