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MODERATE TO SEVERE THROMBOCYTOPENIA IN THE PARTURIENT

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ABSTRACT

Objectives: To analyse patients with moderate to severe thrombocytopenia in labour, to identify the etiology, assess severity, correlate with the maternal disease and management.
Methods: A retrospective study of all pregnant women admitted in labour or in obstetric critical area and found to have a low platelet count were included in a study period of 18 months from July 2013 to Dec 2014.
Results: 25 women out of 2738 deliveries were identified and commonest cause was severe pre-eclampsia with or without HELLP. Coincidental dengue with super added pre-eclampsia was found in 3 women. Severe thrombocytopenia was found in haematological conditions like ITP and aplastic anemia.
Conclusion: Low platelets or fall in platelets showed a worsening of disease condition. Platelet transfusion needs to be done if the cut off is below the desired target level. Timely administration of platelets and discrete use of SDP especially when massive platelet transfusion is required required as mandatory. Delivery should be as atraumatic as possible, avoidance of episiotomy to be practiced. Sometimes treatment can be challenging and involve multi-disciplinary approach.

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INTRODUCTION

Thrombocytopenia is the most common hemostatic abnormality in pregnancy occurring in approximately 10% of all pregnant women. Abnormalities of platelet count may either be mild when the platelet count is between 150,000 and 100,000/mm^3, moderate when the count is between 100,000 and 50,000/mm^{3}or severe when the count is < 50,000/mm^3 (1). Gestational thrombocytopenia is the commonest cause of low platelets in pregnancy, however the count rarely falls below 70,000/mm^3 and is not of much clinical significance. Moderate to severe thrombocytopenia may occur due to either pre-existing disease like immuno thrombocytopenia (ITP), Systemic lupus erythematosus (SLE), anti-phospholipid syndrome (APLA) or pregnancy related conditions like pregnancy induced hypertension (PIH), HELLP, acute fatty liver of pregnancy (AFLP), ect (Kam, 2004). In labour low platelet count is a risk not only to the mother but also to the fetus. Most patients with mild thrombocytopenia do not have any hemostatic risk and do not require treatment unless the degree of thrombocytopenia worsens.

However moderate to severe thrombocytopenia is associated with adverse effects. The threshold for significant spontaneous bleeding is a count of 10,000/mm^3 and in the case of surgical interventions or delivery the threshold is higher >50,000/mm^3. The underlying disorder may manifest as thrombocytopenia and warrant immediate termination. The obstetrician concern is how to obtain hemostasis in the event of delivery and may involve multidisciplinary approach. Many articles describe thrombocytopenia in pregnancy however in labour only few references could be found. The aim of this article is to analyse the etiology of thrombocytopenia in labour, clinical features, management, platelet transfusions and fetal outcome.

MATERIALS AND METHODS

A retrospective study of all pregnant women admitted in labour or in obstetric critical area and found to have a low platelet count were included in a study period of 18 months. Only women with counts less than 1,00,000/mm^3 were included. The cases were analysed for the following:

- Etiology
- Clinical features
- Platelet count on admission
- Correlation with platelet count and maternal disorder.
- Need for platelet transfusion
- Gestational age at presentation.
- Outcome of pregnancy.

The condition of the baby in terms of gestational age, live birth or stillbirth were also assessed. Problems during transfusion were also assessed. The criteria for severe pre-eclampsia were blood pressure > 160/110mmhg, proteinuria +++ or more, oliguria, visual disturbance, epigastric pain, thrombocytopenia or impaired liver function.

Criteria for HELLP were

- Hemolysis as shown by peripheral smear or elevated billirubin > 1.2mg/dl
- Elevated liver enzymes : AST > 72IU/L, LDH > 600 IU/L
- Low platelets : count < 100,000/mm^3.

Management of these women, when and how they were terminated, type of transfusions and problems encountered were also analysed.

RESULTS

Table 1. Analysis of etiology

Cause	Number of cases
Severe pre-eclampsia with and without HELLP	18
PIH with Dengue	3
Megaloblastic anemia	1
ITP	1
Aplastic anemia	1
DIC	1
Total cases	25

Table 2 : Clinical features – combination of clinical features were seen

Clinical feature	Number of cases
Elevated BP	21
HELLP	7
Severe anemia	2
Eclampsia	4
Abruption	2
Renal failure	4
Bleeding episodes	6
Fever	3
Abdominal distention	1

Table 3. Correlation between platelet count on admission and diagnosis

Platelet Count	PIH	PIH with Dengue	Megaloblastic anemia	ITP	Aplastic anemia	DIC
100,000-50,000	10		1			1
50,000-20,000	6					
20,000-10,000	2	1		1		
<10,000		2			1	

The total number of deliveries were 2738 in the study period. The number patients with severe to moderate thrombocytopenia were 25.

