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Original Research Article

Study of changes noted in the platelet count in cord blood of neonates born to hypertensive mothers in a tertiary care hospital, Bangalore, India

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ABSTRACT

Background: Hypertensive disorders of pregnancy pose several problems to both mother and newborn. Complications in new-born like intrauterine death (IUD), intrauterine growth retardation (IUGR), perinatal asphyxia, neonatal sepsis and bleeding disorders are associated with toxemia of pregnancy. To decrease the perinatal morbidity and mortality, babies of hypertensive mothers should be carefully monitored and managed. Aim of this study was to establish the changes in total platelet count in umbilical cord blood.
Methods: This is a hospital based prospective observational study which included the babies born to mothers having hypertensive disorders of pregnancy, total cases accounting about 158. Detailed clinical history taken including details of labour and clinical examination done. In all the subjects, 2 ml of umbilical cord blood anticoagulated with EDTA was collected and haematological tests for total platelet count (TPC) count was done.
Results: This study shows that the incidence of neonatal thrombocytopenia is 43.67%. The incidence of sepsis among thrombocytopenia group accounts for about 60% in gestational hypertension, 64.2% in pre-eclampsia and 50% in eclampsia group.
Conclusions: With respectively, these findings it can be concluded that the incidence of Neonatal Thrombocytopenia is significantly higher in babies born to HDP mothers and it can be taken as a marker to evaluate Sepsis in such a situation in resource limited setting. As less number of studies is available in this area of interest, this study supports the cause.

Keywords: Bleeding, Early onset sepsis, Hypertensive disorders, Neonatal thrombocytopenia, Pre-eclampsia, Prematurity

INTRODUCTION

Hypertensive disorders of pregnancy complicate about 8% of all gestations.[1] Hypertensive disorders are responsible for significant maternal and perinatal morbidity and mortality. Intracranial hemorrhage is the commonest cause of death associated with hypertension.[2]

The classification of hypertensive disorders complicating pregnancy by the Working Group of the National high blood pressure education program [NHBPEP] (2000) consists of four types of hypertensive disease:[3]

- Gestational hypertension (formerly pregnancy-induced hypertension that included transient hypertension).
- Pre-eclampsia and Eclampsia syndrome
- Pre-eclampsia superimposed on chronic hypertension.
- Chronic hypertension.

Pre-eclampsia is currently believed to be a two stage disease with shallow cytotrophoblastic invasion of maternal spiral arterioles initially resulting in placental insufficiency.[4] Acute or chronic uteroplacental insufficiency results in antepartum or intrapartum anoxia that may lead to fetal death, IUGR and /or preterm delivery.[5] Prematurity is the most important factor responsible for increased perinatal morbidity and mortality.[6] Neonatal complications occurring in babies of pre-eclamptic mothers closely relates to the severity of hypertension and proteinuria.

Haematological abnormalities in infants born to hypertensive mothers can lead to serious neonatal complication like sepsis, increased predisposition to infections and disseminated intravascular coagulation (higher in preterm than in term neonates) can occur.[7] Bleeding manifestations including intracranial haemorrhage may result from platelet deficiency due to any cause.[8]

Neonatal thrombocytopenia defined as a platelet count less than 150,000/μL based upon the definition used in adults.[9] The degree of severity of thrombocytopenia can be further subcategorized according to platelet count in the affected individuals:

- Mild thrombocytopenia - platelets count 100,000 to 150,000/μL,
- Moderate thrombocytopenia - platelets count 50,000 to 99,000/μL,
- Severe thrombocytopeni - platelets count <50,000/μL.

The principal mechanism postulated is that preeclampsia and the resultant foetal hypoxia have a direct depressant effect on foetal megakaryocytopoiesis and platelet production the combined effect of impaired megakaryocyte formation and increased platelet activation mediated through cytokines, thrombopoietin, and interleukin-6 are said to be the most likely causative mechanisms.[10]

Hence the purpose of this study is to identify the early hematological changes of the infants pertaining to platelet count, born to mothers with hypertensive disorders of pregnancy, so as to anticipate, diagnose and treat them early to decrease the perinatal morbidity and mortality.

METHODS

It is a prospective observational study. It has a study period from November 2017 to May 2019 in Vani Vilas Hospital and Bowring Hospital attached to Bangalore Medical College and Research Institute, Bangalore.

