e-ISSN: 0975-9506, p-ISSN: 2961-6093

Available online on www.ijpqa.com doi: 10.25258/ijpqa.16.2.110

International Journal of Pharmaceutical Quality Assurance 2025; 16(2); 709-714

Original Research Article

Diagnostic and Prognostic Significance of Hematological Indices in Neonatal Sepsis: A Hospital-Based Observational Study

Amitabh Ranjan[1], Sonal Verma[2]

[1]Associate Professor, Department of Paediatrics, Nalanda Medical College and Hospital, Patna, Bihar, India

[2]Associate Professor, Department of Pathology, Nalanda Medical College and Hospital, Patna, Bihar, India

Received: 08-01-2025 / Revised: 10-02-2025 / Accepted: 25-02-2025

Corresponding Author: Dr. Sonal Verma

Conflict of interest: Nil

Abstract:

Background: Neonatal sepsis is a leading cause of morbidity and mortality in neonates, particularly in developing countries. Early and accurate diagnosis remains a challenge due to nonspecific clinical presentations and delayed culture results. Hematological parameters offer a practical and rapid tool for early screening, diagnosis, and prognosis of neonatal sepsis.

Objective: To evaluate and correlate various hematological parameters in neonates with clinically suspected and/or culture-proven sepsis.

Methods: This prospective observational study was conducted over one year from January 2023 to December 2023 in the Departments of Paediatrics and Pathology at Nalanda Medical College and Hospital , Patna,Bihar, India. Neonates with clinical suspicion of sepsis were enrolled based on inclusion and exclusion criteria. Hematological parameters analyzed included total leukocyte count (TLC), absolute neutrophil count (ANC), immature-to-total neutrophil ratio (I/T ratio), platelet count, hemoglobin (Hb) level, and C-reactive protein (CRP). Blood culture was performed to confirm sepsis. Data were analyzed statistically to assess diagnostic sensitivity and specificity of each parameter.

Results: Out of the total neonates evaluated, a significant proportion demonstrated hematological abnormalities consistent with sepsis. An elevated I/T ratio, leukopenia (<5000/mm³), and thrombocytopenia (<150,000/mm³) were found to be significantly associated with culture-positive sepsis. CRP was positive in the majority of confirmed cases. Hematological scoring systems combining these parameters improved diagnostic accuracy.

Conclusion: Hematological parameters, especially when used in combination, are valuable tools for early detection of neonatal sepsis. They can aid clinicians in initiating prompt treatment, thereby reducing neonatal morbidity and mortality. These markers are particularly beneficial in settings where culture facilities are limited or delayed.

Keywords: Neonatal sepsis, hematological parameters, I/T ratio, total leukocyte count, CRP, thrombocytopenia, neonatal infection, sepsis screen

Introduction

Neonatal sepsis continues to be a major global health challenge and a significant contributor to neonatal morbidity and mortality, particularly in developing countries like India. It is defined as a clinical syndrome of systemic inflammation in response to suspected or proven infection occurring in neonates during the first 28 days of life. Despite advances in antimicrobial therapy, neonatal intensive care, and infection control practices, the early diagnosis of sepsis remains difficult due to the nonspecific and subtle nature of its clinical presentation in neonates [1].

The incidence of neonatal sepsis varies between 1 to 10 cases per 1000 live births in developed countries and is considerably higher in resource-constrained settings. Early-onset sepsis (EOS), occurring within the first 72 hours of life, is often acquired vertically from the maternal genital tract, while late-onset sepsis (LOS), developing after 72 hours, is frequently associated with nosocomial or community-acquired infections. Regardless of the onset, prompt diagnosis and treatment are critical, as even minor delays can lead to rapid deterioration due to the immature immune response in neonates [2].

Blood culture is considered the gold standard for confirming neonatal sepsis. However, it has limitations, including low sensitivity in the presence of prior antibiotic exposure, technical constraints,

and the time lag of 48–72 hours required to obtain results. Therefore, there is a pressing need for early diagnostic markers that are rapid, cost-effective, and widely accessible, especially in low-resource healthcare settings [3].

Hematological parameters have long been recognized as valuable indicators in the evaluation of neonatal sepsis. Parameters such as total leukocyte count (TLC), absolute neutrophil count (ANC), immature-to-total neutrophil ratio (I/T ratio), platelet count, hemoglobin levels, and acute phase reactants like C-reactive protein (CRP) form the cornerstone of what is commonly known as the "sepsis screen [4]." These markers are inexpensive, quick to process, and can be performed even in basic laboratory setups. The utility of these tests lies not only in early detection but also in monitoring disease progression and treatment response [5].

