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NEONATAL THROMBOCYTOPENIA IN MATERNAL PREGNANCY-INDUCED HYPERTENSION: A PROSPECTIVE OBSERVATIONAL STUDY

Pediatrics

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ABSTRACT

Background: Neonates born to mothers with pregnancy induced hypertension (PIH) are at increased risk of thrombocytopenia. The present study was undertaken to evaluate the prevalence of thrombocytopenia in neonates born to mothers with PIH and identify the associated material and neonatal characteristics.

Method: This prospective observational study was conducted in the Department of Pediatrics, at a Tertiary Care Institute during a period of 6 months from 1 July 2019-December 2019. A total 180 neonates born to mothers with PIH were enrolled in the study and detailed history of the mother, physical examination, and platelet count of the newborns was done.

Results: Among total 180 neonates 84 (46.66%) were males and 96 (53.33%) were females. 107 (59.44%) neonates had thrombocytopenia and 17 (9.44%) with severe thrombocytopenia. Higher percentage of thrombocytopenia was associated with neonatal characteristics of low birth weight (LBW) (70.09%); prematurity (63.55%) and male gender (59.81%). Severe thrombocytopenia was significantly associated with low birth weight ($p=0.03$) and prematurity ($p<0.05$). Although a higher percentage of thrombocytopenia was noted with primipara, PIH symptoms at <28 weeks, preeclampsia, and untreated mother, these were not statistically significant.

Conclusion: Thrombocytopenia is the most common complications of PIH, therefore, all neonates especially premature and LBW neonates born to mothers with PIH should be regularly examined for thrombocytopenia during early neonatal period and also, these babies should be closely monitored and managed in order to decrease the perinatal morbidity and mortality.

KEYWORDS

Neonates, Hypertension, Thrombocytopenia, Prematurity, Preeclampsia

INTRODUCTION

Pregnancy induced hypertension (PIH) is one of the most common causes of maternal and neonatal mortality and morbidity. It is a global problem and complicates approximately 10-17% of pregnancies. The incidence of PIH in India ranges from 5% to 15% [1]. New born delivered to mothers with hypertension are more liable for intrauterine growth retardation and may be delivered prematurely [2]. They may also suffer from the consequences of high rate of operative deliveries and the adverse effects of maternal drugs. These neonates may also have a spectrum of hematological changes [3], platelet abnormalities (neonatal thrombocytopenia) are one of them. Neonatal thrombocytopenia is a rare hematologic abnormality, defined as a platelet count less than 150,000/μL of blood [4]. However, 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 (early onset) [5]. The degree of severity of thrombocytopenia can be subcategorized according to platelet count in the affected individuals: Mild thrombocytopenia—platelet counts 100,000 to 150,000/μL; moderate thrombocytopenia—platelet count 50,000 to 99,000/μL; severe thrombocytopenia—platelet count < 50,000/μL [6].

Early onset neonatal thrombocytopenia (<72 hours) has a benign course and predictable outcome whereas late onset (>72 hours) is more severe [7]. Life-threatening bleeding or intracranial hemorrhage (ICH) with a high risk of neurodevelopmental impairment may occur in severe thrombocytopenia [8]. Thus, appropriate diagnosis and therapeutic management is necessary to prevent death. However, thrombocytopenia if not detected and managed appropriately can result in devastating consequences particularly in the preterm baby and leads to death. The paucity of studies from India and the increasing prevalence of this condition in our hospital instigated us to determine the prevalence and to identify the maternal and neonatal factors causing thrombocytopenia in neonates born to PIH mothers.

MATERIALS AND METHODS

After obtaining Institutional Ethical Committee approval and written informed consent from parents or guardian, this prospective observational study was conducted in the Department of Pediatrics, at a Tertiary Care Institute during a period of 6 months from 1 July 2019 to December 2019. A total 180 neonates born to mothers with PIH (BP >140 mmHg Systolic and >90 mmHg and Diastolic after 20 weeks of gestation) were enrolled in the study.

A detailed history of the mother was taken and maternal antenatal data including the details of the hypertension and maternal platelet counts was recorded. The birth details and Apgar score was recorded for all babies and babies were examined in detail and anthropometry recorded. The gestational age (GA) was assessed from maternal dates, sonography and confirmed by clinical examination. 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 of birth. The platelet count was repeated before discharge from hospital and also on follow up at 6 weeks if there was thrombocytopenia discharge. The low counts were confirmed manually using the Neubauer chamber. The neonatal characteristics including sex, birth weight, gestational age and mode of delivery and maternal characteristics including parity, time of onset of PIH and medications used, were recorded. Mothers with ITP and neonates with evidence of early sepsis were excluded.