Inclusion criteria

- Parents / guardians of the new-born willing to give written informed consent.
- Neonates born to mothers having hypertensive disorder of pregnancy
  a. Gestational hypertension - new onset non proteinuria hypertension (systolic pressure elevated more than 140 mm of Hg and diastolic pressure more than 90 mm of Hg) which resolves within 12 hours postpartum.
  b. Pre-eclampsia - hypertension with proteinuria (systolic pressure elevated more than 140 mm of Hg and diastolic pressure more than 90 mm of Hg and proteinuria more than 300 mg in a 24 hour period) or Pre-eclampsia with increasing certainty i.e.:
  - BP more than equal to 160/100 mm Hg
  - Proteinuria 2g/24 hours
  - Serum creatinine > 1.2 mg/dl
  - Persistent headache /cerebral/visual disturbance
  - Persistent epigastric pain.
  c. Eclampsia - seizures that cannot be attributed to other causes in a woman with preeclampsia.

Exclusion criteria

New-born whose mothers had diabetes mellitus, severe anaemia, Rh incompatibility, heart disease, connective tissue disorder, premature rupture of membranes, perinatal infections, and gestational age <28 weeks were excluded and neonates having severe asphyxia and congenital anomalies were excluded from the study.

A neonate born before 37 completed weeks of gestation was taken as preterm. Neonates with birth weight <10th percentile for their gestational age were taken as small for gestational age.

Procedure for this study is as follows, 2 ml of cord blood anti -coagulated with EDTA was collected from neonates of hypertensive after delivery. For each of the samples complete blood count was done pertaining to platelet counts.

As majority of mothers come only during the period of delivery and leave after few days, the follow up of subjects cannot be done. So, pregnant mothers whose blood pressure was ≥140/90 mm of Hg were included as hypertensive.

Data collection procedure was done by collecting relevant information of the pregnant mothers, collected from hospital records and results obtained from the study of cord blood were recorded. The statistical analysis was carried out using t-test for the comparison of differences of the means by SPSS 15.0 for windows.

Methods of statistical analysis

Continuous variables with normal distribution expressed as mean values and standard deviation were compared

using student t test while those not normally distributed were analysed using Mann U Whitney test.

The collected data was analysed by using SAS. Multivariate linear regression, spearman ranks correlation coefficient, paired and unpaired test statistical method was employed to test the defined hypothetical parameters. However, the incumbent changes or association of the variables was tested based on the probability value ($p \leq 0.01$).

I. Multivariate linear regression formula

The formula for linear regression analysis was,

$Y_{ij} = a + b_0 X_0 + b_1 X_1 + b_2 X_2 \ldots . b_n X_n + \in_{IJ}$

a= intercept b_0, b_1, b_2 ...b_n is the coefficients of variables like physical findings, OPE, Biomarkers and ECG features. ∈_IJ=random error associated with variables.

II. Speraman rank correlation

$$r_s = 1 - \frac{6\sum_{i=1}^{n}(d - \bar{d})^2}{n(n^2 - 1)}$$

d=Rank of Xi-Rank of Yi

$$\bar{d} = \frac{\sum_{i=1}^{n} d}{n}$$

where n= the number of observations

RESULTS

Out of 158 cases of hypertensive disorders of pregnancy, gestational hypertension (n=90) with 56.96% constituted the majority, 31.61% (n=50) had pre-eclampsia, remaining 11.39% (n=18) had eclampsia (Table 1).

Table 1: Risk factors attributed to subjects.

Risk factor	No	%
Eclampsia	18	11.39
Pre-eclampsia	43	27.22
Pre-eclampsia with HELLP	07	4.43
PIH	90	56.96
Total	158	100.00

On analyzing the risk factors, it was found that eclampsia was seen in 18 cases (11%), pre- eclampsia was seen in 43 cases (27%), pre- eclampsia with HELLP was seen in 7 cases (4%) and PIH was seen in 90 cases (57%).

In relation to the parity, 74 subjects (47%) were born to primiparous mothers and 84 were born to multiparous mothers (53%) (Table 2). The mean age of the mothers in the study population was 22.82 years.

The majority of the cases were found to be delivered by normal vaginal route, accounting to 68.35% (n=108) and Cesarean section accounted for 31.65% (n=50) (Table 3).

Among 158 newborns, males constitute about 51.9% (n=82) and females about 48.1% (n=76).

Table 2: Subject to parity.

Parity	No	%
Primi	74	46.84
Multi	84	53.16
Total	158	100.00

In relation to the parity, 74 subjects (47%) were born as primiparous and 84 were born as multiparous (53%).

Table 3: Mode of delivery in the study group.

