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Original Research Article

Haematological Markers in Early Diagnosis of Neonatal Sepsis

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Abstract

Background: Neonatal sepsis is a severe systemic infection in newborns, predominantly caused by bacterial, viral, or fungal pathogens. It is a major health issue, especially in preterm or low birth weight infants, due to their underdeveloped immune systems. Despite improvements in neonatal care, the diagnosis of sepsis remains challenging due to its non-specific symptoms and overlaps with other neonatal conditions. The haematological profile, including white blood cell count, platelet count, and inflammatory markers, offers valuable insights for the early identification of sepsis.

Aim: This study aims to evaluate the role of haematological parameters in diagnosing neonatal sepsis, comparing septic and non-septic neonates to determine significant differences in blood profiles and their diagnostic value.

Methodology: A cross-sectional observational study was conducted in the neonatal intensive care unit (NICU) of a Department of Pathology and Pediatrics, Sheikh Bhikhari Medical College, Hazaribagh, Jharkhand, India,The study included 50 neonates diagnosed with sepsis and 50 healthy controls who were matched for gestational stage and age. Samples of blood were examined for the presence of cytoplasmic vacuolations or toxic granules, Band-to-neutrophil ratio, micro erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), platelet count, and total leukocyte count (TLC). In order to identify statistically significant differences between the categories, statistical analysis was implemented.

Results: Septic neonates showed significantly elevated TLC (19.25 ± 5.80 x10^3/µL), CRP (30.15 ± 8.60 mg/L), micro ESR (25.40 ± 11.20 mm), and band-to-neutrophil ratio (0.42 ± 0.18) compared to the control group ($p < 0.001$ for all). Platelet count was markedly lower in the sepsis group (95.00 ± 30.25 x10^3/µL) than in the control group (270.00 ± 45.10 x10^3/µL). Additionally, toxic granules were present in 66% of septic neonates, and positive blood cultures were found in 52%.

Conclusion: The haematological profile, particularly elevated leukocyte count, reduced platelet count, high CRP levels, and the presence of toxic granules, is a crucial diagnostic tool for early detection of neonatal sepsis. The findings highlight the importance of combining these markers to improve diagnostic accuracy and facilitate prompt treatment.

Keywords: C-Reactive Protein, Diagnostic Criteria, Haematological Markers, Infection Biomarkers, Leukocytosis, Neonatal Sepsis, Neonates and Thrombocytopenia.

Introduction

Neonatal sepsis is a severe illness marked by systemic infection in infants, frequently caused by bacterial, viral, or fungal pathogens. It presents a considerable risk to newborns, especially those who are preterm or of low birth weight, owing to their underdeveloped immune systems. The prevalence of neonatal sepsis differs worldwide, with some underdeveloped nations reporting rates as high as 21 per 1,000 live births [1]. The illness is linked to significant morbidity and death, rendering prompt identification and good care essential.

The clinical manifestation of newborn sepsis may be mild and non-specific, frequently overlapping with other prevalent neonatal diseases. Symptoms include Lethargy, respiratory distress, eating difficulties, and temperature instability resistance may provide diagnostic problems [2]. Consequently, there is an immediate want for dependable biomarkers and diagnostic standards to enable early identification. A potential study topic examines the haematological profile of infected newborns, offering essential insights into the physiologic response to infection.

Haematological parameters, such as Inflammatory indicators, platelet count, and white blood cell count including C-reactive protein (CRP), are

crucial in the assessment of sepsis. An increased white blood cell count typically signifies an active immune response, whereas thrombocytopenia, characterized by a low platelet count, is commonly seen in septic neonates [3]. CRP serves as a recognized marker of inflammation, often showing elevated levels in sepsis, thus providing clinicians with a useful means to evaluate infection severity [4]. Studies have shown that specific haematological parameters may function as diagnostic indicators for neonatal sepsis. Scoring systems that integrate these parameters enhance diagnostic accuracy. The criteria for the "sepsis screen," which encompass elevated CRP levels, an increased immature to total neutrophil ratio (I/T ratio), and the presence of toxic granules, offer a systematic method for identifying septic infants [5]. These criteria are essential for differentiating between septic and non-septic infants, especially within high-risk groups.

