

## Research Article

# Neonatal thrombocytopenia associated with gestational hypertension, preeclampsia and eclampsia: a case-control study

Sunil Kumar P.\*, Haricharan K. R.

Department of Pediatrics, Adichunchanagiri Institute of Medical Science, B.G. Nagara, Karnataka, India

**Received:** 15 November 2015

**Revised:** 20 November 2015

**Accepted:** 28 November 2015

**\*Correspondence:**

Dr. Sunil Kumar P.,

E-mail: drpusuku@gmail.com

**Copyright:** © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

### ABSTRACT

**Background:** Gestational hypertension, preeclampsia and eclampsia syndrome is a multi-system disorder associated with adaptive changes in the fetal circulation and causes a marked imbalance in the haemostatic system of the mother and the neonate. These babies may have platelet changes and can lead to serious neonatal complication like sepsis and bleeding manifestations including intracranial hemorrhage. Therefore early platelet screening of these infants is recommended.

**Methods:** This is a prospective study conducted at Sri Adichunchanagiri Institute of Medical Sciences from January 2011 to January 2013. The case group comprised of 150 neonates born to mothers diagnosed either with gestational hypertension, preeclampsia and eclampsia while controls comprised of 150 apparently healthy newborns born to normotensive mothers without maternal complications, born during the same period. Cord blood was collected from these babies and platelet count was studied.

**Results:** Mothers with gestational hypertension, preeclampsia and eclampsia syndrome had a higher number of premature and small for gestational age babies. Platelet counts were significantly decreased in these mothers and babies compared to controls. The platelet count in the baby was affected by the severity of hypertension in the mother. At higher levels of maternal systolic and diastolic blood pressure the number of babies in the case group presenting with thrombocytopenia increased.

**Conclusions:** As these babies are more prone for development of thrombocytopenia during the early neonatal period, these babies should be closely monitored and managed in order to decrease the perinatal morbidity and mortality.

**Keywords:** Neonatal thrombocytopenia, Gestational hypertension, Eclampsia, Preeclampsia

### INTRODUCTION

Hypertensive disorders of pregnancy complicate about 8%-10% of all gestations.<sup>1</sup> Hypertensive disorders are responsible for significant maternal and perinatal morbidity and mortality. Intracranial hemorrhage is the commonest cause of death associated with hypertension.<sup>2</sup> The lower the platelet count, the greater are the maternal and fetal morbidity.<sup>3</sup>

The major mechanism underlying neonatal thrombocytopenia is impaired platelet production. In 75% of all cases, the low platelet count is either present at birth or develops by 72 hours of life.<sup>4</sup> Only a minority of these patients have immunological disorders or coagulopathy causing thrombocytopenia. Most of the remaining patients are preterm neonates born after pregnancies complicated by placental insufficiency and/or fetal hypoxia, for example maternal pre-eclampsia and fetal intrauterine growth restriction. Neonates with

this early onset thrombocytopenia have impaired megakaryocytopoiesis and platelet production; megakaryocytes and their precursor and progenitor cells are considerably reduced at birth and levels of the megakaryocytopoietic cytokine thrombopoietin are therefore elevated.<sup>5</sup>

In pregnancies complicated by gestational hypertension, pre-eclampsia and eclampsia syndrome, thrombocytopenia is generally identified at birth or within the first 2–3 days following delivery, with resolution by 10 days of life in most cases. Severity of thrombocytopenia related to preeclampsia is highly variable, with a small percentage of infants developing severe or clinically significant thrombocytopenia (<50,000/uL).<sup>4,6</sup> One potential mechanism is that the resultant fetal hypoxia, has a direct depressant effect on megakaryocyte proliferation. At present, there is a paucity of evidence-based recommendations to guide clinicians on which platelet counts warrant intervention. Given the inherent risks of platelet transfusions, including the induction of a systemic inflammatory response and worsening of lung function immediately following the transfusion, additional studies are needed to guide clinical management.<sup>7,8</sup>

Platelet abnormalities in infants born to hypertensive mothers can lead to serious neonatal complication like sepsis (higher in preterm than in term neonates) and bleeding manifestations including intracranial hemorrhage from platelet deficiency due to any cause.<sup>9</sup> Therefore early haematological screening of these infants is recommended. Hence the purpose of this study is to identify the early platelet changes of the infants born to mothers with gestational hypertension, preeclampsia and eclampsia syndrome, so as to anticipate, diagnose and treat them early to decrease the perinatal morbidity and mortality.

