DOI: https://doi.org/10.54393/pjhs.v6i4.2993

PAKISTAN JOURNAL OF HEALTH SCIENCES
(LAHORE)
https://thejas.com.pk/index.php/pjhs
ISSN (E): 2790-9352, (P): 2790-9344
Volume 6, Issue 04 (April 2025)

Original Article

OPEN ACCESS

Frequency of Thrombocytopenia in Septic Neonates Admitted to Nursery Section of Pediatric Unit, DHQ Dera Ismail Khan

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ARTICLE INFO

Keywords:
Neonatal Sepsis, Thrombocytopenia, Mechanical Ventilation, Platelet Count

How to Cite:
Yahya, A., Burki, F., Khan, I., Khan, A., & Khan, O. (2025). Frequency of Thrombocytopenia in Septic Neonates Admitted to Nursery Section of Pediatric Unit, DHQ Dera Ismail Khan: Thrombocytopenia in Septic Neonates Admitted to Nursery Section of Pediatric Unit.Pakistan Journal of Health Sciences, 6(4), 170-176. https://doi.org/10.54393/pjhs.v6i4.2993

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Received date: 6th March, 2025
Revised date: 24th April, 2025
Acceptance date: 27th April, 2025
Published date: 30th April, 2025

ABSTRACT

Neonatal sepsis is a major cause of morbidity and mortality, often complicated by thrombocytopenia, which increases the risk of bleeding and worsens prognosis. Reported frequencies of thrombocytopenia in septic neonates vary widely, and local data are limited. **Objectives:** To determine the frequency of thrombocytopenia in septic neonates and its association with clinical and laboratory parameters. **Methods:** This cross-sectional study was conducted at the Department of Paediatrics, DHQ Hospital, Dera Ismail Khan, over six months. A total of 110 septic neonates were enrolled. Demographics, clinical presentations, and laboratory findings were recorded.Blood samples were analyzed for platelet count, white blood cell count, C-reactive protein (CRP), and blood cultures. Data were analyzed using SPSS Version 25, with chi-square and Mann-Whitney U tests applied. Logistic regression identified predictors of thrombocytopenia, with $p<0.05$ considered significant. **Results:** Thrombocytopenia was found in 69.1% of septic neonates. Early-onset sepsis was significantly associated with thrombocytopenia ($p=0.032$), while blood culture results, bacterial pathogen type, CRP, and White Blood Cells (WBC) count were not. Mechanical ventilation showed a significant association ($p=0.033$), and thrombocytopenic neonates had higher mortality ($p=0.053$). Logistic regression identified mechanical ventilation ($p=0.047$, OR=0.386) as a significant predictor, while early-onset sepsis showed borderline significance ($p=0.056$, OR=2.489). **Conclusions:** It was concluded that thrombocytopenia is common in septic neonates, with early-onset sepsis and mechanical ventilation as key risk factors. Routine platelet monitoring in critically ill neonates is essential for timely intervention.

INTRODUCTION

Neonatal sepsis remains a leading cause of neonatal morbidity and mortality, particularly in developing countries, where a significant proportion of neonatal deaths occur within the first 28 days of life [1]. Globally, neonatal sepsis affects approximately 22 per 1,000 live births, with an even higher burden in resource-limited settings. It is a frequent cause of neonatal intensive care unit (NICU) admissions and can progress rapidly to septic shock, contributing to mortality rates as high as 40–70% among critically ill neonates [2]. Diagnosing neonatal sepsis relies on clinical presentation in conjunction with laboratory markers such as C-reactive protein (CRP), total leukocyte count, and blood cultures. It is categorized as early-onset sepsis (EONS), occurring within 72 hours of birth, or late-onset sepsis (LONS), presenting between 4–28 days [3]. EONS often manifests with respiratory distress, poor feeding, lethargy, and temperature instability. Thrombocytopenia is a common hematological abnormality in septic neonates and may exacerbate clinical outcomes by increasing the risk of bleeding [4]. The pathophysiology is multifactorial, involving platelet consumption, bone marrow suppression, and endothelial dysfunction. Reported frequencies of thrombocytopenia in septic neonates vary widely, ranging from 25% to 75%, depending on geographic and institutional differences [5]. Despite these findings, there is a notable lack of

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standardized, region-specific data on the frequency and risk factors of thrombocytopenia in septic neonates in Pakistan.Local studies are scarce and often lack clearly defined diagnostic criteria.

