Original Article

Prevalence and Etiology of Thrombocytopenia in Pregnant Women in Southern Pakistan

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Abstract

Objective: To determine the causes of thrombocytopenia in pregnancy along with the maternal and neonatal outcomes.

Methodology: This descriptive cross-sectional study was conducted in Department of Gynaecology and Obstetrics, unit III Civil hospital Hyderabad from September 2013 to March 2014. Eighty seven pregnant women with thrombocytopenia were included in this study. Samples of blood were collected and analyzed for complete blood count, LFT, PT, and APTT.

Results: The mean age of the women was 26.91±5.28 years. We determined the predominant causes of thrombocytopenia as gestational thrombocytopenia (57.5%), followed by eclampsia (16.1%), preeclampsia (16.1%), HELLP syndrome (12.0%), DIC (3.4%) and immune thrombocytopenic purpura (3.3%). Regarding maternal outcome, antepartum bleeding was observed in 16.0% cases, postpartum bleeding was in 41.3% and maternal mortality was observed in 8.0%. The neonatal outcome showed 77.0% delivered full term whereas 22.9% were preterm. Overall 77.1% neonates were alive, 16.0% were IUD and 6.9% were IUGR.

Conclusion: Thrombocytopenia in pregnancy is associated with maternal and neonatal morbidity and mortality. Therefore, we strongly recommend careful surveillance of these thrombocytopenic mothers and their babies in order to establish the aetiology and timely appropriate intervention.

Key Words: Thrombocytopenia, gestational thrombocytopenia, eclampsia, HELLP syndrome.

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Introduction

Thrombocytopenia is basically defined as a platelet count of less than 150,000/μL.[1,2] Counts from 100,000 to 150,000/μL are considered mildly decreased, 50,000 to 100,000/μL are moderately decreased and less than 50,000/μL are severely decreased.[3] The overall thrombocytopenia occurs in 8% of pregnancies and this incidence falls to 5.1% when patients with obstetric or medical disorders are excluded. [4]

The reason why platelet count decreased in normal pregnancy is not clearly known, but it may be due to low platelet formation or raised platelet "turn over" during pregnancy. [5, 6] In one study it was found that the main causes of thrombocytopenia were

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gestational thrombocytopenia (59.3%), immune thrombocytopenic purpura (11.0%), preeclampsia (10.0%) and HELLP syndrome (12.0%). Thrombocytopenia was associated with higher rates of placental abruption, preterm deliveries, intrauterine growth restriction and stillbirth.[7]

In Pakistan, prior studies demonstrated that main cause of thrombocytopenia in pregnancy is gestational thrombocytopenia, which affects about 6% of pregnancies and constitutes about 75% of cases of pregnancy-related thrombocytopenia.[8,9]The platelet count decreases about 10% and this usually noted in the third trimester and comes to normal within 6 weeks postpartum.[8,9] Immune thrombocytopenia was found in 0.01–0.05% of pregnancies. [8,9] Pregnancy is a procoagulant state induced by raised level of fibrinogen, factor VIII and vonwillebr and factor (VWF), suppressed fibrinolysis and decreased protein S activity. So, women with decreased platelet count during pregnancy are usually less symptomatic due to the procoagulant state. [10] With this background, we designed this study to identify the aetiology of thrombocytopenia in pregnancy and its effect on the fetomaternal outcome.

Methodology

This descriptive cross-sectional study was carried out in Department of Gynaecology and Obstetrics, unit III Civil hospital, Hyderabad from September 2013 to March 2014. A sample size of 87 patients was calculated by the taken prevalence of 8%,[5] 95% confidence level with an absolute precision of 10%.

All pregnant women admitted through emergency and inward fulfilling the inclusion criteria were included after informed consent. Pregnant women with thrombocytopenia having platelets <150x10^9/l were the inclusion criteria. Pregnant women with prior medical disorders like diabetes mellitus, liver impairment, renal disorders, cardiac diseases, and malignancies were excluded. Patients with prior history of thrombocytopenia were also not included in this study.

