

## Evaluation of Red Cell Width in Critically Ill Patients Admitted in Intensive Care Unit

\*Kader A,<sup>1</sup> Islam MS,<sup>2</sup> Ferdoushi S,<sup>3</sup> Chowdhury AA,<sup>4</sup> Mortaz RE,<sup>5</sup> Sultana T,<sup>6</sup> Huda AQ,<sup>7</sup> Nurullah A,<sup>8</sup> Talukder SI,<sup>9</sup> Ahmed AN<sup>10</sup>

Intensive care unit (ICU) patients are heterogenous group with different type of diseases. Morbidity and mortality rate is high in ICU patients. In ICU, critically ill patients are provided with the highest level of monitoring, care and treatment, which are very expensive and consumes many hospital resources. So, various scoring system is used like APACHE-II, SAPS-II, SOFA score to predict outcome of ICU patients and helps physicians for patient admission and management. APACHE-II, SAPS-II, SOFA score contain multiple variables, which are expensive, time consuming, where as RDW is cheaper and easier test. So, it will be beneficial for the patients and helpful for the physicians. This cross sectional study was carried out in the Department of Clinical Pathology, in collaboration with Department of Anesthesia, Analgesia and Intensive Care Medicine, BSMMU, DMCH and BIRDEM, Dhaka from September 2012 to October 2013. Study population was 60 patients selected from intensive care unit, BSMMU, DMCH, BIRDEM according to inclusions criteria. Suspected case of ICU and adult age group were included in the study. After taking informed written consent from patient's attendant blood sample were obtained with all aseptic precaution from all patients and processed in hematology auto analyzer (cell counter). Red cell distribution width, mean cell volume, total leucocytes count, haematocrit were performed in the Department of Clinical Pathology, BSMMU, Dhaka. The study was conducted to assess the RDW as a marker for severity of disease among critically ill patients in ICU. Among the more severely ill patients half were >60 years age group (50.0%). On the other hand among the less severely ill patients majority were 31 to 60 years age group (65.6%). Among the respondents more than half were male (55.0%) and rests were female (45.0%). RDW ranged from 14.70 to 23.00 (median 17.00; mean 17.87±2.41). There was a difference in clinical and laboratory characteristics between the two tertiles of RDW. The higher tertile of RDW were observed in older critical ill patients in ICU. This study showed that the RDW was increased in above four groups. The primary finding of this study showed that increasing RDW levels can serve as a marker to assess the severity of ICU patients. Our study revealed that RDW was significantly associated with severity of diseases of ICU patients. So, RDW may be a reliable marker for assessment the severity of critically ill patients at ICU.

[Dinajpur Med Col J 2015 Jan; 8 (1):67-73]

**Key words:** Intensive care unit, red cell width

1. \*Dr. Abdul Kader, Medical Officer, Department of Medicine, Sir Salimullah Medical College Hospital, Dhaka
2. Dr. Md. Saiful Islam, Assistant Professor, Department of Clinical Pathology, BSMMU, Dhaka, Bangladesh
3. Dr. Sheuly Ferdoushi, Assistant professor, Department of Clinical Pathology, BSMMU, Dhaka, Bangladesh
4. Dr. Abdul Alam Chowdhury, Associate Professor, Department of ENT and Head-Neck Surgery, BSMMU, Dhaka, Bangladesh
5. Dr. Rubaiyat E Mortaz, Research Assistant, Department of Clinical Pathology, BSMMU, Dhaka, Bangladesh
6. Dr. Tuhin Sultana, Associate professor, Department of Clinical pathology, BSMMU Dhaka, Bangladesh
7. Dr. A K Qumrul Huda, Associate Professor, Department of Anesthesia, BSMMU, Dhaka, Bangladesh
8. Dr. AFM Nurullah, Assistant Professor, Department of Radiology & Imaging, Dinajpur Medical College, Dinajpur
9. Dr. Sadequel Islam Talukder, Assistant Professor, Department of Pathology, Dinajpur Medical College, Dinajpur
10. Professor A N Nashimuddin Ahmed, Professor and Chairman, Department of Clinical Pathology, BSMMU, Dhaka, Bangladesh

\* For correspondence

## Introduction

**R**ed cell distribution width (RDW) is a quantitative measure of red cell size variation co-efficient. Higher RDW indicates greater variation of red blood cell size (RBC). It is expressed as percentage and reported as RDW. It is a new routine parameter in fully automated hematology analyzer. It is routinely done by physician in clinical practice as a part of the complete blood count (CBC).<sup>1-3</sup> RDW is a laboratory index used in the differential diagnosis of microcytic hypochromic anaemia. Recently several studies showed that high RDW value predicts the severity of diseases like morbidity and mortality in critically ill patients in intensive care unit (ICU). In recent study, RDW has a potential prognostic power in critically ill patients.<sup>4</sup> RDW is a strong and independent predictor of morbidity and mortality in ICU patients.<sup>4-6</sup>

