

Significance of Hematological Scoring System in Early Diagnosis of Neonatal Sepsis

Bhumika Agrawal¹, Santosh Singh², Jagannath Jatav³, S.K. Sutrakar⁴, Meena Patel⁵,
Monika Kesarwani⁶, Panjap Singh Kirar⁷

¹Post Graduate, Department of Pathology, Shyam Shah Medical College, Rewa, Madhya Pradesh, India

²Associate Professor, Department of Pathology, Shyam Shah Medical College, Rewa, Madhya Pradesh, India

³Associate Professor, Department of Pathology, Shyam Shah Medical College, Rewa, Madhya Pradesh, India

⁴Professor, Department of Pathology, Shyam Shah Medical College, Rewa, Madhya Pradesh, India

⁵Professor, Department of Pediatrics, Shyam Shah Medical College, Rewa, Madhya Pradesh, India

⁶Post Graduate, Department of Pathology, Shyam Shah Medical College, Rewa, Madhya Pradesh, India

⁷Post Graduate, Department of Pathology, Shyam Shah Medical College, Rewa, Madhya Pradesh, India

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Corresponding author: Dr. Bhumika Agrawal

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Abstract

Background: Neonatal sepsis is a major cause of neonatal morbidity and mortality, particularly in developing countries, where delayed diagnosis contributes significantly to adverse outcomes. Clinical manifestations are often subtle and nonspecific, making early diagnosis challenging. Although blood culture remains the gold standard for diagnosis, its delayed turnaround time and low sensitivity limit its utility in emergency settings. The Hematological Scoring System (HSS) proposed by Rodwell et al. provides a rapid, economical, and bedside diagnostic approach for early detection of neonatal sepsis.

Objective: The present study was conducted to evaluate the significance of HSS in the early diagnosis of neonatal sepsis and to compare hematological parameters with blood culture findings.

Material and Methods: This cross-sectional study was conducted in the Department of Pathology, Shyam Shah Medical College, Rewa, over a period of 12 months. A total of 115 neonates clinically suspected of sepsis were included. Blood samples were collected under aseptic precautions for complete blood count, peripheral smear examination, and blood culture. Hematological parameters assessed included Total Leukocyte Count (TLC), Absolute Neutrophil Count (ANC), Immature-to-Total neutrophil ratio (I:T ratio), degenerative changes in neutrophils, platelet count, nucleated red blood cells (NRBCs), and Mean Platelet Volume (MPV). Hematological scoring was interpreted as: score ≤ 2 – sepsis unlikely, score 3–4 – probable sepsis, and score ≥ 5 – sepsis very likely.

Results: Previous studies reviewed in the present work demonstrated high diagnostic utility of HSS. Baruwat S et al. reported sensitivity, specificity, and diagnostic accuracy of 90.48%, 96.83%, and 95.91%, respectively, using a modified HSS cutoff score ≥ 4 . Degenerative changes in neutrophils showed the highest sensitivity (95.23%), while NRBCs demonstrated an accuracy of 91.15%. Elsayed MS et al. reported sensitivity and specificity of 96% and 90%, respectively, for HSS in neonatal sepsis. Elevated I:T ratio (>0.12), thrombocytopenia, neutropenia, increased MPV (>9.5 fL), and presence of toxic granules or Döhle bodies were among the most significant hematological abnormalities associated with culture-positive neonatal sepsis.

Conclusion: The Hematological Scoring System is a rapid, reliable, and cost-effective screening tool for early diagnosis of neonatal sepsis. Incorporation of additional parameters such as NRBCs and MPV further improves diagnostic accuracy and aids timely initiation of therapy, especially in resource-limited settings.

Keywords: Neonatal sepsis, Hematological Scoring System, Blood culture, Immature-to-total neutrophil ratio, Mean Platelet Volume, Nucleated RBCs.

