e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2023; 15 (6); 1350-1359

Original Research Article

Etiological Profile and Outcome of Thrombocytopenia in Neonates Admitted to NICU in A Rural Tertiary Care Centre

Ankitha C[1], Sunil Kumar P[2], Mahendrappa K B[3], Madhunandan Krishnegowda[4*]

[1]Junior Resident, Department of Paediatrics, Adichunchanagiri Institute of Medical Sciences, Bellur, Mandya, Karnataka

[2]Professor, Department of Paediatrics, Adichunchanagiri Institute of Medical Sciences, Bellur, Mandya, Karnataka

[3]Professor and HOD, Department of Paediatrics Adichunchanagiri Institute of Medical Sciences, Bellur, Mandya, Karnataka

[4]Assistant Professor, Department of Paediatrics, Adichunchanagiri Institute of Medical Sciences, Bellur, Mandya, Karnataka

Received: 17-04-2023 / Revised: 19-05-2023 / Accepted: 16-06-2023

Corresponding author: Dr. Madhunandan Krishnegowda

Conflict of interest: Nil

Abstract:

Background: Neonatal thrombocytopenia (NT), accounts for one-third of all admissions to NICU. Mortality due to thrombocytopenia can be decreased by optimal time recognition, early intervention and appropriate management addressing the underlying illness and platelet transfusions.

Objectives: The study aimed to estimate the prevalence, associated maternal and foetal predisposing factors of thrombocytopenia. The study also estimates immediate outcomes among various grades of thrombocytopenia and platelet transfusion cutoffs.

Methodology: A prospective, observational study carried in NICU at Adichunchanagiri Hospital & Research Centre from February 2021 to September 2022. The outcome was measured in terms of need for platelet transfusions, bleeding manifestations, need for parenteral therapy, oxygen support, duration of hospital stay and mortality.

Results: Prevalence of Thrombocytopenia in NICU-admitted neonates was 27.56% with an overall mortality rate of 12.1%. Out of 124 thrombocytopenic neonate mothers, 33.1% (41) had gestational hypertension followed by PROM 32.3%, GDM at 20.2%, Rh Immunization 9.7% and APH 2.4%. In the study, 59.7% of the neonate had sepsis followed by RDS 36.3%, IUGR 33.90%, MAS 16.10%, birth asphyxia 13.70%, and NEC 8.90%. 16.1% required platelet transfusion. The overall mortality rate in our study was 12.1%.

Conclusion: The prevalence of NT is 27.56% among NICU-admitted neonates. Maternal predisposing factors such as gestational hypertension, antepartum haemorrhage, Rh immunization and GDM and the neonatal predisposing factors such as sepsis, premature birth, RDS, NEC, and DIC are associated with neonatal thrombocytopenia. DIC, NEC and birth asphyxia directly influence the severity of thrombocytopenia and thereby the mortality.

Keywords: GDM, MAS.

Introduction

Neonatal thrombocytopenia (NT), one of the most prevalent haematological issues in neonatal intensive care units (NICU), accounts for one-third of all admissions to NICU.[1] The majority of cases are mild and recover on their own in clinically stable neonates, while clinically unstable neonates often have a poor outcome.[1,2] Consequently, it poses a challenge for the treating physician on when to treat and when to ignore. Several variables affect the prognosis of neonatal thrombocytopenia, including the underlying aetiology, platelet count, gestational age, and birth weight.[2] Currently, platelet transfusions remain the cornerstone of therapy.[2]

Thrombocytopenia prevalence in neonates is reported to range between 0.7% and 5%.[3-5] In the NICU, the prevalence of thrombocytopenia ranges from 18 % to 35%.[5-7] The rate of variation in prevalence is totally dependent on the number of study participants. The mortality associated with thrombocytopenia has been reported to range from 1% to as high as 10%.[5-7]

Early NT, which appears within 72 hours of life, is related to complications in pregnancy, including intrauterine growth restriction, maternal diabetes, gestational hypertension, immune thrombocytopenic purpura (ITP), congenital infection, or neonatal alloimmune thrombocytopenia (NAIT).[13] While late-onset NT, which appears beyond 72 hours of life, typically results from sepsis or necrotizing enterocolitis (NEC), it is usually more severe and debilitating.[5-7] Increased destruction/sequestration or decreased platelet synthesis are the two primary underlying pathogenic processes for NT.[7]

The study of association of severity of thrombocytopenia against the above-mentioned etiological factors, could aid early anticipation for platelet transfusion, appropriate management, prevention and decreases the mortality and morbidity. There remains paucity of data to guide cutoffs for platelet transfusion, aetiologies associated with severe thrombocytopenia. Hence, the present study is designed to estimate the prevalence, maternal and fetal risk factors, etiological profile, and clinical outcome of neonatal thrombocytopenia in neonates admitted to the NICU.

