Demystifying Neonatal Thrombocytopenia: An In-Dependent Exploration of Etiological Roots

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ABSTRACT:

Introduction: Neonatal thrombocytopenia, characterised by a low platelet count during the early stages of life, presents a significant clinical challenge with potential risks for affected infants. This original article aims to shed light on the etiology of thrombocytopenia in neonates through a comprehensive study. By investigating the underlying factors that contribute to this condition, we seek to improve our understanding of its origins and provide valuable information for enhanced management strategies. The implications of this research extend beyond understanding etiology; they hold promise for effectively managing neonatal thrombocytopenia. By identifying specific risk factors and their interplay, healthcare practitioners can tailor diagnostic approaches and treatment strategies to optimize patient outcomes. Additionally, this study paves the way for future investigations aimed at targeted interventions and preventive measures.

Methods: A prospective, cross-sectional, single center study was carried out on 180 NICU patients having thrombocytopenia in a tertiary care rural hospital over a period of 2 years

Name, sex, gestational age, age at thrombocytopenia onset, and birth weight were among the demographic information that was noted. The enrolled newborns' parents or guardians were contacted to get information, and specifics regarding their clinical and demographic characteristics were recorded. The structured questionnaire that interviewers used to gather data was pretested and adjusted before being employed in the study. Based on research conducted in laboratories, data was gathered

Data was collected in structured forms and a master sheet was made on Microsoft excel. The data that was evaluated was presented as percentages and figures.

Results: A total of 180 cases of neonates admitted in NICU having thrombocytopenia were studied a male preponderance was observed with 66% (99) males and 44% (81) females. Moderate degree 40% (72 cases) of thrombocytopenia was most commonly encountered followed by mild 35%(63 cases) and then severe degree 25% (45 cases). Highest number of below normal gestational age (below 37 weeks) neonates was observed followed by term neonates(37-42weeks), no neonate having above than normal (more than 42 weeks) gestational age was seen in our study

A number of etiological factors with lots of overlapping leading to thrombocytopenia was seen in neonates sepsis being the most common and consistent aetiology followed by less age of gestation at birth, Meconium aspiration syndrome, birth asphyxia, respiratory distress syndrome, DIC, Jaundice, Intra uterine growth retardation Sepsis was found to be the most common cause of severe thrombocytopenia followed by prematurity the distribution of etiology as per severity of thrombocytopenia as per aetiology can be been in the table below.

Conclusion: This original article offers a comprehensive examination of the etiology of thrombocytopenia in neonates. By unraveling the intricacies of this condition, we provide valuable

insights that contribute to our understanding of the underlying factors involved. Ultimately, this knowledge has the potential to enhance clinical decision-making, improve patient care, and lay the foundation for further advancements in the field of neonatal thrombocytopenia.

Keywords: DIC, Jaundice, Neonatal thrombocytopenia

INTRODUCTION

The most frequent haematological disorder seen in newborn intensive care units (NICUs) is thrombocytopenia, whose frequency varies substantially depending on the population under study. Platelet counts in healthy foetuses and neonates at gestational ages ≥22 weeks are within the adult normal range (150–450×109 /L).[1] Regardless of gestational age, a platelet counts of less than 150×109/L is considered neonatal thrombocytopenia. Still, among healthy newborns, platelet counts between 100 and 150 x 10^9/L are somewhat more typical. In clinically stable infants, most instances are minor and resolve on their own; in clinically unstable neonates, outcomes are frequently dismal[2,3]. As such, it presents a dilemma for the treating physician on whether to intervene and when to take a break. Neonatal thrombocytopenia prognosis is dependent on several factors, such as the underlying aetiology, birth weight, gestational age, and platelet count. Platelet transfusions are still the mainstay of treatment as of right now. Thrombocytopenia affects 0.5–1% of neonates at birth, and 0.1–0.5% of them have severe thrombocytopenia. 5 Between 22 and 35 percent of neonates admitted to NICUs and up to 50 percent of those admitted to NICUs requiring intensive care have thrombocytopenia[4,5]. About 20% of newborns have severe thrombocytopenia, while the majority of newborns have mild or moderate thrombocytopenia (72 hour). Infections, birth asphyxia, prematurity, intrauterine growth retardation, hyperbilirubinemia, respiratory distress syndrome, meconium aspiration syndrome, and low birth weight are among the major causes of thrombocytopenia in newborns. In addition to platelet counts, bleeding symptoms are influenced by underlying illnesses. Regardless of gestational age, early onset neonatal thrombocytopenia is a prevalent condition in the NICU population with a benign course and predictable result. Generally speaking, late onset thrombocytopenia is a more serious condition than early onset[5,6,7]. Though it is one of the complications of the disease process, thrombocytopenia can occasionally be unintentionally discovered, making it a valuable initial assessment for sick newborns. Despite being so common, thrombocytopenia is frequently disregarded in the belief that it would go away on its own, but if it is not identified and treated appropriately, it can have disastrous side effects[4,8,9]. Research on the relationship between thrombocytopenia severity and prevention, effective therapy, early prediction of the need for platelet transfusion, and a reduction in death and morbidity are all aided by this study. There is still a lack of information to advise platelet transfusion cutoffs and aetiologies linked to severe thrombocytopenia. The goal of this study is to shed insight on the pattern, frequency, severity, and potential causes of newborn thrombocytopenia that our hospital has seen.