The study of haematological profiles in neonatal sepsis holds importance that transcends mere diagnosis. Comprehending the pathophysiological alterations that arise in response to infection can guide treatment approaches and enhance clinical results. The presence of immature neutrophils and toxic granules signifies a left shift in the bone marrow response, indicating the body's effort to initiate an effective immune response [6]. These insights can inform monitoring strategies and therapeutic interventions within the NICU environment. Additionally, variations in hematological parameters may offer prognostic insights. Research indicates that specific haematological abnormalities are associated with the severity of disease and outcomes in septic neonates. A higher total leukocyte count correlates with poorer outcomes, whereas a notable reduction in platelet count may suggest a more severe infection or the onset of disseminated intravascular coagulation (DIC) [7]. Identifying these relationships aids clinicians in making informed decisions about resource allocation and treatment escalation.

The significance of prompt identification and handling of neonatal sepsis is highlighted by the effect of inadequate treatment on survival rates. Studies indicate that every hour of delay in starting appropriate antibiotic treatment markedly raises the mortality risk in septic infants [8]. Rapid identification of septic neonates through haematological parameters can enable prompt treatment initiation, thereby enhancing survival outcomes.

There are still many obstacles to overcome in spite of the progress made in comprehending the hematological characteristics of newborn sepsis. The standardization of diagnostic criteria may be complicated by the population's variability, differences in pathogen profiles, and disparate practices in neonatal critical care units. Furthermore, factors like gestational age, birth weight, and underlying comorbidities might affect how haematological values are interpreted; these aspects need to be taken into account in clinical practice. Assessing the importance of the several haematological markers and the haematological scoring system in the early identification of newborn sepsis was the aim of the study.

Methodology

Study Design

This research was structured as a cross-sectional observational study carried out in the neonatal intensive care unit (NICU) of a Department of Pathology and Pediatrics Sheikh Bhikhari Medical College, Hazaribagh, Jharkhand, India for eight months. This design enabled the evaluation of haematological profiles in neonates with a diagnosis of sepsis.

Population Selection

The target population comprised infants diagnosed with sepsis according to clinical criteria and laboratory results. A control group of healthy infants was matched for age and gestational age to facilitate a comparative investigation of hematological markers.

Inclusion Criteria

Neonatal exhibiting symptoms of infection, such as fever, lethargy, respiratory distress, or feeding aversion, were included in the sepsis group as long as they also showed positive blood cultures or increased inflammatory markers (e.g., C-reactive protein). Healthy newborns who were admitted for normal monitoring and showed no symptoms of infection made up the control group.

Data Collection

Demographic and clinical data were systematically documented, encompassing gestational age, birth weight, and clinical symptoms, to guarantee a thorough dataset for analysis. Informed consent was acquired from the parents or guardians of all participants prior to their inclusion in the study.

Blood Sample Collection

Blood samples were collected from both groups for a comprehensive hematological analysis. The tests included C-reactive protein levels, erythrocyte sedimentation rate, total leukocyte count, band-to-mature neutrophil ratio (B: N), platelet count, and the detection of toxic granulations or cytoplasmic vacuolations in peripheral smears. During the first 24 to 36 hours of life, CRP levels were measured semi-quantitatively using the slide agglutination method. Additionally, sterile blood culture samples obtained from a peripheral vein or artery prior to the

administration of antibiotics were examined. As necessary, chest X-rays and other testing were conducted.

Laboratory Analysis

Blood samples were analyzed with automated hematology analyzers to guarantee precision and dependability in the outcomes. Peripheral blood smears were obtained and microscopically analyzed to evaluate cell morphology and detect any unusual cells or abnormalities suggestive of sepsis. The timing of blood sample collection was crucial, with samples obtained during the initial 24 hours of sepsis diagnosis to capture the acute phase response.

A sepsis screen is considered positive when more than two of the following criteria are satisfied: Criteria for elevated inflammatory markers include C-reactive protein levels exceeding 16 mg/l on days 1 and 2 of life or greater than 10 mg/l thereafter. Additionally, a micro ESR greater than [age + 3] mm in the first hour for neonates under 3 days old or exceeding 15 mm in the first hour at any age is noted. Other indicators include leukopenia with a total leukocyte count below 5000/cu mm, neutropenia defined as an absolute neutrophil count below 1500/cu mm, and an immature to total neutrophil ratio (I/T ratio) exceeding 0.20. The presence of toxic granules, cytoplasmic vacuolation, or Dohle bodies in neutrophils, along with a decreased platelet count below 1.5 lacs/cu mm, or a positive blood culture are also significant findings.

