Study of Clinical Profile and Outcome of Neonates Admitted to the NICU with Thrombocytopenia and Abnormal Coagulation Profile

Alikana Deepak Kumar[1], Shaik Karimulla[2], Arumulla Sailusha[3]

ABSTRACT

Introduction: Thrombocytopenia is very common in neonates admitted to the NICU. Even though thrombocytopenia is the most prevalent, other coagulation problems do occur and the two problems often coexist. This study was undertaken to determine the incidence, etiology, clinical profile and immediate outcome of neonates admitted to the NICU with thrombocytopenia with/without abnormal coagulation profile, in a tertiary care hospital.

Material and methods: This is a prospective observational study, conducted in a tertiary care hospital, between November 2017 to September 2019. Seventy (70) neonates admitted to NICU with thrombocytopenia with/without abnormal coagulation profile were included in the study.

Results: Majority of the seventy (70) neonates had grade 3 / severe thrombocytopenia (44.3%). Delivery by LSCS, PIH, maternal anemia and preterm delivery were all significantly associated with thrombocytopenia. Low birth weight (78.6%) was the most common cause of neonatal thrombocytopenia, followed by neonatal sepsis (72.8%). Abnormal PT was observed in 87.1% and abnormal APTT in 82.8% of the study population. Coagulation abnormalities had no significant association with PIH, premature delivery and birth weight. Among the seventy neonates, 52 (74.3%) survived and 18 (25.7%) died. Deaths were significantly more common in severe thrombocytopenia.

Conclusion: In the present study LBW and septicemia were the major etiology associated with both mild and severe thrombocytopenia. Severe thrombocytopenia could be used as a prognostic indicator in sick neonates. But more studies are needed to ascertain this.

Keywords: Neonates, Thrombocytopenia, Coagulation Profile, Low Birth Weight, Septicemia.

INTRODUCTION

The human haemostatic mechanism is dynamic and is profoundly influenced by age. Thrombocytopenia is the most common hematological abnormality seen in neonates admitted to NICU. Even though thrombocytopenia is the most prevalent, other coagulation problems do occur and the two problems often coexist.

Development of haemostasis in the newborn differs from that of adults and coagulation factors do not cross the placental barrier. The coagulation factors are synthesized independently and are dependent on gestational age and level of maturity of the liver. Spontaneous coagulopathy occurs more frequently in the neonatal period than any time. This is because newborns, especially those born preterm or small for gestational age or those with perinatal asphyxia or sepsis tend to experience haemostatic alterations resulting from hepatic or platelet dysfunction and/or derangement of clotting factors.

Thrombocytopenia is defined as a platelet count less than 1.5 lakhs / cu. mm, regardless of gestational age. Early-onset (less than 72 hrs) has a benign and predictable outcome, whereas late-onset (more than 72 hrs) is more severe. In the past decade, there has been a lot of research regarding the etiology, clinical profile and management of neonatal thrombocytopenia[1-3]. But there is a dearth of studies in India, on neonatal thrombocytopenia[4,5].

This study was undertaken to determine the incidence, etiology, clinical profile and immediate outcome of neonates admitted to the NICU with thrombocytopenia with/without abnormal coagulation profile, in a tertiary care hospital.

MATERIAL AND METHODS

This was a prospective observational study conducted in a tertiary care hospital between November 2017 to September 2019. Seventy (70) neonates admitted to NICU with thrombocytopenia with/without abnormal coagulation profile were included in the study. Babies who died within 6 hours of admission and babies with congenital anomalies were excluded from the study.

Institutional ethics committee approval has been obtained for the study. Parental consent was taken at the time of admission. Detailed history inclusive of maternal obstetric history, birth history and perinatal events were recorded in the data entry form. The gestational age of neonates was determined based on New Ballard's scoring system. All neonates underwent thorough clinical examination. Platelet counts were obtained using standard automated cell counter and coagulation profile obtained from automated coagulation analyzer. CBC, sepsis screen and blood culture were also carried out. Low platelet counts were cross-verified by peripheral smear study.

