ORIGINAL RESEARCH PAPER
Volume - 12 | Issue - 02 | February - 2023 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

A STUDY ON RISK FACTORS AND IMMEDIATE OUTCOME OF PRETERM AND TERM NEONATES WITH THROMBOCYTOPENIA IN TERTIARY CARE HOSPITAL

Paediatrics

Dr. K. Mounika Postgraduate, Department of Paediatrics, Alluri Sitarama Raju Academy of Medical Sciences, Eluru, West Godavari District, Andhra Pradesh 534005, India.

Dr. M. Gowtham Assistant Professor, Department of Paediatrics, Alluri Sitarama Raju Academy of Medical Sciences, Eluru, West Godavari District, Andhra Pradesh 534005, India.

Dr. C. S. N. Vittal* Professor, Department of Paediatrics, Alluri Sitarama Raju Academy of Medical Sciences, Eluru, West Godavari District, Andhra Pradesh 534005, India. *Corresponding Author

ABSTRACT

BACKGROUND: Thrombocytopenia (platelet count < 150,000/µL) is one of the most common haematological problems (18-35%) in Neonatal Intensive Care Units (NICUs). The paucity of studies from India and the increasing prevalence of this condition in our NICU, instigated us to determine the risk factors, immediate outcome of the neonates admitted to NICU's in our hospital.

- **OBJECTIVES:**
- To study maternal and fetal risk factors of neonatal thrombocytopenia.
- To study the immediate outcome of term and preterm neonates with thrombocytopenia in our hospital.
- To evaluate the role of NT as a prognostic indicator in NICU graduates.

MATERIAL & METHODS: A Prospective observational study was conducted at Alluri Sitarama Raju Academy of Medical Sciences, Eluru from June 2022 to November 2022 and included 80 newborns admitted in NICU with thrombocytopenia. **RESULTS:** Among the 80 newborns with thrombocytopenia, 47(59%) are preterm and 32 (41%) are terms, majority of cases are due to sepsis 44 (55%), RDS 12 (15%), MAS 8 (10%), PIH 40 (50%), PROM 24 (30%). Out of 80 newborns survival rate is 82.5% and mortality rate is 17.5% among the mortality cases sepsis is the major cause. **CONCULSION:** Thrombocytopenia is one of the most common haematological problems in NICUs. In NT sepsis is the major cause. Among the NT, severe thrombocytopenic neonates had poor immediate outcome. Severe thrombocytopenia can be used as prognostic indicator in sick neonates.

KEYWORDS

NT (neonatal thrombocytopenia), NEC (necrotizing enterocolitis), PROM (premature rupture of membranes), RDS (respiratory distress syndrome), MAS (meconium aspiration syndrome), PIH (pregnancy induced hypertension), LBW (low birth weight).

INTRODUCTION

Thrombocytopenia (platelet count < 150,000/µL) is one of the most common haematological problems in Neonatal Intensive Care Units (NICUs), with 18-35% of the NICU patients developing this problem before hospital discharge. With the exception of phlebotomy induced anemia, thrombocytopenia is the most common hematological abnormality encountered in the NICU. [1]

It might be even more common among Extremely Low Birth Weight neonates (ELBW < or = 1000 grams birth wt) or Preterm babies (GA < or = 34-36 weeks) or Sick neonates in NICUs. In contrast, only 2% of the neonates are thrombocytopenic at birth with Severe Thrombocytopenia (platelet count < 50,000/µL) occurring in less than 3/1000 term infants. [2]

Neonatal thrombocytopenia can result from a variety of disease processes and these can be categorised as early onset (within 72hours) neonatal thrombocytopenia and late onset (> 72 hours).[3] neonates who have sepsis, birth asphyxia, preterm intrauterine growth retardation, hyperbilirubinemia, RDS, MAS, LBW are at risk for developing thrombocytopenia. Bleeding symptoms are dependent on underlying illnesses in addition to platelet count.[4]

Though thrombocytopenia is so prevalent it is often ignored in the assumption that it will resolve spontaneously. However if it is not detected and managed properly can result in devastating complications.