Intensive care unit (ICU) patients are heterogeneous group with different type of diseases. The patients were included mainly from sepsis, septic shock, cardiovascular diseases, pulmonary hypertension, pulmonary embolism, stroke, trauma<sup>7</sup>. Morbidity and mortality rate is high in ICU patients. In Bangabandhu Sheikh Mujib Medical University (BSMMU) 2012, the mortality rate of ICU patients were 46% (from ICU data 2012) and 32.5 % in BIRDEM.<sup>8</sup>

Major manifestations of critically ill patients are circulatory failure, respiratory failure, renal failure, neurological failure and sepsis. According to admission in ICU, most of the patients are admitted with sepsis, cardiovascular disease, neurological diseases, trauma and respiratory disease. Critically ill patients are provided with the highest level of monitoring, care, and treatment which are very expensive. It also consumes many hospital resources. So, various scoring systems have been used for assessing the

severity of critically ill patients in different ICU in the world like APACHE (acute physiology and chronic health evaluation) score, SAPS (simplified acute physiology) score, SOFA (sequential organ failure assessment), MODS (multiple organ dysfunction score) and CIS (cellular injury score) to predict outcome in ICU patients. These are also used for performance of ICU, the assessment of therapies, management guideline and the cost-effectiveness that help physicians for patient admission and management.<sup>9-12</sup>

So, an accurate scoring system is required for assessing the severity of patients and proper effective therapies. It contains variables those can independently predict the outcome or severity of diseases.<sup>13</sup> RDW includes only one variable, widely available to clinician.<sup>3</sup> It is computed directly from the Red blood cell histogram.<sup>3,14</sup>

Raised RDW is found in inflammation (SIRS or sepsis), oxidative stress, malnutrition, neurohormonal response and is associated with pro-inflammatory cytokine, C-reactive protein (CRP). High oxidative stress generates reactive oxygen species by activated leucocyte that release pro-inflammatory cytokines those include tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), interleukine-6 (IL-6), interleukine-1 $\beta$  (IL-1 $\beta$ ). These pro-inflammatory cytokine inhibit erythropoietin production, suppress Red blood cell (RBC) maturation, decrease half-life of RBC and deformability of cell membrane, as a result RBC rapidly damage. So, release of immature RBC in circulation increase RDW and mortality also increased.<sup>3,14-16</sup>

Multivariate analysis demonstrated that RDW was independent predictors of ICU mortality. In recent study, RDW is used for prediction of mortality in ICU patients.<sup>3</sup> If RDW is divided into quartile, higher quartile RDW indicates

higher mortality rate in ICU. For every 1% increase in RDW level the risk of death is 31% higher.<sup>16</sup> High RDW with increase mortality rate 1.6 fold is found in critically ill patients.<sup>15</sup> In statistical analysis, shown from regression analysis in case of multivariable ICU mortality Odd ratio (OR) for RDW was 1.10 (1.06 – 1.15). RDW is significantly associated with ICU mortality.<sup>17</sup>

RDW is the only one variable, simple and cheaper test. It is easily available and can be done rapidly along with complete blood count. Bangladesh is a developing country and most of the patients are unable to bear the costly investigation. So, it would be beneficial for the patients and helpful for the physicians. With this aim, this study was undertaken to evaluate the role of red cell distribution width (RDW) for the assessment of severity of critically ill patients in ICU.

### Methods

This is a cross sectional study done in the Department of Clinical Pathology BSMMU in collaboration with ICU of Anaesthesiology Department, BSMMU and Dhaka Medical College Hospital (DMCH) and ICU of Critical care medicine unit of Bangladesh Institute of Research and Rehabilitation for Diabetes, Endocrine and Metabolic Disorder (BIRDEM), Dhaka. All adult ICU admitted patients in BSMMU, DMCH and Critical care medicine unit of BIRDEM. In initial stage of study we planned to enroll 60 patients. All adult ICU patients (Age >18 years) and normal mean corpuscular volume (MCV) (76-96 fl) was included in this study. Age < 18 years Patients with less than cut-off value of RDW, pregnancy, known hematological disease (leukaemia, myelodysplastic disease, metastatic cancer in bone marrow, some anaemia like iron deficiency anemia, thalassaemia), history of recent blood transfusion (less than 2 weeks) were excluded in this study. Enrolled patient were divided

into four (4) groups according to ICU admission. Initially we thought each group will contain 15 patients, but finally we got

