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Original Research Article

Clinical Outcome of Preterm Neonates with Thrombocytopenia

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Abstract: Thrombocytopenia is a common problem in preterm neonates. Thrombocytopenic neonates are at an increased risk of life threating complications. Hence this study was done with the objective to prospectively analyse clinical outcome of preterm neonates with thrombocytopenia. This prospective study was conducted in Department of Paediatrics, National Institute of Medical Sciences & Research, Jaipur. All intramural, singleton preterm neonates were included in the study. Enrolled neonates were screened for platelet count between 12-24 hour of life and later at 72 hour of life. Platelet count was repeated daily in thrombocytopenic infant. Neonates were followed till discharge. Statistical analysis was done using software SPSS version 23. 168 preterm babies gave the consent for inclusion in the study. 56 (33.3%) neonates had thrombocytopenia. 35 (20.8%) neonates had early onset of thrombocytopenia and 21 (12.5%) had late onset. 24 (42.8%) had mild, 20 (35.7%) had moderate and 12 (21.4%) had severe thrombocytopenia. Thrombocytopenic preterm neonates were diagnoses with sepsis, DIC, NEC and IVH. Severity of thrombocytopenia determined prognosis with severe thrombocytopenia having the highest mortality rate.
Keywords: Preterm Neonate, Thrombocytopenia, DIC, NEC, IVH

INTRODUCTION

Thrombocytopenia is a common haematological problem in neonates, especially in preterms. It is defined as platelet count of less than 150 × 10^9/L and is classified by severity as mild, moderate and severe and by age of onset as early and late [1-4].

0.7-4% of all neonates have thrombocytopenia [2, 5, 6]. Incidence of thrombocytopenia are higher in preterm babies especially those who are sick, ranging widely from 20-40% [7, 8]. Thrombocytopenic preterm neonates are at an increased risk of intraventricular haemorrhage [3, 9] necrotising enterocolitis [3], disseminated intravascular coagulation [3, 7, 10] and mucocutaneous bleed [3]. Even fatality is reported to be quite high in thrombocytopenic preterm neonates [3, 7]. Because of severe morbidity associated with thrombocytopenia in a preterm neonate it is important to identify and know possible clinical outcomes so that clinicians can be prepared and appropriate intervention can be done timely. Our knowledge is also undermined by the lack of prospective studies regarding thrombocytopenia in preterm neonates in this area of this country.

AIMS AND OBJECTIVES

To analyse the clinical outcome of preterm neonates with thrombocytopenia

METHODOLOGY

This Cross-Sectional Observational study was conducted in Neonatal Intensive Care Unit of National Institute of Medical Sciences and Research, Jaipur, India from 01/04/2015 to 31/3/2016. All intramural, singleton preterm neonates of less than 37 weeks of Gestation were included in the study after taking a written, informed consent from one or both parents.

Gestational age was estimated according to last menstrual period, combined with ultrasound and/or Ballard scoring if required. Details of demographic, clinical, laboratory data of mother and neonate

recorded. All mothers were evaluated with respect to age, gravida, para, maternal medical illness, obstetrical illness, infections, medication during pregnancy and details of labour and mode of delivery. Family history of bleeding in parents and sibling was also recorded. Neonatal characteristics including resuscitation detail, Apgar score, birth weight and gestational age at birth were recorded. Complete physical examination was done at enrolment and then once daily to identify the aetiology and risk factors for neonatal thrombocytopenia. All subjects were followed in hospital till recovery/death. Subjects enrolled in the study continued to receive routine management as per unit policy.

Enrolled neonates were screened for platelet count between 12-24 hour of life and later at 72 hour of life. Platelet count was measured by fully automated haematology analyser (KX-21, SYSMEX) along with Neubauer chamber and then confirmed by examination of slide after staining with Leishmen's stain. Platelet Count of less than150×10^9/L was taken as cut off point for thrombocytopenia. Platelet count was repeated daily in thrombocytopenic infant. Data obtained was entred and analysed in a Windows based statistical software IBM SPSS version 23.

