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Original Research Article

A clinical study of spectrum of low platelet count to establish etiology, diagnosis, complications and prognosis in newborns admitted in Al-Ameen medical college hospital NICU, Bijapur, Karnataka, India

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ABSTRACT

Background: In the newborn low platelet count is a common finding in both preterm and term newborn. It has been estimated that as many as 22% of all new borns admitted to NICU develop low platelet counts. A platelet count of less than 150,000/µL is defined as thrombocytopenia irrespective of the age of the individual.
Methods: All the neonates underwent necessary blood investigations like Complete blood counts, (including platelet counts, HB estimation, Red cell indices and PCV), Capsular Polysaccharide - reactive protein. (CRP), Peripheral Smear study, Blood culture, BT, CT, PT, aPPT, Anti-platelet Antibodies.
Results: The prevalence of thrombocytopenia in our study was 28%. The proportion of severe thrombocytopenia among the neonatal thrombocytopenia, 11.2% in our study.
Conclusions: It can be concluded that thrombocytopenia is very much common in among our NICU admissions. Septicemia is its most important and most common cause.

Keywords: Birth asphyxia, Low platelet count, Mucosal bleeding, Neurodevelopment, Septicemia

INTRODUCTION

In the newborn low platelet count is a common finding in both preterm and term newborn. It has been estimated that as many as 22% of all new borns admitted to NICU develop low platelet counts.[1,2]

The present study was done to know the spectrum of low platelet count to establish etiology, diagnosis, complications and prognosis in newborns admitted in Al-Ameen medical college hospital-NICU, Bijapur.

It is a two year prospective observational study, total of 125 newborns delivering at Al-Ameen Medical College Hospital –NICU, Bijapur, irrespective of their underlying morbidity were screened for thrombocytopenia.

METHODS

A detailed history inclusive of maternal history and obstetric history with suggestive of a bleeding and its type in the newborn or the mother was obtained as per the pro forma. Gestational age of all neonates was determined based on the New Ballard's scoring system. All the neonates, except 8 who were lost for follow up, were followed up after their discharge for a period of 6 months.

Exclusion criteria

- Any Multifetal gestation.
- Congenital fetal anomalies.
- Congenital neuromuscular disorders.

- Discharge against medical advice/Not available for follow up.
- Neonates, whose parent or guardian did not agree to be a part of the study.

Growth assessment at birth or admission to detect intrauterine growth restriction was based on Colorado intra uterine growth charts. Every neonate had a detailed physical examination as in the pro-forma with a focus on purpuric / petechial rashes, mucosal bleeding etc. All neonates at admission underwent a gastric lavage to look for any altered blood in the aspirate. Maternal blood was differentiated from neonatal blood using the Apt - Downey test.

All the neonates underwent necessary blood investigations, viz

- Complete blood counts, (including platelet counts, HB estimation, Red cell indices and PCV).
- Capsular Polysaccharide – reactive protein. (CRP)
- Peripheral Smear study.
- Blood culture
- BT, CT
- PT, aPPT
- Anti-platelet Antibodies

Blood was collected in sterile EDTA bulbs by venipuncture after taking all aseptic precautions and swiftly transferred to Al-Ameen Medical College Hospital central laboratory, the time lag between collection and estimation was usually 10 to 15 minutes. CBC was obtained from an automated hematology analyzer (ABX MICOROX OT18- ABX HEMATOLOGIE MONPELLIER CEDEX 04). Peripheral smear study, blood cultures were done using standard laboratory methodology. Measurement of CRP was done by latex turbidimetry using SPINREACT CRP-TURBILATEX. A value of more than 6mg/dl was considered as abnormal. The next Step was to group the neonates, based on their platelet counts at admission. It is shown in the Table 1.

Table 1: Definition of the various groups.

