RESEARCH PAPER

Red Cell Distribution Width as a Prognostic Biomarker for Predicting Clinical Outcomes in Critically Ill Children: A Prospective Observational Study

Running title: *RDW as a Prognostic Biomarker in Paediatric Critical Illness*

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ABSTRACT

Background: Red cell distribution width (RDW), a routinely reported parameter in the complete blood count, has emerged as a prognostic marker across multiple organ systems. Its utility in critically ill paediatric patients admitted to the Paediatric Intensive Care Unit (PICU) warrants further prospective evaluation in resource-limited settings. This study evaluated RDW as a biomarker for predicting mortality, length of PICU stay, mechanical ventilation requirement, and inotrope use in critically ill children.

Methods: A hospital-based prospective observational study was conducted at the PICU of Maharshi Markandeshwar Institute of Medical Sciences and Research, Mullana, Haryana, India, from April 2024 to October 2025. Seventy-five critically ill children were enrolled and stratified into four RDW quartile groups (<13.4%, 13.4–14.3%, 14.4–15.7%, >15.7%). Admission RDW and serial RDW values were correlated with PRISM III severity scores and clinical outcomes using ANOVA, Kruskal–Wallis, chi-square, independent t-test, Spearman's correlation, and ROC curve analysis.

Results: Mean admission RDW was 15.94 ± 3.57%. A significant positive correlation was observed between RDW and PRISM III score ($r = 0.411$, $p < 0.001$). Non-survivors had significantly higher admission RDW than survivors (17.85 ± 4.86% vs 15.55 ± 3.18%, $p = 0.035$). Patients requiring mechanical ventilation and inotropic support had significantly elevated admission RDW ($p = 0.002$ and $p = 0.047$, respectively). Median PICU stay increased from 2 days in the lowest RDW quartile to 12 days in the highest ($p = 0.036$). ROC analysis yielded AUC values of 0.633 for mortality ($p = 0.014$), 0.648 for mechanical ventilation ($p = 0.015$), and 0.696 for inotrope requirement ($p = 0.001$).

Conclusion: RDW at PICU admission is significantly associated with illness severity, prolonged stay, and the need for advanced supportive interventions in critically ill children. Its modest to fair discriminatory ability supports its role as an adjunctive, cost-effective prognostic biomarker, particularly in resource-limited healthcare settings.

Keywords: red cell distribution width; paediatric intensive care unit; critical illness; mortality; PRISM III; prognostic biomarker; mechanical ventilation; inotrope

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1. INTRODUCTION

The Paediatric Intensive Care Unit (PICU) cares for critically ill children requiring advanced organ support and continuous monitoring. Approximately 13.4% of paediatric hospital admissions require PICU-level care, and reported PICU mortality rates range from 2% in well-resourced healthcare systems to over 33% in resource-limited settings, largely driven by healthcare disparities in low- and middle-income countries.[1] Multiple organ dysfunction syndrome (MODS) is a leading cause of PICU morbidity and mortality. Accurate and early risk stratification is therefore essential for timely clinical decision-making and optimized resource allocation.

Several validated prognostic scoring systems—Paediatric Risk of Mortality (PRISM III), Paediatric Index of Mortality (PIM-2), Paediatric Logistic Organ Dysfunction (PELOD-2), and paediatric Sequential Organ Failure Assessment (pSOFA)—have demonstrated good discriminatory ability for PICU mortality.[2] However, their routine application is constrained by the need for multiple variables, computational complexity, and time-intensive data collection, particularly challenging in resource-limited environments.[2] There is consequently an increasing demand for simple, rapid, and universally available biomarkers that can complement or substitute existing scoring systems for early risk stratification.

