International Journal of Contemporary Pediatrics
Meena SL et al. Int J Contemp Pediatr. 2019 May;6(3):1344-1348
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: http://dx.doi.org/10.18203/2349-3291.ijcp20192041

Original Research Article

Clinical profile and outcome of neonatal thrombocytopenia in a tertiary care hospital

Sumarth Lal Meena, Kanwar Singh*, Sanjiv Jain, Anil Jain, B. S. Karnawat

Department of Pediatrics, JLN Medical College and Hospital, Ajmer, Rajasthan, India

Received: 13 March 2019
Accepted: 08 April 2019

***Correspondence:**
Dr. Kanwar Singh,
E-mail: dr_kanwarsingh@rediffmail.com

ABSTRACT

Background: Thrombocytopenia (platelet count <1,50,000/µL) is one of the most common haematological problems in neonatal intensive care units. In contrast, only 2% of the normal neonates are thrombocytopenic at birth with severe thrombocytopenia (platelet count <50,000/µL) occurring in less than 3/1000 term infants. Multiple disease processes can cause thrombocytopenia in neonates. 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. The aims and objective were to study the clinical profile, etiology and outcome of neonatal thrombocytopenia in a tertiary care hospital.
Methods: Prospective study involving 100 neonates with or developed neonatal thrombocytopenia in NICU.
Results: In present study, 100 new-borns with thrombocytopenia 46% were mild, 35% were moderate and 19% were severe thrombocytopenia. 51 (51%) had early onset neonatal thrombocytopenia and 49 (49%) babies had late onset neonatal thrombocytopenia. Anaemia was the dominant maternal predisposing risk factor. Sepsis was the most common cause of neonatal thrombocytopenia. Most common symptom was apnoea. Sepsis, RDS and NEC had significantly contributed to mortality. Most common cause of death was sepsis followed by RDS and NEC.
Conclusions: 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. Anaemia and PROM were the commonest maternal risk factors. Therefore, author recommended that babies born to mothers with these risk factors should be closely monitored for thrombocytopenia.

Keywords: Bleeding, Maternal anaemia, Neonatal thrombocytopenia, Sepsis

INTRODUCTION

Thrombocytopenia (platelet count <1,50,000/µL) is one of the most common haematological problems in Neonatal intensive care units (NICUs).[1] The overall prevalence of thrombocytopenia in neonatal ranges from 1 to 5% and is reported to be much higher in neonates admitted to neonatal intensive care units, ranging from 18 to 35%.[1] It is more common among extremely low birth weight neonates (ELBW <1000 gms birth weight) or preterm babies (GA <36 weeks) or sick neonates in NICUs.[1] In contrast, only 2% of the normal neonates are thrombocytopenic at birth with severe thrombocytopenia (platelet count <50,000/µL) occurring in less than 3/1000 term infants.[2]

Multiple disease processes can cause thrombocytopenia in neonates and these can be classified as early onset (<72

hours) and late onset (>72 hours) neonatal thrombocytopenia.[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]

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]

Considerable number of studies have shown that the average fetal platelet count is above 150,000/µL by second trimester of pregnancy and remain constant then represents thrombocytopenia just as in older children and adults. Neonatal thrombocytopenia classifies into mild (>1,00,000/µl and <1.50,000/µl), moderate (>50,000/µl) and severe (<50,000 µl).[1,2]

The paucity of studies from India and the increasing prevalence of this condition in the NICU, instigated us to determine the etiology, clinical profile and immediate outcome of the neonates with thrombocytopenia admitted in JLN Medical College and Hospital, Ajmer, Rajasthan, India.

METHODS

Prospective study involving 100 neonates with or developed neonatal thrombocytopenia randomly selected in the Neonatal intensive care unit (NICU), Department of Pediatrics, JLN Hospital and NICU of Government Mahila Hospital attached to JLN Medical College, Ajmer, Rajasthan, India from May 2017 to April 2018. Ethical clearance was obtained before starting study.

