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Red Cell Distribution Width in Various Clinical Settings and Correlation with Inflammatory Markers and Serum Parameters: A Prospective Study

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Abstract: Red cell distribution width (RDW) is a measure of degree of variation in the red blood cell size. RDW is recorded as a part of the standard complete blood cell count. The objective of this prospective research study is to find out the independent association of RDW with morbidity in various clinical conditions. This was a fourteen months prospective study done on 450 patients who attended OPD in tertiary care hospital, out of which 306 patients were diagnosed with various clinical conditions, out of which 270 patients showed raised RDW values. In multivariable analysis, RDW remained significantly associated with patient morbidity. In patients, RDW is an independent predictor of morbidity. Considering the fact that RDW is routinely measured in complete blood count without added expenses, this can play role as an "priceless prognostic indicator" in patients.

Keywords: Red Cell Distribution Width, Complete blood picture, Prognostic indicator.

INTRODUCTION

Red cell distribution width (RDW) is a routine parameter and relatively new, which is evaluated in a fully automated hematology analyzer, and it is a part of the standard complete blood count (CBC). RDW expresses small variations and changes in different populations of red cell size. The normal range for measuring the differences in the size of red blood cells is between 11.5% and 15.5%. Elevated red blood cell distribution width could mean that a person is anemic and is at risk of other health conditions. RDW greater than 15.5% states that there is a large degree of variation in red blood cell size.

An increased RDW result from conditions that modify the red blood cells due to premature release of immature cells into the blood stream.

Recent advanced studies have identified RDW as a prognostic indicator in community-acquired pneumonia, septic shock, acute kidney injury, pulmonary hypertension, pulmonary embolism, peripheral artery disease and in patients with clinically significant cardiovascular disease. We need red blood cells to carry oxygen from your lungs to every part of your body. Anything outside of the normal range in red blood cell width or volume indicates a possible problem with bodily function that in turn may affect oxygen getting to various parts of your body [1-4]. However, with certain diseases, you may still have a normal RDW. The RDW test is used to help diagnose types of anemia, example anemia of chronic diseases [5] and other medical conditions including: infections, lung diseases, diabetes, endocrine diseases and obesity [6-12]

METHODS

This is a prospective study done for a period of 14 months in a tertiary care hospital. The Inclusion Criteria was all consecutive individuals who attended tertiary care hospital during this period were considered for study for which a CBC with RDW was available in the laboratory database. Exclusion criteria were those patients who were under radiation therapy and chemotherapy. The study was in accordance with the ethical standards and consent obtained from patients. Univariable analysis was done to determine the association between patient factors and patient morbidity. Chi-square test was done for categorical variables, whereas independent samples *t*-test was used to analyze interval data as appropriate. After evaluating them individually, multivariable logistic regression analysis was done on patient factors that had a significant association with patient morbidity. Those with $P = 0.008$ or less on univariable analysis was included.

RESULTS

Out of 450 patients who were taken for this prospective study were divided into two groups: the normal group and the diseased group. Out of 450 patients the normal were 144 patients and diseased were 306 patients. Out of these 306 diseased group 270(89%) patients had raised RDW values. Table-1 showing number of patients with raised RDW in diseased group. Out of 270 patients with raised RDW, 189 patients showed leucocytosis, raised ESR and C-Reactive Protein. Figure-1 showing number of cases with raised RDW in correlation with inflammation.

The prognostic value of RDW as an indicator of morbidity was investigated for both the groups. The primary end point of this study is to analyze the significant association of RDW with morbidity as an individual factor. The RDW values of the patients were measured in our laboratory, and the reference range is 11.5–15.0. The RDW value of 15.65 was used as a cutoff in our study. A set of variables that might confound the RDW association with the morbidity was analyzed in this study. This includes various co-morbidities. The mean age of the patients was 50.5 ± 20.5 years.

Table-1: showing number of patients with raised RDW in diseased group

S.NO	Clinical condition	Number of patients	Number of patients with raised RDW
1	Endocrine diseases including diabetes	108	94
2	Infections / Tuberculosis	52	46
3	COPD	45	43
4	Hypertension	20	18
5	Renal diseases/UTI	59	52
6	Congestive cardiac failure	16	12
7	HIV	6	5
	Total	306	270

