ORIGINAL RESEARCH

Platelet Count and Indices as Diagnostic Biomarkers in Neonatal Sepsis: A Comprehensive Analysis

[1]Jatadhari Mahar, [2]Satyaranjan Mallick, [3]Rameshwari Das, [4]Narendra NathSoren, [5]Gobinda Hembram

[1,2,5]Assistant Professor, [3]Senior Resident, [4]Professor, Department of Pediatrics, SVPPGIP, S.C.B. Medical College, Cuttack, Odisha, India

Corresponding Author
Gobinda Hembram
Assistant Professor, Department of Pediatrics, SVPPGIP, S.C.B. Medical College, Cuttack, Odisha, India
Email: hembramgobinda@gmail.com

Received: 09 November, 2023 Accepted: 12 December, 2023

ABSTRACT

Background: Neonatal sepsis is a critical condition posing a significant threat to newborns globally, particularly in developing countries. The non-specific symptoms and time-consuming traditional diagnostic methods highlight the need for rapid and reliable biomarkers. Recent studies suggest platelet count and indices such as MPV and PDW as potential indicators for early diagnosis of neonatal sepsis. **Objective:** This study aims to comprehensively analyze the diagnostic value of platelet count and indexes as biomarkers in neonatal sepsis and elucidate their correlation with the severity and mortality of the condition. **Methods:** A hospital-based prospective study was conducted at SVPPGIP & SCB MCH, Cuttack, involving 200 neonates with suspected sepsis. Platelet count, PDW, and MPV were measured and correlated with sepsis severity and outcomes. Statistical analyses were performed using SPSS software, with a significance set at $P<0.05$. **Results:** Of the 200 neonates studied, 60% exhibited thrombocytopenia, more prevalent in culture-positive cases. There was a noteworthy inverse relationship discovered between platelet count and sepsis severity, while MPV and PDW were higher in more severe cases. Gram-negative organisms were the most common cause of sepsis. Notably, severe thrombocytopenia was strongly associated with increased mortality. **Conclusion:** The study confirmed a significant association between platelet count and indices with neonatal sepsis severity and mortality. Platelet count, MPV, and PDW can serve as effective, rapid diagnostic and prognostic biomarkers, potentially improving early detection and outcomes in neonatal sepsis. **Recommendations:** Further multicenter studies are needed to validate these findings across diverse populations and clinical settings. Additionally, enhancing technical expertise at grassroots levels is crucial for the reliable application of these biomarkers in routine neonatal care. This research advocates for the integration of platelet indices in the diagnostic protocol for neonatal sepsis, promising improved patient management and outcomes.

Keywords: Neonatal Sepsis Diagnosis, Platelet Count, Mean Platelet Volume, Thrombocytopenia and Mortality, Platelet Distribution Width

INTRODUCTION

Around the world, neonatal sepsis continues to be a major cause of morbidity and mortality in infants, especially in underdeveloped nations. It is a systemic infection that manifests as a range of clinical and laboratory characteristics in newborns under 28 days of age. Early and accurate diagnosis is crucial for timely intervention and improved outcomes. However, the non-specific clinical presentation and the time-consuming nature of current diagnostic methods, such as blood cultures, pose significant challenges to early detection and treatment [1]. In this context, there's a growing interest in identifying reliable, rapid biomarkers for early diagnosis of neonatal sepsis. Among these, platelet count and indices such as mean platelet volume (MPV) and platelet distribution width (PDW) have emerged as potential diagnostic tools.

Platelets, traditionally recognized for their role in hemostasis, have recently been appreciated for their function in the immune response, particularly in sepsis. A typical observation in sepsis is thrombocytopenia, or a drop in platelet count, which has been linked to a higher risk of morbidity and mortality in newborns [2, 3]. Platelet indices like MPV and PDW reflect platelet activation and have been studied in various adult populations as indicators of inflammatory and infective conditions [4, 5]. However, their role in neonatal sepsis is less clear and has been the subject of fewer studies.

Recent research has indicated that changes in platelet indices can be an early sign of sepsis and may correlate with its severity [6, 7]. A higher MPV, for instance, has been associated with bacterial infections and could reflect an increased turnover of platelets in response to septic conditions [2]. Similarly, PDW, a measure of the variability in platelet size, has been shown to increase in the presence of infection and inflammation [4]. Despite these promising findings, there is a need for more comprehensive studies to validate the utility of platelet count and indices as diagnostic biomarkers in neonatal sepsis, especially in diverse clinical settings.