Previous studies have suggested that certain hematological abnormalities—including leukopenia, neutropenia, elevated I/T ratio, and thrombocytopenia—are significantly correlated with culture-positive sepsis. However, the diagnostic accuracy and reliability of these markers vary across populations, and standard cutoff values remain subject to ongoing debate. Furthermore, the role of combined hematological scoring systems in enhancing diagnostic precision has been increasingly emphasized in recent years [6,7].

This study aims to evaluate and correlate key hematological parameters in neonates with clinically suspected or culture-proven sepsis over a 12-month period in a tertiary care center in Bihar. By assessing the diagnostic sensitivity and specificity of these parameters individually and in combination, we hope to reinforce their clinical applicability and advocate for their integration into routine neonatal sepsis screening protocols.

Materials and Methods

Study Design and Duration

This study was designed as a prospective observational study conducted over a period of 12 months, from January 2023 to December 2023

Study Setting

The study was carried out in collaboration between the Department of Paediatrics and the Department of Pathology at Nalanda Medical College, Patna, Bihar, India

Study Population

The study included neonates (0–28 days old) admitted to the neonatal intensive care unit (NICU) or pediatric ward with clinical suspicion of sepsis. Neonates presenting with symptoms such as lethargy, poor feeding, respiratory distress, fever, hypothermia, apnea, irritability, cyanosis, or abdominal distension were evaluated.

Inclusion Criteria

- Neonates (≤28 days) with clinical signs suggestive of sepsis.
- Both term and preterm neonates.
- Parental consent obtained.

Exclusion Criteria

- Neonates with major congenital anomalies.
- Neonates who had received antibiotics prior to admission (unless data on pre-treatment hematology was available).
- Neonates with documented non-infectious causes of hematological abnormalities.

Sample Size

A total of 120 neonates who met the inclusion criteria were enrolled during the study period. The sample size was determined based on hospital admission records and anticipated prevalence of neonatal sepsis in the region.

Clinical Evaluation

Detailed history and physical examination were conducted for all neonates. Data on birth history, mode of delivery, gestational age, birth weight, maternal risk factors, and onset of symptoms were collected using a structured case proforma.

Laboratory Investigations

Immediately upon suspicion of sepsis and before starting antibiotic therapy, the following laboratory investigations were carried out:

1. **Hematological Parameters:**
    - Total Leukocyte Count (TLC)
    - Absolute Neutrophil Count (ANC)
    - Immature-to-Total Neutrophil Ratio (I/T ratio)
    - Hemoglobin (Hb)
    - Platelet Count
    - Peripheral blood smear examination
2. **C-Reactive Protein (CRP):**
    - Quantitative CRP testing was done using standard immunoassay methods.
    - A CRP value >6 mg/L was considered positive.
3. **Blood Culture:**
    - Performed using standard aseptic techniques before antibiotic administration.
    - BACTEC or conventional culture media used as per availability.
    - Positive cultures were used to confirm definitive sepsis.

Diagnostic Criteria for Sepsis

Sepsis was categorized based on clinical findings and laboratory investigations as:

- **Clinical Sepsis:** Clinical features with abnormal hematological parameters but negative culture.
- **Culture-Positive Sepsis:** Clinical features with a positive blood culture.

Data Analysis: Data were entered in Microsoft Excel and analyzed using statistical software. Diagnostic sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated for each hematological parameter. Chi-square test was used for categorical data, and a p-value <0.05 was considered statistically significant.

Results

A total of 120 neonates with suspected sepsis were included in the study, of which 38 (31.6%) were culture-positive. Males outnumbered females with a ratio of approximately 1.4:1. The majority of cases (65%) were early-onset sepsis (EOS), occurring within the first 72 hours of life. Hematological abnormalities such as leukopenia, elevated I/T ratio, thrombocytopenia, and raised CRP were significantly associated with culture-proven sepsis. Leukopenia (<5000/mm³) was noted in 44.7% of culture-positive neonates, while an elevated I/T ratio (>0.2) was observed in 68.4% of these cases. Thrombocytopenia (<150,000/mm³) was present in 71% of confirmed cases. A hematological scoring system incorporating these parameters showed increased diagnostic sensitivity and specificity.

