Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.47750/jptcp.2023.30.03.013

Prognostic Significance of Red Blood Cell Distribution width (RDW) in Critically ill Paediatric Patients at Sohag University Hospital

Shaimaa Mohammed Mahmoud[1], Rezk Atalla Massoud[2], Al Zahraa El Sayed Ahmed[3], Amr Ahmed Othman[4*]

[1,2,3,4]Department of Paediatrics, Faculty of Medicine, Sohag University, Sohag, Egypt.

***Corresponding author:** Amr Ahmed Othman, Department of Paediatrics, Faculty of Medicine, Sohag University, Sohag, Egypt, Email: amrothman190@gmail.com

Submitted: 14 November 2022; Accepted: 16 December 2022; Published: 20 January 2023

ABSTRACT

Background: RDW has been recently reported as a strong prognostic factor in several diseases of various organ systems , In critically ill children, it is crucial to assess the severity of illness and organ dysfunction.

Aim: this study aimed to evaluate RDW as a marker for illness severity in critically ill paediatric patients

Patients and methods: One hundred and eleven children, 55 males (49.5 %). were included in this cross-sectional hospital-based study. All critically ill paediatric patients, 1 month to 12 years of age, which were admitted to the Paediatric intermediate & Intensive Care Unit (PICU), at Sohag University Hospital, over six months period were included in the study, Investigations performed ; Complete Blood Count, Serum electrolytes, Blood gases, Coagulation profile , Liver and kidney functions, CRP, Serum lactate, serum fibrinogen, Blood urea nitrogen (BUN) and b-type natriuretic peptide. Observation for the patient if a mechanical ventilation and or inotropes were needed, and for the duration of hospital stay and for the outcome of the case. Calculation of critical illness scores including pediatric multiple organ dysfunction syndrome (PMODS), the pediatric risk of mortality (PRISM), pediatric sequential organ failure assessment (PSOFA) and pediatric logistic organ dysfunction-2 (PELOD-2).

Results: Mortality among critically ill children was significantly associated with high RDW >16.9 with p-value <0.001.Critically ill children with low RDW <16.9 had significantly longer duration of PICU admission with p-value =0.015.Critically ill children with high RDW >16.9 had significantly lower GCS during their PICU admission with p-value<0.001. There was a statistically significant positive correlation between R DW level, PRISM III, SOFA, PLEOD II, and PMODS scores with p-value <0.001. High RDW > 16.9 had a statistically significant predictor for survival of critically ill children with p-value <0.001.Univariate regression analysis shows that PRISM III, PSOFA, PLEOD II, PMODS and RDW% had statistically significant effect on PICU survival among critically ill children with p-value <0.001.

Conclusion: Red blood cell distribution width (RDW) is a good predictor of critical illness severity in pediatrics being significantly correlated with severity scores including SOFA, PLEOD II, and PRISM scores

Keywords: *critically ill children, RDW, severity scores.*

INTRODUCTION

In critically ill children, it is crucial to assess the severity of illness and organ dysfunction accurately and predict outcomes for adequate management, so a lot of studies have investigated proper prognostic factors including several scoring systems such as pediatric multiple organ dysfunction syndrome (PMODS), the pediatric risk of mortality (PRISM), pediatric sequential organ failure assessment (PSOFA) and pediatric logistic organ dysfunction-2 (PELOD-2) (1) However, these scoring systems could be slightly complex and inconvenient for use in practice and the qualification of a good clinical parameter for predicting outcomes should be easily assessable, reproducible, widely accessible, and acceptable. (2)

RDW has been recently reported as a strong prognostic factor in several diseases of various organ systems, including the cardiovascular, respiratory, renal, neurologic, and gastrointestinal systems (3). It is also associated significantly with ventilator-free days, postoperative outcomes, all causes of mortality in critically ill patients, and outcomes of intensive care unit (ICU), traditionally, the clinical use of RDW has been limited to help in the differentiation between certain types of anemia's (e.g., β-thalassemia minor and iron deficiency anemia) (4). However, most studies were conducted on adult patients. Only a few studies have investigated RDW in children, especially in the critically ill pediatric population (5)

There is growing evidence of the understanding of the crosstalk between the inflammatory and hematologic systems, it was well established that inflammatory cytokines interfere with the maturation of RBCs in the bone marrow through multiple mechanisms, such as the inhibition of the response to erythropoietin, which impairs iron metabolism and shortens RBCs survival, in turn contributing to high RDW (6).

