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Association between Red Cell Distribution Width and Mortality in Pediatric Patients Admitted to Intensive Care Units

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ABSTRACT

Background: Red cell distribution width (RDW) is a routine laboratory measure that could be used as a predictor of mortality in critically ill patients. Identification of patients at risk for mortality early in the course of PICU admission is an important step in improving the outcome. We aimed to assess the use of RDW as an early biomarker for outcome in pediatric critical illnesses.
Methods: A retrospective study by extracting administrative and laboratory data from patients admitted to PICU of an academic pediatric teaching hospital was accomplished. After exclusion of 64 patients according to our exclusion criteria, 304 pediatric patients with PICU admissions over the 6 months of study period were included in the study.
Results: The mean RDW for all patients was 14.9%±2.5%. PICU mortality was 13.3%. The rate of mortality in the quartile of RDW>15.7% was 20.1%. Elevated RDW was associated with longer duration of PICU admission (P<0.001). Tracheal intubation and ventilator support was needed in 34.2% of the patients. This was also correlated with elevated RDW (P=0.043).
Conclusion: We observed that higher RDW was strongly linked to higher mortality risk in pediatric patients admitted in PICU. Higher RDW was associated with longer duration of PICU admission.

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Introduction

Pediatric intensive care units (PICU) with growing life-sustaining technologies have resulted in advanced 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 laboratory and patient's age. Elevated RDW on complete blood count reflects marked anisocytosis on peripheral blood smear review, which can be caused by any disease involving red blood cell (RBC) destruction or production.[1]

Studies have revealed that RDW could be used as a predictor of mortality in critically ill patients.[2,3] Although the mechanism of this relationship is not fully apparent, it seems that in critical illnesses, the acute systemic inflammatory response can alter both erythropoiesis and erythrocyte maturation.[4-9] In different contexts including sepsis, cardiovascular disease, cancer, and

chronic lower respiratory tract disease, RDW has shown to have association with increased risk of mortality.[4,10-15] In patients admitted to PICU, RDW is associated with risk of death and is suggested as an independent prognostic marker.[14,16-18] The prognostic value of RDW in adult patients with medical conditions such as heart failure admitted to ICU has been studied previously;[19,20] however, information about the value of RDW as a predictor of clinical outcomes in pediatric patients is more limited. We aimed to study the association between RDW parameter in pediatric patients admitted to PICU with mortality.

Materials and Methods

A retrospective study by extracting administrative and laboratory data from patients admitted to PICU of an academic pediatric teaching hospital between September 2015 and February, 2016 was accomplished. Approval for the study was obtained from the Institutional Review Board of Mofid Children's Hospital.

The medical records of all patients were reviewed for the following data: Demographic data, vital signs including body temperature, blood pressure, respiratory rate and pulse rate, a CBC, including RDW, measured within 24 hours of PICU admission, blood gas results, blood bank reports, microbiology reports, mortality, and duration of PICU admission.

RDW is reported as a coefficient of variation (percentage) of red blood cell volume. The normal reference range for RDW in this hospital laboratory was 11.5-14.5%. Patients were categorized into four RDW quartiles based on previously published studies as a priori cut-points (RDW<13.4%, 13.4–14.3%, 14.4–15.7%, and >15.7%).[4,13,14] Anemia was defined in accordance with World Health Organization (WHO) recommendations.[21]

Exclusion criteria were: Age more than 16 years, chronic renal failure, chronic metabolic disease, cancer, chronic hematologic diseases with the potential to change RDW, history of RBC transfusion within previous 72 hours.

SPSS software, version 16.0, was adopted for statistical analysis. The obtained measurement data in line with the normal distribution were expressed as mean±standard deviation. Univariate analysis was performed using Mann-Whitney U and Chi-square tests when appropriate. P<0.05 was considered statistically significant.

Results

After exclusion of 64 patients according to our exclusion criteria, 304 pediatric patients with PICU admissions over the 6 months of study period were included in the study. Demographic, clinical, and laboratory characteristics of the patients are summarized in Table 1. The mean age of the patients was 2.9±3.6 years and 42.9% were female. Nonsurgical, surgical and neurosurgical diseases were recorded in 50.5%, 29.3% and 20.1% of the cases, respectively. The mean RDW for all patients was 14.9%±2.5%. The RDW range was between 11.6%-25%.