Red cell distribution width (RDW) quantifies erythrocyte size heterogeneity (anisocytosis) and is a standard component of the complete blood count (CBC)—one of the most universally available laboratory investigations at all levels of healthcare.[3] Traditionally used as an adjunctive parameter in anaemia classification, recent evidence has greatly expanded its clinical relevance. Elevated RDW reflects systemic inflammation, impaired erythropoiesis, nutritional deficiencies, and oxidative stress, making it a sensitive, non-specific indicator of overall physiological derangement.[4] A large body of adult critical care literature has established RDW as an independent predictor of mortality, length of intensive care unit stay, and organ dysfunction across diverse disease states.[4]

In paediatric critical care, RDW has shown promising but somewhat inconsistent prognostic value. Ramby et al. demonstrated that admission RDW was independently associated with PICU mortality and prolonged length of stay in a cohort of 596 children, with predictive accuracy comparable to the PIM-2 score.[5] Gauchan and Basnet, and Rudrappa et al. subsequently reported significant associations between elevated admission RDW and adverse outcomes—including higher mortality rates and greater resource utilization—in critically ill paediatric patients in South Asian tertiary care settings.[6,7] Hassan et al. further evaluated RDW as a predictor of MODS development in a retrospective paediatric PICU cohort, suggesting that elevated RDW reflects the overall inflammatory burden and illness severity.[8]

Despite this growing evidence base, prospective paediatric data from northern India remain limited. A recent prospective study from central India by Nagaraju et al. highlighted the prognostic relevance of RDW in critically ill children,[9] but comparison with established PICU scoring systems across key clinical endpoints in a North Indian tertiary care setting has not been reported. The present study was designed to prospectively evaluate admission RDW and its serial changes in relation to mortality, PICU length of stay, mechanical ventilation requirement, and inotrope use, and to correlate RDW with PRISM III scores, in critically ill children admitted to a tertiary care PICU in Haryana, India.

2. MATERIALS AND METHODS

2.1 Study Design and Setting

A hospital-based prospective observational study was conducted in the PICU of the Department of Paediatrics, Maharshi Markandeshwar Institute of Medical Sciences and Research (MMIMSR), Mullana, District Ambala, Haryana, India. The study period extended from April 2024 to October 2025 (18 months).

2.2 Study Population and Eligibility

All critically ill children admitted to the PICU whose parents or legal guardians provided written informed consent were eligible for enrolment. Patients discharged from the PICU within 24 hours of admission or who died within the first 24 hours of admission were excluded to ensure clinically meaningful outcome data. Additional exclusion criteria were: (i) chronic haematological disorders known to affect RDW values (thalassemia, immune thrombocytopenic purpura, red cell membrane defects, haemolytic anaemia, leukaemia, or other haematological malignancies); (ii) blood transfusion within the preceding three months; and (iii) current treatment with iron supplementation or other medications for anaemia correction.

2.3 Sample Size Determination

As a time-bound feasibility-based study, sample size was estimated from historical PICU records showing approximately 30 admissions per month. Accounting for anticipated exclusions due to early death, discharge within 24 hours, or other protocol violations, a minimum enrolment target of 75 patients was set. A total of 75 eligible participants were enrolled during the study period.

2.4 Data Collection and Variables

Socio-demographic data (age, sex, body weight) and vital parameters were recorded at admission. Laboratory investigations included a complete blood count with emphasis on RDW estimation, along with serum electrolytes. Disease severity was assessed using the Paediatric Risk of Mortality (PRISM III) score, calculated at 12 hours following PICU admission.

Clinical outcome variables documented prospectively throughout PICU admission included: duration of mechanical ventilation, requirement for inotropic support, need for blood transfusion, total PICU length of stay (LOS), and final outcome (discharge or death). RDW was measured at the time of admission and recorded serially during hospitalization. All data were entered into Microsoft Excel, cross-checked for completeness, and used for statistical analysis.

2.5 RDW Quartile Classification

Patients were categorized into four RDW quartile groups based on their admission RDW value: Group 1 (RDW <13.4%); Group 2 (RDW 13.4–14.3%); Group 3 (RDW 14.4–15.7%); and Group 4 (RDW >15.7%).

2.6 Statistical Analysis

Data were analysed using SPSS version 22.0. Continuous variables were expressed as mean ± standard deviation (SD) or median with range; categorical variables as frequencies and percentages. Between-group comparisons were performed using one-way ANOVA (parametric continuous variables), Kruskal–Wallis test (non-parametric continuous variables), and chi-square test (categorical variables). Two-group continuous comparisons were made using the independent t-test. Serial RDW changes within groups were assessed using the paired t-test. Spearman's rank correlation coefficient (r) was used to evaluate the association between RDW and PRISM III score. Receiver operating characteristic (ROC) curve analysis was performed to assess predictive ability, and area under the curve (AUC) values with 95% confidence intervals (CI) were reported. A two-tailed p-value <0.05 was considered statistically significant.

