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INCIDENCE OF THROMBOCYTOPENIA AND ASSOCIATED MATERNAL RISK FACTORS IN PRETERM NEONATES ADMITTED IN NICU IN A TERTIARY CARE HOSPITAL IN JAIPUR: A PROSPECTIVE OBSERVATIONAL STUDY

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Abstract

Introduction: Neonatal thrombocytopenia is common haematological abnormality and associated with severe morbidity and mortality in preterm neonates, so this study was conducted to find incidence of neonatal thrombocytopenia and associated maternal risk factors in preterm neonates admitted in N.I.C.U.

Methodology: This Prospective observational study was conducted among 274 preterm neonates admitted in N.I.C.U., Department of Pediatrics R.D.B.P Jaipuria Hospital Jaipur over a period of 12 months. Exclusion criteria were Gross Congenital Malformations and birth injuries, maternal alcohol and abusive drug addiction and Neonates whose parents or guardians did not agree to be a part of study. Maternal and neonatal record files and charts were analysed and various laboratory tests were conducted as per protocol to obtain demographic, clinical and laboratory data.

Results: Out of 274 study participants, 108 (39.42%) were having thrombocytopenia. Out of 108 cases, 58.33% were mild, 23.15% were moderate and 18.52% were having severe thrombocytopenia. Mean gestational age was 34.28±1.818 weeks in thrombocytopenia group. Mean total platelet count was 0.989±0.389 in thrombocytopenia group. There was

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significant difference in mean platelet count in mild (1.278±0.143), moderate (0.75±0.16) and severe thrombocytopenia group (0.376±0.065) (p<0.001). PIH and IUGR was significantly higher in thrombocytopenia group (p=0.012, 0.002). PROM was significantly higher in no thrombocytopenia group (15.06%) (p=0.049). GDM was more in thrombocytopenia group (12.04%) as compared to no thrombocytopenia group (7.83%) (p=0.342). PIH was maximum (40%) in moderate thrombocytopenia and minimum 11.11% in mild thrombocytopenia. PIH was significantly associated with severity of thrombocytopenia (p=0.009). GDM (p=0.085), IUGR (p=0.067) and PROM (p=0.919) was not found significantly associated with severity of thrombocytopenia.

Conclusion: Screening of neonates for risk factors of neonatal thrombocytopenia for platelets count is beneficial in the early diagnosis and management of thrombocytopenia.

Keywords: neonates, thrombocytopenia, platelet count

INTRODUCTION

Neonatal thrombocytopenia is common haematological abnormality[1]. It is defined as platelet count less than $150x10^9$ /L regardless gestational age.[2,] 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).[3] Of neonates admitted to neonatal intensive care units (NICUs), the platelet count drops below 150 $\times 10^9$/L in one in four babies and to below 50 × 10^9/L in one in twenty.[4] Overall incidence of thrombocytopenia in neonates is 0.7-2% in general population.[5] This is one of the common hematological problems in a neonatal intensive care unit particularly in premature and sick newborns. [3] Incidence in various studies varies from 22 to 42 per cent of the newborn admissions to NICU.[6,7]

The probable cause of this thrombocytopenia is the initial period of fetal hypoxia secondary to placental insufficiency. It affects the hematopoietic microenvironment which may lead to disruption of commitment of multipotent hematopoietic progenitors to megakaryopoiesis.[8] Broadly 3 primary mechanisms responsible leading to thrombocytopenia[9] are Decreased production of platelets, Increased destruction /consumption of platelets, Sequestration of platelets. Various associated maternal risk factors are maternal age, number of pregnancies, maternal autoimmune diseases, maternal drugs, as non-steroidal anti-inflammatory agents and heparin, pregnancy-induced

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hypertension (PIH), premature rupture of membrane (PROM), Gestational Diabetes Mellitus (GDM) and Intrauterine growth retardation (IUGR).[10]

There is wide variation in the incidence of platelet count between healthy infants and sick neonates in NICU and it is vital to understand the mechanism behind the incidence of neonatal thrombocytopenia. Because of severe morbidity and mortality associated with thrombocytopenia in a preterm neonate, identification of risk factors is 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 indicates need for further studies. So we conducted this study to find the incidence of neonatal thrombocytopenia and association of thrombocytopenia in preterm neonates with various maternal conditions.