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Introduction

Neonatal sepsis is a life-threatening clinical syndrome characterized by systemic signs of

infection occurring during the first 28 days of life and remains a major cause of neonatal morbidity

and mortality worldwide, particularly in developing countries. [1] The incidence ranges from 1% to 8% of all live births, with early-onset sepsis occurring within the first 72 hours of life and late-onset sepsis presenting thereafter. [2] Prematurity, low birth weight, premature rupture of membranes, maternal infection, low APGAR score, and poor perinatal hygiene are among the major risk factors contributing to neonatal sepsis. [3] In South Asian countries, Gram-negative organisms such as *Klebsiella* spp., *Escherichia coli*, and *Acinetobacter* are the predominant pathogens, contributing substantially to neonatal deaths. [4] In India, neonatal sepsis accounts for nearly 36% of neonatal mortality, emphasizing the need for early and accurate diagnosis. [5]

Early diagnosis of neonatal sepsis remains challenging because of nonspecific clinical manifestations during the initial stages of disease. Blood culture is considered the gold standard diagnostic modality; however, its utility is limited due to delayed reporting time, low sensitivity, and false-negative results. [3,6] Therefore, a rapid, reliable, and cost-effective screening tool is essential, especially in resource-limited settings.

Rodwell et al. introduced the Hematological Scoring System (HSS) in 1988 for early identification of neonatal sepsis using hematological parameters such as total leukocyte count, absolute neutrophil count, immature-to-total neutrophil ratio, degenerative changes in neutrophils, and platelet count. [7] Subsequent modifications incorporated nucleated red blood cells (NRBCs) and mean platelet volume (MPV), thereby improving diagnostic accuracy. [8,9] Studies have demonstrated that elevated I:T ratio, neutropenia, thrombocytopenia, degenerative neutrophilic changes, increased NRBCs, and raised MPV are significantly associated with neonatal sepsis. [8-13] The modified HSS thus serves as an economical and practical bedside tool for early diagnosis and timely initiation of treatment. [14]

Aims and Objectives

1. To evaluate the role of Hematological Scoring System (HSS) in the early diagnosis of neonatal sepsis.
2. To study various hematological parameters and peripheral smear changes in neonates clinically suspected of sepsis.
3. To compare hematological scoring system findings with blood culture results.

Material and Methods

This hospital-based cross-sectional study was conducted in the Department of Pathology, Sanjay Gandhi and Gandhi Memorial Hospital associated with Shyam Shah Medical College, Rewa, Madhya Pradesh, over a period of 12 months. A total of 115 neonates clinically suspected of neonatal sepsis were included in the study. The sample size was calculated using the prevalence of neonatal sepsis reported by Murthy et al. [15] with a prevalence rate of 17% and allowable error of 7%.

Neonates presenting with clinical features suggestive of sepsis, including fever or hypothermia, lethargy, poor feeding, respiratory distress, requirement of supplemental oxygen, low APGAR score, or maternal risk factors such as intrapartum fever, prolonged rupture of membranes, prematurity, and maternal urinary tract infection were included in the study. Neonates with major congenital anomalies, hemolytic disorders, Rh incompatibility, inborn errors of metabolism, or steroid therapy were excluded.

Under strict aseptic precautions, 3 mL of peripheral venous blood was collected from each neonate. Of this, 2 mL was transferred into EDTA vials for hematological investigations and 1 mL was inoculated into pediatric blood culture bottles for culture and sensitivity testing. Complete blood count was performed using the Zybco Z3 automated hematology analyzer. Peripheral blood smears were prepared immediately, stained with Leishman stain, and examined under oil immersion microscopy. Differential leukocyte count was performed manually by counting 200 leukocytes per smear.

The hematological parameters assessed included total leukocyte count (TLC), absolute neutrophil count (ANC), immature-to-total neutrophil (I:T) ratio, degenerative changes in neutrophils (toxic granules, Döhle bodies, cytoplasmic vacuolization), platelet count, nucleated red blood cells (NRBCs), and mean platelet volume (MPV). Hematological scoring was performed according to the modified Hematological Sepsis Score based on Rodwell et al. [7] Blood cultures were processed using the BacT/ALERT 3D 60 automated blood culture system and served as the gold standard for diagnosis.

Statistical analysis was performed using appropriate statistical tests, and p-value <0.05 was considered statistically significant.

Results

Table 1: Distribution of Neonates According to Blood Culture and Hematological Scoring System (HSS)

Parameter	Number of Cases (n=115)	Percentage (%)
Culture Positive	71	61.73
Culture Negative	44	38.27
HSS ≤2 (Sepsis unlikely)	28	24.34
HSS 3-4 (Sepsis possible)	64	55.65
HSS ≥5 (Sepsis very likely)	23	20.00

Out of 115 neonates, 71 (61.73%) were culture positive. Majority of neonates (55.65%) had HSS scores between 3–4 indicating probable sepsis, while 20% had scores ≥ 5 suggestive of definite sepsis. These findings support the usefulness of HSS as an early screening tool for neonatal sepsis.