Overall PICU mortality was 13.3%. However, the rate of mortality in the quartile of RDW>15.7% was 20.1%. Elevated RDW was significantly more encountered in nonsurgical patients (P=0.046).

The median length of PICU stay was 7.2 days. Elevated RDW was associated with longer duration of PICU admission (P<0.001). Tracheal intubation and ventilator support was needed in 34.2% of patients. This was also correlated with elevated RDW (P=0.043).

Anemia was detected in 52.7% of the patients; it was more frequent in patients with elevated RDW (P=0.048). Thrombocytopenia and thrombocytosis was observed in 13.1% and 19.6% of the patients, respectively. Abnormal platelet counts significantly correlated with elevated RDW (P=0.001).

Leukocyte counts lower than 5×10^3 /µL was reported in 9.3% of patients and leukocyte counts more than 15×10^3 /µLin 24%. There was no correlation between RDW and leukocyte counts.

The patients in the quartile of RDW>15.7% had significantly more hypotension according to their age, but RDW did not correlate with body temperature and pulse rate at the time of PICU admission.

Discussion

Elevated RDW reflects anisocytosis and higher variability in size of circulating RBCs. The results of our study was compatible with the literature that elevated RDW in pediatric patients admitted in PICU is associated with a higher risk for mortality in critically ill pediatric patients.[2,3]

Many studies have evaluated diverse prognostic markers for early recognition of ICU patients who have high morbidity and mortality risk. A variety of approaches including clinical scoring systems such as the Pediatric Risk of Mortality (PRISM) score, and Pediatric Index of Mortality score and also specific routine laboratory tests have been evaluated in former studies for identifying their potential role in prediction of outcome in critically ill pediatric patients.[22,23]

RDW has been proposed to be a prognostic factor influencing mortality in a spectrum of diseases including cardiovascular, pulmonary, renal, infectious and oncologic diseases and also in critically ill patients.[24-27] Studies have shown that RDW is an independent predictor of mortality and its addition to the "Acute Physiologic and Chronic Health Evaluation (APACHE)" score; which is one of the most commonly used ICU scoring systems, has improved its power for mortality prediction.[28]

Although the precise pathophysiological mechanism of the correlation between higher RDW and mortality is vague, it seems that chronic subclinical inflammation affects iron metabolism as well as bone marrow function and its response to erythropoietin. On the other hand, erythrocyte maturation is suppressed by the inflammatory cytokines and high oxidative stress leading to the entry of newer, larger reticulocytes into the circulation and elevation of RDW.[10] Additionally, RBC membrane glycoproteins and ion channels are altered by inflammation contributing to the change of RBC morphology.[29,30]

Previous studies have established that RDW values increased with age.[17] This relationship; although not fully defined, could depend on several factors