Neonatal sepsis is a major cause of neonatal morbidity and mortality, often complicated by thrombocytopenia, which further increases the risk of bleeding and poor clinical outcomes. However, the reported frequency and associated risk factors of thrombocytopenia vary widely across different populations, and there is limited region-specific evidence from resource-constrained settings such as Pakistan. Moreover, existing studies show inconsistent findings regarding its predictors, especially in relation to sepsis type, inflammatory markers, and need for respiratory support. This study aims to determine the frequency of thrombocytopenia and its association with clinical and laboratory parameters among septic neonates admitted to DHQ Hospital, Dera Ismail Khan. The findings aim to improve early detection and management of hematologic complications in neonatal sepsis in similar resource-constrained healthcare settings.

METHODS

This cross-sectional study was conducted at the Department of Paediatrics, District Headquarters (DHQ) Hospital, Dera Ismail Khan, a tertiary care facility with a specialised neonatal unit.It aimed to assess the prevalence of thrombocytopenia among septic neonates admitted to the pediatric ward's nursery over six months from August 2023 to January 30, 2024. Ethical approval for this study was obtained from the Ethical Review Committee of Gomal Medical College, MTI, Dera Ismail Khan (Approval No: 147/GJMS/JC)and the Research Evaluation Unit, College of Physicians and Surgeons Pakistan (Ref No: CPSP/REU/PED-2023-029-7541). Written informed consent was obtained from parents or guardians of all enrolled neonates. Patient confidentiality was maintained throughout the study, and data were anonymized for analysis. The sample size was calculated using the WHO Sample Size Calculator, with a confidence level of 95%, margin of error of 8%, and expected frequency of thrombocytopenia at 25.6% based on previous literature [6]. The final sample included 110 neonates to allow for potential dropouts. A non-probability consecutive sampling technique was applied. Inclusion Criteria were Neonates aged 1 to 28 days (both male and female). Clinically diagnosed with neonatal sepsis, defined as neonates presenting with poor feeding, lethargy, sluggish reflexes, poor perfusion, and temperature instability >12 hours. C-reactive protein (CRP) >10 mg/L. and a positive blood culture confirming infection. Exclusion Criteria were Neonates with autoimmune or alloimmune thrombocytopenia (assessed via maternal CBC). Syndromic neonates or those with congenital skeletal deformities. And neonates who received plasma transfusions before enrollment. Thrombocytopenia was defined as a platelet count below 150,000/µL. Severity was categorized as follows: mild (100,000–149,999/µL), moderate (50,000–99,999/µL), and severe (<50,000/µL). Demographic and clinical data were recorded on a structured proforma and included: Age, gender, gestational age, birth weight, and mode of delivery. Maternal risk factors (diabetes, preeclampsia, prolonged rupture of membranes). And clinical findings and comorbidities (jaundice, RDS, NEC). Laboratory Investigations CBC including platelet count, WBC count, and CRP levels, were performed. And blood cultures were analyzed to identify bacterial organisms. Clinical Outcomes NICU stay duration, hospital stay, mechanical ventilation requirement, mortality, and thrombocytopenia resolution time were documented. Blood samples (2–3 mL) were drawn in EDTA tubes and processed using standard hospital laboratory procedures. CRP was assessed through immunoassay, and blood cultures were incubated and examined using microbiological methods. Radiographic evaluation was done in cases with respiratory distress. To ensure reliability, CBC reports were manually verified by a senior hematologist. Inter-observer reliability was maintained, and data entry was done in duplicate to minimize errors. Data were analyzed using IBM SPSS Statistics, version 25. Continuous variables were assessed for normality using the Kolmogorov-Smirnov and Shapiro-Wilk tests. Since the data were not normally distributed, non-parametric tests were applied. The Mann-Whitney U test was used to compare continuous variables such as neonatal age at admission, NICU stay duration, hospital stay duration, and thrombocytopenia resolution time between thrombocytopenic and non-thrombocytopenic neonates. For categorical variables, the Chi-square test (χ^2) was used to examine associations between thrombocytopenia and variables including gender, gestational age, birth weight, mode of delivery, maternal risk factors, clinical comorbidities, sepsis type, CRP levels, WBC count, and mechanical ventilation. Where expected cell counts were less than 5, Fisher's Exact Test was applied. To identify independent predictors of thrombocytopenia, binary logistic regression analysis was performed. Variables included in the model were sepsis type (early vs. late onset), mechanical ventilation, platelet count categories, CRP level, WBC count, NICU stay duration, mortality outcome, and need for platelet transfusion. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. A p-value less than 0.05 was considered statistically significant. Model fitness was assessed using the Hosmer-Lemeshow goodness-of-fit test, and variance was explained using Nagelkerke's R^2 and Cox and Snell R^2 values. Overall classification accuracy was also reported to evaluate model performance.

