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Evaluating the Role of Novel Haematological Parameters with Disease Activity in Rheumatoid Arthritis

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ABSTRACT
BACKGROUND- RA affects approximately 0.5 – 1% of the adult population worldwide with a female-to-male ratio of 2-3:1, showing a female preponderance like other autoimmune disorders. Assessing the Disease activity regularly in these patients is a very important aspect in management and it can be calculated by different scales such DAS 28, CDAI, SDAI and RAPID3. Various indices are available from hematological parameters, which are not well studied for evaluating disease activity in RA. Hence, we conducted this study to evaluate the role of NHL score, NLR, PLR and RDW in RA, and its correlation with existing disease activity scores of DAS28CRP, DAS 28 ESR and CDAI.
METHODS- this is a hospital-based cross-sectional study performed in AJ Institute of Medical Sciences, Mangalore. All the patients with Rheumatoid arthritis were included.
RESULTS- This study was used to compare the various methods of assessing Rheumatoid disease activity, while evaluating the utility of NHL score, NLR, PLR and RDW in RA. When we correlated NLR and RDW with DAS28CRP, DAS28ESR and CDAI we found that the values were statistically significant (p-value using ANOVA and Pearson's correlation is 0.002*). Similarly, when we correlated PLR and NHL scorewith the above indices, we found that there was no statistical significance.
CONCLUSION- In our study, we found that NLR and NHL correlate strongly with indices of disease activity in RA, while PLR and RDW score do not. Hence NLR and NHL can be alternative indices of disease activity in a third world country with limited resources.

I. INTRODUCTION

Rheumatoid arthritis (RA) is a systemic autoimmune disorder characterized by disabling inflammatory arthritis and some extra-articular involvement. RA affects approximately 0.5 – 1% of the adult population worldwide with a female-to-male ratio of 2-3:1, showing a female preponderance like other autoimmune disorders.

Though considered to be a disease of the joints RA exhibits features of systemic disease by involving several major organ systems. Despite the advances in treatment, the life expectancy of patients with RA is reduced by 3-10 years because of the comorbidities. The risk factors can be non-modifiable factors like genetic factors and female gender and modifiable factors like environmental and lifestyle factors.[1] C-reactive protein (CRP), the erythrocyte sedimentation rate (ESR), and the rheumatoid factor (RF) have been considered as the markers that estimate disease activity in patients with RA.

Activated platelets play a critical role in the atherogenesis. The association of platelet to lymphocytes ratio with outcomes of patients with ankylosing spondylitis, non-small cell lung cancer, and acute coronary syndrome have been attested in many studies. Inflammation may be a hidden factor that can explain this correlation as Patients with RA present with increasing platelet counts during active stages and decreasing counts during remission of inflammation. [2]

Assessing the Disease activity regularly in these patients is a very important aspect in management and it can be calculated by different scales such as ACR 20,50,70 improvement criteria ,Disease Activity Score employing 28 joint count (DAS28) simplified disease activity index (SDAI), Clinical Disease Activity Index (CDAI) and routine assessment of patient index data 3 (RAPID3).DAS 28, CDAI, SDAI and RAPID3 are continuous measures of disease activity useful in clinical practice whereas ACR 20 50 70 improvement criteria gives a dichotomous response variable and is used mainly in clinical trials . Also, DAS28 (ESR/CRP) scale includes acute phase reactants in its calculations such as the use of erythrocyte sedimentation rate (ESR) or C reactive protein (CRP) and uses a complicated calculation which requires a calculator and laboratory assistance.

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A systemic autoimmune disease, rheumatoid arthritis (RA) is characterised by debilitating inflammatory arthritis and some extra-articular involvement. The cause of RA is unknown, but the inflammation and cytokines that are released as a result of CD4+ T cells and antibodies against self-antigens cause ankylosis and progressive joint destruction by the proliferation of synovial cells, which results in synovitis and pannus formation and ultimately results in cartilage loss. [3]

Patients' disease activity can be determined using a variety of scales, including the Clinical Disease Activity Index and the Disease Activity Score employing a 28 joint count (DAS28) (CDAI).

