Original Research Article

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

Purushottam Rathi

Associate Professor, Department of Pediatrics, SBH Government Medical College, Chakkarbardi, Dhule, INDIA.
Email: drpprathi@gmail.com

Abstract

Background: Neonatal thrombocytopenia is a significant cause of morbidity and mortality particularly in the sick newborns, premature babies and neonates admitted in neonatal intensive care units and usually indicate an underlying pathologic process. 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. Present study was undertaken to determine the etiology, clinical profile and outcome of the neonates with thrombocytopenia admitted in our tertiary care hospital. **Material and Methods:** Present study was prospective, observational study conducted in Neonatal intensive care unit (NICU), in neonates with or developed neonatal thrombocytopenia (platelet count <1.5lakhs/µl). **Results:** In present study total 204 neonates, fulfilling inclusion and exclusion criteria were admitted in NICU. Incidence of thrombocytopenia (platelets < 1.5 lacs/µl)) in NICU admissions was 27.2 %. In present study 45% neonates were preterm (less than 37 weeks) and 55 % were term. According to birth weight 14% neonates were very low birth weight (less than 1000 gms), 46% were low birth weight (1001-2500 gms) and rest 41 % had birthweight > 2500 gms. In present study prematurity (45 %) was most common cause noted for neonatal thrombocytopenia, followed by sepsis (24 %) and respiratory distress (14 %). Depending on the grade of thrombocytopenia neonates with mild thrombocytopenia (1-<1.5 lacs/µl) were 30%, while Moderate thrombocytopenia (50,000-<1 lacs/µl) were 25% and severe thrombocytopenia (<50,000/µl) were 45%. Depending on the time of onset of thrombocytopenia, neonates were labelled as early onset (within 72 hours) and late onset (after 72 hours). Early onset (within 72 hours) were 56% and late onset (after 72 hours) were 44%. In present study 53 (26%) neonatal deaths were noted in neonates with thrombocytopenia. Sepsis (60%), prematurity (13%), birth asphyxia (11%) and respiratory distress (8%) were common causes of death neonates with thrombocytopenia. Sepsis along with thrombocytopenia noted with poor outcome in present study. **Conclusion:** Prematurity, sepsis and perinatal asphyxia are common causes of neonatal thrombocytopenia and associated mortality. Severe thrombocytopenia, sepsis, prematurity were found to be an independent risk factor for poor outcome in NICU admitted neonates.

Key Words: neonatal thrombocytopenia, septicemia, prematurity, neonatal mortality.

Address for Correspondence:
Dr Purushottam Rathi, Associate Professor, Department of Pediatrics, SBH Government Medical College, Chakkarbardi, Dhule, INDIA.
Email: drpprathi@gmail.com
Received Date: 06/01/2020 Revised Date: 30/01/2020 Accepted Date: 12/02/2020
DOI: https://doi.org/10.26611/10141713

Access this article online	
Quick Response Code:	Website: www.medpulse.in
	Accessed Date: 10 January 2021

INTRODUCTION

Neonatal thrombocytopenia is a significant cause of morbidity and mortality particularly in the sick newborns, premature babies and neonates admitted in neonatal intensive care units and usually indicate an underlying pathologic process. 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.[1] Multiple disease processes can cause thrombocytopenia in neonates and these can be

How to cite this article: Purushottam Rathi. Clinical profile and outcome of neonatal thrombocytopenia in a tertiary care hospital. *MedPulse International Journal of Pediatrics.* January 2021; 17(1): 10-14. http://medpulse.in/Pediatrics/index.php

classified as early onset (<72 hours) and late onset (>72 hours) neonatal thrombocytopenia.[2] Early onset neonatal thrombocytopenia has a benign course and predictable outcome. Whereas late onset is more severe.[3] Thrombocytopenia (platelet count (<1.5lakhs/µl) is one of the most common haematological problems in NICU with 18-35% of neonates developing this problem.[4] The overall prevalence of thrombocytopenia in neonates ranges from 1 to 5% and is reported to be much higher in neonates admitted to neonatal intensive care units, ranging from 22 to 35%.[5] The evaluation and management of neonatal thrombocytopenia is a frequent challenge for neonatologists since one out of each four neonates develops thrombocytopenia at some point of hospital stay.[6] Present study was undertaken to determine the etiology, clinical profile and outcome of the neonates with thrombocytopenia admitted in our tertiary care hospital.

