

# Role of Platelet Indices as a Diagnostic Marker of Neonatal Sepsis: A Case-Control Study in a Tertiary Railway Hospital of Eastern India

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## Abstract

**Background:** Neonatal sepsis continues to be a major contributor to morbidity and mortality in almost all parts of the world in both low and middle-income nations. The non-specific clinical presentation and constraints of the traditional diagnostics make it hard to detect the disease at earlier stages. Platelet indices have emerged as potential biomarkers of early sepsis. **Material and Methods:** The proposed study is a prospective case-control study to be conducted at the Department of Pediatrics, B. R. Singh Hospital, and the Centre of Medical Education and Research, Kolkata, between January and December 2024. One hundred and twenty-two term neonates (122) were enrolled, including 61 who developed culture-proven sepsis and 61 controls who did not. Platelet indices and total platelet count (TPC), mean platelet volume (MPV), and platelet distribution width (PDW), and the proportions of MPV to total platelet count TPC (MPV/TPC ratio) were evaluated. The receiver operating characteristic (ROC) curve analysis was used to evaluate diagnostic performance. **Results:** Septic neonates demonstrated significantly lower TPC ( $1.40 \pm 0.43$  vs.  $2.55 \pm 0.54$  lakhs/mm<sup>3</sup>;  $p < 0.001$ ), higher MPV ( $10.45 \pm 1.63$  vs.  $9.11 \pm 0.90$  fL;  $p < 0.001$ ), elevated PDW ( $19.80 \pm 1.42$  vs.  $17.96 \pm 1.45\%$ ;  $p < 0.001$ ), and increased MPV/TPC ratio ( $8.12 \pm 2.47$  vs.  $3.78 \pm 1.04$ ;  $p < 0.001$ ) compared to controls. The MPV/TPC ratio exhibited the highest diagnostic accuracy (AUC = 0.961) with 80.3% sensitivity and 96.7% specificity at a cut-off of  $\geq 5.84$ . **Conclusion:** Platelet indices, especially MPV/TPC ratio, have good diagnostic capabilities for neonatal sepsis and could be considered useful supplementary procedures to the traditional screening techniques, where limited resources are available.

**Keywords:** Neonatal sepsis, Neonatal sepsis platelet indices, platelet distribution width, platelet indices, platelet distribution width, platelet high-resolution computed tomography, platelet indices, platelet mean platelet volume, platelet indices, platelet high-resolution computed tomography, platelet mean platelet volume, platelet indices.

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## INTRODUCTION

Neonatal sepsis is a potentially fatal systemic inflammatory disease that develops when microbes enter the bloodstream during the first 28 days of life.<sup>[1]</sup> It is the second leading cause of neonatal death in the world because it causes 15 percent of all neonatal deaths.<sup>[2]</sup> Neonatal sepsis has been estimated to be 2,202 per 100,000 live births worldwide, with the highest burden experienced in the low- and middle-income countries, where 99 per cent of neonatal mortality is seen.<sup>[3]</sup> The incidence of neonatal sepsis cases is higher in India as it has the highest absolute cases of the condition in the world, whereas the case fatality is 25 to 65 percent.<sup>[4]</sup>

Neonatal sepsis is a condition that is difficult to diagnose because of its non-specific presentation, lethargy, poor feeding, temperature variation, respiratory distress, and hemodynamic instability are just some of the manifestations.<sup>[5]</sup> Blood culture, which is the gold standard for diagnosis, has numerous limitations, including a long turnaround time of 48-72 hours, low sensitivity due to intermittent bacteremia, and the risk of contamination.<sup>[6]</sup> Traditional sepsis screening markers such as C-reactive protein, procalcitonin, and total leukocyte count exhibit

varying sensitivity and specificity and are usually insufficient to support timely patient clinical decision-making.<sup>[7]</sup>

Platelets have important non-hemostatic functions, as they are significant agents of inflammation and are involved in immune responses.<sup>[8]</sup> In sepsis, platelets respond to interactions with the pathogen and immune cells, releasing inflammatory mediators and contributing to microvascular thrombosis.<sup>[9]</sup> Thrombocytopenia caused by sepsis occurs through various mechanisms, including increased platelet consumption, bone marrow inhibition, and sequestration.<sup>[10]</sup> Recent research has shown changes in platelet indices (mean platelet volume [MPV] and platelet distribution width [PDW]).<sup>[11,12]</sup> in septic neonates.

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MPV is a measure of platelet size and activation status; a high MPV value indicates greater platelet turnover and the release of more and larger platelets active in the bone marrow.<sup>[13]</sup> PDW measures platelet anisocytosis and increases with heterogeneous platelet populations during inflammatory states.<sup>[14]</sup> The MPV/TPC ratio has been proposed as a composite marker with enhanced diagnostic performance compared to individual parameters.<sup>[15]</sup>

Despite promising preliminary evidence, studies evaluating platelet indices in neonatal sepsis from the eastern region of India remain limited. Therefore, this study aimed to evaluate the diagnostic utility of platelet indices as potential markers for neonatal sepsis in term neonates admitted to a tertiary care hospital.