Platelets are small anucleate fragments that are formed from the cytoplasm of megakaryocytes and have a characterisitic discoid shape.[5]Megakaryopoiesis includes the production of megakaryocytes from stem cells, while thrombopoiesis is the production of platelets from megakaryocytes. Platelet production begins to the yolk sac and, like the remainder of hematopoiesis shifts to the fetal liver and then to the marrow at the time of gestation.[6]

In the past decade there have been a lot of research article pouring in regarding the etiology, clinical profile and management of Neonatal Thrombocytopenia in the NICU's. The influence of thrombocytopenia on the outcome of neonate is a subject that has not been studied in detail in the past. Neither have articles assessed the value of neonatal thrombocytopenia as a prognostic indicator in sick neonates. After a detailed search of the indexed medical literature, it was found that there have been only few articles on this topic from India.

One article is a study of the association between maternal PIH and neonatal thrombocytopenia while the others are case reports and case series reports. The paucity of studies from India and the increasing prevalence of this condition in our NICU, instigated us to determine the etiology, immediate outcome of the neonates admitted to NICU's in our hospital.

OBJECTIVES

- To study maternal and fetal risk factors of neonatal thrombocytopenia.
- To study the outcome (mortality and morbidity) of term and preterm neonates with thrombocytopenia in our hospital.
- To evaluate the role of neonatal thrombocytopenia as a prognostic indicator in NICU graduates.

MATERIAL & METHODS

Study Design: Prospective hospital based observational study.
Study Area: The Neonatal Intensive Care Unit, Department of Paediatrics, Alluri Sita Rama Raju Academy of Medical Sciences, Malkapuram, Eluru, West Godavari (dist.), Andhra Pradesh.
Study Period: June 2022- November 2022.
Study Population: All neonates with thrombocytopenia admitted to NICU
Sample size: Study consisted a total of 80 cases.
Inclusion criteria: All neonates born in our hospital and admitted to NICU with thrombocytopenia

Exclusion Criteria

1. Those neonates, with major congenital malformations.
2. Babies born outside our hospital and admitted to our NICU(extramural)
3. Maternal medications like aspirin, warfarin
4. Congenital cardiac malformations and surgical conditions in neonate

Ethical Consideration: Institutional Ethical committee permission was taken prior to the commencement of the study.

Study Tools And Data Collection Procedure

At admission the parents and/or the guardian were informed about the study and written consent was obtained. A detailed history inclusive of maternal and obstetric history, with a focus on history suggestive of a bleeding and its type in the newborn or the mother was obtained as per the proforma. Information regarding a number of conditions that have been implicated by past studies to be associated with neonatal thrombocytopenia was prospectively recorded e.g history of PIH, gestational diabetes mellitus, premature rupture of membranes, anemia, history of drug intake in the mother was asked for.

Gestational age of all neonates was determined based on the New Ballard's scoring. Growth assessment at birth or admission by recording birth weight to detect intrauterine growth restriction was based on Fenton intrauterine growth charts. All the neonates underwent necessary blood investigations as complete blood count, platelet count, blood culture and Septic screen.

Blood was collected in sterile EDTA bulbs by venepuncture after taking all aseptic precautions and transferred to Central Laboratory of our hospital, the time lag between collection and estimation was usually 10 to 15 minutes.

CBC was obtained from an automated haematology analyser. The automated haematology analyser used in our laboratory was sysmex kx-21. Blood cultures were done using standard laboratory methodology. Low platelet counts were cross verified by peripheral smear study. Quantitative determination of CRP was done by latex turbidimetry using SPINREACT CRP- TURBILATEX

A septic work up inclusive of absolute neutrophil count, total WBC count, micro ESR, C reactive protein was done on all patients. If any two of the above mentioned were positive then the neonate was labelled as having septicemia. In most of the cases with severe thrombocytopenia investigations such as prothrombin time (PT), aPTT were done by automated CL analyser. Platelet counts were repeated every 24 hours in babies with severe thrombocytopenia and every 48hrs in those with moderate thrombocytopenia.

All diagnoses were based on standard diagnostic criteria laid down in indexed medical literature. All the neonates were managed according to standard NICU protocol as per recent recommendations in the medical literature

Definition Of The Various Groups

- Group 1/mild thrombocytopenia: 1- 1.5 Lakh/
- Group 2/moderate thrombocytopenia:50,000 to 1 lakh
- Group 3/severe thrombocytopenia: less than 50,000

The pattern of onset of neonatal thrombocytopenia was classified as early if it developed less 72 hours of birth and late onset if presented after 72 hours. Maternal and neonatal risk factors were analysed with respect to severity of thrombocytopenia. The data so collected was recorded in the case proforma, tabulated and statistically analysed.