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RESULTS

The results show no significant association between thrombocytopenia and gender (p=0.311), gestational age (p=0.158), or birth weight (p=0.876). However, preterm and low-birth-weight neonates had slightly higher thrombocytopenia frequencies. Mode of delivery, maternal risk factors, Apgar scores, and place of birth also did not show significant associations (all p>0.05). Neonatal age at admission was analyzed using the Mann-Whitney U test and was not significantly different between groups (p=0.260)(Table 1).

Table 1: Association of Demographic Characteristics with Thrombocytopenia

Variables	Category	Thrombocytopenia n (%)	Thrombocytopenia n (%)	p-value	Significance
		Yes	No		
Gender	Female	30 (39.5%)	10 (29.4%)	0.311	No Association
	Male	46 (60.5%)	24 (70.6%)		
Gestational Age	Preterm (<37 Weeks)	57 (75.0%)	21 (61.8%)	0.158	No Association
	Term (≥37 Weeks)	19 (25.0%)	13 (38.2%)		
Birth Weight	Low Birth Weight	48 (63.2%)	22 (64.7%)	0.876	No Association
	Normal Weight	28 (36.8%)	12 (35.3%)		
Mode of Delivery	Cesarean Section	43 (56.6%)	17 (50.0%)	0.522	No Association
	Normal Vaginal Delivery	33 (43.4%)	17 (50.0%)		
Maternal Risk Factors	Multiple Categories	-	-	0.549	No Association
Apgar Score at Birth	>6	65 (85.5%)	28 (82.4%)	0.670	No Association
Place of Birth	In-Hospital	62 (81.6%)	25 (73.5%)	0.337	No Association
Neonatal Age at Admission	Mean Rank (MWU)	57.76	50.46	0.260	No Difference

The study presents the association between various clinical and laboratory parameters with thrombocytopenia in septic neonates. A significant relationship was observed between sepsis type and thrombocytopenia (p=0.032), with early-onset sepsis being more prevalent among thrombocytopenic neonates.However, blood culture results did not show a significant association (p=0.234), indicating that thrombocytopenia was not necessarily linked to the presence of a positive blood culture. Similarly, organism type isolated from blood cultures (E. coli, Klebsiella, Staphylococcus, and others) had no significant impact on thrombocytopenia (p=0.710), suggesting that the presence of thrombocytopenia was independent of the specific bacterial pathogen. Inflammatory markers such as C-reactive protein (CRP) levels did not significantly differ between thrombocytopenic and non-thrombocytopenic neonates (p = 0.808), indicating that elevated CRP levels, a marker of infection, may not predict thrombocytopenia in sepsis. Similarly, white blood cell (WBC) count categories (elevated, low, and normal) showed no significant association with thrombocytopenia (p=0.486), suggesting that leukocyte abnormalities do not necessarily correlate with platelet reduction. Additionally, platelet count severity categories (mild, moderate, and severe thrombocytopenia) were not statistically significant in their association with thrombocytopenia (p=0.339), indicating that overall platelet reduction may not be directly influenced by its severity category in this study population. Finally, the need for platelet transfusion did not show a significant difference between groups (p=0.628), suggesting that thrombocytopenia management may not vary significantly in septic neonates requiring transfusion. Overall, only sepsis type showed a significant association with thrombocytopenia, highlighting its potential role as a contributing factor. However, other clinical and laboratory parameters, such as blood culture results, inflammatory markers, and platelet severity levels, were not significantly associated with thrombocytopenia, indicating that additional factors may influence its development in septic neonates (Table 2).

