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THE INCIDENCE AND RISK FACTORS OF NEONATAL THROMBOCYTOPENIA IN NEWBORNS ADMITTED TO NICU – AN INSTITUTIONAL ANALYSIS

Paediatrics

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ABSTRACT

Introduction: Neonatal thrombocytopenia is a common clinical entity in the NICU. The incidence among neonates admitted to the NICU is much higher than the overall incidence and widely varies depending on the underlying population studied.

Aims: To find out the incidence rate and the associated risk factors of neonatal thrombocytopenia in the new-borns admitted to the NICU.

Materials and Methods: All the in-born neonates that required NICU admission were included in the study. Samples for platelet analysis were sent on day 1 and day 3 of life as per NICU protocol. Beyond day 3 of life, in the presence of risk factors platelet counts were analysed once every 48 hours. If at any point, laboratory thrombocytopenia was encountered platelet counts were sent for analysis once every 24 hours. The data collected was tabulated and relevant statistical analysis was carried out.

Results: 47.27% of the neonates had thrombocytopenia. 86.5% thrombocytopenic neonates were pre-term babies and only 13.5% were term neonates. The thrombocytopenic neonates also had a significantly lower mean gestational age of 32.7 weeks compared to 35.1 weeks among the non-thrombocytopenic new-borns. The mean birth weight of thrombocytopenic babies was 1.7 kg compared to 2.5 kg in the non-thrombocytopenic neonates with a significant p value of <0.001. The occurrence of necrotizing enterocolitis was also significantly higher among the thrombocytopenic neonates. Among the maternal risk factors, pregnancy induced hypertension was present in 42.3% of thrombocytopenic neonates.

Conclusion: Neonatal thrombocytopenia is a common clinical entity whose incidence depends on the underlying population studied. The establishment of the incidence rate and the most commonly associated risk factors in the institute has helped us in early recognition of underlying risks and prompt initiation of appropriate treatment.

KEYWORDS

neonate, NICU, thrombocytopenia

INTRODUCTION

Thrombocytopenia in neonates is defined as a platelet count of less than 150×10^9/L. Though the overall incidence of neonatal thrombocytopenia is <1%, the incidence among neonates admitted to the neonatal intensive care unit (NICU) is much higher and is about 22-35%.[1]

In most cases, neonatal thrombocytopenia is secondary to an underlying cause. It is needless to stress the importance of a meticulous approach in order to establish the cause and direct our treatment correctly.

In spite of there being many studies to determine the risk factors for neonatal thrombocytopenia, many a times the cause remains unknown. Thrombocytopenia, if undetected, has many potential dangers, including, intra-cranial haemorrhage, gastrointestinal bleeds, respiratory tract haemorrhages, umbilical cord haemorrhage, and circumcisional haemorrhage, warranting early detection and treatment of not only thrombocytopenia, but also the underlying cause.

Thrombocytopenia may be broadly classified on basis of aetiology into congenital and acquired. The acquired causes may be immune or non-immune.[2]

Our study aims to specifically deal with the acquired, non-immune causes of thrombocytopenia in neonates. The primary aim of our study is to find the incidence of neonatal thrombocytopenia in NICU admissions at our hospital and to study maternal and neonatal risk factors along with the clinical course of neonatal thrombocytopenia during hospital stay. The secondary aims are to produce current data on outcome (mortality and morbidity) of thrombocytopenic neonates in our hospital, to evaluate the role of neonatal thrombocytopenia as a prognostic indicator in NICU graduates and to objectively judge the efficacy of treatment protocol practiced in our NICU.

MATERIAL AND METHODS

The study was a hospital based prospective observational study conducted in the NICU of Durgabai Deshmukh Hospital and Research Institute, Hyderabad over a period of 12 months from June 2016 to May 2017. During the study period, all the in-born neonates who required NICU admission were included in the study. Extra-mural deliveries, neonates with birth injuries or congenital malformations and neonates with maternal history of anti-platelet or anti-coagulant medications were excluded from the study. Neonates that died or who were discharged before 72 hours of life were also excluded.