Table 2: Comparison of Hematological Parameters with Culture Results

Hematological Parameter	Culture Positive n=71 (%)	Culture Negative n=44 (%)	χ^2 value	p value
Abnormal TLC (≤ 5000 or $\geq 21000/\text{cumm}$)	40 (56.33)	22 (50.00)	0.435	0.509
Abnormal PMN Count (<1800 or $>5400/\mu\text{L}$)	61 (85.91)	35 (79.55)	0.792	0.373
I:T Ratio ≥ 0.12	53 (74.64)	25 (56.81)	3.92	0.047
Degenerative Changes in PMN Present	44 (61.97)	21 (47.73)	2.75	0.097
Platelet Count <1.5 lakh/ μL	34 (47.89)	21 (47.73)	0.0002	0.99

Among all hematological parameters studied, elevated I:T ratio (≥ 0.12) showed statistically significant association with culture-proven neonatal sepsis ($p=0.047$). Abnormal PMN count and

degenerative changes in neutrophils were more frequently observed in culture-positive cases, suggesting their supportive diagnostic role in neonatal sepsis.

Table 3: NRBC Count and MPV in Comparison with Culture Results

Parameter	Culture Positive n=71 (%)	Culture Negative n=44 (%)	χ^2 value	p value
NRBC $\geq 5\%$	15 (21.13)	9 (20.45)	0.01	0.92
MPV >9.5 fL	49 (69.01)	20 (45.45)	6.41	0.011

Raised MPV (>9.5 fL) showed a statistically significant association with culture-positive neonatal sepsis ($p=0.011$), indicating its usefulness as an adjunctive hematological marker. However, NRBC count did not show significant association with blood culture positivity.

Table 4: Clinical Presentation in Comparison with Culture Results

Clinical Features	Culture Positive n=71 (%)	Culture Negative n=44 (%)	Total n=115 (%)
Respiratory Distress	32 (45.07)	20 (45.45)	52 (45.22)
Birth Asphyxia	26 (36.62)	11 (25.00)	37 (32.17)
Feeding Issues	8 (11.27)	8 (18.18)	16 (13.91)
Clinical Sepsis	5 (7.04)	5 (11.36)	10 (8.70)

Respiratory distress was the most common presenting complaint in both culture-positive and culture-negative neonates. Birth asphyxia was more commonly associated with culture-positive sepsis cases, highlighting its importance as a significant clinical risk factor.

Table 5: Risk Factors and Mode of Delivery in Relation to Culture Results

Variable	Culture Positive n=71 (%)	Culture Negative n=44 (%)	p value
Preterm Neonates	21 (29.58)	17 (38.64)	0.317
Term Neonates	50 (70.42)	27 (61.36)	
Normal Vaginal Delivery	41 (57.74)	27 (61.36)	0.702
LSCS Delivery	30 (42.26)	17 (38.64)	

No statistically significant association was observed between maturity status or mode of delivery with culture positivity. However, term neonates and neonates delivered vaginally constituted the majority of culture-positive cases in the present study.

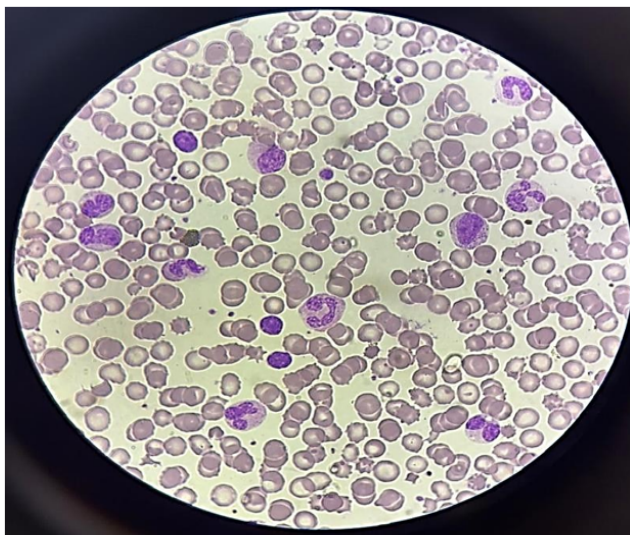


Figure 1: Peripheral blood smear showing Leucocytosis with left shift in neutrophils (promyelocyte, myelocyte, metamyelocytes and band form) in leishman stain 100x oil immersion

