Frequency of Thrombocytopenia in Neonates Presenting with Neonatal Sepsis

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ABSTRACT

Background: Neonatal sepsis is a leading cause of morbidity and mortality in neonates, often associated with thrombocytopenia. Early recognition and management are critical for improving outcomes. Thrombocytopenia is a frequent hematological abnormality in septic neonates, yet its frequency and associated factors require further investigation.

Objective: To determine the frequency of thrombocytopenia in neonates with sepsis at a tertiary care hospital and evaluate its association with demographic and clinical factors.

Methods: A cross-sectional study was conducted over six months at the Department of Pediatrics, Balochistan Institute of Child Health Services, Quetta. A total of 246 neonates with confirmed neonatal sepsis, aged less than 28 days, were included using non-probability consecutive sampling. Blood samples were collected for platelet count and bacterial culture. Thrombocytopenia was defined as a platelet count $<150 \times 10^9$/L. Data were analyzed using SPSS version 25, with Chi-square tests and logistic regression applied to assess associations.

Results: The mean age of the neonates was 8.92 ± 5.40 days; 117 (47.56%) were male, and 129 (52.44%) were female. Thrombocytopenia was identified in 63 (25.61%) neonates. Gram-negative sepsis was predominant (63.82%). No statistically significant association was found between thrombocytopenia and gender ($p = 0.991$) or culture type ($p = 0.141$).

Conclusion: Thrombocytopenia was observed in a quarter of septic neonates. Routine platelet monitoring in neonatal sepsis is essential for early detection and management to improve outcomes.

INTRODUCTION

Neonatal thrombocytopenia is a significant clinical concern, often encountered in neonatal intensive care units, particularly in neonates with sepsis. It is a multifaceted condition influenced by various etiologies, including infections caused by bacterial, viral, fungal, and parasitic pathogens, as well as non-infectious causes. Thrombocytopenia in neonates can present early, typically within the first 72 hours of life, as a consequence of placental insufficiency and reduced platelet production. In such cases, the condition is often mild to moderate and resolves spontaneously. Conversely, thrombocytopenia developing after 72 hours is frequently associated with neonatal sepsis or necrotizing enterocolitis, often presenting with more severe and prolonged clinical manifestations, necessitating interventions such as platelet transfusions (1, 2).

Neonatal sepsis, a leading cause of neonatal morbidity and mortality, significantly impacts platelet dynamics. Pathophysiologically, bacterial endotoxins and other microbial products cause endothelial damage, leading to platelet adhesion, aggregation, and rapid clearance from circulation. This process is particularly pronounced in Gram-negative infections, which are more commonly associated with prolonged and severe thrombocytopenia. Studies have shown that neonates with Gram-negative infections not only exhibit a higher incidence of thrombocytopenia but also face an increased risk of persistent bacteremia, multi-organ failure, and mortality. Notably, thrombocytopenia in septic neonates is an independent predictor of mortality, quadrupling the risk of adverse outcomes (3-6). Despite its clinical importance, there is still no consensus regarding the safe lower limits of platelet counts in septic neonates or the subset of patients who would benefit most from therapeutic interventions such as platelet transfusions (7).

The role of platelet indices such as mean platelet volume (MPV), platelet distribution width (PDW), and plateletcrit (PCT) has also been explored as diagnostic and prognostic markers in neonatal sepsis. These indices, when carefully evaluated, can aid in the timely diagnosis, monitoring, and therapeutic management of septic neonates, potentially improving clinical outcomes (8). Neonatal thrombocytopenia affects up to 35% of admissions to neonatal intensive care units and varies considerably in prevalence across studies, reflecting differences in sample size, environmental factors, and neonatal care practices (9, 10). Variability in the clinical and pathogenic characteristics of causative organisms further complicates the generalizability of findings and emphasizes the need for context-specific research (11).

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This study was designed to address the paucity of local data regarding the frequency of thrombocytopenia in neonates with sepsis, particularly in the context of Gram-negative versus Gram-positive infections. Understanding the association between neonatal thrombocytopenia and sepsis is crucial for early identification and prompt management of high-risk neonates. Given the high burden of neonatal mortality associated with sepsis-related thrombocytopenia, especially in resource-limited settings, this study aims to provide critical insights that can inform clinical guidelines and improve patient outcomes (12-15).