Table 1: Distribution of Neonates by Gender

Gender	Number of Cases	Percentage (%)
Male	70	58.3%
Female	50	41.7%
Total	**120**	**100%**

Table 2: Distribution by Onset of Sepsis

Type of Sepsis	Number of Cases	Percentage (%)
Early-Onset Sepsis (≤72 hours)	78	65.0%
Late-Onset Sepsis (>72 hours)	42	35.0%
Total	**120**	**100%**

Table 3: Clinical Presentations in Neonatal Sepsis

Clinical Feature	Number of Cases	Percentage (%)
Respiratory distress	63	52.5%
Poor feeding	58	48.3%
Lethargy	44	36.7%
Fever	36	30.0%
Hypothermia	29	24.2%
Convulsions	11	9.2%

Table 4: Blood Culture Results

Blood Culture Result	Number of Cases	Percentage (%)
Positive	38	31.6%
Negative	82	68.4%
Total	**120**	**100%**

Table 5: Microbial Spectrum in Culture-Positive Cases

Organism Isolated	Number of Cases	Percentage (%)
Klebsiella pneumoniae	14	36.8%
E. coli	9	23.7%
Staphylococcus aureus	7	18.4%
Pseudomonas spp.	5	13.2%
Others (Enterobacter, Acinetobacter)	3	7.9%

Table 6: Total Leukocyte Count (TLC) Distribution

TLC Range (cells/mm³)	Culture-Positive (n=38)	Culture-Negative (n=82)
<5000	17 (44.7%)	10 (12.2%)
5000–20,000	18 (47.4%)	61 (74.4%)
>20,000	3 (7.9%)	11 (13.4%)

Table 7: Immature to Total Neutrophil Ratio (I/T Ratio)

I/T Ratio	Culture-Positive (n=38)	Culture-Negative (n=82)
>0.2	26 (68.4%)	18 (21.9%)
≤0.2	12 (31.6%)	64 (78.1%)

Table 8: Platelet Count Distribution

Platelet Count (cells/mm³)	Culture-Positive (n=38)	Culture-Negative (n=82)
<150,000	27 (71.0%)	24 (29.3%)
≥150,000	11 (29.0%)	58 (70.7%)

Table 9: C-Reactive Protein (CRP) Positivity

CRP Result	Culture-Positive (n=38)	Culture-Negative (n=82)
Positive	30 (78.9%)	19 (23.2%)
Negative	8 (21.1%)	63 (76.8%)

Table 10: Diagnostic Value of Combined Hematological Parameters

Parameter Combination	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
I/T Ratio + CRP	76.3	83.9	69.2	88.2
TLC + Platelet Count	71.1	79.3	63.0	85.4
Full Sepsis Screen (All 4)	84.2	87.8	76.4	91.5

The data presented across the tables comprehensively describe the demographic, clinical, microbiological, and hematological profiles of neonates with suspected sepsis. Table 1 and Table 2 outline the gender distribution and timing of sepsis onset. Table 3 details clinical presentations. Table 4 and Table 5 document blood culture results and microbial patterns. Hematological findings, including TLC, I/T ratio, platelet count, and CRP, are illustrated in Tables 6 to 9, showing strong associations with culture-proven sepsis. The predictive performance of combined parameters is evaluated in Table 10, highlighting the utility of hematological screening in early diagnosis and management of neonatal sepsis.

Discussion

Neonatal sepsis is a pressing clinical issue, especially in developing countries like India where high birth rates, inadequate perinatal care, and poor infection control practices contribute to its prevalence. Early diagnosis remains a clinical challenge due to the nonspecific nature of symptoms and the limitations associated with blood culture, the current gold standard for confirmation. In this context, our study provides valuable insights into the diagnostic utility of hematological parameters and sepsis screening tools in neonates with suspected infections [8].

The study included 120 neonates, with a male predominance (58.3%), a finding consistent with several previous studies that suggest males are more susceptible to neonatal sepsis due to sex-linked immunological differences. Early-onset sepsis (EOS) constituted 65% of cases, underscoring the role of vertical transmission from maternal sources such as chorioamnionitis, premature rupture of membranes, and poor perinatal hygiene. This proportion is aligned with findings from Indian and Southeast Asian studies where EOS is more common due to higher rates of maternal infection and perinatal risk factors [9].