A pro-inflammatory cytokine, tumor necrosis factor-alpha, promotes hypoferremia and enhances erythrophagocytosis. Other cytokines, such as interleukin-1ß, have been shown to directly and negatively affect the survival of RBCs in the circulation, promote deformity of the RBC membrane, and suppress erythrocyte maturation (6). These inflammatory mediators can thus lead to newer and larger reticulocytes entering the peripheral circulation and increasing RDW, indicating that RDW also reflects the severity of inflammation (7).

Another possible explanation that links RDW and critical illness is oxidative stress; although the erythrocytes usually have an excellent antioxidant capacity. Oxidative stress plays a role in RBC homeostasis such as fragility, maturation, and a lifespan that reduces RBCs survival. It also affects many biological processes, including apoptosis and inflammatory reactions, which could change the size of RBC, consequently, increasing RDW (8).

In addition, there were several other suggestions for possible pathophysiology for high RDW, such as poor nutritional status, activation of the renin-angiotensin system, and impaired renal function . In different contexts including sepsis, cardiovascular disease, cancer, and chronic lower respiratory tract disease, RDW has been shown to have an association with an increased risk of mortality (9). Additionally, RDW has been demonstrated to be strongly associated with the length of hospital stay, the incidence of respiratory failure, the incidence of multiple organ dysfunction syndrome (MODS), and mortality in critically ill children in PICUs. Besides that, some studies have discussed RDW prognosis value in some children with severe infectious diseases and compared it with some classical indexes, such as Pediatric Index of Mortality version 2(PIM2) score, Acute Physiology And Chronic Health Evaluation II (APACHE II) score, lactate, and others (4). This study aimed to evaluate RDW as a marker for illness severity in critically ill pediatric patients.

PATIENTS AND METHOD

One hundred and eleven children, 55 males (49.5 %). were included in this cross-sectional hospital-based study. All critically ill pediatric patients, 1 month to 12 years of age,which were admitted to the Paediatric intermediate & Intensive Care Unit (PICU), at Sohag University Hospital. , over six months period were included in the study. Patients who received a blood transfusion before admission to PICU and patients with incomplete data for pediatric risk of mortality (PRISM), pediatric sequential organ failure assessment (sofa),

J Popul Ther Clin Pharmacol Vol 30(3):e106–e116; 20 January 2023.

paediatric logistic organ dysfunction-2 (PELOD-2), and pediatric multiple organ dysfunction syndrome (PMODS) scores were excluded.

All patients included in this study were subjected to the following. Clinical History: focusing on Demographic factors, especially age, gender, residence, and underlying disease such as cardiac, respiratory, neurological, gastrointestinal, endocrine, nephrology, or another disease. Clinical examination: focusing on General examination; including anthropometric measures (weight & height) & Vital signs (Including HR, BP, and Body temperature). Neurological examination; Including GCS & pupillary reaction. Heart examination and abdominal examination. This study was approved by the research ethics committee of the Sohag Faculty of Medicine. Oral and written consent was taken from the guardians of children who were included in the study.

The following investigations were performed for the patients at admission in the Paediatric intermediate and intensive Care Unit (PICU). Complete Blood Count. focusing on: WBC, MCV, HGB, RDW, and PLT. Serum electrolytes including Na, K, and Ca. Blood gases. Pt, Ptt, INR. Liver and kidney functions. CRP. Serum lactate and serum fibrinogen. Blood urea nitrogen (BUN) and b-type natriuretic peptide.