Table 2: Association of Clinical and Laboratory Findings with Thrombocytopenia

Variables	Category	Thrombocytopenia n (%)	Thrombocytopenia n (%)	p-value	Significance
		Yes	No		
Sepsis Type	Early-Onset (<72 hrs)	56 (73.7%)	18 (52.9%)	0.032	Significant
	Late-Onset (≥72 hrs)	20 (26.3%)	16 (47.1%)		
Blood Culture Result	Negative	29 (38.2%)	9 (26.5%)	0.234	No Association
	Positive	47 (61.8%)	25 (73.5%)		
Organism Identified	*E. coli*	28 (36.8%)	9 (26.5%)	0.710	No Association
	Klebsiella	15 (19.7%)	7 (20.6%)		
	Staphylococcus	26 (34.2%)	15 (44.1%)		
	Others	7 (9.2%)	3 (8.8%)		

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CRP Level	Elevated	64 (84.2%)	28 (82.4%)	0.808	No Association
	Normal	12 (15.8%)	6 (17.6%)		
WBC Count	Elevated	43 (56.6%)	23 (67.6%)	0.486	No Association
	Low	15 (19.7%)	4 (11.8%)		
	Normal	18 (23.7%)	7 (20.6%)		
Platelet Count	Mild (100,000–149,999)	28 (36.8%)	11 (32.4%)	0.339	No Association
	Moderate (50,000–99,999)	35 (46.1%)	13 (38.2%)		
	Severe (<50,000)	13 (17.1%)	10 (29.4%)		
Need for Platelet Transfusion	Yes	44 (57.9%)	18 (52.9%)	0.628	No Association
	No	32 (42.1%)	16 (47.1%)		

The study examined additional clinical variables. Neonatal comorbidities (p=0.261) and antibiotic therapy (p=0.847) were not significantly associated with thrombocytopenia. However, mechanical ventilation was significantly linked to thrombocytopenia (p=0.033). Mortality was higher in thrombocytopenic neonates, with borderline significance (p=0.053), suggesting a possible association with adverse outcomes (Table 3).

Table 3: Association of Additional Factors with Thrombocytopenia

Variables	Category	Thrombocytopenia n (%)	Thrombocytopenia n (%)	p-value	Significance
		Yes	No		
Neonatal Comorbidities	Jaundice	18 (23.7%)	11 (32.4%)	0.261	No association
	NEC	15 (19.7%)	5 (14.7%)		
	None	17 (22.4%)	11 (32.4%)		
	Others	10 (13.2%)	5 (14.7%)		
	RDS	16 (21.1%)	2 (5.9%)		
Antibiotic Therapy Given	Yes	68 (69.4%)	30 (30.6%)	0.847	No Association
	No	8 (66.7%)	4 (33.3%)		
Mechanical Ventilation	Yes	22 (56.4%)	17 (43.6%)	0.033	Significant
	No	54 (76.1%)	17 (23.9%)		
Mortality Outcome	Expired	30 (81.1%)	7 (18.9%)	0.053	Borderline
	Survived	46 (63.0%)	27 (37.0%)		

Research examines the relationship between thrombocytopenia and clinical outcomes, including NICU stay duration, hospital stay duration, and thrombocytopenia resolution time. The Mann-Whitney U test revealed that there were no significant differences in NICU stay duration (p=0.306), hospital stay duration (p=0.765), or thrombocytopenia resolution time (p=0.609) between neonates with and without thrombocytopenia. These findings suggest that thrombocytopenia does not independently impact hospital or NICU stay duration, nor does it significantly affect the time taken for platelet levels to recover (Table 4).

Table 4: Association of Clinical Outcomes with Thrombocytopenia

Variables	Thrombocytopenia Mean ± SD	Thrombocytopenia Mean ± SD	p-value	Significance
	Yes	No		
NICU Stay Duration (Days)	8.86 ± 3.20	9.56 ± 2.87	0.306	No Difference
Hospital Stay Duration (Days)	12.09 ± 3.77	11.91 ± 4.14	0.765	No Difference
Thrombocytopenia Resolution Time (Days)	5.68 ± 2.16	5.41 ± 2.32	0.609	No Difference

Results present the results of logistic regression analysis to determine potential predictors of thrombocytopenia. The findings indicate that sepsis type (early vs. late-onset) was borderline significant (p=0.056), with early-onset sepsis showing a trend toward increasing the likelihood of thrombocytopenia (OR=2.489). The need for mechanical ventilation emerged as a significant predictor (p=0.047), with neonates requiring ventilation having lower odds of thrombocytopenia (OR=0.386). Other variables, including platelet count, mortality outcome, gender, CRP levels, WBC count, need for platelet transfusion, NICU stay duration, and thrombocytopenia resolution time, did not show statistically significant associations (p>0.05). This suggests that while mechanical ventilation and sepsis type may play a role in thrombocytopenia risk, other commonly suspected factors did not appear to be strong predictors in this study population (Table 5).

