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Correlation between Red Cell Band Width and Disease Severity in Rheumatoid Arthritis

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ABSTRACT

Objective: To determine the correlation between red cell band width and disease severity in patients suffering from rheumatoid arthritis.

Study Design: Cross sectional study.

Place and Duration of Study: Rheumatology/General Medicine Department, Pak Emirates Military Hospital, Rawalpindi Pakistan, from Jul 2019 to Feb 2020.

Methodology: Patients of rheumatoid arthritis, who were already diagnosed as per 2010 ACR/EULAR (American college of Rheumatology/European League Against Rheumatism) classification criteria were included in the study. Red cell band width was determined in all the patients from laboratory of own hospital. Severity of rheumatoid arthritis was determined on the basis of Disease Activity Score-28 (DAS-28).

Results: Mean age of the study participants was 36.37±7.822 years. 99(39.6%) patients had mild activity disease, 115(46%) had moderate while 36(14.4%) had severe activity of illness. 137(54.8%) had red cell band width within normal range while 113(45.2%) had increased with. Pearson chi-square test revealed that increasing age, long duration of illness and increased red cell band width had a statistically significant association with severity of illness (p-value <0.05).

Conclusion: Considerable number of patients suffering from rheumatoid arthritis had severe form of illness. Increased red cell band width emerged as a predictor of severe form of illness among the study participants in addition to the advancing age of patient and long duration of illness.

Keywords: Red Cell Band Width, Rheumatoid Arthritis, Severity.

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INTRODUCTION

Rheumatoid arthritis has been a common chronic immunological disease in all parts of the world.[1] Epidemiological statistics have not been different in our part of the world and a lot of patients get diagnosed for this chronic disease by the general physicians, medical specialists and rheumatologist each year.[2] Routine blood investigations, specific immunological tests, targeted x rays and musculo-skeletal ultrasound are the modalities which have been commonly adopted to support the clinical findings to make the diagnosis of rheumatoid arthritis.[3] Biochemical markers of disease severity for rheumatoid arthritis other than the clinical findings have been an area of interest for the physicians and researchers for long.[4]

Red cell band width has been one of those blood indices which is usually less discussed as it is not directly linked to or considered as a diagnostic marker for any of the clinical conditions. But this parameter surely is of importance as it gets affected by number of clinical conditions and it may be used as a prognostic marker to see the treatment response or the disease severity in a lot of diseases especially the immune mediated disorders.[5,6]

Immune mediated diseases have been under research for years now from a lot of aspects. Predicting disease severity with help of Biochemical markers is gaining importance with each passing day as most of these diseases cannot be cured so aim usually is to keep the disease in remission or at lowest disease activity to help patient achieve best possible quality of life. Lin *et al.,* in 2018 performed a case control study and concluded that RDW (Red blood cells distribution width) is increased only in Rheumatoid Arthritis patients, but not in those with Ankylosing Spondylitis and Osteoarthritis. However, increased RDW and its association with C-reactive protien may be mainly due to reduced hemoglobin. Therefore, whether RDW could be used as useful inflammatory index for RA, AS and OA remains to be evaluated.[7] Yunchun *et al.,* in 2016 evaluated the significance of red blood cell distribution width (RDW) and other factors for the disease activity in rheumatoid arthritis and revealed

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an association between RDW and levels of inflammatory factors and autoantibodies in RA. This association may be related to the underlying pro-inflammatory state and increased oxidative stress, both of which correlate with impaired erythrocyte maturation. RDW, Rheumatoid factor and anti-CCP antibodies are key players in the pro-inflammatory and pro-atherogenic status of RA, and they may represent useful markers to improve characterization of disease activity in RA patients, thereby helping the clinician to define more appropriate therapeutic strategies.[8] Hoorta-Baas *et al.,* in 2019 did a study with the objective to evaluate RDW in patients with osteoarthritis (OA), fibromyalgia (FM), rheumatoid arthritis (RA) and spondyloarthritis (SpA) and to evaluate its clinical importance. They came up with the conclusion that in subjects with articular pain, RDW interpretation is a useful tool in clinical practice to distinguish between articular inflammatory and non-inflammatory joint diseases, as with C-reactive protien. RDW seems to be a surrogate marker of the chronic inflammatory process.[9]

Rheumatoid arthritis is a commonly diagnosed clinical condition in our part of the world.[10] Despite multiple options available as disease specific treatment, this disease is notorious to progress and may appear in severe form during the course of time. Most of our population lives in rural area so sometimes it is difficult for them to follow up routinely and may present when disease takes a severe form. Limited work has been done in our set up to look for the laboratory parameters which could predict the disease severity in patients suffering from rheumatoid arthritis. We therefore planned this study with the rationale to determine the correlation between red cell band width and disease severity in patients suffering from rheumatoid arthritis presenting in general medicine/rheumatology outpatient department at Pak Emirates Military Hospital (PEMH) Rawalpindi.