- **Statistical Analysis**
- Descriptive data was 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 <0.05 was considered significant.

OBSERVATIONS & RESULTS

Out of 80 newborns with thrombocytopenia admitted in our NICU were divided into 3 groups based on their platelet counts.

Table 1: Distribution Of Newborns In To 3 Groups According To Severity

Group	Severity	No. of cases	Percentage
Group 1	Mild	40	50%
Group 2	Moderate	28	35%
Group 3	Severe	12	15%

Out of 80 babies, 42 (52.5%) were male babies and 48 (47.5%) were females. We found a larger proportion of male babies (1.27:1 male to female ratio). Male gender was associated with moderate and severe thrombocytopenia, however it was statistically not significant (p value 0.23).

Table 2: Distribution Of Cases In Three Groups According To Their Maternal Risk Factors.

Maternal Risk Factors		Group 1	Group 2	Group 3	No. of cases	Chi Square Value, P Value
PIH	Yes	24	8	8	40	8.0762, 0.0176
	No	16	20	4	40	
Prom	Yes	9	8	7	24	5.6859, 0.0582
	No	31	20	5	56	
Oligohydramnios	Yes	1	3	1	5	2.0013, 0.3676
	No	39	25	11	75	
Eclampsia	Yes	1	2	1	4	1.0777, 0.5832
	No	39	26	11	76	
Anemia	Yes	5	4	1	10	0.2721, 0.8727
	No	35	24	11	70	

Among maternal risk factors, PIH was the commonest cause. 40 (50%) babies had PIH as the maternal risk factor followed by PROM in 24 (30%), anemia 10 (12%), oligohydramnios 5 (6%), eclampsia 4 (5%).

According to gestation, 36 (45%) were preterm and appropriate for gestation babies,11 (14%) preterm and small for gestation babies, 25 (36%) were full term and appropriate for gestation and 4(5%) were full term and small for gestation babies. Full term babies had moderate thrombocytopenia and preterm babies had severe neonatal thrombocytopenia which was statistically significant (P value 0.014)

Babies with low birth weight (<2.5 kg) constituted 49 (62%) of total babies and babies with birth weight ≥2.5 kg constituted 31 (38%) of total babies with neonatal thrombocytopenia. Low birth weight was significantly associated with moderate to severe thrombocytopenia (P value 0.007).

According to onset of neonatal thrombocytopenia, 34 (42%) babies had early onset neonatal thrombocytopenia and 46 (58%) babies had late onset neonatal thrombocytopenia. Late onset neonatal thrombocytopenia was more common and it was associated with moderate to severe neonatal thrombocytopenia, however it was statistically not significant (P value 0.958).

Table 3: Distribution Of Cases In Three Groups According To Their Neonatal Risk Factors.

Neonatal Risk Factors		Group 1	Group 2	Group 3	Total	Chi Square, P Value
Sepsis	Yes	12	22	10	44	20.279, 0.00039
	No	28	6	2	36	
NEC	Yes	1	2	2	5	3.2203, 0.1998
	No	39	26	10	75	
Birth Asphyxia	Yes	5	1	1	7	1.6476, 0.4387
	No	35	27	11	73	
RDS	Yes	10	1	1	12	6.8175, 0.033
	No	30	27	11	68	
MAS	Yes	5	1	2	8	2.1561, 0.3402
	No	35	27	10	72	

Among multiple neonatal risk factors, sepsis was the most common cause of neonatal thrombocytopenia and was found in 44(55%) babies, RDS 12 (15%), MAS 8 (10%), NEC 5 (6%), Birth asphyxia was present in 7 (9%), babies.

Sepsis was associated with severe neonatal thrombocytopenia and it was statistically significant (P value 0.0003). Birth asphyxia was associated with moderate neonatal thrombocytopenia however it was statistically not significant (P value 0.4).RDS was associated with mild to moderate neonatal thrombocytopenia and it was statistically significant (P value 0.033). Out of 44 babies with sepsis, 25 (57.14%) babies significantly had late onset neonatal thrombocytopenia (P value 0.007).

Table: 4 Correlation Of Neonatal Risk Factors With Outcome

Etiology	No. Of Cases	Deaths	Percentage
Sepsis	47	11	78%
Birth Asphyxia	7	1	7%
RDS	12	2	15%

The mortality was significantly high in severe thrombocytopenia as compared to other two groups.