Materials and methods:

A prospective, cross-sectional, single center study was carried out on 180 NICU patients having thrombocytopenia in a tertiary care rural hospital over a period of 2 years. The study excluded neonates with congenital abnormalities, born to mothers with idiopathic thrombocytopenic purpura and with thrombocytopenia who were born outside of the hospital and had platelet transfusion prior to admission in our NICU and were excluded from the research. The sample size for this study was calculated with reference to statistical data using the Finite Population Correction Factor formula: $n = (Z^2 * p * (1-p))/E^2$ [10].

Name, sex, gestational age, age at thrombocytopenia onset, and birth weight were among the demographic information that was noted. The enrolled newborns' parents or guardians were contacted to get information, and specifics regarding their clinical and demographic characteristics were recorded. The

structured questionnaire that interviewers used to gather data was pretested and adjusted before being employed in the study. Based on research conducted in laboratories, data was gathered. Convenience sampling was the method used to get the sample. Before every newborn was given antibiotics, a blood sample was taken from them. The sepsis workup required blood samples for the following tests: platelet count, blood culture, antibiotic sensitivity, total leukocyte count (TLC), absolute neutrophil count (ANC), immature neutrophils to total neutrophil count ratio (I/T ratio), and C-reactive protein (CRP) calculation.

After drawing one millilitre of blood, it was placed in a cell counter to be analysed for platelet count, differential leukocyte count, and total blood count. The newborns were divided into three groups based on their platelet counts: those with mild thrombocytopenia (100–149*103 /µL), moderate thrombocytopenia (50–99*103 /µL), severe thrombocytopenia (<50*103 /µL) [11].

A baby's APGAR score of less than 7 at five minutes of life was deemed to indicate birth asphyxia. Neonatal Sepsis criteria were used to define sepsis, and a blood culture was submitted for a conclusive diagnosis. Other investigations like blood gas, Chest X - ray, Serum electrolytes, neurosonogram were performed upon need, on case-to-case basis.

Data was collected in structured forms and a master sheet was made on Microsoft excel. The data that was evaluated was presented as percentages.

Results:

Demographic- A total of 180 cases of neonates admitted in NICU having thrombocytopenia were studied a male preponderance was observed with 66% (99) males and 44% (81) females (table 1)

Table 1: Gender wise distribution of cases

Sex	Number of cases	Percentage
Males	99	66%
Females	81	44%
Total	180	100%

Severity- Among the thrombocytopenic neonates, moderate degree 40% (72 cases) of thrombocytopenia was most commonly encountered followed by mild 35%(63 cases) and then severe degree 25% (45 cases) (table 2)

Table 2: Severity wise distribution of cases

Grade of Thrombocytopenia	No of Cases	Percentage
Mild	73	40.55
Moderate	82	45.55
Severe	25	45

Gestational age- Among the thrombocytopenic neonates, highest number of below normal gestational age (below 37 weeks) neonates was observed followed by term neonates(37-42weeks), no neonate having above than normal (more than 42 weeks) gestational age was seen in our study(Table 3)

Table 3: Distribution as per Gestational age

Gestational age	No of Cases	Percentage
below 37 weeks	93	62
37-42weeks	72	38
more than 42 weeks	0	0

Etilogic factors- A number of etiological factors with lots of overlapping leading to thrombocytopenia was seen in neonates sepsis being the most common and consistent aetiology followed by less age of gestation at birth, Meconium aspiration syndrome, birth asphyxia, respiratory distress syndrome, DIC, Jaundice, Intra uterine growth retardation (Table 4)

Table 4: Showing Etiological distribution

Etiology	No of Cases	Percentage
Sepsis	148	82.22
Prematurity	93	51.66
Meconium aspiration syndrome	18	10
birth asphyxia	15	8.33
respiratory distress syndrome	13	7.77
DIC	12	6.66
Jaundice	4	2.22
Intra uterine growth retardation	4	2.22

Sepsis was found to be the most common cause of severe thrombocytopenia followed by prematurity the distribution of etiology as per severity of thrombocytopenia as per aetiology can be been in the table below (Table 5)

Table 5: Distribution of etilogies of thrombocytopenia according to severity

Aetiology	Mild (Percentage)	Moderate (Percentage)	Severe (Percentage)
Sepsis	42 (28.37)	84(56.7)	22(14.86)
Prematurity	53(56.9)	21(22.58)	9(9.67)
Meconium aspiration syndrome	8(44.44)	5(27.77)	5(2.77)
birth asphyxia	7(46.66)	6(40)	2(13.33)
respiratory distress syndrome	3(23.07)	5(38.46)	5(38.46)
DIC	8(66.66)	4(33.33)	0(00)
Jaundice	4(100)	0(00)	0(00)
Intra uterine growth retardation	3(75)	1(25)	0(00)

Discussion

Clinically stable newborns often have a good result, but clinically unstable neonates frequently have minor cases that go away on their own. As a result, the treating physician is faced with the dilemma of knowing whether to treat and when to disregard the condition. The underlying aetiology, platelet count, gestational age, and birth weight are some of the factors that influence the prognosis of neonatal thrombocytopenia. For now, platelet transfusions continue to be the mainstay of treatment[12].

