



Frequency and Severity of Thrombocytopenia in Neonatal Sepsis

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ABSTRACT

Background: Neonatal sepsis is serious infection in first 28 days of life and it can cause many hematological problems. One common problem is thrombocytopenia which increase risk of bleeding and poor outcome. **Objective:** To determine the frequency and severity of thrombocytopenia in neonates with sepsis. **Study Design:** Descriptive cross-sectional study. **Duration and Place of Study:** Conducted from 5 April 2024 to 5 October 2024 at Neonatal Intensive Care Unit, Combined Military Hospital Abbottabad. **Methodology:** A total of 136 culture positive septic neonates aged ≤ 28 days were included by calculated sample size. Demographic and clinical data were recorded. Thrombocytopenia was noted. Data was analyzed by Statistical Package for Social Sciences version 26. Mean \pm standard deviation was calculated for quantitative variables. Chi-square test was applied after stratification and $p \leq 0.05$ was taken significant. **Results:** Mean age was 14.49 ± 7.99 days and mean weight 2.97 ± 0.51 kg. Thrombocytopenia was found in 85 (62.50%) neonates. Among them, mild was 23 (27.10%), moderate 31 (36.50%) and severe 31 (36.50%). Age > 14 days showed higher thrombocytopenia 49 (71.0%) compared to ≤ 14 days 36 (53.7%) ($p=0.037$). Gender, mode of delivery and feeding type had no significant association ($p>0.05$). **Conclusion:** Thrombocytopenia is common in neonatal sepsis and most cases are moderate to severe. Increasing age is significant associated factor.

INTRODUCTION

Neonatal sepsis is a severe systemic infection occurring during the neonatal period.¹ It is one of the most important causes of neonatal morbidity and mortality, especially in developing countries.² Sepsis in neonates is usually classified as early-onset sepsis or late-onset sepsis, depending on the time of onset after birth. The infection can be caused by several gram-positive and gram-negative bacteria, leading to a systemic inflammatory response syndrome.³ In the course of this inflammatory response, several hematologic changes can occur, with thrombocytopenia being one of the most common manifestations.⁴ Thrombocytopenia is defined by platelet counts lower than $150,000/\mu\text{L}$, which can occur in neonates with sepsis, leading to platelet consumption, decreased platelet production, and increased platelet destruction in disseminated intravascular coagulation.⁵

The prevalence of thrombocytopenia in neonatal sepsis has been found to be quite high, as indicated by several studies done at different hospitals.⁶ The studies found that a considerable number of septic neonates suffered from mild to severe thrombocytopenia. Severe, moderate, and mild thrombocytopenia can be defined as platelet counts less than $50,000/\mu\text{L}$, $50,000-100,000/\mu\text{L}$,

and $100,000-150,000/\mu\text{L}$, respectively.⁷ Severe thrombocytopenia in septic neonates can be caused by gram-negative bacterial infections, and it can lead to bleeding manifestations such as petechiae, gastrointestinal bleeding, and intraventricular hemorrhage.⁸

The assessment of the incidence and degree of thrombocytopenia in neonatal sepsis can be clinically significant, as it can be used as a diagnostic and prognostic tool.⁹ Low platelet counts in neonatal sepsis have shown a positive association with the degree of disease, shock, and high mortality rates.¹⁰ The monitoring of platelet counts can be useful in early detection of disease complications and timely intervention, including platelet transfusions.¹⁰ Platelet counts can be used as a diagnostic tool in resource-constrained facilities, where other biomarkers are not readily available.¹¹

Neonatal sepsis is common in tertiary care hospitals of Abbottabad, but local data about frequency and severity of thrombocytopenia is limited. Most evidence is from other regions and may not reflect local infection pattern and neonatal characteristics. This study is needed to determine the burden of thrombocytopenia in septic neonates in Abbottabad so early identification and proper

management can be improved and neonatal morbidity and mortality can be reduced.

METHODOLOGY

This descriptive cross-sectional study was conducted at CMH Abbottabad from 5th April 2024 to 5th October 2024 in the Neonatal Intensive Care Unit. Approval was obtained from the Institutional Ethical Review Committee of CMH Abbottabad before starting the study. The research was conducted according to hospital ethical standards and principles for human research. The sample size of 136 neonates was calculated by using WHO sample size software, taking 95% confidence level, 8% margin of error, and expected prevalence 65.29% of thrombocytopenia among neonates with sepsis.¹² Neonates aged ≤ 28 days of either gender, admitted with neonatal sepsis and having positive blood culture were included. Neonatal sepsis was considered when the neonate had clinical features such as fever, poor feeding, lethargy, respiratory distress, temperature instability or seizures along with positive blood culture report. Early-onset sepsis was taken when symptoms appeared within first 72 hours of life and late-onset sepsis when symptoms appeared after 72 hours up to 28 days. Neonates with maternal history of immune thrombocytopenic purpura, systemic lupus erythematosus, intake of drugs during pregnancy known to cause thrombocytopenia, congenital malformations, chromosomal abnormalities or family history of inherited bleeding disorders were excluded. Written informed consent was obtained from parents or legal guardians before enrollment. Confidentiality of patient information was maintained throughout the study. Demographic variables were recorded including age (in days), gender, weight (kg), mode of delivery and feeding type (exclusive breastfeeding, formula feeding or mixed feeding).