The etiology was predominantly PIH seen in 18 women. PIH with super added dengue was seen in 3 women. Hematological disorders like ITP, aplastic anemia and megaloblastic anemia were seen in one each. One patient was found to have hemoperitoneum after caesarean and was found to have DIC. The clinical features at presentation were predominantly those of severe pre-eclampsia as shown in table 2. Combination of features like elevated blood pressure, HELLP, eclampsia, abruption and renal failure were seen. Bleeding episodes like haematuria, malena, bleeding from IV sites, bleeding gum, purpuric spots were seen in 6 women. Fever with elevated BP, abdominal distention following caesarean were also seen.

Table 3 shows the correlation between the platelet count on admission and diagnosis. The platelet count was moderate thrombocytopenia in 12 women, severe thrombocytopenia in 13 women. In the severe thrombocytopenic group 3 women had counts <10,000 cells/mm^3 and 4 women had counts between 10,000 to 20,000 cells/mm^3. In the PIH group platelet count was moderate thrombocytopenia in 10 out of 18 women. 6 women had counts between 50,000 to 20,000 cells/mm^3 and only 2 women had counts between 20,000 to 10,000 cells/mm^3. In patients with dengue and superadded PIH (3 women) the platelet count was <20,000 cells/mm^3 in all. The woman with megaloblastic anemia and dilutional coagulopathy had counts of 60,000/mm^3. Woman with ITP and aplastic anemia had very low counts <20,000cells/mm^3 and <10,000cells/mm^3 respectively. On analysis of platelet transfused in PIH women only 8 received transfusion and 10 did not. All women with dengue received multiple transfusions of 20 to 24 units. The woman with ITP received 44 units of platelet transfusion and the women with aplastic anemia received 40 units of platelets and 10 units of single donor platelets (SDP) as shown in table 4. There was one spontaneous expulsion at 26 weeks of pregnancy, live births were seen in 19 women and 5 women had IUD or stillbirth. 8 women delivered before 34 weeks and 16 women delivered 34 to 38 weeks of pregnancy. Table 5 shows the gestational age at presentation and fetal outcome.

DISCUSSION

Pregnancy is a hypercoagulable state with increased level of clotting factors. However platelet count declines as pregnancy advances. A platelet count < 150,000/mm^3 occurs in 1% of population but occurs in 6 to 12% of pregnancy women at term (McCrae, 2003; Boehlen, 2000). Approximately 1% of all pregnancy women have a count <100,000/mm^3 and about 1 in 1000 to 2000 have a count <50,000/mm^3. In our series also the incidence was similar around 1% of all patients had counts <100,000/mm^3 and severe thrombocytopenia was seen in 4-5/1000 women. In general, patients with a platelet count < 20,000//mm^3 are at risk of spontaneous bleeding. Platelet counts between 20,000 to 50,000/mm^3 have a risk of bleeding during procedures or delivery (Andra, 2013). Patients with counts >50,000/mm^3 generally have minimal risk of bleeding. PPH is the leading cause of maternal mortality (Lale, 2014) and when a patient enters the labour room with a low platelet there is great fear as to whether she would bleed during delivery, how much and how to prevent PPH. Therefore there is great concern to ascertain the diagnosis and immediate treatment. In our study pre-eclampsia was the commonest cause of severe and moderate thrombocytopenia.