Statistical Analysis

Statistical analysis was conducted utilizing tool by SPSS version 27.0 to assess the data. Descriptive statistics detailed the demographic features of both groups, whereas inferential statistics, including t-tests, were utilized to ascertain significant changes in hematological profiles between the sepsis and control groups.

Result

The demographic characteristics of the study participants are presented in Table 1, which delineates the profiles of two distinct groups: the Sepsis Group (n=50) and the Control Group (n=50).

Table 1: Demographic Characteristics

Characteristic	Sepsis Group (n=50)	Control Group (n=50)
Mean Gestational Age (weeks)	31.8 (± 2.7)	32.9 (± 2.5)
Mean Birth Weight (grams)	1,750.50 (± 400.75)	2,150.00 (± 350.50)
Temperature Instability (%)	82	-
Respiratory Distress (%)	68	-
Lethargy (%)	64	-
Feeding Intolerance (%)	54	-

The mean gestational age of the infants in the Sepsis Group is reported as 31.8 weeks (± 2.7), indicating a preterm population with a relatively lower gestational age compared to the Control Group, which has a mean gestational age of 32.9 weeks (± 2.5). This slight difference suggests that the Sepsis Group may exhibit additional vulnerabilities due to their earlier gestational age. In terms of birth weight, the Sepsis Group presents a mean of 1,750.50 grams (± 400.75), which is significantly lower than the mean birth weight of the Control Group at 2,150.00 grams (± 350.50). This disparity highlights the potential impact of sepsis on fetal development and subsequent neonatal health outcomes, as lower birth weight is often associated with increased morbidity.

The incidence of clinical symptoms further underscores the differences between the two groups. Notably, the Sepsis Group exhibits alarming rates of temperature instability at 82%, alongside respiratory distress in 68% of the participants, lethargy in 64%, and feeding intolerance in 54%. These percentages indicate a pronounced burden of acute physiological challenges among the sepsis-affected infants, which are not recorded in the Control Group, suggesting a stark contrast in clinical presentation and health status between the two cohorts.

Table 2 presents the haematological parameters of the studied groups.

Table 2: Haematological Parameters

Parameter	Sepsis Group (n=50)	Control Group (n=50)	p-value
Total Leukocyte Count (TLC) (x10^3/µL)	19.25 (± 5.80)	8.90 (± 2.50)	< 0.001
Platelet Count (x10^3/µL)	95.00 (± 30.25)	270.00 (± 45.10)	< 0.001
Micro ESR (mm)	25.40 (± 11.20)	10.80 (± 4.20)	< 0.001
C-Reactive Protein (mg/L)	30.15 (± 8.60)	7.20 (± 3.00)	< 0.001
Band to Neutrophil Ratio (B)	0.42 (± 0.18)	0.05 (± 0.03)	< 0.001

A striking contrast in the total leukocyte count (TLC) is observed, with the Sepsis Group exhibiting a mean of 19.25 (± 5.80) $x10^3/\mu L$, significantly elevated compared to the Control Group's mean of 8.90 (± 2.50) $x10^3/\mu L$ ($p < 0.001$). This finding indicates a pronounced leukocytosis characteristic of sepsis, reflecting an active immune response to infection. The platelet count further underscores the haematological abnormalities in the Sepsis Group, with a mean of 95.00 (± 30.25) $x10^3/\mu L$, which is substantially lower than the Control Group's mean of 270.00 (± 45.10) $x10^3/\mu L$ ($p < 0.001$). This thrombocytopenia is often associated with sepsis and may signify a consumption of platelets due to ongoing inflammatory processes or disseminated intravascular coagulation. In terms of inflammation markers, the micro erythrocyte sedimentation rate (ESR) is notably higher in the Sepsis Group, with a mean of 25.40 (± 11.20) mm compared to 10.80 (± 4.20) mm in the Control Group ($p < 0.001$). This elevation in ESR reflects an acute phase response, indicative of underlying infection or inflammation.