A detailed history inclusive of maternal obstetric history, birth history, perinatal events with a focus on history suggestive of bleeding and its type in the newborn was obtained as per the proforma.

Information regarding a number of conditions that have been associated with neonatal thrombocytopenia was prospectively recorded e.g., history of PIH, gestational diabetes mellitus, premature rupture of membranes, anaemia and SLE. Any consumption of drugs by the mother that can predispose to neonatal thrombocytopenia was also documented. Gestational age of all neonates was determined based on the New Ballard's scoring system till 14 days of life. All the neonates underwent blood investigations, CBC by automated haematology analyzer, peripheral blood smear study, blood culture, sepsis screen (total WBC count, absolute neutrophil count, IT ratio, micro ESR by done using micro pipette and CRP done by latex turbidimetry). Low platelet counts were cross verified by peripheral smear study.

Platelet counts were repeated every 24 hours in babies with severe thrombocytopenia and every 48 hours in those with moderate thrombocytopenia. PT and APTT were obtained by automated CL analyzer. Other investigations such as urine culture, chest X-ray, neurosonogram and CT brain were performed whenever the need arises.

The data was recorded in the case proforma and tabulated. Statistical analysis was done using chi square test, one-way ANOVA test, students t-test. Software used for analysis was SPSS 17.0 version, Graph pad prism 6 version and EPI-INFO 6 version. 'P' value below 0.05 was considered significant.

RESULTS

The study was conducted on 100 newborns with thrombocytopenia admitted in the NICU and subjects were divided into 3 groups based on their platelet counts. 46 (46%) patients had mild thrombocytopenia, 35 (35%) babies had moderate and 19 (19%) babies had severe thrombocytopenia (Table 1).

Table 1: Distribution of babies in to 3 groups according to severity.

Groups	Severity	N=100	%
Group 1	Mild (1-<1.5 lacs/µl)	46	46%
Group 2	Moderate (50,000-<1 lacs/µl)	35	35%
Group 3	Severe (<50,000/µl)	19	19%

Male and female's ratio was 1.7 to 1.0. Low birth weight (<2.5 kg) constituted 66 (66%) of total babies with neonatal thrombocytopenia.

According to gestation, 27 (27%) preterm were appropriate for gestational age and 36 (36%) preterm were small for gestational age. 35 (35%) full term were appropriate for gestational age and 2 (2%) full term were small for gestational age. Thrombocytopenia in pre term was statistically significant (P value <0.05).

The most common maternal risk factor was anaemia which was present in 48 (48%) babies followed by PROM 30 (30%), PIH 19 (19%), oligohydramnios 2 (2%) babies and eclampsia in 2 (2%) babies. Out of these risk factors, association of anaemia with severe neonatal thrombocytopenia was statistically significant (P value <0.05) (Table 2).

About 51 (51%) babies had early onset neonatal thrombocytopenia and 49 (49%) babies had late onset neonatal thrombocytopenia. Early onset neonatal

thrombocytopenia was more common, and it was associated with mild to moderate neonatal thrombocytopenia, it was statically significant (P value 0.00001).

Table 2: Distribution of patients in three group according to their maternal risk factors.

Maternal factors		Group			Total	X^2 value	P value
		Group 1	Group 2	Group 3			
PIH	Yes	9	9	1	19	3.3644	0.1859
	No	37	26	18	81		
Eclampsia	Yes	0	2	0	2		
	No	46	33	19	98		
PROM	Yes	11	10	9	30	3.574	0.1673
	No	35	25	10	70		
Anaemia	Yes	26	11	11	48	5.9944	< 0.05
	No	20	24	8	52		
Oligohydroamnios	Yes	1	1	0	2		
	No	45	34	19	98		

Sepsis was the commonest cause of neonatal thrombocytopenia and was found in 53 (53%) babies. RDS in 15 (15%), Birth asphyxia was present in 11 (11%) babies, MAS in 10 (10%) babies, neonatal hyperbilirubinemia in 6 (6%) babies and NEC in 5 (5%).