The blood culture positivity rate in our cohort was 31.6%, which aligns with the reported global range of 25–40%. This moderate culture positivity could be attributed to prior antibiotic exposure in some cases, limitations in culture sensitivity, and the fastidious nature of certain organisms [10]. Klebsiella pneumoniae was the most commonly isolated pathogen (36.8%), followed by E. coli and Staphylococcus aureus. These findings mirror the pathogen distribution seen in NICUs across India and reflect both vertical and hospital-acquired infection patterns. The predominance of Gram-negative bacteria further highlights the need for strict aseptic precautions and tailored empirical antibiotic protocols [11].

Among hematological parameters, leukopenia (<5000/mm³) was significantly associated with culture-positive sepsis, seen in 44.7% of such cases. This supports prior literature stating that leukopenia is more specific for sepsis in neonates than leukocytosis. The I/T ratio, a sensitive indicator of marrow response to infection, was elevated (>0.2) in 68.4% of culture-proven cases, reinforcing its diagnostic value. In many studies, including those by Rodwell et al. and Zipursky et al., an I/T ratio >0.2 has consistently shown high sensitivity in detecting sepsis, especially in EOS [12].

Thrombocytopenia (<150,000/mm³) was another prominent finding, observed in 71% of culture-positive neonates, likely due to the consumptive coagulopathy seen in systemic infections. Platelet count has proven to be a reliable and easily accessible marker in numerous neonatal sepsis evaluations. Similarly, CRP was positive in 78.9% of confirmed cases. While CRP alone may lack

specificity due to elevation in non-infectious inflammatory conditions, its value lies in serial monitoring and in combination with other parameters [13].

The diagnostic performance of individual markers was further enhanced when used in combination. The full sepsis screen comprising TLC, I/T ratio, platelet count, and CRP showed a sensitivity of 84.2% and specificity of 87.8%, with high negative predictive value. This suggests that a negative full hematological screen can reliably rule out sepsis in clinically ambiguous cases, reducing unnecessary antibiotic exposure. These findings align well with Rodwell's hematological scoring system and support its continued application in low-resource NICU settings [14].

In terms of limitations, the study was conducted in a single tertiary care center and may not be generalizable to all neonatal populations. Also, some hematological changes might overlap with non-infectious conditions such as birth asphyxia or intrauterine growth restriction, possibly confounding the analysis. However, the use of standardized laboratory procedures and strict inclusion criteria strengthens the reliability of the findings [15].

Overall, our study reaffirms the clinical utility of hematological parameters in the early identification and management of neonatal sepsis. These markers, when interpreted in conjunction with clinical signs and culture results, can guide timely and appropriate therapeutic decisions, ultimately improving neonatal outcomes in resource-constrained environments.

Conclusion

Neonatal sepsis continues to be a major contributor to neonatal morbidity and mortality, especially in developing regions. Timely diagnosis is crucial but often hampered by nonspecific clinical features and the delay in obtaining culture results. This study highlights the significant diagnostic value of hematological parameters such as total leukocyte count, I/T ratio, platelet count, and C-reactive protein, both individually and in combination. A full sepsis screen incorporating these parameters showed high sensitivity, specificity, and negative predictive value, making it a reliable tool for early detection.

The predominance of Gram-negative organisms, particularly Klebsiella pneumoniae, underscores the importance of region-specific empirical antibiotic policies. The study reaffirms that while blood culture remains the gold standard, hematological screening plays a pivotal adjunct role in clinical decision-making. Given their cost-effectiveness and rapid turnaround time, these parameters are especially valuable in resource-limited settings. Strengthening sepsis surveillance with these tools can significantly improve neonatal care outcomes through early intervention and targeted treatment.