Data collection procedure: Eligible pregnant women were enrolled. All patients underwent detailed history and examination. Detailed history like age, gravida, parity, LMP, gestational age any complication antepartum haemorrhage, hypertension in current pregnancy, history of antipartum haemorrhage and post partum haemorrhage in previous pregnancies and outcome of previous pregnancies. Samples of blood were collected and analysed for complete blood count along with peripheral smear examination, LFT, PT and APTT. The above information was recorded by the researcher. The study was approved from an ethical review committee of the institute.

Data analysis Procedure: Data was entered and analyzed using SPSS version 18. Frequency and percentages was recorded for qualitative variables like the cause of thrombocytopenia and maternal and neonatal outcome. Mean ± SD was recorded for quantitative variables like age, gestation age and platelet counts.

Results

During study duration, 1431 patients visited, out of which 87 (6.0%) pregnant women having thrombocytopenia were included in this study.

The mean age of the women was 26.91±5.28 years with the range of 16 to 42 years. The median age was 26 years. Age distribution of the women showed that 45.9% [n=40] were under 25 years, 48.2% [n=42] were between 26 to 35 years and only 5.7% [n=5] were above 35 years.

Mean gestational age was 35.63±4.17 weeks; minimum gestational age was 22 weeks while maximum gestational age was 41 weeks (table-I).

Table I: Statistics of Gestational Age & Platelets Counts

Statistics	Results
Mean gestational age	35.63±4.17 weeks
Minimum gestational age	22 weeks
Maximum gestational age	41weeks
Mean platelets counts	117x10^9/l
Median count	128x10^9/l
Minimum platelets count	35x10^9/l
Maximum platelets count	141x10^9/l

Most of the women were primigravida accountable in 72.3% of cases and multiparity was in 27.59% of cases.

The mean platelets counts were 117x10^9/l with the median count of 128x10^9/l. The minimum platelets count was 35x10^9/l while the maximum was 141x10^9/l. In this study, most common causes of

thrombocytopenia were gestational thrombocytopenia (57.5%), eclampsia (16.1%), preeclampsia (16.1%), HELLP syndrome (12.0%), DIC (3.4%) and immune thrombocytopenic purpura (3.3%) as shown in figure-1.

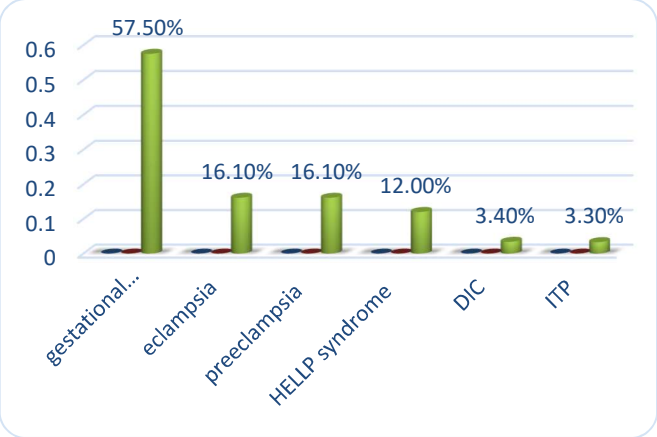

Figure 1. Causes of Thrombocytopenia in Pakistani Pregnant Patients

Regarding maternal outcome, antepartum bleeding was observed in 16.0% cases, post partum bleeding was 41.3% and maternal mortality was observed in 8.0% (table-II). While neonatal outcome showed 77.0% delivered at term whereas 22.9% delivered preterm. Neonatal outcomes showed 14 (16%) cases of IUD and 6 (6.9%) were IUGR, remaining all were healthy alive. Neonatal outcome in term of median Apgar score at 5 minutes was 7 (IQR=1) as shown in table III.

