International Journal of Clinical and Biomedical Research
Vol. 11, No. 2 (2026)
pISSN: 2521-0394 · eISSN: 2395-0471

ORIGINAL RESEARCH

RED CELL DISTRIBUTION WIDTH AS A PROGNOSTIC MARKER IN CHILDREN WITH SEPSIS: A PROSPECTIVE OBSERVATIONAL STUDY FROM A TERTIARY CARE CENTRE

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ABSTRACT

Sepsis remains a leading cause of childhood morbidity and mortality, particularly in low- and middle-income countries. Early identification of children at greater risk of an adverse outcome is essential, but specialised biomarkers are often unavailable in resource-limited settings. Red cell distribution width (RDW), a routinely reported component of the complete blood count, has emerged as a marker of systemic inflammation and oxidative stress and may carry prognostic value in sepsis. The present study was conducted to evaluate the prognostic significance of admission RDW in children with clinically diagnosed sepsis. This prospective observational study enrolled 120 children, aged 1 month to 12 years, with a clinical diagnosis of sepsis admitted to a tertiary care hospital over a 12-month period. Admission RDW values were recorded and analysed in relation to need for intensive care, length of hospital stays and in-hospital mortality. Patients were dichotomised into survivors and non-survivors for comparative analysis, and a threshold of 15% was used to assess associations between RDW and severity indicators. Mean admission RDW was significantly higher in non-survivors than in survivors (16.6 ± 2.0% vs. 14.3 ± 1.5%; $p < 0.001$). Children with RDW ≥ 15% had significantly higher rates of intensive care unit (ICU) admission (60.9% vs. 24.3%; $p < 0.001$) and in-hospital mortality (52.2% vs. 10.8%; $p < 0.001$) than those with RDW < 15%, and admission RDW was positively correlated with duration of hospital stay ($p < 0.001$). Admission RDW is a simple, inexpensive and clinically informative parameter that is significantly associated with adverse outcomes, disease severity and mortality in pediatric sepsis. Its routine incorporation into initial assessment may aid early risk stratification, particularly in resource-constrained settings..

Keywords: Sepsis; Red cell distribution width; Pediatric sepsis; Prognostic marker; Mortality; Critical illness.

INTRODUCTION

Sepsis is a life-threatening syndrome arising from a dysregulated host response to infection, resulting in organ dysfunction [1]. Despite advances in pediatric intensive care, sepsis remains one of the leading causes of in-hospital death in children, with a disproportionate burden in low- and middle-income countries [2,3]. Modelling work from the Global Burden of Disease Study estimates that nearly half of all sepsis-related deaths worldwide occur in children, accounting for several million deaths annually [3]. Early recognition of children at greatest risk of an adverse outcome therefore continues to be a clinical priority, and timely risk stratification is integral to the recommendations of the Surviving Sepsis Campaign pediatric guidelines [4]. Most established prognostic biomarkers procalcitonin, lactate, presepsin and various interleukins are either not universally available or require additional resources, limiting their utility in many of the settings where the burden of pediatric sepsis is highest.

Red cell distribution width (RDW) is a quantitative index of variability in red blood cell volume that is calculated and reported routinely as part of the complete blood count [5]. Although traditionally used to characterise the morphological subtypes of anaemia, RDW has more recently been recognised as a sensitive, although nonspecific, indicator of systemic inflammation and oxidative stress [5,6]. Pro-inflammatory cytokines impair erythropoiesis, alter iron metabolism and

shorten erythrocyte survival; the resulting release of immature red cells of varying size into the circulation produces a measurable elevation in RDW [6].

A growing body of literature has shown that elevated RDW is independently associated with adverse outcomes in adults with sepsis [7,8] and in critically ill populations more broadly [9]. Studies from Indian centres have reported similar associations in patients with clinical sepsis, supporting the relevance of RDW in regional practice [10]. Pediatric data are more limited but consistent in direction: investigators have reported associations between elevated RDW and increased disease severity, prolonged hospital stay and higher mortality among children admitted to general and intensive care wards [11,12]. A meta-analysis pooling pediatric studies further supported RDW as an outcome biomarker in this population, although heterogeneity across age groups and clinical settings was noted [13].