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Table 5: Logistic Regression for Thrombocytopenia (Yes/No)

Variables	B (Coefficient)	Wald χ^2	p-value	Odds Ratio (Exp (B))	95% CI (Lower – Upper)	Significance
Sepsis Type (Early vs. Late-Onset)	0.912	3.645	0.056	2.489	(0.976 – 6.346)	Borderline
Mechanical Ventilation (Yes vs. No)	-0.952	3.954	0.047	0.386	(0.151 – 0.986)	Significant
Platelet Count (Mild vs. Severe)	-0.908	2.017	0.156	0.403	(0.115 – 1.412)	No Effect
Platelet Count (Moderate vs. Severe)	-1.107	3.117	0.077	0.331	(0.097 – 1.130)	No Effect
Mortality Outcome (Expired vs. Survived)	-0.908	2.861	0.091	0.403	(0.141 – 1.155)	No Effect
Gender (Female vs. Male)	-0.844	2.461	0.117	0.430	(0.150 – 1.234)	No Effect

DISCUSSION

The findings of this study highlight the frequency and risk factors associated with thrombocytopenia in septic neonates. Thrombocytopenia was significantly associated with early-onset neonatal sepsis, reinforcing the role of sepsis severity in platelet consumption and bone marrow suppression. This aligns with previous studies reporting higher rates of thrombocytopenia in early-onset sepsis due to maternal-fetal transmission of infections, systemic inflammation, and endothelial dysfunction [7-9]. Blood culture positivity and specific bacterial pathogens *(E. coli, Klebsiella, Staphylococcus)* did not show a significant association with thrombocytopenia.This suggests that the development of thrombocytopenia may be more closely related to the neonate's inflammatory response than the infecting organism. Although gram-negative infections are often associated with severe thrombocytopenia, gram-positive organisms can also trigger cytokine activation, leading to platelet changes [10, 11]. In this study, CRP levels and WBC counts were not significantly different between neonates with and without thrombocytopenia, indicating that traditional inflammatory markers may not reliably predict thrombocytopenia severity. This finding supports earlier literature emphasizing the diagnostic value of CRP for neonatal sepsis but not for its hematologic complications [12-14]. The severity of thrombocytopenia (mild, moderate, or severe) was not significantly linked to its presence, suggesting that other factors, such as cytokine storms, endothelial activation, and coagulation abnormalities, may contribute more to clinical severity. This supports the idea that multi-marker approaches may better predict sepsis-related hematological complications. Mechanical ventilation was significantly associated with thrombocytopenia, reflecting the impact of respiratory distress, hypoxia, and systemic inflammation on platelet counts. Previous studies have similarly reported higher thrombocytopenia rates in ventilated neonates, possibly due to ventilator-induced lung injury and prolonged inflammation [15-17]. Mortality outcomes approached statistical significance (p=0.053), with a higher proportion of thrombocytopenic neonates experiencing adverse outcomes. This aligns with other studies that identify thrombocytopenia as a predictor of poor prognosis, likely due to its link with systemic instability and multi-organ dysfunction [18-20].

This study has several limitations, including its single-center design, relatively small sample size, and use of non-probability consecutive sampling, which may limit generalizability. The short study duration and exclusion of certain high-risk neonatal subgroups may also have affected the ability to detect stronger associations. Future research should involve large-scale, multicenter prospective studies with longer follow-up periods to improve external validity. Additionally, incorporating advanced inflammatory and hematological biomarkers may help better predict thrombocytopenia and guide early targeted interventions in septic neonates.

CONCLUSIONS

It was concluded that thrombocytopenia was common in septic neonates, especially those with early-onset sepsis and requiring mechanical ventilation. Routine platelet monitoring is essential to guide timely interventions and reduce adverse outcomes in critically ill neonates.

Authors' Contribution

Conceptualization: AY
Methodology: IK, AK, OK
Formal analysis: AY, FB
Writing and Drafting: AY, FB, IK, AK
Review and Editing: AY, FB, IK, AK

All authors approved the final manuscript and take responsibility for the integrity of the work

DOI: https://doi.org/10.54393/pjhs.v6i4.2993

Conflicts of Interest

All the authors declare no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

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