All the thrombocytopenic neonates were graded into three categories based on their platelet counts. Grade 1 (Mild)

[1]Assistant Professor, Department of Pediatrics, Guntur Medical College, Guntur, [2]Assistant Professor, Department of Pediatrics, Guntur Medical College, Guntur, [3]Senior Resident, Department of Pediatrics, Guntur Medical College, Guntur, Andhra Pradesh, India

Corresponding author: Dr Shaik Karimulla. Flat No: C513, Golden Homes, Krishna Nagar, Opp. Jute mill, Guntur, Andhra Pradesh 522006, India

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with platelet count between 1.5 lakhs & 1.0 lakh/cu mm, Grade 2 (Moderate) with platelet count between 1.0 lakh & 0.5 lakh/cu mm, Grade 3 (Severe) with platelet count less than 0.5 lakh/cu mm. These neonates also underwent coagulation profile study and Prothrombin time (PT) 13.5 – 16.4 seconds, Activated partial thromboplastin time (APTT) 29.5 – 42.2 seconds and INR 1.05 – 1.35 were taken as normal range. Neonates with values above these ranges were considered to have abnormal coagulation profile.

Statistical Package for Social Sciences (SPSS) software version 21.0 was used for the final analysis. The presentation of the Categorical variables was done in the form of number and percentage (%). The presentation of the continuous variables was done as mean ± SD. The association of the variables which were quantitative in nature was analyzed using Independent t test (for two groups) and ANOVA (for more than two groups). Repeated measure ANOVA was used to compare repeated measurements across follow up. The association of the variables which were qualitative in nature was analyzed using Chi-Square test/Fisher's exact test. For statistical significance, p value of less than 0.05 was considered as significant.

RESULTS

Of the seventy (70) neonates with thrombocytopenia, the majority were of grade 3 (44.3%), followed by grade 2 (37.1%) neonatal thrombocytopenia (Table 01).

Maternal & neonatal risk factors for thrombocytopenia –

Mode of delivery was by cesarean section for a majority (92.3%) in Grade 1 neonatal thrombocytopenia and this difference in the mode of delivery with the grade of thrombocytopenia was statistically significant ($p<0.05$).

Pregnancy-induced hypertension *(PIH)* was high in both moderate and severe groups of neonatal thrombocytopenia (69.2% &32.2% respectively) ($p <0.05$).

GDM was seen in 15.7% of the thrombocytopenic group (p-value was statistically insignificant).

Anemia was seen in a majority (65.4%) of mothers among the neonates with grade 2 neonatal thrombocytopenia, and this difference of anemia in mothers with the grade of thrombocytopenia was statistically significant ($p<0.05$).

Pre-term deliveries were more (83.9%) among the grade 3 neonatal thrombocytopenia, and this difference of gestational age with the grade of thrombocytopenia was statistically significant ($p<0.05$).

Early-onset (<72hrs) was observed in 55.7%, where as late-onset was observed in 44.3% (the P-value observed was statistically insignificant).

Gender – No statistical significance was observed between gender and thrombocytopenia.

Low birth weight was seen in the majority (93.5%) of grade 3 neonatal thrombocytopenia, and this difference of birth weight with the grade of thrombocytopenia was statistically significant ($p<0.05$).

Birth Asphyxia – 40% of thrombocytopenic neonates had birth asphyxia, but this was statistically insignificant.

Meconium aspiration was observed in only 17.1% and the association was statistically insignificant.

Sepsis was seen in the majority of moderate (80.7) and severe (80.6) thrombocytopenia, and the p-value (0.008) is statistically significant.

Clinico-etiological profile of neonates with neonatal thrombocytopenia –

Among the 70 study subjects with neonatal thrombocytopenia, clinical profile showed that those presenting with bleeding were 32.9%, and with petechiae/ purpura were 35.7%. Those diagnosed with sepsis were 72.9%, and those needing assisted ventilation and ≥ 2 platelet transfusions were 62.9% and 47.1% respectively (Table 02).

Outcome in neonates with neonatal thrombocytopenia – Deaths were more (45.2%) among the grade 3 neonatal thrombocytopenia, and this difference in death rate with the grade of thrombocytopenia was statistically significant ($p<0.05$) (Table 03).

