

# THROMBOCYTOPENIA AS AN EARLY MARKER OF NEONATAL SEPSIS: A PROSPECTIVE OBSERVATIONAL STUDY

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## ABSTRACT

**Background:** Neonatal Sepsis is an important cause of mortality and morbidity in newborns. Thrombocytopenia is found in approximately 20-35% of babies who present in NICU. It is the commonest hematological abnormality in neonates with sepsis. Thrombocytopenia related to late onset sepsis is severe and associated with higher mortality. Thus, the objective of our study is to identify thrombocytopenia as a predictive, earliest marker for neonatal sepsis. **Materials and Methods:** A prospective observational study was conducted in the NICU at Tertiary care center, from January 2024 to June 2024. Neonates with culture-proven sepsis and thrombocytopenia (platelet count  $<1,50,000/\text{mm}^3$ ) were enrolled; those with other causes of thrombocytopenia or contaminated/multiple-organism cultures were excluded. After informed consent, clinical evaluations and blood cultures were obtained along with the initial platelet count, followed by daily platelet measurements. The second platelet count was noted at 72 hours. Thrombocytopenia was classified as mild ( $50,000\text{--}1,50,000/\text{mm}^3$ ), moderate ( $20,000\text{--}49,999/\text{mm}^3$ ), or severe ( $<20,000/\text{mm}^3$ ). Data were analyzed to examine the relationship between thrombocytopenia severity and neonatal sepsis outcomes. **Result:** In this study total of 107 neonates with culture-positive sepsis were included, among which 45.79% had thrombocytopenia (platelet count  $<150,000/\text{mm}^3$ ). Certain isolates (e.g., *Acinetobacter*, *Candida*) showed no association with thrombocytopenia, while others (e.g., *Citrobacter diversus*) presented moderate correlations. Overall mortality was significantly higher in neonates with thrombocytopenia (36.73%) compared to those with normal platelet counts (8.62%;  $p<0.001$ ), indicating a strong link between thrombocytopenia and adverse outcomes in neonatal sepsis. **Conclusion:** Thrombocytopenia in neonates with sepsis serves as a significant indicator of disease severity. Its presence underscores the importance of vigilant monitoring, prompt diagnosis, and timely intervention. By recognizing thrombocytopenia as a critical clinical marker, neonatal care teams can potentially improve the outcomes of newborns with sepsis through more targeted treatment and supportive measures.

## INTRODUCTION

Neonatal sepsis remains a significant global health concern, contributing to approximately 1.6 million deaths annually. The burden is particularly high in developing countries, where nearly 60% of neonatal deaths are attributed to sepsis. The incidence of neonatal sepsis in these regions ranges from 2.2 to 8.6 per 1,000 live births, with low birth weight infants being especially vulnerable.<sup>[1-3]</sup>

According to the International Sepsis Definition Conference, sepsis is characterized as a clinical syndrome involving both infection and systemic inflammatory response syndrome (SIRS). In

neonates, SIRS is identified by signs such as tachypnea, temperature instability, prolonged capillary refill time, abnormal white blood cell counts ( $<5000/\mu\text{l}$  or  $>34,000/\mu\text{l}$ ), elevated C-reactive protein (CRP), and increased procalcitonin levels. Severe sepsis is associated with organ dysfunction, hypoperfusion, or hypotension, while septic shock results from hypotension and impaired organ perfusion. The source of neonatal sepsis is often traced to organisms detected in blood, cerebrospinal fluid (CSF), or urine cultures.<sup>[4,5]</sup>

Thrombocytopenia is one of the most common hematological abnormalities encountered in critically ill neonates admitted to the NICU. It often indicates

an active underlying disease process, with its primary cause being increased platelet consumption due to infection, thrombosis, immune-mediated mechanisms, or reduced platelet production. In neonatal sepsis, thrombocytopenia can occur in both early and late stages and is observed in infections caused by both gram-positive and gram-negative organisms.<sup>[6]</sup> Notably, thrombocytopenia can develop even before a positive blood culture result, making it a potential early predictor of neonatal sepsis.<sup>[7]</sup>

A normal platelet count in neonates ranges from 150,000 to 450,000 platelets per microliter of blood, while thrombocytopenia is defined as a platelet count below 150,000 per microliter, regardless of gestational age. Given its high prevalence in NICU settings, thrombocytopenia may serve as an important marker for neonatal sepsis.<sup>[8]</sup>

### Aim

To study the association between thrombocytopenia and sepsis in neonates.