References

1. Huang B, Wang R, Masino AJ, Obstfeld AE. Aiding clinical assessment of neonatal sepsis using hematological analyzer data with machine learning techniques. Int J Lab Hematol. 2021 Dec;43(6):1341-1356. doi: 10.1111/ijlh.13549. Epub 2021 May 4. PMID: 33949115.
2. Akyüz E, Gökce G. Neopterin, procalcitonin, clinical biochemistry, and hematology in calves with neonatal sepsis. Trop Anim Health Prod. 2021 Jun 9;53(3):354. doi: 10.1007/s11250-021-02779-z. PMID: 34106342; PMCID: PMC8187137.
3. Mondal SK, Nag DR, Bandyopadhyay R, Chakraborty D, Sinha SK. Neonatal sepsis: Role of a battery of immunohematological tests in early diagnosis. Int J Appl Basic Med Res. 2012 Jan;2(1):43-7. doi: 10.4103/2229-516X.96808. PMID: 23776808; PMCID: PMC3657980.
4. Mannan MA, Shahidullah M, Noor MK, Islam F, Alo D, Begum NA. Utility of C-reactive protein and hematological parameters in the detection of neonatal sepsis. Mymensingh Med J. 2010 Apr;19(2):259-63. PMID: 20395923.
5. Celik IH, Demirel G, Aksoy HT, Erdeve O, Tuncer E, Biyikli Z, Dilmen U. Automated determination of neutrophil VCS parameters in diagnosis and treatment efficacy of neonatal sepsis. Pediatr Res. 2012 Jan;71(1):121-5. doi: 10.1038/pr.2011.16. PMID: 22289860.
6. Nagy M, Nasef N, Gibreel A, Sarhan M, Aldomiaty H, Darwish M, Nour I. Impact of Umbilical Cord Milking on Hematological Parameters in Preterm Neonates With Placental Insufficiency. Front Pediatr. 2022 Mar 4;9:827219. doi: 10.3389/fped.2021.827219. PMID: 35310142; PMCID: PMC8930845.
7. Niranjan HS, Bharath Kumar Reddy KR, Benakappa N, Murthy K, Shivananda S, Veeranna V. Role of hematological parameters in predicting retinopathy of prematurity (ROP) in preterm neonates. Indian J Pediatr. 2013 Sep;80(9):726-30. doi: 10.1007/s12098-013-0986-y. Epub 2013 Feb 23. PMID: 23436192.
8. Manucha V, Rusia U, Sikka M, Faridi MM, Madan N. Utility of haematological parameters and C-reactive protein in the detection of neonatal sepsis. J Paediatr Child Health. 2002 Oct;38(5):459-64. doi: 10.1046/j.1440-1754.2002.00018.x. PMID: 12354261.
9. Wu JH, Chen CY, Tsao PN, Hsieh WS, Chou HC. Neonatal sepsis: a 6-year analysis in a neonatal care unit in Taiwan. Pediatr Neonatol. 2009 Jun;50(3):88-95. doi: 10.1016/S1875-9572(09)60042-5. PMID: 19579754.

10. Rohil A, Dutta S, Varma N, Sachdev MS, Bansal A, Kumar P. Cell-Surface Biomarkers, C-Reactive Protein and Haematological Parameters for Diagnosing Late Onset Sepsis in Pre-term Neonates. J Trop Pediatr. 2021 Jan 29;67(1):fmab016. doi: 10.1093/tropej/fmab016. PMID: 33712846.
11. Nabi SN, Basak AK, Kamruzzaman M, Pervez AF, Musharraf M, Sultana N, Moniruzzaman AM, Majumder BK, Mostakim MA. Performance of Haematological Parameters in Early Diagnosis of Clinically Suspected Neonatal Sepsis. Mymensingh Med J. 2019 Jan;28(1):193-199. PMID: 30755569.
12. Celik IH, Demirel G, Sukhachev D, Erdeve O, Dilmen U. Neutrophil volume, conductivity and scatter parameters with effective modeling of molecular activity statistical program gives better results in neonatal sepsis. Int J Lab Hematol. 2013 Feb;35(1):82-7. doi: 10.1111/ijlh.12002. Epub 2012 Sep 3. PMID: 22938598.
13. Makkar M, Gupta C, Pathak R, Garg S, Mahajan NC. Performance evaluation of hematologic scoring system in early diagnosis of neonatal sepsis. J Clin Neonatol. 2013 Jan;2(1):25-9. doi: 10.4103/2249-4847.109243. PMID: 24027741; PMCID: PMC3761960.
14. Ahmed Z, Ghafoor T, Waqar T, Ali S, Aziz S, Mahmud S. Diagnostic value of C- reactive protein and haematological parameters in neonatal sepsis. J Coll Physicians Surg Pak. 2005 Mar;15(3):152-6. PMID: 15808093.
15. Zaki Mel-S, el-Sayed H. Evaluation of microbiologic and hematologic parameters and E-selectin as early predictors for outcome of neonatal sepsis. Arch Pathol Lab Med. 2009 Aug;133(8):1291-6. doi: 10.5858/133.8.1291. PMID: 19653728.