Males predominated the female population in our study. Males were more likely than females to have thrombocytopenia (99, 66%) (81, 44%)

respectively. Similar findings were made by Tirupathi et al. [13] and Dahat et al [14]; in their investigation, the proportion of male participants was 56% and 59%, respectively, and that of female participants was 44% and 41%. Addil et al [15]. discovered that thrombocytopenia was present in 68.9 percent of neonates and was more common in females, despite the contrary findings. It has been noted that males predominate over females in the majority of research on neonatal thrombocytopenia; however, we were not able to pinpoint the reason for this male predominance.

According to our research, thrombocytopenia was more common in preterm infants (93, 62 percent) than in term babies (73, 38 percent).

Madhavi et al. [16] and Sharma and Thapar [17] observed similar outcomes; in their investigations, thrombocytopenia was observed in 63.3% and 58.2% of preterm infants, respectively. In our study, the majority of preterm newborns had moderate thrombocytopenia; however, in a study by Meena et al.[18], the majority of preterm babies had severe thrombocytopenia, while the majority of term babies had moderate thrombocytopenia. Rarely severe, thrombocytopenia is linked to preterm birth and a lower gestational age at birth on its own [19].

The most frequent cause of thrombocytopenia in neonates, according to the etiological profile of our study, was newborn sepsis (148, 82.22 percent); other prominent causes were preterm (93, 51.66 percent), Meconium aspiration syndrome (18, 10 percent), and Birth Asphyxia (15, 8.33 percent). Similar findings were made by Gupta et al. [20], Sanii et al. [21], and Madhavi et al. [16], who reported that sepsis was the most common cause of neonatal thrombocytopenia in 42, 241, and 74.5 percent of newborns, respectively. However, birth asphyxia (33.3%) and jaundice were the most common etiologies, according to a study by Jeremiah and Oburu [22]. (19.7 percent). Consequently, decreased gestational age, birth hypoxia, infection, and preterm are prevalent and independent conditions that may cause neonatal thrombocytopenia.

In our investigation, the majority of patients with both early- and late-onset sepsis—14 (36.84 percent) and 21 (36.84 percent), respectively—had moderate thrombocytopenia. But in contrast to early-onset sepsis, severe thrombocytopenia was more common in late-onset sepsis. Sepsis was discovered in 33.3 percent of neonates with severe thrombocytopenia in a research by Bagale and Bhandari [23]. Sepsis was found in 27.9 percent of neonates with mild thrombocytopenia, and hypoxia was found in 37.2 percent of neonates.

While persistent foetal hypoxia is a prevalent cause of early-onset thrombocytopenia, sepsis and NEC have been identified as significant risk factors for late-onset thrombocytopenia.

Nevertheless, a sizable fraction of thrombocytopenia in ELBW newborns had no known cause[24]. Neonatal sepsis linked to thrombocytopenia causes a four-fold increase in mortality, which rises to a six-fold increase in cases of Gram-negative sepsis [25]. Since one in four newborns experiences thrombocytopenia at some point during their stay in the NICU, paediatricians and neonatologists have ongoing challenges in accurately identifying, assessing, and treating the illness in a timely manner[26].

Failure to include the clinical profile and detailed maternal history in the study was the limitation of the study. The referral of neonates from outside of the study setting who already presented with sepsis could have led to selection bias. It was a single-center, small-scale study where the sample size was few. A multicentric study with a large sample size needs to be done for a detailed understanding of the etiology of thrombocytopenia considering both maternal and neonatal factors that are responsible for thrombocytopenia, which will ultimately lead to a decrease in morbidity and mortality of neonates.

Conclusions

A common and universal clinical finding in neonates admitted to the NICU is neonatal thrombocytopenia, which is a major prognostic factor for a number of illness problems in babies hospitalised to the NICU. Therefore, in order to lower morbidity and mortality, thrombocytopenia must be identified early, evaluated, and treated promptly. It was found that preterm and sepsis were independent, distinct causes of the poor prognosis in infants admitted to the NICU. Since thrombocytopenia is a very frequent condition in infants, it is essential to assess each newborn admitted to the NICU for their platelet count, thrombocytopenia's degree and severity, and its pattern of onset. This will help the neonatologist diagnose patients, schedule treatments, and begin therapy as soon as possible.

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