Statistical Analyses

All data were entered into Microsoft excel sheet and statistically analyzed using SPSS software. Chi-square test and Fischer's exact test were applied accordingly for statistical analysis. P value < 0.05 was taken as significant.

OBSERVATIONS AND RESULTS

A total 180 neonates born to mothers with PIH were enrolled in the study during a period of 6 months**, a**mong them 84 (46.66%) were males and 96 (53.33%) were females. Out of 180 neonates, 107 (59.44%) had thrombocytopenia and these neonates were divided into three groups based on their platelet counts as shown in table 1.

Table 1: Distribution Of Babies In 3 Groups According To Severity Of Thrombocytopenia

Groups	Severity	No.of patients	Percentage
Group1	Mild (1-<1.5lacs/μl	34	18.88

Group2	Moderate(50,000-<1lac/µl	56	31.11
Group3	Severe (<50,000/µl)	17	9.44
Total	-	107/180	59.44

Maternal Characteristics-

Out of 180 neonates, 115 (63.88%) neonates had mothers with preeclampsia and 65 (36.11%) with eclampsia. There was no neonate with the mother having gestational hypertension. There were 105 (58.33%) neonates with primipara mothers as compared to 46 (41.66%) neonates with multipara mothers (Chi-square 6.407, p=0.0109). Thrombocytopenia was observed in 32.22% and 27.22% newborns of primi and multiparous women respectively. Severe thrombocytopenia in them was identical. However, the mothers of 104 (57.77%) neonates developed symptoms and signs before 28 weeks of gestation while mothers of 76 (42.22%) developed later. 97 (53.88%) newborns had mothers who did not receive any antenatal medication. 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. Furthermore the occurrence of severe thrombocytopenia, i.e., 13 (7.22%) was found more in <28 weeks of the onset of PIH in comparison to 4 (2.22%) in >28 weeks of onset. Severe thrombocytopenia in the neonate of an eclamptic group 10 (5.55%) was more than pre-eclamptic group mothers babies (7; 3.88%). Severe thrombocytopenia was found in 8 neonates of treated mothers and 9 of untreated. Maternal characteristics did not seem to be significantly associated with neonatal thrombocytopenia (p>0.05), (Table 2).

Neonatal Characteristics-

Thrombocytopenia was higher in male (35.55%) than female newborns (23.88%). There were 10 (5.55%) male babies with severe thrombocytopenia as compared to 7 (3.88%) female neonates. When birth weight was analyzed, 40.55% were >2500g and 59.44 % were <2500g. Thrombocytopenia was 41.66% among low birth weight (LBW) and 17.77% in >2500g neonates. Severe thrombocytopenia was 5 times higher in LBW babies (7.77%) as compared to normal birth weight babies (7.77% vs. 1.6%). Percentage of severe thrombocytopenia in <37 weeks infants was about twice of that in >37 weeks (6.11% vs 3.33%) of gestation. Thus, thrombocytopenia was significantly associated with male gender, LBW babies and prematurity in this study. Severe thrombocytopenia was significantly associated with (p=0.032) LBW babies and also with birth weight versus gestational age (p=0.0021), (Table 2).

Table 2: Bivariate Relationship Of Thrombocytopenia Between Various Neonatal And Maternal Characteristics

Maternal Characteristics		Total n=180	Thrombocytopenia					
			Total n=107	OR(95%CI)	Pvalue	Severe (n=17)	OR(95%CI)	Pvalue
Parity	Primipara	105	58	06924 (0.3185-1.4723)	0.324	10	0.9997 (0.2365-3.3367)	0.985
	Multipara	75	49			7		
Onset of PIH	<28weeks	104	60	0.9875 (0.4589-2.1310)	0.985	13	2.4132 (0.6125-9.4032)	0.218
	>28weeks	76	47			4		
Type of PIH	Preeclampsia	115	65	1.3168 (0.628-2.8914)	0.482	7	1.3067 (0.3958-4.4214)	0.661
	Eclampsia	65	42			10		
Medications	Yes	83	45	0.7359 (0.3576-1.5653)	0.432	8	1.200 (0.3619-3.9843)	0.775
	No	97	62			9		
Neonatal Characteristics		**Total n=180**	**Thrombocytopenia**					
			Total n=107	**OR(95%CI)**	**Pvalue**	**Severe (n=17)**	**OR(95%CI)**	**Pvalue**
Sex	Male	84	64	0.7901 (0.3784-0.6489)	0.521	10	0.15573(0.4602-5.2217)	0.479
	Female	96	43			7		
Birthweight	<2500g	107	75	1.805 (0.8654-3.8793)	0.030	14	3.8393 (0.7983-18.442)	0.032
	>2500g	73	32			3		
Gestational age	<37weeks	95	68	1.7634 (0.8427-3.6542)	2.208	11	2.6875 (0.7899-9.0678)	0.113
	>37weeks	85	39			6		
Birthweight vs.gestation	SGA	66	37	1.8071 (0.8394-3.8735)	0.207	10	7.2829 (2.0478-25.786)	0.0021
	AGA	114	70			7		