A detailed physical examination was performed. Blood samples were collected for a complete blood cell count, platelet count, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and blood culture under aseptic precautions. The platelet count was performed by automated cell counting and also by examination of a peripheral blood smear. After the laboratory investigations, the incidence and severity of thrombocytopenia were assessed. The criteria for thrombocytopenia were a platelet count of less than $150 \times 10^9/L$. Mild thrombocytopenia was a platelet count of 100 to $150 \times 10^9/L$. Moderate thrombocytopenia was a platelet count of 50 to $100 \times 10^9/L$. Severe thrombocytopenia was a platelet count of less than $50 \times 10^9/L$. A positive result for CRP was a level of more than 6 mg/L. ESR was considered to be elevated if it was more.

All data were entered and analyzed using IBM SPSS version 26. Quantitative variables such as age, weight, platelet count, CRP and ESR were presented as mean \pm standard deviation. Qualitative variables including gender, mode of delivery, feeding type, frequency and severity of thrombocytopenia were presented as frequency and percentage. Post-stratification was done for age, gender, mode of delivery and feeding type to control effect modifiers. After stratification, chi-square test was applied and p-value ≤ 0.05 was taken as significant.

RESULTS

The total of 136 neonates was studied with mean age of 14.49 ± 7.99 days and mean weight of 2.97 ± 0.51 kg. The mean platelet count was recorded as $151.16 \pm 116.32 \times 10^9/L$, while mean CRP was 18.33 ± 14.97 mg/L and mean ESR was 35.57 ± 18.44 mm/hr. Regarding gender distribution, majority of neonates was male 89 (65.4%) while female were 47 (34.6%). The mode of delivery show that vaginal delivery was slightly more common with 70 (51.5%) cases comparing to c-section which was 66 (48.5%). For feeding type, exclusive breastfeeding was the most frequent method observed in 83 (61.0%) neonates, followed by formula feeding in 27 (19.9%) and mixed feeding in 26 (19.1%) neonates (Table-I).

Table I
Patient Demographics

Demographics	Mean \pm SD / n (%)
Age (days)	14.49 \pm 7.99
Weight (kg)	2.97 \pm 0.51
Platelet Count ($\times 10^9/L$)	151.16 \pm 116.32
CRP (mg/L)	18.33 \pm 14.97
ESR (mm/hr)	35.57 \pm 18.44
Gender	
Male n (%)	89 (65.4%)
Female n (%)	47 (34.6%)
Mode of Delivery	
Vaginal n (%)	70 (51.5%)
C-section n (%)	66 (48.5%)
Feeding Type	
Exclusive Breast Feeding n (%)	83 (61.0%)
Formula n (%)	27 (19.9%)
Mixed n (%)	26 (19.1%)

Out of total 136 neonates, thrombocytopenia was present in 85 (62.50%) cases while remaining 51 (37.50%) neonates did not had thrombocytopenia. Among the neonates who was diagnosed with thrombocytopenia, severity analysis revealed that mild thrombocytopenia was found in 23 (27.10%) cases, whereas moderate and severe thrombocytopenia was found equally, each accounting for 31 (36.50%) cases (Table-II).

Table II
Frequency and Severity of Thrombocytopenia in Neonatal Sepsis

Variable	Frequency	%age
Thrombocytopenia		
Yes	85	62.50%
No	51	37.50%
Total	136	100%
Severity of Thrombocytopenia		
Mild	23	27.10%
Moderate	31	36.50%
Severe	31	36.50%
Total	85	100%

When stratified analysis was done for demographic factors associated with thrombocytopenia, age was found to be statistically significant factor ($p=0.037$). Neonates with age more than 14 days had higher proportion of thrombocytopenia with 49 (71.0%) cases as compared to those of age 14 days or less which showed 36 (53.7%) cases. For gender, thrombocytopenia was present in 56 (62.9%) male and 29 (61.7%) female neonates, however this difference was not statistically significant ($p=0.889$). In mode of delivery, vaginal delivery group showed thrombocytopenia in 47 (67.1%) neonates while c-section group had 38 (57.6%) cases, though the association was

not significant statistically ($p=0.249$). Regarding feeding type, exclusive breastfeeding group had highest proportion of thrombocytopenia with 58 (69.9%) cases, while formula fed neonates showed 13 (48.1%) and mixed feeding group had 14 (53.8%) cases, however this association was also not reach statistical significance ($p=0.077$) (Table-III).