Abnormal PT was observed in 87.1% of the study population, and 82.8% had abnormal APTT (Table 04).

Maternal & neonatal risk factors for abnormal coagulation profile – Among the 61 study participants with abnormal PT; in majority (75.4%) the *mode of delivery* was by cesarean section. Similarly, it was 72.4% among the 58 study participants with abnormal APTT.

Among those with abnormal PT, the majority (57.4%) were associated with *PIH*. Similarly, it was 56.9% among the 58 study participants with abnormal APTT.

Only 13.1% with abnormal PT and 15.5% with abnormal APTT were associated with *GDM*.

Gestational age – The incidence of abnormal coagulation profile was high in preterm (63.9%) compared to term neonates (not statistically significant).

Neonatal Thrombocytopenia	Frequency	Percentage (%)
Grade 1	13	18.6
Grade 2	26	37.1
Grade 3	31	44.3
Total	70	100.00

Table-1: Neonatal thrombocytopenia grading among study participants (n=70)

Parameter	Frequency (n=70)	Percentage (%)
Bleeding	23	32.9
Petechiae / Purpura	25	35.7
Diagnosed with Sepsis	51	72.8
Diagnosed with NEC	30	42.8
Diagnosed with DIC	13	18.5
Needed Assisted Ventilation	44	62.9
Prematurity	45	64.3
LBW	55	78.6

Table-2: Clinico-etiological profile in neonatal thrombocytopenia

Outcome	Neonatal Thrombocytopenia			Total	p-value
	Grade 1	Grade 2	Grade 3		
Recovered	11 (84.6)	24 (92.3)	17 (54.8)	52 (74.3)	0.003
Died	02 (15.4)	02 (7.7)	14 (45.2)	18 (25.7)	
Total	13 (100)	26 (100)	31 (100)	70 (100)	

Table-3: Outcome with Neonatal Thrombocytopenia grading (n=70)

Abnormal coagulation profile	Frequency	Percentage (%)
Abnormal PT	61	87.1
Abnormal APTT	58	82.8

Table-4: Abnormal coagulation profile among study participants (n=70)

Parameter	Abnormal PT (n=61)	Abnormal APTT (n=58)
Bleeding	19 (31.1)	17 (29.3)
Petechiae/ Purpura	24 (39.3)	22 (37.9)
Diagnosed with Sepsis	47 (77.0)	44 (75.9)
Diagnosed with DIC	13 (21.3)	13 (22.4)
Needed Assisted Ventilation	38 (62.3)	37 (63.8)

Table-5: Clinico-etiological profile in abnormal coagulation profile

Outcome	Abnormal coagulation profile	
	Abnormal PT	Abnormal APTT
Recovered (n=52)	43 (70.5)	41 (70.7)
Died (n=18)	18 (29.5)	17 (29.3)
Total (n=70)	61 (100)	58 (100)

Table-6: Outcome in neonates with abnormal coagulation profile

In **low birth weight babies,** the majority had prolonged PT (77 %) and APTT (79.3%) though statistical significance was not seen.

Birth asphyxia – 89% of asphyxiated neonates had an abnormal coagulation profile (not statistically significant).

Clinico-etiological profile of neonates with abnormal coagulation profile –

In the present study, among the 61 study subjects with abnormal PT, the clinical profile showed that those presenting with bleeding were 31.1% and with petechiae/ purpura were 39.3%. Those diagnosed with sepsis were 77% and those needing assisted ventilation were 62.3% (Table 05).

Outcome in neonates with abnormal coagulation profile – Among the neonates with abnormal PT 29.5% died and 70.5% recovered. Among the neonates with abnormal APTT 29.3% died and 70.7% recovered (Table 06).

DISCUSSION

Though thrombocytopenia is common in NICU, it often coexists with abnormal coagulation profile. The etiology and predisposing factors are many and they interact in a complex manner. As in any other neonatal illness the manifestations are protean, and severe neonatal thrombocytopenia is known to be associated with a poor outcome[6-9].