Table II: Maternal Outcomes	
Maternal outcomes	**percentages**
Antepartum bleeding	16.0%
Post partum bleeding	41.3%
Maternal mortality	8.0%

Table III: Statistics of Apgar Score At 5 Minutes (n=87)		
Statistics		**Apgar Score**
Mean		6.59
95% Confidence Interval for Mean	Lower Bound	6.33
	Upper Bound	6.85
Median		7
Std. Deviation		1.10
Minimum		4
Maximum		8
Inter quartile Range		1

Discussion

The incidence of thrombocytopenia in pregnancy is 8% with gestational thrombocytopenia being the most leading cause accounting for almost 70% of all cases. Thrombocytopenia is most pronounced in the 3rd trimester, where the platelet count usually remains above 110×10^9/L and rarely goes as low as 70×10^9/l in otherwise healthy pregnant cases. [11] Hypertensive disorders like pre-eclampsia and HELLP syndrome accounts for 21% of cases. Maternal platelet count come to normal level usually within 3-5 days following delivery.[12] Low platelets are responsible for maternal deaths and stillbirths due to placental abruption and preterm delivery. [13]

The other slightly common reasons include systemic lupus erythromatosis, antiphospholipid syndrome, DIC, thrombotic thrombocytopenia purpura, fatty liver, human immune deficiency virus (HIV) infection and medications.[13] The basis of gestational thrombocytopenia is indistinct even though it may be due to increased plasma volume observed in pregnancy.[14] Idiopathic thrombocytopenic purpura (ITP) is an autoimmune disorder characterized by destruction of circulating antibody bound platelets by the reticuloendothelial system, particularly in the spleen.[15] In the pregnant cases, the antibody crosses the placenta placing the infant at risk of thrombocytopenia. [16] Thus, therapy of women with ITP during pregnancy is a complex problem, especially to the potential risk of bleeding in both mother and fetus during the antenatal and peripartum periods.[17]

In this study, the average age of the women was 26.91±5.28 years. Most of the women were primi-gravida in our study. In Brohi et al study, the mean age of patients was 30.8 (±5.594) years. [18] The parity status of these cases was multigravida 38(53.5%), primigravida 29(40.8%) and grand multipara 4 (5.6%).

In this study, most, common causes of thrombocytopenia were gestational thrombocytopenia (57.5%). A similar result was also reported in a study it was found that the main causes of thrombocytopenia were gestational thrombocytopenia (59.3%).[7] In Pakistan, it has been observed that main causes of thrombocytopenia in pregnancy are gestational thrombocytopenia, which affects approximately 6% of pregnancies and

constitutes 75% of cases of pregnancy-associated thrombocytopenia. The platelet count tends to fall by about 10%; this is most pronounced in the third trimester and resolves by 6 weeks postpartum. Immune thrombocytopenia complicates 0.01–0.05% of pregnancies. [8,9] Although the pathophysiology of gestational thrombocytopenia is unknown, it is thought to be related to increased activation and peripheral consumption.

The second most causes of thrombocytopenia were eclampsia (16.1%), and preeclampsia (16.1%). A similar result was also reported in a prior study.[7] Thrombocytopenia is usually moderate and platelet count rarely decreases to less than 20,000/µl. Thrombocytopenia in patients with preeclampsia always correlates with the severity of the disease.