Table III
Association of Thrombocytopenia with Demographic Factors

Demographic Factors	Thrombocytopenia		p-value*
	Yes n(%)	No n(%)	
Age (days)	≤14	36 (53.7%)	0.037
	>14	49 (71.0%)	
Gender	Male	56 (62.9%)	0.889
	Female	29 (61.7%)	
Mode of Delivery	Vaginal	47 (67.1%)	0.249
	C-section	38 (57.6%)	
Feeding Type	EBF	58 (69.9%)	0.077
	Formula	13 (48.1%)	
	Mixed	14 (53.8%)	

*Chi-Square Test

DISCUSSION

In this study, thrombocytopenia was seen in 85 neonates, constituting 62.50% of the study population, which is an alarmingly high percentage. This high percentage of thrombocytopenia in the neonatal period can be explained by the high rate of physiological changes occurring during this period, as well as the inability of the immature bone marrow to increase the production of platelets in response to increased consumption or destruction. It is also known that immune-mediated processes and infections in the neonatal period can increase the rate of destruction of platelets. Out of the neonates with thrombocytopenia, severe and moderate thrombocytopenia were seen in 31 (36.50%), nearly three-fourths of the neonates with thrombocytopenia, indicating that the thrombocytopenia seen in the neonatal period is of significant severity, possibly because the size of the neonatal megakaryocyte is smaller and the number of platelets produced is less than in adults. The frequency of thrombocytopenia found in present study was 85 (62.50%) which is somewhat comparable to findings of Arabdin *et al.*¹² who reported thrombocytopenia in 111 (65.29%) neonates with sepsis, and Zafar *et al.*¹³ who found thrombocytopenia in 63 (25.61%) neonates which is considerably lower than present study. This variation in frequency may be because Zafar *et al.*¹³ included both gram-negative and gram-positive sepsis cases with different platelet consumption patterns, while present study population had different clinical characteristics. On other hand, much higher frequencies was reported by Zehravi *et al.*¹⁴ with 192 (78.4%), Shahalam *et al.*¹⁵ with 88 (85.43%), Malik *et al.*¹⁶ with 68 (75.6%), and Saadi *et al.*¹⁷ with 120 (80%) neonates having thrombocytopenia. These studies mostly focused on culture-proven or gram-negative sepsis which is known to cause more severe endotoxin-mediated platelet destruction through activation of complement system and increased thromboxane production, explaining the higher frequencies in those studies as compare to present study.

Regarding severity of thrombocytopenia, present study found moderate and severe thrombocytopenia each in 31 (36.50%) cases and mild in 23 (27.10%) neonates. Kausar *et al.*¹⁸ similarly reported predominance of severe thrombocytopenia in 23 (27.06%) cases with mild in 12 (14.12%) and moderate in 15 (17.65%), suggesting that neonatal sepsis tend to produce clinically significant platelet reduction rather than mild changes. Arabdin *et al.*¹² also reported moderate thrombocytopenia as most frequent with 43 (25.3%) cases which is consistent with present findings. This similarity across studies suggest that pathophysiological mechanism of platelet destruction in neonatal sepsis, which mainly involve increased splenic sequestration and immune mediated destruction, produce moderate to severe degree of thrombocytopenia more commonly regardless of study setting. In present study age was found as significant demographic factor ($p=0.037$), where neonates older than 14 days had thrombocytopenia in 49 (71.0%) cases compared to 36 (53.7%) in younger age group. This finding is supported by Arabdin *et al.*¹² who also found significant association between age group and thrombocytopenia severity ($p=0.010$), suggesting that prolonged exposure to sepsis related inflammatory mediators with increasing age lead to more platelet consumption. However Zafar *et al.*¹³ did not found significant age association ($p=0.119$) which may be due to their different age grouping criteria and smaller proportion of thrombocytopenic patients in their cohort.

Gender was not found significantly associated with thrombocytopenia in present study ($p=0.889$), with male neonates showing 56 (62.9%) and female 29 (61.7%) frequency. This result is in agreement with Malik *et al.*¹⁶ and Zafar *et al.*¹³ who also reported no significant gender association ($p>0.05$ and $p=0.991$ respectively), and Arabdin *et al.*¹² similarly showed no gender based difference. These consistent findings across multiple studies confirm that thrombocytopenia in neonatal sepsis is not influenced by gender and is rather driven by infectious and inflammatory mechanisms which affect both sexes equally. Mode of delivery and feeding type was also not significantly associated with thrombocytopenia in present study, with $p=0.249$ and $p=0.077$ respectively. Similar non-significant findings for delivery mode was seen in Kausar *et al.*¹⁸ where cesarean delivery was in 42 (49.41%) and vaginal in 43 (50.59%) without significant influence on thrombocytopenia. These results collectively indicate that thrombocytopenia in neonates is more dependent on the severity and type of infecting organism rather than perinatal or feeding related factors.

This study has certain limitations, and the results need to be interpreted with respect to these limitations. Firstly, the study is based on a single center, i.e., in one hospital, and the results may not be applicable to the rest of the neonatal population in various settings. Secondly, the study may have had lower statistical power to show significant associations with thrombocytopenia and demographic variables because of the small number of samples included in the study. Lastly, the study did not include blood cultures in the neonates, which may have shown the causative organisms and their relationship with thrombocytopenia.

CONCLUSION

The present study has shown that thrombocytopenia is a common complication in neonates with sepsis, with the majority of neonates with sepsis having moderate or

severe thrombocytopenia. Age has been found to have significance in the development of thrombocytopenia, but gender, method of delivery, and type of feeding have not shown any significance in the development of thrombocytopenia.

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