RESULTS

During the study period 5170 neonates were born of which 183 were preterm babies. Amongst these preterm neonates parents of 168 preterm babies gave the consent for inclusion in the study. 56 (33.3%) neonates had thrombocytopenia. 35 (20.8%) neonates had early onset of thrombocytopenia (before 72 hours of birth) and 21 (12.5%) had late onset (after 72 hours of birth). 24 (42.8%) had mild thrombocytopenia (Platelet count 150×10^9/L-100×10^9/L), 20 (35.7%) had moderate thrombocytopenia (Platelet count 100×10^9/L-50×10^9/L) and 12 (21.4%) had severe thrombocytopenia (Platelet count $<50\times 10^9$/L). Baseline demographic characteristics of the thrombocytopenic preterm new-borns are depicted in table 1.

Baseline maternal demographic information of thrombocytopenic neonates is depicted in table 2.

Various perinatal characteristics of the thrombocytopenic preterm infants are depicted in Table 3.

13 of the thrombocytopenic neonates had sepsis, 3 had disseminated intravascular coagulation (DIC), 2 had intraventricular haemorrhage (IVH) and 2 had necrotising enterocolitis (NEC) as shown in Table 4.

Out of 56 thrombocytopenic preterms, 38 recovered, 14 died and 4 preterm left against medical advice as shown in Table 5.

Table 1: Description of baseline demographic characteristics of thrombocytopenic preterm neonates

Characteristics	Mean ± SD
Gestational age(in weeks)	34.3 ± 1.54
Birth weight in grams	1707.3 ± .445
Sex; n (%)	
Male	31(55.4)
Female	25(44.6)
Growth status; n (%)	
AGA	52(92.9)
SGA	4 (7.1)

Table 2: Description of baseline maternal demographic characteristics of thrombocytopenic preterm neonates

Characteristics	Values N (%)
Maternal Age (In years) Mean ± SD	 24.54 ± 4.173
Gravida - Primi	28(50.0)
Maternal medical problems	
Hypertension AIDS	7(12.5%) 1(1.8%)
Gestational hypertension	7(12.5%)
Evidence of maternal infection Maternal fever Foul smelling liquor PROM>24hrs	 5(8.9) 4(7.1) 8(14.3)

Table 3: Description of baseline perinatal characteristics of thrombocytopenic preterm neonates (n=56)

Characteristics	Values N (%)
Maternal medication Antenatal steroid Antibiotic Pitocin	 11(19.6%) 5(8.9%) 6(10.7%)
Mode of delivery Vaginal Delivery LSCS (Emergency) LSCS (Elective)	 45(80.3) 9(16.1) 2(3.6)
Resuscitation Required Not Required	 14(25) 42(75)
Delayed cry	20(35.7)
Apgar Score at 5 min. ≤7 >7	 20(35.7) 36(64.3)

Table 4: Clinical diagnosis of thrombocytopenic preterm neonates

	Neonates with Thrombocytopenia	Mild Thrombocytopenia	Moderate Thrombocytopenia	Sever Thrombocytopenia
Sepsis	13	3(23.1%)	3(23.1%)	7(53.8%)
DIC	3	0	0	3(100%)
NEC	2	0	1(50%)	1(50%)
IVH	2	0	0	2(100%)

Table 5: Outcome and mortality associated with thrombocytopenia in preterm neonates

Outcome	Total no. of patients	Mild TP	Moderate TP	Sever TP
Recovered	38	23	14	1
Died	14	0	4	10
LAMA	4	1	2	1

DISCUSSION

Neonatal thrombocytopenia frequently occurs in the preterm sick neonates admitted to neonatal

intensive care unit, and it can contribute to high mortality. To prevent the preterm neonates from neonatal thrombocytopenia, or to evaluate a thrombocytopenic neonate, the mechanism and predisposing factors of thrombocytopenia must be investigated. Since aggressive therapy administered to thrombocytopenic infants also increases the mortality, this study was planned to evaluate the outcome of thrombocytopenic preterm neonates. There are limited prospective Indian studies till date conducted to evaluate clinical outcome of thrombocytopenia in preterm neonate.