## MATERIALS AND METHODS

**Study Design and Setting:** This prospective case-control study was conducted at the Department of Pediatrics, B. R. Singh Hospital and Centre for Medical Education and Research, Kolkata, a tertiary railway hospital in Eastern India, from January 2024 to December 2024.

**Ethical Considerations:** The Institutional Ethics Committee approved the study protocol. Written informed consent was obtained from parents/guardians of all participating neonates after explaining the study purpose in the local vernacular language.

**Sample Size:** The sample size was calculated using the formula for comparing two proportions. Based on previous literature reporting MPV >10.8 fL in 58.6% of septic neonates versus 33.3% of controls, with 95% confidence level and 80% power, the minimum sample size was estimated at 61 per group, totaling 122 participants.

### Participants

#### Inclusion Criteria:

- **Cases:** Term neonates ( $\geq 37$  weeks of gestation) up to 28 days of life with clinical features of sepsis and positive blood culture
- **Controls:** Term neonates admitted for non-infectious conditions without sepsis features

#### Exclusion Criteria:

- Neonates with chromosomal abnormalities, syndromic

conditions, or hydrops fetalis

- Hypoxic-ischemic encephalopathy or intrauterine growth restriction
- Congenital or acquired thrombocytopenia
- Maternal conditions affecting platelet counts (ITP, gestational hypertension, TORCH infections)
- Prior platelet transfusion
- Culture-negative suspected sepsis cases

**Data Collection:** Proforma: The data on demographic characteristics, maternal risk factors, and clinical presentations were recorded using a structured proforma. Presence of fever (greater than 38.0 C) and hypothermia (less than 36.5 C), lethargy and poor feeding, respiratory distress, convulsions, vomiting, jaundice, or abdominal distension were also used to diagnose clinical sepsis.

**Laboratory Investigations:** Aseptically, peripheral venous blood samples (1.5-2 mL) were put in EDTA tubes. The full blood count, including TPC, MPV, and PDW, was analyzed on the Sysmex Automated Hematology Analyzer (System XN1000). Standard microbiological methods were used to obtain blood cultures from all suspected sepsis cases.

**Statistical Analysis:** SPSS version 16.0 was used to analyse the data. The continuous variables have been provided as mean and standard deviation, and analyzed through the Mann-Whitney U test. Frequencies and percentages were used to express categorical variables, and comparisons were performed using the chi-square or Fisher's exact test. Diagnostic performance has been assessed using ROC curve analysis and the determination of the area under the curve (AUC), sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). The level of statistical significance was established at  $p < 0.05$ .

## RESULTS

**Demographic and Birth Characteristics:** One hundred and twenty-two neonates were recruited, including 61 cases and 61 controls. There were also similarities in the mean age at admission ( $3.84 \pm 2.54$  vs.  $3.97 \pm 1.91$  days;  $p = 0.747$ ). There was no difference in gender distribution (males: 47.5 versus 39.3;  $p = 0.361$ ). Cases had significantly lower mean birth weight than controls ( $2.73 \pm 60$  vs.  $2.96 \pm 56$  kg;  $p = 0.029$ ) [Table 1].

**Table 1: Demographic and Birth Characteristics of Study Participants**

Characteristic	Cases (n=61)	Controls (n=61)	p-value
Mean age (days)	3.84 ± 2.54	3.97 ± 1.91	0.747
Male gender, n (%)	29 (47.5)	24 (39.3)	0.361
Mean birth weight (kg)	2.73 ± 0.60	2.96 ± 0.56	0.029*
Low birth weight, n (%)	22 (36.1)	15 (24.6)	0.168
Inborn delivery, n (%)	46 (75.4)	45 (73.8)	0.835

\*Statistically significant ( $p < 0.05$ )

**Maternal Risk Factors:** There were significant maternal risk factors that were correlated with neonatal sepsis, which consisted of premature rupture of membranes (45.9% vs. 19.7;  $p = 0.002$ ), foul-smelling liquor (34.4% vs. 3.3;  $p = 0.001$ ), maternal fever (27.9% vs. 18.0;  $p = 0.023$ ), chorioamnionitis (29.5% vs. 3.3;  $p =$

**Platelet Indices:** Platelet indices were significantly different between septic infants and controls. Thrombocytopenia (TPC < 1.5 lakhs/mm<sup>3</sup>) was found in 39.3 percent of the cases, compared with 6.6 percent of the controls ( $p < 0.001$ ). There were statistically significant discrepancies in all platelet parameters across groups [Table 2].