Observation for the patient if a mechanical ventilation and or inotropes were needed, and for the duration of hospital stay and for the outcome of the case. Calculation of the scores including PRISM III, PSOFA, PELOD II, PMODS. (1)

Statistical analysis

The collected data were computerized and statistically analysed using the SPSS program (Statistical Package for Social Science) version 24 and NCSS 12, LLC, USA. Data were tested for normal distribution using the Shapiro Walk test. Qualitative data were represented as frequencies and relative percentages. The chi-square test ($\chi 2$) and Fisher exact were used to calculate the difference between qualitative variables as indicated. Quantitative data were expressed as median and range. Mann-Whitney test was used to calculate the difference between quantitative variables in two groups for non-normally distributed variables. Kruskal-Wallis Test was used to calculate the difference between quantitative variables in more than two groups for non-normally distributed variables. Spearman's correlation test was used for correlating non-normally distributed variables. (ROC) curve was constructed to permit the selection of threshold values for test results and comparison of different testing strategies. Areas under ROC curves and their standard errors were determined using the method of Centor and compared using the normal distribution, with correction for correlation of observations derived from the same cases. A larger area under a ROC curve (AUC) indicates superior test performance, with 1 representing 100% sensitivity and specificity and 0.5 representing no discriminatory utility. Kaplan and Meier's method was used to estimate time to death in PICU and the log-rank test compared both groups. The Cox proportional hazards model was used for univariate regression analysis. Variables that were statistically significant in the univariate analysis were included in the multivariate Cox proportional hazards model. All statistical comparisons were two-tailed with a significance level of P-value ≤ 0.05 indicating significance, $p < 0.001$ indicates a highly significant difference while $P > 0.05$ indicates a non-significant difference.

RESULTS

TABLE 1: Comparison of clinico-demographic data based on ROC curve-derived RDW levels

		RDW Level		Test	P
		Low RDW ≤ 16.9	High RDW >16.9		
		N=52	N=59		
Age (months)		9.0 (1.0-144.0)	8.0 (2.0-144.0)	-0.58	0.56
Sex	Female	28 (53.8%)	28 (47.5%)	0.451	0.502
	Male	24 (46.2%)	31 (52.5%)		
Weight (kg)		8.5 (2.0-37.0)	7.0 (2.5-35.0)	-0.35	0.727
Height (Cm)		73 (50-170)	73 (50-162)	-0.69	0.489
Duration of Admission (Days)		11 (5-30)	8 (1-100)	-2.43	0.015

Quantitative variables were expressed as Median (range) and compared using the Mann-Whitney U test, while qualitative variables were expressed as numbers and percentages and compared using the Chi-square X2 test

The study was conducted on 111 critically ill children, Age of the studied patients ranged from one month to 12 years, with the median age 9 months (1-144 months) with female to male ratio 1.02:1.This table shows that critically ill children with a low RDW <16.9 had a significantly longer duration of PICU admission with p-value =0.015

TABLE 2: Comparison of PICU prognostic Scores based on survival Outcome

		Outcome		MW Test	P
		Improved	Died		
		N=64	N=47		
		Median (Range)	Median (Range)		
Scores	PRISM III	3 (1-11)	11 (8-14)	-8.63	<0.001
	PSOFA	3 (1-8)	8 (4-11)	-8.35	<0.001
	PELOD II	3 (1-11)	11 (5-15)	-8.37	<0.001
	PMODS	2 (1-7)	6 (3-8)	-7.59	<0.001

There was a statistically significant difference between improved critically ill children and dead critically ill children as regards different scores for severity of disease including; PRISM III with p-value <0.001, PSOFA with p-value <0.001, PLEOD II with p-value <0.001 and PMODS with p-value <0.001 being higher in died children compared to improved children as presented in (table 2)

TABLE 3: The Receiver operating characteristic (ROC) curve analysis of RDW as a diagnostic marker to predict in-hospital outcomes (Mortality, need for MV and Inotropes)

	Cut-off	Sensitivity % 95% CI	Specificity % 95% CI	PPV 95% CI	NPV 95% CI	AUC 95% CI	P
Inotropes	>17.5	96 86.3 - 99.5	83.61 71.9 - 91.8	82.8 73.1 - 89.5	96.2 86.7 - 99.0	0.924 0.857 - 0.965	<0.001
MV	>18.3	93.62 82.5 - 98.7	87.5 76.8 - 94.4	84.6 74.1 - 91.4	94.9 86.2 - 98.2	0.925 0.859 - 0.967	<0.001
Mortality	>16.9	100 92.5 - 100.0	81.25 69.5 - 89.9	79.7 70.2 - 86.7	100	0.956 0.900 - 0.986	<0.001

The area under the ROC curve (AUC), The 95%CI: 95% confidence interval, Positive predictive value (PPV), and negative predictive value (NPV)