## METHODS

This prospective randomized case control study was conducted at Adichunchanagiri Institute of Medical Sciences, B.G. Nagara from January 2011 to January 2013. The case group included 150 neonates born to mothers whose blood pressure was more than or equal to 140/90mmHg, detected after the twentieth week of pregnancy. They were classified as gestational hypertension (new onset non proteinuric Hypertension), preeclampsia (proteinuric Hypertension) and eclampsia (seizures that cannot be attributed to other causes in a woman with preeclampsia). Babies born with congenital malformations and those born to mothers with other problems like diabetes mellitus, severe anaemia, chronic hypertension, chronic disease and nutritional were excluded from the study. Institutional review board approval was obtained for the study and written informed consent was taken from the parents for the study. The control group comprised apparently 150 healthy newborns born to normotensive mothers without maternal

complications, born during the same period. Maternal details like age, parity, immunisation status, gestational age, onset of symptoms, blood pressure recording, presence of seizures and proteinuria, details of labor, mode of delivery and presence of complications if any during labor were also recorded. Baby details like name, sex, date of birth, time of birth, Apgar score, gestational age (by New Ballard's scoring system) were recorded. General and physical examination of the neonates was done, including anthropometric measurements. Cord blood was collected and platelet count of newborn was estimated using automated cell counter method using SYSMEX KX-21 Automated haematology analyser B2584 08/2007 Japan. Platelet count was confirmed by peripheral smear examination and REES ECKER method. Thrombocytopenia refers to a reduction in platelet count to < 150 × 10<sup>9</sup>/L or < 1.5 lakhs/cumm).<sup>10</sup>

Analysis of variance (ANOVA) has been used to find the significance of study parameters between three or more groups of patients, Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups Inter group analysis) on metric parameters. Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups. Pearson's correlation has been used to show the relationship between the mothers and the babies' values. And SPSS 15.0 statistical software was used for the analysis of the data.

## RESULTS

**Table 1: Distribution of Baby Platelet count in two groups of newborns.**

Baby Platelet count	Cases (n=150)	Controls (n=150)
<1 lakh	64(42.7%)	6(4%)
1-1.50	22(14.7%)	10(6.7%)
1.5-2.0	22(14.7%)	54(36%)
2.0-3.0	38(25.3%)	70(46.7%)
>3.0	4(2.7%)	10(6.7%)

A Comparative Case-Control study was undertaken to study the platelet count of new born, which included 150 babies born to mothers with gestational hypertension, preeclampsia and eclampsia syndrome (cases) and an equal number of babies (150) born to mothers without gestational hypertension, preeclampsia and eclampsia syndrome (controls).

Approximately half of the pregnancy induced hypertension mothers in our study were preeclamptic (48%) while eclampsia (14.7%) and gestational hypertension (37.3%) mothers constituted the rest. In this study 64% (96/150) of gestational hypertension, preeclampsia and eclampsia syndrome mothers needed caesarean section for the delivery of their babies while

only 40% (60/150) of mothers in the control group needed caesarean section. This observation was statistically significant (P value = 0.003).

In this study highest rate (45.5%) of prematurity was observed in neonates born to eclamptic mothers, while 27.7% of the preeclamptic mothers gave birth to premature babies. Prematurity was least commonly observed in the gestational hypertension group with a rate of 17.9%. 38 of the cases had intrauterine growth retardation while the rest (112 cases) had normal

intrauterine growth. 15.8%, 57.9% and 26.3% of babies born to mothers with gestational hypertension, preeclampsia and eclampsia respectively had intrauterine growth retardation.

Mothers with gestational hypertension, preeclampsia and eclampsia syndrome showed a lower platelet count than the controls which was found to be statistically significant. The mothers mean platelet count was 1.98 +/- 0.65 lakhs for the cases against 2.45 +/- 0.62 lakhs in the controls which related to a P value of <0.001.

**Table 2: Association of Maternal Platelet count with Baby Platelet count in cases.**

Mother platelet count	Baby platelet count				
	<1 lakhs	1.0-1.50 lakhs	1.5-2.0 lakhs	2.0-3.0 lakhs	>3.0 lakhs
<1 lakh (n=4)	2(50%)	0(0%)	0(0%)	2(50%)	0(0%)
1-1.50 (n=36)	24(66.7%)	0(0%)	4(11.1%)	6(16.6%)	2(5.6%)
1.5-2.0 (n=40)	16(40%)	8(20%)	6(15%)	10(25%)	0(0%)
2.0-3.0 (n=62)	20(32.2%)	12(19.4%)	12(19.4%)	16(25.8%)	2(3.2%)
>3.0 (n=8)	2(25%)	2(25%)	0(0%)	4(50%)	0(0%)

