https://doi.org/10.48047/AFJBS.6.14.2024.7807-7814

African Journal of Biological Sciences

Journal homepage: http://www.afjbs.com

Research Paper Open Access

Thrombocytopenia in Neonates Prevalence Rates and Contributing Factors

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Volume 6, Issue 14, 2024

Received: 15 June 2024

Accepted: 25 July 2024

Published: 15 Aug 2024

doi: 10.48047/AFJBS.6.14.2024.7807-7814

ABSTRACT

Background: A frequent blood disorder detected in the newborn is reduced platelet number. The causes of thrombocytopenia, its treatment methods, and the outcome of the condition should be evaluated for better illness management. Typically, around one-third of platelets are situated within the spleen. Thrombocytopenia is defined by a platelet count below 150x10^9/L.

Objective: To evaluate the frequency of causes of thrombocytopenia in neonates admitted to a tertiary care medical center.

Methods: A cross-sectional investigation was conducted. Blood specimens were gathered in EDTA tube and assessed on hematology analyzer Nihon Kohen for full blood count. Peripheral smear were inspected, serum bilirubin and CRP were measured.

Results: Out of 400 individuals, 232 were male and 168 were female. A majority of the patients, around 88.0%, developed thrombocytopenia due to infections, while 10% had neonatal thrombocytopenia associated with neonatal jaundice, and 2% had other causes for neonatal thrombocytopenia. There were no cases of maternal autoimmune disorders linked to neonatal thrombocytopenia.

Conclusion: Neonatal thrombocytopenia is prevalent among newborns in developing countries, primarily caused by infections, which can be prevented through proper care before and after birth.

Key words: Neonatal thrombocytopenia. Jaundice. Sepsis.

INTRODUCTION:

In fetuses, the platelet count during the trimester (second) and in neonates is comparable to that of healthy children and adults[1, 2].Mild thrombocytopenia is characterized by a platelet count of 100-150x10^9/L, intermediate levels range from 50-100x10^9/L, and profound thrombocytopenia is identified when the count falls below 50x10^9/L. Various factors are included in causing Neonatal thrombocytopenia, including the development of alloantibodies. Sepsis, neonatal jaundice, and it typically manifests as early thrombocytopenia, occurring within the first 72 hours of life, or as late thrombocytopenia, which develops after the initial 72 hours[4].

Neonatal jaundice causes thrombocytopenia in newborns that require careful monitoring and management [5, 6].About 37% of newborns admitted to intensive care units experience thrombocytopenia. The reasons for neonatal thrombocytopenia are diverse, including both immune and non-immune disorders[7, 8].The most common cause of thrombocytopenia in infants is Infection and should be considered in any newborn with a platelet count below 50x10^9/L[9].

Bacterial infections can cause thrombocytopenia through various mechanisms, such as endothelial damage, widespread intravascular clotting, immune-driven destruction, platelet clumping due to bacterial substances attaching to platelet membranes, and reduced platelet production resulting from infected bone marrow. Neonatal sepsis is categorized as either early-stage or late-staget[10,]

Early stage sepsis manifests soon after birth and is linked with trans-placental transmission or an ascending contagion from the cervix. Conversely, late-onset sepsis develops between 4 and 90 days of life and is attained from the environment. These infections may be associated with splenomegaly. The trans-placental transfer of maternal autoantibodies in mothers with idiopathic thrombocytopenic purpura or systemic lupus erythematous can lead to neonatal autoimmune thrombocytopenia, which accounts for approximately 10% of cases[11].

Hyperbilirubinemia can also lead to a reduced platelet count in infants. Various factors, including infant-related, labor-related, maternal, and environmental influences, can affect the severity and progression of jaundice. Kernicterus is a serious condition that can cause death and lifelong disability. Approximately 70% of conditions associated with hyperbilirubinemia occur in individuals of Asian ethnicity[12, 13, 14]

Certain therapeutic drugs have been identified as potential causes of neonatal thrombocytopenia. For instance, quinine therapy administered during pregnancy has been linked to both maternal and neonatal thrombocytopenia. While heparin-induced thrombocytopenia affects around 10% of adults, it is rare in neonates[15, 16].

Assessing the clinical significance of neonatal thrombocytopenia is crucial. The specific lower limit platelet counts for various groups of preterm neonates have not been precisely established. However, platelet transfusion was considered for all neonates if their platelet count dropped below 50 × 10^9/l.

MATERIAL AND METHODS:

The study employed purposive sampling, focusing on neonates aged 1 to 28 days with thrombocytopenia, while excluding all pre-term infants. Patients meeting the inclusion criteria were selected from the inpatient department, with parental consent obtained for all participating neonates. The following assessments were conducted.