Inotropes at cutoff >17.5 had an AUC of 0.924 (95% CI:0.857 to 0.965) with a sensitivity of 96% (95% CI:86.3 - 99.5%) and a specificity of 83.61% (95% CI:71.9 - 91.8%). The PPV was 82.8% (95% CI: 73.1 - 89.5%) and the NPV was 96.2% (95% CI: 86.7 - 99.0%); P= <0.001;MV at cutoff >18.3 had an AUC of 0.925 (95% CI:0.859 to 0.967) with a sensitivity of 93.62% (95% CI:82.5 - 98.7%) and a specificity of 87.5% (95% CI:76.8 - 94.4%). The PPV was 84.6% (95% CI: 74.1 - 91.4%) and the NPV was 94.9% (95% CI: 86.2 - 98.2%); P= <0.001. For outcome at cutoff >16.9 had an AUC of 0.956 (95% CI:0.900 to 0.986) with a sensitivity of 100% (95% CI:92.5 - 100.0%) and a specificity of 81.25% (95% CI:69.5 - 89.9%). The PPV was 79.7% (95% CI: 70.2 - 86.7%) and the NPV was 100% (95% CI: %); P= <0.001(Table 3).

J Popul Ther Clin Pharmacol Vol 30(3):e106–e116; 20 January 2023.

TABLE 4: Comparison of RDW levels derived from ROC curve based on survival Outcome

		Outcome		Total N=111	X2 Test	P
		Improved N (%) N=64	Died N (%) N=47			
RDW Level	Low RDW ≤ 16.9	52 (81.3%)	0 (0.0%)	52(46.8%)	71.8	<0.001
	High RDW >16.9	12 (18.8%)	47 (100.0%)	59(53.2%)		

This table shows that mortality among critically ill children was significantly associated with high RDW >16.9 with a p-value <0.001.

TABLE 5: Comparison of patients' clinical findings based on ROC curve-derived RDW levels

		RDW Level		Test	P
		Low RDW ≤ 16.9	High RDW >16.9		
		N=52	N=59		
Vital Signs	Temperature (°C)	38.2 (36.8-39.5)	38.6 (36.0-39.5)	-1.55	0.122
	Heart Rate (Beat/Min)	130 (98-192)	128 (50-184)	-0.01	0.995
	SBP (mm hg)	85 (65-1001)	84 (48-150)	-0.45	0.65
	DBP (mm hg)	52 (40-100)	51 (34-110)	-0.02	0.983
GCS		15 (8-15)	12 (4-15)	-6.43	<0.001
pupillary reaction	Both fixed	0 (0.0%)	1 (1.7%)	3.657	0.161
	Both reactive	52 (100.0%)	55 (93.2%)		
	One reactive & one fixed	0 (0.0%)	3 (5.1%)		

This table shows that critically ill children with high RDW >16.9 had significantly lower GCS during their PICU admission with a p-value<0.001

TABLE 6: Comparison of the use Vent and Inotropes based on ROC curve-derived RDW levels

		RDW Level		X2 Test	P
		Low RDW ≤ 16.9 N (%) N=52	High RDW >16.9 N (%) N=59		
Vent	No	51 (98.1%)	13 (22.0%)	65.467	<0.001
	Yes	1 (1.9%)	46 (78.0%)		
Inotropes	No	50 (96.2%)	11 (18.6%)	67.080	<0.001
	Yes	2 (3.8%)	48 (81.4%)		

This table shows that critically ill children with higher RDW > 16.9 had a significant association with the use of mechanical ventilation, and inotropes with p-value <0.001

TABLE 7: Linear Correlations between RDW % level and certain studied parameters in the whole group

