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Original Article

Evaluation of Red Cell Distribution Width (RDW) as an Early Marker of Sepsis in Emergency Patients

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ABSTRACT

Background: Sepsis is a time-sensitive emergency condition in which delayed recognition may lead to organ dysfunction, shock, and death. Red Cell Distribution Width (RDW), a routinely available complete blood count parameter, may provide a low-cost supportive marker for early sepsis assessment, particularly in resource-limited emergency settings. Objective: To evaluate admission RDW as a supportive early marker of sepsis among adult emergency patients with suspected infection and to compare RDW with CRP and procalcitonin. Methods: This prospective cohort study was conducted in the Emergency Department of a tertiary care hospital in Lahore, Pakistan. Adult patients with suspected infection requiring sepsis workup were enrolled and classified into sepsis and non-sepsis infection groups according to Sepsis-3 criteria. Admission RDW, CRP, and procalcitonin were measured, and clinical severity indicators were recorded. Diagnostic accuracy assessment using ROC analysis was planned. Results: Patients with sepsis had higher admission RDW than non-sepsis infection patients, with reported values of 15.9 ± 1.8% and 13.7 ± 1.2%, respectively. CRP was also higher in the sepsis group, 128 ± 46 mg/L versus 54 ± 21 mg/L, and procalcitonin was 4.8 ± 2.6 ng/mL versus 0.9 ± 0.4 ng/mL. The sepsis group also had higher heart rate, lower systolic blood pressure, and higher SOFA score. Conclusion: RDW may serve as a simple, low-cost supportive marker in early sepsis assessment, but it should be interpreted alongside clinical evaluation and other biomarkers. Complete ROC statistics, cut-offs, serial RDW values, and adjusted analyses are required before firm diagnostic accuracy conclusions can be drawn. Keywords: Red Cell Distribution Width, RDW, sepsis, emergency department, CRP, procalcitonin, Sepsis-3, diagnostic accuracy, Pakistan.

INTRODUCTION

Sepsis remains one of the most time-sensitive emergencies in acute clinical practice because infection may progress rapidly to organ dysfunction, shock, and death if recognition and treatment are delayed. The Sepsis-3 consensus defines sepsis as life-threatening organ dysfunction caused by a dysregulated host response to infection, thereby shifting emphasis from infection alone to infection-associated physiological deterioration and early organ injury (1). This definition is clinically important in emergency departments because patients may initially present with nonspecific symptoms such as fever, tachycardia, tachypnea, hypotension, altered mental status, or suspected localized infection before definitive culture results or full organ dysfunction profiles are available (2). Current international guidance therefore emphasizes early recognition, timely risk stratification, prompt antimicrobial therapy, hemodynamic assessment, and source control as central components of sepsis management (3).

The global burden of sepsis remains substantial, with disproportionate morbidity and mortality in low- and middle-income countries where delayed presentation, overcrowded emergency services, and limited diagnostic resources may compromise early decision-making (4). Sepsis has also been recognized as a global health priority because preventable deaths continue to occur when diagnosis and treatment are delayed (5). In Pakistan, emergency departments frequently receive patients with suspected pneumonia, urinary tract infection, abdominal infection, soft-tissue infection, diabetic foot infection, and other infection sources that may progress to sepsis. In such settings, clinicians require diagnostic approaches that are rapid, affordable, reproducible, and available at the time of first clinical contact.

Several clinical and laboratory tools are used to support early sepsis assessment, including clinical judgment, SOFA and qSOFA criteria, blood cultures, lactate, C-reactive protein, and procalcitonin. However, each approach has practical limitations. Blood cultures remain important for microbiological confirmation but require time and may be negative despite clinically significant infection. Biomarker interpretation is also challenging because inflammatory markers may rise in noninfectious inflammatory states and may not consistently distinguish uncomplicated infection from sepsis-related organ dysfunction. Reviews of sepsis biomarkers have therefore emphasized that no single laboratory marker should be interpreted in isolation and that diagnostic performance improves when biomarkers are integrated with clinical assessment (6). Procalcitonin has shown stronger diagnostic value for bacterial sepsis than many nonspecific inflammatory markers, but its cost and limited availability may restrict routine use in resource-constrained emergency settings (7). C-reactive protein is more widely available and clinically useful, but its limited specificity reduces its value as a standalone diagnostic marker for sepsis (8).