The mortality was high in late onset thrombocytopenia as compared to early onset thrombocytopenia.

Out of 14 deaths, 11 (78%) due to sepsis followed by birth asphyxia 1 (7%) and RDS 2 (14%).Death due to sepsis was significantly high.

DISCUSSION

Neonatal thrombocytopenia (platelet count <1. 5 lacs/µl) is one of the commonest haematological abnormalities encountered in NICU and if it is not detected and managed properly can result in devastating complications.

The severity of neonatal thrombocytopenia in this study was mild in (50%), moderate in (35%) and severe in (15%). The results were similar to studies conducted by Meena SL et al,[7]Tirupati K et al,[8]Khalessi N et al,[9] and Ghamdi AM et al.[10]

The high prevalence of moderate and sever thrombocytopenia in this study was probably because of higher proportion of septicemic babies in our NICU which is a tertiary care

The high proportion of male babies (male: female ratio 1.2:1) with thrombocytopenia in this study is probably due to high incidence of sepsis among male babies. Meena SL et al,[7]Khalessi N et al,[9] Sheikh MA et al,[11] Chandra A et al,[12]Antoniette BWM et al,[13]Schuchat A et al,[14]and Kuruvilla KA et al,[15]noted that the incidence of neonatal sepsis was higher in males than female neonates.

This is probably due to the fact that the factors regulating the synthesis of gamma globulin are situated on the X- chromosome and male has only one X- chromosome.

In this study, PIH was the commonest maternal risk factor. 50% mother had PIH and it was associated with all type thrombocytopenia. Other maternal risk factors were PROM in 30%, anemia 12%, oligohydramnios in 6% and eclampsia in 5% babies. PROM in mother is a cause of early onset neonatal sepsis eventually leading to neonatal thrombocytopenia.

In present study, 33(42%) had early onset neonatal thrombocytopenia and 58% babies had late onset neonatal thrombocytopenia. Late onset neonatal thrombocytopenia was more common, and it was associated with moderate to severe neonatal thrombocytopenia. In studies conducted by Meena SL et al, Khalessi N et al, Eslami Z et al,[16]Ghamdi AM et al, show early onset thrombocytopenia was more common.

Late onset thrombocytopenia in our study is probably due to high incidence of sepsis

Among neonatal risk factors sepsis was the most common cause of neonatal thrombocytopenia which was found in 55% babies and was associated with severe neonatal thrombocytopenia. In studies conducted by Meena SL et al, Basil M et al,[17]and Gupta A et al, sepsis was associated with thrombocytopenia which was similar to this study

Septicemia leads to thrombocytopenia due to both decreased production and increased consumption of platelets and hence results usually in severe thrombocytopenia.

RDS was in 15%, birth asphyxia was present in 9% and MAS was in 10 %. Birth asphyxia was associated with mild to moderate thrombocytopenia. Instudy conducted by Meena SL et al, showed birth asphyxia was associated with mild to moderate thrombocytopenia whereas in studies conducted by Nandyal SS et al, and Gupta A et al, birth asphyxia was associated with severe thrombocytopenia.

In this study, sepsis was significantly associated with late onset thrombocytopenia and birth asphyxia was significantly associated with early onset neonatal thrombocytopenia which is similar to study conducted by Meena SL et al.

In Nandyal SS et al study, both sepsis and birth asphyxia were associated with late onset neonatal thrombocytopenia.

According to Murray NA et al, one of the most common causes of early onset thrombocytopenia in term neonates is perinatal asphyxia.

Neonates with birth asphyxia have impaired megakaryopoiesis and platelet production. In a recent Cochrane meta-analysis, therapeutic hypothermia was reported to increase the relative risk of thrombocytopenia in neonates with perinatal asphyxia

The overall mortality in thrombocytopenic babies in this study was 17.5%. Mortality in this study was more as compared to other studies. Mortality was high (40.82%) in late onset neonatal thrombocytopenia group, however it was statistically not significant

Out of 14 deaths due to sepsis were 11(78%) followed by RDS 2 (14%), birth asphyxia 1 (7.5%).

CONCLUSION

Neonatal thrombocytopenia is a treatable and reversible condition. Hence, it is important to identify neonates at risk and initiate transfusion therapy to prevent severe bleeding and potentially significant morbidity.