HELLP affects 0.5-0.9% of all pregnancies and develops in 10% of patients with preeclampsia.[19] In our study, it affects (12.0%) of patients. Similar findings were also reported in one previous study (12.06%).[7] It is characterized by hemolysis, elevated liver enzymes, and low platelets. The pathophysiology is similar to preeclampsia, with endothelial damage and release of tissue factor and coagulation activation. A recent study identified mutations in genes that regulate the alternative complement system, suggesting that excessive complement activation may be involved in pathogenesis similar to atypical hemolytic uremic syndrome (atypical HUS).[20]

Immune thrombocytopenia occurs in 1 in 1000-10,000 pregnancies, accounting for 3% of all thrombocytopenic gravidas. [21,22] It is the most common cause of thrombocytopenia in the first and second trimesters. [21] In the present study, it accounts for 3.3%. ITP is an autoimmune disorder caused by the development of immunoglobulin G (IgG) autoantibodies that are directed against several platelet glycoproteins. [23] Antibody-bound platelets are rapidly cleared from maternal circulation once they bind to specific antibody receptors on macrophages, found mainly in the spleen and also in the liver. [9] IgG antibodies can cross the placenta and have the potential to cause thrombocytopenia in the infant. [24]

In Brohi et al study the most common cause of thrombocytopenia was gestational thrombocytopenia seen in 24 (33.8%) patients followed by HELLP syndrome in 19 (26.7%) and hepatitis E in 10(16.3%) patients. [18] There were 11 cases who had platelets below 20,000, 18 had levels between 20-50,000 and 19 had between 50-100,000. [18]

In this study regarding the maternal outcome, antepartum bleeding was observed in 16.0% cases, postpartum bleeding was 41.3% and maternal mortality was observed in 8.0%. Neonatal death was observed in 14 cases and 6 were IUGR. Brohi et al study the common symptoms were bleeding seen in 30 (42.2%) cases and purpura or easy bruising seen in 11(15.4%) cases while 30 cases were asymptomatic. [18] Of 11 cases that had platelets below 20,000, 10 mothers died along with their 7 babies while only 3 surviving babies were those of mothers dying of post-partum hemorrhage. [18] Overall maternal mortality was in 20 (28.1%) patients. [18] Maternal and fetal deaths occurred in almost all cases with DIC, HEV and malaria while, in PPH mothers died but their newborns survived irrespective of platelet count. [18]

In a comparison of neonatal outcomes, Apgar scores of 7 were determined in our study while it was <7 at 5 min noted in infants of mothers with thrombocytopenia, having more chances of intrauterine growth restriction and stillbirth in one previous report. [7] These adverse outcomes were found in rare cases of thrombocytopenia such as disseminated intravascular coagulation, thrombotic thrombocytopenic purpure, anti-phospholipid antibodies (APLA) syndrome and myeloproliferative disease, but not among patients with Gestational thrombocytopenia. [7]

Thrombocytopenia in pregnancy is caused due to accelerated platelet consumption or haemodilution, antiplatelet antibodies; however, their presence or absence cannot determine the disorder or the differentiation from immune thrombocytopenic purpure. [25] Often one has to wait till the postpartum period to differentiate between gestational thrombocytopenia of pregnancy, which resolves itself following delivery or immune thrombocytopenia which does not subside after delivery. [26] The most common cause of thrombocytopenia in our study was gestational thrombocytopenia which has a favourable pregnancy outcome even in the third trimester of pregnancy.

Conclusion

Thrombocytopenia in pregnancy is associated with maternal and neonatal morbidity and mortality. Therefore, we strongly recommend careful surveillance of these thrombocytopenic mothers and their babies in order to establish the aetiology and timely appropriate intervention.