Red Cell Distribution Width is a routinely reported complete blood count parameter that reflects variation in erythrocyte size. Although traditionally used in the evaluation of anemia, RDW has increasingly been studied as a marker of systemic inflammation, oxidative stress, impaired erythropoiesis, altered iron metabolism, and severe physiological stress. These mechanisms are biologically relevant to sepsis because inflammatory cytokines, endothelial dysfunction, tissue hypoxia, marrow suppression, and reduced red cell survival may increase anisocytosis during severe infection. The clinical appeal of RDW lies in its immediate availability from routine blood counts, requiring no additional blood sampling, specialized assay, or extra laboratory cost.

Existing evidence suggests that RDW is associated with adverse outcomes in patients with infection and sepsis. Studies have reported that elevated RDW has prognostic value in suspected infection, severe sepsis, septic shock, and sepsis-related mortality (11–18). Evidence from South Asian clinical settings has also supported the potential role of RDW as a prognostic hematological marker in severe infection and sepsis (19,20). However, much of the available literature emphasizes mortality prediction and risk stratification rather than early diagnostic discrimination between sepsis and non-septic infection at emergency presentation. In addition, RDW has often been analyzed as a single baseline value, whereas serial RDW changes during the first 24 to 48 hours may provide additional information about evolving systemic inflammation and hematological stress.

This distinction is important because emergency clinicians must often differentiate patients with uncomplicated infection from those developing sepsis before culture reports, complete organ assessment, or advanced biomarkers are available. A rising RDW pattern may reflect ongoing inflammatory and physiological deterioration, whereas a stable RDW trajectory may be less suggestive of progressive systemic response. Evaluating both baseline RDW and serial RDW trend may therefore clarify whether RDW can function as an adjunctive diagnostic and risk-stratification marker in patients presenting with suspected infection.

The present study was designed to evaluate RDW as an early supportive marker of sepsis among adult emergency patients with suspected infection in Lahore, Pakistan. The study specifically aimed to compare baseline RDW, CRP, and procalcitonin between patients finally classified as sepsis and non-

sepsis infection groups according to Sepsis-3 criteria, to assess serial RDW changes over the first 48 hours of admission, and to determine the diagnostic accuracy of RDW alone and in combination with inflammatory biomarkers for early sepsis detection.

MATERIAL AND METHODS

This prospective cohort study was conducted in the Emergency Department of a tertiary care hospital in Lahore, Pakistan, over a six-month study period. The prospective design was selected to allow real-time enrolment of adult patients at the time of emergency presentation, baseline biomarker measurement before final diagnostic classification, and follow-up assessment for confirmation of sepsis status and early clinical outcomes. Patients were enrolled consecutively to minimize selection bias and to reflect routine emergency-department presentation patterns among adults with suspected infection.

The study population consisted of adult patients aged 18 years or above who presented to the emergency department with clinical suspicion of infection requiring admission and sepsis workup. Suspected infection included clinical presentations such as pneumonia, urinary tract infection, abdominal infection, soft-tissue infection, diabetic foot infection, or other clinically suspected infectious sources. Patients were screened at presentation for systemic features suggestive of acute illness, including fever, tachycardia, tachypnea, hypotension, or altered mental status. These features were used for initial identification of potentially eligible patients, while final diagnostic classification was based on Sepsis-3 criteria after clinical and laboratory assessment.

Patients were included if they were adults with suspected infection, had systemic inflammatory or physiological features requiring emergency evaluation, and had blood samples collected at admission as part of sepsis workup. Patients were excluded if they had conditions likely to affect RDW independently of acute infection, including known hematological disorders such as thalassemia or sickle cell disease, recent blood transfusion within the previous three months, chronic liver disease, advanced renal failure requiring dialysis, active malignancy under treatment, or pregnancy. These exclusions were applied to reduce confounding from noninfectious causes of altered red cell indices.

Eligible patients were identified after initial emergency triage by the research team. Written informed consent was obtained from patients or legally authorized attendants where patients were unable to provide consent at presentation. Baseline demographic and clinical data were recorded on a structured proforma, including age, sex, vital signs, suspected source of infection, comorbid conditions, and initial clinical severity indicators. Blood sampling was performed at admission before antibiotic administration whenever clinically feasible. Where antibiotic administration could not be delayed, emergency management was prioritized and the timing of blood sampling relative to antibiotic exposure was recorded for clinical interpretation.