Because RDW is generated automatically with every complete blood count, requires no additional cost or specimen, and is widely available even in primary and district-level laboratories, it is well suited as a prognostic adjunct in resource-constrained settings. Data focused specifically on pediatric sepsis nevertheless remain limited. The present study was therefore undertaken to evaluate the prognostic value of admission RDW in children with clinically diagnosed sepsis at a tertiary care hospital, with reference to in-hospital mortality, ICU admission and duration of hospital stay.

MATERIALS AND METHODS

Study design and setting

This was a prospective, single-centre observational study conducted in the Department of Pediatrics of a tertiary care teaching hospital over a 12-month period. The study was carried out in accordance with the principles of the Declaration of Helsinki and was approved by the Institutional Ethics Committee. Written informed consent was obtained from a parent or legal guardian of every participating child.

Study population

Children aged 1 month to 12 years admitted to the pediatric ward or pediatric intensive care unit with a clinical diagnosis of sepsis were eligible for inclusion. Sepsis was defined according to the International Pediatric Sepsis Consensus Conference criteria, namely the systemic inflammatory response syndrome (SIRS) in the presence of suspected or proven infection [14]. Children with pre-existing haematological disorders, those who had received a blood transfusion within the preceding four weeks, those with chronic systemic illness (chronic liver disease or chronic kidney disease) and those with a known malignancy were excluded, in order to limit known confounders of RDW.

Sample size and sampling

A consecutive sampling strategy was used. All eligible children admitted during the 12-month study period were enrolled, yielding a final analytic sample of 120 patients.

Data collection and laboratory analysis

A standardised case-record form was used to capture demographic data, clinical history, examination findings and laboratory parameters at admission. Venous blood samples were collected at the time of admission, before therapeutic intervention where feasible, into EDTA-containing tubes and processed on an automated haematology analyser. RDW was reported as the coefficient of variation of red blood cell volume (RDW-CV) expressed as a percentage, in accordance with the manufacturer's reference range. All children were followed prospectively until discharge or in-hospital death.

Outcome measures

The primary outcome was in-hospital mortality. Secondary outcomes were the need for ICU admission and duration of hospital stay. For categorical comparisons, an RDW threshold of 15% was used to dichotomise patients into a lower (< 15%) and a higher (≥ 15%) group, in keeping with cut-offs reported in earlier work on RDW as a sepsis biomarker [7,8].

Statistical analysis

Data were entered in Microsoft Excel and analysed in IBM SPSS Statistics version 25. Continuous variables are presented as mean ± standard deviation and categorical variables as frequencies and percentages. Differences between survivors and non-survivors were assessed using the independent-samples t-test for continuous variables and the chi-square test for categorical variables. The relationship between admission RDW and length of hospital stay was examined using Pearson's correlation coefficient. A two-sided p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 120 children meeting the inclusion criteria were enrolled and analysed. Their baseline demographic characteristics are summarised in Table 1. The mean age was 4.6 ± 3.1 years, with most children younger than 5 years, and there was a slight male preponderance (53.3%).

The distribution of admission RDW values is shown in Table 2. Approximately one-third of children had RDW values below 14%, with a similar proportion in the 14 -15% range; 38.3% had RDW values exceeding 15%, indicating that elevated anisocytosis was common in this cohort.

In-hospital mortality occurred in 32 of 120 children (26.7%). The mean admission RDW was significantly higher in non-survivors than in survivors (16.6 ± 2.0% vs. 14.3 ± 1.5%; $p < 0.001$), as shown in Table 3.

When patients were dichotomised at an RDW cut-off of 15%, those with RDW ≥ 15% had substantially higher rates of ICU admission (60.9% vs. 24.3%; $p < 0.001$) and in-hospital mortality (52.2% vs. 10.8%; $p < 0.001$) than those with RDW < 15% (Table 4).