MATERIAL AND METHODS

This cross-sectional study was conducted at the Department of Pediatrics, Balochistan Institute of Child Health Services (BICHQ), Quetta, and Bolan Medical College (BMC), over a period of six months, from 24th August 2021 to 24th April 2022. The study utilized non-probability consecutive sampling to recruit a total of 246 neonates who were diagnosed with neonatal sepsis. The sample size was calculated using a 20% expected frequency of thrombocytopenia in neonates, with a 95% confidence interval and a 5% margin of error (5). Only neonates aged less than 28 days, of either gender, with sepsis confirmed by clinical and laboratory criteria, were included in the study. Exclusion criteria comprised neonates with other known causes of thrombocytopenia, such as fetal/neonatal alloimmune thrombocytopenia (FNAITP), maternal immune thrombocytopenic purpura (ITP), congenital anomalies, hyaline membrane disease, hypoxic-ischemic encephalopathy, or cases with probable blood culture contamination defined by a C-reactive protein (CRP) level >10 mg/L without clinical confirmation of sepsis. Data collection was initiated after obtaining informed consent from the parents or legal guardians of all participants. Ethical approval was secured from the institutional review board of Balochistan Institute of Child Health Services, ensuring adherence to the principles outlined in the Declaration of Helsinki for human research. Baseline demographic data, including age, gender, and maternal details, were recorded using a structured study questionnaire. Blood samples were collected aseptically and sent to the hospital laboratory for analysis. Platelet counts were obtained to identify thrombocytopenia, defined as a platelet count $<150 \times 10^9$/L. Concurrently, blood samples were inoculated into blood culture bottles and sent to the microbiology laboratory for culture and sensitivity testing to confirm bacterial etiology. Gram staining was performed to categorize the causative organisms as Gram-positive or Gram-negative. All laboratory investigations were conducted by qualified pathologists following standard operating procedures. Thrombocytopenia was classified based on severity, and the data were stratified by age, gender, and type of bacterial culture. The collected data were carefully reviewed for completeness and accuracy before analysis.

Data analysis was performed using SPSS version 25. Continuous variables, such as age, were expressed as means ± standard deviations, while categorical variables, such as gender, Gram stain results, and the presence of thrombocytopenia, were presented as frequencies and percentages. Chi-square tests were employed to examine associations between thrombocytopenia and categorical variables, such as gender and type of bacterial culture. A p-value <0.05 was considered statistically significant.

Throughout the study, strict confidentiality of participants' data was maintained. The findings aimed to contribute to a better understanding of the frequency and clinical significance of thrombocytopenia in neonatal sepsis, providing valuable insights for early diagnosis and management.

RESULTS

A total of 246 neonates diagnosed with neonatal sepsis were included in the study. The mean age of the neonates was 8.92 ± 5.40 days, with a minimum age of 1 day and a maximum age of 27 days. Of the total participants, 117 (47.56%) were male, and 129 (52.44%) were female. The majority of neonates had Gram-negative bacterial cultures, with 157 (63.82%) cases, compared to 54 (21.95%) with Gram-positive cultures. A total of 63 (25.61%) neonates were diagnosed with thrombocytopenia, while 183 (74.39%) neonates had normal platelet counts.

Table 1: Baseline Characteristics of the Study Population (n = 246)

Variable	Statistic
Mean Age (days)	8.92 ± 5.40
Gender	
- Male	117 (47.56%)
- Female	129 (52.44%)
Gram-positive culture	54 (21.95%)
Gram-negative culture	157 (63.82%)
Thrombocytopenia	
- Present	63 (25.61%)
- Absent	183 (74.39%)

The frequency of thrombocytopenia was further analyzed based on the age groups and bacterial culture types. Among neonates aged less than 14 days, 45 (23.2%) had thrombocytopenia, while 18 (34.6%) neonates aged between 14 and 28 days were thrombocytopenic. Although the incidence of thrombocytopenia appeared higher in older

neonates, this difference was not statistically significant (p = 0.119). Similarly, thrombocytopenia was observed in 35 (22.3%) neonates with Gram-negative sepsis and 18 (33.3%) with Gram-positive sepsis, but the association between culture type and thrombocytopenia was also not statistically significant (p = 0.141).

Table 2: Thrombocytopenia Frequency by Demographic and Culture Characteristics (n = 246)

Variable	Thrombocytopenia Present	Thrombocytopenia Absent	p-value
Gender			
- Male	30	87	0.991
- Female	33	96	
Age Group (days)			
- <14 days	45	149	0.119
- 14–28 days	18	34	
Culture Type			
- Gram-positive	18	36	0.141
- Gram-negative	35	122	0.113

Logistic regression analysis was performed to evaluate potential predictors of thrombocytopenia. The model included age, gender, and culture type (Gram-positive vs. Gram-negative) as independent variables. None of these factors showed a statistically significant association with the presence of thrombocytopenia (p > 0.05 for all).

Further stratification of data based on platelet count severity did not reveal significant differences between groups. However, descriptive trends indicated a higher prevalence of thrombocytopenia in Gram-positive cultures compared to Gram-negative cultures, and older neonates showed slightly increased risk, although these trends were not statistically robust.