Materials and Methods:

The present study was a prospective Observational study conducted at NICU of Adichunchanagiri Institute of Medical sciences, B G Nagara, Karnataka. A total of 124 Neonates were enrolled during the study period of 18 months (February 2021 to September 2022).

A detailed maternal history and neonatal history pertaining to gestational age at birth, birth weight, perinatal asphyxia, history of clinical presentations were documented in the data collection form after taking parents/ guardians written informed consent. Gestational age was calculated using New Ballard's scoring.

Birth asphyxia was considered in babies with APGAR Score < 7 at 5 min of life. Sepsis was defined according to Neonatal Sepsis guidelines and blood culture was sent for definitive diagnosis. Other investigations like blood gas, Chest X - ray, Serum electrolytes, neurosonogram were performed upon need, on case-to-case basis.

The Maternal and neonatal predisposing factors were checked for their association with the severity of thrombocytopenia. Platelet counts were repeated after 48 hours among thrombocytopenic babies. In case of Severe thrombocytopenia requiring platelet transfusions, repeat counts were done after 24 hrs. The mean cutoffs for platelet transfusion were studied among the study subjects. The immediate outcomes were estimated based on bleeding manifestations, requirement of Oxygen

support, duration of stay in the hospital and mortality.

The neonates were classified as per the severity of thrombocytopenia based on platelet counts into those with no thrombocytopenia (>150*10^3/µL), mild thrombocytopenia (100 - 149*10^3/µL), moderate thrombocytopenia (50-99*10^3/µL), and severe thrombocytopenia (<50*10^3/µL).[4]

Statistical analysis was done using SPSS software 26. The categorical variables presented in frequency and percentage and numerical data with mean and SD. The Chi-Square test or Fisher's exact test (in the case where Chi-square test was not possible) was used to find the association between two categorical variables and independent student t test used for numerical variables.

Results

In our study, among 450 neonates who were admitted in NICU, 124 babies had thrombocytopenia who were further taken up for the study.

The Prevalence of Neonatal Thrombocytopenia was estimated to be 27.56% (124/450). The percentage of neonates with mild (100 – 149*10^3/µL), moderate (50 –99*10^3/µL), or severe thrombocytopenia (<50*10^3/µL) was 78.20% (97), 9.7% (12), and 12.10% (15) respectively. (Table 1)

Table 1: Prevalence of neonatal thrombocytopenia Parameters

Thrombocytopenia	Frequency	Percentage
Mild	97	78.20%
Moderate	12	9.70%
Severe	15	12.10%

The prevalence of severe thrombocytopenia according to our study was 12.1%. Out of 124 neonates, male babies were 66.10% (82) and female were 33.90% (42).
The average age at presentation of neonatal thrombocytopenia was 74.71 ± 52.76 hours, about 71.8% (89) had Early onset thrombocytopenia (less than 72 hrs) and 28.20% (35) were Late onset thrombocytopenia (72 hrs of age). The babies were categorized according to Birth weight and gestational age into 4 and 5 groups respectively. (Table 2)

Table 2: Demographic Characteristics of Thrombocytopenic babies

S.No	Parameters		Number	Frequency
1	Gender	Female babies	42	33.9%
		Male babies	82	66.10%
2	Age of Onset	EOT (<72 hrs)	89	71.8%
		LOT (>72hrs)	35	28.2%
3	Birth Weight	>/= 2.5 kg	47	37.9 %
		1.5 - 2.49 kg	57	46 %
		1- 1.49 kg	16	12.9 %
		<0.99 kg	4	3.2 %
4	Gestational Age	< 28 weeks	3	2.4 %
		28-31 weeks + 6 days	10	8.1 %
		32- 33 weeks + 6 days	23	18.5 %
		34 - 36 weeks + 6 days	34	27.4 %
		>37 weeks	54	43.5 %

Maternal predisposing factors: Out of 124 thrombocytopenic neonates, 33.1% (41) mothers had gestational hypertension followed by premature rupture of membranes 32.3% (40), gestational diabetes mellitus 20.2% (25), Rh Immunization 9.7% (12), and antepartum haemorrhage 2.4%. Our study showed statistically significant association between neonatal thrombocytopenia with antepartum haemorrhage ($p< 0.001$), gestational hypertension ($p< 0.05$), Rh Immunization ($p<0.05$), gestational diabetes mellitus ($p<0.05$). Gestational hypertension (60%, 9/15) had tends to cause more severe neonatal thrombocytopenia whereas antepartum haemorrhage (20%, 3/15), Rh Immunization (20%, 3/15), and gestational diabetes mellitus (0/15) caused less severe neonatal thrombocytopenia**.**

