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Original Article

Internal Medicine Section

RDW as a Prognostic Marker of Sepsis and its Comparison with APACHE II Score: A Prospective Observational Cross-sectional Study

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ABSTRACT

Introduction: Sepsis is one of the most important and common cause for Intensive Care Unit (ICU) admission. Life-threatening organ dysfunction is caused by a dysregulated host response to infection. Clinical scoring system is cumbersome for prognosticating sepsis outcome. Red cell Distribution Width (RDW) is a part of routine investigation done in the form of Complete Blood Count (CBC), inexpensive and easily available.

Aim: To evaluate RDW as a prognostic marker of sepsis and its comparison with APACHE II (Acute Physiology and Chronic Health Evaluation II) score.

Materials and Methods: The present study was a prospective observational cross-sectional study was conducted at MLN Medical College and associated Swaroop Rani Nehru Hospital, Prayagraj, Uttar Pradesh, India, which included 110 patients diagnosed with sepsis. The patients were divided into survivors and non survivors group. CBC, liver function test, kidney function test, serum electrolytes, Arterial Blood Gas (ABG) analysis, blood culture, site-specific culture were done and APACHE II was calculated.

Results: Out of the 110 patients enrolled in the study, 61 were males and 49 were females. Mean±SD age of the non survivors (n=42) was 57.45±22.93 years and that of survivors (n=68) was 58.59±17.18 years. APACHE II score in the non survivors was 18.50±6.80 while that among the survivors was 10.51±6.61 (p<0.001). RDW in the non survivors was 17.62±4.29 while that in the survivors was 13.99±1.66 (p<0.001).

Conclusion: The RDW was found to be significantly higher in non survivor group as compared to survivor in this study. So RDW at admission can be used as simple, easy to perform prognostic marker of sepsis.

Keywords: Acute physiology and chronic health evaluation II, Prognosis, Red cell distribution, Sepsis outcome, Survivors

INTRODUCTION

Sepsis is one of the most lethal, difficult-to-treat morbid condition in which patients generally require intensive care. RDW is one of the parameters studied under CBC. RDW is an indicator of heterogeneity in Red Blood Cell (RBC) size. It is calculated in relation to variation in Mean Corpuscular Volume (MCV). The normal range of RDW is generally defined as 11.5-14.5% [1,2]. RDW values higher than the normal range are reflective of a higher heterogeneity in RBC size, which in turn is reflective of dysfunctional erythropoiesis, reduced lifespan of RBCs or premature release of reticulocytes [3]. Inflammation and oxidative stress reduce RBC survival and suppress their maturation. Proinflammatory state play major role in inefficient erythropoeisis leading to structural and functional alteration in RBCs. Plasma cytokines such as Tumour Necrosis Factor α (TNF α), interferon γ, interleukin 1β and interleukin 6 have been shown to effect RBCs survival and production. Erythroid progenitor cell activity is inversely related to amount of circulating cytokines. It is elevated when excess of reticulocytes are released into the circulation. Proinflammatory state of sepsis may elevate RDW by having a negative impact on RBC survival [4].

As far as physiological scoring systems for prediction of outcome are concerned, there are a number of such scoring systems being used, viz., APACHE, Simplified Acute Physiology Score (SAPS), Mortality Probability Model (MPM), Multiple Organ Dysfunction score (MODS), Sequential Organ Failure Assessment Score (SOFA), Logistic Organ Dysfunction Score (LODS), etc., keeping in view the scope of present study, only APACHE score was discussed. The aim of the study was to evaluate RDW as prognostic marker of sepsis and its comparison with APACHE II score.

MATERIALS AND METHODS

This prospective observational cross-sectional study was conducted at MLN Medical College and associated Swaroop Rani Nehru Hospital, Prayagraj, Uttar Pradesh, India, from May 2018 to May 2019. The study was approved by Institutional Ethical Committee (IEC) (Ethics committee Registration No. ECR/922/Inst/UP/2017).

Inclusion criteria: A total of 110 patients diagnosed as sepsis and who gave informed consent were included in the study.

Exclusion criteria:

- History of packed RBCs or whole blood transfusion in the previous week,
- Already taking treatment for anaemia,
- Known haematological disorder (Leukaemia, Myelodysplastic Syndrome (MDS), Metastasis to bone marrow}
- Recent chemotherapy,
- Drugs affecting RBC morphology or survival likes (erythropoietin, pentoxifylline, cyclosporin, nitrates etc.,).
- Critically-ill patients of aetiology other than sepsis.

