Original Article

Red Cell Distribution Width as a Diagnostic Marker in Neonatal Sepsis: A Prospective Cross-Sectional Study at a Tertiary Care Hospital in Northeast India

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Abstract

Background: Neonatal sepsis remains a major cause of neonatal morbidity and mortality, particularly in resource-constrained settings. The nonspecific clinical presentation and limitations of conventional diagnostic tests complicate early diagnosis. Red cell distribution width (RDW), routinely reported in a complete blood count, may serve as an adjunctive marker of systemic inflammation. This study evaluated the diagnostic utility of RDW in neonates investigated for suspected sepsis. The objective is to compare RDW values between sepsis-screen-positive and negative neonates, determine the proportion of screen-positive neonates with elevated RDW, assess associations between RDW and conventional sepsis-screening parameters, and compare RDW and sepsis-screen performance against microbiological culture results. The study also evaluated RDW diagnostic accuracy using receiver operating characteristic (ROC) analysis. **Material and Methods:** A prospective cross-sectional study was conducted in the Neonatal Intensive Care Unit of Silchar Medical College and Hospital, Assam, India, from October 2024 to September 2025. A total of 172 neonates with suspected sepsis or associated risk factors were enrolled using consecutive sampling. RDW and conventional sepsis-screening parameters, including total leukocyte count, absolute neutrophil count, immature-to-total neutrophil ratio, C-reactive protein (CRP), and micro-erythrocyte sedimentation rate, were assessed. Blood culture was used as the primary microbiological reference standard. Urine culture and cerebrospinal fluid (CSF) analysis and culture were recorded as secondary findings when clinically indicated. RDW was compared between sepsis-screen groups and evaluated against blood culture results. ROC and regression analyses were performed to assess diagnostic performance and factors associated with sepsis. **Results:** Of the 172 neonates, 90 (52.3%) were classified in the sepsis group and 82 (47.7%) in the non-sepsis group. Mean RDW was higher among neonates with sepsis than among those without sepsis (17.8 ± 2.0% versus 15.2 ± 1.2%). At an RDW cutoff of 17.5%, the reported sensitivity was 80%, specificity 82%, positive predictive value 81%, negative predictive value 81%, and overall accuracy 81%. The reported area under the ROC curve was 0.85. RDW correlated positively with CRP ($r = 0.42$, $p = 0.003$). **Conclusion:** RDW demonstrated promising diagnostic discrimination in this hospital-based cohort and may complement conventional assessment of neonatal sepsis. Further multicentric studies using clearly defined reference standards are needed to validate its diagnostic performance and independent clinical value.

Keywords: Neonatal sepsis, red cell distribution width, sepsis screen, C-reactive protein, blood culture, newborn.

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Introduction

Neonatal sepsis is a potentially life-threatening systemic infection occurring during the neonatal period and remains an important cause of preventable neonatal morbidity and mortality. Early recognition is essential because clinical deterioration can be rapid, particularly among vulnerable newborns. However, the diagnosis is challenging because manifestations such as respiratory distress, temperature instability, lethargy, feeding intolerance, and poor perfusion are nonspecific and may also occur in non infectious neonatal conditions. The resulting diagnostic uncertainty can delay appropriate treatment or contribute to unnecessary antimicrobial exposure.

Blood culture remains a central method for microbiological confirmation of neonatal bloodstream infection. Nevertheless, its sensitivity may be affected by blood volume, prior antimicrobial administration, and low-level or intermittent bacteraemia. Furthermore, culture results are not immediately available, necessitating initial decisions based on clinical assessment and supportive investigations. Conventional laboratory parameters, including total leukocyte count, absolute neutrophil count, immature-to-total neutrophil ratio, and C-reactive protein (CRP), are commonly incorporated into neonatal sepsis screening. However, their diagnostic performance varies

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with the timing of sampling, gestational age, underlying illness, and the criteria used to define sepsis.[1,2]

The search for accessible and reliable adjunctive biomarkers is therefore clinically important, particularly in settings where advanced diagnostic facilities are limited. Red cell distribution width (RDW) quantifies variation in circulating erythrocyte size and is routinely reported as part of a complete blood count. Although traditionally used in the assessment of haematological disorders, RDW has attracted interest as a potential marker of systemic inflammation and physiological stress.

