OUTCOME OF NEONATAL THROMBOCYTOPENIA AND ASSOCIATED NEONATAL FACTORS IN PRE-TERM NEONATES ADMITTED IN NICU OF A TERTIARY CARE HOSPITAL IN JAIPUR: A PROSPECTIVE OBSERVATIONAL STUDY

Raghav Kumar[1*], Devanshi Rathore[2], Ayushi Gupta[3], Bharat Kumar[4]

Article History: Received: 21.03.2023 **Revised:** 30.06.2023 **Accepted:** 03.07.2023

Abstract

Introduction: Thrombocytopenia is one of the commonest haematological problems in NICU. This study was planned to find the immediate outcome of neonatal thrombocytopenia and associated neonatal factors of thrombocytopenia in preterm neonates admitted in N.I.C.U.
Methodology: We conducted this study to find the immediate outcome of neonatal thrombocytopenia and associated neonatal factors of thrombocytopenia in preterm neonates admitted in N.I.C.U., Department of Pediatrics R.D.B.P Jaipuria Hospital Jaipur over a period of 12 months. Their details were furnished in a predefined study Proforma by reviewing clinical records, examinations and laboratory investigations.
Results: Out of 274 study participants, 108 were having thrombocytopenia. Out of 108, 19.44 % died. Mortality was significantly higher in thrombocytopenia group ($p<0.001$). Mortality was significantly associated with severity of disease. ($p<0.001$) Duration of hospital stay was significantly higher in thrombocytopenia group (11.01±5.376 days) ($p<0.001$). Birth asphyxia, Sepsis, Necrotising enterocolitis and DIC was significantly higher in thrombocytopenia group as compared to without thrombocytopenia group. Neonatal jaundice was significantly higher in no thrombocytopenia group (24.09%). ($p=0.035$). Foetal distress was more in no thrombocytopenia (3.61%) as compared to thrombocytopenia group (2.78%) but this difference was not found statistically significant ($p=0.974$). Birth asphyxia ($p=0.004$), Sepsis ($p=0.003$), Necrotising enterocolitis ($p<0.001$), DIC ($p<0.001$) and Foetal distress ($p=0.006$) was significantly associated with severity of thrombocytopenia.
Conclusion: Screening of neonates with risk factors of neonatal thrombocytopenia for platelets count is beneficial in the early diagnosis and management of thrombocytopenia.

Keywords: neonates, risk factors, thrombocytopenia

[1*]Senior Resident, Department of Pediatrics, Autonomous State Medical College, Firozabad, Uttar Pradesh, India
[2]Senior Resident, Department of Pediatrics, ESIC Medical College, Alwar, Rajasthan, India
[3]Junior Resident, Department of Pediatrics, Uttar Pradesh University of Medical Sciences, Saifai, Uttar Pradesh, India
[4]Junior Resident, Department of Pediatrics, Uttar Pradesh University of Medical Sciences, Saifai, Uttar Pradesh, India

***Corresponding author:**
[1*]Raghav Kumar, Senior Resident, Department of Pediatrics, Autonomous State Medical College, Firozabad, Uttar Pradesh, India

DOI: 10.31838/ecb/2023.12.s3.582

1. Introduction

Thrombocytopenia (platelet count <1.5 lakhs/µl) is one of the commonest haematological problems in NICU. The chances of developing thrombocytopenia rise with a degree of prematurity.[1] The prevalence varies with range of 18-35% in premature neonates in NICU while prevalence is 2% in full-term neonates.[2,3] The important causes of thrombocytopenia in neonates are sepsis, birth asphyxia, prematurity, intra-uterine growth retardation, hyperbilirubinemia, respiratory distress syndrome, meconium aspiration syndrome and low birth weight. Apart from platelet count, bleeding manifestations depend on underlying ailments.[4] Mild thrombocytopenia often spontaneously resolves within the first weeks of life without clinical intervention.[2] Sometimes in case of severe thrombocytopenia, it can cause mortality & morbidity due to severe complication like IVH.[5]

Several approaches to prevention and treatment of the principal conditions that precipitate severe thrombocytopenia are currently under investigation in preterm infants. At a more basic level, however, there remains a need for trials in this area. Because of severe morbidity and mortality associated with thrombocytopenia in a preterm neonate identification of risk factors are important early in the course of treatment so that preventive measures can be initiated early. The paucity of studies from India and the increasing prevalence of this condition and being identifiable as directly causing most mortality and morbidity indicates need for further studies. So, we conducted this study to find the immediate outcome of neonatal thrombocytopenia and association of thrombocytopenia in preterm neonates with various neonatal conditions.