MATERIAL AND METHODS

Present study was prospective, observational study Neonatal intensive care unit (NICU), D Department of Pediatrics, SBH Government Medical College, Chakkarbardi from January 2019 to December 2019 (1 year). Institutional ethical committee clearance was obtained for present study.

Inclusion criteria

Neonates with or developed neonatal thrombocytopenia (platelet count <1.5lakhs/µl).

Exclusion criteria

MOTHER with History s/o ITP, SLE / other autoimmune disorders, on medication during pregnancy (sulfonamides, quinine / quinidine) (thiazides, tolbutamide, vancomycin, hydralazine, and heparin). Neonate with history suggestive of bleeding disorder in family, trisomies, Turner /Noonan's syndromes, RVT, CHD, Congenital leukemia. Conditions associated with sequestration of platelets (Kasabach - merritt syndrome with giant haemangiomas, renal vein thrombosis, polycythemia, CCHD, placental vascular thrombi – PIH /preeclampsia /eclampsia). Massive bleed from causes like birth trauma, accidental slipping of cord clamp causing hemodynamic disturbance/exchange transfusion (dilutional NNT). Sick neonate with. Neonate who received IV antibiotics for ≥ 48 hrs prior to our study.

A written, informed consent was taken from parents/guardians before participation. A detailed history inclusive of maternal obstetric history (history of PIH, gestational diabetes mellitus, premature rupture of membranes, anaemia and SLE.), birth history, perinatal events with a focus on history suggestive of bleeding and its type in the newborn was obtained as per the proforma. 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 analyser, 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 analyser. Other investigations such as urine culture, chest X-ray, neurosonogram and CT brain were performed whenever the need arises. Neonatal details such as clinical symptoms, diagnosis, platelet count and other relevant investigations, duration of the stay and outcome were documented. Follow up was kept till neonatal period. Relevant data was entered in a proforma and analyzed. Statistical analysis was done by chi square test, continuous variables were analyzed using unpaired two tailed student t test or by one-way analysis of variance.

RESULTS

In present study total 204 neonates, fulfilling inclusion and exclusion criteria were admitted in NICU. Incidence of thrombocytopenia (platelets < 1.5 lacs/µl)) in NICU admissions was 27.2 %. Male neonates (59%) were more than female neonates (41%) . In present study 45% neonates were preterm (less than 37 weeks) and 55 % were term. According to birth weight 14% neonates were very low birth weight (less than 1000 gms), 46% were low birth weight (1001-2500 gms) and rest 41 % had birthweight > 2500 gms.

Table 1: Distribution according to gestational age and birth weight

	VLBW	LBW	BW > 2500 gm	
Pre-term	28 (14%)	42 (21%)	22 (11%)	92 (45%)
Term	0	51 (25%)	61 (30%)	112 (55%)

In present study prematurity (45 %) was most common cause noted for neonatal thrombocytopenia, followed by sepsis (24 %) and respiratory distress (14 %). Depending on the grade of thrombocytopenia neonates with mild thrombocytopenia (1-<1.5 lacs/µl) were 30%, while Moderate thrombocytopenia (50,000-<1 lacs/µl) were 25% and severe thrombocytopenia (<50,000/µl) were 45%.