Several mechanisms may contribute to increased RDW during infection, including altered erythropoiesis, changes in erythrocyte maturation, oxidative stress, and inflammatory effects on red-cell survival and production. These mechanisms are biologically plausible but are not specific to sepsis. Anaemia, nutritional deficiencies, gestational age, and other neonatal illnesses may also influence RDW. Consequently, its interpretation requires consideration of the clinical context rather than reliance on an isolated measurement.

Previous investigations have examined RDW in neonatal sepsis, including its diagnostic and prognostic applications. Saleh et al. evaluated RDW in relation to neonatal sepsis and its severity, while Salim et al. investigated the relationship between RDW and neonatal sepsis.[3,4] Golhar et al. specifically examined its diagnostic and prognostic utility in early-onset sepsis among term neonates.[5] Hodeib et al. also investigated elevated RDW in early-onset neonatal sepsis.[6] Collectively, these studies support further evaluation of RDW but do not establish a universally applicable diagnostic threshold. Differences in patient populations, sepsis definitions, laboratory methods, and study designs may account for variation in reported performance.

Biomarkers should therefore be evaluated against clearly specified diagnostic criteria and interpreted alongside clinical findings and microbiological evidence. Sharma et al. emphasized the challenges associated with biomarker-based diagnosis of neonatal sepsis and the potential value of combining clinical and laboratory information.[1] Jain et al. and Gupta et al. similarly examined the diagnostic utility of conventional inflammatory and hematological parameters in neonatal sepsis.[7,8]

In this context, the present study evaluated RDW among neonates admitted with suspected sepsis to a tertiary care hospital in Assam, India.

Aim and Objectives:

1. To evaluate the diagnostic utility of RDW in neonates investigated for suspected sepsis by comparing values between sepsis screen-positive and screen-negative groups.
2. To determine the optimal RDW cutoff and assess its diagnostic performance against microbiological culture results using ROC curve analysis, and examine its association with CRP levels.

Materials and Methods

Study Design: This was a prospective cross-sectional study.

Study Setting and Duration: The study was conducted in the Level II Neonatal Intensive Care Unit (NICU) of Silchar Medical College and Hospital, Assam, India, from October 2024 to September 2025.

Sampling Technique: Consecutive sampling was employed, and eligible neonates were recruited until the study sample was achieved.

Sample Size: The sample size was calculated using an anticipated neonatal sepsis prevalence of 30%, a 95% confidence level and an absolute precision of 7%, yielding a minimum required sample size of 165 neonates. A total of 172 neonates were ultimately enrolled in the study.

Inclusion Criteria

- Term live-born neonates (37–42 weeks) admitted to the Level II NICU with suspected sepsis or associated risk factors.
- Clinical features suggestive of sepsis.
- Birth weight ≥2.5 kg.
- Written informed consent from a parent or legal guardian.

Exclusion Criteria

- Severe birth asphyxia or meconium aspiration syndrome.
- Congenital malformations, metabolic disorders, or chromosomal abnormalities.
- Significant cardiovascular or respiratory disease unrelated to sepsis.
- Previous blood transfusion.
- Discharge before completion of assessment or loss to follow-up.

Definitions of Neonatal Sepsis Onset: Neonatal sepsis was classified into early-onset sepsis (EOS) and late-onset sepsis (LOS) according to the age at which symptoms first appeared.

Early-onset sepsis (EOS): Sepsis presenting within the first 72 hours of life.

Late-onset sepsis (LOS): Sepsis presenting after the first 72 hours of life.

Clinical Assessment and Data Collection: Relevant maternal, perinatal, and neonatal data were collected using a structured proforma. Information regarding clinical manifestations, gestational age, birth weight, age at symptom onset, laboratory findings, and pertinent maternal and perinatal history was recorded.

The following maternal and perinatal risk factors associated with neonatal sepsis were assessed: (1) low birth weight or prematurity; (2) maternal fever above 38°C or suspected intra-amniotic infection; (3) foul-smelling or meconium-stained amniotic fluid; (4) rupture of membranes lasting more than 18 hours; (5) an unclean vaginal examination or more than three sterile vaginal examinations during labour; (6) prolonged labour exceeding 24 hours; and (7) perinatal asphyxia, defined as an Apgar score below 4 at one minute.