**Table 3: Pearson correlation between neonate platelet count with maternal SBP and DBP in cases.**

Maternal BP	Neonate platelet count				
	<1 lakh (n=64)	1.0-1.50 lakh (n=22)	1.50-2.0 lakh (n=22)	2.0-3.0 lakh (n=38)	>3.0 lakh (n=4)
<b>SBP (mm Hg)</b>					
<140	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)
140-149	14(21.9%)	12(54.5%)	9(41.7%)	15(38.9%)	0(0%)
150-159	26(40.6%)	2(9.1%)	4(16.6%)	6(16.7%)	0(0%)
≥160	24(37.5%)	8(36.4%)	9(41.7%)	17(44.4%)	4(100%)
<b>DBP (mm Hg)</b>					
<90	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)
90-99	18(28.1%)	6(27.3%)	10(45.5%)	12(31.6%)	0(0%)
100-109	22(34.4%)	8(36.4%)	8(36.4%)	16(42.1%)	0(0%)
>110	24(37.5%)	8(36.4%)	4(18.2%)	10(26.3%)	4(100%)

The babies born to mothers with gestational hypertension, preeclampsia and eclampsia syndrome had a mean platelet count of 1.42 lakhs for the cases against a mean of 2.09 lakhs for the controls, which was statistically significant with a P value of < 0.001. The mean platelet count was lowest 1.29 lakhs in babies born to eclamptic mothers, while it was lower 1.40 lakhs in babies of preeclamptic mothers than that of babies born to mothers with gestational hypertension (1.50 lakhs). 57.3% (86/150) of babies born to mothers with gestational hypertension, preeclampsia and eclampsia syndrome had thrombocytopenia compared to 10.6% (16/150) in controls. This observation was highly significant with P value <0.001.

Table 2 shows mother platelet count is significantly associated with baby platelet count with P=0.028. The lower the maternal platelet counts the number of babies presenting with thrombocytopenia increased and this observation was statistically significant.

Table 3 shows the platelet count in the baby was affected by the severity of hypertension in the mother. At higher levels of maternal systolic and diastolic blood pressure the number of babies in the case group presenting with thrombocytopenia increased.

In our study 10 of the premature babies and 4 babies with term gestation who had thrombocytopenia developed proven sepsis within 72 hours of life. 3 preterm baby and 7 term babies with thrombocytopenia developed probable

sepsis within 72 hours of life. All of these babies recovered and were discharged following appropriate management.

## DISCUSSION

Hypertensive disorders are one of the most common obstetric complications in pregnancy. These disorders provide great challenges for obstetricians and neonatologists because they are associated with a number of adverse maternal outcomes and short and long term neonatal complications. Gestational hypertension, preeclampsia and eclampsia syndrome have important implications for the mother and her baby, suggesting that it is not a simple gestational disorder but a clinical syndrome involving important maternal and fetal vascular alterations that can persist and cause diseases in later life.<sup>11</sup>

There is concern about the possible relationship between gestational hypertension, preeclampsia and eclampsia syndrome and sepsis, and a higher incidence of sepsis was reported in preterm infants of mothers who have HELLP syndrome (haemolysis, elevated liver enzymes, low platelet count) and severe preeclampsia compared to normotensive mothers.<sup>12</sup> In the Brazilian Network on Neonatal Research cohort study, a similar incidence of early onset sepsis (4.6% vs. 4.2%) and late onset sepsis (24% vs. 22%) was found in very low birth weight infants born to preeclamptic and normotensive mothers respectively.<sup>13</sup> In our study 24 babies developed proven sepsis within 72 hours of life requiring admission and management in the neonatal intensive care unit. 10 of these were preterm babies while 4 babies were of term gestation. All 14 babies recovered following appropriate treatment and were discharged. 10 babies in our study (7 term and 3 preterm) developed probable sepsis and were also discharged following appropriate treatment. All of these 24 babies had thrombocytopenia.

