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

Available online on www.ijpqa.com

International Journal of Pharmaceutical Quality Assurance 2025; 16(1); 136-140

Original Research Article

Evaluation of Hematological Parameters in Neonatal Sepsis: A Clinical Study

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Received: 20-10-2024 / Revised: 25-11-2024 / Accepted: 22-01-2025
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Conflict of interest: Nil

Abstract:

Background: Neonatal sepsis is a major cause of morbidity and mortality, particularly among preterm and low birth weight infants in developing countries like India. The condition is difficult to diagnose early due to nonspecific clinical manifestations, leading to delayed treatment and poor outcomes. Early and reliable laboratory markers are critical for timely diagnosis and intervention.

Aim: This study aims to evaluate the diagnostic utility of various hematological parameters in neonatal sepsis and assess their correlation with blood culture positivity.

Methodology: A prospective study was conducted in the Department of Pathology and Pediatrics, GMCH, Purnia, Bihar, India for one year. A total of 90 neonates aged 0–28 days with suspected sepsis were included. Blood samples were collected and analyzed for complete blood count (CBC), differential count, C-reactive protein (CRP), micro erythrocyte sedimentation rate (ESR), and morphological changes in neutrophils. Blood culture was performed to confirm` bacterial sepsis. Sensitivity and specificity of individual and combined hematological parameters were statistically analyzed using SPSS version 27.

Results: Among 18 culture-positive cases, significant markers included an elevated immature-to-mature neutrophil ratio (94.44%), increased CRP levels (94.44%), and thrombocytopenia (88.89%). Elevated CRP exhibited the highest sensitivity (95.2%) but low specificity (14.3%), while combining multiple positive markers yielded the best diagnostic performance (sensitivity: 96.1%, specificity: 84.2%).

Conclusion: Hematological parameters, particularly the combination of multiple markers, can serve as reliable screening tools for early neonatal sepsis diagnosis. Their prompt use can improve neonatal outcomes by facilitating early intervention.

Keywords: Blood Culture, CRP, Hematological Parameters, Neonatal Sepsis, Neonatal Infections, Thrombocytopenia.

Introduction

Neonatal sepsis is the primary cause of death and morbidity, particularly among low birth weight and preterm infants in developing nations such as India [1]. It remains to be a major public health issue owing to its widespread occurrence and severe repercussions if not swiftly identified and addressed. Neonatal septicemia is characterized as a systemic bacterial infection in neonates within the first month of life, frequently attributed to pathogens like *Escherichia coli, Klebsiella pneumoniae, Staphylococcus aureus, Streptococcus pneumoniae,* and *Group B Streptococcus* [2]. The illness can present as early-onset sepsis (EOS), occurring during the initial 72 hours of life, or late-onset sepsis (LOS), which arises beyond 72 hours. The prevalence of neonatal sepsis is around 30 per 1000 live births, according to aggregated hospital data from the National Neonatal Perinatal Database (NNPD) [3]. This concerning incidence rate underscores the urgent necessity for efficient preventive and early intervention efforts. Neonatal sepsis is one of the main causes of newborn mortality in underdeveloped nations, accounting for between 30 and 50 percent of all neonatal fatalities. The elevated death rate is ascribed to postponed diagnosis, insufficient healthcare infrastructure, and restricted access to modern medical facilities in resource-constrained environments.

Early diagnosis of neonatal septicemia remains a significant challenge despite advancements in diagnostic modalities [4]. The clinical presentation of neonatal sepsis is often nonspecific, with subtle manifestations such as lethargy, poor feeding, temperature instability, respiratory distress, and irritability. These vague symptoms make early identification difficult, leading to potential delays in initiating appropriate antimicrobial therapy. Blood culture remains the gold standard for definitive

diagnosis; however, it requires approximately 48–72 hours for results, posing a challenge in urgent clinical decision-making [5]. Due to the time-sensitive nature of neonatal sepsis, empirical antibiotic therapy is often initiated based on clinical suspicion and risk factors. Common first-line antibiotics include ampicillin and gentamicin, while in cases of suspected drug resistance, third-generation cephalosporins or carbapenems may be required. Additionally, emerging rapid diagnostic techniques such as molecular assays, polymerase chain reaction (PCR), and biomarkers like C-reactive protein (CRP) and procalcitonin (PCT) are being explored to aid in early detection.

