International Journal Dental and Medical Sciences Research
Volume 6, Issue 4, July-Aug 2024 pp 476-480 www.ijdmsrjournal.com ISSN: 2582-6018

Prognostic Significance of Red Cell Distribution Width in Critically ill Children

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Submitted: 20-08-2024 Accepted: 30-08-2024

ABSTRACT:
BACKGROUND: Paediatric intensive care units (PICU) with growing life sustaining technologies have resulted inadvanced care for children and adolescents. Moreover, characterizing the disease severity at admission and assessing risk factors correlating with mortality can help improve the quality of patient care. By means of simple laboratory values this goal seems to be attainable.
Red cell distribution width (RDW) is a laboratory parameter which expresses the variability in red blood cell size and is calculated as the standard deviation in red blood cell (RBC) size divided by the mean corpuscular volume (MCV). Clinically, it is a widely available and low-cost test. Its normal range is between 11.5–14.5%. Reference ranges may vary depending on the individual. RDW has been recently reported as a strong prognostic factor in several diseases.
OBJECTIVES: To study the association between red cell distribution width (RDW) and mortality in critically-ill children admitted in Paediatric Intensive Care Unit at SMCH.
METHODS: 220 participants were recruited consecutively over a 6 monthsperiod. Data collected included demographics, vital parameters, laboratory values, severity and organ failure scores, RDW for the first 5 days of admission, duration of PICU stay and survival outcome.
RESULTS: 20 patients died during study period. High RDW at admission (RDW D1) correlated significantly with mortality (P=0.007). The odds of death increased by 15 to 23 times with rise in RDW D1 from 18% to >21%. The optimal RDW D1 cut-off value for mortality was 18.6%, which yielded sensitivity 90.9%, specificity 70.8%, positive predictive value 27.8%, negative predictive value 98.4%, and area under curve (AUC) 0.83 (95%CI 0.737, 0.925). 29 out of 60 (48.3%) patients with RDW D4 >18% had PICU stay of ≥7 days
INTERPRETATION AND CONCLUSION: High RDW (≥18.6%) at admission and persistently high levels are linked to higher fatality rates and longer stays in the PICU.

KEYWORDS: Risk Factors, Predictors, Critically Ill, Red Cell Distribution Width

I. INTRODUCTION

Red blood cell (RBC) distribution width (RDW), calculated by dividing the standard deviation of RBC volume by the mean corpuscular volume and multiplied by 100, is routinely reported as part of the complete blood count (CBC) using automated flow cytometry. RDW has been traditionally used as additional information in the differential diagnosis of the cause of anaemia.[1] 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.[2] It also showed significant associations with ventilator-free days, postoperative outcome, intensive care unit (ICU) discharge outcome, out-of-hospital outcome, and all-cause mortality in critically ill patients.[3]

However, most studies were conducted in adult patients. Only a few studies have investigated RDW in children, especially in the critically ill paediatric population.[4]In these 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 paediatric risk of mortality (PRISM), paediatric sequential organ failure assessment (pSOFA), paediatric logistic organ dysfunction-2 (PELOD-2), and paediatric multiple organ dysfunction syndrome (pMODS) [5]. 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.[6]

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

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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 [7]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[8]

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 Paediatric Index of Mortality version 2(PIM2) score, Acute Physiology and Chronic Health Evaluation II (APACHE II) score, lactate, and others.[9]

II. OBJECTIVES OF STUDY

To study the association between red cell distribution width (RDW) and mortality in critically-ill children admitted in Paediatric Intensive Care Unit at SMCH.

III. METHODS

Study population-Children aged between 1month to 12 years admitted to the PICU at Silchar Medical College and Hospital, a tertiary care hospital in Assam

Study period February 2024 to July 2024 (6months)
Study design Prospective Cross-sectional study

Sample size -The prevalence of PICU mortality as per previous study was 16.9%. So, for this study p= 0.169

- The formula used for sample size calculation is as follows:
- $n = 4pq/D^2$
- $n = 4pq/D^2 = 0.539/0.0025 = 216$ (approx. 220)

At site : total sample size: 220 children admitted in the PICU at SMCH during the study period

Sampling Method Purposive Sampling
Inclusion criteria
All sick patients admitted in the PICU at SMCH during the study period; ages ranging from 1 month to 12 years.

Exclusion criteria

I. Age more than 12 years
II. Chronic Renal Failure
III. Chronic Metabolic Disease
IV. Cancer
V. Chronic haematological Diseases with the potential to change RDW
VI. History of Blood transfusion within 72 hours

Methodology

- This observational study was conducted in PICU of Silchar Medical College and Hospital, Assam, India.
- Participants were recruited consecutively over 6 months.
- Data included variables like demographics, vital parameters, complete blood count, serum electrolytes, and microbiological profile.
- It further includes Pediatric Risk of Mortality Score (PRISM) score at 12 and 24 hours, daily Pediatric Logistic Organ Dysfunction (PELOD) score, mechanical ventilation days, inotropes, renal replacement therapy, duration of PICU stay and final outcome (discharge or death).
- The RDW values were recorded at admission and for the next 5 days. CBC, including RDW estimation was performed by automatic blood analyzer.