Although none of the mothers in this study had HELLP syndrome, platelet counts were noted to be lower in these mothers than those of controls. Thrombocytopenia (platelet count < 1.5 lakhs) was observed in 40 (24%) mothers; while 24% mothers were found to have platelet counts between 1.5 and 2 lakhs. Thrombocytopenia as a complication of maternal gestational hypertension, preeclampsia and eclampsia syndrome has been well documented-Pritchard JA et al noted thrombocytopenia in 30% of mothers with gestational hypertension, preeclampsia and eclampsia syndrome with 7% having counts below 50,000 which was comparable to our study.<sup>14</sup> Brazy JE et al have documented thrombocytopenia in 57% of such mothers and one fourth of them had platelet counts < 50,000.<sup>15</sup>

The most significant difference found in our study was the presence of thrombocytopenia in the babies born to mothers with gestational hypertension, preeclampsia and eclampsia syndrome. Thrombocytopenia was present in

57.3% of our cases which was almost twice of that observed in other studies. Brazy JE et al noted thrombocytopenia in 36% of infants of mothers with severe preeclampsia- eclampsia, Bhat YR et al and Fraser SH et al reported thrombocytopenia which complicated all maternal hypertension subtypes in 36% and 35% of babies respectively. Sivakumar S et al noted thrombocytopenia in 22% of the cases while Burrows RF et al and Weinstein L et al recorded thrombocytopenia in 9.2% and 16% of babies respectively.<sup>15-20</sup> However Pritchard JA et al have documented thrombocytopenia in only 4.2% of babies even though 30% of mothers had thrombocytopenia.<sup>14</sup>

In the present study thrombocytopenia was observed in 10.6% of the controls and this observation was comparable to that of Brazy JE et al who observed thrombocytopenia in 11% of the controls, while Burrows RF et al observed thrombocytopenia in only 2.2% of the controls.<sup>15,19</sup>

The mean platelet count was lowest 1.29 lakhs in babies born to eclamptic mothers, while it was lower 1.40 lakhs in babies of preeclamptic mothers than that of babies born to mothers with gestational hypertension (1.50 lakhs).

Out of the 86 babies having thrombocytopenia, 64 (42.7%) babies had a platelet count less than 1 lakh while the 22 (14.7%) other babies with thrombocytopenia had counts between 1-1.5 lakhs. 16 of the babies had counts below 50,000. The number of babies in our study having platelet counts less than 1 lakh was almost four times of that of Sivakumar S et al who reported a platelet count of less than 1 lakh in 5 (10%) out of 11 babies with thrombocytopenia, while 6 (12%) of the babies had counts between 1-1.5 lakhs and only one baby had counts below 50,000.<sup>17</sup> 14.7% of the babies in our study had low normal platelet counts between 1.5 and 2 lakhs and this observation was almost half of that noted by Thiagarajah S et al who reported low normal counts (1.5-2 lakhs) in 30% of the babies.<sup>21</sup>

In our study we were able to obtain a statistically significant correlation ( $P=0.028$ ) between the infants platelet count and the maternal platelet count. When the mothers platelet count was in the range of < 1 lakh, 1-1.5 lakhs, 1.5-2 lakhs, 2-3 lakhs and > 3 lakhs, thrombocytopenia was seen in 2, 24, 24, 32, 4 babies respectively. This observation was comparable to that of Brazy JE et al who have noted that the degree of thrombocytopenia in the infant was significantly related to the depression in maternal platelet counts.<sup>15</sup> However Siva Kumar S et al, Burrows RF et al and Pritchard JA et al have not noted similar correlation.<sup>14,18,19</sup>

In this study a statistically significant correlation between the infants' platelet count and severity of maternal hypertension was not obtained though the number of babies born to mothers with gestational hypertension,



preeclampsia and eclampsia syndrome presenting with thrombocytopenia was higher with higher levels of maternal systolic and diastolic blood pressure. This finding was similar to that observed by Sivakumar S et al.<sup>18</sup>

Severe neonatal thrombocytopenia  $<50,000/\text{mm}^3$  can be associated with increased risk of hemorrhage.<sup>21</sup> However none of the babies in our study had any bleeding manifestations and there was no increased risk of intracranial hemorrhage following vaginal delivery/instrumental delivery.

Our study was an attempt to study the platelet count changes that may be seen in neonates born to mothers with gestational hypertension, preeclampsia and eclampsia syndrome and to compare them with babies born to normotensive mothers.

Platelet counts were more affected in babies of eclamptic and preeclamptic mothers than in mothers with gestational hypertension, suggesting that the severity as well as the duration of hypertension play a vital role in influencing the platelets of babies born to mothers with gestational hypertension, preeclampsia and eclampsia syndrome and eventually the final neonatal and perinatal outcome.