References

1. Kadir RA, McLintock C. Thrombocytopenia and disorders of platelet function in pregnancy. *SeminThrombHemost*. 2011;37(6):640-52.
2. Burrows RF, Kelton JG. Thrombocytopenia at delivery: a prospective survey of 6,715 deliveries. Am J Obstet Gynecol. 1990;162:731– 4.
3. Magann EF, Martin JN Jr. Twelve steps to optimal management of HELLP syndrome. ClinObstet Gynecol. 1999;42:532–50.
4. Berkowitz RL, Kolb EA, McFarland JG, et al. Parallel randomized trials of risk-based therapy for fetal alloimmune thrombocytopenia. *Obstet Gynecol*. 2006;107(1):91-6.
5. Boehlen F, Hohlfeld H, Extermann P, Perneger TV, de Moerloose P. Platelet count at term pregnancy: a reappraisal of the threshold. Obstet Gynecol. 2000;95:29 –33.
6. Provan D, Stasi R, Newland AC. International consensus report on the investigation and management of primary immune thrombocytopenia. Blood. 2010;115:168 –86.
7. Parnas M, Sheiner E, Vardi IS, Burstein E, Yermiahu T, Holcberg G. Moderate to severe thrombocytopenia during pregnancy. Eurp J ObstetGynecolReprod Biol. 2006;128:163-8
8. Asif N, Hassan K. Thrombocytopenia in pregnancy. Haematology Updates 2010.
9. Mazhar SB, Emanuel A. Thrombocytopenia in pregnancy. Ann Pak Inst Med Sci 2011;7:163-4
10. Calderwood C. Thromboembolism and thrombophilia in pregnancy. Current obstet and gynaecol(2006) 16 321-326.
11. www.ouhsc.edu/platelets (Accessed on March 01, 2011).
12. Chen Z, Liang MY, Wang JL. Etiology and clinical characteristics of pregnancy emerged thrombocytopenia. Zhonghua Fu Chan KeZaZhi. 2011 Nov;46:834-9.
13. Kam PC, Thompson SA, Liew AC. Review article, thrombocytopenia in the parturient. Anaesthesia.2004;59:255–64.
14. Silver R, Berkowitz R, Bussel J. Thrombocytopenia in pregnancy. Chicago: American College of Obstetrics and Gynecology;1999. (Practice bulletin, No 6.)
15. Lechner K. Management of adult immune thrombocytopenia. Rev ClinExpHematol2001;5:222-35.
16. Schwartz KA. Gestational thrombocytopenia and immune thrombocytopenia in pregnancy. Hematol Oncol Clin North Am 2002;14:1101-16.
17. Kelton GJ. Idiopathic thrombocytopenic purpura complicating pregnancy. Blood Rev 2002;16:43-6.
18. Brohi ZP, Perveen U, Sadaf A. Thrombocytopenia in Pregnancy: An Observational Study . Pak J Med Res. 2013;52(3): 67-70.
19. Kirkpatrick CA. The HELLP syndrome. Acta Clin Belg. 2010 Mar-Apr;65(2):91-7.
20. Fakhouri F, Jablonski M, Lepercq J, Blouin J, Benachi A, Hourmant M, Pirson Y, Dürrbach A, Grünfeld JP, Knebelmann B, Frémeaux-Bacchi V. Factor H, membrane cofactor protein, and factor I mutations in patients with hemolysis, elevated liver enzymes, and low platelet count syndrome. Blood. 2008 Dec1;112(12):4542-5.
21. Gill KK, Kelton JG. Management of idiopathic thrombocytopenic purpura in pregnancy. SeminHematol. 2000 ;37(3):275-89
22. Segal JB, Powe NR. Prevalence of immune thrombocytopenia: analyses of administrative data. J ThrombHaemost. 2006 Nov;4(11):2377-83.
23. Schwartz RS. Immune thrombocytopenic purpure-from agony to agonist. N Engl J Med. 2007 Nov 29;357(22):2299-301
24. Garty BZ, Ludomirsky A, Danon YL, Peter JB, Douglas SD. Placental transfer of immunoglobulin G subclasses. Clin Diagn Lab Immunol. 1994 Nov;1(6):667-9.
25. Khellaf M, Loustau V, Bierling P, Micheal M, Godeau B. Trombocytopenia in pregnancy. Rev Med Interne 2012;33: 446-52.
26. Won YW, Moon W, Yun YS, Oh HS, Choi JH. Clinical aspects of pregnancy and delivery in patients with chronic idiopathic thrombocytopenic purpura (ITP). Korean J Intern Med 2005;20:129-34.