However, the DAS28 scale uses acute phase reactants in its computations, such as the usage of ESR or C-reactive protein (CRP). Although other characteristics including age, gender, serum fibrinogen level, and immunoglobulins can affect ESR, these other factors often have little to no impact on how widely it is utilised. [3] In addition, calculating the DAS28 score takes time because it requires the patient to complete laboratory tests and an online calculator or app. [4,5]While a tool that is solely clinical, like CDAI, can be beneficial without requiring any of the aforementioned laboratory testing. [6,7]

Additionally, the majority of patients who visit government hospitals come from lower socioeconomic classes and occasionally skip having tests done. In these settings with limited resources, a purely clinical index like the CDAI might be an effective indicator. Furthermore, there is a dearth of information regarding the usage trends of disease-modifying anti-rheumatic medications (DMARDs) in our country and in relation to the rheumatoid factor. [2]

Hematological indices, which use a variety of clinical and laboratory indicators, are more practical than disease activity composites, which are frequently employed in RA. Hence, it is essential to create haematological indicators that accurately assess RA activity. The purpose of this study is to ascertain if four different haematological indicators, including RDW, NHL score, NLR, and PLR, can be utilized to evaluate disease activity in RA patients.

II. METHODS AND MATERIALS

Upon enrolment, peripheral venous blood was tested for total and differential white blood cells (neutrophils and lymphocytes), haemoglobin, and platelets. SII, NHL score, NLR, and PLR were calculated using neutrophils, lymphocytes, haemoglobin, and platelets. NHL score = neutrophil/(hemoglobin × lymphocyte), NLR = neutrophil/lymphocyte, and PLR = platelet/lymphocyte. NHL score was g/dL.Datawas reported as mean with standard deviation (SD) or median (interquartile range) for continuous variables and number (% of cases) for categorical variables.

Chi-square or Fisher's exact test was used to compare categorical variables between groups. Student's t-test and Kruskal–Wallis tests were employed to compare RA patients and controls for continuous variables. Hematological indicators and RA disease activity factors were correlated using Pearson's correlation analysis. ROC curve analysis with estimation of area under the curve (AUC) and 95% confidence interval (CI) was used to verify RA diagnosis and remission haematological indicators. ROC analysis using Youden's index determined haematological index cut-off values for RA prediction. SPSS 21.0 performed all statistical analyses (SPSS Inc., Chicago, IL, USA). Statistical significance was considered when p value < 0.05.

III. RESULTS

The study population consisted of 40 patients with RA and 20 control subjects. Themean age of RA patients and controls was 58.7 years and 59.5 years, respectively, whichwas not statistically different. 78.45% of the study population was female, which corroborates with the findings of other studies. The mean diseaseduration of RA was 9.35 years (SD 6.89 years). The levels and these positivity frequencies ofRFwas879 IU/mLand 72.34% respectively.

Hematologically, RA patients had higher RDW and NLR than controls ($p < 0.001$). NHL score and PLR were greater in RA, but not significantly, which may be explained by a smaller sample size may explain this. RA and control groups had substantial haematologicaldifferences.DAS28-ESR and DAS28-CRP showed a statistically significant rise in NHL score and NLR as disease activity deteriorated. RDW and PLR were not statistically significant in DAS28 CRP and CDAI disease activity subgroups ($p > 0.05$ for all), however DAS28-ESR was ($p = 0.021$). Although CDAI disease activity subgroups were statistically significant, no gradually increasing trend in the haematological indices was identified.

When we correlated SII with each of the indices, we found that there was a positive correlation between NLR and NHL, but not with the other scores.

IV. DISCUSSION

ESR, CRP, DAS28, and CDAI are clinically available RA disease activity markers [3]. Peripheral blood lymphocyte, platelet, and neutrophil counts or ratios have been used to estimate or predict systemic inflammatory response. RDW, NHL score, NLR, and PLR were assessed for disease activity in RA patients in this study. Hematological indicators RDW, NHL score, and NLR were strongly linked with ESR, CRP, and composite markers of disease activity. RDW and NHL score, not NLR and PLR, helped diagnose RA and determine remission status.

This study compared RA activity using RDW, NHL score, NLR, and PLR. Hemoglobin, lymphocytes, and neutrophils comprise the NHL score. Pro-inflammatory cytokines limit bone marrow erythropoiesis and diminish circulating erythrocyte survival, causing anaemia.

In previous clinical studies, multiple hematological indices such as NLR, PLR, or meanplatelet volume have been compared with disease activity in RA [10–17]. RA patientsshowed significantly higher NLR compared with controls [10–12,14–17], which is in agreement with the finding in the present study. In most studies, a close association betweenNLR and disease activity indices such as DAS28, ESR, or CRP was reported [11,12,15,16].

V. CONCLUSION

Hematological indices are easily measured and available disease activitymarkers of systemic inflammation in RA. Among hematological indicesNHL score and NLR, but not RDW and PLR were associated with disease activity measures and adequatelyreflected disease activity in RA.

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