Table 2: Distribution of neonates depending on the grade of thrombocytopenia

Etiology	Mild thrombocytopenia (1-<1.5 lacs/µl)	Moderate thrombocytopenia (50,000-<1 lacs/µl)	Severe thrombocytopenia (<50,000/µl)	Total
Prematurity	31 (15%)	20 (10%)	41 (20%)	92 (45%)
Sepsis	9 (4%)	11 (5%)	29 (14%)	49 (24%)
Respiratory distress	8 (4%)	9 (4%)	11 (14%)	28 (14%)
Intra uterine growth retardation	7 (3%)	6 (3%)	3 (1%)	16 (8%)
Birth asphyxia	4 (2%)	2 (1%)	3 (1%)	9 (4%)
Meconium aspiration syndrome	1 (0%)	2 (1%)	2 (1%)	5 (2%)
Jaundice	1 (0%)	1 (0%)	3 (1%)	5 (2%)
Total	61 (30%)	51 (25%)	92 (45%)	204

Depending on the time of onset of thrombocytopenia, neonates were labelled as early onset (within 72 hours) and late onset (after 72 hours). Early onset (within 72 hours) were 56% and late onset (after 72 hours) were 44%. Prematurity, sepsis, respiratory distress and intra uterine growth retardation were common causes for both early onset and late onset thrombocytopenia.

Table 3: Distribution of neonates depending on the time of onset

Neonatal factors	Early onset thrombocytopenia (< 72 hours)	Late onset thrombocytopenia (> 72 hours)	Total
Prematurity	53 (26%)	39 (18%)	92 (45%)
Sepsis	17 (8%)	32 (16%)	49 (24%)
Respiratory distress	19 (9%)	9 (4%)	28 (14%)
Intra uterine growth retardation	11 (5%)	5 (2%)	16 (8%)
Birth asphyxia	8 (4%)	1 (0%)	9 (4%)
Meconium aspiration syndrome	1 (0%)	4 (2%)	5 (2%)
Jaundice	1 (0%)	4 (2%)	5 (2%)
Total	115 (56%)	89 (44%)	204

Anaemia (Hb < 7 gm%) (16%), Hypertensive diseases of pregnancy (14%), Eclampsia (4%), Prolonged rupture of membranes (> 18 hours) (3%) and Oligohydramnios (2%) were common maternal high-risk factors associated with neonatal thrombocytopenia.

Table 4: Distribution of neonates according to their maternal risk factors.

Maternal risk factors	Mild thrombocytopenia (1-<1.5 lacs/µl)	Moderate thrombocytopenia (50,000-<1 lacs/µl)	Severe thrombocytopenia (<50,000/µl)	Total
Anaemia (Hb < 7 gm%)	11 (5%)	13 (6%)	9 (4%)	33 (16%)
Hypertensive diseases of pregnancy	13 (6%)	9 (4%)	6 (3%)	28 (14%)
Eclampsia	2 (1%)	3 (1%)	3 (1%)	8 (4%)
PROM	1 (0%)	3 (1%)	3 (1%)	7 (3%)
Oligohydramnios	1 (0%)	1 (0%)	3 (1%)	5 (2%)

In present study 53 (26%) neonatal deaths were noted in neonates with thrombocytopenia. Sepsis (60%), prematurity (13%), birth asphyxia (11%) and respiratory distress (8%) were common causes of death neonates with thrombocytopenia. Sepsis along with thrombocytopenia noted with poor outcome in present study.

Table 5: Neonatal etiology with outcome.

Neonatal factors	Total cases (n=204)	No. of deaths (n=53)
Sepsis	49 (24%)	32 (60%)
Prematurity	92 (45%)	7 (13%)
Birth asphyxia	9 (4%)	6 (11%)
Respiratory distress	28 (14%)	4 (8%)
Intra uterine growth retardation	16 (8%)	2 (4%)
Meconium aspiration syndrome	5 (2%)	1 (0%)
Jaundice	5 (2%)	1 (0%)
Total	**204**	**53**