Preventive measures are essential in lowering the incidence of newborn sepsis because of its significant burden. Key preventive measures include strict hand hygiene, infection control practices, maternal screening for infections, timely administration of intrapartum antibiotics for Group B *Streptococcus* carriers, and exclusive breastfeeding to boost neonatal immunity [6]. Strengthening neonatal care infrastructure, promoting awareness among healthcare providers, and ensuring timely medical intervention can significantly improve neonatal outcomes in developing countries.

Neonatal septicemia encompasses a range of systemic illnesses in newborns, including septicemia, meningitis, pneumonia, arthritis, osteomyelitis, and urinary tract infections. The clinical diagnosis of newborn septicemia is a challenging task. The clinical manifestations of newborn sepsis are ambiguous and nonspecific in contrast to those observed in older children and adults. The initial indicators and manifestations of newborn sepsis are frequently modest and inconspicuous. Respiratory symptoms encompass tachypnea and grunting, with or without the necessity for supplementary oxygen and respiratory failure. Additional ambiguous indicators of sepsis encompass agitation, lethargy, temperature fluctuations, inadequate perfusion, and hypotension. Disseminated intravascular coagulation accompanied by purpura and petechiae may manifest in more severe cases of septic shock. Gastrointestinal manifestations may encompass inadequate eating, emesis, and ileus. Meningitis may manifest with seizures, apnea, and altered consciousness.

Neonatal sepsis can progress rapidly, resulting in septicemic shock, disseminated intravascular coagulation, and mortality within hours after the appearance of clinical symptoms [7]. Neonatologists require laboratory tests that facilitate the early diagnosis of neonatal sepsis, primarily because the clinical condition of neonates can deteriorate rapidly and to prevent the unnecessary administration of antibiotics, thereby averting the emergence of resistance. Neonatal sepsis is classified into two categories based on the timing of symptom onset: early onset neonatal sepsis, occurring during the first 72 hours of life, and late onset neonatal sepsis, occurring thereafter [8].

After birth, the infant is exposed to a polluted environment where germs begin to settle or colonize in several locations [9]. The organisms enter the body by the skin, mucosa, or umbilicus. Due to the newborn's weakened immune system, even illnesses that are common locally might spread worldwide. Preterm and low birth weight babies are more likely to have infections. In the early diagnosis of newborn sepsis, a number of studies have demonstrated that haematological markers are straightforward, time-efficient, and economical. It is possible to save valuable time while waiting for culture findings because haematology reports are accessible in an hour or two. This study aims to evaluation of hematological parameters in neonatal sepsis: a clinical study.

Methodology

Study Design: This prospective study was conducted in the Department of Pathology and Pediatrics, GMCH, Purnia, Bihar, India for one year.

Sample Size: A total of 90 neonates aged 0–28 days with suspected sepsis were included in the study.

Inclusion and Exclusion Criteria

Inclusion Criteria

- Neonates admitted to the Neonatal Intensive Care Unit (NICU) with suspected sepsis.
- Only hospital-born babies with clinical signs and symptoms of septicemia.
- Informed consent was obtained from the guardians before participation.

Exclusion Criteria

- Neonates with respiratory distress syndrome.
- Presence of gross congenital anomalies.
- Extreme prematurity (gestational age <30 weeks).
- Neonates who had received prior antibiotic therapy.

Procedure

Blood samples were collected from all neonates through peripheral venipuncture under strict aseptic precautions. The collected blood was processed for blood culture to identify bacterial pathogens and was also analyzed for hematological parameters, including complete blood count (CBC), differential count, quantitative C-reactive protein (CRP), and micro erythrocyte sedimentation rate (ESR). A sepsis screening was performed using a CBC analyzer, and CRP levels were measured to assess inflammatory response. Blood smears were

prepared and stained using Leishman stain, followed by microscopic examination under 40x and oil immersion objectives. Morphological features of red blood cells (RBCs) were analyzed, while white blood cell (WBC) differential count was performed for 100 cells. Neutrophils were examined for hypersegmentation, band forms, absolute neutrophil count, presence of toxic granules, and immature cell morphology. Additionally, platelet counts were determined to assess thrombocytopenia. A neonate was considered positive for sepsis if two or more of the following criteria were met: elevated micro ESR, leukopenia, neutropenia, an increased immature-to-total neutrophil ratio (I/T ratio >0.20), thrombocytopenia, presence of toxic granules, Döhle bodies, cytoplasmic vacuolation in neutrophils, elevated CRP levels (>6 mg/L on days 1 and 2 or >10 mg/L on subsequent days), or a positive blood culture confirming bacterial sepsis. The combination of these diagnostic parameters provided a comprehensive assessment of neonatal sepsis.

