ORIGINAL RESEARCH

Investigations of thrombocytopenia among the new born in Neonatal Intensive care unit

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ABSTRACT
Background: Thrombocytopenia (platelet count <1,50,000/µL) is one of the most common haematological problems in neonatal intensive care units (NICUs). It is a significant cause of morbidity and mortality in the sick infants and accounts for up to 20 to 40% of admissions to Neonatal Intensive Care Unit (NICU). **Materials and Methods:** A total of 100 new born patients were enrolled in the study. Complete blood count, thrombocytopenia and sepsis was done on patients. **Results:** It was observed that neonatal thrombocytopenia is the common haematological abnormality seen in NICU, often result into severe complication if not detected and managed properly. Pregnancy induced hypertension and PROM are the important maternal risk factors for thrombocytopenia. **Conclusion:** Pre maturity, low birth weight, small for date babies and birth asphyxia are the important neonatal risk factors for early onset thrombocytopenia.
Keywords: NICU, Thrombocytopenia, platelets, Neonatal

INTRODUCTION

Thrombocytopenia (platelet count <1,50,000/µL) is one of the most common haematological problems in neonatal intensive care units (NICUs). It is a significant cause of morbidity and mortality in the sick infants and accounts for up to 20 to 40% of admissions to Neonatal Intensive Care Unit (NICU). Most of the sick and premature infants have low platelet count.[1] The reported incidence of thrombocytopenia with less than 50,000 platelet count is around 0.12 to 0.14% and severe thrombocytopenia (platelets < 50.000/µL) occurs in 0.1–0.5%.[2,3,4,5] Bacterial infections are one of the most common causes of neonatal septicemia. There are numerous other reasons of thrombocytopenia, such as immune-mediated, chromosomal abnormalities, and genetic disorders. In neonates, thrombocytopenia frequently follows a systemic illness.[6] There may or may not be symptoms in neonates who have thrombocytopenia. It's critical to determine whether pr- eclampsia related thrombocytopenia is the primary cause of a newborn's symptoms or whether they are secondary to other factors in symptomatic newborns.[7,8]

AIM

To evaluate the maternal and neonatal risk factors of thrombocytopenia in new born admitted in NICU as well as pattern of outcome in new born with thrombocytopenia.

MATERIALS AND METHODS

Study Design: This is a prospective study conducted at the Department of Pediatrics, Bebe Nanki Mother and Child Care Centre, Govt. Medical College, Amritsar after receiving approval from the institutional ethics committee. A total of 100 neonates were enrolled in the study, till 28 days of age, admitted to the center following criteria:

Inclusion Criteria:

1. All neonates above 1000 gms admitted in

NICU.
2. Thrombocytopenia <1.5 Lakh.

Exclusion Criteria:

3. Newborn with extremely low birth weight (ELBW) (<1000 gms)
4. Babies born before 28 weeks of gestations.
5. Newborn with any life-threatening congenital deformity.

Study Procedure: A detailed antenatal, medical history along with complete examination will be done as per the prescribed proforma after taking an informed written consent from the parents. The complete blood count and thrombocytopenia was confirmed to exclude the possibility that platelet clumping has caused erroneous thrombocytopenia. Septic screening was performed to assess the prevalence and course of thrombocytopenia in culture positive and culture negative neonatal sepsis in comparison to normal newborn.

Statistical Analysis: All the data noted on proforma was statistically analyzed using the latest SPSS version.

RESULTS

The present study was conducted in Department of Paediatrics, Bebe Nanki Mother and Child Care Centre, Govt. Medical College, Amritsar. The study constituted of 100 neonates admitted to the neonatal intensive care unit with neonatal thrombocytopenia. Out of 100 new born mild thrombocytopenia was reported in 82 (82%), moderate thrombocytopenia was reported in 12 (12%), while severe and very severe thrombocytopenia was observed in 03 (3%) of neonates. In the present study, 61% were males and 39% were females, with male to female ratio was 1.56:1.