Parameters	RDW %	
	r	P
Age (months)	0.021	0.827
Weight (kg)	-0.031	0.749
Height (Cm)	0.011	0.907
Duration Of Admission (Days)	-0.307	0.001
Temprature ("C)	0.156	0.103
Heart Rate (Beat/Min)	0.043	0.656
Random Blood Sugar (Mg/Dl)	0.016	0.872
SBP (mm hg)	-0.118	0.218
DBP (mm hg)	-0.144	0.131
GCS	-0.559	<0.001
WBCS (X1000/ML)	-0.017	0.86
MCV (FL)	-0.136	0.154
HGB (G/DL)	-0.256	0.007
PLT(X1000/ML)	-0.096	0.315
serum lactate (mmol/l)	0.328	<0.001
serum fibrinogen (mg/dl)	-0.358	<0.001
blood urea nitrogen(mg/dl)	0.500	<0.001
b-type natriuretic peptide (pg/ml)	-0.070	0.465
PT (SEC)	0.032	0.739
PTT (SEC)	0.070	0.466
IN	0.011	0.91
total billirubin(mg/dl)	0.281	0.003
PH	-0.091	0.344
PAO2 (MM HG)	-0.001	0.99
PACO2(MM HG)	0.175	0.066
BE (MMOL/L)	-0.013	0.89
HCO3(MMOL/L)	0.053	0.577
FIO2	0.733	<0.001
SPO2 %	-0.355	<0.001
CRP (MG/L)	0.487	<0.001
Na(Mmol/L)	0.092	0.337
K(Mmol/L)	-0.147	0.125
Ionized Ca(Mmol/L)	-0.067	0.485
Total Ca(Mg/Dl)	0.073	0.448
s.Cr. (mg/dl)	0.102	0.286
ALT(U/L)	0.012	0.901
AST(U/L)	0.014	0.885
s.Albumin(g/dl)	-0.147	0.123
PRISM III	0.793	<0.001
PSOFA	0.808	<0.001
PELOD II	0.823	<0.001
PMODS	0.775	<0.001

r = Correlation Coefficient $P \leq 0.05$= significant P <0.001 highly significant and P >0.05 NS

There was a statistically significant negative correlation between RDW level and duration of PICU stay with p-value =0.001. There was a statistically significant positive correlation between RDW level, serum lactate with p-value <0.001and CRP level with p-value <0.001. There is a statistically significant negative correlation between RDW level and serum fibrinogen with a p-value <0.001. There was a statistically significant positive correlation between RDW level and FiO2 with a p-value <0.001.

There is a statistically significant negative correlation between RDW level and SPO2 with a p-value <0.001. There was a statistically significant positive correlation between RDW level, PRISM III, SOFA, PLEOD II, and PMODS scores with a p-value <0.001. High RDW > 16.9 had a statistically significant predictor for the survival of critically ill children with p-value <0.001 as presented in (table 7)

TABLE 8: Kaplan– Meier survival analysis illustrating PICU survival rate differences in patients as regard ROC curve-derived RDW levels

RDW Level	Total N	N of Deaths	Censored		PICU Survival rate%	Log Rank	Sig.
			N	Percent			
Low RDW ≤ 16.9	52	0	52	100.0%	100.0%	51.9	<0.001
High RDW >16.9	59	47	12	20.3%	16.7%		
Overall	111	47	64	57.7%	37.6%		

High RDW > 16.9 has a statistically significant predictor for the survival of critically ill children with a p-value <0.001.

TABLE 9: Univariate Cox-regression analyses of different scores and RDW% for PICU Survival

	β	SE	P	HR	95.0% CI for HR
PRISM III	0.481	0.078	<0.001	1.618	1.388-1.885
PSOFA	0.484	0.074	<0.001	1.622	1.404-1.874
PELOD II	0.312	0.045	<0.001	1.366	1.250-1.493
PMODS	0.534	0.086	<0.001	1.706	1.441-2.019
RDW %	0.349	0.047	<0.001	1.418	1.294-1.553

β: regression coefficient; SE: standard error; HR: hazard ratio; 95%CI: 95% confidence interval, P-value <0.05 is significant

Univariate regression analysis shows that PRISM III, PSOFA, PLEOD II, PMODS, and RDW% had a statistically significant effect on PICU survival among critically ill children with p-value <0.001. as presented in table (9)

TABLE 10: Multivariate Cox-regression analyses models of RDW% with each score and for PICU Survival

	β	SE	P	HR	95.0% CI for HR
Model.1					
RDW %	0.161	0.072	0.026	1.175	1.020-1.353
PSOFA	0.371	0.096	<0.001	1.450	1.202-1.748
Model.2					
RDW %	0.058	0.078	0.453	1.060	0.910-1.234
PRISM III	0.450	0.090	<0.001	1.568	1.315-1.869
Model.3					
RDW %	0.120	0.085	0.157	1.127	0.955-1.331
PELOD II	0.236	0.071	0.001	1.266	1.102-1.453
Model.4					
RDW %	0.220	0.067	0.001	1.246	1.091-1.422
PMODS	0.312	0.114	0.006	1.366	1.093-1.708