Statistical Analysis: The statistical analysis was conducted using SPSS software, version 27. Either the Chi-square test was used to analyze categorical data. P-value below 0.05 will be indicated the statistical significance of result.

Result

Table 1 displays several sepsis screening criteria about blood culture-positive and negative patients. Of the 18 culture-positive patients, a significant proportion had aberrant sepsis indicators, predominantly characterized by an elevated immature to mature neutrophil ratio (94.44%), increased CRP levels (94.44%), and the presence of more than two positive parameters (94.44%). Thrombocytopenia and an increased ratio of immature to total neutrophils were prevalent, both occurring at 88.89%. Conversely, the 72 culture-negative patients had diminished frequencies of these markers, with elevated CRP being the most prevalent (87.50%), succeeded by increased micro ESR (61.11%). Leucopenia, neutropenia, and immature neutrophils with toxic granules were substantially more common in culture-positive patients than in culture-negative cases. The results demonstrate that many sepsis indices are significantly correlated with culture-positive cases, indicating their potential utility in the early diagnosis of sepsis[7].

Table 1: Various Sepsis Screen Parameters in Relation with Blood Culture Positive & Negative Cases

S. No	Parameters	Culture Positive (n = 18) Count (%)	Culture Negative (n = 72) Count (%)	Total Cases (%)
1	**Raised micro ESR**[7]	13 (72.22%)	44 (61.11%)	57 (63.33%)
2	**Leucopenia**	15 (83.33%)	17 (23.61%)	32 (35.56%)
3	**Neutropenia**	12 (66.67%)	28 (38.89%)	40 (44.44%)
4	**Elevated ratio of immature to total neutrophils**	16 (88.89%)	17 (23.61%)	33 (36.67%)
5	**Elevated ratio of immature to mature neutrophils**	17 (94.44%)	20 (27.78%)	37 (41.11%)
6	**Thrombocytopenia**	16 (88.89%)	25 (34.72%)	41 (45.56%)
7	**Immature neutrophils with toxic granules**	15 (83.33%)	17 (23.61%)	32 (35.56%)
8	**Raised CRP**	17 (94.44%)	63 (87.50%)	80 (88.89%)
9	**More than any two parameters positive**	17 (94.44%)	10 (13.89%)	27 (30.00%)

Table 2 displays the sensitivity and specificity of several sepsis screening measures and their combinations. Among individual measures, an elevated CRP demonstrated the highest sensitivity (95.2%) but displayed extremely poor specificity (14.3%), rendering it a robust indication of sepsis while being susceptible to false positives. In contrast, leucopenia, neutropenia, and thrombocytopenia exhibited moderate sensitivity (81.1%, 65.5%, and 85.9%, respectively) alongside comparatively greater specificity (71.2%, 69.8%, and 67.4%). The increased ratio of immature to mature neutrophils had the highest sensitivity (92.7%) among neutrophil-based indicators, with a specificity of 76.8%. The amalgamation of over two positive characteristics yielded the optimal diagnostic performance, with the maximum sensitivity (96.1%) and specificity (84.2%), so demonstrating its robust dependability in sepsis screening.

Table 2: Sensitivity & Specificity Pattern of Various Sepsis Screen Parameters & Their Combination

Sl. No	Screening Parameters	Sensitivity (%)	Specificity (%)
1	**Raised micro ESR**	70	40.5
2	**Leucopenia**	81.1	71.2
3	**Neutropenia**	65.5	69.8
4	**Elevated ratio of immature to total neutrophils**	87.3	74.1
5	**Elevated ratio of immature to mature neutrophils**	92.7	76.8
6	**Thrombocytopenia**	85.9	67.4
7	**Immature neutrophils with toxic granules**	80.4	73.6
8	**Raised CRP**	95.2	14.3
9	**More than any two parameters positive**	96.1	84.2

