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Original Research Article

A study on the predictive value of red blood cell distribution width as a biomarker of outcome in paediatric critical illness

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ABSTRACT

Background: One of the pediatric population's interest group is critically sick children requiring medical aid services, since these children are at an extreme risk of death. Red cell distribution width (RDW) measures the variability in red corpuscle size and is calculated as proportional variation in mean corpuscular cell volume (MCV), with a traditional vary of 11.5-14.5%. The ensuing acute rise in RDW could thus say the degree of the underlying inflammatory state and supply helpful prognostic data regarding intensity of resource utilization and risk of mortality. The aim and objectives were to determine the association between RDW and mortality in critically ill children admitted to PICU.
Methods: A cross sectional observational study was conducted among 103 children in the age group of 2 months to 18 years admitted to PICU at SMIMER Hospital.
Results: In this study, mean age of survivors was 16.8 years. Among survivors group, in 35 (42.1%) cases there was respiratory system involvement followed by CNS involvement in 19 (22.8%) cases while in non-survivors group only in 7 (35%) cases respiratory system was involved, in 2(10%) cases CNS involved. In RDW quartile range of 16.1-19.0, 46 cases had survived and 11 deaths were noted and significant difference was found between RDW quartiles and odd's ratio of survivor and non-survivor group.
Conclusions: Raised RDW levels have been seen strongly associated with mortality and poor clinical parameters, including use of vasoactive-ionotropic drugs, oxygen as well as mechanical ventilator support. Hence, RDW can be used as a biomarker in prediction of risk mortality in PICU.

Keywords: Biomarkers, Critical illness, Paediatrics, Red blood cell, Outcome

INTRODUCTION

One of the pediatric population's interest group is critically sick children requiring medical aid services, since these children are at an extreme risk of death. In recent times, intensive care medicine has become extremely specialized covering many fields of medicine. Whereas the overall variety of hospital beds within the USA diminished by 26.4% from the year 1985 to 2000, while intensive care unit (ICU) beds increased by 26.2% during the same era. This signifies the high demand for intensive care medicine. Mortality rates within the ICU powerfully depends on the severity of the sickness and also the patient population analysed, and 6.4% to 40% of critically sick patients are reported to die.[1]

Mostly, information on specific prognostic criteria for single diseases is revealed. However, very little is thought on the precise causes of death and also the impact of general risk factors that will uniformly complicate the course of critically sick patients no matter the underlying illness.[2] Data of such general determinants of outcome in an exceedingly critically sick patient population wouldn't solely facilitate improve prognostic analysis of ICU

patients, but also indicate what medical aid and analysis will enhance the short and long run outcomes of those patients.[3]

Red cell distribution width (RDW) measures the variability in red corpuscle size and is calculated as proportional variation in mean corpuscular cell volume (MCV), with a traditional vary of 11.5-14.5%.[4] It's an easy, affordable, and easily available measure reported as a part of a whole blood count (CBC). Many recent studies consider that RDW may be helpful as a biomarker of severity of disease and clinical outcomes in critically sick patients. An elevated RDW is an independent predictor of all-cause mortality in infection, congestive heart failure, and adult critical illness, and has been shown to enhance acute physiology grading for risk prediction in critically sick adults.[2-8]

Increased RDW values indicates bigger variability in RBC size, that usually indicates dysfunctional erythropoiesis, shortened lifespan of RBC, or premature release of reticulocytes from the bone marrow into the peripheral circulation. The ensuing acute rise in RDW could thus say the degree of the underlying inflammatory state and supply helpful prognostic data regarding intensity of resource utilization and risk of mortality. The characterization of such as a promptly offered biomarker could give an easy, pragmatic tool to stratify patients by severity of health problem and determine those in danger for who could require higher resource utilization and poor outcomes to facilitate targeted interventions and triage decisions without adding any extra cost or the requirement for a completely unique laboratory assay. Therefore, we opted to study the association of RDW at PICU admission with length of hospitalization (LOH) and mortality to work out its potential application as a practical biomarker within the critically sick paediatric population.[9,10]