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 (From December 2018 to December 2019) among all live preterm neonates admitted in our N.I.C.U considered eligible for the study according to selection criteria. The present study was conducted to determine the incidence and associated maternal factors of preterm thrombocytopenia neonates admitted in N.I.C.U after receiving the clearance from IEC and informed consent from the guardian of the newborn admitted in N.I.C.U under study.

INCLUSION CRITERIA

- All live preterm babies less than 37 weeks born in Govt. R.D.B.P Jaipuria 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.

With reference to previous studies, it was found that incidence of thrombocytopenia in preterm babies ranges between 22- 42%[6,7]. For the purpose of sample size calculation, it is assumed that (p) = 22%, with the precision error of estimation (L) = 5%, and at alpha = 0.05. Thus, a sample size of 274 preterm neonates was planned. Sample size calculation formula is

$n = 4pq/L2$

where: p = prevalence

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q = 1-p

L = allowable error

The details were furnished in a predefined study proforma. Maternal and neonatal record files and charts were analysed to obtain demographic, clinical and laboratory data. Conditions which were mainly focussed included gestational hypertension, intra uterine growth retardation, gestational diabetes mellitus and PROM. 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)[11]If IUGR was documented in pregnancy in fetal ultrasound, growth assessment at birth or admission to confirm intrauterine growth restriction. 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: Complete blood count (Total count, Differential count, Haemoglobin), C-Reactive Protein, Blood culture, Coagulation study and Peripheral smear. Severe thrombocytopenia required investigations such as prothrombin time (PT), activated thromboplastin time and assay for fibrin degradation products (FDP).

Neonatal thrombocytopenia cases (Platelet count <1,50,000/ µL) were 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).

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.

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Results:

Out of 274 study participants, 108 (39.42%) were having thrombocytopenia and 166 (50.58%) were not having thrombocytopenia. 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. [Graph-1]

Graph 1: Distribution of study population according to severity of thrombocytopenia

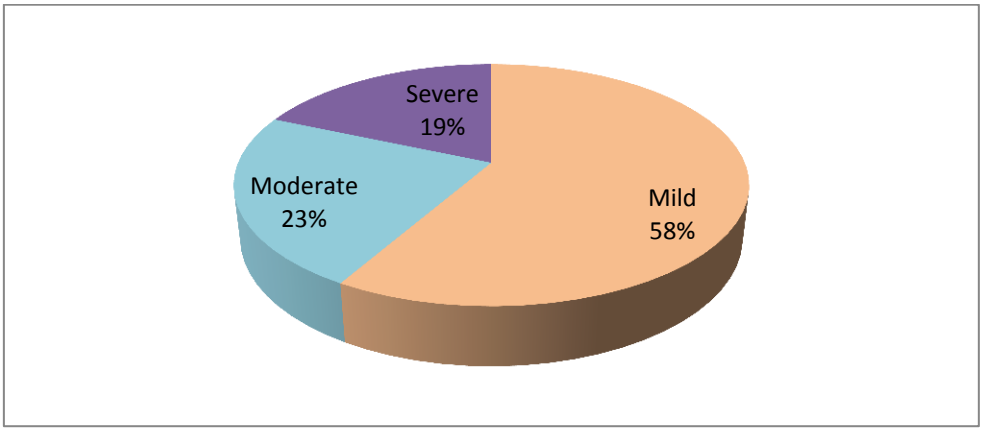

Table-2: Baseline characteristics of study population

Baseline characteristics	**No Thrombocytopenia**		**With Thrombocytopeni**		**P value**
	Mean	SD	Mean	SD	
Age (days)	30.56	35.07	34.96	49.08	0.388
Body weight (Kg)	1.794	0.429	1.716	0.449	0.148
Gestational age (weeks)	35.11	0.908	34.28	1.818	<0.001
Gender	N	%	N	%	
Female Child	81	48.79	40	37.04	0.073
Male Child	85	51.21	68	62.96	
Grand Total	166	100	108	100	

Mean age in no thrombocytopenia group was 30.56±35.07 days and in with thrombocytopenia group was 34.96±49.08 days. Mean body weigh in no thrombocytopenia group was 1.794±0.429 Kg and with thrombocytopenia group was 1.716±0.449 Kg. There was no statistical difference with respect to age and weight in both groups (p=0.388 and 0.148 respectively). Proportion of Male children was more than female in thrombocytopenia group (Male: 62.96%, Female: 37.04%) as well as without thrombocytopenia group (Male: 51.21%, Female: 48.79%). Distribution of participants according to gender was statistically similar in both groups (p=0.073). Mean gestational age was 35.11±0.908 weeks in no thrombocytopenia group and 34.28±1.818 weeks in