METHODOLOGY

This cross-sectional study was conducted during the period of July 2019 to February 2020. Sample size was calculated by using the WHO sample size calculator and keeping the population prevalence proportion of increased RCBW in patients of RA as 95%.[10] Non probability consecutive sampling technique was used to gather the required sample size for this study.

Inclusion Criteria: Patients presenting at General Medicine/Rheumatology Outpatient Department of PEMH, Pakistan who fulfilled the 2010 ACR / EULAR (American college of Rheumatology/ European League Against Rheumatism) classification criteria, with age between 15 and 60 years were included in this study.[11]

Exclusion Criteria: Patients who were in complete remission or without a clear diagnosis or those with comorbid other autoimmune disease or those who were pregnant were excluded from the study. Patients with comorbid malignant disease of any type were also excluded at the start of the study. Patients who were using any kind of illicit or psychoactive substance or those with any hematological disorder due to any cause other than RA or hematological or lymphoid malignancy were also excluded from the study.

Permission from hospital ethics committee via letter number A/28/31 March 2020 was sought prior to commencement of study. All the patients signed the informed consent form before getting enrolled into the study. About 3ml venous blood samples were taken in EDTA potassium tubes from the patients diagnosed as RA. The RDW was determined using an XE-2100 (Sysmex, Kobe, Japan) analyzer for each patient in the laboratory of our own hospital. The normal value for RDW was taken as 13±1.5%.[12] More than this as regarded as increased RDW.

Disease activity score-28 (DAS-28) was developed in 1983 in Holland with a formula that includes number of tender and swollen joints, self-assessment of health using the visual-analog scale (VAS), and erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP). It predicts the activity and severity of underlying rheumatoid arthritis. Due to its complex calculation and variable of contribution of each parameter, a set formula available on online calculators has been used to incorporate all the clinical and laboratory parameters and calculate the final score.[13] Interpratation of the final score was done as Low disease activity: DAS-28 = 2.6 -- < 3.2, Moderate disease activity: DAS-28 > 3.2 -- ≤ 5.1, and High disease activity: DAS-28 >5.1.[13]

Statistical analysis was performed by using the SPSS 23.0. Frequency and percentage were calculated for the qualitative variables like gender, patients with mild, moderate or severe activity of disease or patients with and without the increased red cell band width.

Mean and standard deviation was calculated for the age of the patients and duration of illness. Pearson chi-square test was used to see the association between the age, gender, presence of increased RDW and duration of RA with the severity of illness. The *p*-value less than or equal to 0.05 was considered as significant for this study.

RESULTS

Two hundred and fifty patients of rheumatoid arthritis were recruited in the analysis after inclusion and exclusion criteria were applied. Mean age of the study participants was 36.37±7.822 years. Mean duration of rheumatoid arthritis among the study participants was 3.57±6.125 years. Table-I shows that 187(74.8%) patients were female while 63(25.2%) were male. 99(39.6%) patients had mild activity disease, 115(46%) had moderate while 36(14.4%) had severe activity of illness. 137(54.8%) and red cell band width within normal range while 113(45.2%) had increased with.

Table-I: Characteristics of Patients with Rheumatoid Arthritis Included in the Study

Study Parameters	n(%)
Age (years)	
Mean+SD	36.37±7.822 years
Range (min-max)	15 years-57years
Mean duration of illness	3.57±6.125 years
Gender	
Male	63(25.2%)
Female	187(74.8%)
Red cell band width	
Within range	137(54.8%)
Increased	113(45.2%)
Disease activity	
Low	99(39.6%)
Moderate	115(46%)
Severe	36(14.4%)

Table-II: Relationship of Various Factors with the Severity of Rheumatoid Arthritis among the Target Population

