Clinico-etiological profile of the neonates with thrombocytopenia admitted to NICU in a rural hospital - A cross sectional study

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Abstract
Background: The most common haematological abnormality seen in neonates admitted to neonatal intensive care unit (NICU) is thrombocytopenia. Even though thrombocytopenia is more prevalent many a times it is not treated properly assuming that it will resolve by itself. If this finding is not detected and treated properly can result in serious complications. The present study was performed to determine the maternal and neonatal causes, time of onset and degree of thrombocytopenia. **Materials and methods:** A prospective observational study was conducted for a period of 1 year on neonates admitted to NICU with various causes. Blood samples from these neonates were collected and analysed for time of onset and severity of thrombocytopenia. **Results:** Out of 409 neonates admitted to NICU 264 developed thrombocytopenia with a prevalence of 65.5%. 65% had early onset thrombocytopenia and 35% had late onset thrombocytopenia. The most common neonatal cause was prematurity whereas most common maternal cause was pregnancy induced hypertension (PIH). Severe degree thrombocytopenia was found in 67.8 % in contrast to mild and moderate thrombocytopenia. **Conclusion:** Thrombocytopenia is the common finding seen in neonates with many causes. Significant association was found with prematurity, respiratory distress, sepsis and maternal hypertension. Hence platelet count can be used as a prognostic marker which can help in further diagnostic workup and management.
Key Word: Thrombocytopenia, prematurity, early onset, sepsis.

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INTRODUCTION

Thrombocytopenia is the most common haematological abnormality occurring in the neonatal intensive care unit after phlebotomy induced anaemia.[1] The incidence of neonatal thrombocytopenia varies greatly from<1% in healthy population to around one third of the neonates admitted to NICU.[2] thrombocytopenia is defined as platelet count <150,000/mm^3 regardless of the gestational age.[3,4]

Thrombocytopenia occurs in 1-5% of new-borns at birth and severe thrombocytopenia occurs in 0.1-0.5%.[1] Of 50% neonates admitted to NICU 22 to 35% of the new borns will have thrombocytopenia.[5,6] The incidence of thrombocytopenia in neonates admitted to NICU is high compared to the general population. Many etiological factors lead to neonatal thrombocytopenia and the common causes of are sepsis, preterm, respiratory distress, birth asphyxia, intrauterine growth retardation, hyperbilirubinemia, meconium aspiration syndrome and low birth weight. Apart from these causes at many circumstances the cause is still unknown. Depending on the time of onset this can be early-onset thrombocytopenia (<72hours) or late-onset thrombocytopenia (>72 hours).[7] Early onset neonatal thrombocytopenia has a benign course and predictable outcome. Whereas late onset is more severe.[8] Life-threatening bleeding or intracranial haemorrhage (ICH) with a high risk of neurodevelopmental impairment may occur in severe thrombocytopenia (platelets <50 ×109/L).[9] Thus,

appropriate diagnostic and therapeutic management is necessary to prevent death. However if not detected and managed properly can result in life threatening complications. However, thrombocytopenia, if not managed appropriately, can result in devastating consequences particularly in the preterm baby and leads to death. The present study aim to highlight the prevalence and to identify the maternal and neonatal factors causing thrombocytopenia.

MATERIALS AND METHODS

The study was a prospective observational study conducted for a duration of one year at tertiary care hospital. Institutional ethical clearance was obtained before the start of the study. The study included the neonates who got admitted to NICU. For all the neonates who were included in the study detailed maternal information, neonatal information and consent was taken. Maternal information included details of labour, history of any diabetes, hypertension, drug history, preeclampsia, eclampsia, Rh blood group. Neonatal history included Anthropometric parameters like head circumference, chest circumference, length, height, weight. Thorough clinical examination of the neonates were done. Blood samples were collected in an ethylene diamine tetra acetate (EDTA) anticoagulant containing vacutainer and platelet counts were obtained by using standard Sysmex automated cell counter. Neonates with platelet count less than $150,000/mm^3$ were considered to have thrombocytopenia and graded as mild ($100,000$-$150,000 / mm^3$), moderate ($50,000 – 100,000 / mm^3$) and severe ($<50,000/ mm^3$). [5]Time of onset of thrombocytopenia was divided as early thrombocytopenia

(from birth to 72hours) and late thrombocytopenia (for <72 hours of birth). Data was entered into Microsoft excel data sheet and was analysed and results were expressed as numbers and percentage.