The antenatal records of the mothers were checked and relevant obstetric and medical history noted. Details of the mode of delivery and associated complications if any were also noted. In all neonates a thorough, clinical examination was done and anthropometric parameters charted. Samples for platelet analysis were sent on day 1 and day 3 of life as per our NICU protocol. Beyond day 3 of life, in the presence of risk factors platelet counts were analysed once every 48 hours. If at any point, laboratory thrombocytopenia was encountered platelet counts were sent for analysis once every 24 hours. All other relevant investigations were also sent depending on the clinical condition of the new born.

For platelet count estimation a blood sample of 1ml was collected in EDTA anticoagulated vacutainer and was sent for laboratory analysis. The platelet counts were estimated with an automated haematology analyser, Cellenium junior, manufactured by Trivitron with a software version of 1.3 for haematological analysis. Platelet counts and morphology were confirmed by peripheral smear examination.

All characteristics were summarized descriptively. For continuous variables, the summary statistics of N, mean, standard deviation (SD) were used. For categorical data, the number and percentage were used in the data summaries. Chi-square ($\chi2$)/ Freeman-Halton Fisher exact test was employed to determine the significance of differences between groups for categorical data. The difference of the means of analysis variables was tested by unpaired t test and ANOVA. If the p-value was < 0.05, then the results were considered to be significant. Data was analysed using SPSS software v.23.0.

RESULTS

Out of the NICU admissions 110 neonates that satisfied the inclusion criteria were studied. Out of them 52(47.27%) had thrombocytopenia. Among the thrombocytopenic neonates 11(21.2%) had mild, 19(36.5%) had moderate and 22(42.3%) had severe

thrombocytopenia. Twenty (38.5%) had thrombocytopenia that was early in onset and 32(61.5%) had thrombocytopenia that was late in onset (Table 1).

Table 1: Onset and severity of thrombocytopenia

Onset	Number(N)	Percentage
Early	20	38.5
Late	32	61.5
Total	52	100.0
Severity	**Number**	**Percent**
Mild	11	21.2%
Moderate	19	36.5%
Severe	22	42.3%
Total	52	100 %

Forty five of the 52(86.5%) thrombocytopenic neonates were pre-term babies and only 7(13.5%) were term neonates. Prematurity was significantly associated with an increased risk of thrombocytopenia with a p value of <0.001. These pre-term, thrombocytopenic neonates also had a significantly lower mean gestational age of 32.7weeks (with a p value of < 0.001) compared to 35.1 weeks among the pre-term, non-thrombocytopenic new-borns.The mean birth weight of thrombocytopenic babies was 1.7kg compared to 2.5kg in the non-thrombocytopenic neonates with a significant p value of <0.001 (Table 2).

Table 2: Comparison of foetal characteristics

Variables		Thrombocytopenic (N=52)		Non- thrombocytopenic (N=58)		Total		p value
		N	Percent	N	Percent	N	Percent	
Term/ Preterm	Term	7	13.5	29	50.0	36	32.7	<0.001*
	Preterm	45	86.5	29	50.0	74	67.3	
Mean preterm Gestational age (weeks)		**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	<0.001**
		32.7	2.3	35.1	1.2	33.6	2.2	
Mean birth Weight (kg)		**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	
		1.7	0.6	2.5	0.7	2.1	0.7	<0.001**

The number of SGA babies in the thrombocytopenic group was 20(38.5%) and the non-thrombocytopenic group was 14(24.1%). However, this difference was not significant with a p value of 0.105.

Culture positive sepsis was present in 31 of the 52(59.61%) thrombocytopenic neonates compared to only 2 of the 58(3.4%) non-thrombocytopenic neonates. Prevalence of culture positive sepsis was significantly higher among the thrombocytopenic group with a p value of < 0.001. Among the various organisms isolated, the prevalence of Klebsiella pneumoniae sepsis was the highest and was significantly high in thrombocytopenic neonates with a p value <0.001. The occurrence of necrotizing enterocolitis was also significantly higher among the thrombocytopenic neonates with a p value of 0.047.