- Group-1: 10 cases of sepsis (septic shock)
- Group-2: 21 cases of neurological (stroke, sub-arachnoid hemorrhage, meningitis, encephalitis, brain tumor)
- Group-3: 18 cases of cardiovascular (myocardial infarction, heart failure, hypertension)
- Group-4: 11 cases of Trauma (head injury, road traffic accidents)

After measuring RDW value, ICU patients were divided into two tertiles. Patients who had  $\leq 17.5$  considered as less severe group and who had  $> 17.5$  considered as more severe. 2.0 ml venous sample with EDTA for RDW and CBC. Measurement of RDW and CBC were done after collection. RDW and CBC were done by automated hematology analyzer, calibrated according to manufacturer instruction. Sample were presented to the haematology analyzer Sysmex-XT 4000i, where 20 microlitre ( $\mu$ l) blood was aspirated directly. CBC includes Hb, red cell count, white blood cell count, platelet count, haematocrit, MCV, MCH, MCHC and RDW was done. RDW was derived from pulse height analysis and can be expressed as the coefficient of variation (CV) percentage of the measurement of the red cell volume. RDW plotted as a histogram, deviation from a unimodal gaussian curve was inspected. All data were recorded systematically in a preformed data collection sheet and quantitative data was expressed as mean  $\pm$  Standard deviation and qualitative data was expressed as frequency and percentage. We divided RDW into two groups on basis of severity below 17.5 RDW and above 17.5 RDW values and compared demographics, clinical characteristics, laboratory test result.

All statistical computations were performed by using SPSS.17.

## Results

Patients' age range was 18 to 86 years. Table I shows age distribution of the study patients and among the more severely ill patients half were >60 years age group (50.0%). On the other hand among the less severely ill patients majority were 31 to 60 years age group (65.6%). But these differences were not statistically significant in chi-square test. But the mean age was found  $53.81 \pm 15.15$  years in less severe group and  $53.56 \pm 19.44$  years in more severe group. The mean age difference was statistically significant ( $p < 0.05$ ) between the two groups in unpaired t- test.

Table I: Relation of age with severity of disease

Age (in years)	Less severe* N(%)(n=32)	More severe** N(%)(n=28)	p
18 - 30	4(12.5)	2((7.1%)	0.071
31 - 60	21(65.6)	12(42.9)	
>60	7(21.9)	14(50.0)	
Total	32(100.0)	28(100.0)	
Mean age $\pm$ SD	53 .81 $\pm$ 15.15	53.56 $\pm$ 19.44	0.019

\*Less severe group = Patient with lower RDW value  $\leq 17.5$ , here 32 patients were included.

\*\*More severe group = patient with higher RDW value  $> 17.5$ , here 28 patients were included.

Table II: Sex distribution of the study patients (n=60)

Sex	No of the respondents(N)	Percent (%)
Male	33	55.0
Female	27	45.0
Total	60	100.0

Table II shows sex distribution of the patients. Among the patients more than half were male (55.0%) and rests were female (45.0%).

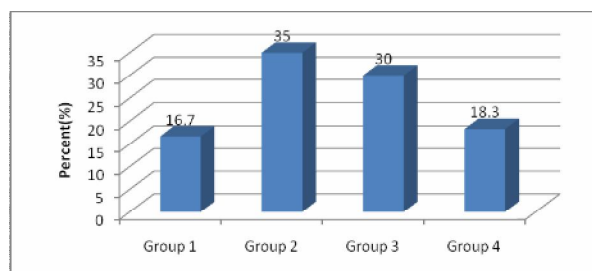


Figure 1. Distribution of patients according to Group (group-1=10, group-2= 21, group-3= 18, group-4= 11).

The total patients were grouped into four as follows

Group 1- sepsis (e.g, septic shock), 10 patients.

Group 2- Neurological diseases (e.g. stroke, subdural haemorrhage, meningitis, encephalitis), 21 patients.

Group 3 - Cardiovascular diseases (e.g, myocardial infarction, heart failure, hypertension), 18 patients.

Group 4 - Trauma patients (e.g. head injury, road traffic accidents), 11 patients.

Fig 1 shows distribution of patients in different groups. Among the total patients (n=60) more than one third 21 (35.0%) was in group-2, more than one fourth 18(30%) was in Group-3, more than eighteen percent 11(18.3) were in Group-4 and 10(16.7%) were in Group-1.