Clinical Features of Neonatal Sepsis: Neonatal sepsis may present with non-specific clinical manifestations, making early diagnosis challenging. The clinical features assessed included:

- Temperature instability: Fever or hypothermia.
- Lethargy: Reduced activity, weak crying, or poor sucking.
- Poor perfusion: Prolonged capillary refill time (CRT), potentially progressing to septic shock.
- Hypotonia: Reduced muscle tone and diminished or absent neonatal reflexes.

- Heart rate abnormalities: Tachycardia or bradycardia.
- Respiratory manifestations: Apnoea, grunting, or gasping respiration.
- Blood glucose abnormalities: Hypoglycaemia or hyperglycaemia.
- Metabolic acidosis: An acid–base disturbance that may occur in severely ill neonates.

Laboratory Investigations: Laboratory evaluation included a sepsis screen, complete blood count and blood culture. RDW was recorded as a percentage from the CBC. CSF analysis, urine cultures, and chest radiography were performed when clinically indicated.

The sepsis screen comprised the following parameters:

- Total leukocyte count (TLC).
- Absolute neutrophil count (ANC).
- Immature-to-total neutrophil ratio (I/T ratio).
- C-reactive protein (CRP).
- Micro-erythrocyte sedimentation rate (micro-ESR).

A screen was considered positive when two or more parameters were abnormal according to the predefined criteria. Blood culture results were classified as positive or negative and used as the reference standard to assess the diagnostic performance of RDW and the sepsis screen.

Study Groups : Neonates were classified into two groups based on clinical assessment and laboratory findings:

- Sepsis Group: Neonates diagnosed with sepsis based on clinical and laboratory evaluation.
- Non-Sepsis Group: Neonates initially suspected of having sepsis but in whom the diagnosis was subsequently excluded.

RDW values were compared between the two groups to evaluate its diagnostic utility. The diagnostic performance of RDW and the sepsis screen was assessed against blood culture as the reference standard. Neonates diagnosed with sepsis were further classified into early-onset sepsis (EOS) and late-onset sepsis (LOS) according to the age at symptom onset, and RDW values were compared between these groups.

Statistical Analysis: Data were analysed using appropriate statistical methods. Continuous variables were summarized as means and standard deviations or medians and interquartile ranges, as appropriate. Categorical variables were expressed as frequencies and percentages. Continuous variables were compared using the Student's t-test or an appropriate non-parametric test, while categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate.

Receiver operating characteristic (ROC) curve analysis was used to evaluate the diagnostic performance of RDW and determine its discriminatory ability. Sensitivity, specificity, positive predictive value, negative predictive value, and overall diagnostic accuracy were assessed where applicable. Correlation analysis was used to examine the relationship between RDW and CRP. Logistic regression was used to assess associations between selected clinical or laboratory variables and neonatal sepsis. A p-value of less than 0.05 was considered statistically significant.

Ethical Considerations: Ethical approval for the study was obtained from the Institutional Ethics Committee, Silchar Medical College and Hospital, Silchar, Assam, India (Approval No. SMC/ETHICS/M2/2023/55 Dated 13/10/2023). Written informed consent was obtained from the parent or legal guardian of each participating neonate before enrolment.

Results

Demographic Characteristics: A total of 172 neonates were enrolled, comprising 90 males (52.3%) and 82 females (47.7%).

Table 1: Gender distribution

Characteristic	n	%
Male	90	52.3
Female	82	47.7
Total	172	100.0

Maternal Risk Factors: Prolonged rupture of membranes was reported in 50 cases (29.1%), followed by multiple vaginal examinations (>3) in 40 (23.3%), maternal fever/chorioamnionitis in 30 (17.4%), foul-smelling liquor in 20 (11.6%), and prolonged labour in 15 (8.7%). No risk factors were recorded in 17 cases (9.9%).

Table 2: Distribution of Neonates According to Maternal and Perinatal Risk Factors

Risk factor	n	%
Prolonged rupture of membranes	50	29.1
Multiple vaginal examinations (>3)	40	23.3
Maternal fever/chorioamnionitis	30	17.4
Foul-smelling liquor	20	11.6
Prolonged labour	15	8.7
No recorded risk factor	17	9.9

Clinical Presentations: Respiratory distress was the most common recorded feature (100/172, 58.1%), followed by lethargy/weak cry (80, 46.5%), poor feeding (70, 40.7%), and temperature instability (60, 34.9%). Hypotension occurred in 20 neonates (11.6%), while other features, including jitteriness, were recorded in 25 (14.5%). Features were not mutually exclusive.