DISCUSSION

Neonatal thrombocytopenia is one of the most common haematological abnormalities seen in NICU [7]. The aetiology predisposing factors encountered are many and they interact to produce neonatal thrombocytopenia [9]. Previous studies report a prevalence of thrombocytopenia of 1–5% of all newborns. However, the prevalence varies depending upon the population studied. In neonates of mother with PIH, an incidence of thrombocytopenia up to 36% has been reported previously [10-12]. In another study, the incidence of neonatal thrombocytopenia in infants born to mothers with PIH has been purported to be in the range of 1 per 100 live births, and it is more commonly seen in preterm and low-birth-weight infants [13]. In present study, the prevalence of thrombocytopenia was 59.44% which was in concordance with study done by Chaurasiya et al (53.15%) [14]. The majority of neonates will have mild or moderate thrombocytopenia. However, 5–10% will have severe thrombocytopenia at birth (platelets <50 109/L) and require urgent investigation to identify the cause and institute prompt treatment to prevent long-term disability or death [15]. In current study, the neonates were divided into 3 grades based on the severity of thrombocytopenia. Among which the prevalence of mild and moderate thrombocytopenia was found in 34 (18.88%) and 56 (31.11%) neonates respectively followed by severe thrombocytopenia was found in 17 (9.44%) neonates. This finding is correlated with the study done by Chaurasiya et al [14] and Tirupathi et al [16].

Pre-eclampsia is one of the major maternal and perinatal mortality and morbidity worldwide, particularly in developing countries [17]. Preeclampsia affects approximately 6% of all the pregnancies, more often in primigravidas in the age group of 20-30 years. Approximately 50% of patients with preeclampsia will develop thrombocytopenia, in current study, higher percentage of thrombocytopenia was observed with pre-eclamptic mothers (36.11%). Severity will be usually proportionate to that of the underlying pathology. But in few cases, onset of thrombocytopenia precedes other manifestations of pre-eclampsia [18]. Though the pathogenesis of thrombocytopenia in patients with preeclampsia is not well understood, recent studies suggest that megakaryocytopoiesis impairment as a pathogenic factor [19-21]. 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 [22]. In present study, it was observed that 58.33% of neonates had primigravida mother which is comparable with the previous studies [14, 23, and 24]. The signs and symptoms of PIH appeared earlier i. e. at <28-week gestation (57.77%) as compared to after 28 weeks as similar to Chaurasiya et al [14] and Mehta et al study [25]. Increased risk associated with mothers not receiving medications was statistically not significant. Further, maternal characteristics did not seem to be significantly associated with neonatal thrombocytopenia.

Present study observed a higher percentage of overall and severe thrombocytopenia in male newborns. LBW infants were at 5 times increased risk for severe thrombocytopenia compared to normal weight infants, only three neonates weighing >2500 g had severe thrombocytopenia which is comparable with the other studies [26,

27]. Prematurity was reported as another major risk associated with neonatal thrombocytopenia and maternal hypertension by earlier studies [3, 28]. In existing study, premature infants were at two times increased risk for severe thrombocytopenia compared to term infants likewise Sola et al [13] and Bhat et al [27]. 114 (63.33%) newborns were AGA, 66 (36.66%) were SGA and 107 (59.44%) 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 [27, 29]. The risk of thrombocytopenia was not found to be different in SGA or AGA newborns. However, severe thrombocytopenia was significantly associated with SGA babies. 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

Thrombocytopenia is the most common complications of PIH and at times is life threatening. Therefore, all neonates especially premature and LBW neonates born to mothers with PIH should be regularly examined for thrombocytopenia during early neonatal period, because these babies are more prone for development of thrombocytopenia during the early neonatal period. This would reduce neonatal morbidity and mortality.

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