Table III: Relation of mean RDW ((Mean  $\pm$  SD)) between in less and more severe group in total patients.

Less severe	More Severe	p
16.04 $\pm$ 0.70	19.75 $\pm$ 1.90	0.001

p value reached from unpaired t-test

Table III shows distribution of RDW in both less and more severe group. The mean RDW was found  $16.04 \pm 0.70$  in less severe group and  $19.75 \pm 1.90$  in more severe group. The mean RDW difference was statistically significant ( $p < 0.001$ ) between the two groups in unpaired t test which indicates raised RDW was associated with severity of disease.

Table IV: Relation of RDW of individual group with severity of the disease

Groups	Less severe (RDW $\leq 17.5$ ) Mean $\pm$ SD	More severe (RDW $> 17.5$ ) Mean $\pm$ SD	P-value
Group-1 (n=10)	$16.30 \pm 0.60$	$19.74 \pm 2.20$	0.003
Group-2 (n=21)	$15.90 \pm 0.696$	$21.23 \pm 1.87$	0.001
Group-3 (n=18)	$15.97 \pm 0.89$	$19.08 \pm 1.05$	0.001
Group-4 (n=11)	$16.28 \pm 0.53$	$19.85 \pm 0.65$	0.008

p value reached from independent t-test

Table IV shows distribution of mean RDW in both less and more severe group patients among the individual group. The mean RDW in group-1 was found  $16.30 \pm 0.60$  in less severe group and  $19.75 \pm 1.90$  in more severe group patients,  $15.90 \pm 0.696$  was in less severe,  $21.23 \pm 1.87$  was in more severe in group-2,  $15.97 \pm 0.89$  was in less severe,  $19.08 \pm 1.05$  was in more severe in group-3 and  $16.28 \pm 0.53$  was in less severe,  $19.85 \pm 0.65$  was in more severe group patient in group-4. The mean RDW difference in less and more severe group patients among the individual group were statistically significant ( $p < 0.05$ ) in unpaired t-test.

### Discussion

This cross sectional study was conducted to assess the RDW as a marker for severity of disease among critically ill patients in ICU. Our study was enrolled in 60 patients from

intensive care unit, Dhaka. Among 60 patients who participated in our study were divided into four (4) groups on the basis of ICU admission primarily based on clinical evaluation and lab diagnosis. Among them 10 (16%) patients were in group-1 (sepsis), 21 (35%) were in group-2 (neurological disease), 18 (30%) were in group-3 (cardiovascular diseases) and 11 (18.3%) were in group-4 (trauma patients). This cross sectional study evaluated RDW for assessing the severity of diseases of ICU patients that correlated with APACHE-II score. After measuring RDW value, ICU patients were divided into two tertiles. Patients who had  $\leq 17.5$  (RDW), considered as less severe patients and who had  $> 17.5$  (RDW) considered as more severe patients.<sup>14</sup>

In our study, mean age was  $53.81 \pm 15.15$  in less severe patients and  $53.56 \pm 19.44$  in more severe patients. The mean age difference was statistically significant ( $P < 0.05$ ) between less and more severe patients in unpaired t-test which indicate increase RDW was associated with critically ill patients with age. Similar findings were found in other studies.<sup>3,14,15,17</sup> According to their study mean age was  $70.39 \pm 16.73$  years, 67.4 years, 63 years, and  $61.7 \pm 18.3$  years respectively. These finding were nearly consistent with our study.

The present study showed that male were 33 (55%) and female 27 (45%). Predominance male patient of ICU was also found in other studies.<sup>17,15,3,14</sup> These findings were nearly consistent with our study.

This study revealed that mean RDW value in less severe patients were  $16.04 \pm 0.70$  and mean RDW value in more severe patients were  $19.75 \pm 1.90$ . The mean RDW difference in both groups was statistically significant ( $P < 0.001$ ) in unpaired t-test which indicates raised RDW was associated with severity of disease. Also significant finding were

observed the other studies.<sup>3,14,17,15,4,16</sup> Previous studies showed that high mortality rate were associated with higher RDW tertile compared with low RDW tertile. This finding was consistent with our study.