According to gestation age, 15 (15%) were pre term having gestation age in range of >28-32 weeks, 57(57%) were near term having gestation in between 33-36 weeks, while 28 (28%) were term having gestation ≥ 37 weeks. Preterm babies had more severe and very severe neonatal thrombocytopenia as compared to term and near term babies with significant p value 0.03(p< 0.05). Babies with very low birth weight (<1.5 kg) constituted 15 (15%) of total babies, babies with low birth weight (>1.5-2.5) constituted 34 (34%) and babies with birth weight ≥2.5 kg constituted 43 (43%) of total babies with neonatal thrombocytopenia. Low birth weight was significantly associated with severe to very severe thrombocytopenia with p-value 0.06 (p<0.05).

Among all maternal risk factors, pregnancy induced hypertension (PIH) was the most common for neonatal thrombocytopenia with p value 0.022 (p <0.05); followed by maternal thrombocytopenia with p value 0.046 (p < 0.05). In our study, PROM was reported in 29 (29%) mothers and it was the most significant maternal risk factor for late onset neonatal thrombocytopenia in 21 neonates with significant p-value 0.001 (p< 0.05) as compared to 08 neonates who had early onset thrombocytopenia Among multiple neonatal risk factors, association between severity of thrombocytopenia and neonates born pre term was statistically significant (p- value 0.000). Similarly, low birth weight of babies (<

2.5 Kgs) was also significant risk factor for neonatal thrombocytopenia with statistically significant p- value 0.00001 (p< 0.05). Also, when pre term, appropriate for age babies and severity of thrombocytopenia was compared, it was found to be statistically significant (p-value 0.0236).

Out of 100 neonates with thrombocytopenia, blood culture positive sepsis was present in 50 (50%) babies. Among these 39 neonates had mild thrombocytopenia and 07 neonates had moderate thrombocytopenia. Severe and very severe thrombocytopenia was reported in 03 and 01 neonates respectively. Severity of neonatal thrombocytopenia was significantly higher in blood culture positive neonates as compared to blood culture negative neonates with significant p value 0.0012 (p< 0.05).

Similarly birth asphyxia was present in 30(30%) babies resulting into mild to moderate thrombocytopenia with significant p value 0.0296 (p <0.05) as compared to neonates who cried immediately at birth.

Table 1: Gestation age and its relation with early and late onset thrombocytopenia

Neonatal Gestational age (in weeks)	Early onset Thrombocytopenia (< 72 hrs)	Late onset Thrombocytopenia (> 72 hrs)	p-value
28-32	11	03	
33-36	27	31	
≥37	27	01	0.00001

In the present study, among 100 neonates, 14 (14%) neonates were having gestation age between 28- 32 weeks. Pre mature babies had early onset thrombocytopenia as compared to late pre term and term babies with highly significant p- value 0.00001(p< 0.05).

In the present study, late onset neonatal thrombocytopenia was present in 10 (71.4%) very low birth weight babies and 26 (60.4%) low birth weight babies. The incidence of late onset thrombocytopenia was more in very low birth weight and low birth weight babies as compared

to AGA babies with significant p- value 0.00013 ($p< 0.05$)

Table 2: Birth asphyxia and its relation with early and late onset neonatal thrombocytopenia

	Early onset Thrombocytopenia (< 72 hrs)	Late onset Thrombocytopenia (> 72 hrs)	p-value
Birth Asphyxia (H/O PNA)	25	05	
No Birth Asphyxia	32	38	0.000497

In the present study, out of 100 neonates, birth asphyxia was present in 30(30%) neonates. Among these 30 neonates, early onset thrombocytopenia was present in 25 (83.33%) neonates with significant p- value 0.000497 ($p< 0.05$) as compared to 05 (16.66%) neonates who had late onset thrombocytopenia.