### Objectives

1. To assess the prevalence of thrombocytopenia in culture-positive neonatal sepsis.
2. To determine the association between thrombocytopenia and neonatal sepsis.
3. To evaluate the outcomes of neonates with sepsis and thrombocytopenia.

## MATERIALS AND METHODS

This study was conducted in the Level III Neonatal Intensive Care Unit (NICU) at Government Medical College, Miraj. It was designed as a prospective observational study and was carried out over six months, from January 2024 to June 2024. The study population included newborns admitted to the NICU with neonatal sepsis. Total 107 neonates diagnosed with neonatal sepsis during the study period were enrolled.

The study specifically focused on neonates with culture-positive sepsis who also had thrombocytopenia. Certain newborns were excluded from the study, including those with other known

causes of thrombocytopenia such as maternal thrombocytopenia, HELLP syndrome, systemic lupus erythematosus (SLE), pre-eclampsia and eclampsia, congenital infections, necrotizing enterocolitis (NEC), and polycythemia. Additionally, neonates whose blood cultures grew contaminants or two or more microorganisms were also excluded.

Culture-proven sepsis is defined as a neonate exhibiting clinical signs suggestive of septicemia, pneumonia, or meningitis, with a confirmed isolation of a pathogen from the blood culture. Thrombocytopenia is characterized by a platelet count below 1,50,000/mm<sup>3</sup>. Prevalence refers to the proportion of disease observed in a specific population.

Before enrollment, informed consent was obtained from the parents or guardians of eligible neonates. Once enrolled, a detailed history was recorded, followed by a thorough physical examination. Blood culture samples were collected using aseptic precautions. The first platelet count, referred to as the 'Initial Platelet Count,' was measured from the same blood sample collected for culture. This served as the reference point for tracking platelet count trends. Subsequent platelet counts were monitored every 24 hours. The 'Second Platelet Count' was recorded at 72 hours after the initial count. The severity of thrombocytopenia was classified as mild (platelet count between 50,000/mm<sup>3</sup> to 1,50,000/mm<sup>3</sup>), moderate (platelet count between 20,000/mm<sup>3</sup> to 50,000/mm<sup>3</sup>), or severe (platelet count below 20,000/mm<sup>3</sup>). The collected data was further analyzed to establish trends and associations.

## RESULTS

### 1. Prevalence of Thrombocytopenia in Culture-Positive Neonatal Sepsis:

The prevalence of thrombocytopenia (defined as platelet count < 150,000) in culture-positive neonatal sepsis is 45.79%.

### 2. Association between Thrombocytopenia and Neonatal Sepsis (by Isolate).

**Table 1**

Blood Culture Isolate	No	Yes	No (%)	Yes (%)
Acinetobacter	1	0	100.00%	0.00%
Candida	1	0	100.00%	0.00%
Citrobacter diversus	1	1	50.00%	50.00%
Citrobacter freundii	5	2	71.42%	28.58%
Coagulase-negative Staphylococcus	40	7	85.11%	14.89%
E. coli	5	1	83.33%	16.67%
Enterococcus	3	1	75.00%	25.00%
Klebsiella aerogenes	4	0	100.00%	0.00%
Klebsiella pneumoniae	15	1	93.75%	6.25%
Non-fermenting Gram-negative rods	1	0	100.00%	0.00%
Pseudomonas aeruginosa	1	0	100.00%	0.00%
Staphylococcus aureus	9	1	90.00%	10.00%
Streptococcus pneumoniae	1	0	100.00%	0.00%
Streptococcus viridans	3	0	100.00%	0.00%
klebsiella oxytoca	3	0	100.00%	0.00%

The relationship between thrombocytopenia and neonatal sepsis varies by the type of blood culture isolate identified. For isolates such as *Acinetobacter* and *Candida*, there is a consistent observation where 100% of the cases did not exhibit thrombocytopenia, suggesting no association. In contrast, *Citrobacter diversus* shows an equal distribution, with 50% of the cases associated with thrombocytopenia and 50% without. *Citrobacter freundii* has a higher prevalence of cases without thrombocytopenia, at 71.42%, compared to 28.58% with it.