In our study, out of 168 preterm babies 56 (33.3%) were found to be thrombocytopenic. Previous studies have revealed that incidence of thrombocytopenia in healthy preterm was found to be similar as compared to the incidence in healthy term neonate [10]. Beiner ME *et al.;* [9] found that 93 (31%) preterm neonates were thrombocytopenic out of 305 babies (gestational age between 27-35 weeks). Bonifacio L [3] studied 1054 preterm neonates, out of which 94 (8.9%) had at least one episode of thrombocytopenia.

Sepsis was found 13 (23.21%) preterm neonates with thrombocytopenia. Sepsis associated thrombocytopenia is principally a problem in preterm and in very low birth weight babies (<1500gm). Incidence of sepsis in thrombocytopenic preterm neonate ranges from 22.8% [11] to 45% [12] and in term neonate incidence ranges from 15% [10] to 60% [13]. Sepsis is more in late onset thrombocytopenia and associated with severe thrombocytopenia (63.2%) [3] 25% of VLBW babies develop at least one episode of late onset bacterial sepsis [14] and thrombocytopenia complicates 50% of such septic episodes [15]. Benzamin *et al.;* [16] showed that fungal sepsis is associated with greater degree of thrombocytopenia than with coagulase negative staphylococcus sepsis.

In the study we found that 3 preterm had DIC and all three were severely thrombocytopenic. Previous studies revealed that mucocutaneous bleed was seen only in preterm with severe and late onset thrombocytopenia (18.4 %.) [3]. Incidence was higher in preterm which are <28 week of gestation (85.7%) [3]. NICU preterm are at high risk for thrombosis due to increased susceptibility to DIC, use of indwelling vascular catheter, use of extracorporeal membrane oxygenation. Exchange transfusion preformed frequent in NICU also contributes to thrombocytopenia [17].

Intraventricular haemorrhage occurred in 2 thrombocytopenic preterm neonates. Andrew *et al.;* [7] investigated the impact of thrombocytopenia on low birth weight babies and found significant higher incidence of IVH among thrombocytopenic neonate and more over severe grader of IVH were found in thrombocytopenic group. But till now no data demonstrate a clear relationship between IVH and thrombocytopenia [18-20]. Mcdonald *et al.;* [19] reported a significant higher incidence of IVH in 50 infants of gestational age less than 33 weeks in whom platelet counts were less than 150,000/ml within first 8 hour of life.

In the current study, 2 preterm had necrotising enterocolitis and out of which 1 had severe and 1 had moderate thrombocytopenia. NEC is common in very low birth weight babies and <28 weak of gestation with incidence of 12% in preterm thrombocytopenic neonate [3]. In has also been reported that in early stage of NEC, degree of thrombocytopenia correlates with its severity [17, 21]. In addition Vervendis *et al.;* [22] demonstrated fall of platelet count during the course of NEC. Studies also demonstrated that those infants who have persistent and progressive severe thrombocytopenia by 3wk after the initial diagnosis of NEC, have increased mortality, morbidity and more likely to require laparotomy for Bowel necrosis [21].

In our study, out of 56 thrombocytopenic preterm, 23 with mild and 14 with moderate thrombocytopenia recovered. However, but only one preterm recovered from severe thrombocytopenia. Out of 56 thrombocytopenic preterm, 13 died. Out of which, 10 had severe and 4 had moderate thrombocytopenia. Previous studies also demonstrate that mortality rate among the non-thrombocytopenic was 1.4% as compared to 16.7%, 32.4%, and 45.8% in preterm neonates with mild, moderate and severe thrombocytopenia [3] and in other study incidence of mortality found to be 34% in preterm [6].

CONCLUSION

33.3% preterm neonates were found to be thrombocytopenic. 20.8% had early onset of thrombocytopenia and 12.5% had late onset of thrombocytopenia. Thrombocytopenic preterm neonates were diagnoses with sepsis, DIC NEC and IVH. Severity of thrombocytopenia determined prognosis with severe thrombocytopenia having the highest mortality rate.

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