Neonatal predisposing factors: The average APGAR score at 5 minutes of birth was 8.62 ± 0.9. In the study, 59.7% (74) of the neonate had sepsis followed by hyperbilirubinemia 47.6% (59), respiratory distress syndrome 36.3% (45), intrauterine growth restriction 33.90% (42), meconium aspiration syndrome 16.10% (20), birth asphyxia 13.70% (17), and necrotizing enterocolitis 8.90% (11). (Figure 1)

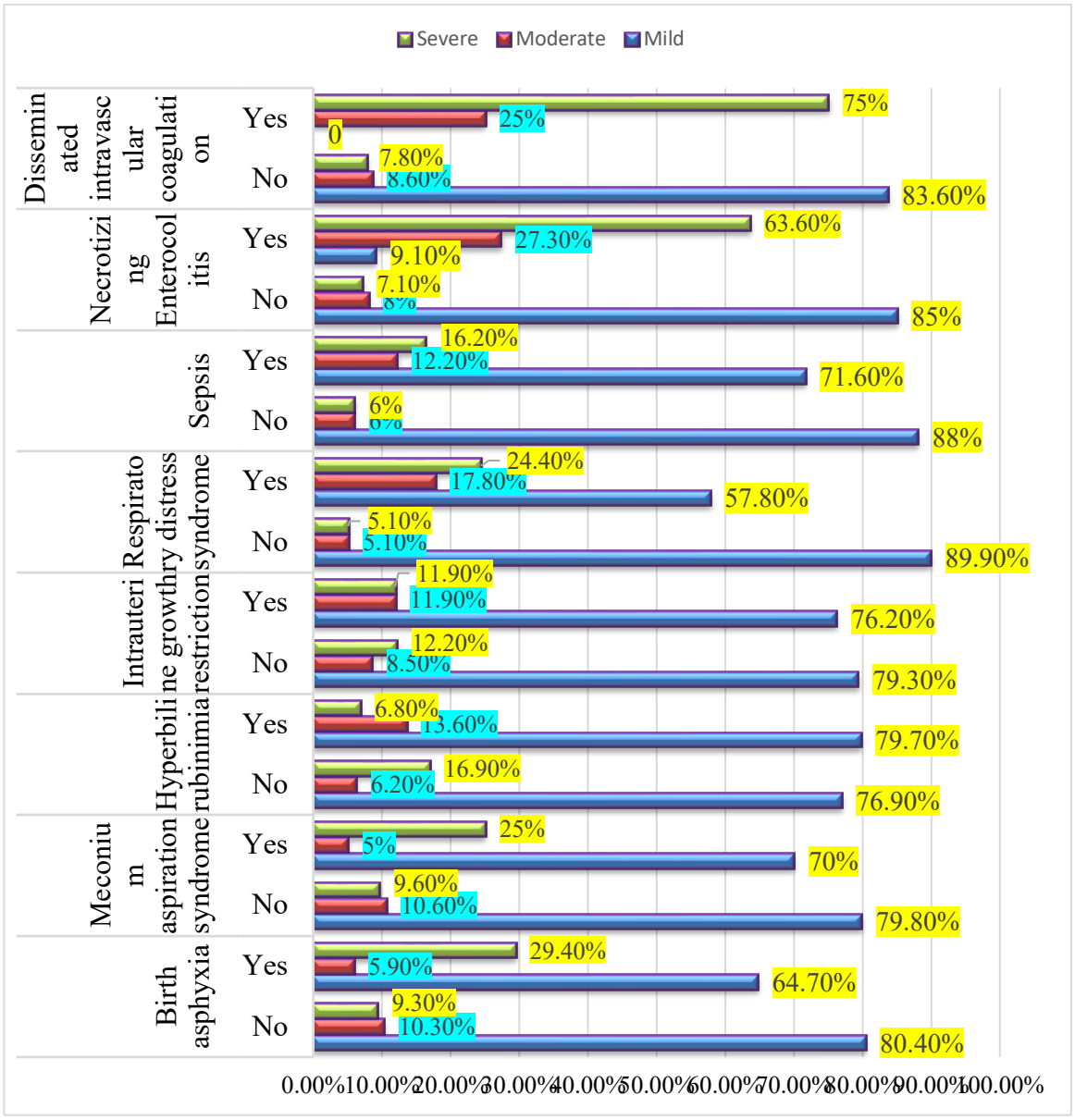

Figure 1: Different neonatal predisposing factors distributed as per severity of thrombocytopenia