Group	Platelet count at admission
(Non thrombocytopenia) NTHR	≥150,000/µL
(Thrombocytopenia) THR	<150,000/µL
(Mild to moderate thrombocytopenia)	<150,000/µL, ≥50,000/µL
(severe thrombocytopenia) STHR	<50,000/µL

All cases in group B (STHR) investigations such as prothrombin time (PT), activated thromboplastin time (aPTT) were done as mentioned below. 1.8 ml of venous blood was collected in a bottle containing 0.2 ml of 3.8% sodium citrate so that a ratio blood and citrate is 9:1. In the present study PT, aPTT were obtained by automated coagulation analyzer ERBA COAG UNO, using Dade actin cephaloplastin for aPTT and Thromborel S, brain thromboplastin reagent marketed by Dade Behring with the ISI value of 1.15 for PT. (Normal PT: 14-22 sec., Normal aPTT: 30-55 sec).

Platelet counts were repeated 24 hours after medical intervention in all cases in Group A (THR). Other investigations such as urine sediment examination for candiduria, chest Xray, neurosonogram and CT (Computed tomography) brain were performed whenever the need arised.

However for 2 cases, in whom Neonatal alloimmune thrombocytopenia was strongly suspected, platelet genotyping was done. On the day of discharge all the neonates underwent a detailed clinical examination. The neonates were classified at discharge based on their immediate outcome as below.

Satisfactory

If the patient fulfills all the criteria laid down below the outcome was considered to be satisfactory.

- All acute problems should have become passive
- Baby should be accepting breast feed or spoon feeds
- Adequate weight gain for 3 consecutive days.
- At discharge baby weight should be more than or equal to 1.5kg.
- There is no associated morbidity such as hypoxic ischemic encephalopathy, persistent seizures, intra cranial bleed etc.

Not satisfactory

If the patient does not fulfill even one of the above mentioned criteria

Table 2: Definition of the various neurodevelopmental outcomes.

Outcome	Denver II	Weight and/or head circumference
Good (g)	Normal(N)	≥ 3rd centile
Fair (f)	Normal	≥ 3rd centile
Poor (p)	Suspect(S)/expired	< or > or =3rd centile(irrespective of their growth)

Expired - self explanatory

All neonates were followed up at least once in two weeks for a period of 6 months. In each visit a detailed physical examination was done. Weight and head circumference were measured. Growth parameter at a point of time lying below the 3rd percentile was considered to be abnormal. Neurodevelopment was assessed using the Denver II scale as shown in (Table 2).

Normal

No delays and a maximum of one caution in the various test items

Suspect

2 or more precautions and/or 1 or more delays.

In all the neonates their final performance at the sixth month of follow up documented and this performance was used to assess the overall outcome of the infant.

Statistical analysis

Descriptive data are presented as number or percentages. Comparison of the groups for categorical variables was done by Chi-square test. Continuous variables were analyzed using unpaired two tailed student t test or by one way analysis of variance (ANOVA). A p value below 0.05 was considered significant.

Chi-square test

$\chi^2 = \sum (O-E)^2/E$ O is observed
E is expected

One way ANOVA (analysis of variance)

F = between group variance/ within group variance

Variance = SD^2 SD is standard deviation

Student t test

t = Difference in means/ standard error of difference

SE = SD/√n SE is Standard error, SD is Standard deviation

The independent variables were those that showed significant association in the univariate analysis and those that are known to be influence the outcome of NICU graduates These factors were subsequently subjected to a stepwise logistic regression analysis using SPSS version 13.0, to evaluate the independent factors associated with outcome. The dependent variable was the outcome which was classified into good (0), fair (1) and expired or poor neurodevelopment irrespective of the physical growth (2). A p value below 0.05 was considered significant.

RESULTS

A total of 125 consecutive neonatal admissions were included in our study as per the inclusion and exclusion criteria laid down. The subjects were divided into four groups based on their platelet counts, as has already been mentioned in (Table 3).

Table 3: Subject distribution in the various groups.