Among the maternal risk factors, pregnancy induced hypertension was present in 22(42.3%) of thrombocytopenic neonates compared to 19(32.8%) in non- thrombocytopenic group, although this difference was not significant.

Table 3: Complications and mortality among thrombocytopenic neonates

Variables		Thrombocytopenic patients (N=52)		Non-thrombocytopenic patients (N=58)		Total		p value
		N	Percent	N	Percent	N	Percent	
PETECHIAE		2	3.8	0	0.0	2	1.8	0.132
ICB	IVH 1	1	1.9	0	0.0	1	0.9	0.221
	IVH2	1	1.9	0	0.0	1	0.9	
PULMONARY		3	5.8	0	0.0	3	2.7	0.102
GI		13	25.0	2	3.4	15	13.6	0.001**

The incidence of bleeding manifestations was high and occurred in 20(38.4%) of thrombocytopenic neonates. GI bleed was noted to be the most common bleeding manifestation and was observed to be significantly higher among thrombocytopenic neonates with a p value of 0.001.

The mortality rate was 7.7% among the thrombocytopenic new-borns compared to none in the non-thrombocytopenic neonates which was significant with a p value of 0.047 (Table 3).

Twenty-two (42.3%) of the thrombocytopenic neonates required single donor platelets making the transfusion rate significantly higher among the thrombocytopenic neonates with a p-value of <0.001.

DISCUSSION

The focus of our study was to obtain the incidence rate of thrombocytopenia in our NICU set up and also to find the prevalence rate of the acquired, non-immune causes of thrombocytopenia associated with our study population.

In our study, we observed a high incidence of thrombocytopenia similar to other Indian studies like that of Gupta et al.[3] and Nandyal et al.[4] A higher incidence of severe thrombocytopenia and late onset thrombocytopenia was consistent with that of Nandyal et al.[4]

Our study findings were correlating closely with that of Khalessi et al.[5] where in preterm neonates constituted a high percent of the thrombocytopenic population. Rameshbabu et al.[6] also noted a higher number of pre-terms compared to terms among the thrombocytopenic population. The mean gestational age among preterm neonates with thrombocytopenia was significantly low in our study, suggesting that the incidence of thrombocytopenia is inversely related to the gestational age and this was consistent with the results of Khalessi et.al.[5]

The results of our study can be closely compared with Baer et al.[7] who also observed that the mean birth weight in the thrombocytopenic neonates was significantly lower.

The results of our study were consistent with that of Bolat et al.[8] and Ververidis et al.[9] suggesting necrotizing enterocolitis to be an important risk factor for neonatal thrombocytopenia.

In our study culture positive sepsis was noted to be the most common risk factor of neonatal thrombocytopenia. Similar findings were observed in studies conducted by Gupta et al.[3], Patil et al.[10], Tirupathi et al.[11] and Amutha et al.[12] The prevalence of bleeding manifestations in our study were closest to that of Rameshbabu et al.[6] the most common site of bleeding being GI bleed.

Our study was similar to that of the Bolat et al.[8] and Bonifacio et al.[13] with respect to the fact that the transfusion rates were significantly high among the severely thrombocytopenic neonates.

The overall mortality rates in our study are similar to that of Rameshbabu et al.[6], Selvan et al.[14], Bolat et al.[8] with significantly higher mortality among the thrombocytopenic neonates.

CONCLUSION

To conclude, incidence of thrombocytopenia varies depending on the underlying population studied. Thrombocytopenia in a neonate is most often associated with an underlying illness. Early identification and treatment of the underlying cause is essential for the management of thrombocytopenia.

Our study paves way for many future research considerations. Though neonatal thrombocytopenia has been a subject of interest for many years, the immune causes need to be studied more in detail especially in resource poor NICU settings. Platelet transfusion has been the mainstay of treatment of thrombocytopenia for many years. Further research is required to establish newer treatment options like the use of rTPO and in vitro stem cell derived platelets.

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