RESULTS

There were 409 neonatal admissions in 1 year duration for the NICU out of which 264 neonates were found to have thrombocytopenia due to various causes. The overall prevalence of neonatal thrombocytopenia was 65.5%. The common cause of neonatal thrombocytopenia was prematurity (41%) followed by respiratory distress (28%) and neonatal sepsis (15%) [Figure 1]. Among the maternal factors 30 (11%) neonatal mothers had pregnancy induced hypertension (PIH) followed by infection caused by premature rupture of membranes (PROM) which was seen in 8(3%) cases. Remaining did not have any maternal risk factors. Out of 264 neonatal thrombocytopenia cases 172 (65%) developed early onset thrombocytopenia and 92 (35%) developed late onset thrombocytopenia. Prevalence of prematurity was high in early onset thrombocytopenia (45.3%) whereas the prevalence of respiratory distress was high in late onset thrombocytopenia (57.6%). Sepsis and birth asphyxia were significantly associated with early onset thrombocytopenia [Table 1]. The neonates were divided into 3 grades based on the severity of thrombocytopenia. Among which the prevalence of severe thrombocytopenia was found in 68% followed by mild and moderate thrombocytopenia with a prevalence of 17% and 15% respectively. Severe thrombocytopenia was predominantly observed in respiratory distress (72%) and prematurity (65%) [Table 2].
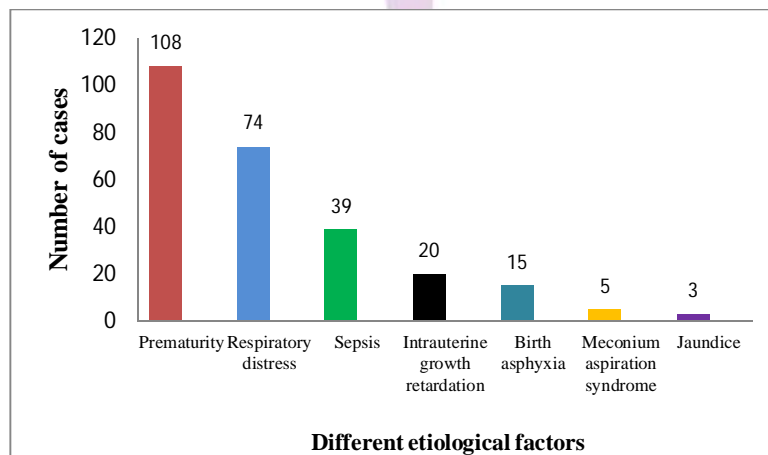

Figure 1: Chart showing various neonatal etiological factors causing thrombocytopenia

Table 1: Distribution of cases depending on the time of onset

Neonatal factors	Early onset thrombocytopenia	Late onset thrombocytopenia
Prematurity	78 (45.3%)	18 (19.5%)
Respiratory distress	30(17.4%)	53(57.6%)
Sepsis	27(15.6%)	9 (9.7%)
Intra uterine growth retardation	18(10.4%)	5(5.4%)
Birth asphyxia	13(7.5%)	5(5.4%)
Meconium aspiration syndrome	3(1.7%)	2(2.1%)
Jaundice	3(1.7%)	0
Total	172	92

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

Etiology	Mild thrombocytopenia	Moderate thrombocytopenia	Severe thrombocytopenia
Prematurity	21(19%)	17 (15.7%)	70 (64.8%)
Respiratory distress	12 (11%)	11 (10%)	51 (47.2%)
Sepsis	4 (8.8%)	5 (12.8%)	31(79%)
Intra uterine growth retardation	2 (4.4%)	2 (13%)	14 (70%)
Birth asphyxia	3 (20%)	2 (13%)	10 (66.6%)
Meconium aspiration syndrome	2(4.4%)	1(2.5%)	2(1.1%)
Jaundice	1(2.2%)	1(2.5%)	1(0.5%)
Total	**45**	**40**	**179**

DISCUSSION

Neonatal thrombocytopenia is one of the most common haematological abnormality seen in NICU. [8] The aetiology and predisposing factors encountered are many and they interact to produce neonatal thrombocytopenia. [10]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.[11, 12] In our study the prevalence of thrombocytopenia is 65.5% which was in concordance with study done by Gupta *et al* (70.5%).[13] Table 3 shows the comparison of prevalence with other studies. In the study done by Beiner *et al* prevalence of thrombocytopenia was found to be more in preterm neonates.
[14]