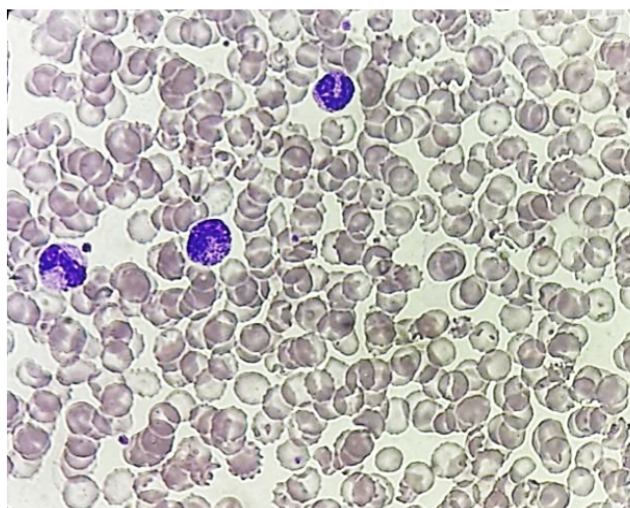


Figure 2: Peripheral smear showing band form with toxic granulation in neutrophil (Leishman stain 100x oil immersion)

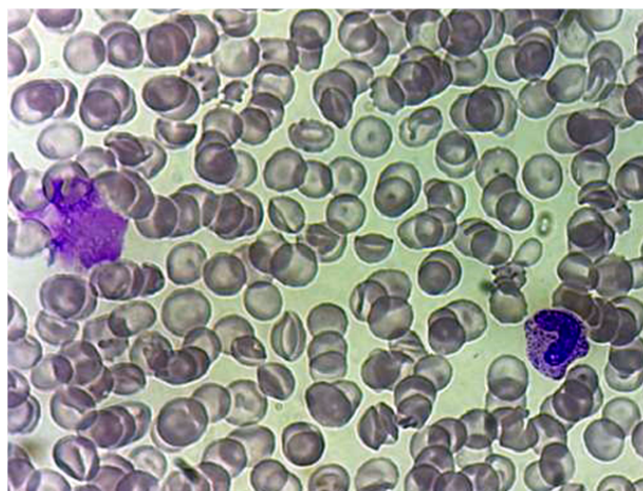


Figure 3: Peripheral blood smear showing band form with Thrombocytopenia (Leishman stain 100x oil immersion)

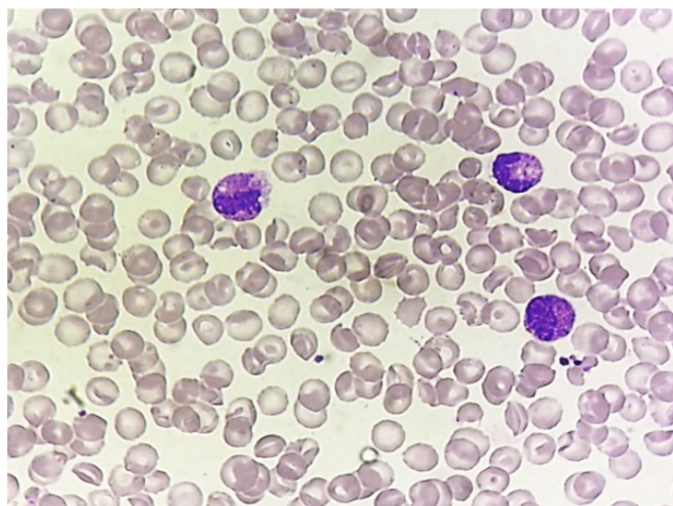


Figure 4: Peripheral smear showing cytoplasmic vacuolation and toxic granulation in neutrophil (Leishman stain 100x oil immersion)

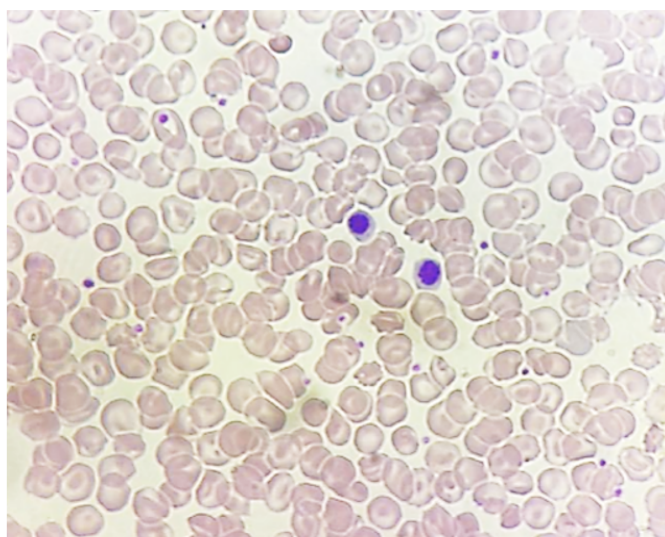


Figure 5: Peripheral smear showing nucleated RBCs (Leishman stain 100x oil immersion)