For Coagulase-negative *Staphylococcus*, a significant majority of cases, 85.11%, are not associated with thrombocytopenia, while only 14.89% are. Similarly, *E. coli* and *Enterococcus* predominantly show cases without thrombocytopenia, at 83.33% and 75% respectively. *Klebsiella* species, including *K. aerogenes*, *K. pneumoniae*, and *K. oxytoca*, as well as other isolates like Non-fermenting Gram-negative rods, *Pseudomonas aeruginosa*, *Streptococcus pneumoniae*, and *Streptococcus viridans*, also

predominantly show no thrombocytopenia, with rates ranging from 90% to 100%. Only a small fraction of *Staphylococcus aureus* cases, 10%, show thrombocytopenia, indicating a generally lower association compared to other isolates.

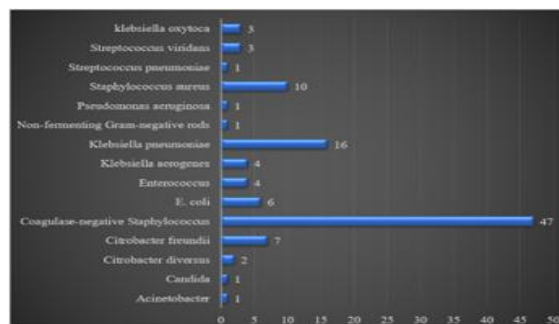


Figure 1

**Primary Outcome:** Correlation between Thrombocytopenia and Neonatal Sepsis  
**Secondary Outcome:** Discharge / Death.

Table 2: Outcome of Neonates with Sepsis (based on Platelet Counts).

		Outcome				Total	%
		Death		Discharge			
		No.	%	No.	%		
Platelet Category	Thrombocytopenia	18	36.73	31	63.27	49	45.79
	Normal	5	8.62	53	91.38	58	54.21
Total		23	21.50	84	78.50	107	100.00

Chi-square = 12.44, df= 1, P value = <0.001

The outcomes of neonates with sepsis based on platelet counts reveal a stark contrast between those with thrombocytopenia and those with normal platelet levels. In the thrombocytopenia group, out of 49 neonates, 18 (36.73%) resulted in death, while 31 (63.27%) were discharged. Conversely, among the 58 neonates with normal platelet counts, only 5 (8.62%) resulted in death, and the majority, 53 (91.38%), were discharged.

This distribution results in a total of 23 deaths and 84 discharges out of 107 cases, corresponding to death and discharge rates of 21.50% and 78.50%, respectively. The chi-square statistical test yielded a value of 12.44 with 1 degree of freedom, and the P value is less than 0.001, indicating a statistically significant association between platelet count and outcomes in neonatal sepsis. This significant result suggests that thrombocytopenia in neonates with sepsis is associated with a higher risk of mortality compared to those with normal platelet counts.

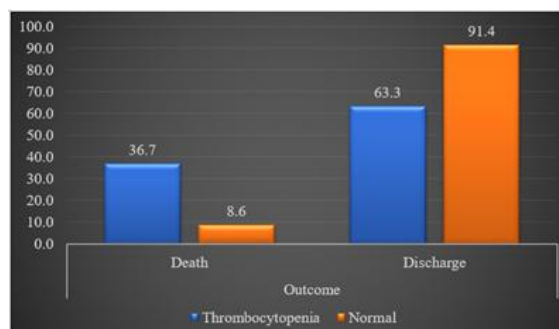


Figure 2

## DISCUSSION

Thrombocytopenia is one of the most common hematopoietic conditions observed in newborns admitted to the NICU. In fetal development, platelets begin to circulate around the fifth week of gestation and gradually reach normal adult levels of  $150\text{--}450 \times 10^9/\text{L}$  by the second trimester. This platelet count remains consistent throughout life. While severe thrombocytopenia (platelet count  $<50 \times 10^9/\text{L}$ ) in neonates is recognized as a condition requiring special clinical attention, there is limited understanding of the correlation between the severity of thrombocytopenia and the risk of bleeding.<sup>[9,10]</sup> In the present study, the prevalence of thrombocytopenia, defined as a platelet count of less than  $150,000/\text{mm}^3$ , in neonates with culture-positive sepsis was found to be 45.79%. A similar study