Scoring systems are utilized for analysis of the patient's mortality risk within the ICU by giving a score to patient and predicting the end result. However, patient's mortality isn't solely tormented by ICU performance, instead also depends on several alternative factors like demographic and clinical characteristic of population, infrastructure and non-medical factors (management and organization), case mix and admission practice. Many grading systems just like the paediatric risk of mortality (PRISM) and paediatric index of mortality (PIM) are used to predict the danger of a patient's mortality within the PICU. However, these grading systems are long and cumbersome; thus there's a desire to seek out an easy technique that may facilitate in characterizing the patients having a high risk of mortality.[11]

Ever since the introduction of mortality scores within the ICU, they been used a lot often these days and the scores are a part of the methodology of quality control and research.[12] They're helpful for evaluating the standard of care, prognosis and to estimate the danger of mortality and to evaluate different services regarding to the complexity underlying illness.[13,14]

Aim and objectives

The aim and objectives of the study were to determine the association between RDW and mortality in critically ill children admitted to PICU.

METHODS

A cross-sectional observational study was conducted among 103 children in the age group of 2 months to 18 years admitted to PICU at SMIMER hospital. Patient death within 1 hour of PICU admission, lack of complete blood count (CBC) report within 24 hours of PICU admission, elective admission to PICU after elective surgery and re-admission to PICU during the study period were excluded.

The institutional ethical committee permission was taken prior to the study. The procedure to be performed was explained to the patient's guardian/relatives and written informed consent was taken. Data included variables like demographics, vital parameters, complete blood counts, serum electrolytes and microbiological profile were collected. Paediatric risk of mortality 3 (PRISM 3) score was used to estimate mortality risk on PICU admission using physiologic and laboratory variables within first 24 hours of admission in PICU.

Data entry and analysis

Data were netted into Microsoft excel sheet and analyzed by using statistical package for the social sciences (SPSS) software version 24. Qualitative data were described as a frequency and percentages and analyzed by using Chi square test. Quantitative data were described as mean and SD and analyzed by using Z test. Receiver operator curve (ROC) was used to determine optimal cut off value for RDW on admission. The area under curve (AUC) with 95% confidence interval (CI), sensitivity, specificity, positive and negative predictive values were calculated to analyze the accuracy of RDW to predict the mortality.

RESULTS

The total number of patients admitted in PICU during the study period were 513 after which excluding the patients according to exclusion criteria, 103 patients were enrolled. Out of the total patients enrolled, 83 (80.5%) were survivors and 20 (19.4%) were non-survivors.

In our study, out of the total among survivors, majority of the participants (27) belonged to 1-5 years of age, while 7 participants belonged to more than 12 years of age. Mean age of survivors was 16.8 years. In non-survivor group, most (30%) of the study cases belonged to 1 to 5 years age group. Only 4 deaths were noted in 6 to 12 years of age group children. The mean age of non-survivor group was 3.2 years. There were 40 and 8 males in survivors and non-

survivor group respectively. There was no significant difference found between Gender and survival probability (Figure 1).

In the study, among survivors group, 35 cases were having respiratory involvement followed by 19 cases having CNS involvement and 12 cases having GIT involvement. While in non-survivors group only in 7 cases respiratory involvement, in 2 cases CNS involvement as well as in 4 cases GIT involvement was found. There was a significant association found between respiratory system, CNS, GIT as well as poisoning system involvement and both the groups. The mean PRISM 3 score among survivors and non-survivors was respectively 5.65 and 7.94. a significant difference was found between PRISM 3 score of both the groups. Statistically significant difference was found among respiratory rate of both the groups. While, other all vital parameters were statistically not significant among both the groups. In PRISM 3 score, statistical significant difference was found among both the groups (Table 1).