There was statistically significant association between respiratory distress syndrome, necrotizing enterocolitis, sepsis, disseminated intravascular coagulation with neonatal thrombocytopenia ($p < 0.05$). Disseminated intravascular coagulation (40%, 6/15) shows to cause less severe neonatal thrombocytopenia. Necrotizing enterocolitis (63.6 %, 7/11), respiratory distress syndrome (73.33%, 11/15), and sepsis (100%, 15/15) were tends to cause more severe thrombocytopenia.(Table 3) In the study, out of 124 neonates, 89 had early onset thrombocytopenia, while the rest had late onset thrombocytopenia. Late onset thrombocytopenia was associated with more severe thrombocytopenia than early onset. But there was no statistically significant association between the 2 groups. (Figure 2)

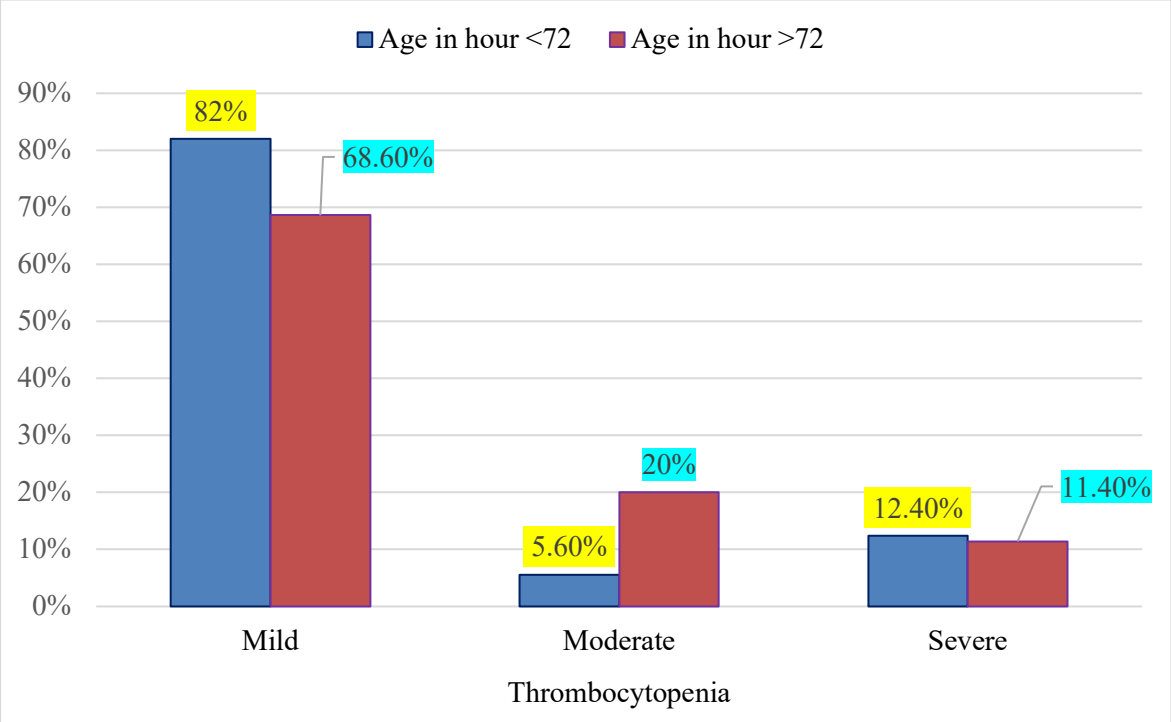

Figure 2: Association of age at onset with severity of Thrombocytopenia

Table 3: Association of Maternal and Neonatal Risk factors with Neonatal thrombocytopenia

Maternal predisposing factors		Neonatal thrombocytopenia				P-value
		Mild	Moderate	Severe	Total	
Gestational hypertension	Yes	27 (65.9%)	5 (12.2%	9 (22%)	41 (100%)	0.038*
	No	70 (84.3%)	7 (8.4%)	6 (7.2%)	83 (100%)	
Gestational diabetes mellitus	Yes	20 (80%)	5 (20%)	0	25 (100%)	0.014*
	No	77 (77.8%)	7 (7.1%)	15 (15.2%)	99 (100%)	
Rh Immunization	Yes	6 (50%)	3 (25%)	3 (25%)	12 (100%)	0.036*
	No	91 (81.3%)	9 (8%)	12 (10.7%)	112 (100%)	
Premature rupture of membranes	Yes	27 (67.5%)	6 (15%)	7 (17.5%)	40 (100%)	0.135
	No	70 (83.3%)	6 (7.1%)	8 (9.5%)	84 (100%)	
Maternal thrombocytopenia	Yes	0	0	1 (100%)	1(100%)	0.218
	No	97 (78.9%)	12 (9.8%)	14 (11.4%)	123 (100%)	
Antepartum haemorrhage	Yes	0	0	3 (100%)	3 (100%)	<0.002**
	No	97 (80.2%)	12 (9.9%)	12 (9.9%)	121 (100%)	