All variables with P-value <0.05 in univariate analysis were entered in the multivariate regression model Four multivariate cox regression models were constructed to avoid multicollinearity with the covariates

Multivariate regression analysis shows that RDW % and PSOFA score together had a statistically significant predictor for PICU survival among critically ill children, and RDW% with PMODS score together had a statistically significant predictor for PICU survival among critically ill children with p-value <0.001and 0.006. RDW % was an independent predictor for PICU Survival in models 1, 4 including PSOFA and PMODS, respectively (table 10)

DISCUSSION

Red blood cell (RDW) has been reported as a strong prognostic factor in several diseases of various organ systems, including the cardiovascular, respiratory, renal, neurologic, and gastrointestinal systems (4) However, few studies have investigated RDW in children, especially in the critically ill pediatric population (5)

In critically ill children, it is crucial to promptly and accurately assess the severity of illness and organ dysfunction and predict outcomes for prompt management. For this purpose, many studies have investigated proper prognostic factors including several scoring systems such as the pediatric risk of mortality (PRISM), pediatric sequential organ failure assessment (pSOFA), pediatric logistic organ dysfunction-2 (PELOD-2), and pediatric multiple organ dysfunction syndrome (p-MODS) (1).

The current study found statistically significant increased RDW among non-survived critically ill children with p-value <0.001. this goes in run with Sachdev et al. study which was conducted on 101 critically ill children to evaluate the association between RDW and mortality among critically ill children and found statistically significant elevated RDW among non-survived children with p-value =0.007 (10). Similarly, Ramby et al. found that RDW was independently associated with PICU mortality with p-value=0.001 (11). Sukewanti et al. study also found statistically significant higher RDW among non-survived critically ill children with p-value =0.001 (12).

The current study found a statistically significant association between higher RDW group critically ill children and longer duration of admission with p-value =0.015. This goes in run with Said et al. which was conducted on 3913 critically ill children to investigate the association of RDW with morbidity and mortality in critically ill children and found a statistically significant association between high RDW >14.8 and length of PICU stay with p-value <0.001 (13).

The current study found a statistically significant association between higher RDW group critically ill children and lower Hb with p-value =0.037. This goes in a run with Said et al. which found a statistically significant association between high RDW >14.8 and lower Hb with a p-value <0.001 (13).

The current study found a statistically significant association between higher RDW group critically ill children and higher lactate with p-value =0.016. this goes in a run with Sukewanti et al. study which was conducted on 68 critically ill children to evaluate the correlation between lactate level and RDW in critically ill children and found a statistically significant positive correlation between RDW and lactate level with p-value <0.001 (12). This can be explained as both RDW and lactate increase in similar conditions such as hypoxemia, inflammation, and altered tissue perfusion, which are found in various underlying diseases in critically ill patients, which supports that RDW might be used as a prognostic marker in critically ill patients (12).

The current study found a statistically significant association between higher RDW group critically ill children and higher CRP with a p-value <0.001. this goes in run with Ha et al. study which revealed a statistically significant association between high RDW and high CRP with a p-value <0.001 (14). Similarly, RDW was reported to have a strong association with inflammatory markers (15). This can be explained as inflammatory mediators can lead to newer and larger reticulocytes entering the peripheral circulation and increasing RDW, indicating that RDW also reflects the severity of inflammation (7).

Another explanation is oxidative stress as erythrocytes usually have an excellent antioxidant capacity and serve as the primary (oxidative sink) which could be prone to oxidative damage (14). Oxidative stress plays a role in RBC homeostasis such as fragility, maturation, and a lifespan that reduces RBC survival. It also affects many biological processes, including apoptosis and inflammatory reactions, which could change the size of RBC, consequently increasing RDW (8).

Also, this can be attributed to poor nutritional status, activation of the renin-angiotensin system, and impaired renal function (8).

The current study found a statistically significant association between higher RDW group critically ill children and higher FIO2 and SPO2 with p-value <0.001, and 0.001. Similarly, Hartawan et al. conducted a study on 60 critically ill children to the evaluated correlation between RDW and duration of mechanical ventilation and found a statistically significant positive correlation between RDW and FiO2 with p-value <0.05, r=0.82 (16).