Table 3: Distribution of Neonates According to Clinical Presentation

Feature	n	%
Respiratory distress	100	58.1
Lethargy/weak cry	80	46.5
Poor feeding	70	40.7
Temperature instability	60	34.9
Hypotension	20	11.6
Other features (e.g., jitteriness)	25	14.5

Sepsis-Screen Parameters: Elevated CRP was the most frequent abnormal parameter (95, 55.2%). An I/T ratio >0.2 was recorded in 73 neonates (42.4%), abnormal TLC in 66 (38.3%), and abnormal ANC in 63 (36.6%).

Table 4: Distribution of Individual Sepsis-Screen Parameters Among the Study Neonates

Parameter	n	%
Abnormal TLC	66	38.3
Abnormal ANC	63	36.6
I/T ratio >0.2	73	42.4
Elevated CRP	95	55.2
Elevated Micro-ESR	40	23.2

Sepsis-Screen Outcomes: A positive sepsis screen was recorded in 90 neonates (52.3%), while 82 (47.7%) had a negative screen.

Table 5: Distribution of Neonates According to Sepsis-Screen Results

Screen result	n	%
Positive	90	52.3
Negative	82	47.7
Total	172	100.0

RDW in Sepsis and Non-Sepsis Groups: Mean RDW was higher in the sepsis group (17.8 ± 2.0%) than in the non-sepsis group (15.2 ± 1.2%), a reported difference is 2.6%.

Table 6: Comparison of RDW Values Between Sepsis and Non-Sepsis Groups

Group	n	Mean RDW (%) ± SD
Non-sepsis	82	15.2 ± 1.2
Sepsis	90	17.8 ± 2.0

RDW in Early- and Late-Onset Sepsis: Among neonates with sepsis, 40 were classified as EOS and 50 as LOS. Mean RDW was 17.5 ± 1.8% in EOS and 18.1 ± 2.1% in LOS; the reported difference was statistically significant (p=0.045).

Table 7. RDW in EOS and LOS

Parameter	EOS (n=40)	LOS (n=50)	p-value
Mean RDW (%) ± SD	17.5 ± 1.8	18.1 ± 2.1	0.045

Blood Culture Findings: Blood cultures were positive in 72 neonates and negative in 100. Among positive cultures, coagulase-negative staphylococci accounted for 35 (48.6%), Staphylococcus aureus for 15 (20.8%), Gram-negative bacilli including E. coli and Klebsiella for 12 (16.7%), and other organisms for 10 (13.9%).

Table 8. Organisms in positive blood cultures

Organism	n	% of positive cultures
Coagulase-negative staphylococci	35	48.6
Staphylococcus aureus	15	20.8
Gram-negative bacilli (E. coli, Klebsiella)	12	16.7
Other organisms	10	13.9
Total positive cultures	72	100.0

Correlation Between RDW and CRP: RDW showed a positive correlation with CRP among septic neonates.

Table 9. Association Between RDW and CRP Levels Among the Study Neonates

Comparison	r	p-value
RDW and CRP	0.42	0.003

RDW Cut-off Analysis: At the reported thresholds, sensitivity ranged from 68% to 80% and specificity from 75% to 82%. The highest reported sensitivity and specificity were at 17.5% (80% and 82%, respectively); PPV and NPV were both reported as 81%. Verify these estimates against the original ROC output and diagnostic cross-tabulations before submission.

Table 10. Diagnostic Performance of RDW at Different Cut-off Values for Identifying Neonatal Sepsis

Cut-off (%)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
16.0	68	75	70	73
16.5	72	78	74	76
17.0	78	80	79	79
17.5	80	82	81	81

Sepsis Screen Versus Blood Culture: Among 90 screen-positive neonates, 60 had positive blood cultures and 30 had negative cultures. Among 82 screen-negative neonates, 12 were culture-positive and 70 culture-negative. From this cross-tabulation, sepsis screen sensitivity was 83.3% and specificity was 70.0%, with a positive predictive value of 66.7%, negative predictive value of 85.4%, using blood culture as the reference.