2. Methodology

This Prospective observational study was conducted in N.I.C.U, Department of Pediatrics R.D.B.P Jaipuria Hospital Jaipur over a period of 12 months (December 2018 to December 2019). The present study was conducted to determine the immediate outcome of neonatal thrombocytopenia and association of thrombocytopenia in preterm neonates admitted in N.I.C.U with various neonatal conditions. Further clinical course and assessment of factors predisposing to thrombocytopenia were also assessed. The study was conducted after receiving the clearance from IEC and informed consent from the guardian of the newborn admitted in N.I.C.U under study

All live preterm neonates admitted in our N.I.C.U considered eligible for the study according to selection criteria. Study population was divided into Thrombocytopenia group (Preterm babies with any one or more sample suggestive of thrombocytopenia) and No Thrombocytopenia group (Preterm babies with no sample suggestive of thrombocytopenia)

Inclusion Criteria

- All live preterm babies less than 37 weeks born in Hospital
- All preterm babies born outside and admitted in our NICU on day 1.
- All the preterm whom parents willing for participation

Exclusion Criteria:

- Gross congenital Malformations and birth injuries
- Maternal alcohol and abusive drug addiction
- Neonates whose parents or guardians did not agree to be a part of study.

After approval of ethical committee & institutional scientific committee, 274 patients were taken for the study as per the admission census of preterm babies in NICU during the entire study duration. After informing patients/guardians about the study, informed consent was taken.

Their details were furnished in a predefined study Proforma. For the study, maternal and neonatal record files and charts were analysed to obtain demographic, clinical and laboratory data. History of consumption of drugs by the mother that can predispose to neonatal thrombocytopenia were also be documented and these babies were excluded from the study. Apgar score was recorded for all babies. The gestational age (GA) was assessed from maternal dates and confirmed by clinical examination as described by Ballard (New Ballard Score)[6] Information regarding the clinical data of neonates e.g development of clinical signs of birth asphyxia, sepsis, NEC was noted prospectively from neonatal record files during NICU stay. Every neonate had a detailed physical examination to rule out any gross congenital anomaly. Any evidence of cutaneous bleed or mucosal bleed during stay in NICU was also be noted.

Platelet count was done in all the babies on every alternate day till day 5 of life and further as per need. Platelet count before discharge was also be recorded in cases where it was required. In cases where thrombocytopenia was documented, peripheral smear was used to collaborate the finding. All neonates underwent necessary blood investigations as per NICU protocol whenever needed as Complete blood count, C-Reactive Protein, Blood culture, Coagulation study, Peripheral smear. A septic work up to confirm sepsis inclusive of total WBC count, C reactive protein, was done in patients showing signs of clinical sepsis. The next step was to group the neonates, based on their platelet counts. Neonatal thrombocytopenia can be classified as Mild (Platelet count 1,50,000/ µL to 1,00,000/ µL), Moderate (Platelet count 1,00,000/ µL - 50,000/ µL), and Severe (Platelet count: <50,000/ µL).[2] Some of the cases of group Severe thrombocytopenia required investigations such as prothrombin time (PT), activated thromboplastin time and assay for fibrin degradation products (FDP). Treatment including platelet transfusions was done as per the standard NICU protocol as per the recent recommendations in the medical literature.