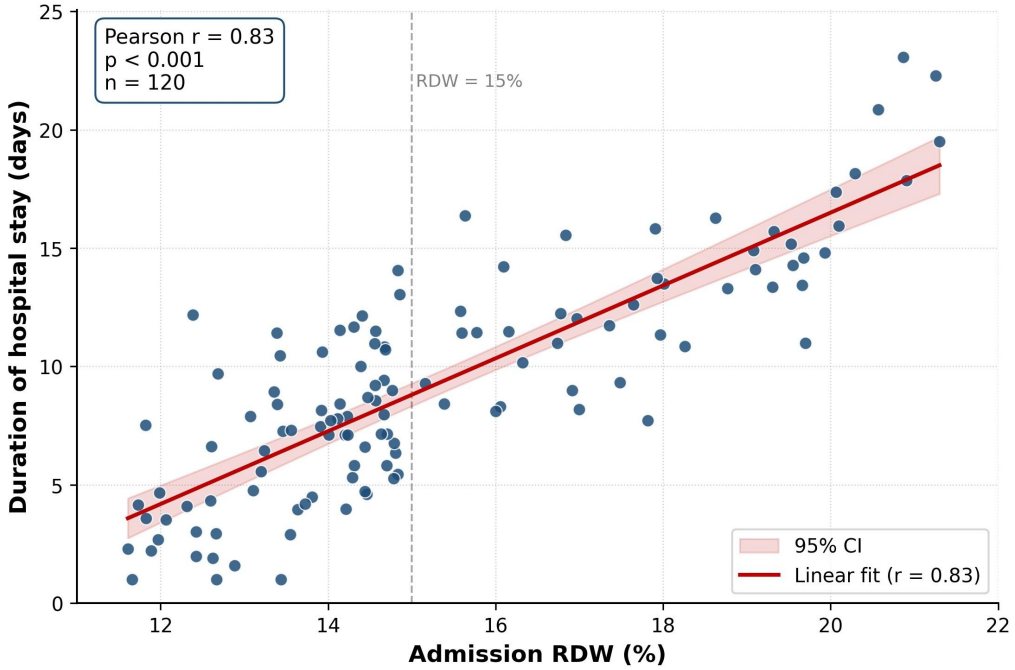

Figure 1. *Correlation between admission red cell distribution width (RDW) and duration of hospital stay among children with sepsis*

Table 1. Baseline demographic characteristics of the study population (n = 120).

Parameter	Value	Percentage / SD
Mean age (years)	4.6 ± 3.1	
Male sex	64	53.3%
Female sex	56	46.7%
Total	120	100.0%

Table 2. Distribution of admission red cell distribution width (RDW) values.

Admission RDW (%)	Number of patients (n)	Proportion (%)
< 14	38	31.7
14 – 14.9	36	30.0
≥ 15	46	38.3
Total	120	100.0

Table 3. Admission red cell distribution width (RDW) and in-hospital outcome.

Outcome	Mean admission RDW (%)	p-value
Survivors (n = 88)	14.3 ± 1.5	< 0.001
Non-survivors (n = 32)	16.6 ± 2.0	

Table 4. Association between admission red cell distribution width (RDW) thresholds and severity indicators.

Variable	RDW < 15% (n = 74)	RDW ≥ 15% (n = 46)	p-value
ICU admission, n (%)	18 (24.3)	28 (60.9)	< 0.001
In-hospital mortality, n (%)	8 (10.8)	24 (52.2)	< 0.001

DISCUSSION

In this prospective single-centre cohort of 120 children with sepsis, admission RDW was significantly higher in those who died than in those who survived, and an RDW threshold of 15% identified a subgroup of children with markedly higher rates of ICU admission and in-hospital mortality. Admission RDW was also positively correlated with length of hospital stay. Taken together, these findings support the use of RDW as a simple, widely available prognostic marker in pediatric sepsis.