An increased RDW can lead to hypoxemia as a transient decrease in PaO2 will lead to erythropoietin release through hypoxia-inducible transcription factors. These will trigger the release of immature reticulocytes into the circulation, leading to an anisocytosis pathway, elevated RDW values have been found in diverse respiratory diseases. Schepens et al. reported that patients with higher RDW upon admission are associated with a greater need for invasive mechanical ventilation, lower 28-day ventilator-free days, and lower P/F ratios (5).

The current study found a statistically significant association between higher RDW group critically ill children and higher severity scores (PRISM III, PSOFA, PLEOD II, and PMODS) with a p-value <0.001. This goes in run with the Ha et al. study which was conducted on 960 critically ill children who were admitted to PICU to evaluate RDW as a strong predictor marker of severity of critical illness and found that high RDW >16.5 was significantly related to severity scores (PRISM III, pSOFA, PELOD II, and pMODS) with p-value <0.001, 0.001, 0.017 and <0.001 respectively (14).

The current study found a statistically significant association between higher RDW group critically ill children and the use of MV and inotropes with p-value <0.001. This goes in run with Ha et al. study which evaluated RDW in 960 critically ill children and revealed statistically significant higher RDW among critically ill children who needed vasoactive drugs and mechanical ventilation with p-value <0.05 (14).

Our study revealed that higher RDW>16.9 was significantly associated with mortality with a p-value <0.001. Bazick et al. study reported that RDW was a strong predictor of mortality among critically ill children with 2.8-5 fold higher mortality in patients with RDW values >15.8% (17). Another study by Khanbabaee et al. also revealed a statistically significant association between high RDW and mortality among critically ill children with sepsis with a p-value =0.017 (18). This goes in run with Ha et al. study which found that high RDW >16.5 was significantly related to PICU mortality with a p-value =0.002 (14).

RDW is a simple routinely reported measurement without additional effort or costs, it is advantageous as a prognostic factor. furthermore, although it has been controversial whether or not adding RDW improves the discrimination and performance for outcome prediction of some previously used scores or models, our study shows a significant improvement in the performance of prediction of PICU mortality assessed using the cNRI test, which could prove its validity (19).

The current study found a statistically significant negative correlation between RDW and Hb level with p-value =0.007. This goes in run with Sukewanti et al. study which found that RDW inversely correlated with hemoglobin with p-value=0.002 (12). This can be explained as the associated inflammation and sepsis among critically ill children leading to proinflammatory cytokines such as tumor necrosis factor α, interleukin 6, and interleukin 1B which could suppress RBC maturation and decrease the half-life of RBCs. Therefore, the inflammatory response could lead to elevated RDW (20).

CONCLUSION

Red blood cell distribution width (RDW) is a simple non-invasive reliable marker that is already a part of routine complete blood picture (CBC). Its measurement is simple, inexpensive, non-invasive, and convenient, thus, it could be a promising additional prognostic factor in critically ill children. RDW is a good predictor of critical illness severity in paediatrics being significantly correlated with severity scores including SOFA, PLEOD II, and PRISM scores, and with different laboratory and inflammatory markers such as haemoglobin, platelets, C-reactive protein, Erythrocyte Sedimentation Rate, Ferritin, fibrinogen, and procalcitonin. RDW in critically ill children is strongly associated with PICU mortality and poor clinical parameters such as higher severity scores, use of inotropic drugs, and MV support. RDW is a significant predictor for mortality being high among non-survived critically ill children.