Figure 6: Colony growth of Gram positive (Staphylococcus aureus) on blood agar



Figure 7: Growth of lactose fermenting Gram negative bacteria (*E. coli*) on MacConkey agar

Discussion

Table 1: Distribution of Cases According to Culture Result and Hematological Scoring System

In the present study, out of 115 neonates clinically suspected of sepsis, 71 cases (61.73%) were culture positive, while 44 cases (38.27%) were culture negative. Majority of neonates belonged to the HSS score category of 3–4 (55.65%), indicating probable sepsis, whereas 20% neonates had scores ≥ 5 suggestive of definite sepsis. These findings support the utility of Hematological Scoring System (HSS) as an effective early screening tool for neonatal sepsis.

The findings of the present study are comparable with the study conducted by Baruwat S et al. [16] who observed culture positivity in 21 neonates and reported high diagnostic accuracy of modified HSS with sensitivity of 90.48% and specificity of 96.83%. Similarly, Sharma R et al. [17] reported that HSS score >3 and >4 had better specificity and negative predictive value for early neonatal sepsis diagnosis. Elsayed MS et al. [18] also demonstrated high sensitivity (96%) and specificity (90%) of HSS in neonatal sepsis diagnosis.

The higher proportion of neonates with moderate to high HSS scores in the present study indicates that hematological parameters can provide rapid and reliable evidence of infection before blood culture reports become available. Thus, HSS can be effectively utilized in resource-limited settings for early diagnosis and prompt initiation of treatment.

Table 2: Hematological Parameters in Comparison with Culture Results

In the present study, abnormal Total Leukocyte Count (≤ 5000 or ≥ 21000 cells/cumm) was

observed in 56.33% culture-positive neonates. However, the association was statistically insignificant ($p=0.509$). Similar findings were reported by Buch et al. [19] who found low sensitivity and specificity of TLC alone in diagnosing neonatal septicemia. Bhat RY et al. [20] also observed abnormal leukocyte counts in only 29.7% of septic neonates. This suggests that TLC alone has limited diagnostic value.

Abnormal PMN count was seen in 85.91% culture-positive cases, though the association was not statistically significant ($p=0.373$). Comparable observations were made by Kushwaha R et al. [21] who reported high sensitivity of total PMN count (74.70%) in neonatal sepsis. Gregory J et al. [22] also observed that neutrophil counts outside normal range were strongly associated with serious bacterial infection.

The Immature to Total neutrophil (I:T) ratio ≥ 0.12 was present in 74.64% of culture-positive neonates and showed statistically significant association with neonatal sepsis ($p=0.047$). Similar findings were observed by Mondal SK et al. [23] who reported elevated I:T ratio in 63.2% proven sepsis cases. Narasimha A et al. [24] also identified abnormal I:T ratio as the most sensitive hematological indicator of neonatal sepsis. Likewise, Sharma R et al. [17] observed I:T ratio as one of the most common abnormalities in septic neonates. Degenerative changes in neutrophils were observed in 61.97% culture-positive neonates, though statistical significance was not achieved ($p=0.097$). However, Baruwat S et al. [16] reported degenerative changes as the most sensitive parameter in modified HSS. These changes reflect increased inflammatory activity and may support diagnosis when interpreted with other parameters. Thrombocytopenia (<1.5 lakh/cumm) was observed

in 47.89% culture-positive neonates, but no significant association was found ($p=0.99$). Similar findings were noted by Kavehmanesh Z et al. [25] who demonstrated thrombocytopenia in septic neonates, especially in gram-negative infections. However, platelet count alone may not reliably differentiate septic from non-septic neonates.

Overall, among all hematological parameters evaluated, I:T ratio emerged as the most significant marker associated with culture-proven neonatal sepsis in the present study.