1. Hematologic Analysis: Blood specimens were gathered in EDTA-containing vials and processed using a semi-automated hematology analyzer manufactured by Nihon Kohen.

2. Peripheral Blood Film Examination: Peripheral blood smears were prepared and stained using May-Grunewald Giemsa stain to confirm platelet counts and to detect the presence of schistocytes.

3. Serum bilirubin levels were utilized to assess neonatal jaundice.

4. C-Reactive Protein (CRP) Measurement: Levels of C-reactive protein were assessed, with values above 6 mg/L indicating a potential infection.

5. Radiographic Imaging: X-rays were conducted to identify any skeletal anomalies potentially linked to genetic abnormalities.

Data analysis was performed using Statistical Package for the Social Sciences (SPSS) version 20.0. Mean ± Standard deviation (SD) were expressed as quantitative variables such as age and platelet count, while qualitative variables like gender and causes of neonatal thrombocytopenia, including infections, autoimmune factors, neonatal jaundice and additional factors (such as genetic abnormalities or maternal medication usage, were displayed as percentages and frequencies.

RESULTS:

In the Neonatal Nursing Unit (NNU) of Children's Hospital ICH Lahore, 400 newborns, comprising 232 males (58%) and 168 females (42%), were admitted. Platelet counts were conducted for neonates with thrombocytopenia and various provisional diagnoses in the laboratory.

Platelet counts were conducted in the laboratory for neonates experiencing thrombocytopenia alongside multiple provisional diagnoses. The most prevalent provisional diagnosis was severe neonatal sepsis infections (88%), with neonatal jaundice accounting for 12% of cases. Maternal autoimmune diseases were not identified, and occurrences of TARS, heparin-induced thrombocytopenia, or drug-induced thrombocytopenia were observed in 0.9% of cases.

Patients were classified according to the commencement of the illness. Out of the 232 male patients, 52% encountered early-stage disease, whereas 49.1% encountered late-stage disease. Within the 168 female patients, 58% demonstrated early-stage disease, and 43% displayed late-stage disease. In total, 54% of patients manifested early-stage disease, and 46% demonstrated late-stage disease.

	Stage Early	**Late stage**	**Overall**
Male	52%	49.1%	232
Female	58%	43%	168
Total	54%	46%	400

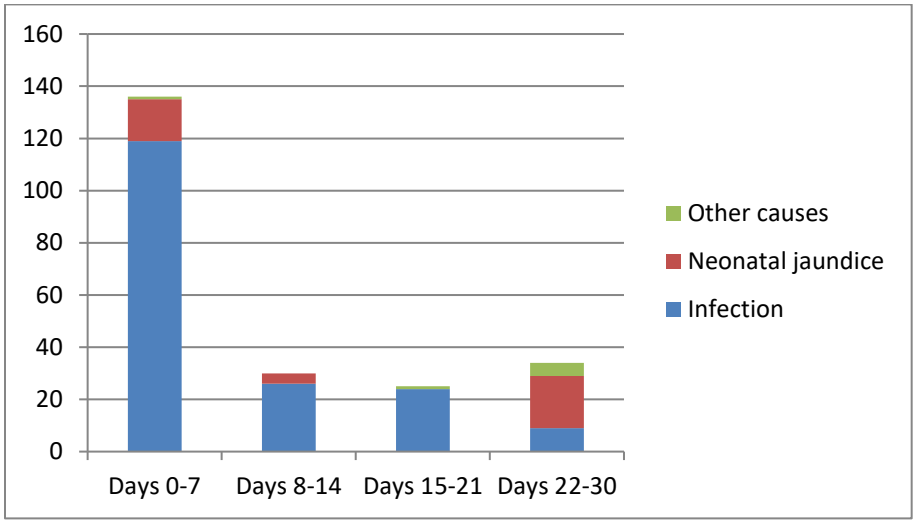
The average age with standard deviation (SD) was calculated for all participants involved in the study, yielding 6.38 ± 7.14 days.