Statistical analysis was performed by the SPSS program for Windows, version 17.0 (SPSS, Chicago, Illinois). Continuous variables were presented as mean ± SD, and categorical variables are presented as absolute numbers and percentage. Unpaired t test for continuous data and chi-square test for categorical data was used to evaluate the significance of the differences in variables among group. For all statistical tests, a p value less than 0.05 was taken to indicate a significant difference.

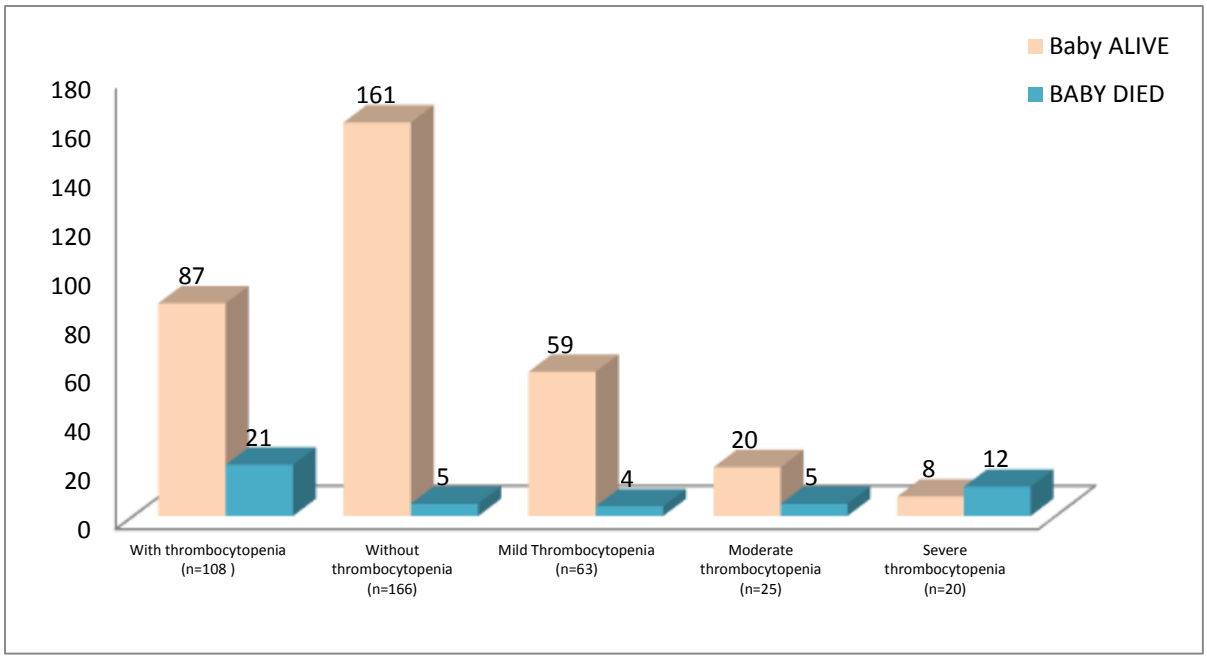
3. Results

Out of 274 study participants, 108 (39.42%) were having thrombocytopenia. Mortality was 19.44 % (21 cases) among 108 thrombocytopenia cases and 3.01% (5 cases) among 166 no thrombocytopenia cases. Mortality was significantly higher in thrombocytopenia group ($p<0.001$). Mortality was highest in severe thrombocytopenia (60%) followed by moderate thrombocytopenia (20%) and minimum in mild thrombocytopenia cases (6.34%) and difference in distribution was found significantly different according to severity of disease. ($p<0.001$) [Table-1, Graph-1]

Table-1: Outcome according to severity of Thrombocytopenia

Outcome	**Baby Alive**		**Baby Died**		**P value**
	N	**%**	**n**	**%**	
With thrombocytopenia (n=108)	87	80.56	21	19.44	<0.001

Without thrombocytopenia (n=166)	161	96.99	5	3.01	
Mild Thrombocytopenia (n=63)	59	93.66	4	6.34	<0.001
Moderate thrombocytopenia (n=25)	20	80	5	20	
Severe thrombocytopenia (n=20)	8	40	12	60	