conducted by Babji NS et al. reported a comparable prevalence of thrombocytopenia at 39.47% among the participants.<sup>[11]</sup> In contrast, a study by Arabdin M et al. observed a higher prevalence, with 65.29% of neonates developing thrombocytopenia.<sup>[12]</sup>

In present study the association between thrombocytopenia and neonatal sepsis varies by the type of blood culture isolate. *Acinetobacter* and *Candida* showed no cases of thrombocytopenia (100%). *Citrobacter diversus* had an equal distribution (50% with and 50% without thrombocytopenia), while *Citrobacter freundii* showed a higher prevalence of cases without thrombocytopenia (71.42%). Coagulase-negative *Staphylococcus* (85.11%), *E. coli* (83.33%), and *Enterococcus* (75%) predominantly lacked thrombocytopenia. *Klebsiella* species, Non-fermenting Gram-negative rods, *Pseudomonas aeruginosa*, *Streptococcus pneumoniae*, and *Streptococcus viridans* had thrombocytopenia rates of only 0-10%. *Staphylococcus aureus* showed thrombocytopenia in just 10% of cases, indicating a lower association.

A study conducted by Arabdin M et al. also highlighted the variation in thrombocytopenia severity based on the causative bacterial pathogen. Their findings demonstrated that gram-negative sepsis was associated with a significantly higher incidence of early thrombocytopenia compared to gram-positive sepsis. Specifically, severe early thrombocytopenia was observed in 30.43% of gram-negative sepsis cases, whereas only 4.34% of gram-positive sepsis cases exhibited severe thrombocytopenia. These results align with previous research indicating that thrombocytopenia is more prevalent in gram-negative sepsis, reinforcing the understanding that bacterial type plays a crucial role in the hematological response to neonatal sepsis.<sup>[12]</sup>

In the present study, neonates with sepsis and thrombocytopenia had a significantly higher mortality rate (36.73%) compared to those with normal platelet counts (8.62%). Among 107 cases, 23 (21.50%) resulted in death, while 84 (78.50%) were discharged. The chi-square test (12.44, df = 1) yielded a P value < 0.001, indicating a statistically significant association between thrombocytopenia and increased mortality in neonatal sepsis. Similarly, a study by Singh et al.<sup>[13]</sup> reported a mortality rate of 37.1% among neonates with sepsis, aligning with the findings of the present study. However, in contrast, Babji NS et al. observed a lower mortality rate of 7.4% among neonates with sepsis.<sup>[11]</sup>

This study observes a strong association between thrombocytopenia and neonatal sepsis outcomes. Thrombocytopenia emerges as a frequent hematological abnormality in septic neonates and appears to be an early marker of disease severity. The severity of thrombocytopenia seems to vary based on the causative pathogen, with gram-negative sepsis showing a higher prevalence of early thrombocytopenia. The findings suggest that

neonates with lower platelet counts face an increased risk of mortality, highlighting the importance of early detection and continuous monitoring of thrombocytopenia in septic neonates. Statistical analysis indicates a significant correlation between thrombocytopenia and adverse outcomes, reinforcing the potential role of platelet count trends as a prognostic indicator. Further observations and research are needed to better understand the underlying mechanisms and to develop targeted management strategies for improving neonatal sepsis outcomes.

## CONCLUSION

This study highlights thrombocytopenia as a significant hematological abnormality in neonatal sepsis, with a strong association between low platelet counts and increased mortality. The findings suggest that thrombocytopenia can serve as an early predictive marker for disease severity, emphasizing the need for timely detection and monitoring. Given its prognostic value, incorporating platelet count trends into routine neonatal sepsis management may aid in early intervention and improved clinical outcomes. Further research is necessary to explore targeted therapeutic strategies and optimize neonatal care.

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