DISCUSSION

Neonatal thrombocytopenia is a common clinical problem and is a prognostic marker of many disease conditions in neonates. Platelets appear in fetal circulation as early as 5 weeks of gestation. It reaches an adult value of 150 000 to 450 000/ μL by the second trimester and remains constant throughout life. Despite the general acceptance of neonatal platelet counts of $<50X10^9$/L as an indicator for special clinical attention, the correlation between the severity of thrombocytopenia and risk of bleeding remains unclear.[4] In our study the prevalence of thrombocytopenia is 27.2% which is less than in study done by Gupta *et al.* (70.5%).[2] The leading causes of neonatal thrombocytopenia include prematurity, sepsis, respiratory distress syndrome, birth asphyxia, meconium aspiration syndrome, and hyperbilirubinemia, among which sepsis and prematurity contribute to a significant number of severe thrombocytopenia. In present study prematurity (45 %) was most common cause noted for neonatal thrombocytopenia, followed by sepsis (24 %) and respiratory distress (14 %). Among preterm born infants admitted to the NICU, lower gestational age, SGA birth weight, hypoxia at birth, and age greater than 72 hours are major factors that increase the risk for the development of severe thrombocytopenia, which is also associated with NEC and culture proven sepsis, especially that caused by Candida infection.[7,8] Neonatal sepsis (24 %) was found to be second common cause in the present study. Gupta *et al*.[2] and Khalessi *et al*.[6] found sepsis to be the most common cause of neonatal thrombocytopenia with a proportion of 42% and 24.1% respectively. Septicemia leads to thrombocytopenia because of both decreased production and increased consumption of platelets, thereby resulting usually in severe thrombocytopenia.[2] The cause of sepsis is mainly infections which could be bacterial, viral or fungal. The pathogenesis for thrombocytopenia in sepsis is endothelial damage which accelerates platelet consumption, impaired platelet production and their sequestration in the enlarged spleen.[9] It is estimated that up to 20% of neonates develop sepsis and approximately 1% die of sepsis related causes[2]. Sepsis related mortality is largely preventable with rational antimicrobial therapy and aggressive supportive care. Respiratory distress and birth asphyxia accounted for 18% cases in present study. Perinatal asphyxia is reported to be widely associated with neonatal thrombocytopenia. Sharma and Thapar demonstrated that perinatal asphyxia was significantly associated with thrombocytopenia.[10] New-borns with respiratory distress and birth asphyxia also develop thrombocytopenia because of hypoxic injury caused to neonatal megakaryocytes.[11] In present study neonatal thrombocytopenia cases with early onset (within 72 hours) were 56% and late onset (after 72 hours) were 44%. While another study demonstrated, that neonatal thrombocytopenia was 43.4% in early onset group and 56.5% in late onset group, majority of the severity of the thrombocytopenic infants presented only after 72 hours of life and the most common etiology was the late onset of sepsis.[12] In present study, sepsis was significantly associated with late onset thrombocytopenia and prematurity, birth asphyxia was significantly associated with early onset neonatal thrombocytopenia. In Sonam S *et al.* study, both sepsis and birth asphyxia were associated with late onset neonatal thrombocytopenia.[1] Depending on the grade of thrombocytopenia neonates with mild thrombocytopenia were 30%, while moderate thrombocytopenia were 25% and severe thrombocytopenia were 45%. Sonam *et al*..[1] had shown severe thrombocytopenia to be found in 65.6% of infants in their study. The proportion of severe thrombocytopenia in present study are less than above study, because of a higher contribution of prematurity and septicemia in admission cases, more cases with severe thrombocytopenia in above study. The predisposing factors associated with neonatal thrombocytopenia were maternal PIH, maternal drug intake, septicemia, necrotizing enterocolitis, and perinatal asphyxia. In present study 26% neonatal deaths were noted in neonates with thrombocytopenia. Sepsis (60%), prematurity (13%), birth asphyxia (11%) and respiratory distress (8%) were common causes neonatal mortality. Sepsis along with thrombocytopenia noted with poor outcome in present study. Thrombocytopenia has been reported as an independent risk factor for sepsis related death among neonates.[13] Increased platelets destruction, an impaired platelet production or a combination may be the underlying mechanism of thrombocytopenia. [14]

CONCLUSION

Prematurity, sepsis and perinatal asphyxia are common causes of neonatal thrombocytopenia and associated mortality. All these are preventable conditions. Early identification and management is must to reduce mortality and morbidity. Severe thrombocytopenia, sepsis, prematurity were found to be an independent risk factor for poor outcome in NICU admitted neonates.

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Source of Support: None Declared
Conflict of Interest: None Declared