Table 11. Association Between Sepsis-Screen Results and Blood Culture Findings Among the Study Neonates

Screen result	Culture Positive	Culture Negative	Total
Positive	60	30	90
Negative	12	70	82
Total	72	100	172

Multivariable Logistic Regression: In the reported model, RDW >17% was associated with higher odds of sepsis (OR 3.5, 95% CI 1.8–6.8; p=0.0002). CRP >1 mg/dL was also associated with sepsis (OR 2.8, 95% CI 1.5–5.4; p=0.001).

Table 12. Multivariable Logistic Regression Analysis of Factors Associated with Neonatal Sepsis

Predictor	OR	95% CI	p-value
RDW >17%	3.5	1.8–6.8	0.0002
CRP >1 mg/dL	2.8	1.5–5.4	0.001

Overall Diagnostic Performance of RDW: The reported diagnostic performance of RDW included sensitivity of 80%, specificity of 82%, overall accuracy of 81%, and an AUC of 0.85.

Table 13. Diagnostic Performance of RDW at Different Cut-off Values for Identifying Neonatal Sepsis

Measure	Reported value
Sensitivity	80%
Specificity	82%
Overall accuracy	81%
AUC	0.85

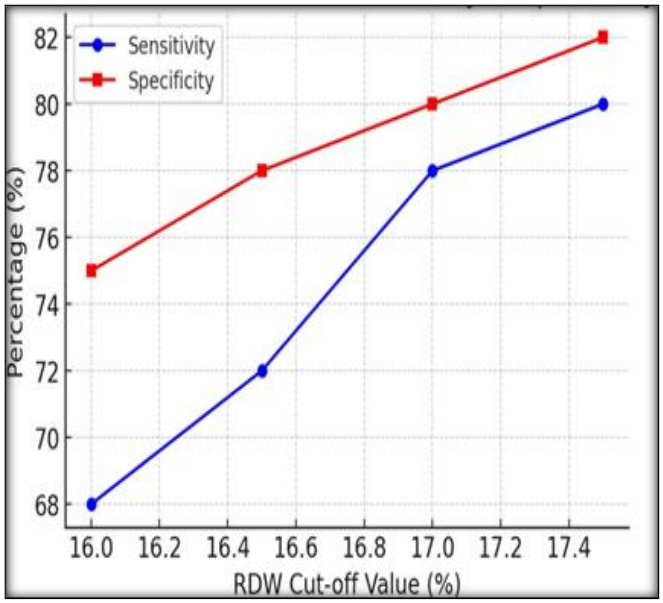


Figure 1: Sensitivity and Specificity of RDW at Different Cut-off Values for the Diagnosis of Neonatal Sepsis.

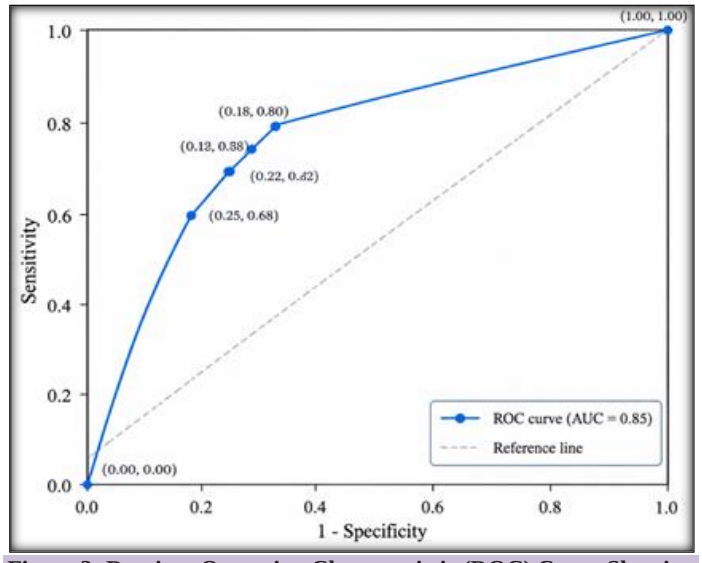


Figure 2: Receiver Operating Characteristic (ROC) Curve Showing the Diagnostic Performance of RDW in Predicting Neonatal Sepsis (AUC = 0.85).

Association Between Sepsis-Screen Results and Blood Culture Findings Among the Study Neonates

Discussion

The present study evaluated red cell distribution width (RDW) as

an adjunctive marker for neonatal sepsis in 172 neonates. The principal findings were higher mean RDW values among septic neonates, a positive correlation between RDW and C-reactive protein (CRP).