C-reactive protein (CRP) levels are also markedly elevated in the Sepsis Group, with a mean of 30.15 (± 8.60) mg/L versus 7.20 (± 3.00) mg/L in the Control Group ($p < 0.001$). Elevated CRP is a well-known marker of systemic inflammation and infection, reinforcing the clinical picture of sepsis in these patients. The band to neutrophil ratio (B) is significantly higher in the Sepsis Group, with a mean of 0.42 (± 0.18) compared to 0.05 (± 0.03) in the Control Group ($p < 0.001$). This ratio is indicative of a left shift in the neutrophil population, which is often observed in bacterial infections and sepsis.

Overall, the haematological parameters delineate a clear differentiation between the Sepsis and Control Groups, with significant alterations indicative of the inflammatory and immunological response characteristic of sepsis, which are critical for understanding the pathophysiology and management of this condition.

Table 3 outlines the criteria used for sepsis screening within the Sepsis Group, providing a comprehensive overview of the clinical and laboratory indicators associated with this condition.

Table 3: Sepsis Screen Criteria

Criteria	Sepsis Group Positive (%)
Elevated C-reactive protein	92
Elevated Micro ESR	88
Leukopenia	28
Neutropenia	36
Elevated I/T Ratio	80
Presence of Toxic Granules	66
Presence of Cytoplasmic Vacuolations	58
Positive Blood Culture	52

The data reveals that an overwhelming 92% of the infants in the Sepsis Group exhibit elevated C-reactive protein (CRP) levels, underscoring its utility as a prominent marker of systemic inflammation and infection. Similarly, elevated micro erythrocyte sedimentation rate (ESR) is present in 88% of the cohort, further corroborating the inflammatory response characteristic of sepsis. In contrast, leukopenia is observed in only 28% of the infants, while neutropenia, indicative of a specific reduction in neutrophils, is seen in 36%. These findings suggest that, although leukopenia and neutropenia are relevant parameters, they are less frequently observed compared to the inflammatory markers.

The elevated immature-to-total (I/T) neutrophil ratio, a critical indicator of bacterial infection, is found in 80% of the infants, indicating a significant shift in neutrophil maturation consistent with sepsis. Additionally, the presence of toxic granules, which reflects the activation of neutrophils in response to infection, is noted in 66% of the participants, while cytoplasmic vacuolations are present in 58%. These morphological changes in neutrophils are characteristic of severe infections and emphasize the underlying immune response. Lastly, positive blood cultures, confirming the presence of pathogens, are identified in 52% of the Sepsis Group. This finding is crucial, as it provides direct evidence of the infectious agent responsible for sepsis.

In summary, the sepsis screen criteria reveal a high prevalence of inflammatory markers and specific neutrophil changes in the Sepsis Group, with elevated CRP and micro ESR being particularly prevalent. These criteria collectively highlight the multifaceted nature of sepsis diagnosis and the importance of a comprehensive screening approach to identify affected infants.

Table 4 summarizes the key findings from the comparative analysis between the Sepsis and the Control Group, highlighting significant differences in haematological and clinical parameters.

Table 4: Key Findings			
Finding	**Sepsis Group (n=50)**	**Control Group (n=50)**	**p-value**
Mean WBC Count (x10³/μL)	19.25 (± 5.80)	8.90 (± 2.50)	< 0.001
Mean Platelet Count (x10³/μL)	95.00 (± 30.25)	270.00 (± 45.10)	< 0.001
Mean C-Reactive Protein (mg/L)	30.15 (± 8.60)	7.20 (± 3.00)	< 0.001
Presence of Toxic Granules (%)	66	0	-
Positive Blood Culture (%)	52	0	-

The mean white blood cell (WBC) count in the Sepsis Group is markedly elevated at 19.25 (± 5.80) x10³/μL, compared to a substantially lower mean of 8.90 (± 2.50) x10³/μL in the Control Group, with a p-value of less than 0.001 indicating a highly statistically significant difference. This elevation is consistent with a robust immune response typically observed in septic conditions. In terms of platelet count, the Sepsis Group shows a mean of 95.00 (± 30.25) x10³/μL, which is significantly lower than the Control Group's mean of 270.00 (± 45.10) x10³/μL ($p < 0.001$). This thrombocytopenia is a common finding in sepsis, suggesting a depletion of platelets possibly due to consumption during inflammatory processes.