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thrombocytopenia group. Gestational age was significantly higher in no thrombocytopenia group as compared to thrombocytopenia group (p<0.001). [Table-1]

Table-2: Total platelet count according to severity of thrombocytopenia

TPC mean	**Total**	**Mean**	**Std. Deviation**	**P value**
Without thrombocytopenia	166	2.044	0.514	< 0.001
With thrombocytopenia	108	0.989	0.389	
Mild	63	1.278	0.143	< 0.001
Moderate	25	0.75	0.160	
Severe	20	0.376	0.065	

Mean total platelet count was significantly higher in no thrombocytopenia group (2.044±0.514) as compared to thrombocytopenia group (0.989±0.389) (p<0.001). There was significant difference in mean platelet count in mild (1.278±0.143), moderate (0.75±0.16) and severe thrombocytopenia group (0.376±0.065) (p<0.001). [Table-2]

Table-3: Maternal complication in both groups

Maternal complication	No Thrombocytopenia (n=166)		With Thrombocytopenia (n=108)		P value
	N	%	N	%	
GDM	13	7.83	13	12.04	0.342
PIH	15	9.04	22	20.37	0.012
IUGR	18	10.84	28	25.93	0.002
PROM	25	15.06	7	6.48	0.049

GDM was more in Thrombocytopenia group (12.04%) as compared to no thrombocytopenia group (7.83%) but this difference was not found significant (p=0.342). PIH was significantly higher in thrombocytopenia group (20.37%) as compared to no thrombocytopenia group (9.04%) (p=0.012). IUGR was also significantly higher in thrombocytopenia group (25.93%) as compared to no thrombocytopenia group (10.84%) (p=0.002). PROM was significantly higher in no thrombocytopenia group (15.06%) as compared to thrombocytopenia group (6.48%) (p=0.049). [Table-3, Graph-2]

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Graph-2: Maternal complication in both groups

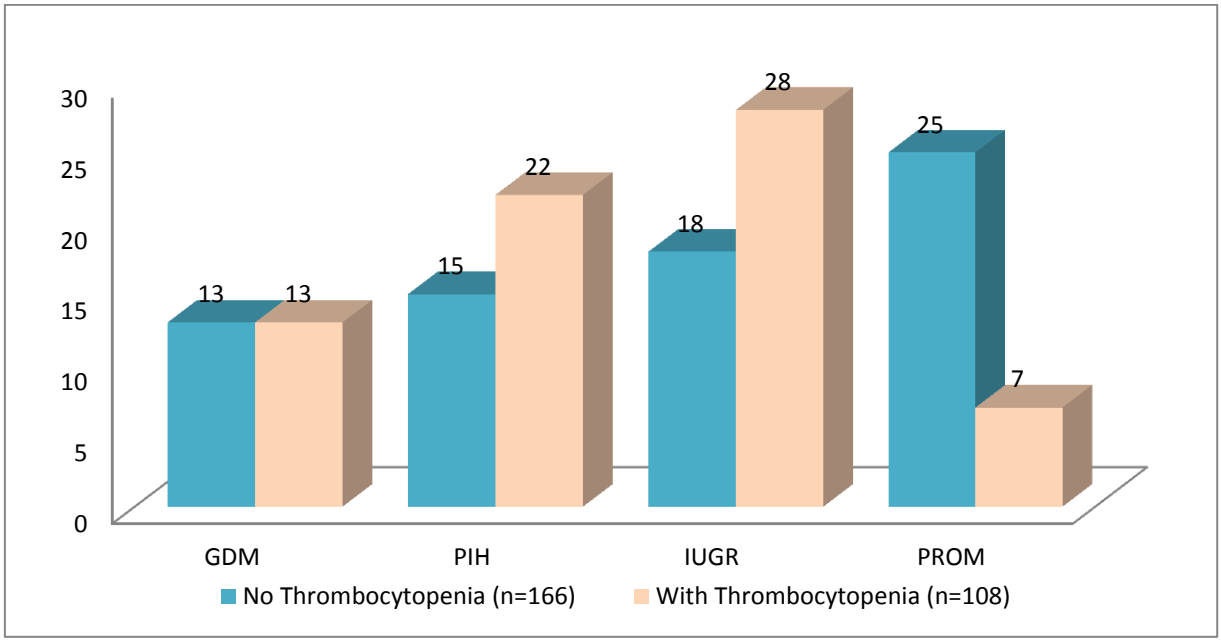

Table-4: Maternal complication according to severity of Thrombocytopenia

Maternal complication	Mild Thrombocytopenia (n=63)		Moderate Thrombocytopenia (n=25)		Severe Thrombocytopenia (n=20)		P value
	N	%	N	%	n	%	
GDM	9	14.29	0	0	4	20	0.085
PIH	7	11.11	10	40	5	25	0.009
IUGR	12	19.05	7	28	9	45	0.067
PROM	4	6.35	2	8	1	5	0.919