Neonatal predisposing factors						P value
		Mild	Moderate	Severe	Total	
Birth asphyxia	Yes	11 (64.7%)	1 (5.9%)	5 (29.4%)	17 (100%)	0.063
	No	86 (80.4%)	11 (10.3%)	10 (9.3%)	107 (100%)	
Meconium aspiration syndrome	Yes	14 (70%)	1 (5%)	5 (25%)	20 (100%)	0.138
	No	83 (79.8%)	11 (10.6%)	10 (9.6%)	104 (100%)	
Hyperbilirubinemia	Yes	47 (79.7%)	8 (13.6%)	4 (6.8%)	59 (100%)	0.13
	No	50 (76.9%)	4 (6.2%)	11 (16.9%)	65 (100%)	
Respiratory distress syndrome	Yes	26 (57.8%)	8 (17.8%)	11 (24.4%)	45 (100%)	0.000***
	No	71 (89.9%)	4 (5.1%)	4 (5.1%)	79 (100%)	
Sepsis	Yes	47 (63.5%)	12 (16.2%)	15 (20.3%)	74 (100%)	0.049*
	No	41 (82%)	6 (12%)	3 (6%)	50 (100%)	
Intrauterine growth restriction	Yes	32 (76.2%)	5 (11.9%)	5 (11.9%)	42 (100%)	0.835
	No	65 (79.3%)	7 (8.5%)	10 (12.2%)	82 (100%)	
Necrotizing Enterocolitis	Yes	1 (9.1%)	3 (27.3%)	7 (63.6%)	11 (100%)	0.000***
	No	96 (85%)	9 (8%)	8 (7.1%)	113 (100%)	
DIC	Yes	0	2 (25%)	6 (40%)	8 (100%)	0.001***
	No	97 (83.6%)	10 (8.6%)	9 (7.8%)	116 (100%)	
Age of neonates	< 72 hrs	73 (82%)	5 (5.6%)	11 (12.36%)	89 (100%)	0.063
	>72 hrs	24 (68.6%)	7 (20%)	4 (11.4%)	35 (100%)	

Clinical features: Among the clinical features, there was statistically significant association between apnea, respiratory distress, seizures, feed intolerance, abdominal distension, and Hypoglycemia ($p<0.05$). Apnea (53.33%, 8/15), respiratory distress (93.33%, 14/15), Seizures (53.33%, 8/15), feed intolerance (73.33%, 11/15), abdominal distension (53.33%, 8/15), blood transfusion and Hypoglycemia (73.33%, 11/15) had the positive association and were more predictive of severe neonatal thrombocytopenia.

Lethargy shows no statistically significant association to neonatal thrombocytopenia ($p >0.05$). (Table 4)

Table 4: Association of clinical features among neonatal thrombocytopenia

Clinical manifestation	Thrombocytopenia			P-value
	Mild	Moderate	Severe	
Apnoea	0	0	8 (100%)	<0.001***
Respiratory distress	41 (68.3%)	5 (8.3%)	14 (23.3%)	<0.001***
Lethargy	42 (72.4%)	9 (15.5%)	7 (12.1%)	0.116
Seizures	3 (23.1%)	2 (15.4%)	8 (61.5%)	<0.001***
Feed intolerance	44 (68.8%)	9 (14.1%)	11 (17.2%)	0.031*
Abdominal distension	6 (35.3%)	3 (17.6%)	8 (47.1%)	<0.001***
Hypoglycaemia	12 (52.2%)	3 (13%)	8 (34.8%)	<0.001***
Platelet transfusion	2 (10%)	4 (20%)	14 (70%)	<0.001***

Outcomes*:* Out of 124 thrombocytopenic neonates 9.68% (12) had bleeding manifestation and 16.10% (20) required the transfusion, 25.8% (32) of the total neonatal thrombocytopenia required oxygen, and 2.4% (3) of the total neonatal thrombocytopenic babies lost their life. 7.26% (9/124) of the total neonatal thrombocytopenic patients showed bacterial growth.

The average IV fluids requirement for thrombocytopenic neonates was 4.1 ± 4.02 days, oxygen supplementation was 2.83 ± 2.49 days, and duration of hospital stay in days is 11.13 ± 7.42. (Figure 3)