This study aims to provide a comprehensive analysis of the diagnostic value of platelet count and indices in neonatal sepsis. By examining these hematological parameters in a cohort of neonates with suspected sepsis, we seek to elucidate their potential as rapid, cost-effective tools for early diagnosis. Understanding the relationship between platelet metrics and sepsis can contribute to developing more effective diagnostic strategies, ultimately improving the clinical outcomes for affected neonates.

METHODOLOGY

Study Design: This was a hospital-based prospective study aimed at evaluating the relationship between neonatal sepsis and various platelet indices, including platelet count, MPV, and PDW.

Study Setting: The study was conducted at SVPPGIP & SCB MCH, Cuttack, from December 2020 to November 2022.

Participants: The target population comprised 200 neonates admitted to the neonatal unit of SVPPGIP & SCB MCH during the study period. The inclusion criteria were neonates with clinical signs and symptoms of sepsis, confirmed through positive culture or other laboratory findings indicative of probable sepsis. Neonates with causes of thrombocytopenia other than sepsis or those who died before a diagnosis could be established were excluded from the study.

Inclusion criteria:

Neonates admitted in NICU and newborn ward with probable sepsis and proven sepsis.

Exclusion criteria:

- Neonates having causes of thrombocytopenia other than sepsis
- Neonate died before establishing diagnosis

Ethical Considerations: The SCB MCH, Cuttack institutional ethical committee approved the project. Every newborn whose guardian met the inclusion criteria gave their informed permission.

Data Collection Procedure

- **Blood Sample Collection:** Approximately 2 ml of venous blood was drawn from each suspected septic neonate using aseptic precautions from peripheral veins into ethylenediamine-tetra acetic acid (EDTA) tubes.
- **Sepsis Screen:** The collected samples were analyzed for sepsis screen and complete blood count (CBC) for platelet indices using a hematology analyzer.
- **Blood Culture:** A portion of the collected blood was used for culture to confirm sepsis.

Aseptic Measures: Prior to the collection of a sample, a 5 cm by 5 cm patch of skin over the venipuncture site was cleaned with 70% isopropyl alcohol, povidone-iodine, and alcohol three times. Prior to venipuncture, the skin was let at least a minute to dry.

Statistical Analysis: Software from SPSS was used to gather and examine data (version 25). The data was displayed in the study using suitable tables and graphical representations. ANOVA, the chi-squared test, and the Student's t-test were used to compare categorical data. P-values less than 0.05 were regarded as statistically significant.

RESULTS

A total of 200 neonates admitted with clinical signs of sepsis were included in the study. The mean age of presentation was 72.46 ± 57.23 hours, with a nearly equal distribution among males (130, 65%) and females (70, 35%). The majority (53%) presented within the first 24 hours of life.

Table 1: Demographic Profile of Neonates

Age in Hours	Male (n=130)	Female (n=70)	Total (n=200)
24	66 (50.7%)	40 (57.1%)	106 (53%)
48	12 (9.2%)	6 (8.6%)	18 (9%)
72	14 (10.8%)	8 (11.4%)	22 (11%)
96	12 (9.2%)	6 (8.6%)	18 (9%)
120	10 (7.7%)	4 (5.7%)	14 (7%)
>120	16 (12.4%)	6 (8.6%)	22 (11%)
Total	130 (100%)	70 (100%)	200 (100%)
Mean ± SD	74.51 ± 64.52	71.03 ± 53.49	72.46 ± 57.23

*T-test (T=0.78), P=0.34 (NS).

Among the 200 neonates, 118 (59%) were diagnosed with early-onset sepsis (EOS), while 82 (41%) had late-onset sepsis (LOS). The majority of sepsis cases were found in neonates born outside the hospital (55%).

Table 2: Onset of Neonatal Sepsis Based on Place of Delivery

Place of Delivery	EOS (n=118)	LOS (n=82)	Total
Intramural (Hospital)	50 (42.4%)	40 (48.8%)	90
Extramural (Outside)	68 (57.6%)	42 (51.2%)	110

The mean platelet count on day 1 of sepsis was significantly lower in culture-positive neonates compared to culture-negative cases. A progressive increase in the platelet count was observed by day 7 post-antimicrobial therapy.