GDM was maximum in severe Thrombocytopenia (20%) followed by 14.29% in mild thrombocytopenia group and no case in moderate thrombocytopenia and GDM was not found significantly associated with severity of thrombocytopenia (p=0.085). PIH was maximum (40%) in moderate thrombocytopenia group followed by 25% in severe thrombocytopenia group and minimum 11.11% in mild thrombocytopenia group. PIH was significantly associated with severity of thrombocytopenia (p=0.009). IUGR was maximum (45%) in severe thrombocytopenia and 28% in moderate thrombocytopenia and 19.05% in mild thrombocytopenia. IUGR was not significantly associated with severity of thrombocytopenia (p=0.067). PROM was maximum in moderate thrombocytopenia (8%) followed by severe thrombocytopenia (5%) and mild thrombocytopenia (4%) and PROM

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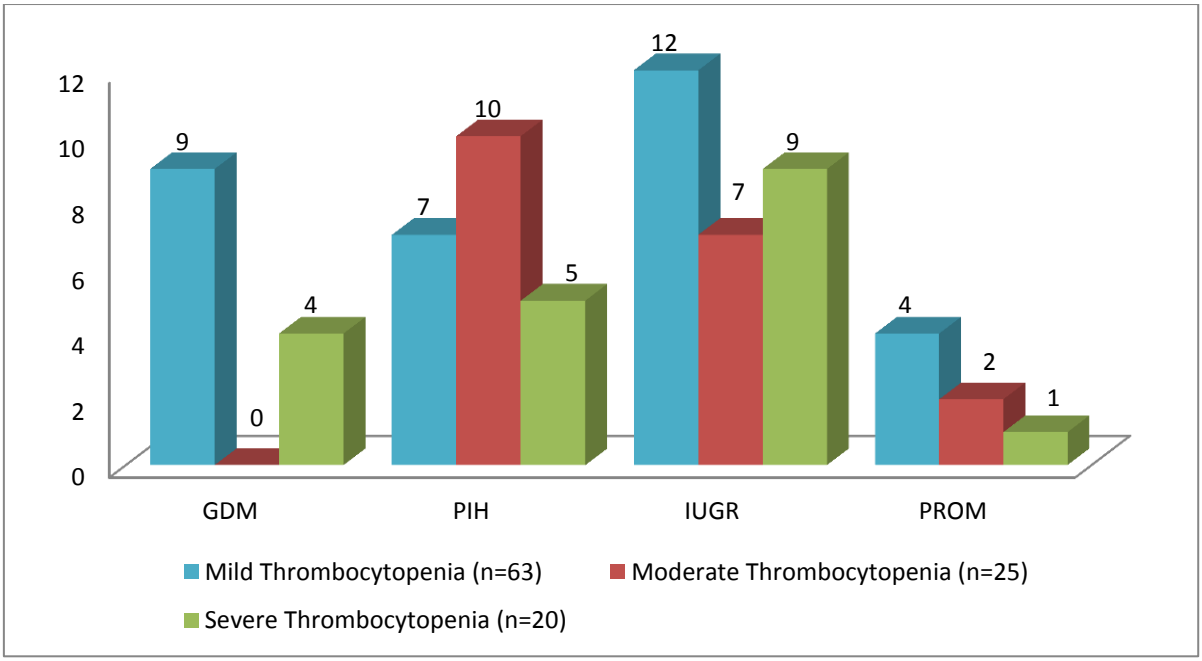
was not significantly associated with severity of thrombocytopenia (p=0.919). [Table-4, Graph-3]

Graph-3: Maternal complication according to severity of Thrombocytopenia



DISCUSSION

Neonatal thrombocytopenia frequently occurs in the preterm sick neonates admitted to neonatal intensive care unit, and it can contribute to high mortality. To prevent the preterm neonates from neonatal thrombocytopenia, or to evaluate a thrombocytopenic neonate, the mechanism and predisposing factors of thrombocytopenia must be investigated. Since aggressive therapy administered to thrombocytopenic infants also increases the mortality, this study was planned to evaluate the outcome of thrombocytopenic preterm neonates. There are limited prospective Indian studies till date conducted to evaluate maternal and neonatal factors association and outcome of thrombocytopenia in preterm neonate.