Table 4: Transfusion chart

Platelet Count	PIH		Dengue		Megaloblastic anemia		ITP		Aplastic anemia		DIC	
	R	NR	R	NR	R	NR	R	NR	R	NR	R	NR
100,000-50,000	2	8			1						1	
50,000-20,000	4	2										
20,000-10,000	2		1				1					
<10,000			2						1			

R – Received, NR – Not Received

Table 5. Gestational age at presentation & fetal outcome

Gestational age	PIH	Others	IUD/Still birth
< 28 weeks	1	0	1
28 to 34 weeks	7	1	3
34 to 38 weeks	13	3	2
>38 weeks	0	0	0

Pre-eclampsia is said to be present in 21% of maternal thrombocytopenia[6]. Thrombocytopenia occurs in 50% of pre-eclampsia and occasionally precedes other manifestation of the disease. A decrease in platelet count is considered as an early sign of worsening of pre-eclampsia and may occur even before other clinical manifestation of disease are apparent (McCrae, 2003). The severity of thrombocytopenia directly correlates with the severity of the lesion. HELLP syndrome is often considered to be a variant of pre-eclampsia and in 1982 Weinstein coined the term HELLP and also stated that its presence is an indication for delivery as there is increased risk of maternal and fetal mortality (Weinstein, 1982). The hallmark of HELLP is microangiopathic hemolytic anemia, elevated liver enzymes and low platelet count. The reported cutoff value have ranged from 75,000/mm^3 to 229,000/mm^3 with a level of <100,000/mm^3 most often cited. HELLP may be complete with all the elements or partial with one or two components. HELLP occurs in 0.5 to 0.9 of all pregnancies and in 20% of all cases with severe pre-eclampsia.

The Mississippi Triple class system classifies this syndrome based on platelet counts (Joshi, 2010).

- Class I< 50,000/mm^3
- Class II50,000 to 1,00,000/mm^3
- Class III1,00,000 to 1,50,000/mm^3

In our study of 21 women with PIH, 7 women had HELLP, 5 belonging Mississippi Class I and 2 to Class II. Abruption was found in 2 and eclampsia was found in 4. HELLP, abruption and eclampsia require immediate termination irrespective of the gestational age. All our patients were terminated before 38 weeks of pregnancy, most of them were early or late preterm. Only one patient expelled at 26 weeks. M Sibai et al also states the same in his analysis of 442 pregnancies with HELLP syndrome [9]. In a study of 437 women who had 442 pregnancy with HELLP syndrome, serious maternal morbidity including DIC (21%), abruption 16%, ARF 8%, Pulmonary edema 6%, liver haematoma 1%, retinal detachment 1%. 55% of patients required blood component therapy and 2% required laparotomy for bleeding. Maternal mortality was 1%. Of 21 patients with low platelets with PIH, transfusion was done only in 11 patients, 9 of them had counts <50,000/mm^3 and only 2 had counts >50,000/mm^3 - one had 55,000/mm^3 and other had 62,000/mm^3, since LSCS had to be performed platelet transfusion was done as per British guidelines. Platelet count of > 80,000/mm^3 is recommended for epidural anesthesia by the British committee for the standards in hematology [10]. The count that was aimed in our patients was 50,000/mm^3 for vaginal delivery and 80,000/mm^3 for LSCS.

Dengue with super added PIH was seen in 3 patients. 2 of these patients in addition had HELLP-one complete and another partial. These patients had extremely low platelet counts (7,000/mm^3). The counts were much lower than those seen in severe pre-eclamsia. All of them had bleeding tendencies and all required transfusions. 24 units were given for the patient with 9000/mm^3, 22 units for a patient with twins and a count of 7,000 cells and 7 units for a patient with partial HELLP and previous caesarean. The rise in platelet count was very slow in this group, it took 10 days for platelet count to stablise. Dengue is a common tropical disease in our country. All our 3 patient had secondary dengue with super added pre-eclampsia and presented with bleeding tendencies. No reports of dengue with pre-eclampsia have been reported so far. The compounded effect of pre-eclampsia and dengue lead to very low platelet count and massive platelet transfusion was required in these women. The interval between the diagnosis and delivery was within 2 to 3 days. Termination was done immediately for all case of abruption, eclampsia, renal failure and HELLP after platelet correction to the desire level. In preterm mothers steroid administration was done for lung maturity and subsequently induction or LSCS was resorted to based on other parameters.