**Table 2: Comparison of Platelet Indices Between Cases and Controls**

Parameter	Cases (n=61)	Controls (n=61)	p-value
TPC (lakhs/mm <sup>3</sup> )	1.40 ± 0.43	2.55 ± 0.54	<0.001*
TPC <1.5 lakhs/mm <sup>3</sup> , n (%)	24 (39.3)	4 (6.6)	<0.001*
MPV (fL)	10.45 ± 1.63	9.11 ± 0.90	<0.001*
PDW (%)	19.80 ± 1.42	17.96 ± 1.45	<0.001*
MPV/TPC ratio	8.12 ± 2.47	3.78 ± 1.04	<0.001*

\*Statistically significant (p < 0.05); TPC: Total platelet count; MPV: Mean platelet volume; PDW: Platelet distribution width

**Diagnostic Performance:** The examination of all ROC curves indicated that the platelet index has good diagnostic performance. The AUC was highest for the MPV/TPC ratio (0.961), followed by TPC (0.914), PDW (0.818), and MPV

(0.734). At a cut-off value of 5.84 or higher, the MPV/TPC yielded sensitivity of 80.3%, specificity of 96.7%, and diagnostic accuracy of 88.5% [Table 3].

**Table 3: Diagnostic Performance of Platelet Indices for Neonatal Sepsis**

Parameter	AUC (95% CI)	Cut-off	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
TPC (lakhs/mm <sup>3</sup> )	0.914 (0.862-0.967)	<1.5	82.0	98.4	84.5	98.0	90.2
MPV (fL)	0.734 (0.641-0.827)	≥9.75	67.2	75.4	73.2	69.7	71.3
PDW (%)	0.818 (0.746-0.890)	≥19.85	52.5	93.4	88.9	66.3	72.9
MPV/TPC ratio	0.961 (0.932-0.991)	≥5.84	80.3	96.7	96.1	83.1	88.5

AUC: Area under curve; PPV: Positive predictive value; NPV: Negative predictive value

## DISCUSSION

The paper tested platelet indices as variables in neonatal sepsis diagnostics and found that TPC, MPV, PDW, and the MPV/TPC ratio showed significant changes in septic newborn infants. The results confirm the use of these easily obtained parameters as supplements to the traditional diagnosis measures.

The finding of decreased birth weight in neonates with septicemia is consistent with the literature on the definition of low birth weight as the key risk factor in the infection of newborns.<sup>[16]</sup> The correlation is probably a manifestation of immunological immaturity and decreased transplacental immunoglobulin transmission in smaller infants.<sup>[17]</sup>

The maternal risk factors we found to be associated with PROM, chorioamnionitis, and maternal infections are also consistent with prior studies, which highlight the significance of intrapartum factors in the pathogenesis of early sepsis.<sup>[18]</sup> These results support the necessity of extreme maternal screening and prevention.

Thrombocytopenia in 39.3% of septic neonates is a finding supported by numerous studies reporting rates of 38-81%.<sup>[19,20]</sup> The pathophysiology is characterized by decreased platelet consumption due to disseminated intravascular coagulation, primary inhibition of bone marrow function by proinflammatory cytokines, and platelet aggregation with pathogens.<sup>[21]</sup>

The elevated MPV in discharged neonates indicates thrombopoiesis compensation, in which platelets produce larger, more reactive platelets.<sup>[22]</sup> Meta-analysis by Wang et al. established that there was a significant increase in MPV in neonates with septicemia as compared to normal controls.<sup>[23]</sup> We report an MPV of 9.75 fL or higher as the best cut-off and 67.2 as the sensitivity, which agrees with pooled estimates from recent meta-analyses.<sup>[24]</sup>

High PDWs reflect greater heterogeneity in platelet size under inflammatory conditions and have been linked to a

range of infectious and inflammatory diseases.<sup>[25]</sup> The specificity (93.4) of PDW in our study is high, indicating that it can be used rule out the diagnosis of sepsis.

The most accurate diagnostic marker, based on AUC, was the MPV/TPC ratio, with an AUC of 0.961. This composite variable represents a reduction in platelet number and an increase in platelet volume, which enhances discriminant ability.<sup>[26]</sup> The same report was replicated by Kaur et al., who reported a 96.67% specificity for the MPV/TPC ratio in the diagnosis of neonatal sepsis.<sup>[27]</sup>

Our findings have important clinical ramifications, especially in resource-constrained environments—platelet indices. The platelet indices are traditionally obtained by performing a standard complete blood count and do not require any additional cost or specialized equipment. Their prompt access is in contrast to blood culture turnaround times, which may delay timely therapy changes.

Limitations of the study include its single-center design, which did not distinguish between early- and late-onset sepsis. Moreover, gestational age associations among neonates during the term period may affect platelet parameters. It is justified to conduct multicenter research involving larger numbers of people in the future to confirm these results.

## CONCLUSION

This paper shows that platelet indices, specifically the MPV/TPC ratio, have strong diagnostic value, with high sensitivity and specificity for neonatal sepsis. These parameters are cost-effective and readily available and could be useful as adjuncts to traditional diagnostic methods to recognize and intervene in sepsis more quickly. Incorporating platelet indices into neonatal sepsis screening guidelines would greatly enhance the quality of diagnostic systems, particularly in health facilities with limited resources, and ultimately reduce the rates of neonatal morbidity and mortality.

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**Conflicts of interest**

There are no conflicts of interest.

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