Table 3: Platelet Indices in Neonatal Sepsis

Parameter	Culture Positive Sepsis	Culture Negative Sepsis
Mean Platelet Count (Day 1)	1.23 ± 0.51 lac/µl	1.91 ± 0.72 lac/µl
Mean Platelet Volume (MPV)	10.5 ± 1.3 fL	9.6 ± 1.1 fL
Platelet Distribution Width (PDW)	15.4 ± 2.1%	14.2 ± 1.9%

*P<0.05 for all comparisons between culture-positive and negative sepsis.

A statistically significant correlation was found between lower platelet counts and increased severity of sepsis. Similarly, higher MPV and PDW values were associated with more severe cases and poorer outcomes.

Table 4: Correlation of Platelet Indices with Sepsis Severity

Platelet Index	Correlation Coefficient	P-value
Platelet Count	-0.63	<0.001
MPV	0.59	<0.001
PDW	0.55	<0.001

Gram-negative organisms were predominant (57%), with E. coli being the most common isolate. Gram-positive infections accounted for 40% of the culture-positive cases.

Table 5: Organisms Isolated in Culture-Positive Sepsis

Organisms	No. of Patients (n=94)	Percentage (%)
Staphylococcus aureus	20	21.3%
E. coli	27	28.7%
Others	47	50.0%

Thrombocytopenia was present in 60% (120/200) of the neonates with sepsis. Severe thrombocytopenia (<50,000/µl) was associated with a higher mortality rate.

Table 6: Thrombocytopenia and Mortality in Neonatal Sepsis

Thrombocytopenia Level	Mortality
Absent (n=80)	5 (6.25%)
Mild (n=86)	15 (17.4%)
Severe (n=34)	30 (88.2%)

*Chi-squared test, P<0.001

The results indicate a significant association between various platelet indices and the diagnosis and severity of neonatal sepsis. Thrombocytopenia, particularly when severe, was a strong predictor of mortality in this cohort. These findings support the potential of platelet count and indices as diagnostic and prognostic biomarkers in neonatal sepsis.

DISCUSSION

In the present study conducted at SVPPGIP & SCB MCH, Cuttack, a tertiary care hospital in Odisha, 200 newborns with features of sepsis were considered to explore the diagnostic potential of platelet count and indices as markers of neonatal sepsis. The purpose of this study was to determine the frequency of thrombocytopenia and the variations in different platelet indices in newborn sepsis, particularly concerning the duration of illness, specific organisms, and their effect on neonatal mortality and morbidity.

Consistent with the findings of Guida*et al.* [1], the study noted that 60% of neonatal sepsis cases had thrombocytopenia, with a majority being culture proven. This prevalence underscores the frequent occurrence of thrombocytopenia in septic neonates and its potential as a diagnostic marker.

It was observed that thrombocytopenia was common on day 1 of sepsis and showed improvement by day 3, which was statistically significant ($p<0.05$). Murray NA *et al.* [8] also observed a statistically relevant relationship between platelet count and the duration of illness. This pattern might indicate the body's response to infection and the efficacy of treatment over time.

The findings that the majority of thrombocytopenia cases were mild, with a smaller percentage being moderate or severe, align with the observations of Charoo BA *et al.* [9]. Severe thrombocytopenia was

particularly associated with higher mortality, highlighting its prognostic value.

Gram-negative organisms were most commonly associated with thrombocytopenia. This aligns with the studies of Guida*et al.* [1] and Bhat *et al.* [3], which also found a predominance of gram-negative organisms in thrombocytopenic septic neonates. The variety of organisms causing thrombocytopenia underscores the need for broad-spectrum diagnostic markers.

The study found that decreased platelet count was associated with increased mean platelet volume (MPV) in cases of septicemia. Similar to observations by Nelson and Kehl*et al*., [7] and Becchi *et al*., [5]it was found that MPV has an important prognostic value in the early stage of sepsis. Increased PDW was also noted in septic neonates, aligning with findings from Gucluet *al*. [2] and Patrick CH *et al*., [6] who reported significant increases in PDW in the presence of bacteremia.

