Neonatal thrombocytopenia in neonates born to the mothers with pregnancy-induced hypertension

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ABSTRACT

Introduction: Neonatal thrombocytopenia is a common clinical problem. Thrombocytopenia presenting in the first 72 h is usually secondary to placental insufficiency and caused by reduced platelet production. **Objective:** The objective is to evaluate the thrombocytopenia and it is associated neonatal and maternal factors in neonates born to mothers with pregnancy-induced hypertension (PIH). **Methods:** This study was conducted in a tertiary care hospital over a period of 1 year. Mothers with PIH were included in the study. A detailed history of the mother, physical examination, and platelet count of the newborns was done and data collected. **Results:** A total 111 neonates born to 106 mothers (5 pair of twin babies) with PIH were included in the study. The male-to-female ratio in these newborns was 1:1.05 with 59.4% being low birth weight (LBW), 63% term babies, and 20.72% small for gestational age babies. 59 (53.15%) neonates had thrombocytopenia and 12 with severe thrombocytopenia. Although a higher percentage of thrombocytopenia was noted with primipara, PIH symptoms at <28 weeks, preeclampsia, and untreated mother, these were not statistically significant. Severe thrombocytopenia was 5 times higher in <2.5 kg neonates as compared to >2.5 kg babies (9.0% vs. 1.8%) and 1.5 times in infants <37 weeks vis-a-vis > 37-week infants (8.3 vs. 4.5%). Thrombocytopenia was significantly associated with LBW (odd ratio [OR] - 1.8056; 95% confidence interval [CI]: 0.8395–3.8834, p=0.0305). Severe thrombocytopenia was significantly associated with LBW (OR - 3.08393; 95% CI: 0.7993–184.442; p=0.0329) and with small for gestational age (OR - 7.2625; 95% CI: 2.0471–25.7651; p=0.0021). **Conclusion:** Premature and LBW neonates born to mothers with PIH should be regularly scrutinized for thrombocytopenia during the early neonatal period. This would reduce neonatal morbidity and mortality. PIH in mothers should be ruled out as a cause of thrombocytopenia in early neonatal life.

Key words: *Neonatal mortality, Neonatal thrombocytopenia, Neonates, Pregnancy-induced hypertension*

Hypertension is one of the most prevalent complications met within pregnancy and contributes significantly to maternal and perinatal morbidity and mortality [1]. Preeclampsia is a multisystem disorder of the mother that affects the fetus because of uteroplacental insufficiency [2]. These fetuses are at risk of intrauterine growth retardation, premature delivery, and other hematological disorders. Thrombocytopenia due to reduced platelet production is seen in the first 72 h of the life of these neonates [3-6]. Fortunately, most of these episodes are mild or moderate and resolve spontaneously [5].

The American College of Obstetrics and Gynecology defined that preeclampsia is the development of hypertension with proteinuria, edema or both, induced by pregnancy after 20 weeks of gestational and sometimes earlier when there are extensive hydatidiform changes in chorionic villi. Eclampsia is diagnosed when a patient with preeclampsia has convulsions in the absence of neurological disease [7]. In this study, an attempt has been made to evaluate the various maternal and neonatal factors associated with thrombocytopenia in a neonate born to mothers with pregnancy-induced hypertension (PIH).

METHODS

This observational study was conducted in the Department of Pediatrics, at a tertiary care institute during a period of 1 year, i.e., from April 2017 to March 2018. Ethical clearance and permission to conduct this study were taken from the institute's ethical committee before the commencement of the study. Babies born to mothers with PIH were enrolled in the study. Perinatal data were collected after taking a detailed history from the mother or a close relative with respect to maternal age, pregnancy details, past medical history, antenatal visits, and examination details (blood pressure and presence of edema). Natal history was recorded as to the mode of delivery, presentation, placental anomaly or umbilical vessel anomaly, obstetric analgesia or anesthesia, birth trauma, and meconium stained liquor. Postnatal history was also recorded with regard to Apgar score at 1 and 5 min, cry after birth, seizures, apnea, lethargy, and abnormal cry. Mother's relevant investigations such as complete blood count, urine routine, blood urea, and liver function test were noted. All neonates were subjected to anthropometric examination

along with gestational age assessment and detailed general and systemic examinations.

Platelet count sampling was done in the labor room in all neonates born to PIH mother from cord blood or within the 1st h of life, subsequently 72 h and or on the 7th day of life if required. The low counts were confirmed manually using the Neubauer chamber. Platelet count of <150,000/mm^3 was defined as thrombocytopenia. Platelet count of <50,000/mm^3 with bleeding or <30,000/mm^3 without bleeding was considered as severe thrombocytopenia [8,9]. Mothers with immune thrombocytopenia purpura and neonates with congenital anomalies and evidence of sepsis such as respiratory distress, lethargy, temperature instability, and seizure activity along with positive sepsis screen (leukopenia, neutropenia, positive C-reactive protein, and growth on blood culture) were excluded from the study along with those who refused to give consent for the study.

