A STUDY ON ETIOLOGICAL FACTORS OF NEONATAL THROMBOCYTOPENIA IN A TERTIARY CARE HOSPITAL

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ABSTRACT

INTRODUCTION: - Thrombocytopenia (platelet count<1.5 lakhs/µL) is one of the most common hematological problems in NICUs, with 18-35% of the neonates developing this problem. More common among ELBW (< or = 1000 grams birth wt.) or Preterm babies (GA < or = 32-36 weeks) or Sick neonates. In contrast, only 2% of neonates are thrombocytopenic at birth with Severe Thrombocytopenia (platelet count<50,000/µL) in less than 3/1000 term infants.

AIMS AND OBJECTIVES: - To determine the etiological correlation to neonatal thrombocytopenia.

MATERIAL AND METHODS: - 70 neonates, having platelet count (<1.5 lakhs/µL), were selected from NOVEMBER 2017 to SEPTEMBER 2019 among those admitted to NICU. Initial platelet count is done on admission and counts repeated after any therapeutic intervention.

OBSERVATION AND RESULTS: - Severe thrombocytopenia (<50,000/µL) is present in 44.3%. Of the thrombocytopenic neonates (n=70), 64.3% were preterm, 78.6% were LBW, 72.8% had Septicemia, 40% had Birth asphyxia, 17.1% MAS, 18.5% had DIC and 42.8% had NEC.

CONCLUSION: - Significant association is observed with Maternal PIH, NEC, LBW, Sepsis and prematurity. Factors leading to Sepsis directly influence platelet counts.

KEYWORDS

Platelets, Thrombocytopenia, Septicemia, Neonatal Intensive Care Unit.

INTRODUCTION

The human hemostatic mechanism is dynamic and is profoundly influenced by age. Thrombocytopenia most common hematological abnormality seen in neonates admitted to NICU. The development of hemostasis in newborn differs from that of adults, and the coagulation factors do not cross the placental barrier. The coagulation factors are synthesized independently and are dependent on gestational age and level of maturity of the liver. Thrombocytopenia is defined as a platelet count <1.5 lakhs/µm, regardless of gestational age. Early-onset (<72 hrs) has a benign and predictable outcome, whereas late-onset (>72 hrs) is more severe. 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. Platelets are small anucleate fragments that are formed from the cytoplasm of megakaryocytes and have a characteristic discoid shape. 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. After a detailed search of the indexed medical literature, it was found that there have been only a few articles on this topic from India. One article is a study of the association between maternal PIH and neonatal thrombocytopenia while the others are case reports and case series reports. The paucity of studies from India and the increasing prevalence of this condition in our NICU, instigated us to determine the etiology, of the neonates admitted to NICU in a tertiary care hospital.

AIMS AND OBJECTIVES:

- To determine the etiological correlation to neonatal thrombocytopenia.

PATIENTS AND METHODS:

Present study was done to know the frequency, etiological profile of neonates admitted to NICU with thrombocytopenia and abnormal coagulation profile.

STUDY DESIGN:

The study was a prospective observational study conducted on 70 neonates.

STUDY PERIOD:

From November 2017 to September 2019 at a tertiary care hospital, for a duration of 22 months

INCLUSION CRITERIA:

Neonates with thrombocytopenia admitted in NICU from November 2017 to September 2019.

EXCLUSION CRITERIA:

- Babies died within 6 hours of admission in whom investigations were not done.
- Babies with congenital anomalies.

METHOD OF COLLECTION OF DATA:

At admission, parents/guardians were informed about the study, and oral informed consent was obtained. A detailed history inclusive of maternal obstetric history, birth history, perinatal events were obtained as per proforma. Information regarding the number of conditions that have been associated with neonatal thrombocytopenia were recorded, e.g., history of PIH, gestational diabetes mellitus, premature rupture of membranes, and anemia. The gestational age of neonates was determined based on New Ballard’s scoring system. All the neonates underwent thorough clinical examination, platelet counts were obtained using standard Sysmex automated cell counter, coagulation profile obtained from automated coagulation analyzer, CBC by automated hematology analyzer, blood culture, sepsis screen (total WBC count, absolute neutrophil count, I/T ratio, micro ESR did by using micropipette and CRP did by latex turbidimetry). Low platelet counts were cross verified by peripheral smear study.

