

## **Role of Red Blood Cell Distribution Width for Assessment of the Severity of Critically Ill Patients in Intensive Care Unit and to Correlate with Acute Physiology and Chronic Health Evaluation-II (Apache-II) Score**

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### **Abstract:**

*Morbidity and mortality rate is high in ICU patients. 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 score are used in our country. APACHE-II, SAPS-II, SOFA score contain multiple variable,*

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*which are expensive, time consuming, where as RDW is cheaper, rapidly and easily test. The study was cross sectional conducted to assess the RDW as a marker for severity of disease among critically ill patients in ICU. Study population was 60 patients selected from intensive care according to inclusion 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). 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%). RDW ranged from 14.70 to 23.00 and the mean APACHE-II score was ranged from 15.0 to 32.0. The higher tertile of RDW were observed in older critical ill patients in ICU. The primary finding of this study showed that increasing RDW levels can serve as a marker to assess the severity of ICU patients. This association remained significant even after adjustment for APACHE-II score. RDW is less expensive and common measurement found on the complete blood count. The RDW fared better than APACHE II for morbidity or mortality prediction of ICU patients. RDW is widely available test, no additional cost and found in routinely performed with complete blood cell count and is highly reproducible, RDW has the potentially clinical utility to predict outcome for ICU patients.*

**Key words:** Red Blood Cell Distribution Width, Critically Ill Patients, Acute Physiology and Chronic Health

## **Introduction**

Red 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.<sup>1-3</sup> RDW is a laboratory index used in the differential diagnosis of microcytic hypochromic anemia. 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>5</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>6</sup> Morbidity and mortality rate is high in ICU patients and about 15% mortality rate found in ICU patient in France.<sup>7</sup> 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 (From statistical Year Book 2011-12 of DAB). 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 system 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>8</sup> APACHE-II or SOFA or other score contain multiple variables and those are more expensive, very costly and time consuming. On the other hand, 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 will 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 for the assessment of severity of critically ill patients in ICU and to correlate with APACHE-II score.

## **Methodology**

**Study design:** Cross sectional analytical study

**Place of study:** This study was done in the Department of Clinical Pathology BSMMU in collaboration with ICU of Anesthesiology 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.

**Study duration:** One year (1) from September 2012 to August 2013

**Study population:** All adult ICU admitted patients in BSMMU, DMCH and Critical care medicine unit of BIRDEM.

**Sample size:** 60

**Sampling Technique:** Purposive sampling was applied. As per inclusion criteria the patients were enrolled in this study. The particulars of the patients and clinical data were recorded in a pre-designed data-sheet and were kept until the end of the study. The whole procedure was explained to the patient and informed written consent was taken

### **Patient selection:**

#### **Inclusion criteria:**

Eligible patients are those needed to be hospitalized to ICU who are transferred from the emergency department or the other hospital including medical and trauma patient like-

- Adult ICU patients (Age >18 years)
- Patient with more than cut-off value of RDW & APACHE-11 (cut-off value RDW is  $\geq 14.8\%$  and APACHE-11 is  $\geq 15$  points).
- Normal mean corpuscular volume (MCV) (76-96 fl)

#### **Exclusion criteria:**

- Age <18 years
- Patients with less than cut-off value of RDW & APACHE-11 score (cut-off value RDW is  $\geq 14.8\%$  and APACHE-11 is  $\geq 15$  points).
- 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)

#### **Grouping of Patients:**

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-aracnoid 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.

### Data collection:

Data was collected by a predesigned Proforma. Blood samples were collected from all ICU patients during admission within 24 hours. Patient's information was obtained through using patient's information sheet which involves questionnaire, clinical findings and laboratories reports.

### Result

**Table 1: Age distribution of the study subjects and relation of age with severity of the disease assessed by RDW (n=60)**

Age (in years)	Less severe* N(%)( n=32)	More severe** N%(n=28)	$\chi^2$	df	P value
18-30	4(12.5)	2((7.1%)	5.211	2	0.071
31- 60	21(65.6)	12(42.9)			
>60	7(21.9)	14(50.0)			
<b>Total</b>	<b>32(100.0)</b>	<b>28(100.0)</b>			
Mean age $\pm$ SD Age Range = 68, (Min 18, Max 86)	53.81 $\pm$ 15.15	53.56 $\pm$ 19.44			0.019 s

\*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-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.