Mode of delivery	No	%	p-value
Cesarean	50	31.65	0.000
Vaginal	108	68.35	0.000
Total	158	100	

The majority of the cases were found to be delivered by normal vaginal route, accounting to 68.35% and Cesarean section accounted for 31.65%

On comparing the body weight of the 158 newborns in the study it was found that 8 (5%) had body weight less than or equal to 1.0 kg whereas, 58 (37%) had body weight ranging between 1- 1.5kg. 66 subjects (42%) had body weight ranging from 1.5- 2.5 kg and 26 (16%) had body weight greater than 2.5 kg (Table 4). Mean birth weight is 1.62kgs.

Table 4: Distribution of birth weight (kgs) for subjects.

Body weight	No	%	p-value
< 1.0 Kg	8	5.06	0.312
1.0-1.5 Kg	58	36.71	0.006
1.5-2.5Kg	66	41.77	0.003
>2.50Kg	26	16.46	0.012
Total	158	100.0	

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Table 5: Distribution of GA.

GA	No	%	p-value
E- preterm	5	3.16	0.632
Late preterm	22	13.92	0.0002
Preterm	100	63.29	0.0006
Term	31	19.62	0.0021
Total	158	100.00	

On analyzing the gestational age of the study subjects, it was found that, 5 were early preterm (3%), 22 were late preterm (14%), 100 were preterm (63%) and 31 were term (20%) (Table 5).

The most significant findings observed in this study were the incidence of thrombocytopenia among the study group and its severity associated with the severity of hypertension. Overall incidence was about 43.67% (n=69).

It was observed that 11 subjects (7%) had severe thrombocytopenia, 33 (21%) had moderate thrombocytopenia and 25 (16%) had mild thrombocytopenia. The platelet counts were normal in 89 (56%) subjects (Figure 1).

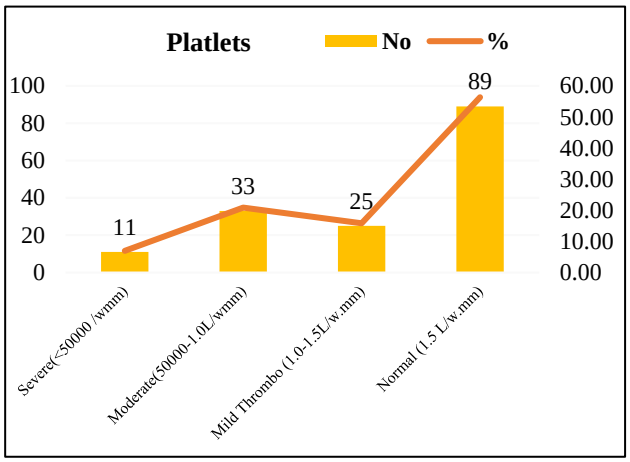

Figure 1: Thrombocytopenia severity wise classification.

In Gestational Hypertension group of about 90 cases, 25 newborns had thrombocytopenia accounting for about 22.7% incidence with grading of MILD thrombocytopenia 56% (14 cases), moderate 36% (9 cases) and severe 8% (2 cases).

In Pre-Eclampsia group of about 50 cases, 28 newborns had thrombocytopenia accounting for about 56% incidence with grading of MILD thrombocytopenia 17.8% (5 cases), moderate 57.1% (16 cases) and severe 25% (7 cases).

Table 6: Distribution of thrombocytopenia among hypertensive disorders of pregnancy groups.

Variable	Mild	Moderate	Severe	p-value
PIH	14	09	02	0.0032
Pre-eclampsia	05	14	06	0.0017
Pre-eclampsia (HEELP)	00	02	01	0.2784
Eclampsia	06	08	02	0.0000

In Eclampsia group of about 18 cases, 16 newborns had thrombocytopenia accounting for about 88% incidence with grading of mild thrombocytopenia 37.5% (6 cases), moderate 50% (8 cases) and severe 12.5% (2 cases) (Table 6).

Table 6 shows the distribution of thrombocytopenia among gestational hypertension, pre-eclampsia and eclampsia group. This table also shows the severity of thrombocytopenia into mild, moderate and severe in the above-mentioned groups.

Gestational Hypertension group having Neonatal Thrombocytopenia (n=25), the incidence of Sepsis accounts for 60% and Respiratory distress about 24%. Pre-Eclampsia group having Neonatal Thrombocytopenia (n=28), the incidence of Sepsis accounts for 64.2%, Respiratory distress about 10.7% and bleeding 7.1% respectively. Eclampsia group having Neonatal Thrombocytopenia (n=16), the incidence of Sepsis accounts for 50% and Respiratory distress about 32% (Figure 2).