Groups	Description	No. of subjects	Percentage of the total
Group A	No Thrombocytopenia (≥150,000/μL)	83	66.4%
Group B	Thrombocytopenia (<150,000/μL)	42	33.6%
Group B1	Mild to moderate thrombocytopenia (<150,000/μL&≥ 50,000/μL)	31	22%
Group B2	Severe Thrombocytopenia (<50,000/μL)	11	11.2%

Prevalence of thrombocytopenia in our NICU

The prevalence of thrombocytopenia on the whole was 28%. Severe thrombocytopenia, accounted for 11% of all the neonatal thrombocytopenia. The mean platelet count for all the groups was 1.624 with a standard deviation-of ±- 0.72 as shown in (Table 4).

Table 4: Mean platelet count in each of the groups.

	Group A	Group B1	Group B2
Mean platelet count	2.04	1.15	0.37
Standard deviation	0.47	0.27	0.096

Etiologic profile

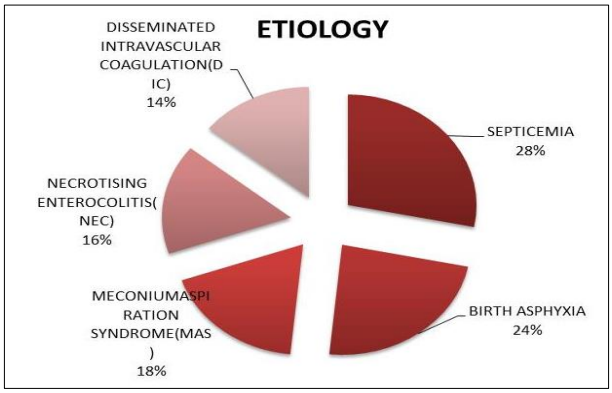

Figure 1: Etiology.

Septicemia and thrombocytopenia

Septicemia, as proven by blood culture, was significantly associated with thrombocytopenia. While the prevalence of septicemia was 60% in the severely thrombocytopenia group, Platelet counts in septicemia and nonsepticemic

neonates were also compared, by student t test, and the association was highly significant as shown in (Table 5).

Birth asphyxia and thrombocytopenia

There was statistical correlation between the diagnosis of birth asphyxia and thrombocytopenia as shown in (Table 6).

Meconium Aspiration Syndrome (MAS) and thrombocytopenia

There was significant association between thrombocytopenia and MAS as shown in (Table 7). Relation of NEC with low platelet count as shown in (Table 8).

Table 5: Septicemia and thrombocytopenia.

Septicimia	Group A (Non-thrombo)	% within group	Group B1 (Non-thrombo)	% within group	Group B2 (Non-thrombo)	% within group
No	54	65.06	24	77.41	08	72.72
Yes	29	34.93	07	22.50	03	27.27

Table 6: Birth asphyxia and thrombocytopenia.

Birth asphyxia	Group A	% with group	Group B1	% with group	Group B2	% with group
Yes	20	30.20	15	25.0	10	23.40
No	35	86.80	25	75.00	20	68.00

Table 7: Meconium Aspiration Syndrome (MAS) and thrombocytopenia.

MAS	Group A	% with group	Group B1	% with group	Group B2	% with group
Yes	15	7.05	10	6.05	08	5.0
No	45	33.25	25	27.05	22	21.60

Table 8: NEC with thrombocytopenia.

	Group A	% within group	Group B1	% within group	Group B 2	% within group
NEC	21	7.05	16	5.0	11	4.05
No NEC	33	40.45	26	29.15	18	83.90

Table 9: DIC and thrombocytopenia.

DIC	Group A	% with group	Group B1	% with group	Group B2	% with group
Yes	24	7.01	19	5.0	13	2.19
No	31	35.25	23	28.40	15	22.15

Table 10: Mucosal bleeding.

	Group A (Non-thrombo)	% within group	Group B1 (Non-thrombo)	% within group	Group B2 (Non-thrombo)	% within group
Mucosal bleed	24	28.91	06	19.35	08	72.72
No Mucosal bleed	59	71.08	25	80.06	03	27.27

Clinical impact of thrombocytopenia

Mucosal bleeding was significantly associated with thrombocytopenia. The prevalence of bleeding was 65.95% in the severely thrombocytopenia group.