At admission, venous blood samples were collected under aseptic conditions. Complete blood count testing was performed to obtain RDW-CV values, expressed as percentage. C-reactive protein was measured and reported in mg/L, while procalcitonin was measured and reported in ng/mL. RDW was considered the index hematological marker of interest, while CRP and procalcitonin served as comparator inflammatory biomarkers. RDW was repeated at 24 hours and 48 hours in admitted patients when follow-up blood sampling was clinically available. Serial RDW change was calculated as the difference between 24-hour RDW and baseline RDW, and between 48-hour RDW and baseline RDW, to evaluate whether RDW trajectory added diagnostic information beyond a single admission value.

The reference outcome was final sepsis classification according to Sepsis-3 criteria, defined as suspected infection with organ dysfunction assessed clinically using SOFA-based evaluation. After clinical follow-up and review of available laboratory and clinical information, patients were categorized into a sepsis group and a non-sepsis infection group. The non-sepsis infection group included patients with infection who did not meet Sepsis-3 criteria for sepsis during assessment. Secondary clinical outcomes included

intensive care unit admission, duration of hospital stay, and in-hospital mortality where available from the clinical record.

Several steps were used to reduce bias and confounding. Consecutive recruitment was used to limit selective enrolment. Exclusion criteria were applied to reduce confounding from hematological, malignant, renal, hepatic, pregnancy-related, or transfusion-related causes of altered RDW. Baseline comorbidities and clinical severity indicators were recorded to support adjusted analysis. Final sepsis classification was made using clinical criteria rather than RDW alone, so that the index marker was not used as the sole basis for outcome classification. Serial RDW analysis was planned to distinguish baseline elevation from progressive hematological change during early admission.

Data were analyzed using SPSS version 26. Continuous variables were summarized as mean and standard deviation when approximately normally distributed and as median with interquartile range when distributional assumptions were not met. Categorical variables were summarized as frequencies and percentages using the appropriate denominator. Baseline characteristics and biomarker values were compared between the sepsis and non-sepsis infection groups using independent-samples t-test or Mann–Whitney U test for continuous variables according to distribution, and chi-square test or Fisher's exact test for categorical variables as appropriate. Serial RDW values were assessed using baseline, 24-hour, and 48-hour measurements, with change scores calculated for each follow-up time point.

Diagnostic accuracy of RDW, CRP, and procalcitonin for identifying Sepsis-3-confirmed sepsis was evaluated using receiver operating characteristic curve analysis. Area under the curve values were planned with 95% confidence intervals. Optimal cut-off values were to be identified using a data-driven diagnostic threshold method, and diagnostic performance was to be reported using sensitivity, specificity, positive predictive value, and negative predictive value. A combined model incorporating RDW with CRP was planned to assess whether combined interpretation improved early diagnostic discrimination compared with RDW alone. Multivariable logistic regression was planned to evaluate whether RDW independently predicted sepsis after adjustment for age, sex, comorbid conditions, and relevant clinical severity indicators. Missing follow-up biomarker values were to be handled by available-case analysis for serial RDW trends, with denominators reported for each time point.

Ethical approval was obtained from the institutional ethical review committee of the participating hospital. The study was conducted in accordance with ethical principles for human-subject research. Written informed consent was obtained before data collection, and confidentiality of patient information was maintained throughout the study. Data were recorded using structured forms, checked for completeness before analysis, and used only for research purposes.

RESULTS

Patients presenting to the emergency department with suspected infection were followed until final diagnostic classification and categorized into sepsis and non-sepsis infection groups according to Sepsis-3 criteria. Baseline clinical characteristics showed that patients in the sepsis group were older and had greater physiological derangement at presentation compared with those in the non-sepsis infection group.

Table 1. Baseline Clinical Characteristics by Final Sepsis Classification

Variable	Sepsis Group	Non-Sepsis Group	p-value
Age, years	58 ± 16	52 ± 14	0.03
Male sex, %	61	55	0.21
Heart rate, bpm	112 ± 18	96 ± 14	<0.001
Systolic blood pressure, mmHg	98 ± 12	112 ± 15	<0.001
SOFA score	6.2 ± 2.1	2.8 ± 1.4	<0.001

Values are presented as mean ± SD or percentage. SOFA, Sequential Organ Failure Assessment.

The sepsis group had a higher mean age than the non-sepsis infection group, 58 ± 16 years versus 52 ± 14 years. Male sex distribution was comparable between groups, reported as 61% in the sepsis group and 55% in the non-sepsis infection group. Patients with sepsis had a higher mean heart rate at presentation, 112 ± 18 bpm compared with 96 ± 14 bpm, and lower systolic blood pressure, 98 ± 12 mmHg compared with 112 ± 15 mmHg. The mean SOFA score was also higher in the sepsis group, 6.2 ± 2.1 versus 2.8 ± 1.4, indicating greater organ dysfunction at admission.