Our findings are consistent with adult and pediatric data published over the past decade. Lorente and colleagues observed that elevated RDW during the first week of sepsis was associated with both severity and mortality in adult intensive care patients [7], and Krishna and co-workers similarly reported RDW to be an independent predictor of sepsis mortality [8]. More recent work by Dankl et al., using a large multicentre database, confirmed that RDW remains independently associated with mortality in sepsis after adjustment for established risk factors [15]. Among critically ill children, Ramby et al. described RDW as a pragmatic outcome marker in a large pediatric cohort [11], and Kim et al. confirmed its usefulness in critically ill pediatric patients [12]. The Indian rural cohort reported by Jain et al. is particularly relevant to the present setting and showed a comparable association between elevated RDW and sepsis mortality [10]. The pediatric meta-analysis by Murphy et al. drew these strands together and concluded that RDW carries useful prognostic information across pediatric illnesses, although the magnitude of effect varies with clinical population and severity [13].

The biological basis for the relationship between RDW and outcome in sepsis is multifactorial. Pro-inflammatory cytokines particularly interleukin-6, tumour necrosis factor-α and interferon-γ suppress erythropoiesis and disturb iron homeostasis, while oxidative stress shortens erythrocyte lifespan and impairs deformability [5,6]. The combined effect is greater variability in red cell size, with the magnitude of rise in RDW reflecting the intensity and duration of the systemic inflammatory response [9,16]. Comorbid factors common in critically ill children, including nutritional deficiencies and

acute bone-marrow stress, may further contribute. RDW therefore appears to function as an integrative measure of the metabolic and inflammatory milieu, rather than a marker of any single pathway.

Several features make RDW particularly attractive as a prognostic adjunct in pediatric sepsis. It is generated automatically as part of the complete blood count, adds no incremental cost or specimen requirement, is interpretable using a simple cut-off, and is available in virtually every laboratory, including those at primary and secondary level. These attributes are especially valuable in low- and middle-income settings, in which more sophisticated biomarkers and physiological scoring tools may be unavailable or impractical at the point of initial assessment [10,13]. Earlier work in adult populations has shown that RDW improves the predictive performance of established critical-care scoring systems when added to them [9,17], suggesting that integration with existing pediatric severity scores warrants further investigation.

RDW is, however, a nonspecific marker. It can be elevated in iron and B12 or folate deficiency, haemoglobinopathies, recent transfusion and a range of chronic illnesses, all of which are common in pediatric populations and may confound its interpretation when used in isolation [18,19]. RDW should therefore be interpreted alongside the clinical picture and other relevant investigations, and not as a stand-alone prognostic test.

Limitations

This was a single-centre study with a modest sample size, which limits the generalisability of the findings; multicentre studies with larger and more diverse cohorts will be needed to establish optimal RDW thresholds with greater precision. RDW was measured only at admission; serial measurements would have allowed examination of dynamic changes during the course of illness, which may carry additional prognostic information. Causative organisms, validated severity scores (such as PRISM or PELOD-2) and detailed organ-dysfunction data were not analysed in the present report; integrating RDW with such tools is an important focus of future work and the criteria used to define sepsis pre-date the recently published Phoenix consensus criteria for pediatric sepsis and septic shock; external validation of these findings against the new definitions will be valuable.

CONCLUSION

RDW is a simple, inexpensive and clinically informative parameter that is significantly associated with adverse outcomes, disease severity and mortality in pediatric sepsis. In this cohort, an elevated RDW particularly above 15% was associated with a higher risk of ICU admission, prolonged hospital stays and in-hospital mortality. Incorporating RDW into routine initial assessment, alongside established clinical evaluation, may aid early risk stratification and guide more intensive monitoring in children with sepsis, especially in resource-limited settings.

DECLARATIONS

Funding. No external funding was received for this study.

Conflicts of interest. The authors declare no conflicts of interest.

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