Sepsis was associated with severe neonatal thrombocytopenia and it was statistically significant (P value 0.0001). Out of 53 babies with sepsis, 36 (67.92%) babies had late onset thrombocytopenia and it was statically significant (P value 0.00003) (Table 3).

Table 3: Distribution of patients in three group according to their etiology (neonatal factors).

Etiology		Group			Total	X^2 value	P value
		Group 1	Group 2	Group 3			
Sepsis	Yes	14	24	15	53	17.94	0.0001
	No	32	11	4	47		
Birth Asphyxia	Yes	7	3	1	11	1.6853	0.4305
	No	39	32	18	89		
RDS	Yes	13	2	0	15		
	No	33	33	19	85		
Neonatal hyperbilirubinemia	Yes	4	1	1	6	1.223	0.5422
	No	42	34	18	94		
MAS	Yes	7	3	0	10		
	No	49	32	19	90		
NEC	Yes	1	2	2	5	2.03	0.361
	No	45	33	17	95		

The most common symptom of thrombocytopenia was apnoea in 28 (28%) followed by lethargy in 24 (24%), feeding difficulty in 23 (23%) and convulsions in 20 (20%) babies. All the above symptoms were predominantly present in moderate and severe neonatal thrombocytopenia.

In this study, 22 (22%) presented with peteciae/purpura, 17% with GI bleeding and 2% babies with pulmonary bleeding. Peteciae/purpura is statistically significant (P value 0.000735).

PT INR, appt was done in 36 and it was abnormal in 17 (47.22%) babies. This was statically significant (P value 0.05).

Blood transfusion was given in 5 (5%), platelet transfusion in 13 (13%) and FFP in 27 (27%) babies.

The mortality was significantly high in severe thrombocytopenia group (47.37%) as compared to other 2 groups and it was not statistically significant (p value 0.2286). The mortality was high in late onset neonatal thrombocytopenia group (40.82%) as compared to early onset neonatal thrombocytopenia group (27.45%) but it was statistically not significant. Out of 34 deaths, 23 (67.64%) due to sepsis followed by NEC 3 (8.82%), RDS 3 (8.82%), MAS 2 (5.88%), birth asphyxia 2 (5.88%) and neonatal hyperbilirubinemia 1 (2.9%). Death due to sepsis was significantly high (Table 4).

Table 4: Correlation of etiology with outcome.

Etiology	No. of cases	No. of deaths	%
Sepsis	53	23	67.64%
Birth Asphyxia	11	2	5.88%
RDS	15	3	8.82%
Neonatal hyperbilirubinemia	6	1	2.9%
MAS	10	2	5.88%
NEC	5	3	8.82%

DISCUSSION

Neonatal thrombocytopenia (platelet count <1.5 lacs/µl) is one of the commonest haematological abnormality 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 (46%), moderate in (35%) and severe in (19%). The results were similar to studies conducted by Khalessi N et al, and Ghamdi AM et al.[7,8] 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 centre.

The high proportion of male babies (male: female ratio 1.7:1) with thrombocytopenia in this study is probably due to high incidence of sepsis among male babies. Khalessi N et al, Sheikh MA et al, Chandra A et al, Antoniette BWM et al, Schuchat A et al, and Kuruvilla KA et al, 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- chromosone and male has only one X- chromosone.[8-12]

In this study, anaemia was the commonest maternal risk factor. 48% mother had anaemia and it was associated with all type thrombocytopenia. Other maternal risk factors were PROM in 30%, PIH 19%, oligohydramnios in 2% and eclampsia in 2% babies. All these risk factors were associated with severe thrombocytopenia. Among all these factors, association of anaemia with severe neonatal thrombocytopenia was statistically significant (P value <0.05). In a study conducted by Tirupath K et al, an association has been documented between anaemia and thrombocytopenia. PROM in mother is a cause of early onset neonatal sepsis eventually leading to neonatal thrombocytopenia.[14]