Incidence of neonatal thrombocytopenia in our study was 39.42%. Beiner et al[12] estimated the prevalence of thrombocytopenia 31%, only among preterm neonates. This was 22% in Castle V et al's study[13] and 36.4% in Bilal M et al's study[14]. It is evident that in our study there is a relatively higher prevalence of neonatal thrombocytopenia.

In our study, maximum cases were having mild thrombocytopenia (58.33%) while 23.15% were having moderate and 18.52% were having severe thrombocytopenia as compared to study of Hanoudi BM's[15] where maximum cases were of moderate

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thrombocytopenia (55.8%) while 26.31% were having mild and 17.9% were having severe thrombocytopenia. 52.7% of patient had mild and 43.9% moderate and 3.29% of the neonates had severe thrombocytopenia in Bilal M et al's study.[14] 42.8% had mild thrombocytopenia, 35.7% had moderate thrombocytopenia 21.4% had severe thrombocytopenia In Goyal P et al's study[16]. 49% had mild, 34% had moderate and 17% had severe thrombocytopenia in Saini R et al's study.[17] In study of Madavi D and Subuhi S,[18] mild thrombocytopenia was observed in 32.85 % neonates, moderate thrombocytopenia in 8.57 % & severe thrombocytopenia in 3.57 %.

Mean gestational age was 35.11±0.908 weeks in no thrombocytopenia group and 34.28±1.818 weeks in thrombocytopenia group in this study. Gestational age was significantly higher in no thrombocytopenia group as compared to thrombocytopenia group ($p<0.001$) similar to the study of Goyal P et al[16] where neonates with lower gestational age had a statistically highly significant association with thrombocytopenia as compared to neonates without thrombocytopenia (33.46±1.81 versus 34.72 ± 1.19, p=<.001). Beiner ME et al[12] found that average gestational age was slightly lower though statistically significant in thrombocytopenic group (30.5 weeks) as compare to nonthrombocytopenic group (31.6 weeks).

PIH was significantly higher in thrombocytopenia group (20.37%) as compared to no thrombocytopenia group (9.04%) (p=0.012). Saini R et al[17] revealed that PIH was higher in thrombocytopenia group as compared to no thrombocytopenia group but the difference was statistically not significant (p=0.641). PIH was maximum (40%) in moderate thrombocytopenia group followed by 25% in severe thrombocytopenia group and minimum 11.11% in mild thrombocytopenia group. Hanoudi BM[15] found that hypertension was 20% in mild, 11.3% in moderate and 11.76% in severe thrombocytopenia. Madavi D and Subuhi S[18] were revealed that among all maternal risk factors, PIH was seen to be more commonly associated with thrombocytopenia. 48.33% babies of PIH mother had thrombocytopenia but it was not statistically significant.

GDM was more in Thrombocytopenia group (12.04%) as compared to no thrombocytopenia group (7.83%) but this difference was not found significant (p=0.342) similar to the study of Madavi D and Subuhi S[18] (p=0.99). GDM was more in no Thrombocytopenia group as compared to thrombocytopenia group but this difference was not found significant (p=0.903) in study of Saini R et al[17] . GDM was maximum in severe Thrombocytopenia (20%) followed by 14.29% in mild thrombocytopenia group and no

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case in moderate thrombocytopenia and this distribution was not found significantly associated with severity of thrombocytopenia (p=0.085). Three of the mothers (3.16%) had gestational diabetes mellitus, including zero case in mild, 3.77% in moderate and 5.88% in severe thrombocytopenia but was not significantly associated in study of Hanoudi BM.[15]

IUGR was also significantly higher in thrombocytopenia group (25.93%) as compared to no thrombocytopenia group (10.84%) (p=0.002) in agreement with study of Madavi D and Subuhi S[18] (p<0.05). IUGR was maximum (45%) in severe thrombocytopenia and 28% in moderate thrombocytopenia and 19.05% in mild thrombocytopenia. Distribution of IUGR was statistically similar in all 3 groups (p=0.067). In study of Sonam S et al[19] there were 25% cases in mild, 25% in moderate and 50% cases of IUGR in severe thrombocytopenia.