The severity of neonatal thrombocytopenia in the NICU was moderate to severe type. Late onset neonatal thrombocytopenia was more common than early onset neonatal thrombocytopenia.

Low birth weight babies were more prone to severe thrombocytopenia. Preterm babies had severe thrombocytopenia whereas term babies had moderate thrombocytopenia.

PIH and PROM were the commonest maternal risk factors. Sepsis and RDS were the commonest neonatal factors associated with thrombocytopenia. Sepsis was associated with late onset thrombocytopenia

Mortality was significantly high in babies with severe neonatal thrombocytopenia, in those with late onset neonatal thrombocytopenia and in cases where thrombocytopenia was due to sepsis.

Babies born to mothers with PIH and PROM and those with sepsis, birth asphyxia, and other risk factors should be closely monitored for thrombocytopenia and early intervention should be done.

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.

LIMITATIONS

Single centre study
Relatively smaller sample size

REFERENCES

1. Roberts I, Murray NA. Neonatal thrombocytopenia: causes and management. Arch Dis Childhood-Fetal Neonatal Ed. 2003;88(5):F359-64.
2. Roberts I, Murray NA. Neonatal thrombocytopenia: new insights into pathogenesis and implications for clinical management. Current Opinion Pediatr. 2001;13(1):16-21.
3. Gupta A, Mathai SS, Kanitkar M. Incidence of thrombocytopenia in neonatal intensive care unit. Med J Armed Forces India. 2011;67(3):234-6.
4. Sonam S. Nandyal, Shashikala P, Vidhushi Sahgal. Study of thrombocytopenia in neonatal intensive care unit. Ind J Pathology Oncol. 2016;3(1);55-9.
5. Israels SJ, Rand ML, Michelson AD. Neonatal platelet function. Semin ThrombHemost. 2003;29(4):363-72.
6. Nathan DG, Stuart HO, Look AT. Nathan and Oski's hematology of infancy and childhood. 6 th ed. Philadelphia: Saunders; 2003.
7. Meena SL, Singh K, Jain S, Jain A, Karnawat BS. Clinical profile and outcome of neonatal thrombocytopenia in a tertiary care hospital. Int J ContempPediatr 2019;6:1344-8.
8. Tirupathi K, Swarnkar K, Vagha J. Study of risk factors of neonatal thrombocytopenia. Int J ContempPediatr 2017;4:191-6
9. Khalessi N, Khosravi N, Sanni S. The prevalence and risk factors for neonatal thrombocytopenia amougnewbornsasmitted to intensive care unit of aliasghar children's hospital. Iran J Blood Cancer. 2013;5(2):41-5.
10. Ghamdi AM, Umran KA, Buali WA. A practical approach to assessment of neonatal thrombocytopenia in NICU. J Neonatal-Perinatal Med. 2008;1(3);175-80.
11. Younis S, Sheikh MA, Raza AA. Diagnostic accuracy of C-reactive protein in neonatal sepsis. J Biores Man. 2014;1(1):33-42.
12. Chandra A, Rao MN, Srinivas M, Shyamala S. Rapid diagnostic test in neonatal septicemia. Ind J Pediatr. 1988;55(6);947-53.
13. Antoniette BWM, Flora DIP. Clinical correlation of neonatal and maternal haematological parameters as predictors of neonatal sepsis. Pediatric infect Dis Soc Philippines J. 2005;9(2)36-43.
14. Schuchat A, Zywicki SS, Dinsmoor MJ. Mercer B, Romagurea J, O' Sullivan MJ. Risk factors and opportunities for the prevention of prevention of early onset neonatal sepsis: a multicentercasecontrol study. Paediatrics. 2000;105:21-6.
15. Kuruvilla KA, Pillai S, Jesudasan M, Jana AK. The bacterial profile of sepsis in a neonatal unit in south India. Ind Paediatr. 1998;35:851-8.
16. Eslami Z, Lookzadeh MH, Noorishadkam M, Hashemi A, Ghilian R, Dehghan PA. Thrombocytopenia and associated factors in neonates asmitted to NICU during years 2010-2011. Iran J Ped Hematol Oncol. 2013;3(1);205-15.
17. Basil M. Hanoudi CABP. Study of risk factors for neonatal thrombocytopenia in preterm infants. Mustansiriya Med J. 2015;14(1):64-9.