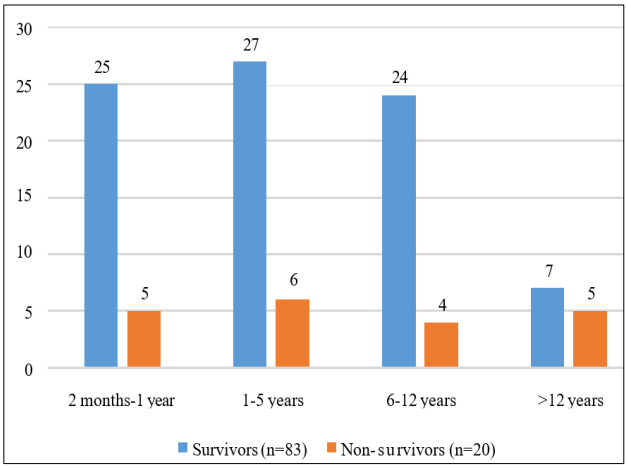

Figure 1: Age wise distribution of study participants.

There was statistically significant difference found between admission RDW level among both the groups as well as peak RDW level among both the groups. The relative change in RDW were 0.54 and 0.71, respectively among survivors and non-survivors groups. Also no significant difference was found between relative change in RDW among both groups (Table 2).

At the time of admission according to RDW level <16.4, 2 cases were found who required ionotropics support while in >16.4 RDW level, 2 cases were found who required ionotropics support. The oxygen requirement was almost similar in both the groups at the time of admission. It was observed that mechanical ventilator support requirement was higher in cases having RDW less than 16.4. Also, the length of hospital stay was more in the group who had more than 16.4 RDW. There was no association found between ionotropics use, oxygen and ventilator support among group A having RDW less than and more than 16.4 mg/dl. At the time of peak RDW according to RDW level <19.5, 1 case was found who required ionotropics support while in >19.5 RDW level, 3 cases were found who required ionotropics support. The oxygen requirement was higher in group who had more than 19.5 RDW level. It was observed that mechanical ventilator support requirement was higher in cases having RDW more than 19.5. Also, the length of hospital stay was more in the group who had more than 19.5 RDW level. There was association found between ionotropics use, oxygen and ventilator support among group B having RDW less than and more than 19.5 mg/dl (Table 3).

In this study, 13.1-16 RDW quartile was found among 27 patients in which 19 were survivors and 8 were non-survivors. There was no significant difference found between RDW quartiles and odd's ratio of survivors and non-survivors group. Among 16.1-19 RDW quartile level, 46 cases had survived and 11 deaths were noted. In this quartile range, there was significant difference found between RDW quartiles and odd's ratio of survivors and non-survivors group. Among >19 RDW quartile level, 18 cases had survived and 1 death was noted. In this quartile range, there was significant difference found between RDW quartiles and odd's ratio of survivors and non-survivors group (Table 4).

There was a satisfactory association found by ROC curve analysis among admission RDW level and mortality of patients in PICU. Overall sensitivity of RDW is 80.6% and specificity was 69.7% found. The AUC was 0.833 (Figure 2).

Table 1: Clinical characteristics.

Parameters	Survivors (n=83)	Non survivors (n=20)	P value
Reason for admission			
Respiratory	35 (42.1)	7 (35)	0.0445
CNS	19 (22.8)	2 (10)	0.002
CVS	0 (0)	1 (5)	0.128
GIT	12 (14.4)	4 (20)	0.031
Renal	0 (0)	1 (5)	0.27
Endocrine	5 (6)	0 (0)	0.34
Poisoning	4 (4.8)	0 (0)	0.014
Hematology	2 (2.4)	1 (5)	0.245

Continued.

Parameters	Survivors (n=83)	Non survivors (n=20)	P value
Infectious	7 (8.4)	0 (0)	0.14
Vital signs (mean±SD)			
Temperature	99.15 (1.11)	99.048 (1.01)	0.716
Pulse rate	115.75 (22.5)	110.88 (25.24)	0.474
Respiratory rate	48.061 (3.9)	37.28 (15.18)	0.013
BP	104 (10.05)	101.6 (10.7)	0.439
DBP	62.6 (11.26)	63.5 (9.06)	0.805
SpO_2	96.56 (3.21)	106.5 (97.7)	0.684
PRISM 3 score (mean±SD)	5.65 (3.8)	7.94 (5.81)	0.0001

Table 2: Admission and peak survivors: RDW amongst survivors and non survivors.