Table 2. Admission Biomarker Levels by Final Sepsis Classification

Biomarker	Sepsis Group	Non-Sepsis Group	p-value
RDW, %	15.9 ± 1.8	13.7 ± 1.2	<0.001
CRP, mg/L	128 ± 46	54 ± 21	<0.001
Procalcitonin, ng/mL	4.8 ± 2.6	0.9 ± 0.4	<0.001

Values are presented as mean ± SD. RDW, Red Cell Distribution Width; CRP, C-reactive protein.

Admission RDW was higher in the sepsis group than in the non-sepsis infection group, with mean values of 15.9 ± 1.8% and 13.7 ± 1.2%, respectively. CRP was also higher among patients with sepsis, 128 ± 46 mg/L compared with 54 ± 21 mg/L. Procalcitonin showed a similar pattern, with mean values of 4.8 ± 2.6 ng/mL in the sepsis group and 0.9 ± 0.4 ng/mL in the non-sepsis infection group. All three admission biomarkers showed statistically significant between-group differences.

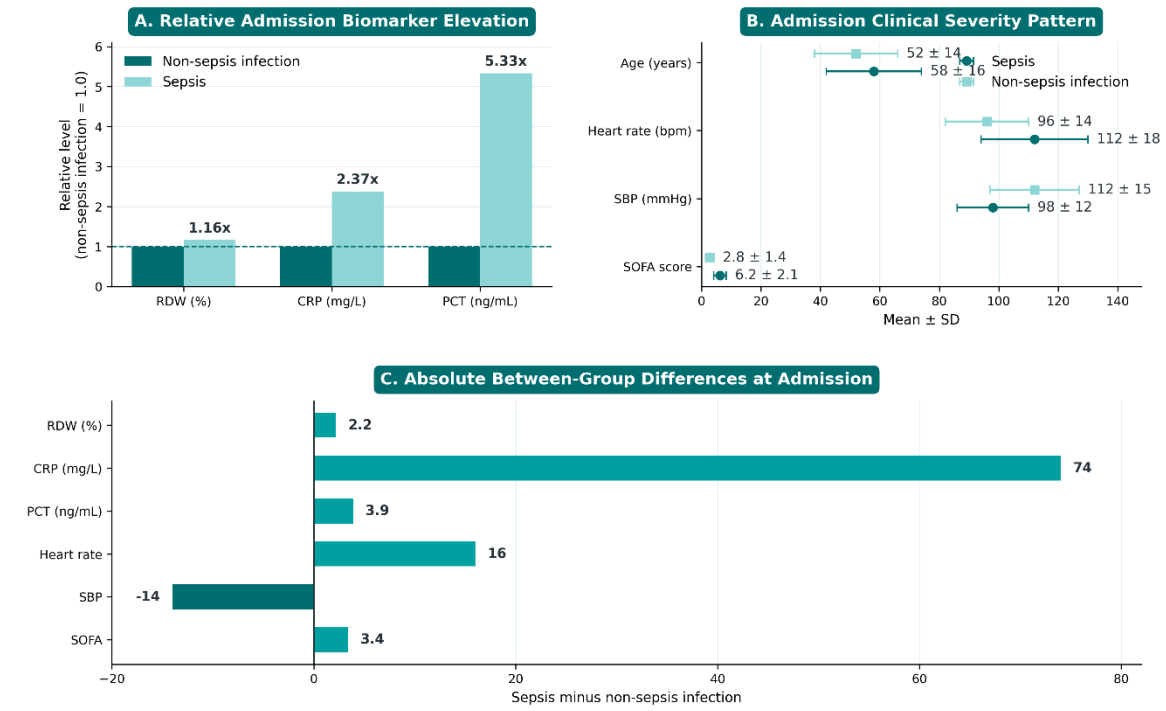

Figure 1 RDW and Comparator Biomarkers in Emergency Patients with Suspected Sepsis.