Haematological disorders must always be borne in mind especially when the clinical situation rules out pregnancy related conditions like PIH. In cases of severe anemia, megaloblastic anemia must always be thought of as was done in our case. In case of megaloblastic anemia the patient was referred as severe anemia with hemoglobin of 4.3gm/dl, platelet count showed 60,000cells/mm^3 . Anemia was more profound in this case and peripheral smear and bone marrow confirmed the diagnosis. A patient with known ITP presented at 28 weeks with PROM. She was on steroids. After delivery she developed hemothorax. She was treated as per ASH guidelines (The American Society of Hematology, 2011) Since she did not respond to steroids, Anti Rh immunoglobulin was given. She received a total of 44 units of platelets. Splenectomy was done as a last resort. A normotensive woman was referred as severe anemia with low platelet count. Dengue and drug history were ruled out. ITP was initially thought of, but inspite of transfusion the platelet count never raised. The expected rise was 5000cell/mm^3 after the single unit of transfusion but in this patient even after 4-5 units the counts did not raise. Further evaluation was done and ultimately a bone marrow confirmed aplastic anemia. We had to delivery her for fear of abruption or bleeding elsewhere and planned to refer her for bone marrow transplant. The patient was delivered under cover of single donor platelet.

However following delivery the counts fell to <2000/mm^3, she developed huge vulval haematoma, multiple bleeds, cerebral bleed and could not be resuscitated. Sometimes massive bleeding as in PPH may result in dilution coagulopathy as seen in our patient. This patient was referred from outside with abdominal distention after caesarean section, was found to have hemoperitoneum with platelet count of 60,000cells/mm^3, hemoglobin of 5gm/dl, fibrinogen of 150mg/dl, INR 1.6, she was diagnosed as DIC. NIH consensus conference report noted that pathological haemorrhage in a patient receiving massive transfusion is caused more frequently by thrombocytopenia than by depletion of coagulation factors. This may be due to hemodilution using crystalloids or using only packed cells. In such a situation it is always worthwhile to serially check for platelet count, PT & INR to see if dilution coagulopathy has occurred, since unless it is corrected bleeding would not stop (Platelet Transfusion Therapy, 1986). Still birth and IUD were seen in 6 women all in the PIH group. The high perinatal mortality was due to prematurity and IUGR. Similar reports are quoted by Kubilay Ertan (A Kubilay Ertan, 2002). However thrombocytopenia was not related to the preterm birth.

Factors to be considered in thrombocytopenic patients in the last trimester are

- When to terminate?
- What is the mode of termination?
- What is the ideal count to be obtained?
- What is the type of transfusion to be given?

Termination needs to be thought of only for maternal conditions like PIH, HELLP or abruption. The severity of thrombocytopenia directly correlates with the severity of the lesion[(14)]. Patient with severe PIH need to be serially monitored and a drop in platelet count may heralds the onset of HELLP. Careful surveillance is necessary. Vaginal birth is the preferred mode delivery. The chance of bleeding is less when trauma is minimal. Even episiotomy need to be given only where necessary because 1 patient with aplastic anemia had huge vulval haematoma after delivery. Both British and American guidelines suggest a platelet count >50,000/mm^3 is safe for vaginal delivery. British guidelines suggest aiming at a platelet count >80,000/mm^3 for a caesarean section. The count that was aimed in our patients was 50,000/mm^3 for vaginal delivery and 80,000/mm^3 for LSCS.

A single unit of platelet transfusion rises the platelet count by 5,000/mm^3. A unit obtained by apheresis of a single donor (SDP) contains an equivalent of 5 to 6 units raising the platelet count by around 30,000 to 60,000/mm^3. Platelet should be ABO and Rh compatible. Since stored platelets have a very short shelf- life, procuring many units may be a problem as the blood bank may not have that many bags. When requirement of platelet is large SDP is preferred as the risk of blood born pathogenesis is low, as also alloimmunisation. Where aphaeresis unit is not available, obtaining one required a lot of effort and co-ordination. Since the presentation varied interdepartmental assistance was often required. Good co-ordination with blood bank was required for procuring blood and blood products. In addition consultation with intensivist, haematologist, nephrologist, anesthetists and pediatrician was required. Team approach was the secret of success of survival of these patients.

Conclusion

Unlike in the antenatal period, moderate to severe thrombocytopenic patients near term are in a grave situation – one because the diagnoses has still to be made and secondly due to limited time constraints as delivery is imminent. A detailed history & physical examination is necessary in evaluating a patient with thrombocytopenia. Timely administration of platelets and discrete use of SDP especially when massive platelet transfusion is required helps prevent risk of infection and alloimmunisation. A platelet count of above 10,000cells/mm^3 must be maintained even after delivery to prevent spontaneous bleeding. Delivery should be as atraumatic as possible, avoidance of episiotomy to be practiced. Any pregnancy with a low platelet count less than 50,000cells/ml requires to be shifted to a tertiary centre, since etiology is varied and treatment is multidisciplinary.

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