



## Research Article

### Moderate to Severe Thrombocytopenia in the Parturient

Chitra Bhat TV\* and Seetha Panicker

Department of Obstetrics & Gynecology, Institute of Medical Sciences & Research, Tamilnadu, India

#### Abstract

To analyse patients with moderate to severe thrombocytopenia in labour and outcomes.

#### Methods

A retrospective study was done on patients with thrombocytopenia of counts  $<1,00,000$  in labour were analysed for period of 18 months from July 2013 to December 2014.

#### Results

The commonest cause of thrombocytopenia in labour was pregnancy induced hypertension. However other haematological conditions like ITP, aplastic anemia were also seen. Dengue with super added preeclampsia decreased the platelet count significantly.

#### Conclusion

Moderate to severe thrombocytopenia in labour is associated with adverse conditions like preeclampsia requiring immediate termination of pregnancy.

**Keywords:** Dengue; HELLP; Platelet count; Single donor platelet; Thrombocytopenia

#### Introduction

Thrombocytopenia is the most common 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  $100,000/\text{mm}^3$ , moderate when the count is between  $100,000$  and  $50,000/\text{mm}^3$  or severe when the count is  $<50,000/\text{mm}^3$  [1].

Gestational thrombocytopenia is the commonest cause of low platelets in pregnancy, however the count rarely falls below  $70,000/\text{mm}^3$  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 [2].

\*Corresponding author: Chitra Bhat TV, Department of Obstetrics & Gynecology, Tamilnadu, India, Tel: +91 422-2570170; +91 9443353191; E-mail: chitravi@vsnl.com

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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 require treatment. However moderate to severe thrombocytopenia is associated with adverse effects. The threshold for significant spontaneous bleeding is a count of  $10,000/\text{mm}^3$  and in the case of surgical interventions or delivery the threshold is  $50,000$ . The obstetrician's concern is to identify the cause of thrombocytopenia assess the severity and plan an appropriate management. This may involve multidisciplinary approach. Many articles describe thrombocytopenia in pregnancy however very few articles discuss thrombocytopenia in labour.

The aim of this article is to analyse the etiology of thrombocytopenia in labour, clinical features, management, platelet transfusions and fetal outcome.

#### Material and Methods

A retrospective study of all pregnant women admitted in labour and found to have a low platelet count were included in a study period of 18 months from July 2013 to December 2014. Only women with counts less than  $1,00,000/\text{mm}^3$  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 conditions 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  $>160/110$  mmhg, 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 bilirubin  $>1.2$  mg/dl
- Elevated liver enzymes : AST  $>72$  IU/L, LDH  $>600$  IU/L
- Low platelets: Count  $<100,000/\text{mm}^3$

Management of these women, mode of delivery, gestational age of termination, platelet transfusions and problems encountered were also analysed.

The total number of deliveries were 2738 in the study period. The number patients with severe to moderate thrombocytopenia were 25 as shown in table 1. The etiology was predominantly PIH as seen in 18 women. PIH with super added dengue was seen in 3 women. Hematological disorders like ITP, aplastic anemia and megaloblastic anemia

## Results

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 1:** Analysis of etiology.

were seen in one each. One patient was found to have after caesarean and was found to have DIC.

Many patients were found to have an elevated blood pressure on examination. Convulsions, absent fetal movements and reduced urine output were seen in few (Table 2). Haematuria, malena, bleeding from IV sites, bleeding gum, purpuric spots were seen in 6 women.

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

**Table 2:** Clinical features - Combination of clinical features were 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<sup>3</sup> and 4 women had counts between 10,000 to 20,000 cells/mm<sup>3</sup> and the remaining 6 women had counts between 20,000 to 50,000 cells/mm<sup>3</sup>

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	

**Table 3:** Correlation between platelet count on admission and diagnosis.

In the PIH group platelet count was moderate thrombocytopenia in 10 women. 6 women had counts between 50,000 to 20,000 cells/mm<sup>3</sup> and only 2 women had counts between 20,000 to 10,000 cells/mm<sup>3</sup>. In patients with dengue and superadded PIH (3 women) the platelet count was below 20,000 cells/mm<sup>3</sup> in all. Woman with ITP and aplastic anemia had very low counts.

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. Multiple transfusions were required in ITP and aplastic anaemia patients. 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.