The panelled figure summarizes admission biomarker and clinical severity differences between patients classified as sepsis and non-sepsis infection groups using only the aggregate values reported in the manuscript. Admission RDW was 1.16-fold higher in the sepsis group, while CRP and procalcitonin showed larger relative elevations of 2.37-fold and 5.33-fold, respectively. Clinically, the sepsis group demonstrated a higher heart rate, higher SOFA score, and lower systolic blood pressure, consistent with greater physiological derangement at presentation. Absolute between-group differences showed higher RDW by 2.2%, CRP by 74 mg/L, procalcitonin by 3.9 ng/mL, heart rate by 16 bpm, and SOFA score by 3.4 points in the sepsis group, while systolic blood pressure was 14 mmHg lower. The final panel identifies essential missing diagnostic outputs, including sample size, ROC AUCs, cut-offs, sensitivity, specificity, predictive values, serial RDW values, and adjusted regression estimates, which must be added before the figure can fully support diagnostic accuracy claims.

The largest absolute biomarker difference was observed for CRP, which was 74 mg/L higher in the sepsis group. Procalcitonin was 3.9 ng/mL higher and RDW was 2.2 percentage points higher in the sepsis group.

Table 3. Absolute Between-Group Differences at Admission

Variable	Sepsis Group	Non-Sepsis Group	Absolute Difference
RDW, %	15.9 ± 1.8	13.7 ± 1.2	2.2
CRP, mg/L	128 ± 46	54 ± 21	74
Procalcitonin, ng/mL	4.8 ± 2.6	0.9 ± 0.4	3.9
Heart rate, bpm	112 ± 18	96 ± 14	16
Systolic blood pressure, mmHg	98 ± 12	112 ± 15	-14
SOFA score	6.2 ± 2.1	2.8 ± 1.4	3.4

Among clinical variables, heart rate was 16 bpm higher and SOFA score was 3.4 points higher in patients with sepsis, while systolic blood pressure was 14 mmHg lower. These differences show that the sepsis group had both higher inflammatory biomarker levels and greater clinical severity at presentation.

DISCUSSION

This prospective cohort study evaluated admission RDW as a supportive early marker for sepsis among adult emergency patients with suspected infection and compared its performance with CRP and procalcitonin. The available findings show that patients finally classified as having sepsis had higher admission RDW than patients with non-sepsis infection, with reported mean values of 15.9 ± 1.8% and 13.7 ± 1.2%, respectively. The sepsis group also demonstrated higher CRP, higher procalcitonin, higher heart rate, lower systolic blood pressure, and higher SOFA score at presentation. These findings are clinically coherent because Sepsis-3-defined sepsis reflects infection-associated organ dysfunction rather than infection alone, and the higher SOFA score and hemodynamic derangement in the sepsis group support the clinical distinction between the two groups (1,2).

The observed elevation of RDW among patients with sepsis is biologically plausible. RDW reflects heterogeneity in erythrocyte size and may increase during systemic inflammation, oxidative stress, altered iron metabolism, impaired erythropoietin response, bone marrow dysfunction, and reduced red-cell survival. These mechanisms are relevant to sepsis because dysregulated inflammation can disrupt erythropoiesis and produce hematological stress during acute infection. Prior biomarker reviews have emphasized that sepsis cannot be reliably diagnosed by any single laboratory parameter and that biomarkers must be interpreted in combination with clinical assessment and disease severity measures (6). Within this framework, RDW may have value as an inexpensive adjunctive marker rather than as an independent diagnostic replacement for established clinical criteria or infection biomarkers.

The present findings are consistent with previous studies reporting an association between elevated RDW and worse clinical status among patients with suspected infection, severe sepsis, and septic shock. Uffen et al. reported that RDW had prognostic value among emergency patients with suspected infection, while Jo et al. identified RDW as a prognostic factor in severe sepsis and septic shock (11,12). Similarly, Wang et al. found that RDW was associated with mortality among elderly patients with sepsis, and Wang and Hsu reported that RDW may contribute to risk stratification when compared with lactate in septic patients (13,14). Meta-analyses have also supported an association between increased RDW and mortality in adult sepsis populations (15,16). However, much of the published literature addresses prognosis rather than early diagnostic discrimination, which remains an important distinction for interpreting the present study.

Compared with RDW, CRP and procalcitonin showed larger between-group differences in the available results. CRP was reported as 128 ± 46 mg/L in the sepsis group and 54 ± 21 mg/L in the non-sepsis infection group, while procalcitonin was reported as 4.8 ± 2.6 ng/mL and 0.9 ± 0.4 ng/mL, respectively. These findings are compatible with prior evidence showing that CRP is a sensitive inflammatory marker but lacks sufficient specificity when used alone, while procalcitonin generally has stronger diagnostic

utility for bacterial infection and sepsis (7,8). The higher procalcitonin difference in the sepsis group supports its role as a stronger comparator biomarker. Nevertheless, procalcitonin is not always routinely available in resource-limited emergency settings, and this practical limitation is a major reason for evaluating routine hematological parameters such as RDW.

