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Original Research Article

Clinico-Etiologic Spectrum and Outcome of Neonatal Thrombocytopenia: an Observational Study

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Abstract

Aim: The aim of the present study was to determine the etiology, clinical profile and outcome of the neonates with thrombocytopenia admitted in the tertiary care hospital.

Methods: The present study was prospective, observational study Neonatal intensive care unit (NICU), Department of Pediatrics, Nalanda Medical College and Hospital, Patna, Bihar, India for the period of six months . In present study total 200 neonates, fulfilling inclusion and exclusion criteria were admitted in NICU.

Results: According to birth weight 27 neonates were very low birth weight (less than 1000 gms), 42 were low birth weight (1001-2500 gms) and rest 21 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 29%, while Moderate thrombocytopenia (50,000-<1 lacs/µl) were 25% and severe thrombocytopenia (<50,000/µl) were 46%. 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) was 55% and late onset (after 72 hours) was 45%. Prematurity, sepsis, respiratory distress and intra uterine growth retardation were common causes for both early onset and late onset thrombocytopenia. 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.

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.

Keywords: neonatal thrombocytopenia, septicemia, prematurity, neonatal mortality

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]

Thrombocytopenia is one of the frequent and universal hematopoietic entities found in neonates in the neonatal intensive care unit (NICU).[7] Neonatal thrombocytopenia is characterized by a platelet count of <150×109/L in any neonate of viable gestational age. The incidence of thrombocytopenia in newborns is 1%-5% at birth, while severe thrombocytopenia exists in 0.1%-0.5% of neonates. [7] The incidence of thrombocytopenia is inversely proportional to the gestational age and birth weight of a newborn. Most of the neonates in NICU manifest mild (100-150×109/L) to moderate (50-99×109/L) thrombocytepenia, while in about 20% of neonates, severe thrombocytopenia (<50×109/L) is seen. Neonates are more predisposed to develop thrombocytopenia in response to illness, which may be because of the limited ability of the neonatal megakaryopoietic axis to increase the production of platelets in response to platelet consumption. [8]

The causative factors responsible for early-onset thrombocytopenia (first 72 hours of life) are different from those of late-onset thrombocytopenia (after 72 hours of life). [9] Most of the episodes of neonatal thrombocytopenia are relatively self-resolving and mild, and they last for a shorter duration. However, sometimes, it may cause morbidity and mortality because of serious complications such as intraventricular hemorrhage (IVH). [10] The incidence of IVH was as high as 60% in neonates with severe thrombocytopenia, and mortality was directly proportional to the severity of thrombocytopenia. Since the etiology determines the clinical course and outcome, early identification and appropriate diagnostic evaluation are essential for the improved survival of the neonates. [10]

The aim of the present study was to determine the etiology, clinical profile and outcome of the neonates with thrombocytopenia admitted in the tertiary care hospital.

Materials and Methods

The present study was prospective, observational study Neonatal intensive care unit (NICU), Department of Pediatrics, Nalanda Medical College and Hospital, Patna, Bihar, India for the period of six months.In present study total 200 neonates, fulfilling inclusion and exclusion criteria were admitted in NICU.

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

Table 1: Distribution according to gestational age and birth weight

	VLBW (less than 1000 gms)	LBW (1001-2500 gms)	BW > 2500 gm	Total
Pre-term	27	42	21	90 (45%)
Term	0	50	60	110 (55%)

According to birth weight 27 neonates were very low birth weight (less than 1000 gms), 42 were low birth weight (1001-2500 gms) and rest 21 had birthweight > 2500 gms.

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	30	20	40	90 (45%)
Sepsis	8	10	30	48 (24%)
Respiratory distress	7	9	12	28 (14%)
Intra uterine growth retardation	7	6	3	16 (8%)
Birth asphyxia	4	3	3	10 (5%)
Meconium aspiration syndrome	1	1	2	4 (2%)
Jaundice	1	1	2	4 (2%)
Total	58	50	92	200

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 29%, while Moderate thrombocytopenia (50,000-<1 lacs/µl) were 25% and severe thrombocytopenia (<50,000/µl) were 46%.

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	52	38	90 (45%)
Sepsis	16	32	48 (24%)
Respiratory distress	18	10	28 (14%)
Intra uterine growth retardation	10	6	16 (8%)
Birth asphyxia	8	2	10 (5%)
Meconium aspiration syndrome	1	3	4 (2%)
Jaundice	1	3	4 (2%)
Total	110 (55%)	90 (45%)	200

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) was 55% and late onset (after 72 hours) was 45%. Prematurity, sepsis, respiratory distress and intra uterine growth retardation were common causes for both early onset and late onset 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%)	10	12	10	32 (16%)
Hypertensive diseases of pregnancy	12	10	8	28 (14%)
Eclampsia	2	3	3	8 (4%)
PROM	1	2	3	6 (3%)
Oligohydramnios	1	1	2	4 (2%)

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 5: Neonatal etiology with outcome

Neonatal factors	Total cases (n=200)	No. of deaths (n=50)
Sepsis	48 (24%)	30 (60%)
Prematurity	90 (45%)	6 (12%)
Birth asphyxia	8 (4%)	6 (12%)
Respiratory distress	28 (14%)	4 (8%)
Intra uterine growth retardation	18 (9%)	2 (4%)
Meconium aspiration syndrome	4 (2%)	1 (2%)
Jaundice	4 (2%)	1 (2%)
Total	**200**	**50**

In present study 50 (25%) neonatal deaths were noted in neonates with thrombocytopenia. Sepsis (60%), prematurity (12%), birth asphyxia (12%) and respiratory distress (8%) were common causes of death neonates with thrombocytopenia. Sepsis along with thrombocytopenia noted with poor outcome in present study.

Discussion

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. [11] 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. [12] Early onset neonatal thrombocytopenia has a benign course and predictable outcome. Whereas late onset is more severe. [13] Thrombocytopenia (platelet count (<1.5lakhs/µl) is one of the most common haematological problems in NICU with 18-35% of neonates developing this problem. [14]

According to birth weight 27 neonates were very low birth weight (less than 1000 gms), 42 were low birth weight (1001-2500 gms) and rest 21 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 29%, while Moderate thrombocytopenia (50,000-<1 lacs/µl) were 25% and severe thrombocytopenia (<50,000/µl) were 46%. Depending on the time of onset of thrombocytopenia, neonates were labelled as early onset (within 72 hours) and late onset (after 72 hours). 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. [15,16]

Early onset (within 72 hours) was 55% and late onset (after 72 hours) was 45%. Prematurity, sepsis, respiratory distress and intra uterine growth retardation were common causes for both early onset and late onset thrombocytopenia. 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. 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. [17] It is estimated that up to 20% of neonates develop sepsis and approximately 1% die of sepsis related causes2. 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. [18] New-borns with respiratory distress and birth asphyxia also develop thrombocytopenia because of hypoxic injury caused to neonatal megakaryocytes. [19]

In present study 50 (25%) neonatal deaths were noted in neonates with thrombocytopenia. Sepsis (60%), prematurity (12%), birth asphyxia (12%) and respiratory distress (8%) were common causes of death neonates with thrombocytopenia. Sepsis along with thrombocytopenia noted with poor outcome in present study. 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. [20] Increased platelets destruction, an impaired platelet production or a combination may be the underlying mechanism of thrombocytopenia. [21]

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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