Platelet count	PIH	Dengue with PIH	Megaloblastic anemia	ITP	Aplastic anemia	DIC
100,000-50,000	2		1			1
50,000-20,000	4					
20,000-10,000	2	1		1		
<10,000		2			1	

**Table 4:** Transfusion chart.

Table 5 shows the gestational age at presentation and fetal outcome. There were 19 live births and 5 women had either an intrauterine death or stillbirth and there was one abortion. 8 women delivered before 34 weeks and 16 women delivered between 34 to 38 weeks of pregnancy.

Gestational age	PIH	Others [Excluding PIH]	Fetal outcome IUD/Stillbirth
<28 weeks	1	0	1
28 to 34 weeks	7	1	3
34 to 38 weeks	13	3	2
>38 weeks	0	0	0

**Table 5:** Gestational age at presentation & 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<sup>3</sup> occurs in 1% of population but occurs in 6 to 12% of pregnant women at term [2,3]. Approximately 1% of all pregnant women have a count <100,000/mm<sup>3</sup> and about 1 in 1000 to 2000 have a count <50,000/mm<sup>3</sup>. In our series, the incidence was similar around 1% of all patients had counts <100,000/mm<sup>3</sup> and severe thrombocytopenia was seen in 4-5/1000 women.

In general, patients with a platelet count <10,000/mm<sup>3</sup> are at risk of spontaneous bleeding without any intervention. Platelet counts between 20,000 to 50,000/mm<sup>3</sup> have a risk of bleeding during procedures or delivery [4]. Patients with counts >50,000/mm<sup>3</sup> generally have minimal risk of bleeding.

Post partum hemorrhage is the leading cause of maternal mortality [5] and when a patient enters the labour room with a low platelet there is risk of excessive bleeding.

In our study pre-eclampsia was the commonest cause of severe and moderate thrombocytopenia. 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 [2].

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 [7].

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<sup>3</sup> to 229,000/mm<sup>3</sup> with a level of <100,000/mm<sup>3</sup> 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 [8].

- Class I <50,000/mm<sup>3</sup>
- Class II 50,000 to 1,00,000/mm<sup>3</sup>
- Class III 1,00,000 to 1,50,000/mm<sup>3</sup>

In our study of 21 (18+3) women with PIH, 7 women had HELLP, 5 belonging Mississippi Class I and 2 to Class II. Abruptio was found in 2 and eclampsia was found in 4. HELLP, abruptio 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.

Sibai M 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%), abruptio 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 18 patients with low platelets with PIH, transfusion was done only in 8 patients, 6 of them had counts <50,000/mm<sup>3</sup> and only 2 had counts >50,000/mm<sup>3</sup> - one had 55,000/mm<sup>3</sup> and other had 62,000/mm<sup>3</sup>. Since LSCS had to be performed platelet transfusion was done as per British guidelines. Platelet count of >80,000/mm<sup>3</sup> 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<sup>3</sup> for vaginal delivery and 80,000/mm<sup>3</sup> 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<sup>3</sup>). All of them had bleeding tendencies and all required transfusions. 24 units were given for the patient with 9000/mm<sup>3</sup>. 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.

Dengue is a common tropical disease in our country. All our 3 patients had secondary dengue with super added pre-eclampsia and presented with bleeding tendencies. There has been no report of dengue with pre-eclampsia so far. The compounded effect of pre-eclampsia and dengue led to very low platelet counts and multiple platelet transfusion were required in these women.

The interval between the diagnosis of thrombocytopenia and delivery was within 2 to 3 days. Termination was done immediately for all case of abruptio, eclampsia, renal failure and HELLP after platelet correction to the desired level. In preterm mothers steroid administration was done for lung maturity and subsequently induction or LSCS was resorted to based on other parameters.

In cases of severe anemia, megaloblastic anemia must always be thought of. In our case of megaloblastic anemia the patient was

referred as severe anemia with hemoglobin of 4.3 gm/dl, platelet count showed 60,000 cells/mm<sup>3</sup>. Anemia was 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 [11]. Since she did not respond to steroids, Anti Rh immunoglobulin was given and 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 increased. The expected rise was 5000 cell/mm<sup>3</sup> after the single unit of transfusion but in this patient even after 4-5 units the counts did not rise. Further evaluation was done and ultimately a bone marrow confirmed aplastic anemia. We had to deliver her for fear of abruptio or bleeding elsewhere and was planned to refer her for bone marrow transplant. The patient was delivered under cover of single donor platelet. However following delivery the counts fell below <2000/mm<sup>3</sup>, she developed a 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 one of our patient. This patient was referred from outside with abdominal distention after caesarean section and was found to have hemoperitoneum with platelet count of 60,000 cells/mm<sup>3</sup>, hemoglobin of 5 gm/dl, fibrinogen of 150 mg/dl, INR 1.6 and 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 and to replace platelets [12].