Statistical Analysis-Quantitative variables were compared using unpaired t-test/Mann-Whitney test. Qualitative variables were compared using Chi-square/ Fisher exact test. A receiver operating characteristic (ROC) curve was used to determine the optimal cut-off value for RDW at admission (RDW D1). The area under curve (AUC) with 95% confidence interval (CI), sensitivity, specificity, positive predictive value and negative predictive value were calculated to analyse the diagnostic accuracy of RDW D1 to predict mortality. A two-sided P value of less than 0.05 was considered statistically significant. All analyses were performed with SPSS version 17.0.

IV. RESULTS

One hundred fifteen children admitted in PICU wereassessed; Fifty patientspresented with shock at admission; 20 (9%) children died during study period.**TableI** compares the variables between survivors anddeaths. Admission haemoglobin was inversely related toRDW D1 (r=–0.3, P=0.02) but there was no significantdifference in the haemoglobin levels between survivorsand deaths. High RDW at admission (RDW D1)correlated significantly with mortality (P=0.007). Theodds of death increased to 15 to 23 times with rise inRDW D1 from 18% to more than

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21% (**Table II**). Of the 20 patients who died, 16 had RDW D1 >18.6%(P<0.001). The optimal RDW D1 cut-off value formortality was 18.6% with sensitivity 90.9%, specificity70.8%, positive predictive value 27.8% and negativepredictive value 98.4%. The area (95% CI) under ROCwas 0.83 (0.737, 0.925).The median stay in PICU was 3.6 days. Twenty-nineout of 60 (48.3%) patients on day 4 with RDW >18% hadPICU stay of ≥7 days. 90 patients hadevidence of infection at admission. The median RDW onday 3 (18 vs 15.4; P=0.02), day 4 (18.4 vs 15.4; P=0.02)and day 5 (18.1 vs 15.2; P=0.02) were significantlyhigher among children with infection as compared to children without infection.

Table I Characteristics of Survivors and Non-Survivors

VARIABLE	DEATHS (n=20)	SURVIVORS (n=200)
Age (Months)	36	60
Male n(%)	14 (70)	120 (54)
Female n(%)	6 (30)	80 (36)
Heart Rate (/min)	154	142
SBP(mmHg)	87.2	89.5
DBP(mmHg)	56.3	61
MAP(mmHg)	65	68.7
RR(/min)	54	40
Temp(°C)	37.8	37.5
RDW		
Day 1	20	16.5
Day 2	21	17.6
Day 3	21	20.5
Day 4	20.7	18.2
Day 5	18	17.7
Hb(g/dl)	9.4	9.8
CRP(>6mg/dl) n(%)	20 (100)	98 (44)
PRISM 12	22.4	6.9
PRISM 14	22.5	4.1
PELODS		
Day 1	31.4	7.6
Day 2	33.2	7.1
Day 3	27.5	6.6
Day 4	22	5.2
Day 5	14.9	5
MODS n(%)	18 (90)	20 (09)
MV n(%)	20 (100)	80 (36)
Inotropes ,n(%)	20 (100)	60 (27)

Table II Admission Red Cell Distribution Width (Day 1) Quantiles and Odds Ratio of Death

Day 1 RDW Quantiles	Survivor, n=200	Non-Survivor,n=20	Odds Ratio (95% CI)	P value
15.7-18.04	38	2	1.05 (0.95,1.16)	1.00
18.04-21.5	30	8	1.26 (1.00,1.59)	0.04
≤21.5	30	10	1.4 (1.06,1.83)	0.02

V. DISCUSSION

Discussion

This observational study demonstrated that high RDW levels at admission can predict death in the PICU, and persistently elevated RDW values are related with longer PICU stays. The study's limitations include its short duration and limited sample size.Other limitations include a lack of disease-specific data and failure to statistically control for other risk variables associated with death.

Elevated RDW has been linked to several causes of death and long-term mortality in specific demographics and disease sub-populations [10].Elevated RDW has been linked to inflammation markers such as interleukin-6 and

CRP [11], increased erythrocyte sedimentation, impaired iron mobilisation, oxidative stress, ineffective red cell production, and increased red cell destruction [12–14]. Pro-inflammatory cytokines reduce erythrocyte maturation, shorten half-life, and distort the RBC membrane, allowing bigger reticulocytes to enter the peripheral circulation and raise RDW [15].RDW may indicate membrane integrity, while high RDW may indicate membrane instability [16]. The release of immature cells with low oxygen-binding capacity indicates a poor response to oxidative stress. This may explain why the link between RDW and clinical outcome is independent of acute disease severity and inflammation level [17]. Although anaemia is a risk factor for death in the under-5 age group [18], haemoglobin levels above 7 g/dL do not necessarily correspond with mortality [19].

In our investigation, a high RDW was linked to death but not to haemoglobin levels. Patients with and without infections did not significantly differ in their entrance RDW values; however, the former group had persistently high RDW values, which are likely indicative of a prolonged inflammatory response. High RDW at admission and levels that remain high over time appear to be linked to mortality and extended PICU stays. In areas with limited resources, red cell distribution width may be utilised as a predictor of outcome for children admitted to the PICU.

VI. LIMITATIONS

The study's limitations include its short duration and limited sample size. additional limitations were a lack of segregated data by disease profile and a failure to statistically adjust additional risk factors for mortality.

VII. CONCLUSION

High RDW (≥18.6%) at admission and persistently high levels are linked to higher fatality rates and longer stays in the PICU.

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