In our study we have found the mean RDW  $16.30 \pm 0.60$  in less severe group and  $19.75 \pm 1.90$  in more severe group patients,  $15.90 \pm 0.696$  in less severe,  $21.23 \pm 1.87$  in more severe in group-2,  $15.97 \pm 0.89$  in less severe,  $19.08 \pm 1.05$  in more severe in group-3 and  $16.28 \pm 0.53$  in less severe,  $19.85 \pm 0.65$  in more severe group patient in group-4. The mean RDW difference in less and more severe group patients among the individual group were statistically significant ( $p < 0.05$ ) in unpaired t-test which indicate raised RDW was associated with severity of disease.  $P < 0.05$  were observed in the other studies.<sup>14,15,16,17</sup> Their studies showed that higher mortality rate were associated with higher RDW tertile compared with low RDW tertile. This finding was similar to our study.

### Conclusion

This study revealed that RDW is an effective parameter for prediction the adverse outcome in ICU patients. Increased RDW likely reflects the presence of pro-inflammatory cytokines and oxidative stress. RDW is less expensive, available, routinely done with CBC, no additional cost is needed and highly reproducible. It is also helpful for daily follow up of the patients by only evaluating CBC. From this study, we concluded that higher RDW levels can serve as a marker for assessing the severity of diseases and can be used for prediction of adverse outcomes of ICU patients.

### References

1. Patel KV, Ferrucci L, Ershler WB, Longo DL, Guralnik JM, 2009, 'Red blood cell distribution width and the risk of death in middle-aged and older adults', Arch Intern Med; 169: 515–523.
2. Forhecz Z, Gombos T, Borgulya G, Pozsonyi Z, Proha'szka Z, Ja'noskuti L, 2009, 'Red cell distribution width in heart failure: prediction of clinical events and relationship with markers of ineffective erythropoiesis, inflammation, renal function, and nutritional state', Am Heart J; 158(4): 659-666.
3. Wang F, Pan W, Pan S, Ge J, Wang S, Chen M, 2011, 'Red cell distribution width as a novel predictor of mortality in ICU patients', Ann Med; 43(1):40-46.
4. Jackson CE, Bezlyak V, Tsorlalis IK, Dalzell JR, Myles RC, Spooner R, Ford I, Petrie MC, Cobbe SM, McMurray JJV, 2009, 'The novel biomarker red cell distribution width (RDW) has incremental prognostic value, in addition to B-type natriuretic peptide (BNP), in patients with acute decompensated heart failure', Eur Heart J; 30 (Suppl. abstract):14.
5. Perlstein TS, Weuve J, Pfeffer MA, Beckman JA, 2009, 'Red blood cell distribution width and mortality risk in a community-based prospective cohort', Arch Intern Med; 169(6):588-594.
6. Braun E, Domany E, Yael Kenig, Mazor Y, Makhoul B F and Zaher S Azzam, 2011, 'Elevated red cell distribution width predicts poor outcome in young patients with community acquired pneumonia', critical care; 15: R194.
7. Scharte M, Fink MP, 2003, 'Red blood cell physiology in critical illness', Crit Care Med; 31: S651–S657.
8. From statistical Year Book; 2011-12 of DAB
9. Shrestha GS, Gurung R, Amatya R, 2001, 'Comparison of acute physiology, age, chronic health evaluation III score with

- initial sequential organ failure assessment score to predict ICU mortality', *Nepal Med Coll J*;13(1):50-54.
10. Keegan MT, Gajic O, Afessa B, 2011, 'Severity of illness scoring systems in the intensive care unit' , *Crit Care Med*; 39(I):233-236.
  11. Deakin C D, *Clinical notes for the FRCA*, 2000, 2<sup>nd</sup> edition; 238-140.
  12. Rao SM, Suhasini T, 2003, 'Organization of intensive care unit and predicting outcome of critical illness', *Indian J anaesthesia*; 47(5):328-337.
  13. Al-Najjar Y, Goode KM, Zhang J, Cleland JG, Clark AL, 2009, 'Red cell distribution width an inexpensive and powerful prognostic marker in heart failure', *Eur J Heart Fail*;11: 1155–1162.
  14. Sadaka F, Jacklyn O, Sumi P, 2012, 'Red Cell Distribution Width and Outcome in Patients With Septic Shock', *J Intensive Care Med*; 1-7.
  15. Bazick HS, Chang D, Mahadevappa K, 2011, 'Red cell distribution width and all-cause mortality in critically ill patients', *Crit Care Med*; 39(8):1913-1921.
  16. Ani C, Ovbiagele B, 2009, 'Elevated red blood cell distribution width predicts mortality in persons with known stroke', *Journal of the Neurological Sciences*; 277 :103–108.
  17. Hunziker S, Leo A, Joon I, 2012, 'Red cell distribution width improves the simplified acute physiology score for risk prediction in unselected critically ill patients', *Critical care*; 16: R89.