Study Procedure

All registered participant underwent clinical examination (Glasgow Coma Scale (GCS), respiratory rate, pulse rate), and investigation CBC (Haemoglobin (Hb), Total Leukocyte Count (TLC), Differential Leukocyte Count (DLC), Platelet count, haematocrit, RDW) ABG (PaO_2, pH, Serum Bicarbonate) Serum electrolyte (serum sodium, serum potassium) KFT (serum creatinine), Granule Basic Proteins (GBP) with toxic granulation, blood culture, site-specific culture, urine routine/microscopy, X-ray, Ultrasound abdomen, Electrocardiogram (ECG) and 2D-ECHO.

APACHE II score calculated at the time of admission was analysed using study population which was divided into survivors group and non survivors group and the predicted normal RDW group (<14.5%) and higher RDW group (>14.5%). Between these groups, continuous and categorical variables were analysed.

STATISTICAL ANALYSIS

For continuous variable Student's t-test and for categorical variables Chi-square test was used and a p-value <0.05 was considered to be statistically significant. The individual discriminatory values of RDW and APACHE II score for predicting mortality was studied using Receiver Operating Characteristic (ROC) curve analyses with calculation of Area Under the Curve (AUC).

RESULTS

A total of the 110 patients were enrolled in the study, 61 were males and 49 were females. Mean±SD age of the non survivors (n=42) was 57.45±22.93 years and mean age of survivors (n=68) was 58.59±17.18 years. The age and gender showed no significant variation among the survivors and non survivors (p>0.05) [Table/Fig-1]. However, mean TLC and pulse rate were significantly higher among those who died as compared to those who were discharged (p<0.001). Mean arterial pressure of those who died was significantly lower as compared to that of patients who were discharged (p<0.001). Incidence of organ dysfunction was also significantly higher in those who died (83.3%) as compared to those who were discharged (36.8%) (p<0.001) and serum creatinine levels was found to be significantly higher in those who died as compared to those who were discharged (p=0.013). APACHE II score in the non survivors was significantly higher than in the survivors. RDW in the non survivors was 17.62±4.29 while RDW in the survivors was 13.99±1.66 and this difference was also statistically significant (p<0.001) [Table/Fig-1].

Fact or/Characteristic	Non survivors (n=42)	Survivors (n=68)	p-value
Age (years) Mean±SD	57.45±22.93	58.59±17.18	0.768
TLC (Th/cumm) Mean±SD	22.2±10.1	15.2±4.3	<0.001
MAP (mmHg) Mean±SD	70.36±10.1	80.56±13.44	<0.001
GCS Mean±SD	10.98±3.02	13.09±2,41	<0.001
APACHE II Mean±SD	18.50±6.80	10.51±5.61	<0.001
RDW (%) Mean±SD	17.62±4.29	13.99±1.66	<0.001

[Table/Fig-1]: Demographic and characteristics of study participants (n=110).

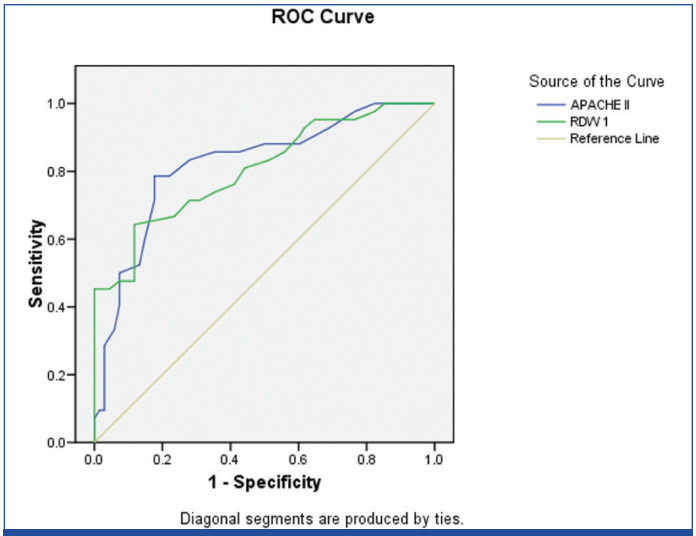
On ROC curve analysis to predict the outcome on the basis of APACHE II and RDW scores, the projected cut-off value of APACHE II and RDW (%) >14.50 and >14.35 were found to have a sensitivity and specificity of 78.6% and 82.4% and 71.4% and 72.1%, respectively. Statistically, there was no significant difference between two predictors with respect to AUC values (p=0.800) [Table/Fig-2-4].