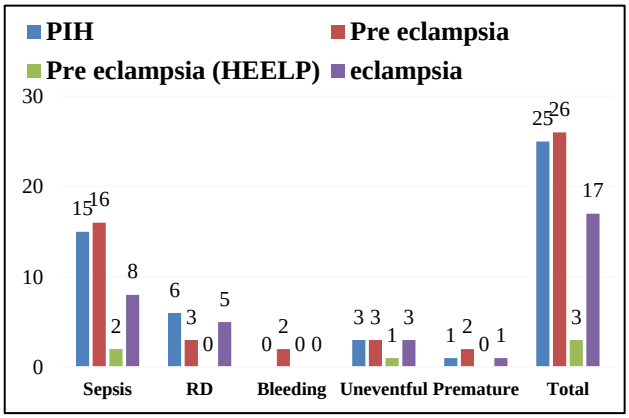

Figure 2: Distribution of clinical courses among thrombocytopenia population.

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.[11] 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.[12]

In this study, maximum number of mothers were found to be multigravida (53%) and below 23 years. This result is in accordance with the study of Sivakumar et al.[13] It was also found that most of the pregnant mothers of study group (62%) were belonged to low socioeconomic status.

Thus, under nutrition, poverty and ignorance have got definite relation to Hypertensive disorders of pregnancy.

The most important finding in this study was significant fall of Total Platelet count in the babies born to HDP mothers. Out of the 69 babies having thrombocytopenia, 34 (49.2%) babies had a platelet count less than 1 lakh/mm3 while the 35 (50.8%) other babies with thrombocytopenia had counts between 1-1.5 lakhs/mm^3.

Severe neonatal thrombocytopenia <50,000/mm^3 can be associated with increased risk of hemorrhage.[14] However, none of the babies in this study had any bleeding manifestations and there was no increased risk of intracranial hemorrhage following vaginal delivery/instrumental delivery.

In this study a statistically significant correlation between the newborn's platelet count and severity of maternal hypertension was not obtained though the number of babies born to HDP mothers with thrombocytopenia was higher. This finding was similar to that observed by Gelband et al.[15] Although the exact pathophysiologic mechanism is not known, it was reported that utero-placental insuffiency secondary to pregnancy induced hypertension is responsible for the development of thrombocytopenia.[16] Bleeding in neonates occurs if the platelet count decrease to <50,000/mm^3.[17]

The study of Kleckner et al, reported that cause of this thrombocytopenia was thrombocyte destruction due to platelet adherence to abnormal placental endothelium.[18] But study of Burrow et al, reported that there was no significant change in total platelet count in term babies of hypertensive mothers and normotensive mothers.[19] Moodley et al, reported that an undefined factor which leads to disseminated intravascular coagulation (DIC) was transported by the placenta and caused thrombocytopenia in the neonates.[20] Akcan et al, suggested the role of mediators in developing thrombocytopenia.[21]

Normally, vascular endothelial growth factor (VEGF) and placental growth factor (PlGF) are responsible for maturation of megakaryocyte and participate in the regulation of megakaryocyte development.[22] The activity of these two factors is suppressed by sFlt 1 and soluble Enderlin, which are found to be raised in pre-eclampsia pregnancies. Low levels of PlGF and VEGF are shown in the cord blood of pre-eclampsia mothers' neonates.[27-30]

Platelet counts were more affected in neonates of eclamptic and pre-eclampsia mothers than in mothers with gestational hypertension, suggesting that the severity as well as the duration of hypertension is important in influencing the platelets of neonates born to HDP mothers and eventually the final neonatal and perinatal outcome.[23,24] This result is similar to a study done by Bhat and Cherian (2008) who reported that in neonates of mothers with preeclampsia, the percentage of neonatal thrombocytopenia was 36% and it is more likely to occur in preterm and low birth weight infants.[25]

Increased risk of sepsis was found in cases and in the neonates with neutropenia. Study results were similar to Bhaumik et al, who reported an increased RR (non-significant) of sepsis in neonates born to PIH mothers.[26]

CONCLUSION

In the setup (resource limited setting) authors continually seek to determine the early markers of haematological changes noted in neonates born to Hypertensive disorders of pregnancy, which contribute to adverse neonatal outcome.

This study was an attempt to analyse the hematological changes pertaining to the platelet counts that may be seen in neonates born to HDP mothers.

As less number of studies is available in this area of interest, this study supports the cause. And this will be a cost-effective tool in predictor of hematological abnormalities and serve as an early marker even before pricking the babies and for early management in order to decrease the perinatal morbidity and mortality.

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