Demographic and Clinical Characteristics: A slight male predominance was observed, with 90 (52.3%) males and 82 (47.7%) females. This finding is consistent with reports by Sharma et al,.[1] Respiratory distress (58.1%) and lethargy (46.5%) were the most common clinical manifestations, consistent with findings reported by Sankar et al,.[15] These findings highlight the nonspecific clinical presentation of neonatal sepsis and the importance of early recognition.

Prolonged rupture of membranes was the most frequent maternal risk factor (29.1%), followed by repeated vaginal examinations (23.3%) and maternal fever or chorioamnionitis (17.4%). Similar associations were reported by Sharma et al,.[1] Roy et al,.[9]

Sepsis Screening and Blood Culture Findings: Elevated CRP was the most frequent screening abnormality (55.2%), followed by an increased immature-to-total neutrophil ratio (42.4%), abnormal total leukocyte count (38.3%), and abnormal absolute neutrophil count (36.6%). These findings support the role of CRP and haematological indices in neonatal sepsis screening, as reported by Jain et al,.[7] Gupta et al,.[8] and Sharma et al.[1] However more than one parameter has to be positive to label as sepsis screen positive. Blood cultures were positive in 66% of neonates with positive sepsis screens, compared with 15% of those with negative screens. Staphylococcus aureus (48.6%) and coagulase-negative staphylococci (20.8%) were the predominant isolates, followed by Gram-negative bacilli (16.7%). These findings emphasize the importance of blood culture confirmation and local microbiological surveillance to guide antimicrobial therapy.

Correlation Between RDW and CRP: An observational research comparing RDW levels in newborns with septic shock and those in healthy neonates was carried out by Lazarus Monica et al. (2020),.[13] They discovered that RDW levels were much greater in infants diagnosed with sepsis. Elevated C-reactive protein levels were associated with increased RDW values. Their results provide credence to the theory that RDW might serve as a useful early indicator of sepsis in infants.

Diagnostic Performance of RDW: The mean RDW was 17.8% in neonates with sepsis and 15.2% in those without sepsis. Similar differences were reported by Martin et al. [10], Deka and Aravind.[11] Bulut et al,.[12] Mofied et al,.[14] and Ratridewi et al,.[16]

An RDW cut-off of 17.5% demonstrated the best diagnostic performance in the present study, with a sensitivity of 80%, specificity of 82%, positive predictive value of 82%, and negative predictive value of 81%. Deka et al,.[11] reported a cut-off of approximately 17.25%, supporting the potential diagnostic utility of RDW. Nevertheless, differences in study populations and diagnostic criteria may influence optimal cut-off values. RDW should therefore be interpreted alongside clinical findings, CRP, and blood culture results rather than used as a standalone diagnostic test.

Overall, the present study suggests that RDW is a readily available and cost-effective adjunctive marker for neonatal sepsis, with potential applications in diagnosis and severity assessment. Further prospective studies involving larger populations are required to validate the optimal cut-off and establish its independent diagnostic and prognostic value.

Limitations of the Study: The study was limited by its single-centre design and relatively small sample size (172 neonates), which may restrict generalizability. RDW is a nonspecific parameter influenced by factors such as gestational age, birth weight, and anemia. Although RDW correlated with CRP and sepsis severity, its independent prognostic value remains uncertain. Therefore, RDW should be used as an adjunctive rather than standalone diagnostic marker. Larger multicentre prospective studies are needed to validate the optimal cut-off and clinical utility of RDW in neonatal sepsis.

Conclusion

In this prospective cross-sectional study of 172 neonates admitted to a tertiary care hospital in Assam, RDW was higher among neonates classified as having sepsis than among those without sepsis. An RDW cutoff of 17.5% was associated with reported sensitivity of 80%, specificity of 82%, and an area under the ROC curve of 0.85. RDW also showed a moderate positive correlation with CRP.

These findings suggest that RDW may have potential as an accessible adjunctive marker in the assessment of suspected neonatal sepsis. However, the results do not establish RDW as a standalone diagnostic test or demonstrate that its use improves clinical outcomes. External validation in larger multicentre cohorts are necessary before the proposed cutoff can be recommended for routine clinical use.

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Conflicts of interest

There are no conflicts of interest.

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