The prevalence of thrombocytopenia in the present study was 27.5%. This prevalence is slightly higher than 8% to 35% reported in other studies[6-9,10]. This higher prevalence is probably due to higher proportion of septicemic neonates in our NICU admissions. The proportion of severe thrombocytopenia (44.3%) in the present study also falls on the higher side. This is once again probably a reflection of septicemia contributing to the majority of cases of neonatal thrombocytopenia in our NICU. Sepsis is reported to result in moderate to severe thrombocytopenia in various studies[11].

The etiological profile was similar to other NICU studies from India[12,13], with septicemia accounting for the majority of the admissions. Neonates with prematurity, IUGR and perinatal asphyxia in our setting are more frequently exposed to infections than neonates with the same problems in Western countries. Hence in neonates with an already compromised hematological environment, exposure to an infection probably leads to a precipitous fall in platelet count resulting in severe thrombocytopenia.

Maternal PIH was significantly associated with neonatal thrombocytopenia. This finding is in agreement with studies conducted by Burrows et al[14] and Gupta AK et al[12]. In this study, anemia was the commonest maternal risk factor. 41.2% of mothers had anemia, and it was associated with all types of thrombocytopenia. In a study conducted by Tirupathi K et al[15], an association has been documented between anemia and thrombocytopenia.

Prematurity is known to be associated with lower platelet counts[6-9]. In the present study gestational age was associated with low platelet counts with a statistically significant p-value. Incidence of thrombocytopenia was twice in preterm neonates than term neonates in studies by Beiner et al[8], Eslami Z et al[16] & Bonafacio et al[17].

The high proportion of male babies with thrombocytopenia in this study is probably due to a high incidence of sepsis among male babies. Chandra A et al[18], Antoniette BWM et al[19], Schuchat A et al[20] and Kuruvilla KA et al[21] noted that the incidence of neonatal sepsis was higher in males than females.

The present study showed early-onset thrombocytopenia as predominant, which was in concordance with the studies done by Khalessi et al[22] and Eslami et al[16].

Mechanical ventilation can lead to thrombocytopenia due to mechanical reasons; shearing effect on the pulmonary vasculature producing increasing platelet consumption[23]. There was a significant prevalence (62.9%) of thrombocytopenia in mechanical ventilated neonates. This association has been documented by other studies done in this regard[24].

The prevalence of petechiae and purpura in thrombocytopenic neonates was 35.7%. This association has been well reported and documented in the past[25]. The mortality rate was very high (45.2%) among the severely thrombocytopenic neonates while it was only 15.4% and 7.7% respectively in mild & moderate groups of thrombocytopenia. This was similar to other studies[8-10].

In the present study, unlike thrombocytopenia, prothrombin time and activated partial thromboplastin time are not influenced by age, sex, maternal PIH and NEC.

Among the seventy neonates, 52 (74.3%) survived and 18 (25.7%) died. Thirteen neonates expired even after multiple transfusions; four neonates expired without receiving any transfusions. The association of increased mortality rates with an increasing number of platelet transfusions mainly reflects the severity of the underlying disease. Three studies from the USA, UK and Mexico reported higher mortality rates in neonates who had received platelets compared with those who did not[26,27,28].

CONCLUSION

In the present study, the prevalence of thrombocytopenia was high (27.5%), and that of severe thrombocytopenia was 44.3%. Low birth weight followed by septicemia was the major etiology associated with both mild and severe thrombocytopenia. The predisposing factors associated with neonatal thrombocytopenia were maternal PIH, prematurity, septicemia, NEC, DIC and assisted ventilation. Glaringly perinatal asphyxia was not associated with neonatal thrombocytopenia in the present study.

The mortality rate (21.05%) was far more common in the severe thrombocytopenic group. Moreover, low platelet count was found to be an independent risk factor for a poor outcome in our cohort.

Though thrombocytopenia and abnormal coagulation profile often coexist, coagulation abnormalities have no significant association with PIH, prematurity, and birth weight. Severe thrombocytopenic neonates with abnormal coagulation profile bleed more frequently and can have nonspecific signs such as respiratory distress at presentation.

The most significant conclusion of the present study was that severe thrombocytopenia could be used as a prognostic indicator in sick neonates. But to generalize this statement, and apply to all neonatal admissions, more studies are required in this regard with similar results.

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