Graph-1: Outcome according to severity of Thrombocytopenia

Duration of hospital stay was significantly higher in thrombocytopenia group (11.01±5.376 days) as compared to no thrombocytopenia group (8.102±4.584 days) (p<0.001) [Graph-2]

Graph-2: Mean duration of hospital stay in both groups

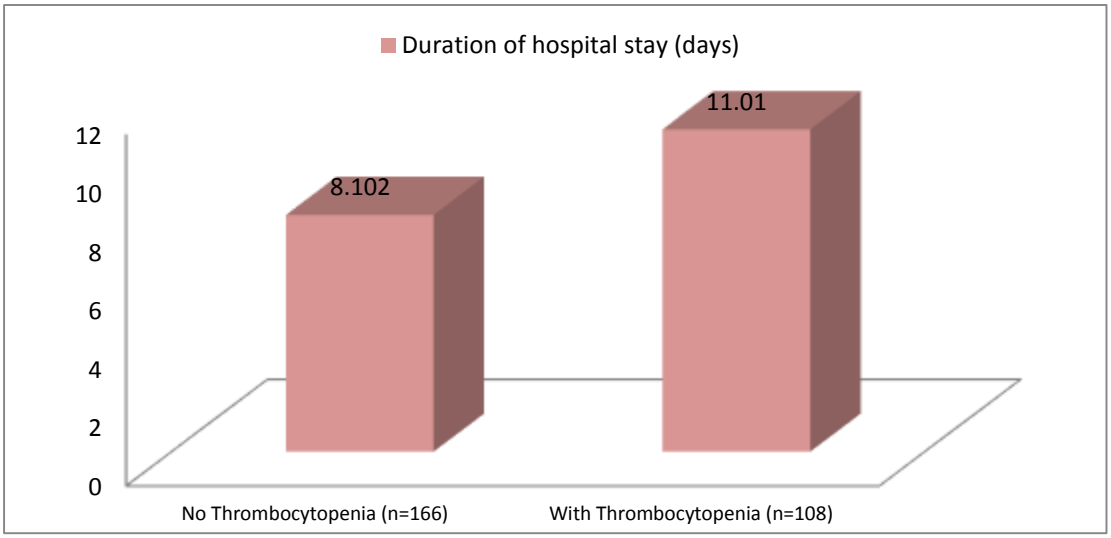


Table-3: Foetal complications in both groups

Foetal complication	No Thrombocytopenia (n=166)		Thrombocytopenia (n=108)		P value
	n	%	n	%	
Birth asphyxia	48	28.92	45	41.67	0.041
Sepsis	45	27.11	55	50.93	<0.001
Necrotising enterocolitis	0	0	18	16.67	<0.001
Neonatal Jaundice	40	24.09	14	12.96	0.035
DIC	0	0	10	9.26	<0.001
Foetal distress	6	3.61	3	2.78	0.974

Sepsis was the most common foetal complication (50.93%) among thrombocytopenic group followed by Birth asphyxia (41.67%), Necrotising enterocolitis (16.67%), Neonatal Jaundice (12.96%), DIC (9.26%) and least common was Foetal distress (2.78%). Birth asphyxia was significantly higher in thrombocytopenia group (41.67%) as compared to without thrombocytopenia group (28.92%) (p=0.041). Sepsis was significantly higher in thrombocytopenia group (50.93%) as compared to without thrombocytopenia group (27.11%) (p<0.001). Necrotising enterocolitis and DIC was also significantly higher in thrombocytopenia group (16.67% and 9.26% respectively) as compared to without thrombocytopenia group (0% and 0% respectively) (p<0.001 and <0.001 respectively). Neonatal jaundice was significantly higher in no thrombocytopenia group (24.09%) than with thrombocytopenia group (12.96%) (p=0.035). Foetal distress was more in no thrombocytopenia (3.61%) as compared to thrombocytopenia group (2.78%) but this difference was not found statistically significant (p=0.974). [Table-3, Graph-3]