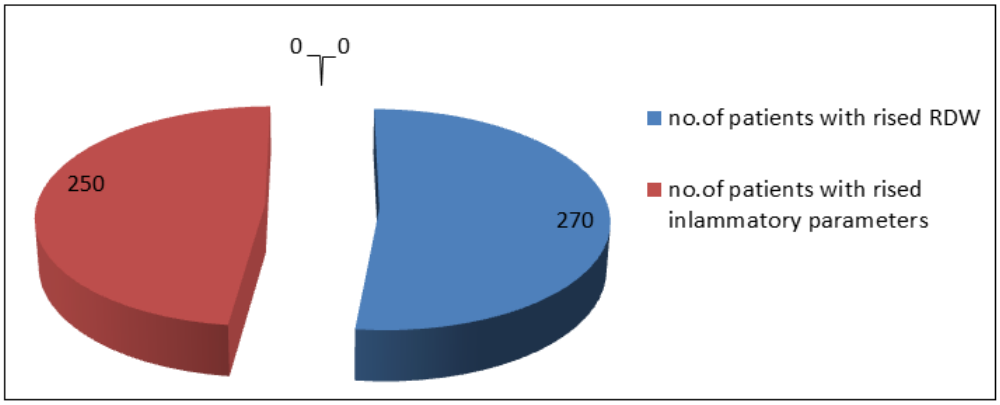

Fig-1: showing number of cases with raised RDW in correlation with inflammatory markers

DISCUSSION

In the present prospective study, we measured and calculated the multivariable in different patient co-morbidities, which we commonly encountered. This includes hypertension, diabetes mellitus, human immunodeficiency virus infection, chronic obstructive pulmonary disease, end-stage renal disease, congestive cardiac failure, tuberculosis, thyroid disease, dyslipidemia and acute pancreatitis. Similarly in Wang D and Ucar et al in their studied compared RDW value with different co-morbidities [13, 14]. However, the above variables were included in the study essentially to investigate the independent association of RDW with the morbidity in correlation with ESR, in which Lippi G et al study also showed similar objective [1-3].

In the present study, out of 450 individuals, 144 were normal and 306 were diseased of which 270 patients showed raised RDW. It has been hypothesized that an increase in oxidative stress contributed to the increased release of inflammatory cytokines leading to iron immobilization which may act an important role in increasing the RDW value. RDW therefore serves as an extensively available, "priceless prognostic indicator" which if raised in a clinical setting is in favour of an underlying complex hyper inflammatory pathologic process [1-4]. Similarly in our study also showed 270 patients with raised RDW out of which 250 patients had increased inflammatory parameters such as leucocytosis, ESR and CRP

Taking into consideration the fact that the RDW is routinely measured in the automated complete blood count (CBC) analyses and has no added price, this makes our study of RDW as a prognostic indicator efficacious and attractive. Risk-stratification of patients can be potentially made by the measure of an inexpensive serologic indicator, i.e., RDW, to give

support in taking prognosticating clinical decisions. The target of this research study is to derive the prognostic value of RDW as an independent factor in determining prognosis in patients. However, Shteinshnaider M et al. in their study showed the importance of RDW as a prognostic indicator [15].

In this study, our results showed that the RDW value at the time of visit is significantly associated with increased morbidity with $P = 0.008$. The mean RDW in the deceased group is 16.20 and 15.0 in the normal group, validating the RDW cutoff value as 15.65. The exact pathophysiology that makes increased RDW a potential marker of prognosis of mortality in acute illness is not very clear. In conditions related to increased red blood cell destruction, blood loss, or after blood transfusions, RDW can be elevated. However, many studies in the medical literature have revealed that the relationship between RDW and morbidity of RDW is independent of anemia. A plausible explanation is that RDW is a surrogate marker of inflammation-related oxidative stress [3]. Severe inflammatory conditions such as severe pneumonia and sepsis have been known to increase the degree of Anisocytosis by causing a disruption in erythropoiesis, changing the red blood cell membrane deformability and red blood cell circulation half-life, and this eventually causes an increased RDW.

Bion [16] suggested that RDW can also be possibly used to give some insight into the patient's degree of physiological reserve, one of three main determinants of clinical outcome. Hunziker *et al., [17]* suggested that the physiological reserve is a reflection of the collective cellular response to an acute stressor state of hypoxia and ischemia. This results in a cascade of necessary events to improve the delivery of oxygen to target organs including increasing erythropoietin production which in turn leads to the increased manufacture and release of mature erythrocytes from the bone marrow into the bloodstream. The faster and more efficient process of reactive erythropoiesis carried out under oxidative stress, the more effective will be the patient's ability to physiologically deal with the acute stressor event. This is interesting because the release of large immature red cells that possess poor oxygen-binding capacity, which manifests as an increased RDW, implies suboptimal and ineffective response to the oxidative stress such as sepsis. It may also give a tenable explanation for why an increased RDW is associated with increased morbidity in patients. In the present study, sensitivity and specificity are 85% and 80% respectively. The current study does, however, have some limitations. Inflammatory markers other than ESR, CRP were not included and there can be biologic variability.

CONCLUSION

To conclude RDW acts as a good prognostic marker in patients and helps to improve decision making in use of effective therapeutic intervention. This also helps in making clinical decisions at the earliest. However, taking the fact into consideration that RDW is routinely measured as part of CBC analysis and thus is free of additional expensive costs.

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