Table 3: Sepsis and its relation with early and late onset thrombocytopenia

	Early onset Thrombocytopenia (< 72 hrs)	Late onset Thrombocytopenia (>72 hrs)	p-value
Blood Culture positive	11	39	0.00001
Blood Culture negative	46	04	
Fungal sepsis	01	03	

In the present study, out of 100 neonates, blood culture was positive in 50 (50%) babies. Among these 50 babies, late onset thrombocytopenia was present in 39 (78%) neonates, while 11 (22%) neonates who had early onset thrombocytopenia. In blood culture negative babies, only 04 (8.69%) had late onset thrombocytopenia. So, the incidence of late onset thrombocytopenia as compared to early onset thrombocytopenia was high in blood culture positive neonates as compared to blood culture negative neonates with significant p-value 0.00001 ($p< 0.05$). Our study reported fungal sepsis in 04 neonates. Among these, 03(75%) had late onset neonatal thrombocytopenia while 01 (25%) had early onset thrombocytopenia.

Table 4: Outcome with severity of neonatal thrombocytopenia

Outcome	Neonatal thrombocytopenia				Total	p-value
	Mild	Moderate	Severe	Very Severe		
Recovered	83	10	02	00	95	
Died	00	02	01	02	05	
Total	83	12	03	02	100	0.00001

In the present study, Out of 100 neonates, 95(95%) of neonates with neonatal thrombocytopenia recovered fully with specific treatment or no specific treatment was given to asymptomatic neonates. Only 05 (5%) neonates died during treatment. Among these, 02 (2%) had moderate thrombocytopenia, 01 (1%) had severe thrombocytopenia and 02 (2%) had very severe thrombocytopenia. However no death was reported in neonates with mild thrombocytopenia. Mortality was significantly high among neonates with moderate, severe and very severe thrombocytopenia with highly significant p value 0.00001 (p values< 0.05).

DISCUSSION

Thrombocytopenia is one of the most common haematological problems in neonatal intensive care units (NICUs). In the sick neonates the frequency of thrombocytopenia is as high as 15 percent, and it is most severe after several days of delivery. Thrombocytopenia is a risk factor for ICH (Intracranial Haemorrhage). IVH is more common in VLBW (very low birth weight) neonates and most are due to immune mediated thrombocytopenia. If left untreated, thrombocytopenia can cause serious problems. In this present study, 100 neonates were divided into 4 groups based on their platelet count. Our study found that 82 (82%) neonates had mild thrombocytopenia. The prevalence of mild thrombocytopenia was higher in study by Khalessi et al (2013)[9], Ghamdi et al (2008)[10] and Gupta et al (2011)[11] which is in accordance with our study. As compared to our study, low prevalence of mild thrombocytopenia (32.85%) was noted by Madavi et al (2021)[12] in their study, followed by moderate thrombocytopenia in 8.57 % and severe thrombocytopenia in 3.57%.These were in accordance with our study in which moderate thrombocytopenia was reported in 12 (12%), while severe and very severe thrombocytopenia was observed in 03 (3%) of neonates. In contrast to our study, Nandyal et al

(2016)[13] in their research on 99 newborns noted that, 65.6% of the newborns had severe thrombocytopenia, and in a study by Bonifacio et al (2007)[14] 51% of the newborns had severe thrombocytopenia.

In the present study, out of 100 neonates with neonatal thrombocytopenia, 61 (61%) were males and 39 (39%) were females; the male to female ratio was 1.56:1.In research by Basil et al (2015)[15] similar findings were seen, showing that the proportion of male babies with thrombocytopenia was higher than that of female neonates (1.37:1). Prematurity is a well-documented risk factor for neonatal thrombocytopenia. In the present study, preterm babies had more severe and very severe neonatal thrombocytopenia as compared to term and near-term neonates with significant p-value 0.038149 ($p<0.05$). In a study by Jeremiah et al (2010)[16], out of 140 neonates 60 (42.8%) neonates were premature of which 38 (63.3%) had thrombocytopenia. Similar findings were reported by Anubha Sharma et al (2015)[17], where 58.2% preterm babies developed thrombocytopenia. Incidence of thrombocytopenia was twice in preterm neonates than term neonates in studies by Beiner et al (2003)[18], Eslami Z et al (2013)[19] and Bonafacio et al (2007)[14]. The result of our study was comparable to Arif et al (2020)[20] research, they also reported that 13 (56.2%) of premature neonates develop severe thrombocytopenia.