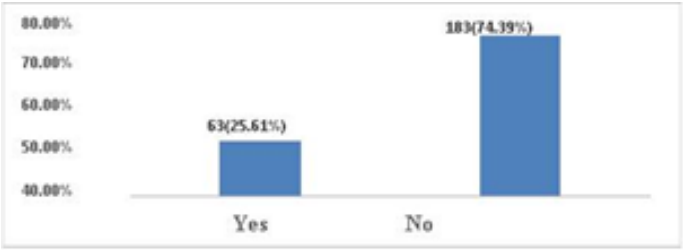

Figure 1 Frequency of thrombocytopenia among septic neonates n=246

In this study, the frequency of thrombocytopenia among neonates with sepsis was 25.61%. The condition was slightly more prevalent among females and neonates aged 14–28 days. However, gender, age, and type of bacterial culture were not found to be statistically significant predictors of thrombocytopenia. These findings underscore the need for larger studies with more granular data to better delineate risk factors and clinical implications of thrombocytopenia in neonatal sepsis.

DISCUSSION

The current study revealed that thrombocytopenia was present in 25.61% of neonates diagnosed with sepsis, aligning with previous findings that reported frequencies ranging from 20% to 35% among similar populations (5, 8). This prevalence underscores the clinical relevance of thrombocytopenia as a common hematological abnormality in neonates with sepsis. While the majority of cases were associated with Gram-negative bacterial infections, consistent with prior studies highlighting the higher pathogenicity and prolonged effects of Gram-negative organisms, the association between culture type and thrombocytopenia in this study did not reach statistical significance (3, 6). Gram-negative organisms are known to produce endotoxins that disrupt endothelial integrity, promote platelet activation, and increase platelet clearance, which may explain their more frequent association with thrombocytopenia in neonatal sepsis (4). However, the lack of a statistically significant correlation in this study may be attributable to the sample size or variations in bacterial strains and neonatal care practices.

Gender did not emerge as a significant factor in the occurrence of thrombocytopenia, which is consistent with some reports, though others have suggested a slightly higher prevalence in male neonates due to potential sex-based immunological differences (10, 13). Similarly, age was not a significant predictor, although a trend toward higher thrombocytopenia rates in neonates aged 14 to 28 days was noted. This trend might reflect the natural progression of sepsis and its complications in older neonates, warranting further investigation in larger cohorts.

The findings of this study were supported by previous literature emphasizing thrombocytopenia as an independent risk factor for neonatal morbidity and mortality. Neonates with severe thrombocytopenia have been shown to experience increased rates of multi-organ dysfunction and persistent bacteremia, both of which contribute to poor clinical outcomes (5, 7). Platelet indices, including mean platelet volume and platelet distribution width, were not assessed in this study, representing a limitation, as these parameters have been demonstrated to serve as early and sensitive markers of sepsis-related complications in neonates (2, 8). Future studies incorporating these indices could provide more comprehensive insights into the hematological alterations associated with neonatal sepsis.

One of the strengths of this study was its focus on a resource-limited setting, providing data from a population that is often underrepresented in neonatal sepsis research. The rigorous exclusion criteria minimized confounding factors, ensuring that the observed thrombocytopenia was predominantly attributable to sepsis. However, the study was limited by its single-center design, which may restrict the generalizability of the findings.

Additionally, the use of non-probability sampling and the absence of longitudinal follow-up data limited the ability to assess the progression and clinical outcomes of thrombocytopenia in the included neonates.

Another limitation was the reliance on culture-positive sepsis as the primary diagnostic criterion, which may have excluded cases of culture-negative sepsis, a known challenge in neonatal populations (6). The lack of advanced molecular diagnostic tools to identify specific bacterial strains or quantify endotoxin levels also constrained the depth of analysis. Furthermore, environmental and care-related factors unique to the study setting, such as infection control practices and antibiotic resistance patterns, may have influenced the results and should be considered when interpreting the findings.

Based on these results, it was evident that thrombocytopenia remains a significant and clinically relevant complication in neonates with sepsis. It is recommended that clinicians adopt a proactive approach to monitoring platelet counts and indices in septic neonates, particularly in those with Gram-negative infections. Early detection and targeted management of thrombocytopenia, including the judicious use of platelet transfusions, could mitigate its impact on neonatal outcomes. Future multicenter studies with larger sample sizes and more advanced diagnostic modalities are necessary to validate these findings, explore the underlying mechanisms further, and identify potential therapeutic targets. In addition, efforts to standardize neonatal sepsis management protocols and improve infection prevention measures could play a pivotal role in reducing the burden of thrombocytopenia and its associated complications in this vulnerable population.

CONCLUSION

The study concluded that thrombocytopenia was observed in approximately one-quarter of neonates with sepsis, emphasizing its significance as a common hematological complication and independent risk factor for neonatal morbidity and mortality. While no statistically significant associations were found with gender, age, or bacterial culture type, the findings underscore the importance of early identification and management of thrombocytopenia in septic neonates to improve clinical outcomes. These results highlight the need for routine platelet monitoring in neonatal sepsis protocols, particularly in resource-limited settings, and advocate for further research to optimize care strategies. Addressing thrombocytopenia promptly could reduce the burden of complications and enhance survival rates, contributing to improved neonatal health outcomes globally.

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