PROM was significantly higher in no thrombocytopenia group (15.06%) as compared to thrombocytopenia group (6.48%) (p=0.049). In study of Saini R et al[17] PROM was higher in thrombocytopenia group (26.32%) as compared to no thrombocytopenia group (17.65%) but this difference was not statistically significant (p=0.156). In study of Goyal P et al[16] PROM was higher in thrombocytopenia group (14.3%) as compared to no thrombocytopenia group (6.2%) but this difference was not statistically significant (0.078).

Neonatal jaundice was 80% in mild thrombocytopenia, 20% in moderate and 0% in severe thrombocytopenia in Sonam S et al's study.[19]

CONCLUSION AND RECOMMENDATIONS

Our study indicated a high prevalence (39.42%) of thrombocytopenia among neonates admitted to NICU. Most cases were having mild to moderate Thrombocytopenia. Among maternal factors PIH, PROM and IUGR 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.

BIBLIOGRAPHY

1. Roberts IA, Murray NA. Thrombocytopenia in the newborn. Curr Opin Pediatr. 2003;15(1):17-23.
2. Sola MC, Del Vechio A, Rimsza K. Evaluation and treatment of thrombocytopenia in neonatal intensive care unit. Clin Perinatology. 2000; 27:655-670.

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3. Roberts I, Murray NA Neonatal thrombocytopenia: causes and Management. Arch Dis Child Fetal Neonatal Ed. 2003;88(5): F359 - 64.
4. Roberts I, Murray NA. Neonatal thrombocytopenia. Semin Fetal Neonatal Med. 2008;13(4):256-64.
5. Uhrynowska M, Maslanka K, Zupanska B. Neonatal thrombocytopenia: incidence, serological and clinical observations. Am J Perinatol. 1997;14(7):415-418.
6. Mehta P, Vasa R, Neumann L, Karpatkin M. Thrombocytopenia in the high-risk infant. J Pediatr 1980;97(5): 791-4.
7. Gupta A, Mathai S, Kanitkar M. Incidence of thrombocytopenia in the neonatal intensive care unit. Medical journal armed forces India. 2011;67(3):234-6
8. Inagaki K, Oda T, Naka Y, Shinkai H, Komatsu N. Induction of megakaryocytopoiesisand thrombocytopoiesis by ITZ -132, a novel small molecule with thrombopoietin mimetic activities. Blood. 2004;104(1): 58 – 64.
9. Sola MC, Rimsza LM. Mechanisms underlying in the neonatal thrombocytopenia intensive care unit. Actapaediatr Suppl. 2002;91(438):66- 73.
10. Sequeira AIR, Rocha D, Dias CJ, Carreira L, Cleto E. Immune neonatal thrombocytopenia-review. Nascer e CrescerBirth and Growth Medical Journal. 2020;29(1):29-35
11. Ballard JL, Khoury JC, Wedig K, et al. New Ballard Score, expanded to include extremely premature infants. J Pediatrics 1991; 119:417-423.
12. Beiner ME, Simchen MJ, Sivan E, Chetrit A, Kuint J, Schiff E. Risk factors for neonatal thrombocytopenia in preterm infants. Am J Perinatol. 2003;20(1): 49- 54.
13. Castle V, Andrew M, Kelton J, Giron D, Johnston M, Carter C. Frequency and mechanism of neonatal thrombocytopenia . J Pediatr. 1986;108:749-56.
14. Bilal M, Raj B, Shreyan A. Maternal and neonatal factors causing thrombocytopenia in neonates admitted to NICU during 2013-2014. International Journal of Scientific Research. 2016;5(5):376-77.
15. Hanoudi BM. Study of risk factors for neonatal thrombocytopenia in preterm infants. Mustansiriya Medical Journal. 2015;14(1): 64-69
16. Goyal P, Natani BS, Agarwal A, Bhatia S, Kumar M. Evaluation of gestational age as a risk factor for thrombocytopenia in preterm neonates. International Journal of Medical and Health Research. 2017;3(9):08-10

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 07, 2023

17. 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.
18. Madavi D, Subuhi S. Prevalence and etiology of neonatal thrombocytopenia in tertiary care NICU. Paripex - Indian Journal F Research 2019;8(9);38-40.
19. Nandyal SS, Shashikala P, Sahgal V. Study of thrombocytopenia in neonatal intensive care unit. Indian Journal of Pathology and Oncology 2016;3(1);55-59