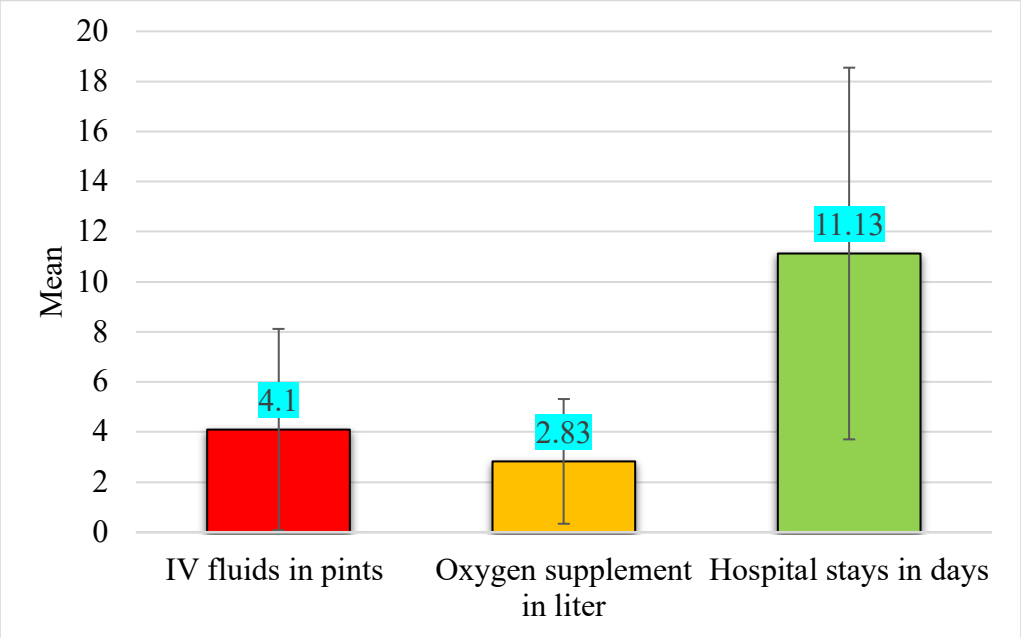

Figure 3: Requirement of IV fluids, Oxygen supplement, and hospital stay for neonatal thrombocytopenia

Average platelet count for those, not requiring transfusion, required transfusion and after transfusion of blood: The average platelets for those who did not require blood transfusion was 1.29 ± 0.20 × 105 cells per mm^3, and those who required platelet transfusion was 0.43±0.29 × 105 cells per mm^3. After transfusion, the platelet value increased in an average by 0.7 ± 0.29 × 105 cells per mm3. There was a statistically significant difference between the levels of platelets among no requirement and requirement of transfusion group using student t test ($p < 0.001$). There was no statistically significant difference between platelet values among early onset and late onset thrombocytopenia ($p > 0.05$). (Table 5)

Table 5: **Average platelet count of neonates requiring transfusion and after transfusion platelets**

Parameters		Mean ± SD	P value
Platelet Transfusion	No	1.29±0.20	<0.001
	Required	0.43±0.29	
	After	0.7 ± 0.29	
Age	> 72 hrs	1.10 ± 0.422	0.377
	< 72 hrs	1.17 ± 0.368	

Discussion

The study aimed to estimate the prevalence of thrombocytopenia in neonates admitted to the NICU and any associated maternal or foetal predisposing factors. In the study we observed, 27.56% (124/450) of NICU-admitted neonates had thrombocytopenia. Lindern J S et al., reported similar incidence, Gupta AK et al., and Castle V et al., observed a lower incidence, and Mehta P et al., and Beiner et al reported a higher incidence. [6, 9, 17, 10,14]

Maternal predisposing factors associated with neonatal thrombocytopenia:

In the study, we observed, there was a statistically significant association between neonatal thrombocytopenia and a variety of maternal conditions, including gestational diabetes mellitus ($p<0.05$), antepartum hemorrhage ($p<0.001$), Rh Immunization and gestational hypertension ($p<0.05$). Other maternal predisposing factors, such as premature rupture of membranes (46.67%,7/15), and maternal thrombocytopenia, were statistically non-significant ($p>0.05$).

Our study shows a lower prevalence of gestational hypertension than reported by Bhat R et al., Burrows RF et al., Chakraborty A et al., and Nandeeswari S et al., (33.1% vs. 36.1% vs. 68.1% vs. 72.17% vs. 72%).[23-25,8] However, other maternal risks such as Rh immunization, and antepartum hemorrhage are statistically significantly negatively associated with thrombocytopenia. Maternal Rh immunization (20% vs. 80%, $p<0.05$) tends to cause less severe thrombocytopenia. Gestational hypertension (60% vs. 40%, $p<0.05$) and antepartum haemorrhage (100% vs. 0%, $p<0.001$) tend to cause more severe thrombocytopenia.