Graph-3: Foetal complications in both groups

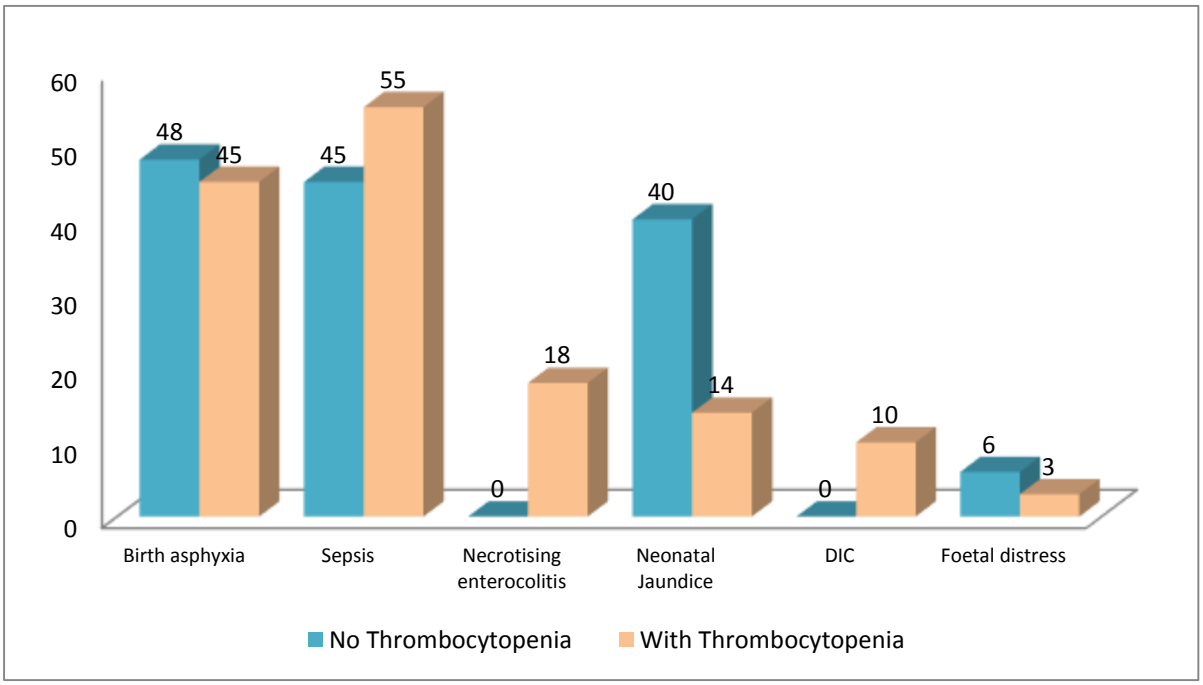
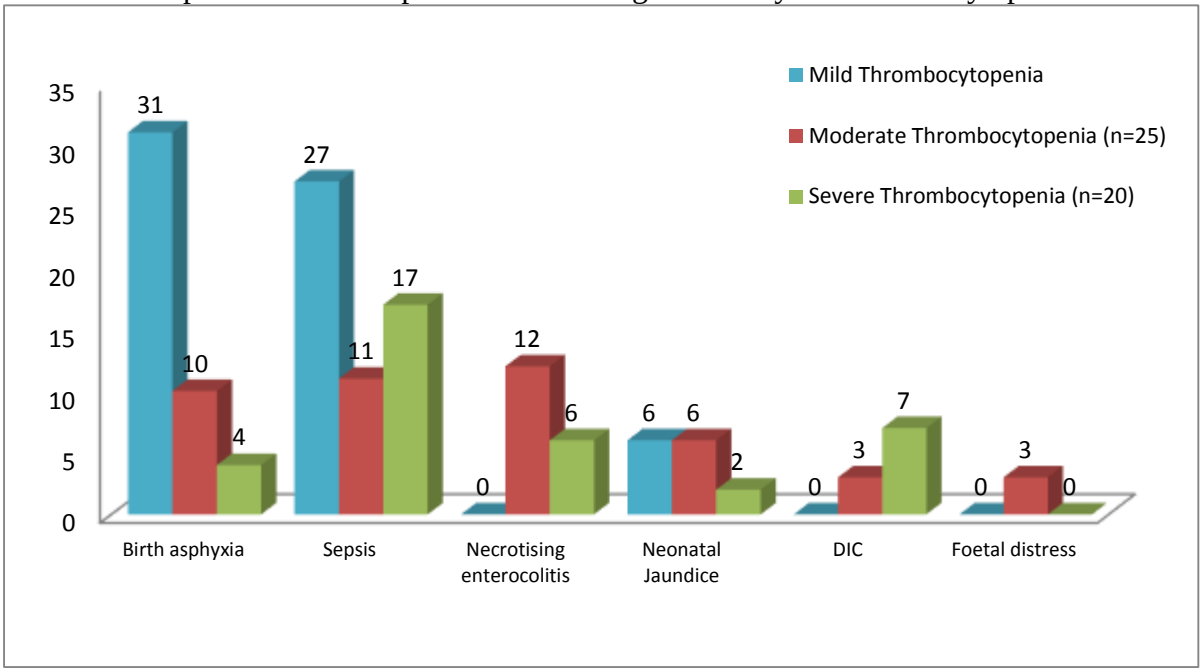