Test variables	Area Under the Curve (AUC)±SE	Projected cut-off value	Projected sensitivity	Projected specificity
APACHE II	0.821±0.042	>14.50	78.6%	82.4%
RDW (%)	0.805±0.044	>14.35	71.4%	72.1%

[Table/Fig-2]: Receiver-operator characteristic curve analysis to calculate cut-off value of APACHE II and RDW for prediction of mortality as outcome.

DISCUSSION

The mean APACHE II and RDW values were significantly higher in non survivors as compared to survivors. Shaikh MA and Yadavalliin DR in their study, on univariate analysis reported heart rate, blood pressure, respiratory rate, oxygen saturation, platelet count and total bilirubin levels to be significantly associated with mortality and they also found a significant association between mortality and higher RDW values similar to present study [5]. Zhang J et al., in their study, did not find a significant difference in APACHE II scores between survivors and non survivors but found mean RDW levels of non survivors to be significantly higher as compared to survivors, as observed in the present study participants [6]. A relationship of higher RDW values with high mortality rate and higher APACHE II scores was also observed by Jandial A et al., and Han Y et al., [7,8]. In this study, on univariate assessment higher mean TLC values, pulse rate, and S. creatinine were associated with mortality significantly. Patients who died had significantly higher proportion of organ dysfunction as compared to those who survived. Mean GCS scores of patients who died were significantly lower as compared to those who survived. In this study, on ROC analysis, for mortality as an outcome, APACHE II and RDW showed AUC values of 0.821 and 0.805, respectively. However, AUC values for RDW and APACHE III scores were considerably lower in the study of Han Y et al., who reported these to be only 0.64 and 0.58, respectively [7]. On the other hand, Jandial A et al., reported AUC value of 0.606 and 0.822 for RDW and APACHE II, respectively [8]. As far as comparison with APACHE II is concerned, the present study shows APACHE II to be relatively superior both in terms of sensitivity as well as specificity as compared to RDW, thus showing that APACHE II had higher discriminatory ability as compared to RDW which was in agreement with the observations of Jandial A et al., [8]. Although, APACHE II has higher discriminatory power as compared to RDW but it requires evaluation of a total of 13 parameters. While RDW value is very simple to obtain from CBC report which is the most commonly performed haematological test. Thus, it may offer the prognosis by measurement of only one parameter. So, RDW might be a cost-effective solution in low resource settings as compared to APACHE II as a prognostic marker of sepsis.



[Table/Fig-3]: Receiver-operator characteristic curve.

S. No.	Variables	TP	FP	FN	TN	Sens	Spec	PPV	NPV	Accuracy
1.	APACHE II >14.5	33	12	9	56	78.6	82.4	73.3	86.2	80.9
2.	RDW >14.5 (Preselected)	28	16	14	52	66.7	76.5	63.6	78.8	72.7
3.	RDW >14.35 (Study-derived)	30	19	12	49	71.4	72.1	61.2	80.3	71.8

[Table/Fig-4]: Calculation of efficacy of APACHE II and RDW (at preselected cut-off and study-derived cut-off) for the outcome mortality.
'z'=0.253; p=0.800 (NS); TP: True positive; FP: False positive; FN: False negative; TN: True negative; Sens: Sensitivity; Spec: Specificity; PPV: Positive predictive value; NPV: Negative predictive value

Limitation(s)

The present study was done in a small sample size, so larger sample data needed to validate the sensitivity. Secondly, sepsis is the most common cause of hospitalisation and has varied organ involvement,

so predicting the outcome on the basis of single haematological parameter may be questionable by various experts.

CONCLUSION(S)

The present study showed that RDW may be a good prognostic marker of sepsis and it is useful in predicting the mortality in septic patients. On comparison with APACHE II, this study showed that APACHE II is relatively superior in terms of sensitivity, specificity and discriminatory power. But APACHE II is cumbersome scoring system as it requires multiple parameters and has to be done within 24 hours while RDW is simple, routinely done as a part of CBC, inexpensive, easily available. So, RDW may be a good simple prognostic marker of sepsis in developing country like India.

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