Neonatal risk factors for Neonatal thrombocytopenia:

In the study, we observed that neonatal predisposing factors such as respiratory distress syndrome, necrotizing enterocolitis, and sepsis were statistically significant and positively associated with thrombocytopenia. Respiratory distress syndrome (73.33% vs. 26.67%, $p<0.001$), necrotizing enterocolitis (63.6% vs. 36.36%, $p<0.001$), and sepsis (20% vs. 6%, $p<0.05$) tend to cause more severe thrombocytopenia. Nandeeswari S et al., reported a higher prevalence than our study (88.46% vs. 36.3%).[8] Similar to our finding, Kohelet D et al., reported the positive association to the severity of thrombocytopenia.[26]

In the study, 59.70% (74) of the neonatal thrombocytopenic patients had sepsis, and among them, 7.26% (9) of blood cultures were positive for bacterial pathogens. In contrast to the study, Castle V et al., (10%) reported a higher and Hale O et al., (5.4%) reported a lower rate of blood culture for bacterial infections.[17,11] There is decrease production and increase consumption of platelets in septicaemia which leads to thrombocytopenia.[41] However, there is no statistically significant difference in the occurrence of early onset or late onset neonatal thrombocytopenia among sepsis (56.2% vs. 68.6%, $p>0.05$).

The overall prevalence of necrotizing enterocolitis was 8.9%. The study shows a higher prevalence of severe thrombocytopenia among NEC than reported by Charoo B A et al.[17] However, disseminated intravascular coagulation was significantly associated with severe thrombocytopenia (40%, $p<0.001$). Neonatal predisposing factors like birth asphyxia, meconium aspiration syndrome, hyperbilirubinemia, intrauterine growth restriction, and the age of neonates do not have a statistically significant association with thrombocytopenia ($p>0.05$).

In our study, premature birth was more associated with severe thrombocytopenia than term birth (73.33% vs. 26.67%). Chakraborty A et al., and Bonafacio L et al., reported similar findings in their studies.[25-27] Similar to our finding, Nandeeswari S et al. reported no association between intrauterine growth restriction and severity of thrombocytopenia whereas Maruyama H et al., reported contrast to our finding.[8,28]

Outcome measures

Out of total thrombocytopenic neonates, 12.10% (15) developed severe thrombocytopenia and 16.10% (20) received the platelet transfusions. The study showed a statistically significant difference in the platelet count between those who required the platelet transfusion and those who did not require the platelet transfusion ($0.43 \pm 0.29 \times 10^5$ Vs $1.29 \pm 0.20 \times 10^5$, P

<0.001) . We observed platelet transfusion given to those who have platelet level less than 0.5 × 10^5 which is similar to the guideline given by the National Health Service 2020 guideline.[18-22]

The study shows an overall mortality rate of 12.1%, which is comparatively lower than Beiner et al., Mehtha et al., Castle et al., and Chakraborty A et al., (12.1% vs. 22.05% vs.31% vs. 24.61% vs. 39.92%).[14,10,17,25] Among severe thrombocytopenic neonates, 20% was the mortality rate, which is comparatively lower than that reported by Chakraborty A et al., (20% vs. 37%) . It may be the reason of strict follow the National Health Service 2020 guideline to treat neonatal thrombocytopenia.

Conclusions

The prevalence of neonatal thrombocytopenia was 27.56% among NICU admitted neonates. Late onset thrombocytopenia was more severe in nature and strongly associated with sepsis. The maternal risk factors, gestational hypertension tends to cause more severe neonatal thrombocytopenia, whereas Rh immunization and antepartum hemorrhage tend to cause less severe thrombocytopenia. The neonatal predisposing factors such as respiratory distress syndrome, necrotizing enterocolitis, premature birth, and sepsis tend to cause more severe thrombocytopenia, whereas disseminated intravascular coagulation tends to cause severe thrombocytopenia but invariably requiring transfusions.

The study showed a overall mortality rate of 12.1% among the thrombocytopenic neonates. A multi-center study with a larger sample size is required to confirm the results. The lack of facility, fetomaternal platelet alloimmunization was not performed on suspected cases to rule out neonatal alloimmune thrombocytopenia which is the limitation of our study.