2.7 Ethics Statement

Ethical clearance was obtained from the Institutional Review Board of MMIMSR, Mullana, Haryana, India. Written informed consent was obtained from the parents or legal guardians of all enrolled participants prior to data collection. Patient management and therapeutic interventions were performed exclusively in accordance with standard institutional PICU protocols; no additional diagnostic or therapeutic procedures were introduced as part of the study.

3. RESULTS

3.1 Patient Characteristics Across RDW Quartile Groups

A total of 75 critically ill children were enrolled. The median age was 108 months (range: 1–204 months); males constituted 54.7% of the cohort. Mean body weight was 26.48 ± 15.10 kg. Age ($p = 0.809$), sex distribution ($p = 0.693$), weight ($p = 0.844$), and all haemodynamic parameters at admission—heart rate, respiratory rate, SpO_2, temperature, systolic blood pressure, and diastolic blood pressure—did not differ significantly across RDW quartile groups ($p > 0.05$ for all). Mean admission RDW was 15.94 ± 3.57% for the total cohort.

Statistically significant differences across RDW quartile groups were observed for white blood cell count (WBC, $p = 0.040$), red blood cell count (RBC, $p = 0.048$), and mean corpuscular volume (MCV, $p = 0.029$). WBC count rose progressively from 12.45 ± 6.27 × 10^3/µL in Group 1 to 19.90 ± 7.15 × 10^3/µL in Group 4, while MCV declined from 90.36 ± 5.20 fL to 80.86 ± 10.73 fL across the same groups. PRISM III scores increased significantly with higher RDW quartile (from 14.18 ± 3.68 in Group 1 to 19.28 ± 4.26 in Group 4; $p < 0.001$). Table 1 summarises baseline characteristics and clinical outcomes stratified by RDW quartile.

Table 1: Baseline Characteristics and Clinical Outcomes Across RDW Quartile Groups

Characteristic	Total (n = 75)	RDW <13.4 % (n = 11)	RDW 13.4–14.3 % (n = 18)	RDW 14.4–15.7 % (n = 17)	RDW >15.7 % (n = 29)	p-value
Age (months), median (range)	108 (1–204)	108 (96–192)	132 (72–192)	96 (1–204)	60 (4–204)	0.809
Male sex, n (%)	41 (54.7)	6 (54.5)	8 (44.4)	11 (64.7)	16 (55.2)	0.693
Weight (kg), mean ±SD	26.48 ±15.10	26.64 ±14.46	28.78 ±11.77	27.00 ±16.08	24.69 ±17.02	0.844
WBC (×10^3/µL)	17.00 ±8.16	12.45 ±6.27	15.06 ±8.73	17.06 ±8.88	19.90 ±7.15	0.040*
RBC (×10^6/µL)	4.77± 0.76	4.27± 0.65	4.52± 0.67	4.76± 0.66	5.00± 0.85	0.048*
MCV (fL)	83.83 ±9.41	90.36 ±5.20	85.33 ±8.18	83.06 ±8.45	80.86 ±10.73	0.029*

Haemoglobin (g/dL)	13.01 ±1.83	13.00 ±1.10	13.17 ±1.54	12.94 ±1.52	12.97 ±2.37	0.983
Platelet (×10³/μL)	254.8 ±159.8	234.0 ±84.8	293.3 ±150.5	280.2 ±207.6	224.0 ±155.0	0.441
RDW at admission (%)	15.94 ±3.57	12.69 ±0.49	13.88 ±0.30	14.92 ±0.36	19.05 ±3.99	<0.001*
PRISM III score	16.81 ±4.40	14.18 ±3.68	14.61 ±2.91	16.65 ±4.36	19.28 ±4.26	<0.001*
Mechanical ventilation, n (%)	23 (30.7)	1 (9.1)	3 (16.7)	5 (29.4)	14 (48.3)	0.040*
Inotrope use, n (%)	12 (16.0)	0 (0)	1 (5.6)	2 (11.8)	9 (31.0)	0.034*
Mortality, n (%)	13 (17.3)	1 (9.1)	2 (11.1)	2 (11.8)	8 (27.6)	0.320
PICU LOS (days), median (range)	6 (2–19)	2 (2–7)	6 (2–18)	9 (3–16)	12 (2–18)	0.036*