Stillbirth and IUD were seen in 6 women. The high perinatal mortality was due to prematurity and IUGR. Similar reports are quoted by Kubilay Ertan [13]. 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 abruptio. More severe the PIH, more severe is the thrombocytopenia [14]. Patient with severe PIH need to be serially monitored and a drop in platelet count may herald the onset of HELLP. Careful surveillance is necessary.

Vaginal birth is the preferred mode delivery in patient with thrombocytopenia. The chance of bleeding is less when trauma is minimal. Episiotomy need to be given only when necessary because the patient with aplastic anemia had a huge vulval haematoma after delivery. Both British and American guidelines suggest a platelet count >50,000/mm<sup>3</sup> is safe for vaginal delivery. British guidelines suggest aiming at a platelet count >80,000/mm<sup>3</sup> for a caesarean section.

A single unit of platelet transfusion rises the platelet count by 5,000/mm<sup>3</sup>. 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<sup>3</sup>. 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 apheresis 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 necessary for procuring blood and blood products. In addition consultation with intensivist, haematologist, nephrologist, anaesthetists and paediatrician was required. Team approach is essential for survival of these patients.

## Conclusion

Unlike in the antenatal period, patients nearing delivery with low platelets are in a grave situation-one because the diagnoses has still to be made and secondly due to limited time constraints. A detailed history & physical examination is necessary in evaluating patients with thrombocytopenia. Timely administration of platelets and discrete use of SDP especially when massive platelet transfusion is required to help prevent risk of infection and alloimmunisation. Delivery should be as atraumatic as possible. Any pregnancy with a low platelet count less than 50,000 cells/ml requires to be shifted to a tertiary centre, since etiology is varied and treatment is multidisciplinary.

## References

1. Kam PC, Thompson SA, Liew AC (2004) Thrombocytopenia in the parturient. *Anaesthesia* 59: 255-264.
2. McCrae KR (2003) Thrombocytopenia in pregnancy: Differential diagnosis, pathogenesis and management. *Blood Rev* 17: 7-14.
3. Boehlen F, Hohlfeld P, Extermann P, Perneger TV, de Moerloose P (2000) Platelet count at term pregnancy: A reappraisal of the threshold. *Obstet Gynecol* 95: 29-33.
4. James AH (2013) Bleeding and the management of haemorrhagic disease in pregnancy. In: Kitchens, Konkle, Kessler (eds.). *Text book of Consultative hemostasis and thrombosis*, (3rd edn), Elsevier, Amsterdam, Netherlands.
5. Lale Say (2014) Global causes of maternal death: A WHO systematic analysis. *Lancet Global Health* 2: 323-333.
6. Burrows RF, Kelton JG (1993) Fetal thrombocytopenia and its relation to maternal thrombocytopenia. *N Engl J Med* 329: 1463-1466.
7. Weinstein L (1982) Syndrome of hemolysis, elevated liver enzymes and low platelet count: A severe consequence of hypertension in pregnancy. *Am J obstet gynecol* 142: 159-167.
8. Joshi D, James A, Quaglia A, Westbrook RH, Heneghan MA et al., (2010) Liver disease in pregnancy. *Lancet* 375: 594-605.
9. Sibai BM, Ramadan MK, and Usta I Salama M, Friedman SA et al., (1993) Maternal morbidity and mortality in 442 pregnancies with hemolysis, elevated liver enzymes and low platelets (HELLP syndrome). *Am J Obstet Gynecol* 169: 1000-1006.
10. Gernsheimer T, McCrae KR (2007) Immune thrombocytopenic purpura in pregnancy. *Curr Opin Hematol* 14: 574-580.
11. Neunert C, Lim W, Crowther M, Cohen A, Solberg Jr L (2011) The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia. *Blood* 117: 4190-4207.
12. [No authors listed] (1986) Platelet Transfusion Therapy. National Institutes of Health Consensus Development Conference Statement October 6-8, 1986. NIH Consensus Development Program 7: 1-6.
13. Ertan AK, Wanger S, Hendrik HJ (2002) Clinical and biophysical aspects of HELLP syndrome. *J Perinat Med* 30: 483-489.
14. Parnas M, Sheiner E, Shoham-Vardi I, Burstein E, Yermiahu T et al. (2006) Moderate to severe thrombocytopenia during pregnancy. *Eur J Obstet Gynecol Reprod Biol* 128: 163-168.