REFERENCES

1. Matics TJ, & Sanchez-Pinto LN. Adaptation and validation of a pediatric sequential organ failure assessment score and evaluation of the sepsis-3 definitions in critically ill children. JAMA pediatrics. 171(10), e172352-e172352. 2017
2. Graciano AL, Balko JA, Rahn DS, Ahmad N, & Giroir BP. The Pediatric Multiple Organ Dysfunction Score (P-MODS): development and validation of an objective scale to measure the severity of multiple organ dysfunction in critically ill children. Critical care medicine, 33(7), 1484-1491. 2005.
3. Jo YH, Kim K, Lee JH, Kang C, Kim T, Park HM, & Rhee, J. E. Red cell distribution width is a prognostic factor in severe sepsis and septic shock. The American journal of emergency medicine, 31(3), 545-548. 2013.
4. Wang B, Lu H, Gong Y, Ying B, & Cheng B. The association between red blood cell distribution width and mortality in critically ill patients with acute kidney injury. BioMed Research International, 2018.
5. Schepens T, De Dooy JJ, Verbrugghe W, & Jorens PG. Red cell distribution width (RDW) as a biomarker for respiratory failure in a pediatric ICU. Journal of Inflammation. 14(1), 1-7. 2017.
6. Fujita B, Strodthoff D, Fritzenwanger M, Pfeil A, Ferrari M, Goebel B, & Jung C. Altered red blood cell distribution width in overweight adolescents and its association with markers of inflammation. Pediatric obesity, 8(5), 385-391. 2013.
7. Sadaka F, O'Brien J, & Prakash S. Red cell distribution width and outcome in patients with septic shock. Journal of intensive care medicine, 28(5), 307-313. 2013.
8. Semba RD, Patel KV, Ferrucci L, Sun K, Roy CN, Guralnik JM, & Fried L. P. Serum antioxidants and inflammation predict red cell distribution width in older women: the Women's Health and Aging Study I. Clinical nutrition, 29(5), 600-604.2010
9. Kumar S, Sudhakar A, Mohan M, Balachandran R, Raj B, Sumangala SG, Kumar RK. Elevated red cell distribution width is associated with delayed postoperative recovery after correction of Tetralogy of Fallot. Annals of pediatric cardiology. 6(2):121. Jul 2013.
10. Sachdev A, Simalti A, Kumar A, Gupta N, Gupta D, & Chugh P. Outcome prediction value of red cell distribution width in critically-ill children. Indian pediatrics, 55(5), 414-416. 2018.
11. Ramby AL, Goodman DM, Wald EL, Weiss SL. Red Blood Cell Distribution Width as a Pragmatic Marker for Outcome in Pediatric Critical Illness. PLoS One . 10(6):e0129258.2015
12. Sukewanti NM, Hartawan INB, Wati DK, Suparyatha IBG, & Ryalino C. Correlation of red cell distribution width and serum lactate levels in critically ill pediatric patients. Bali Journal of Anesthesiology, 4(3), 104. 2020.
13. Said AS, Spinella PC, Hartman ME, Steffen KM, Jackups Jr R, Holubkov R & Doctor A. Red blood cell distribution width: biomarker for red cell dysfunction and critical illness outcome?. Pediatric critical care medicine: a journal of the Society of Critical Care Medicine and the World Federation of Pediatric Intensive and Critical Care Societies, 18(2), 134. 2017.
14. Ha EJ, Park SJ, & Jhang WK. Evaluation of the usefulness of red blood cell distribution width in critically ill pediatric patients. Medicine, 99(36). 2020
15. Jo YH, Kim K, Lee JH, Kang C, Kim T, Park HM, & Rhee, J. E. Red cell distribution width is a prognostic factor in severe sepsis and septic shock. The American journal of emergency medicine, 31(3), 545-548. 2013.
16. Hartawan INB, Saputra Y, & Ryalino C. Correlation of red cell distribution width value with the duration of mechanical ventilator usage in patients treated in pediatric intensive care unit. Bali Journal of Anesthesiology, 4(3), 99.2020
17. Bazick HS, Chang D, Mahadevappa K, Gibbons FK, & Christopher KB. Red Cell Distribution Width and all cause mortality in critically ill patients. Critical care medicine, 39(8), 1913.2011

18. Khanbabaee G, Hashemi SM, Salarian S, Fariborzi MR, & Kiumarsi A. Red cell distribution width elevation and sepsis in pediatric critically ill patients. Archives of Pediatric Infectious Diseases, 6(2). 2018
19. Hunziker S, Celi LA, Lee J, Howell MD. Red cell distribution width improves the simplified acute physiology score for risk prediction in unselected critically ill patients. Crit Care . 16(3):R89.2012
20. Agarwal AM. Diagnostic approach to Anemia. University of Utah School of Medicine, Department of Pathology, ARUP Laboratories. 2014.

J Popul Ther Clin Pharmacol Vol 30(3):e106–e116; 20 January 2023.