Since babies born to mothers especially with preeclampsia and eclampsia are more prone for development of prematurity, low birth weight and intrauterine growth retardation and thrombocytopenia during the early neonatal period, these babies should be closely monitored so as to facilitate early detection and management of sepsis and bleeding tendencies in order to attempt to provide these babies with decreased morbidity and improved growth, development and survival.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: The study was approved by the Institutional Ethics Committee*

## REFERENCES

1. Sibai BM. Diagnosis and management of gestational hypertension and preeclampsia. *Obstet Gynecol.* 2005;110-21.
2. Steer P, Lupton M, Oteng-Ntim E. Hypertensive diseases in pregnancy. In: Rennie and Robertson's Textbook of neonatology. 4<sup>th</sup> ed. Philadelphia: Churchill livingstone. 2008:179-81.
3. Weinstein L. Syndrome of hemolysis, elevated liver enzymes and low platelets: a severe consequence of hypertension in pregnancy *Obstet Gynecol.* 1982;142:159-63.
4. Castle V, Andrew M, Kelton J, Girdon D, Johnston M, Carter C. Frequency and mechanism of neonatal thrombocytopenia. *J Pediatr.* 1996;108:749-55.
5. Murray NA, Roberts AG. Circulating Megakaryocytes and their Progenitors in early thrombocytopenia in preterm neonates. *Pediatr Res.* 1996;40:112-9.
6. Mehta P, Vasa R, Neumann L, Karpatkin M. Thrombocytopenia in the high-risk infant. *J Pediatr.* 1980;97(5):791-4.
7. Khan H, Belsher J, Yilmaz M, Afessa B, Winters JL, Moore SB, et al. Fresh-frozen plasma and platelet transfusions are associated with development of acute lung injury in critically ill medical patients. *Chest.* 2007;131(5):1308-14.
8. Weksler BB. Platelets and the inflammatory response. *Clin Lab Med.* 1983;3(4):667-76.
9. Raizada N, Lal A, Bhatia RC, Jain BK, Chander K, Goyal A. Neonatal thrombocytopenia due to pregnancy induced hypertension. *Indian J Pediatr.* 1996;63:226-8.
10. Scott JP and Montgomery RR. Platelet and Blood Vessel disorders. In: Nelson textbook of pediatrics. 19<sup>th</sup> ed. Philadelphia: Elsevier Saunders. 2012;478:1714.
11. de Souza Rugolo LM, Bentlin MR, Petean Trindade CE. Preeclampsia: Effect on the fetus and newborn. *Neo Reviews.* 2011;12(4):e198-e206.
12. Kim HY, Sohn YS, Lim JH, Kim EH, Kwon JY, Park YW, et al. Neonatal outcome after preterm delivery in HELLP syndrome. *Yonsei Med J.* 2006;47(3):393-8.
13. Procianny RS, Silveira RC, Mussi-Pinhata MM, Souza Rugolo LM, Leone CR, de Andrade Lopes JM, et al. Brazilian network on neonatal research. Sepsis and neutropenia in very low birth weight infants delivered of mothers with preeclampsia. *J Pediatr.* 2010;157(3):434-8.
14. Pritchard JA, Cunningham FG, Pritchard SA, Mason RA. How often does maternal preeclampsia incite thrombocytopenia in the fetus? *Obstet Gynecol.* 1987;69:292-5.
15. Brazy JE, Grimm JK, Little VA. Neonatal manifestations of severe maternal hypertension occurring before the thirty sixth week of pregnancy. *J Pediatr.* 1982;100(2):265-71.
16. Bhat YR, Cherian CS. Neonatal thrombocytopenia associated with maternal pregnancy induced hypertension. *Indian J Pediatr.* 2008;75(6):571-3.
17. Fraser SH, Tudehope D. Neonatal neutropenia and thrombocytopenia following maternal hypertension. *J Paediatr Child Health.* 1996;32:31-4.
18. Sivakumar S, Bhat BV, Badhe BA. Effect of pregnancy induced hypertension on mothers and their babies. *Indian J Pediatr.* 2007;74(7):623-5.
19. Burrows RF, Andrew MD. Neonatal thrombocytopenia in hypertensive disorders of pregnancy. *Obstet Gynecol.* 1990;76:234-7.
20. Weinstein L. Syndrome of hemolysis, elevated liver enzymes and low platelets, a severe consequence of

hypertension in pregnancy. *Am J Obstet Gynecol.* 1982;142:159-63.

21. Thiagarajah S, Bourgeois FJ, Harbert GM, Caudle MR. Thrombocytopenia in preeclampsia: associated abnormalities and management principles. *Am J Obstet Gynecol.* 1984;150(1):1-7.

**Cite this article as:** Sunil Kumar P, Haricharan KR. Neonatal thrombocytopenia associated with gestational hypertension, preeclampsia and eclampsia: a case-control study. *Int J Contemp Pediatr* 2016;3:16-21.