In present study, very low birth and low birth weight neonates had severe thrombocytopenia as compared to neonates with birth weight more than 2.5 kgs who had mild to moderate thrombocytopenia. In our study, low birth weight was significantly associated with severe to very severe thrombocytopenia with p-value 0.066458 ($p<0.05$). This is similar to the study done by Khaleesi et al in which 59.1% babies with thrombocytopenia were low birth weight babies. The result in our study is comparable to the studies conducted by Charoo BA et al and Robert and Murray, they also found that neonatal thrombocytopenia was more common among low birth weight babies. Low birth weight and prematurity are closely related. In this present study, low birth weight was significantly associated with severe to very severe thrombocytopenia with p-value 0.066458 ($p<0.05$). Similar findings were reported by Roberts I and Murray NA (2006)[21], Tirupati K et al (2017)[22], Khalessi et al (2013)[23] Eslami Z et al (2013)[19] and Christensen et al (2006)[21]. The ability of premature low birth weight neonates to repair the harm produced by increased platelet breakdown is limited. With maturation, there is an increase in IgG transfer from placenta to foetal circulation. Neonates who are born prematurely or with low birth weight have this process slowed, making them more susceptible to neonatal thrombocytopenia.

Our study revealed among all maternal risk factors, pregnancy induced hypertension was the most common risk factor for neonatal thrombocytopenia with significant p value 0.022 ($p <0.05$). The results of our study are comparable to the study conducted by Eslmai at al (2013)[19] where 46.4% had pregnancy induced hypertension. The findings of our study are correlating with similar studies conducted by Madavi D et al (2021)[12] where authors observed that PIH (64.8%) was seen to be more commonly associated with thrombocytopenia. The findings of our study were in concordance with studies conducted by Burrows et al (1990)[4] and Kumar et al (2018)[24] where maternal PIH was significantly associated with neonatal thrombocytopenia. In contrast to our study, Bagale BB and Bhandari A (2018)[25] noted that 89.2% had no any maternal risk factor contributing to neonatal thrombocytopenia, whereas pregnancy induced hypertension was observed in only 9.5% of cases which less as compare to our study.

In our study, the second most common maternal risk factor for neonatal thrombocytopenia was maternal thrombocytopenia which was seen in 05 (5%) mothers. Out of these 05 neonates born to mothers having thrombocytopenia, 04 (80%) neonates had mild thrombocytopenia while 01 (20%) neonate had very severe thrombocytopenia (p-value 0.046). In present study, PROM was present in 29 (29%) mothers. Among the newborns born to mothers with PROM, 23 neonates had mild neonatal thrombocytopenia, while moderate and severe neonatal thrombocytopenia was present in 02 and 03 neonates respectively. None of the neonates had very severe thrombocytopenia. p-value was 0.176 ($p>0.05$). In their study, Meena SL et al (2019)[26] noted that anaemia (48%) was common maternal factor followed by PROM in 30%, PIH 19%, oligohydramnios in 2% and eclampsia in 2%.

Our study reported neonatal sepsis was the second most common cause of neonatal thrombocytopenia, which was observed in 50 (50%) neonates and was linked to moderate to severe neonatal thrombocytopenia. Severity of neonatal thrombocytopenia was significantly higher in blood culture positive neonates as compared to blood culture negative neonates with significant p value 0.0012 ($p<0.05$). The results of our study were comparable with studies conducted by Nandyal et al (2013)[13], Gupta et al (2012)[11], and Khalessi et al (2013)[23] which showed sepsis was present in 22.2%, 42%, and 24.1% of thrombocytopenic neonates in the