Socio-demographic factors	Low activity	Moderate activity	Severe activity	*p*-value
Age				
<40 years	66(66.7%)	51(44.4%)	15(41.7%)	0.002
>40 years	33(33.3%)	64(55.6%)	21(58.3%)	
Gender				
Female	73(73.7%)	85(73.9%)	29(80.5%)	0.678
Male	26(26.3%)	30(26.1%)	07(19.5%)	
Duration of illness				
<5 years	56(56.6%)	41(35.6%)	17(47.2%)	0.009
>5 years	43(43.4%)	74(64.4%)	19(52.8%)	
Red cell band width				
Within range	67(67.7%)	61(53.1%)	09(25%)	<0.001
Increased	32(32.3%)	54(46.9%)	27(75%)	

Pearson chi-square test (Table-II) revealed that increasing age (*p*-value-0.002), long duration of illness (*p*-value-0.009) and increased red cell band width (*p*-value<0.001) had a statistically significant association with severity of illness among the patients suffering from rheumatoid arthritis while gender had no statistically significant relationship with the severity of illness (*p*-value>0.678).

DISCUSSION

Rheumatology is an emerging specialty in our country with limited number of trained doctors available to manage a huge number of patients which mostly rely on the general practitioners or the medial specialists. Adequate knowledge about all the aspects of rheumatology diseases can only enable the doctors to manage the patients effectively and screen and pick up the cases with advanced disease early for aggressive management plan. Various immune based or blood indices have been used in the diagnosis and prediction of severity of illness in rheumatoid arthtiirs.[3-5] We planned this study with the rationale to determine the correlation between red cell band width and disease severity in patients suffering from rheumatoid arthritis presenting to our teaching hospital from all parts of the country.

Lee *et al.*, in 2010 published an interesting study and concluded that RDW has a strong association with the presence and severity of rheumatoid arthritis. It has also been linked to raised CRP among the target population.[14] Our findings were quite similar to them as RDW has strong association with more severe diseases in our study population. Our scope was limited so we did not study correlation of other parameters like CRP and ESR.

Salvagno *et al.*, in 2015 and Patel *et al.*, in 2018 published that an increased RDW mirrors a profound deregulation of erythrocyte homeostasis involving both impaired erythropoiesis and abnormal red blood cell survival, which may be attributed to a variety of underlying metabolic abnormalities such as shortening of telomere length, oxidative stress, inflammation, poor nutritional status, dyslipidemia, hypertension, erythrocyte fragmentation and alteration of erythropoietin function.[15,16] Our findings also suggest that RDW should be incorporated when a patient of RA is investigated because it can predict the severity of illness.

Rodríguez-Carrio *et al.*, in 2015 did a very interesting study and incorporated the cardiovascular risk in addition to severity of RA in their study design

and came up with the findings that RDW at disease onset may be used as an early marker of CV risk in RA, whereas in patients with established disease it was related to the activity of the disease. These findings suggest that RDW can be considered as a surrogate marker of inflammation and, consequently, CV risk in RA patients.[17] Our results supported their results from the point of view that RDW predicted disease severity in our study. For cardiovascular risk factors prediction studies with a longitudinal design need to be conducted in local population to fill the gap. Same authors in same year published another study highlighting the underlying mechanism that RDW was associated to Endothelial Progenitor Cells (EPC) depletion and increased levels of different mediators linked to endothelial damage and vascular repair failure, thereby shedding new light on the nature of RDW as cardiovascular and disease severity predictor.[18]

Lin *et al.*, in 2018 and Yunchun *et al.*, in 2016 performed studies with a similar design as that of ours and came up with the similar results that RDW had a strong link with presence of active inflammation and more severe disease among the patients suffering from RA.[7,8] Our results were similar to their results and showed that this phenomenon has not been different in our population and with more studies we could be able to make our local guidelines to incorporate this parameter in routine investigation of RA.

Small sample size, cross-sectional study design, ample population from a single center and lack of availability of RDW values prior to the onset of RA or at the time of diagnosis of RA are some of the limitations which need to be addressed in future studies to generate the results which could be generalized to the local population.

CONCLUSION

Considerable number of patients suffering from rheumatoid arthritis had severe form of illness. Increased red cell band width emerged as a predictor of severe form of illness among the study participants in addition to the advancing age of patient and long duration of illness.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

SR & AF: Data acquisition, data analysis, critical review, approval of the final version to be published.

AR & AK: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

AB: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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