RDW	Survivors	Non survivors	P value
Admission RDW	16.81±2.47	17.43±3.51	0.0345
Peak RDW	17.51±4.78	22.43±1.39	0.028
Relative change in RDW	0.54±0.558	0.71±0.632	0.2361

Table 3: Relation of admission and peak RDW to various outcome parameters.

RDW quartile	Survivors (n=83)	Non survivors (n=20)	Odds ratio (95% confidence interval)	P value
13.1-16.0	19	8	0.44 (0.12 – 1.3)	0.115
16.1-19.0	46	11	1.01 (0.88-1.4)	0.00012
>19.1	18	1	5.26 (3.8-6.7)	0.084

Table 4: RDW quartile and ODD ratios among study participants.

Variables	Admission RDW		P value	Peak RDW		P value
	<16.4	>16.4		<19.5	>19.5	
Ionotropics support (n=4)	2 (47)	2 (52)	0.6807	1 (25)	3 (75)	0.008
Oxygen support (n=90)	44 (11.1)	46 (88.9)	0.3938	10 (11.1)	80 (88.9)	0.0001
Mechanical ventilatory support (n=9)	6 (22.2)	3 (77.7)	0.3946	2 (2.22)	7 (77.7)	0.0001
Length of stay (mean±SD)	4.83±0.92	5.33±1.7	0.07	3.33±6	5±4.71	0.5180

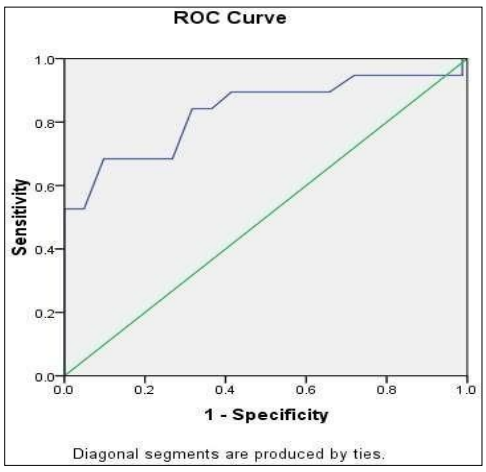

Figure 2: ROC Curve based on admission RDW cutoff of 16.4.

RDW cut off: 16.4, AUOC: 0.833, sensitivity: 80.6%, specificity 69.7%

The AUC of the given ROC is suggestive of excellent (0.967) association between peak RDW level and mortality. The sensitivity is 100% and specificity is 91.95% (Figure 3).

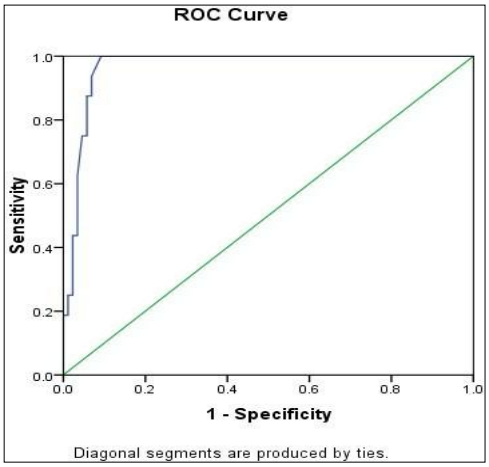

Figure 3: ROC curve based on peak RDW cutoff of 19.5.

Peak RDW cut off: 19.5, AUOC: 0.967, sensitivity: 100%, specificity 91.95%

DISCUSSION

This study was conducted to predict the mortality based on RDW value. Total 103 patients were enrolled out of which 83 (80.5%) survived. In present study mortality rate was 19.6% while in study of Rudrappa et al, Gauchan et al, and Sachdeva et al studies mortality rates were 14.28%, 17.6% and 10.89% respectively.

In the present study, mean age of survivors was 16.8 years. The mean age of non-survival group was 3.2 year. While in the study of Rudrappa et al, in survivor group, mean age was 4.5 years and in the non-survivor group mean age was 5.47 years. In Gauchan et al study the mean age of survivor and non-survivor group was 12.4 and 6.3 years, respectively.[15,16]

In present study, there were 40 and 8 males in survivors and non-survivors group respectively. Also, 43 and 8 females were respectively in survivors and non-survivors group. In Wang at al study, 35 and 15 were males, as well as 45 and 5 females in survivors and non-survivors group respectively.