studies respectively. Sepsis was associated to severe thrombocytopenia in studies by Patil et al (2014)[27], Basil and Zaccheaus et al (2010)[28], which was comparable to the outcomes in our investigation. Due to both increased consumption and decreased production of platelets, septicemia causes thrombocytopenia, which typically has severe consequences. In present study, birth asphyxia was associated with mild to moderate thrombocytopenia with significant p value 0.0296 ($p<0.05$) as compared to neonates who cried immediately at birth. Meena SL et (2019)[26] in their study revealed that birth asphyxia and sepsis were substantially linked to early-onset neonatal thrombocytopenia and late-onset thrombocytopenia, respectively and it was similar to our study. In Nandyal SS et al (2016)[13] study, both sepsis and birth asphyxia were associated with late onset neonatal thrombocytopenia. However, in our study, birth asphyxia was associated with early onset thrombocytopenia while sepsis was associated with late onset thrombocytopenia. Bagale et al (2018)[25] in their study observed that 27% neonates had early onset neonatal sepsis while only 2.7% had late onset neonatal sepsis. 35.1% had asphyxia and 9.5% were IUGR babies. This is in contrast to our study, which showed that birth asphyxia was linked to early onset thrombocytopenia and sepsis was mainly linked to late onset thrombocytopenia. In a study by Eslami et al (2013)[19], 31.9% had neonatal sepsis, 20.8% were IUGR and 13.9% had asphyxia as neonatal risk factors. In our study, 50% had blood culture proven sepsis and 30% had birth asphyxia as risk factor for neonatal thrombocytopenia. Tirupati K et al (2017)[22] found that sepsis was the commonest cause of neonatal thrombocytopenia which was found in 97 (48.5%) babies and was associated with severe neonatal thrombocytopenia, which was quite similar to our study.

In the present study, out of 100 neonates, 95 (95%) of neonates with neonatal thrombocytopenia recovered fully with specific treatment or no treatment was given to asymptomatic neonates and only 05 (5%) neonates expired during treatment. Among these, 02 (2%) had moderate thrombocytopenia, 01(1%) had severe thrombocytopenia and 02 (2%) had very severe thrombocytopenia. However, no death was reported in neonates with mild thrombocytopenia. In our study, mortality rate was significantly high among neonates with moderate, severe and very severe thrombocytopenia with highly significant p-value 0.00001 ($p<0.05$). The findings of our study were comparable to the studies conducted by Bagale BB and Bhandari A (2018)[25], they also found that 77.03% of the neonates recovered and only 5.40% neonates died. Similar findings were observed by Madavi et al (2021)[12] where mortality rate was only 3.6%. However, Patil et al (2014)[27] reported that mortality rate was very high 37%, among the severely thrombocytopenic neonates, while it was only 3.72% and 3.92% respectively in the mild to moderate and no thrombocytopenia groups. Bonifacio L et al (2007)[131] observed that the mortality rate was 16.7%, 32.4% and 45.8% in neonates with mild, moderate and severe thrombocytopenia, respectively. Kumar et al (2018)[24] found that among the 70 neonates, 52 (74.3%) survived and 18 (25.7%) died. Our study results were in contrary to the findings of Arif et al (2020)[20] and Meena SL et al (2019)[26] research, where authors reported very higher percentage of mortality rate (35% and 34%) respectively, inadequate prenatal and foetal evaluation other associated factors like very low birth weight, prematurity and nosocomial sepsis along with severe thrombocytopenia may be the cause.

CONCLUSION

Thus, it was concluded that thrombocytopenia is due to impaired megakaryopoiesis, inadequate platelet production, and increased platelet destruction. NT within 72 hrs of childbirth is usually due to fetal hypoxia. Among the maternal risk factors, pregnancy induced hypertension is the most common cause of early onset thrombocytopenia. Pre maturity, low birth weight, small for date babies and birth asphyxia are the important neonatal risk factors for early onset thrombocytopenia. Bleeding risk is minimal in fetal hypoxia as compared to sepsis. Detection of thrombocytopenia is a useful in initial assessment of sick neonates. So timely detection and management helps in improving the neonatal outcome and thus helps in decreasing the neonatal mortality.

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