Table 1: Patient characteristics

Characteristic	All patients	RDW Quartile <13.4	RDW Quartile 13.4-14.3	RDW Quartile 14.4-15.7	RDW Quartile >15.7	P value
Number (%)	304	85(28)	75(24)	68(22)	76(25)	
Age(years)	2.9(0.1-16)	3.4(0.15-16)	2.13(0.1-14)	2.1(0.1-13)	3.1(0.1-16)	0.046
Gender (%)						0.9
Male	169(55.)	50(58.8)	41(54.7)	36(52.9)	42(55.3)	
Female	135(44.)	35(41.2)	34(45.3)	32(47.1)	34(44.7)	
Admit category (%)						0.004
Nonsurgical	140(46.)	37(43.5)	26(34.7)	31(45.6)	46(60.5)	
Surgical	94(30.9)	20(23.5)	28(37.3)	23(33.8)	23(30.3)	
Neurosurgical	70(23)	28(32.9)	21(28)	14(20.6)	7(9.2)	
CRP						0.01
<10	68(58.6)	22(73.3)	12(66.7)	23(63.9)	11(34.4)	
>10	48(41.4)	8(26.7)	6(33.3)	13(36.1)	21(65.6)	
Anemia (%)	159(52.)	39(45.9)	35(46.7)	35(51.5)	50(65.8)	0.048
WBC						0.128
<5000/mm3	25(8.2)	8(9.4)	5(6.4)	3(4.4)	9(11.8)	
5000-15000/mm3	205(67.4)	61(71.8)	54(72)	49(72.1)	41(53.9)	
>15000/mm3	74(24.3)	16(18.8)	16(21.3)	16(23.5)	26(34.2)	
Platelet						0.001
<150000/mm3	35(11.6)	3(3.6)	4(5.3)	13(19.1)	15(19.7)	
150000-450000/mm3	207(68.5)	67(79.8)	61(80.6)	38(55.9)	41(53.9)	
>450000/mm3	61(20.1)	14(16.7)	10(13.3)	17(25)	20(26.3)	
PICU Length of stay mean (days)	7.2(0.1-90)	5.39(0.5-60)	6.4(0.5-56)	9.1(1-51)	8.45(0.1-90)	<0.001
PICU Length of stay >48 hrs	164(53.9)	45(52.9)	30(40)	41(60.3)	48(63.2)	0.022
Mortality(%)	34(11.1)	8(9.4)	5(6.6)	5(7.3)	16(21.1)	0.016
Respiration						0.043
Normal	153(50.3)	46(54.1)	45(60)	34(50)	28(36.8)	
Tachypnea	51(16.8)	17(20)	12(16)	8(11.8)	14(18.4)	
Intubation	100(32.9)	22(25.9)	18(24)	26(38.2)	34(44.7)	
Tachycardia(%)	185(60.9)	53(62.4)	45(60)	42(61.8)	45(59.2)	0.975
Tempreture	37.36(35-40.5)	37.36(36.39.4)	37.22(35-40)	37.43(35-40)	37.44(35.4-40.5)	0.7
Blood pressure						0.017
Normal	267(87.8)	79(92.9)	67(89.3)	59(86.8)	62(81.6)	
Hypotention	11(3.6)	0(0)	1(1.3)	2(2.9)	8(10.5)	
Hypertention	28(8.6)	6(7.1)	7(9.3)	7(10.3)	6(7.9)	
PTT						0.017
<35 sec	134(76.6)	42(89.4)	33(78.6)	30(76.9)	29(61.7)	
>35 sec	41(23.4)	5(10.6)	9(21.4)	9(23.1)	18(38.3)	
INR						0.017
<1.5	167(91.3)	49(98)	45(95.7)	34(89.5)	39(81.3)	
>1.5	16(8.7)	1(2)	2(4.3)	4(10.5)	9(10.8)	
Albumin						0.003
<3.5 gr	47(44.3)	7(28)	13(56.5)	5(21.7)	22(62.9)	
>3.5 gr	59(55.7)	18(72)	10(43.5)	18(78.3)	13(37.1)	

including inflammation, anemia, nutritional status and age associated diseases.[31,32] In a study by Buyukkocak an colleagues, the correlation between RDW and age in patients admitted in ICU was significant especially among the patients who had expired.[16] In our study, age correlated positively with RDW and the mean age of patients in the quartile of RDW>15.7% was significantly higher.

An association between increasing levels of acute phase reactants such as erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and interleukin-6 with elevated RDW has been confirmed in adults.[4-6,33,34] In our study, elevated RDW was correlated positively with raised CRP but not with ESR.

In the study by Ramby et al. Al in Italy the Overall PICU mortality was 6.5% which was much less than what we had in our hospital. They also found that there was a significant increase in mortality rate across all RDW quartiles and RDW measured within 24 hours of PICU admission was independently associated with PICU duration of admission >48 hours and higher mortality

in a general PICU population.[35] In our patients, elevated RDW was also associated with longer duration of PICU admission more than 48 hours.

Increase in RDW may be a sign of cytomembrane instablity which may cause multiple organ dysfunction, consequently leading to a poorer prognosis and increase in mortality.[36] Instability of cell membrane could be due to lack of some materials such as blood albumin and cholesterol.[19,39] In our study hypoalbuminemia was associated with elevated RDW (P=0.003).

Different cohorts reveal that poor medical conditions requiring mechanical ventilation is one of the most important risk factors of mortality in PICU patients.[38] In our study, tracheal intubation and mechanical ventilation was associated with elevated RDW (P=0.043).

In summary, we observed that higher RDW was associated with higher mortality rate in pediatric patients admitted to PICU. This study should prompt further prospective evaluation of the association between high RDW and prediction of mortality in pediatric patients in order to improve risk-stratification of the ill patients.

There is no citation for ref #37 and the order of 38 and 39 is wrong

Conflict of Interest: None declared.

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