The above data were collected and tabulated using Microsoft Excel sheet. The data were then analyzed using SPSS software, Chi-square test and Fischer's exact test were applied accordingly for statistical analysis.

RESULTS

A total of 181 cases of PIH were admitted during the study period; among those, 106 mothers were considered for the study due to their full follow-up from the birth of a baby to 7 days of life. A total of 111 babies was delivered from 106 mothers (5 pair of twin babies); out of them, 71 (63.96%) neonates had mothers with preeclampsia and 40 (36.04%) with eclampsia. There was no neonate with the mother having gestational hypertension. There were 65 (58.55%) neonates with primipara mothers as compared to 46 (41.55%) neonates with multipara mothers (Chi-square 6.505, p=0.0107). In this study, mothers of 64 (57.65%) neonates developed symptoms and signs before 28 weeks of gestation while mothers of 47 (42.35%) developed later. 60 (54%) newborns had mothers who did not receive any antenatal medication (Table 1).

A total of 49 of these neonates were delivered normally while 62 were delivered through lower segment cesarean section. 97 of these neonates (87.39%) had immediate cry after birth, 51.36% (57) were female, and 48.64% (54) were male with the male-to-female ratio of 1:1.05. There were 70 (63.07%) term babies and 41 (36.93%) preterm babies in this study. Sixty-six (59.45%) of 111 neonates were low birth weight (LBW) babies. Most of these (88, 79.28%) neonates were appropriate for gestational age (AGA) as compared to 23 neonates (20.72%) who were small for gestational age (SGA). Seven of these babies were born to mothers who had taken antenatal treatment while 16 neonates were born from mothers who did not receive any antenatal care. Two of these 111 neonates had head circumference and length of <3rd centile while the rest above 3rd centiles. In the present study, 59 (53.15%) neonates born to mothers with PIH had thrombocytopenia while 12 (10.81%) had severe thrombocytopenia.

Table 1 represents a bivariate relationship of thrombocytopenia to various maternal characteristics. Thrombocytopenia was observed in 32 (28.83%) and 27 (24.33%) newborns of primi and multiparous women, respectively (p=0.3257). Severe thrombocytopenia in them was identical. A higher percentage of thrombocytopenia was observed with <28-week onset of symptoms, pre-eclamptic mothers, and untreated mothers, and these were not statistically significant. The occurrence of severe thrombocytopenia, i.e., 9 (8.1%) was found more in <28 weeks of the onset of PIH in comparison to 3 (2.7%) in >28 weeks of onset. Severe thrombocytopenia in the neonate of an eclamptic group 7 (6.30%) was more than pre-eclamptic group mothers babies. Severe thrombocytopenia was found in 6 neonates of each untreated as well as treated mothers. Maternal characteristics did not seem to be significantly associated with neonatal thrombocytopenia (p>0.05).

Thrombocytopenia was observed more in female 32 (28.83%) than in male 27 (24.32%). Furthermore, thrombocytopenia was observed more in <2.5 kg, term, AGA newborns. There were 7 (6.30%) male babies with severe thrombocytopenia as compared to 5 (4.5%) female neonates. Severe thrombocytopenia was 5 times higher in LBW babies (9%) as compared to normal birth weight babies (9% vs. 1.8%). Percentage of severe thrombocytopenia in preterm infants was about 1.5 times higher than term infants (8.3% vs. 4.5%). Thrombocytopenia was significantly associated with LBW babies in this study (odds ratio [OR] - 1.8056; 95% confidence interval [CI]: 0.8395–3.8834; p=0.0305) and so was severe thrombocytopenia (OR 3.8393; 95% CI: 0.7993–18.442; p=0.0329). Severe thrombocytopenia was also significantly associated with birth weight versus gestational age (OR 7.2625; 95% CI: 2.0471–25.7651; p=0.0004).

DISCUSSION

Severe hypertension in pregnant women is a multisystem disease and a threat to the well-being of both mother and child. Although the exact mechanism of action continues to be elusive, many factors may contribute to PIH such as abnormal trophoblast invasion, uteroplacental hypoperfusion, prostaglandin imbalance, endothelial dysfunction, inappropriate intravascular coagulation, and unexplained immunologic injury [7]. The presence of severe hypertension in pregnancy causes a marked imbalance in maternal homeostasis and unfavorable uterine environment for the fetus. The severity of uteroplacental insufficiencies experienced by these fetuses may be reflected in the low Apgar score, high hematocrit and increase in hemoglobin level, leucopenia, and thrombocytopenia [10].

This study was hence conducted in a tertiary care institute over a period of 1 year so as to evaluate neonatal thrombocytopenia in neonates of mothers with PIH and also to study the various maternal and neonatal factors associated with it. A total of 111 neonates were included in the study with 5 pair of twin babies; out of them, 59 had thrombocytopenia with 12 (10.81%) having severe thrombocytopenia.