**Figure 1: Distribution of patients according to Group**

**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.

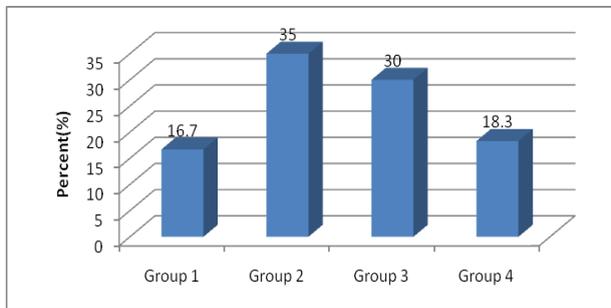


Figure 1 shows distribution of patients in different groups. Among the total patients (n=60) more than one third 21 (35.0%) was in group-2, more than one fourth 18(30%) was in Group-3, more than eighteen percent 11(18.3) were in Group-4 and 10(16.7%) were in Group-1.

**Table 2: Relation of mean RDW between in less and more severe group in total patients**

RDW	Less severe	More Severe	t	df	P value
RDW (Mean ± SD)	16.04 ± 0.70	19.75 ± 1.90	-10.85	58	0.001

P value reached from unpaired t-test

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.

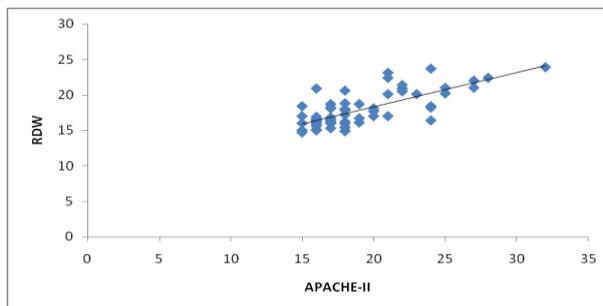
**Table 3: Relation of RDW of individual group with severity of the disease**

Group	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

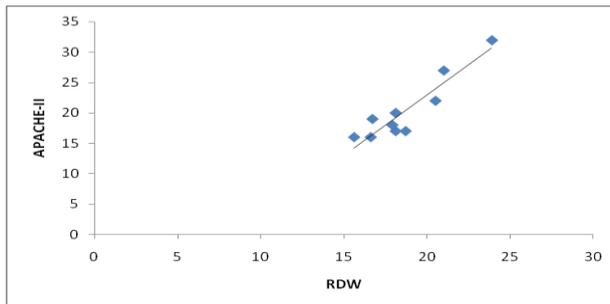
The mean RDW in group-1 was found  $16.30 \pm 0.60$  in less severe group and  $19.75 \pm 1.90$  in more severe group patients,  $15.90 \pm 0.696$  was in less severe,  $21.23 \pm 1.87$  was in more severe in group-2,  $15.97 \pm 0.89$  was in less severe,  $19.08 \pm 1.05$  was in more severe in group-3 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.

**Figure 2: Correlation between RDW and APACHE-II among the respondents**



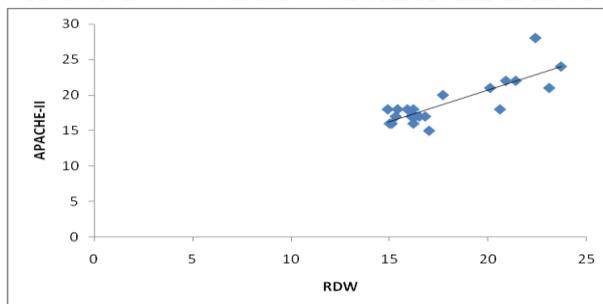
Scatter diagram shows positive correlation between RDW and APACHE-II. Pearson correlation test showed that it is statistically highly significant ( $p < 0.01$ ,  $r = 0.733$ ). This result indicates when APACHE-II score is increased than RDW value also increased stepwise.

**Figure 3: Correlation between RDW and APACHE-II in Group-1**



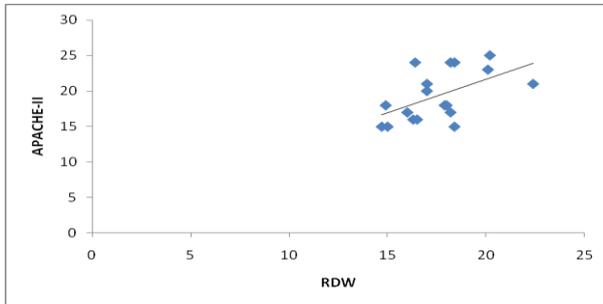
Scatter diagram shows positive correlation between RDW and APACHE-II in Group 1. Pearson correlation test showed that it is statistically highly significant ( $p < 0.01$ ,  $r = 0.923$ ).