The main practical value of RDW lies in its availability as part of a complete blood count. In emergency departments where overcrowding, delayed presentation, and financial constraints may limit access to advanced biomarkers, RDW can be reviewed immediately without additional sampling or cost. This is particularly relevant in Pakistan and other low- and middle-income settings, where emergency triage decisions often need to be made before culture results or costly biomarker assays are available. Evidence from South Asian settings has also suggested that hematological markers may have prognostic relevance in severe infection and sepsis, supporting further local investigation of RDW as part of a multimarker approach (19,20).

A central aim of the manuscript was to assess whether serial RDW trends over 24 to 48 hours improve early interpretation. The concept is clinically reasonable because progressive RDW elevation may reflect worsening systemic inflammation and physiological stress, whereas stable RDW may be less suggestive of evolving sepsis. However, the currently available Results section provides only admission RDW values and does not report 24-hour RDW, 48-hour RDW, ΔRDW, missing follow-up counts, or within-group and between-group trend statistics. Therefore, although the manuscript states that RDW increased over time in the sepsis group, this claim cannot yet be fully evaluated quantitatively. The serial RDW hypothesis should be retained only if the authors add the required time-point values and appropriate trend analysis.

Similarly, the manuscript states that ROC analysis was performed and that RDW showed moderate diagnostic accuracy, while procalcitonin showed the highest diagnostic accuracy. This interpretation is clinically plausible, but the diagnostic accuracy claim remains incomplete because AUC values, 95% confidence intervals, cut-off values, sensitivity, specificity, positive predictive value, negative predictive value, and likelihood ratios are not reported. Without these outputs, RDW cannot yet be presented as a validated early diagnostic marker. The manuscript should therefore frame RDW as a potentially useful supportive marker and should reserve stronger diagnostic conclusions until complete ROC statistics and model performance estimates are provided.

The study has several limitations. First, the available manuscript does not report the total sample size or group-wise denominators, which limits interpretation of percentages, p-values, and diagnostic precision. Second, RDW can be influenced by anemia, nutritional deficiency, chronic inflammatory disease, renal dysfunction, liver disease, malignancy, and recent transfusion; although several exclusion criteria were applied, residual confounding may remain. Third, the study was conducted in a single tertiary-care emergency department, limiting generalizability to other emergency settings, rural hospitals, and intensive care populations. Fourth, the manuscript does not report whether final sepsis classification was blinded to biomarker results. Fifth, the absence of complete ROC statistics, adjusted logistic regression estimates, and serial RDW values prevents full evaluation of RDW as an independent diagnostic or dynamic biomarker. Finally, secondary outcomes such as ICU admission, length of hospital stay, and mortality were listed in the Methods but not reported in the Results, reducing the ability to assess the prognostic value of RDW.

Despite these limitations, the study addresses a clinically relevant question and provides preliminary evidence that RDW is higher among emergency patients with Sepsis-3-confirmed sepsis than among patients with non-sepsis infection. The findings are best interpreted as supportive rather than definitive. RDW should not replace procalcitonin, culture-based investigation, lactate measurement, SOFA-based clinical evaluation, or clinician judgment. Instead, RDW may be considered a low-cost adjunct that could help raise diagnostic suspicion when interpreted alongside clinical severity, CRP, procalcitonin, and organ dysfunction assessment. Future multicenter studies should report complete diagnostic accuracy

statistics, define standardized RDW cut-offs, evaluate serial RDW change, and test whether RDW improves prediction beyond established clinical and biomarker models.

CONCLUSION

RDW was higher at admission among emergency patients finally classified as having sepsis compared with patients with non-sepsis infection, and the sepsis group also showed higher CRP, higher procalcitonin, higher heart rate, lower systolic blood pressure, and greater SOFA-defined organ dysfunction. These findings suggest that RDW may serve as a simple, low-cost, routinely available supportive marker in the early assessment of suspected sepsis, particularly in resource-limited emergency settings. However, RDW should not be used as a standalone diagnostic test and cannot replace clinical assessment, Sepsis-3-based organ dysfunction evaluation, procalcitonin, CRP, lactate, microbiological testing, or clinician judgment. Complete reporting of sample size, group denominators, ROC AUCs, diagnostic cut-offs, sensitivity, specificity, predictive values, serial RDW values, and adjusted regression estimates is required before firm diagnostic accuracy conclusions can be drawn.

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