**p < 0.05 (statistically significant). WBC = white blood cell count; RBC = red blood cell count; MCV = mean corpuscular volume; PRISM III = Paediatric Risk of Mortality score III; PICU = paediatric intensive care unit; LOS = length of stay. Statistical tests: Kruskal–Wallis for age and PICU LOS; chi-square for sex, mechanical ventilation, inotrope use, and mortality; one-way ANOVA for all other continuous variables.*

3.2 Correlation Between RDW and PRISM III Score

Spearman's correlation analysis demonstrated a significant moderate positive correlation between admission RDW and PRISM III score ($r = 0.411$, $p < 0.001$). This indicates that higher RDW values at PICU admission were associated with greater severity of illness as measured by the PRISM III scoring system.

3.3 RDW and Length of PICU Stay

Median PICU length of stay increased progressively across RDW quartile groups: 2 days (Group 1), 6 days (Group 2), 9 days (Group 3), and 12 days (Group 4), with a statistically significant difference ($p = 0.036$). Patients with PICU stays exceeding 10 days had a significantly higher mean admission RDW (17.93 ± 4.29%) compared with those staying 2–5 days (14.61 ± 2.25%; $p = 0.012$). This gradient was maintained for RDW measured during hospitalization (16.16 ± 4.04% vs 13.20 ± 2.03%; $p = 0.017$), suggesting that elevated RDW reflects greater disease burden and prolonged recovery time.

3.4 Association Between RDW and Clinical Outcomes

Non-survivors (n = 13, 17.3%) had significantly higher mean admission RDW compared with survivors (17.85 ± 4.86% vs 15.55 ± 3.18%; $p = 0.035$). RDW during hospitalization also remained significantly higher in non-survivors (16.15 ± 4.62% vs 14.08 ± 2.94%; $p = 0.041$). Although mortality was highest in Group 4 (27.6% vs 9.1% in Group 1), the categorical comparison of mortality across RDW quartile groups did not reach statistical significance ($p = 0.320$).

Patients requiring mechanical ventilation (n = 23, 30.7%) had significantly higher admission RDW than non-ventilated patients (17.87 ± 4.70% vs 15.10 ± 2.61%; $p = 0.002$). This difference persisted for RDW measured during hospitalization (16.13 ± 4.53% vs 13.69 ± 2.36%; $p = 0.003$). The proportion of patients requiring mechanical ventilation rose from 9.1% in the lowest RDW quartile to 48.3% in the highest ($p = 0.040$). Patients requiring inotropic support (n = 12, 16.0%) had higher admission RDW than those who did not (17.83 ± 4.69% vs 15.59 ± 3.28%; $p = 0.047$). The proportion requiring inotropes increased from 0% in the lowest RDW quartile to 31.0% in the highest ($p = 0.034$). Table 2 summarises these associations.

Table 2: Association Between Admission RDW and Clinical Outcomes

Outcome	Group	n (%)	RDW at Admission Mean± SD (%)	RDW During Stay Mean± SD (%)	p-value
Mortality	Non-survivors	13 (17.3)	17.85±4.86	16.15±4.62	0.035 / 0.041
	Survivors	62 (82.7)	15.55±3.18	14.08±2.94	—
Mechanical Ventilation	Required	23 (30.7)	17.87±4.70	16.13±4.53	0.002 / 0.003
	Not required	52 (69.3)	15.10±2.61	13.69±2.36	—
Inotrope Use	Required	12 (16.0)	17.83±4.69	16.17±4.43	0.047 / 0.050
	Not required	63 (84.0)	15.59±3.28	14.11±3.03	—

p-values are expressed as: RDW at admission / RDW during hospitalization. Independent t-test used for all comparisons.