Table-4: Foetal complication according to severity of Thrombocytopenia

Foetal complication	Mild Thrombocytopenia (n=63)		Moderate Thrombocytopenia (n=25)		Severe Thrombocytopenia (n=20)		P value
	n	%	N	%	N	%	
Birth asphyxia	31	49.21	10	40	4	20	0.004
Sepsis	27	42.86	11	44	17	85	0.003
Necrotising enterocolitis	0	0	12	48	6	30	<0.001
Neonatal Jaundice	6	9.52	6	24	2	10	0.172
DIC	0	0	3	12	7	35	<0.001
Foetal distress	0	0	3	12	0	0	0.006

Birth asphyxia was among 49.21% in mild thrombocytopenia, 40% in moderate thrombocytopenia and 20% in severe thrombocytopenia and this was significantly associated with severity of thrombocytopenia (p=0.004). Sepsis was highest in severe thrombocytopenia (85%) followed by moderate thrombocytopenia (44%) and mild thrombocytopenia (42.86%). Sepsis was significantly associated with severity of thrombocytopenia (p=0.003). Necrotising enterocolitis was maximum in moderate thrombocytopenia (48%) followed by severe thrombocytopenia (30%) and no case of Necrotising enterocolitis in mild thrombocytopenia. Necrotising enterocolitis was significantly associated with severity of thrombocytopenia (p<0.001). Neonatal jaundice was highest in moderate thrombocytopenia (24%) followed by severe (10%) and mild thrombocytopenia (9.52%) and this was not significantly associated with severity of thrombocytopenia (p=0.172). DIC was 35% in severe thrombocytopenia and 12% in moderate thrombocytopenia and no case in mild thrombocytopenia and this was significantly associated with severity of thrombocytopenia (p<0.001). Foetal distress was significantly higher in moderate thrombocytopenia group (12%) (p=0.006) [Table-4, Graph-4]

Graph-4: Foetal complication according to severity of Thrombocytopenia



4. Discussion

This study was conducted to find the immediate outcome of neonatal thrombocytopenia and association of thrombocytopenia in preterm neonates with various neonatal conditions. Out of 108 thrombocytopenia participants in our study, 21 (19.44 %) died in our study. Mortality was highest in severe thrombocytopenia (60%) followed by moderate thrombocytopenia (20%) and minimum in mild thrombocytopenia (6.34%) and difference in distribution was found significantly different according to severity of disease (p<0.001). Madavi D and Subuhi S[7] revealed that out of 140 neonates the mortality was in 5 (3.7%) of which 3 babies were having severe thrombocytopenia. Bonifacio L et al[8] observed that the mortality rate was 16.7%, 32.4% and 45.8% in neonates with mild, moderate and severe thrombocytopenia, respectively. In study of Saini R et al[9] mortality was found more in newborn with thrombocytopenia (36.84%) than newborn without thrombocytopenia (20.86%). In study of Meena SL et al.[10] mortality was significantly high in severe thrombocytopenia group (47.37%) as compared to other groups and it was not statistically significant (p value 0.228).