In this study, it was observed that 58.5% of neonates had primigravida mother. Derham and Hawkin and Prakash *et al*. observed that PIH was more common in primiparous mothers (57.64% and 57%, respectively) which is, however, lower than

Table 1: Bivariate relationship of thrombocytopenia to various maternal characteristics

Characteristic	Total neonates (111)	Thrombocytopenia					
		Total (59)	OR (95% CI)	p-value	Severe 12	OR (95% CI)	p-value
Parity			0.6824(0.3184–1.4623)	0.3257		0.9897 (0.2935–3.3366)	0.9866
Primipara	65	32			7		
Multipara	46	27			5		
Onset of PIH			0.9973(0.4690–2.1210)	0.9945		2.4000 (0.6126–9.4022)	0.2089
<28 weeks	64	34			9		
>28 weeks	47	25			3		
Type of PIH			1.3154(0.6026–2.8714)	0.4913		1.3061 (0.3858–4.4214)	0.661
Preeclampsia	71	36			5		
Eclampsia	40	23			7		
Medications			0.7353(0.3474–1.5563)	0.4215		1.200 (0.3619–3.979)	0.7656
Yes	51	25			6		
No	60	34			6		
Sex			0.7813(0.3701–0.6492)	0.5173		0.15489 (0.4602–5.2219)	0.4797
Male	54	27			7		
Female	57	32			5		
Birth weight			1.8056(0.8395–3.8834)	0.0305		3.8393 (0.7993–18.442)	0.0329
<2500 g	66	39			10		
>2500 g	45	20			2		
Gestational age			1.6544(0.7559–3.6208)	0.2077		2.6765 (0.7899–9.0687)	0.1138
<37 weeks	41	25			7		
>37 weeks	70	34			5		
Birth weight versus gestational age			1.8056(0.8395–3.8834)	0.2077		7.2626 (2.0471–25.7651)	0.0021
SGA	23	17			7		
AGA	88	42			5		

SGA: Small for gestational age, AGA: Appropriate for gestational age, PIH: Pregnancy-induced hypertension, CI: Confidence interval, OR: Odd ratio

as concluded by Pritchard *et al*. (85%) [11-13]. Primigravid condition is one of the high-risk factors for PIH. Its etiology is not clear but is proposed to occur due to dysfunction of the placental trophoblast and endothelial dysfunction with the maternal systemic vasculature [14]. The present study indicated that signs and symptoms of PIH appeared earlier that is at <28-week gestation (57.65%) as compared to after 28 weeks. Mehta *et al*. a rural-based study reported significantly higher incidence with gestational period ≤20 weeks (10%) than with >20-week gestational period (5.3%) [15]. In various hospital-based studies, the frequency was found to be higher after 28 weeks of gestation [12,16,17].

In our study, 88 (79.28%) newborns were AGA, 23 (20.22%) were SGA, and 59.45% were LBW babies. Higher incidence of somatic growth retardation, LBW, and prematurity in babies of PIH mothers have been perceived by other authors as well [2,10]. Compromised placental perfusion from uterine vasospasm is considered to be the most important causative factor for this. We observed thrombocytopenia in 53% neonates born to PIH mothers and 10.81% had severe thrombocytopenia. Bhat and Cherian demonstrated thrombocytopenia in 36% neonates born to PIH mothers with severe in 20% [18]. The combined effect of impaired megakaryocytic formation and increased platelet activation mediated through cytokines, thrombopoietin, and interleukin 6 was said to be most likely causative mechanisms [5,19].

A total of 32.43% of thrombocytopenic infants were born to pre-eclamptic mothers in our study while 22% in a study by Sivakumar *et al*. [20]. Raizada *et al*. also demonstrated that preterm infants born to pre-eclamptic mothers had thrombocytopenia; however, no significant correlation was found between the infants' platelet count and severity of hypertension [21]. An incidence of up to 36% has been reported previously by other researchers [3,5,18,22].

LBW and prematurity were significantly associated with thrombocytopenia in our study. LBW infant was 5 times at increased risk of thrombocytopenia. Bhat and Cherian also reported 4.5 times increased risk of severe thrombocytopenia with decreasing birth weight while Roberts and Murray have proven that LBW infants are at 2.52 times increased risk for thrombocytopenia [4,18]. Tsao *et al*. concluded that birth weight is negatively associated with thrombocytopenia [19].

Prematurity was reported as another major risk linked with neonatal thrombocytopenia and maternal hypertension by many authors [6,10,22]. In our present study, premature newborns were at 1.5 times increased risk of severe thrombocytopenia compared to term infant. Previously, Bhat and Cherian inferred that premature infants were at 2.52 times increased the risk for

severe thrombocytopenia compared to term infant [18]. The risk of thrombocytopenia was not found to be different in SGA or AGA newborns. However, in the present study, severe thrombocytopenia was significantly associated with SGA babies. Sola *et al*. observed that premature neonates are more prone to develop thrombocytopenia as compared to their term counterparts [23].

This study is restricted by its small sample size. Furthermore, the frequency of thrombocytopenia due to other causes was not compared to neonates born to PIH mothers. Platelet transfusion requirement and outcome of these newborns were also not analyzed in this study.

CONCLUSION

In this study, we infer that LBW and premature newborns born to mothers with PIH are prone to severe thrombocytopenia and require scrutiny during the 1st week of life.

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