Table 3: Comparison of prevalence of neonatal thrombocytopenia

Studies on Neonatal thrombocytopenia in NICU	Prevalence
Gupta *et al*	70.5%
Sharan gouda Patil *et al*	25.45%
Shashikala *et al*	63.8%
Selvan *et al*	38.4%
Present study	65.5%

Table 4: Comparison of timing of onset of thrombocytopenia

Neonatal thrombocytopenia in NICU studies	Early onset thrombocytopenia	Late onset thrombocytopenia
Khalessi *et al*	67.7%	32.4%
Eslami *et al*	75.3%	24.7%
Amutha *et al*	87.9%	12.1%
Present study	65%	35%

Table 5: Comparison of different grades/degrees of neonatal thrombocytopenia

Neonatal thrombocytopenia in NICU studies	Mild	Moderate	Severe
Gupta *et al*	84.4%	13.0%	2.6%
Ghamdi *et al*	60%	20%	20%
Present study	17%	15.1%	67.8%

The present study showed early onset thrombocytopenia as predominant which was in concordance with the studies done by Khalessi *et al* and Eslami *et al*[12,6] [Table 4]. Severe degree thrombocytopenia was higher in our study whereas Gupta *et al* and Ghamdi *et al* studies [Table 5] showed mild thrombocytopenia as predominance.[13, 15] In our study most common neonatal risk factor causing thrombocytopenia was prematurity. Khalessi *et al* and Gupta *et al* studies [12,13] found sepsis to be the most common cause of neonatal thrombocytopenia with prevalence of 24.1% and 42% respectively. Eslami Z *et al* recorded intrauterine growth retardation and neonatal sepsis as the important causes for thrombocytopenia. [6] The second most cause was respiratory distress in the present study. New-borns with respiratory distress and birth asphyxia also develop thrombocytopenia because of hypoxic injury caused to neonatal megakaryocytes.[16] Neonatal sepsis was found to be third common cause in the present study. 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] Other neonatal causes were found to be intrauterine growth retardation, birth asphyxia, meconium aspiration syndrome and jaundice Many maternal conditions also results in thrombocytopenia. In our study maternal pregnancy induced hypertension (PIH) was significantly associated with neonatal thrombocytopenia which was in concordance with the study done by Bilal *et al*.[18]The cause for thrombocytopenia in this condition is mainly due to placental insufficiency.[17] Multiple disease processes can cause thrombocytopenia. A practical approach to the diagnosis and management of thrombocytopenia in the neonate can be based on the time of onset of thrombocytopenia (early onset<72 hours after birth or late onset >72 hours after birth).[7] In our study early onset thrombocytopenia was predominantly observed (65.5%) which was in concordance with the studies done by Khalessi *et al* and Eslami *et al* which was 67.5% and 75% respectively.[12,6] The causes associated with early onset are (Haemolysis, elevated liver enzymes and low platelet count) HELLP syndrome, intra uterine growth retardation, drug abuse and maternal diabetes.[6] Late onset thrombocytopenia common causes are sepsis and necrotizing enterocolitis. The onset is rapid within 1 to 2 days and can lead to severe thrombocytopenia. The clinical manifestation is mucosal bleeding which requires treatment with platelet transfusion when compared to early onset thrombocytopenia which will resolve by itself.[19] According to studies done by Gupta *et al* and Ghamadi *et al* mild thrombocytopenia was more common in contrast to our study in which severe thrombocytopenia was found

to be predominant.[13, 15] The cause of severe thrombocytopenia in perinatal period is mainly due to viral infections. Viral neuraminidase causes sialic acid loss from the platelet membranes and also leads to intravascular platelet aggregation and degeneration of megakaryocyte which causes decreased production of platelets.[17] Patients with severe thrombocytopenia or a platelet count lower than 50,000/mL should be evaluated for sepsis disseminated intravascular coagulation (DIC), or neonatal alloimmune thrombocytopenia (NAIT). [17]

CONCLUSION

The most common laboratory finding seen in neonates admitted to NICU is thrombocytopenia. Both neonatal and maternal factors can lead to thrombocytopenia. Since the prevalence of neonatal thrombocytopenia is high and severe thrombocytopenia can lead to life threatening complications it is very important to know the platelet count, grade and time of onset of thrombocytopenia in all the cases of thrombocytopenia admitted to NICU so that it aids the clinician in diagnosis, planning further investigations and also helps in appropriate management.

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