In present study, the mean temperature among survivor group was 99.15 degree Celsius and in non-survivor group was 99.04 Celsius (p=0.716). While in study of Sachdeva et al, the mean temperature was respectively 98.9 and 97.9 among survivor and non-survivor group (p=0.684). In present study, the mean pulse rate among survivor group was 115.75 /minutes and in non-survivor group was 110.88/minutes (p=0.474). While in study of Sachdeva et al, the mean pulse rate was respectively 164.3 and 140.4 among survivor and non-survivor group (p=0.002). In present study, the mean respiratory rate among survivor group was 48.06/minutes and in non-survivor group was 37.28/minutes (p=0. 013). While in study of Sachdeva et al, the mean respiratory rate was respectively 50.2 and 41 among survivor and non-survivor group (p=0.001). In present study, the mean PRISM 3 score among survivor group was 5.65 and in non-survivor group was 7.94 (p=0.0001). While in study of Sachdeva et al, the mean PRISM 3 score was respectively 4.76 and 7.81 among survivor and non-survivor group (p=0.000).[17]

At the time of admission, the mean RDW in survivor group was 16.87 and in non-survivor group was 17.43. While peak RDW within first seven days of admission in survivor group was 17.51 and in non-survivor group was 22.43. Statistically significant difference was found between admission RDW level as well as peak RDW level among both the groups. As well as in study of Rudrappa et al, Gauchan et al, Sachdeva et al, studies there was a significant difference found between RDW at admission and RDW at peak level among both groups.[15-17]

There was a satisfactory association found by ROC analysis among admission RDW level and mortality of patients in PICU. Overall sensitivity of RDW is 80.6% and specificity 69.7%. The AUC was 0.833. The AUC of given the ROC showed excellent (0.967) association between peak RDW level and mortality. The sensitivity was 100% and specificity was 91.95%. In the research of Rudrappa et al, the AUC was 0.71.[15] While in the study of Gauchan et al, the AUC was 0.762, with sensitivity of 83.3% and specificity 59.7% which was on lower side than our study.[16] In the study of Rambey et al, the AUROC for RDW to predict LOS >48 hours and mortality was 0.61 (95% CI 0.56, 0.66) and 0.65 (95% CI 0.55, 0.75), respectively.[18]

In our study, there was no association found between ionotropics used, oxygen support and mechanical ventilator support among groups A and B that is RDW less than and more than 16.4 mg/dl. There was no association found between length of stay among both the groups in condition of RDW less than 16.4 mg/dl. While in the study of Gauchan et al, similar findings were seen in patients having RDW less than 14.5 mg/dl.[16] Although several previous studies reported an association of RDW with various clinical parameters in adults, there are few studies that included children.[19,20]

The elevation of RDW can occur from any disease process that reasons ineffective RBC production and releasing more premature RBCs into the blood circulation. This could be attributable to inflammatory and related process. It was well recognized that inflammatory cytokines interfere with the maturation of RBCs in the bone marrow through multiple mechanisms, such as the inhibition of the production of or response to erythropoietin, which damages iron metabolism and shortens RBC survival, in turn leading to high RDW.[21]

Limitations

It included only non-surgical patients. It was conducted at a single tertiary care centre. Additionally, the study was carried out over a relatively short duration, which may have restricted the assessment of long-term outcomes. Furthermore, the relatively small sample size may have reduced the statistical power of the study.

CONCLUSION

Raised RDW levels have been seen strongly associated with mortality and poor clinical parameters, including use of vasoactive-ionotropic drugs, oxygen as well as mechanical ventilator support. Hence, RDW can be used as a biomarker in prediction of risk mortality in PICU. RDW measurement is simple, inexpensive, and convenient as included in routine CBC. Thus, it could be a promising additional analytical factor in these patients. Furthermore, large studies with longer duration of follow-up are needed for the Indian setup.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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