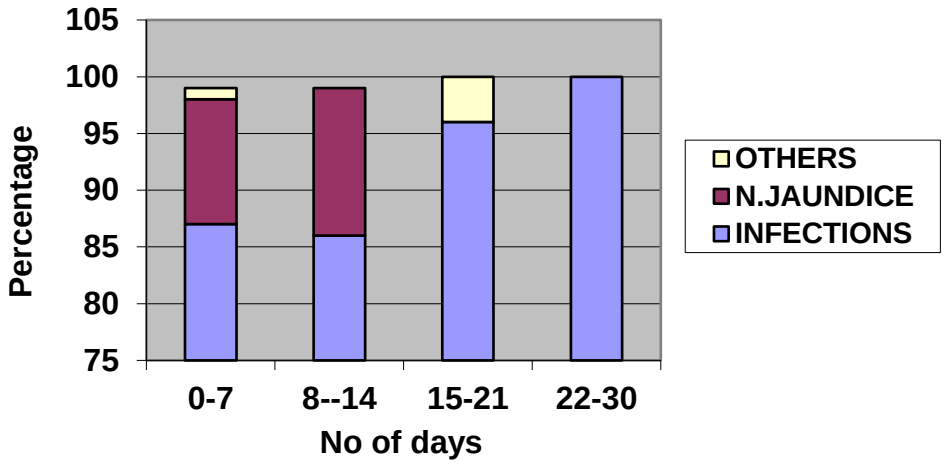
The distribution of causes of neonatal thrombocytopenia was analyzed across all patients. Infection emerged as the most prevalent cause, accounting for 356 cases (88%). Neonatal jaundice was identified in 40 cases (10.0%), while other causes were observed in only 4 cases (2.0%). Autoimmune maternal diseases were not reported.

Thrombocytopenia in neonatal (frequency of causes)

Reasons or causes of thrombocytopenia in neonatal	**Frequency**	**Percentage(100)**
Contagion or Infection	356	88.0
Jaundice(Neonatal)	40	10.0
Additional	4	2.0
Total	400	100.0

All individuals were categorized based on age ranges and diagnoses. In the 0 to 7-day age bracket, roughly 87.4% exhibited infections, 11.6% displayed neonatal jaundice, and only 1.0% demonstrated alternative origins of thrombocytopenia. Among those aged 8 to 14 days, 85.6% showcased infections, while 14.4% presented with neonatal jaundice. In the 15 to 21-day age group, 96.0% manifested infections, with merely two patients (4.0%) showing alternate causes of thrombocytopenia. For individuals aged 22 to 30 days, all patients (100%) were diagnosed with infections.





Graph 1, 2: Diagnosis of patient according to age groups

Neonates in the neonatology unit of a tertiary care hospital exhibited varying degrees of thrombocytopenia frequency. Approximately 21% (n=82) experienced mild thrombocytopenia, whereas 37.0% (n=146) and 42% (n=172) encountered moderate and severe thrombocytopenia, respectively.

Categories of thrombocytopenia	**Number of neonate**	**Out of 100**
Mild	82	21.0%
Intermediate	146	37.0%
Profound	172	42.0%
Overall	400	100%

DISCUSSION:

Thrombocytopenia stands as the predominant hemostatic abnormality among newborns, impacting approximately 25% of infants in neonatal intensive care units. The primary causes of thrombocytopenia include infections and disseminated intravascular coagulation. Severe thrombocytopenia is commonly encountered, necessitating platelet transfusions for any infant whose platelet count falls below 20 x 10^9/L. Infections, identified as the most common cause in this study, can be prevented with proper prenatal and postnatal care and timely treatment, which remains challenging for low-income families.

Although neonatal jaundice accounted for only 10 to 12 %, it remains significant, as affected patients may require exchange transfusions, placing additional demands on blood banks.

Infections were the leading cause of thrombocytopenia, accounting for 89.0% of cases. Neonatal jaundice emerged as the second most prevalent factor, accounting for 10.0% of cases, while alternative factors were accountable for merely 1.0%.

The severity of thrombocytopenia varied among the patients in our study. We observed that 21.0% of patients experienced a mild degree of thrombocytopenia, while 37.0% and 42% developed moderate and severe degrees, respectively.

Conclusion:

Thrombocytopenia is a serious finding in neonates, often prompting aggressive interventions. Establishing a comprehensive differential diagnosis list for thrombocytopenic neonates is crucial for pediatricians, neonatologists, and hematologists to identify the underlying cause and determine appropriate management strategies. While international literature offers extensive causes, our local context, marked by unhygienic conditions, malnutrition, and inadequate antenatal care, is likely to present unique etiologies and frequencies. Effective management can alleviate the burden on blood banks by promoting judicious use of platelet transfusions. Furthermore, it can mitigate unnecessary risks associated with overtreatment in neonates.

Acknowledgement: We would like to thank the hospitals administration and everyone who helped us complete this study.

Disclaimer: Nil

Conflict of Interest: There is no conflict of interest.

Funding Disclosure: Nil

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