Several studies have highlighted the role of platelet indices in diagnosing neonatal sepsis. Guida*et al*. [1] and Bhat *et al*. [3] have documented the utility of platelet count, MPV, and PDW as markers of neonatal sepsis, with variations observed in culture-positive and culture-negative sepsis cases. The findings are consistent with these studies, reinforcing the potential of these indices as useful, rapid diagnostic tools in neonatal sepsis.

The significant association of thrombocytopenia with neonatal sepsis, especially its correlation with severity and mortality, indicates that platelet count and indices can be valuable additions to the diagnostic and prognostic toolkit for neonatal sepsis. Their routine assessment in suspected cases could lead to earlier diagnosis and more targeted treatment, potentially improving outcomes.

CONCLUSION

In conclusion, this study highlights the diagnostic and prognostic significance of platelet count and indices in neonatal sepsis. By confirming and expanding upon the findings of previous research, it provides a strong basis for considering these hematological parameters in the routine evaluation of septic neonates. As neonatal care continues to advance, incorporating such efficient and accessible markers could significantly improve the outcomes for one of the most vulnerable patient populations.

Limitations and Future Directions: The constraints of being a single-center investigation and the pre-treatment of some neonates with antibiotics, which may have affected the platelet indices, should be noted even though the study offers insightful information. Future multicenter studies are necessary to validate these findings across different populations and settings. Additionally, further research should explore the relationship between platelet indices and other clinical and laboratory parameters to enhance the understanding and utility of these markers in neonatal sepsis.

Recommendations: The study being conducted in single center and one of the referral tertiary institute & majority of septic new-born had received one or more antibiotic treatment prior to the investigations. Although complete blood count (CBC) is one of the routine investigations for all sick neonates but it is difficult to judge the reliability and validity of test performed in grass route level i.e. PHC and CHC, since the lack of technical expert to conduct the test. However, there is definite positive relation of changes of different indices of platelet between duration of infection, severity and mortality due to neonatal sepsis. There is further multicenter study is needed to know the actual relation of changes in different platelet indices with that of organisms, duration of infections and mortality.

REFERENCES

1. Guida, J. D., Kunig, A. M., Leef, K. H., McKenzie, S. E., & Paul, D. A. (2003). Platelet count and sepsis in very low birth weight neonates: is there an organism-specific response? Pediatrics, 111(6 Pt 1), 1411-1415.
2. Guclu, E., Durmaz, Y., &Karabay, O. (2010). Main inflammatory parameters in acute appendicitis: are they predictable? Polish Journal of Surgery, 82(5), 278-282.
3. Bhat, S. A., Lone, R., & Mir, M. S. (2017). Platelet indices in neonatal sepsis: a review. Journal of Pediatric and Neonatal Individualized Medicine, 6(2), e060237.
4. Korniluk, A., Koper-Lenkiewicz, O. M., Kamińska, J., Kemona, H., &Dymicka-Piekarska, V. (2016). Mean Platelet Volume (MPV): New Perspectives for an Old Marker in the Course and Prognosis of Inflammatory Conditions. Mediators of Inflammation, 2019, 9213074.
5. Becchi, C., Al Malyan, M., Fabbri, L. P., Marsili, M., Boddi, V., &Boncinelli, S. (2006). Mean platelet volume trend in sepsis: is it a useful parameter? Minerva Anestesiologica, 72(9), 749-756.
6. Patrick, C. H., Lazarchick, J., & James, M. O. (2012). Use of platelet indices in the differential diagnosis of neonatal thrombocytopenia. Journal of Perinatology, 32(7), 514-519.
7. Nelson, A., &Kehl, D. (2011). The role of mean platelet volume in the early diagnosis of acute appendicitis. American Journal of Emergency Medicine, 29(9), 1003-1005.
8. Murray NA, Roberts IA, circulating megakaryocytes and their progenitors 1996.
9. Charoo BA, Iqbal JI, Iqbal Q, Mushtaq S, Bhat AW, Nawaz I. Nosocomial sepsis-induced late onset thrombocytopenia in a neonatal tertiary care unit: a prospective study. HematolOncol Stem Cell Ther. 2009; 2(2):349-353.