3.5 Serial RDW Changes in Survivors and Non-Survivors

Serial paired analysis revealed that RDW declined significantly from admission to hospital stay in both survivors (15.55 ± 3.18% to 14.08 ± 2.94%; $p < 0.001$) and non-survivors (17.85 ± 4.86% to 16.15 ± 4.62%; $p < 0.001$). However, non-survivors maintained persistently and significantly higher RDW levels throughout their PICU stay compared with survivors. Table 3 presents these data.

Table 3: Serial RDW Values in Survivors and Non-Survivors

Group	RDW at Admission Mean±SD (%)	RDW During Stay Mean±SD (%)	Mean Change (%)	p-value
Survivors (n = 62)	15.55 ± 3.18	14.08 ± 2.94	−1.47	<0.001
Non-survivors (n = 13)	17.85 ± 4.86	16.15 ± 4.62	−1.70	<0.001

Paired t-test used for within-group comparison of admission RDW vs RDW during hospitalization. Non-survivors maintained persistently elevated RDW throughout hospitalization relative to survivors.

3.6 ROC Curve Analysis

ROC curve analysis demonstrated statistically significant predictive ability of admission RDW for all three adverse outcome endpoints. The AUC for predicting mortality was 0.633 (95% CI: 0.470–0.795; $p = 0.014$), indicating modest discriminatory ability. The AUC for mechanical ventilation requirement was 0.648 (95% CI: 0.533–0.762; $p = 0.015$). The highest predictive performance was observed for inotrope requirement (AUC = 0.696; 95% CI: 0.585–0.807; $p = 0.001$), indicating fair discriminatory ability. Table 4 summarises the ROC curve parameters.

Table 4: ROC Curve Analysis of Admission RDW for Predicting Clinical Outcomes

Outcome	AUC	95% Confidence Interval	p-value
Mortality	0.633	0.470 – 0.795	0.014
Mechanical ventilation	0.648	0.533 – 0.762	0.015
Inotrope requirement	0.696	0.585 – 0.807	0.001

AUC = area under the receiver operating

characteristic curve; CI = confidence interval.

4. DISCUSSION

This prospective observational study evaluated the prognostic utility of RDW in 75 critically ill children admitted to a tertiary care PICU in northern India. The principal findings were: (i) admission RDW correlated significantly with PRISM III illness severity scores ($r = 0.411$, $p < 0.001$); (ii) elevated admission RDW was significantly associated with mortality, prolonged PICU stay, mechanical ventilation requirement, and inotrope use; and (iii) ROC analysis confirmed modest to fair predictive accuracy of RDW for all three adverse clinical outcomes studied, with the highest AUC observed for inotrope requirement (0.696).

The pathophysiological basis of the association between elevated RDW and adverse outcomes in critical illness is multifactorial. Pro-inflammatory cytokines such as interleukin-6, tumour necrosis factor-α, and interleukin-1β suppress erythroid precursor maturation, resulting in heterogeneous erythrocyte populations and elevated RDW. Oxidative stress—a hallmark of critical illness—shortens erythrocyte lifespan and promotes release of immature reticulocytes, increasing anisocytosis. Functional iron deficiency, mediated through hepcidin upregulation in response to inflammation, further contributes to ineffective erythropoiesis.[1,2] These converging mechanisms explain why RDW serves as an integrative marker of overall systemic physiological derangement.

The significant positive correlation between admission RDW and PRISM III score observed in our study aligns with findings by Kim et al., who reported significantly higher PRISM III, pSOFA, PELOD-2, and pMODS scores in paediatric PICU patients with elevated RDW values, supporting RDW as a marker of systemic rather than disease-specific severity.[2]

Our finding that non-survivors had significantly higher admission RDW than survivors ($17.85 \pm 4.86\%$ vs $15.55 \pm 3.18\%$, $p = 0.035$) is consistent with several paediatric critical care studies. Said et al., in a large cohort of 3,913 paediatric PICU patients, reported that admission RDW (OR = 1.13, 95% CI: 1.03–1.24) and relative RDW change during hospitalization were both independent predictors of ICU mortality after adjusting for severity of illness.[10] Hashemi et al. found PICU mortality to be 20.1% in the highest RDW quartile (>15.7%)—closely mirroring our observed rate of 27.6% in the equivalent quartile.[11] Sachdev et al. demonstrated that an RDW cut-off of 18.6% predicted PICU mortality with 90.9% sensitivity and an AUC of 0.83; the higher cut-off and AUC relative to the present study likely reflect differences in illness severity profile and patient mix.[12]