**Figure 4: Correlation between RDW and APACHE-II in Group-2**



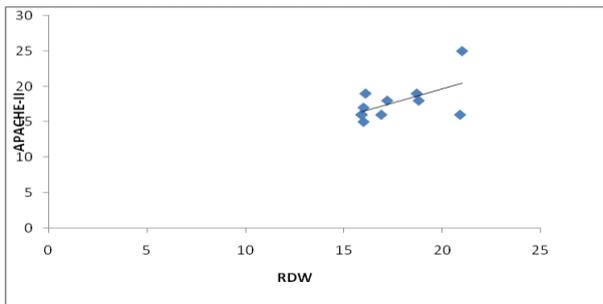
Scatter diagram shows positive correlation between RDW and APACHE-II in Group 2. Pearson correlation test showed that it is statistically highly significant ( $p < 0.01$ ,  $r = 0.823$ ).

**Figure 5: Correlation between RDW and APACHE-II in Group-3**



Scatter diagram shows positive correlation between RDW and APACHE-II in Group 3. Pearson correlation test showed that it is statistically significant ( $p < 0.05$ ,  $r = 0.538$ ).

**Figure 6: Correlation between RDW and APACHE-II in Group-4**



Scatter diagram shows positive correlation between RDW and APACHE-II in Group-4. Pearson correlation test showed that it is statistically significant ( $p < 0.05$ ,  $r = 0.576$ ).

## 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 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>9</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>3,10,11</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. 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>11-12</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 indicates raised RDW was associated with severity of disease. P value  $< 0.05$  were observed in the other study.<sup>12</sup> Our study revealed that the mean RDW difference in less and more severe group patients in septicemia was statistically significant ( $p$  value  $< 0.05$ ) in unpaired t-test which indicates raised RDW was associated with severity of septicemia. P value  $< 0.05$  was observed in the other studies.<sup>9,11</sup> These studies showed that higher mortality rate were associated with higher RDW tertile compared with low RDW tertile. This finding was consistent with our study. Among the patients with neurological disorders like stroke, RDW is high due to inflammatory states, infection of atherosclerotic plaque that causes cytokines production and those cytokine impede RBC maturation. Elevated RDW predict mortality in person with known stroke.<sup>11</sup> This study showed that mean RDW difference in both less and more severe group in neurological diseases was statistically significant ( $p < 0.001$ ). This result indicates raised RDW was associated with severity of neurological diseases were demonstrated that higher mortality rate were associated with higher RDW tertile compared with low RDW tertile.<sup>9</sup> P value was  $< 0.001$  in their studies. This finding was similar to our study. In cardiovascular diseases increased RDW is not clear but RDW may represent inflammation.<sup>10</sup> In some previous study, RDW is found to be a new prognostic marker in heart failure, coronary cardiac diseases.<sup>4</sup> Higher value of RDW were associated with increased risk of death. The present study revealed that mean RDW difference in both less and more severe group in cardiovascular diseases was statistically significant ( $p$  value  $< 0.001$ ), which indicates raised RDW was associated with severity of cardiovascular diseases. P value was  $< 0.05$  in their study.<sup>13</sup> Previous studies showed that higher mortality rate were associated with higher RDW tertile compared with low RDW tertile. This finding was similar with our study. The APACHE-

II score system has shown positive correlation with ICU mortality and is one of the most common models to evaluate patient's disease severity. In accordance with previous studies APACHE-II score had demonstrated a strong power to predict ICU mortality. Patients with high APACHE-II score and high RDW levels carry the higher risk of mortality. For predicting ICU mortality, predicting power of RDW was relatively low than APACHE-II. But previous studies had shown that there was stepwise increased APACHE-II score with increased RDW tertiles (all  $p < 0.05$ ) and when adding RDW to APACHE-II score strongly predict ICU mortality.<sup>3</sup> We found positive correlation among the total patients between RDW and APACHE-II in pearson correlation test that is statistically highly significant ( $P < 0.01$ ,  $r = 0.77$ ). This result was consistent with other study.<sup>3</sup> We also found positive correlation among the individual group between RDW and APACHE-II in pearsons correlation test that is statistically highly significant ( $P < 0.01$ ,  $r = 0.923$ ) in group-1, ( $P < 0.01$ ,  $r = 0.823$ ) in group-2, ( $P < 0.01$ ,  $r = 0.538$ ) in group-3 and ( $P < 0.01$ ,  $r = 0.576$ ) respectively. These results were consistent with other study.<sup>3</sup>

## **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. There was a positive correlation between RDW and APACHE-II score. RDW is better than APACHE-II for morbidity or mortality prediction in ICU patients, moreover RDW is less expensive, available, routinely done with CBC and 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 like APACHE-II score.

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