References

1. Roberts I, Stanworth S, Murray NA. Thrombocytopenia in the neonate. Blood reviews. 2008 Jul 1;22(4):173-86.
2. Roberts IA, Chakravorty S. Thrombocytopenia in the newborn. 4th-ed. Academic Press. 2019. pp. 813-31.
3. Saber AM, Aziz SP, Almasry AZ, Mahmoud RA. Risk factors for severity of thrombocytopenia in full term infants: a single center study. Italian Journal of Pediatrics. 2021 Dec; 47(1): 1-7.
4. Cloherty JP, Eichenwald EC, Stark AR. Manual of Neonatal Care. Philadelphia, PA: Lippincott Williams & Wilkins; 2008.
5. Eltawel M, AlHarbi T, AlJamaan K, Alsaif S, Ali Y, Salam M. A Prospective Study on the Incidence and Outcomes of Neonatal Thrombocytopenia at a Tertiary Care Facility in Central Saudi Arabia. Adv Neonatal Care. 2018;18(5): E3-E12.
6. von Lindern JS, van den Bruele T, Lopriore E, Walther FJ. Thrombocytopenia in neonates and the risk of intraventricular hemorrhage: a retrospective cohort study. BMC Pediatr. 2011; 11:16.
7. Roberts IA, Murray NA. Neonatal thrombocytopenia: new insights into pathogenesis and implications for clinical management. Current opinion in pediatrics. 2001;13(1):16-21.
8. Nandeeswari S. Incidence and clinic-etiological profile of thrombocytopenia in neonates admitted to the NICU of Cheluvama hospital attached to Mysore medical college and research institute, Mysore [Dissertation]. Rajiv Gandhi University of Health sciences; 2016.
9. Gupta AK, Kumari S, Singhal A, Bahl A. Neonatal thrombocytopenia and platelets transfusion. Asian J Transfus Sci. 2012 Jul;6(2):161-4.
10. Mehta P, Vasa R, Neumann L, Karpatkin M. Thrombocytopenia in the

high-risk infant. The Journal of pediatrics. 1980 Nov 1;97(5):791-4.
11. Ören H, Irken G, Ören B, Olgun N, Özkan H. Assessment of clinical impact and predisposing factors for neonatal thrombocytopenia. The Indian Journal of Pediatrics. 1994 Sep;61(5):551-8.
12. Arif H, Ikram N, Riaz S, Nafisa A. Risk factors and outcome of neonatal thrombocytopenia. Journal of Rawalpindi Medical College. 2020 Sep 30; 24(3):229-34.
13. Tirupathi K, Swarnkar K, Vagha J. Study of risk factors of neonatal thrombocytopenia. Int J Contemp Pediatr. 2017 Jan; 1:191-6.
14. Beiner ME, Simchen MJ, Sivan E, Chetrit A, Kuint J, Schiff E. Risk factors for neonatal thrombocytopenia in preterm infants. American journal of perinatology. 2003;20(01):049-54.
15. Yamada H, Kato EH, Kishida T, Negishi H, Makinoda S, Fujimoto S. Risk factors for neonatal thrombocytopenia in pregnancy complicated by idiopathic thrombocytopenic purpura. Annals of hematology. 1998;76(5):211-4.
16. Bhat Y R, Cherian C S. Neonatal thrombocytopenia associated with maternal pregnancy-induced hypertension. Indian J Pediatr. 2008; 75(6): 571–573.
17. Castle V, Andrew M, Kelton J, Giron D, Johnston M, Carter C. Frequency and mechanism of neonatal thrombocytopenia J Pediatr 1986108(5 Pt 1):749–755.
18. Andrew M et al. A randomized, controlled trial of platelet transfusion sin thrombocytopenic premature infants. J Pediatr 1993;123; 285-291.
19. Murray NA et al. Platelet transfusion in the management of severe thrombocytopenia in neonatal intensive care unit patients. Transfus med 2002;12;35-41
20. New HV, Berryman J, Bolton-Maggs PH, Cantwell C, Chalmers EA, Davies T, Gottstein R, Kelleher A, Kumar S, Morley SL, Stanworth SJ. Guidelines on transfusion for fetuses, neonates and older children. British journal of haematology. 2016Dec;175(5):784-828
21. Curley, A, et al. Randomized trial of Platelet-Transfusion Thresholds in Neonates. N Engl J Med. 2019; 380:242-251.
22. Neunert C, Terrell DR, Arnold DM, Buchanan G, Cines DB, Cooper N, et al. American Society of Hematology 2019 guidelines for immune thrombocytopenia. Blood Adv. 2019; 3: 3829-3866.
23. Burrows RF, Andrew M. Neonatal thrombocytopenia in the hypertensive disorders of pregnancy. Obstet Gynecol 1990;76(2): 234-8.
24. Bhat YR, Cherian CS. Neonatal thrombocytopenia associated with maternal pregnancy induced hypertension. Indian J Pediatr 2008; 75(6):571-3.
25. Chakraborty A et al. Immediate outcome and a short term follow up study of neonates with neonatal thromb-ocytopenia [Dissertation]. Rajiv Gandhi University of Health sciences; 2010.
26. Kohelet D, Perlman M, Hanna G, Ballin A. Reduced platelet count in neonatal respiratory distress syndrome. Biol Neonate. 1990;57(6):334-342.
27. Bonifacio L, Petrova A, Nanjundaswamy S, Mehta R. Thrombocytopenia Related Neonatal Outcome in Preterms. Indian J Paediatr 2007;74(3) :269-274.
28. Maruyama H, Shinozuka M et al. Thrombocytopenia in preterm infants with intrauterine growth retardation. Acta med. 2008;62(5):313-317.