In present study, 51% had early onset neonatal thrombocytopenia and 49% babies had late onset neonatal thrombocytopenia. Early onset neonatal thrombocytopenia was more common, and it was associated with mild to moderate neonatal thrombocytopenia. In studies conducted by Khalessi N et al, Eslami Z et al, Ghamdi AM et al, show early onset thrombocytopenia was more common. Authors also found early onset thrombocytopenia was more common.[7,8,15]

Among neonatal risk factors sepsis was the most common cause of neonatal thrombocytopenia which was found in 53% babies and was associated with severe neonatal thrombocytopenia. In studies conducted by Basil M et al, and Gupta A et al, sepsis was associated with thrombocytopenia which was similar to this study.[3,16] Septicaemia 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 11%, MAS in 10% and neonatal hyper bilirubinemia in 6% babies. Birth asphyxia was associated with mild to moderate thrombocytopenia. In studies conducted by Nandyal SS et al, and Gupta A et al, birth asphyxia was associated with severe thrombocytopenia.[3,4]

In this study, sepsis was significantly associated with late onset thrombocytopenia and birth asphyxia was significantly associated with early onset neonatal thrombocytopenia.

In Nandyal SS et al study, both sepsis and birth asphyxia were associated with late onset neonatal thrombocytopenia.[4] According to Murray NA et al, one of the most common causes of early onset thrombocytopenia in term neonates is perinatal asphyxia.[1] 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.

Blood transfusion was given in 5%, platelet transfusion in 13% and FFP in 27% babies. Severe neonatal thrombocytopenia required platelet and FFP transfusion.

The overall mortality in thrombocytopenic babies in this study was 34%. 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 34, deaths due to sepsis were 23 (43.40%) followed by NEC 3 (60%), RDS 3 (20%), MAS 2 (20%), birth asphyxia 2 (18.18%) and neonatal hyperbilirubinemia 1 (16.67%).

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. Anaemia and PROM were the commonest maternal risk factors. Therefore, authors recommended that babies born to mothers with these risk factors should be closely monitored for thrombocytopenia.

Sepsis and RDS were the commonest neonatal factors associated with thrombocytopenia. Sepsis was associated with late onset thrombocytopenia and RDS was associated with early onset thrombocytopenia. The most common symptom in all forms of thrombocytopenia was apnoea. The most common sign was cutaneous bleeding (petechiae/purpura). Mortality was significantly high in babies with severe neonatal thrombocytopenia, in those with early onset neonatal thrombocytopenia and in cases where thrombocytopenia was due to sepsis and birth asphyxia.

Severe thrombocytopenia can be used as a prognostic indicator in sick neonates. But to generalize this statement and apply to all neonatal admission, more studies are required in this regard with similar results.

ACKNOWLEDGEMENTS

Authors would like to thank all newborn's parents and hospital staff who provide unconditional support during study.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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 Thromb Hemost. 2003;29(4):363-72.
6. Nathan DG, Stuart HO, Look AT. Nathan and Oski's hematology of infancy and childhood. 6th ed. Philadelphia: Saunders; 2003.
7. 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.
8. Khalessi N, Khosravi N, Sanni S. The prevalence and risk factors for neonatal thrombocytopenia amoug newborns asmitted to intensive care unit of aliasghar children's hospital. Iran J Blood Cancer. 2013;5(2):41-5.
9. Younis S, Sheikh MA, Raza AA. Diagnostic accuracy of C-reactive protein in neonatal sepsis. J Biores Man. 2014;1(1):33-42.
10. Chandra A, Rao MN, Srinivas M, Shyamala S. Rapid diagnostic test in neonatal septicemia. Ind J Pediatr. 1988;55(6);947-53.
11. 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.
12. 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 multicenter case-control study. Paediatrics. 2000;105:21-6.
13. 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.
14. Tirupathi K, Swarnkar K, Vagha J. Study of risk factors of neonatal thrombocytopenia. Int J Contemp Pedaitr. 2017;4:191-6.
15. 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.
16. Basil M. Hanoudi CABP. Study of risk factors for neonatal thrombocytopenia in preterm infants. Mustansiriya Med J. 2015;14(1):64-9.

Cite this article as: 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.