C-reactive protein (CRP) levels in the Sepsis Group also reflect a significant inflammatory response, with a mean value of 30.15 (± 8.60) mg/L, contrasting sharply with the Control Group's mean of 7.20 (± 3.00) mg/L ($p < 0.001$). This elevation in CRP reinforces its role as a biomarker for infection and inflammation. The presence of toxic granules in neutrophils is observed in 66% of the Sepsis Group, whereas no instances are reported in the Control Group (0%), indicating a significant association between toxic granulation and septic conditions. This finding highlights the activation of neutrophils in response to severe infection. Additionally, positive blood cultures were noted in 52% of the Sepsis Group, again with no positive cultures in the Control Group (0%). This finding is critical as it confirms the presence of infectious agents in a substantial portion of the septic population.

The findings emphasize the significant differences in haematological and clinical parameters between the Sepsis and Control Groups, underscoring the diagnostic importance of these indicators in identifying and managing sepsis effectively.

Discussion

Neonatal sepsis is a critical condition characterized by systemic infection in infants, leading to significant morbidity and mortality. The haematological profile of affected neonates provides essential insights into the pathophysiological processes underlying this condition. The findings from the current study delineate notable differences in the haematological parameters and clinical presentations between the Sepsis Group and a Control Group.

The demographic data indicate that the Sepsis Group exhibited a lower mean gestational age of 31.8 weeks and a birth weight of 1,750.50 grams, in contrast to the Control Group, which had a mean gestational age of 32.9 weeks and a birth weight of 2,150.00 grams. This aligns with existing literature that suggests preterm infants face an elevated risk of sepsis attributable to their immature immune systems and reduced physiological reserves (Ganatra et al., 2010). [9]. The high prevalence of clinical symptoms in the Sepsis Group, including temperature instability (82%), respiratory distress (68%), lethargy (64%), and feeding intolerance (54%), underscores the serious physiological challenges encountered by these infants (Goldstein et al., 2005) [10].

In this result, the finding presents the haematological parameters of the two groups, highlighting significant differences. The Sepsis Group demonstrated a Total Leukocyte Count (TLC) of 19.25 (± 5.80) x10³/μL, which was significantly higher than the Control Group's count of 8.90 (± 2.50) x10³/μL ($p < 0.001$). Leukocytosis indicates an immune response to infection, reflecting heightened neutrophil production in reaction to inflammatory stimuli (Cuenca et al., 2013). [11]. The platelet count in the Sepsis Group was significantly lower at 95.00 (± 30.25) x10³/μL, in contrast to 270.00 (± 45.10) x10³/μL in the Control Group ($p < 0.001$). Thrombocytopenia frequently occurs in sepsis and can arise from heightened consumption linked to disseminated intravascular coagulation (DIC) or direct suppression of bone marrow (Cohn, 1976) [12].

The Micro Erythrocyte Sedimentation Rate (ESR) and C-Reactive Protein (CRP) levels were significantly elevated in the Sepsis Group, measuring 25.40 (± 11.20) mm and 30.15 (± 8.60) mg/L, respectively. These findings underscore their function as acute-phase reactants that increase in response to systemic inflammation (Nabulsi et al., 2012) [13]. The Band to Neutrophil Ratio (B) was elevated at 0.42 (± 0.18) in the Sepsis Group, indicating a left shift typically associated with bacterial infections. The presence of toxic granules in neutrophils (66% in the Sepsis Group compared to 0% in the Control Group) further confirms the increased activation of neutrophils, which is characteristic of severe infections (Van et al., 1997) [14].

The criteria for sepsis screening presented in Table 3 indicate a significant prevalence of elevated inflammatory markers, specifically CRP (92%) and ESR (88%) within the Sepsis Group. The presence of these markers highlights their significance in diagnosing sepsis and assessing treatment responses (Xie et al., 2021) [15]. The immature-to-total (I/T) ratio was elevated in 80% of cases, underscoring its significance as a diagnostic criterion in neonatal sepsis (Bender et al., 2008) [16].

Conclusion

The study highlights the significant role of haematological markers in the early diagnosis of neonatal sepsis. Neonates with sepsis demonstrated markedly distinct parameters, including an elevated total leukocyte count, decreased platelet count, increased C-reactive protein levels, and a higher band-to-neutrophil ratio, in comparison to the control group. Toxic granules and positive blood cultures served to further differentiate septic infants. The results demonstrate that integrated haematological markers serve as efficient diagnostic instruments for the prompt detection of neonatal sepsis, enabling timely intervention and improving outcomes.

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