Table 3: NRBC Count and MPV in Comparison with Culture Results

In the present study, NRBC count $\geq 5\%$ was observed in 21.13% culture-positive neonates and 20.45% culture-negative neonates, with no statistically significant association ($p=0.92$). Although elevated NRBCs are considered markers of hypoxic stress and inflammatory marrow stimulation, their isolated diagnostic role appeared limited in this study. Similar observations were discussed by Baruwat S et al. [16] who incorporated NRBCs into modified HSS and reported high overall diagnostic accuracy.

Mean Platelet Volume (MPV) >9.5 fL was observed more frequently among culture-positive neonates (69.01%) compared to culture-negative neonates (45.45%), and this association was statistically significant ($p=0.011$). Elevated MPV reflects increased platelet activation and turnover during systemic inflammation and sepsis.

These findings are supported by studies cited in the review literature, where Indian neonatal studies [26-27] demonstrated significantly higher MPV values in culture-positive neonatal sepsis and emphasized its usefulness as an economical adjunctive marker in modified hematological scoring systems. Increased MPV may therefore improve the sensitivity of HSS when combined with conventional hematological parameters.

Thus, MPV proved to be a useful additional hematological marker for early diagnosis of neonatal sepsis in the present study, whereas NRBC count showed limited independent significance.

Table 4: Clinical Presentation in Comparison with Culture Results

In the present study, respiratory distress was the most common presenting complaint among both culture-positive (45.07%) and culture-negative neonates (45.45%). Birth asphyxia was more commonly associated with culture-positive cases (36.62%) compared to culture-negative neonates (25%). These findings indicate that respiratory symptoms and perinatal stress are important clinical indicators associated with neonatal sepsis.

The observations of the present study are comparable with Sharma R et al. [17] and Chaware SA et al. [28] who also reported predominance of early-onset neonatal sepsis with respiratory manifestations being among the commonest presenting features. Neonates with respiratory distress often require prompt sepsis evaluation because clinical manifestations in neonatal sepsis are usually nonspecific and overlap with pulmonary conditions.

Birth asphyxia contributes to neonatal immune compromise and increases susceptibility to infection. Asphyxiated neonates may also show altered neutrophilic responses, affecting hematological parameters such as I:T ratio and ANC. Therefore, careful interpretation of hematological findings is essential in such cases.

The present study highlights that clinical features alone are insufficient for diagnosis and should be interpreted along with hematological scoring and blood culture findings for accurate early diagnosis of neonatal sepsis.

Table 5: Risk Factors and Mode of Delivery in Comparison with Culture Results

In the present study, term neonates constituted the majority of culture-positive cases (70.42%), whereas preterm neonates accounted for 29.58% cases. However, the association between maturity status and culture positivity was statistically insignificant ($p=0.317$). Similarly, mode of delivery also showed no significant association with culture positivity ($p=0.702$).

These findings differ slightly from many previous studies where prematurity and low birth weights were considered important risk factors for neonatal sepsis. Murthy et al. [15] identified prematurity as a significant contributor to neonatal sepsis risk in developing countries. However, the present study possibly reflects increased admission of term neonates with perinatal complications in the study setting. Regarding mode of delivery, normal vaginal delivery accounted for the majority of both culture-positive and culture-negative cases. Similar observations were reported by Chaware SA et al. [28] where delivery mode did not significantly alter sepsis incidence.

Thus, although prematurity and delivery-related factors are recognized risk factors for neonatal sepsis, no statistically significant association was observed in the present study. This suggests that neonatal sepsis is multifactorial and influenced by several maternal, neonatal, and environmental factors.

Conclusion

The present study demonstrates that the Hematological Scoring System (HSS) is a rapid,

simple, economical, and effective screening tool for early diagnosis of neonatal sepsis. Among the hematological parameters studied, Immature to Total neutrophil ratio (I:T ratio) and Mean Platelet Volume (MPV) showed statistically significant association with culture-proven neonatal sepsis and emerged as valuable early diagnostic markers.

Although parameters such as total leukocyte count, platelet count, degenerative changes in neutrophils, and NRBC count individually showed limited statistical significance, their combined assessment through HSS improved diagnostic utility. The study further emphasizes that hematological parameters interpreted alongside clinical findings can facilitate early identification and prompt management of neonatal sepsis, especially in resource-limited settings where advanced biomarkers may not be readily available.

Therefore, modified HSS incorporating newer parameters like MPV and NRBCs can serve as a reliable adjunct to blood culture for early neonatal sepsis diagnosis and may help reduce neonatal morbidity and mortality through timely intervention.

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