Sepsis was significantly higher in thrombocytopenia group (50.93%) as compared to without thrombocytopenia group (27.11%) (p<0.001). This higher incidence is probably due to higher proportion of septicemic neonates in our NICU preterm admissions, while it was lower in the other studies, for e.g the incidence of septicaemia was just 7.5% in the study conducted by Castle V et al[11] and 5.4% in study of Oren H et al.[12] The role of neonatal factors among the etiological profile for preterm thrombocytopenia was similar to other NICU studies from India, with septicaemia, and perinatal asphyxia being the most common risk factor. Septicaemia accounted for most of the cases in both the severe and mild to moderate thrombocytopenia group.

Sepsis was highest in severe thrombocytopenia (85%) followed by moderate thrombocytopenia (44%) and mild thrombocytopenia (42.86%) in our study. Sepsis was significantly associated with severity of thrombocytopenia

(p=0.003). Out of 108, 63 (58.33%) were having mild thrombocytopenia, 25 (23.15%) were having moderate thrombocytopenia and 20 (18.52%) were having severe thrombocytopenia. Madavi D and Subuhi S[7] revealed that 74.5% cases of sepsis were found in thrombocytopenia group and 25.5% in no thrombocytopenia group and sepsis was significantly higher in thrombocytopenia group (p<0.05). Sepsis was 88% in mild, 66.03% in moderate and 76.47% in severe thrombocytopenia in study of Hanoudi BM[13] but this was not significantly associated with severity of thrombocytopenia. (p=0.003). Sepsis was significantly associated with severity of thrombocytopenia in study of Meena SL et al[10] (p<0.001)

Birth asphyxia was significantly higher in thrombocytopenia group (41.67%) as compared to without thrombocytopenia group (28.92%) (p=0.041). Madavi D and Subuhi S[7] in their study found similar results that that Birth asphyxia was significantly higher in thrombocytopenia group (61.53%) as compared to without thrombocytopenia group (39.47%) (p=0.2). Birth asphyxia was among 49.21% in mild, 40% in moderate and 20% in severe thrombocytopenia. Birth asphyxia was significantly associated with severity of thrombocytopenia. (p=0.004). Birth asphyxia was 12.5% in mild, 12.5% in moderate and 75% in severe thrombocytopenia in Sonam S et al's study.[14] Birth asphyxia was significantly associated with mild TCP (p=0.001) in study of Basil M et al.[13] Birth asphyxia was not significantly associated with severity of thrombocytopenia in study of Meena SL et al.[10] (p=0.43)

Necrotising enterocolitis (NEC) was significantly higher in thrombocytopenia group (16.67%) as compared to without thrombocytopenia group (0%) (p<0.001) in agreement to the study of Madavi D and Subuhi S[7] where NEC was significantly higher in thrombocytopenia group (100%) as compared to no thrombocytopenia (0) (p=0.001). Necrotising enterocolitis was maximum in moderate thrombocytopenia (48%) followed by severe thrombocytopenia (30%) and no case of Necrotising enterocolitis in mild thrombocytopenia. Distribution of Necrotising enterocolitis was significantly different according to severity of thrombocytopenia (p<0.001). NEC was 0% in mild, 3.77% in moderate and 5.88% in severe thrombocytopenia in study of Hanoudi BM [13] but this was not significantly associated with severity of thrombocytopenia (p=0.523) similar to the study of Meena SL et al[10] (p=0.361). Bonifacio L et al[8] found that 14 out of 90 cases and none out of controls had NEC.