The next step was to group neonates based on their platelet counts.

DISTRIBUTION OF THROMBOCYTOPENIC NEONATES INTO THREE GRADES ACCORDING TO SEVERITY GRADES

GRADE 1: MILD (1-<1.5 Lakhs/µL)
GRADE 2: MODERATE (50,000-<1Lakhs/µL)
GRADE 3: SEVERE (<50,000/µL)

STATISTICAL METHODS:

The information collected regarding all the selected cases were
10 had severe thrombocytopenia. Maternal PIH is associated with

**OBSERVATION AND RESULTS:**
Among the total of 70 study participants with neonatal thrombocytopenia, the majority were of grade 3 (44.3%), followed by grade 2 (37.1%) neonatal thrombocytopenia.

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Gr-1</th>
<th>Gr-2</th>
<th>Gr-3</th>
<th>X value</th>
<th>P value</th>
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</thead>
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<tr>
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<td>32</td>
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<tr>
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<td>17</td>
<td>09</td>
<td>9.916</td>
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</table>

Table 2: Distribution of patients in the three groups according to their maternal factors:

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<th>ETOLOGY</th>
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<th>Gr-2</th>
<th>Gr-3</th>
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<th>P value</th>
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**DISCUSSION:**
Neonatal thrombocytopenia is a common hematological abnormality encountered in the NICU. Though thrombocytopenia is common in NICU, it often coexists with abnormal coagulation profile. The etiology and predisposing factors are many, and they interact in a complex manner. As in any other neonatal illness, the manifestations are protean, and severe neonatal thrombocytopenia is known to be associated with a poor outcome.\(^6\)

**PREVALENCE:**
The prevalence of thrombocytopenia in the present study was 27.5%. This prevalence is slightly higher than that, 08-35%, reported in other studies.\(^7\)

Beiner et al. estimated the prevalence of thrombocytopenia only among Preterm neonates (between 27 and 35 weeks of gestational age). It is evident from the table that in the present study, there is a slightly higher prevalence of neonatal thrombocytopenia. This higher prevalence is probably due to higher proportion of septicemic neonates in our NICU admissions, while it was lower in the other studies, for e.g., In a prospective study conducted by Castle et al. on 807 consecutive neonates admitted into a regional neonatal intensive care unit over a one year period, thrombocytopenia developed in 22% of the infants. The prevalence of sepsis in his study was just 7.5%.\(^8\)

The proportion of severe thrombocytopenia (44.3%) in the present study also falls on the higher side. This is once again probably a reflection of sepsis contributing to the majority of cases of neonatal thrombocytopenia in our NICU. Sepsis is reported to result in a moderate and severe group of thrombocytopenia rather than its milder form in various studies.\(^9\)

**ETOLOGICAL PROFILE: MATERNAL PIH:**
Maternal PIH was significantly associated with neonatal thrombocytopenia (P<0.009). This finding is in agreement with studies conducted by Burrows et al.\(^1\) In a study done by Gupta AK et al. on 870 neonates in Delhi, he noticed 146 babies with thrombocytopenia, out of which 43.8% (p<0.04) had a history of maternal pregnancy-induced hypertension. This is in agreement with the present study. Maternal PIH was present in 32 cases (45.7%) with thrombocytopenia, of which 10 had severe thrombocytopenia. Maternal PIH is associated with moderate thrombocytopenia rather than severe thrombocytopenia in other studies, which was similar to the present study.

**ANEMIA:**
In this study, anemia was the commonest maternal risk factor. 41.2% mother had anemia, and it was associated with all type thrombocytopenia. The association of anemia with severe neonatal thrombocytopenia was statistically significant (P-value <0.05). In a study conducted by Tirupati K et al,\(^1\), an association has been documented between anemia and thrombocytopenia.