Hence, showing that severely thrombocytopenia neonates bled more frequently. The 'p' value for this association was 0.002 as derived by Chi square test and it was significant as shown in (Table 10).

Platelet count and bleeding

To objectively assess the statistical relationship between platelet count and bleeding in neonates, student T test was used. The results are depicted in the table below. It

was found that there is a statistically significant association between platelet count and bleeding in the neonates in our study as shown in (Table 11).

Table 11: Platelet count and bleeding.

Status	Mean platelet count (*10*/µL)	Number of neonates	
No Bleed	1.70	87	T=3.72
Bleed	1.16	38	P=0.001

Mortality analysis in various groups due to low platelet count as shown in (Table 12).

Immediate outcome

While the proportion of mortality was high in the severely thrombocytopenia group. The proportion of babies with a not satisfactory immediate outcome was higher in the mild to moderate thrombocytopenia group and no thrombocytopenia group as shown in (Table 13).

Table 12: Mortality analysis in various groups.

Mortality	Septicemia	MAS	RDS	NEC	DIC	Prematurity	Total
Group A	4	3	1	0	0	7	15
Group B1	1	1	1	0	0	2	5
Group B2	8	2	4	2	1	2	19
Mortality	10.4	4.8	4.8	1.6	0.8	8.8	39

Table 13: Immediate outcome.

Immediate outcome	Group A(Non-thrombo)	% with group	Group B1 (moderate)	% with group	Group B2 (severe)	% with group
Expired	15	18.07	11	35.04	05	45.45
Non satisfactory	07	5.6	05	36.12	04	36.36
Satisfactory	61	73.49	15	48.38	02	18.18

Table 14: Outcome analysis in the study groups.

Group	Mortality	Lost for follow up	Regularly follow up
B1 moderate	3 (9.67%)	8	82
Severe	5 (45.4%)	10	20

Outcome at 3 months after discharge

Out of the 125 cases there were 20 mortalities, 18 of them were lost for follow up. Those 18 cases that were lost for follow up were excluded while assessing the outcome in the different groups.

The outcome was classified as good, fair, poor and expired, based on the physical growth and neurodevelopment as shown in (Table 14).

Neurodevelopment

Among the cases followed up, the proportion of cases with poor neurodevelopmental outcome (i.e. suspect outcome in Denver II) was higher in group B2, i.e. severely thrombocytopenic group, in relation to the other group.

Response to the treatment protocol

The efficacy of the treatment protocol practiced in our NICU was assessed based on the percentage increase in platelet count, 24 hours after blood or platelet transfusion.

Percentage increment in platelet count

Comparison of the percentage increase (increment in platelet count/ original platelet count* 100) in platelet count after blood and platelet transfusion group, given as a part of the management of severe thrombocytopenia, was done using student paired t test and there was no significant difference.

The percent increment in platelet count after 24 hours of blood transfusion, platelet transfusion and exchange transfusion is illustrated in (Table 15).

Table 15: Increment in platelet count.

Increment	Platelet transfusion (PRP / FFP)	Blood transfusion (Whole blood)
Mean increase %	92.6%	

DISCUSSION

Neonatal thrombocytopenia remains a common clinical problem. The etiology and predisposing factors are many and they interact in a complex manner to produce neonatal thrombocytopenia.[3,4]

Prevalence

The prevalence of thrombocytopenia in our study was 28%. Beiner et al estimated the prevalence of thrombocytopenia, only among preterm neonates, while it was lower in the other studies.[5-7] For e.g. analysis done by Castle et al, septicemia was just 7.5%. This higher prevalence of septicemia probably leads to a higher prevalence of neonatal thrombocytopenia in our admissions.[8,9]

The proportion of severe thrombocytopenia among the neonatal thrombocytopenia, 11.2% in our study, is also on the higher side. Septicemia is reported to result in severe thrombocytopenia rather than its milder form in various studies as shown in (Table 16).

Table 16: Prevalence of thrombocytopenia in various studies.

Studies on neonatal thrombocytopenia in NICUs	Prevalence of thrombocytopenia
Castle et al	22%
Hale Oren et al	5.4%
Beiner et al[2]	31%
Our study	28%

The mean platelet count among our NICU admissions was 1.603*105/µl. This is once again on the lower side compared to other studies. This might just be a reflection of the higher prevalence of severe thrombocytopenia in our NICU. Septicemia was strongly associated with thrombocytopenia, especially the severe variety (p=0.008), 28% of neonates in the severe thrombocytopenia group were observed. This finding is in agreement with other studies where septicemia has been recognized to be one of the risk factors for thrombocytopenia in neonates admitted to NICU. In western studies only 10% of septicemia with severe thrombocytopenia had lab evidence of DIC whereas in our study it was 27%.[10,11] As been shown in various other studies DIC was strongly associated with severe thrombocytopenia (p<0.001). Severe thrombocytopenia cases had evidence of DIC.[12] In our study there was significant association between perinatal asphyxia and thrombocytopenia. NEC, as diagnosed by Bell's criteria, was significantly associated with thrombocytopenia (p<0.001). Neonates in our study with radiological evidence of NEC had neonatal thrombocytopenia.

Mucosal bleeding was significantly associated with thrombocytopenia (p=0.002). While 72% of the neonates with thrombocytopenia had mucosal bleeding. The types of bleeding included G.I bleed, bleed from the E.T tube (pulmonary hemorrhage) and bleeding from the oral cavity. Investigations to rule out IC bleed, neurosonogram and CT brain, where done only in 28 cases of the 125. Among these cases the majority had severe thrombocytopenia.

Among severe thrombocytopenia cases 11 underwent neurodiagnostic work up, 7 turned out to have IC bleed. Hence there was as a strong correlation between IC bleed and severe thrombocytopenia (p<0.01). In our study neurodiagnostic tests were done only in the event of a suspicion of an intracranial pathology. The incidence of petechiae and purpura was significantly associated with severe thrombocytopenia (p<0.001) with 72% of these neonates having them. This association has been well reported and documented in the past. The most common symptom other than bleeding was "not feeding well". Hence this finding is of not much clinical significance. The most common sign other than bleeding in severe thrombocytopenia group was delayed capillary refill (>3 sec.).

Course in the hospital

It was assessed based on the duration of stay and the time spent by the neonate on intravenous fluid therapy and supplemental oxygen. While 87.5% of the neonates with severe thrombocytopenia had to stay longer than a week they also spent more time on IV fluids and supplemental oxygen. Mortality rate was very high, among the neonates with severe thrombocytopenia. This association might be due to the higher degree of severity of the underlying illness or due to an increased susceptibility of the neonates to complications, in those with severe thrombocytopenia.

Short term outcome at 6 months

Proportion of poor neurodevelopmental outcome was significantly higher among the neonates with severe thrombocytopenia compared to the other two groups. But 36.36% of neonates with both severe thrombocytopenia and poor outcome did not have radiological evidence of IC bleed. So probably the underlying pathology, that produced a low platelet count, might have also affected the developing brain detrimentally.

It was found that the prevalence of thrombocytopenia was high (28%) and percentage of severe thrombocytopenia was 11%. Septicemia was the major etiology associated with both severe and mild to moderate thrombocytopenia. The predisposing factors associated with neonatal thrombocytopenia were maternal PIH, prematurity, birth asphyxia, septicemia, NEC, DIC & IUGR. Bleeding of any sort either mucosal, cutaneous or intracranial was significantly associated with severe thrombocytopenia. Delayed capillary refill was the most common sign other than bleeding that was associated with thrombocytopenia.

Mortality rate and poor neurodevelopmental outcome were far more common in the severe thrombocytopenia group. Moreover low platelet count was found to be an independent risk factor for a poor outcome in our NICU graduates.

Hence it can be concluded that thrombocytopenia is very much common in among our NICU admissions. Septicemia is its most important and most common cause. The most significant conclusion of our study was that severe thrombocytopenia can 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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Ethical approval: The study was approved by the Institutional Ethics Committee

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