DIC was among 9.26% in our study while 18.5% in study of Kumar AD et al.[14] Foetal distress was not significantly associated with thrombocytopenia in our study but Foetal distress was significantly associated with severity of thrombocytopenia in study of Bonifacio L et al[8] (p=0.01). Respiratory distress syndrome was 7.1% in mild, 21.4% in moderate and 71.4% in severe thrombocytopenia in study of Sonam S et al.[4] In study of Madavi D and Subuhi S,[7] Respiratory distress syndrome was 60% in thrombocytopenia group and 40% in no thrombocytopenia group and this difference was statistically not significant. (p=0.32). In this study, mortality was significantly associated with severity of thrombocytopenia.

5. Conclusion

Our study concluded that proportion of mortality was 19.44% among neonates with thrombocytopenia admitted to NICU and mortality was significantly associated with severity of thrombocytopenia. Among Neonatal factors, Sepsis, Birth asphyxia, Necrotising enterocolitis, Neonatal Jaundice and DIC were significantly associated with thrombocytopenia.

Thrombocytopenia is very common in preterm babies and should be actively looked for so that it can be managed appropriately. Platelet count should be regularly followed up in preterm babies with associated risk factors. Screening of neonates with risk factors of neonatal thrombocytopenia for platelets count is beneficial in the early diagnosis and management of thrombocytopenia.

6. References

[1] Sola MC, Del Vecchio A, Rimsza LM. Evaluation and treatment of thrombocytopenia in the neonatal intensive care unit. Clinics in perinatology. 2000;27(3):655-79.

[2] Roberts I, Murray NA. Neonatal thrombocytopenia: causes and management. Arch Dis Child Fetal Neonatal Ed 2003; 88 (5): F359-64.

[3] Resch E, Hinkas O, Urlesberger B, Resch B. Neonatal thrombocytopenia—causes and outcomes following platelet transfusions. Eur J Pediatr. 2018;177(7):1045-52.

[4] Nandyal SS, Shashikala P, Vidhushi Sahgal. Study of thrombocytopenia in neonatal intensive care unit. Ind J Pathology Oncol. 2016;3(1);55-9.

[5] Madhavi D, Subuhi S, Zubair M. Outcome of neonatal thrombocytopenia in tertiary care NICU. J Pediatr Neonatal Care. 2020;10(3):92–96.

[6] Ballard JL, Khoury JC, Wedig K et al. New Ballard Score, expanded to include extremely premature infants. J Pediatrics 1991; 119:417-423.

[7] Madavi D, Subuhi S. Prevalence and etiology of neonatal thrombocytopenia in tertiary care NICU. Paripex - Indian Journal F Research. 2019;8(9);38-40.

[8] Bonifacio L, Petrova A, Nanjundaswamy S, Mehta R. Neonatal Thrombocytopenia Related outcome in preterms. Indian J Pediatr. 2007; 74:269-76.

[9] Saini R, Saini P, Sehra RN, Saini L, Gehlot Y. Thrombocytopenia burden and its associating Risk factors: A cross-sectional study at a tertiary care set up. International Multispecialty Journal of Health.2017;3(7):237-43.

[10] Meena SL, Singh K, Jain S, Jain A, Karnawat BS. Clinical profile and outcome of neonatal thrombocytopenia in a tertiary care hospital. Int J Contemp Pediatr 2019;6:1344-8.

[11] Castle V, Andrew M ,Kelton J , Giron D , Johnston M , Carter C . Frequency and mechanism of neonatal thrombocytopenia . J Pediatr 1986; 108 : 749-56.

[12] Oren H, Irken G, Oren B, Olgun N, Ozkan H. Assesment of clinical impact and predisposing factors for neonatal thrombocytopenia. Indian J Pediatr. 1994;61(5):551-558.

[13] Hanoudi BM. Study of risk factors for neonatal thrombocytopenia in preterm infants. Mustansiriya Medical Journal. 2015;14(1): 64-69.

[14] Kumar AD, Karimulla S, Sailusha A. Study of clinical profile and outcome of neonates admitted to the NICU with thrombocytopenia and abnormal coagulation profile. International Journal of Contemporary Medical Research 2021;8(12):L1-L5.