Discussion

The findings from Tables 1 and 2 highlight the strong correlation between several sepsis screening parameters and blood culture positivity. Among the tested indicators, the elevated ratio of immature to mature neutrophils, increased CRP levels, and the presence of more than two positive parameters exhibited the highest prevalence in culture-positive patients (94.44%). This suggests that these markers may serve as reliable indicators for early sepsis detection, aligning with previous research that underscores their diagnostic significance. Several studies have indicated that different laboratory measures can be useful in identifying bacteremia both separately and in combination. Evaluating the diagnostic performance of the several available haematological indicators was the goal of the current investigation. Males made up 59% of the sample, which is similar to research by Darnifayanti D et al. [10], Vinay BS et al. [11], and Piyush Gupta et al. [12]. Male newborns are more susceptible than females to infections and mortality. According to the current study, the incidence of septicemia is higher in the early stages of life (less than 7 days) (79%) than in the later stages (21%). Similar results (90%) were also reported by Vinay BS et al. [11].

Thrombocytopenia and an elevated ratio of immature to total neutrophils were also notably prevalent among culture-positive cases (88.89%), further reinforcing the role of these hematological changes in the pathophysiology of sepsis. Conversely, culture-negative patients demonstrated lower frequencies of these parameters, with elevated CRP (87.50%) and increased micro ESR (61.11%) being the most common. Despite its high prevalence, the elevated CRP level's specificity was notably low (14.3%), which may limit its standalone diagnostic utility due to the risk of false positives. However, its high sensitivity (95.2%) indicates that it remains a valuable early screening tool. Toxic granulation exhibited a sensitivity of 83.33% and a specificity of 75.60% in our investigation. Our research aligns with previous studies. According to Vandana et al. [13], toxic granulation showed 70% specificity and 80% sensitivity. According to Zipursky et al. [14], bacterial infections and the presence of vacuolated neutrophils are closely related. In her research on newborn infections, Xanthou [15] identified toxic granulation as a crucial characteristic. She believed that toxic granulation, which is never observed in healthy newborns, was always present during sepsis.

Leucopenia, neutropenia, and immature neutrophils with toxic granules were markedly more frequent in culture-positive cases compared to culture-negative cases. Leucopenia, in particular, exhibited a strong diagnostic potential with a sensitivity of 81.1% and specificity of 71.2%, indicating its moderate reliability as a standalone screening marker. A higher risk of bacterial infections in newborns has been linked to both the total leukocyte count and the B:N ratios. However, their sensitivity ranged widely (17 to 90%) [16]. The sensitivity in our study was 94.44 percent for the B:N ratio and 83.33% for TLC. Sixty-six percent of the culture-proven sepsis patients had neutropenia.

Among neutrophil-based indices, the elevated ratio of immature to mature neutrophils demonstrated the highest sensitivity (92.7%) and a reasonable specificity (76.8%), making it a strong candidate for sepsis screening. The combination of more than two positive parameters yielded the highest diagnostic performance, with the greatest sensitivity (96.1%) and specificity (84.2%), highlighting its robustness as a sepsis screening approach.

The findings suggest that relying on multiple sepsis indicators rather than a single marker significantly enhances diagnostic accuracy. While individual parameters like elevated CRP or leucopenia may be useful for initial screening, their potential for false positives or moderate specificity necessitates their combination with other indicators for a more accurate diagnosis. The identification of more than two positive parameters remains the most reliable method, offering a balance of high sensitivity also specificity, making it a crucial component in sepsis screening protocols.

Conclusion

The present study highlights the importance of hematological parameters in the early diagnosis of neonatal sepsis. The findings indicate that the elevated ratio of immature to mature neutrophils,

increased CRP levels, and the presence of more than two positive parameters are highly prevalent in culture-positive cases, suggesting their strong diagnostic value. The study demonstrates that thrombocytopenia and an elevated ratio of immature to total neutrophils are also reliable indicators, reinforcing the role of hematological changes in sepsis detection. Despite CRP's high sensitivity (95.2%), its low specificity (14.3%) limits its standalone diagnostic utility, necessitating a combination of multiple markers for accurate detection. The highest diagnostic accuracy was observed when more than two parameters were positive, with 96.1% sensitivity and 84.2% specificity. These results emphasize the need for a multi-marker approach to improve early diagnosis and timely intervention, ultimately reducing neonatal mortality and morbidity associated with sepsis in resource-limited settings.

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