The association between elevated RDW and mechanical ventilation requirement in our study (48.3% in the highest quartile vs 9.1% in the lowest, $p = 0.040$; AUC = 0.648) is consistent with prior reports. Rudrappa et al. and Mahendrappa et al. both observed significantly higher RDW values among mechanically ventilated paediatric patients, with the latter specifically reporting mean RDW of $16.1 \pm 2.1\%$ versus $12.9 \pm 2.5\%$ in ventilated versus non-ventilated neonatal PICU patients ($p < 0.001$).[7,13] The fair predictive value of RDW for inotrope requirement (AUC = 0.696, $p = 0.001$) further underscores its utility as a surrogate marker for haemodynamic compromise and the need for cardiovascular support.

The significant association between elevated admission RDW and prolonged PICU stay in our cohort—with median stay rising from 2 to 12 days across quartile groups ($p = 0.036$)—parallels observations by Gauchan and Basnet, who identified higher ΔRDW (relative change from admission) as a predictor of complicated hospital course and mortality in critically ill Nepalese children.[6] The persistent elevation of RDW in non-survivors throughout their PICU stay, despite a statistically significant decline in both groups, suggests that the trajectory of RDW over time may provide additional prognostic information beyond a single admission measurement.

The AUC of 0.633 for mortality prediction in our study is broadly consistent with published values: Said et al. reported an AUC of 0.611[10] and Bazick et al. 0.67 for mortality prediction in adult critically ill populations.[14] Higher AUCs reported by Gauchan and Basnet (0.721)[6] and Mahendrappa et al. (0.810 in a neonatal cohort)[13] likely reflect differences in patient age range, disease spectrum, and illness severity thresholds. Purtle et al. demonstrated that an elevated discharge RDW independently predicted out-of-hospital mortality following critical illness in adult patients,[15] supporting the value of serial RDW monitoring beyond the admission measurement alone.

Although the categorical association between RDW quartile groups and mortality did not reach statistical significance ($p = 0.320$) in this study, this is most plausibly attributable to the relatively modest sample size and the uneven distribution of mortality events. The statistically significant finding from continuous comparisons of RDW between survivors and non-survivors ($p = 0.035$ for admission RDW) provides a directionally consistent and clinically meaningful signal.

Key strengths of this study include the prospective design with systematic real-time data collection, serial RDW measurements throughout the PICU stay, strict exclusion of patients with haematological confounders, and the simultaneous evaluation of multiple clinically relevant outcomes alongside a validated illness severity score. The primary limitation is the single-centre design with a modest sample size,

which constrains statistical power for subgroup analyses—particularly for mortality—and limits generalizability. The absence of concurrent inflammatory biomarkers (interleukin-6, C-reactive protein, serum ferritin) restricted mechanistic interpretation of RDW elevation. Long-term post-discharge follow-up was not performed.

5. CONCLUSION

RDW at PICU admission is significantly associated with illness severity (as measured by PRISM III), prolonged PICU stay, mechanical ventilation requirement, inotrope use, and mortality in critically ill children. A modest to fair predictive ability was confirmed by ROC analysis for all three adverse outcome endpoints. As a simple, inexpensive, and universally available haematological parameter routinely reported in the complete blood count, RDW has significant potential as an adjunctive bedside prognostic biomarker in the PICU, particularly in resource-limited settings where complex severity scoring systems may be difficult to apply. Larger multicentre prospective studies with standardized serial RDW monitoring, concurrent biomarker profiling, and long-term post-discharge follow-up are warranted to validate these findings and determine optimal cut-off thresholds for clinical application.

DECLARATIONS

Ethics approval and consent to participate: Ethical clearance was obtained from the Institutional Review Board of Maharshi Markandeshwar Institute of Medical Sciences and Research, Mullana, Haryana, India. Written informed consent was obtained from parents or legal guardians of all enrolled participants prior to study commencement.

Consent for publication: Not applicable (no individual-level patient identifiers published).

Availability of data and materials: The datasets supporting the conclusions of this article are available from the corresponding author upon reasonable request.

Competing interests: The authors declare no competing interests.

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