**AGE AT PRESENTATION:**
It was shown that 51.6% of the severely thrombocytopenic neonates presented before 72 hours of life, and 48.4% of them presented after 72 hours of life. This finding doesn't reiterate the well-documented association that majority of the severely thrombocytopenic neonates present after 72 hours and the common etiology, in these neonates, are acquired ones such as sepsis and NEC.\(^1\)

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.\(^1\). The probable etiology could be due to a higher incidence of low birth weight babies, prematurity, early onset of sepsis, and NEC. Eslami Z et al., in a retrospective study of 350 neonates and noted 75.3% early-onset thrombocytopenia and 24.7% late-onset thrombocytopenia, most of them had mild to moderate thrombocytopenia which correlates with the present study.

**PREMATURITY:**
Prematurity is known to be associated with lower platelet counts.\(^1\) In the present study gestational age was associated with low platelet counts with a statistically significant p-value (0.006). Incidence of thrombocytopenia was twice in preterm neonates than term neonates in Beiner et al., Eslami Z et al.,\(^2\), Bonafacio et al.\(^3\). Similar to this present study showed a significant association of prematurity with thrombocytopenia. The association between gestational age and thrombocytopenia is most likely explained by maternal conditions that cause placental insufficiency, such as PIH and preeclampsia. These can result in fetal growth retardation and are often managed with induced preterm delivery, which explains the relationship between thrombocytopenia and lower gestational age at birth.

**SEPTICEMIA:**
The etiological profile was similar to other NICU studies from India, with sepsisemia accounting for the majority of the admissions. Sepsis was accounted for most of the cases in mild, moderate & severe thrombocytopenia groups.

Sepsisemia led to thrombocytopenia due to both decreased production and increased consumption of platelets and hence, results usually in severe thrombocytopenia. Probably, due to the higher incidence of sepsisemia in our admissions, the neonates with prematurity, IUGR, and perinatal asphyxia had also been exposed to infections more frequently than neonates with the same problems in western countries. Hence in neonates with an already compromised hematological environment, exposure to an infection probably leads to a precipitous fall in platelet count resulting in severe thrombocytopenia rather than to its milder variety. But to prove this hypothesis, the interaction between the above-mentioned factors with sepsisemia should be assessed.

**NECROTIZING ENTEROCOLITIS:**
NEC, as diagnosed by Bell's criteria, was significantly associated with thrombocytopenia (P<0.02). All the neonates in the present study with radiological evidence of NEC had thrombocytopenia. This finding is in agreement with the well-known fact that thrombocytopenia is one of the major lab markers of NEC.\(^1\)

**CONCLUSION:**
The prevalence of severe thrombocytopenia in the NICU is inversely proportional to birth weight, and most cases are acquired consumptive thrombocytopenia. In the present study, the prevalence of thrombocytopenia was high (27.5%), and that of severe thrombo cytopenia was 44.3%. Low birth weight followed by septicemia was the major etiology associated with both severe and mild to moderate thrombocytopenia. The predisposing factors associated with neonatal thrombocytopenia were maternal PIH, prematurity, age at presentation, septicemia, NEC, DIC, and assisted ventilation. Glari

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\(^{1}\) Beiner et al.
\(^{2}\) Eslami et al.
\(^{3}\) Bonafacio et al.
\(^{4}\) Khalessi et al.
\(^{5}\) Eslami Z et al.
\(^{6}\) Bell's criteria.
ngly perinatal asphyxia not associated with neonatal thrombocytopenia in the Present Study. 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. Low birth weight babies were more prone to severe thrombocytopenia. Preterm babies had severe thrombocytopenia whereas term babies had moderate thrombocytopenia. Anemia and PIH 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 Prematurity were the commonest neonatal factors associated with thrombocytopenia in present study.

REFERENCES: