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Assessment of Disease Activity in Rheumatoid Arthritis Patients Using Neutrophil-to-Lymphocyte Ratio and Platelet-to-Lymphocyte Ratio.

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Abstract

Background: Systemic symptoms, increasing joint degradation, and persistent synovitis are the hallmarks of RA (Rheumatoid Arthritis), a chronic autoimmune inflammatory disease. Timely treatment and disability prevention depend on accurate disease activity assessment. The standard instrument for assessing the severity of an illness is the Disease Activity Score-28 (DAS-28), although it requires a number of clinical and laboratory criteria. Derived from regular complete blood counts, the NLR (Neutrophil-to-Lymphocyte Ratio) and PLR (Platelet-to-Lymphocyte Ratio) have become widely accessible and reasonably priced inflammatory indicators. The purpose of this study was to assess the relationship between NLR and PLR and disease activity in rheumatoid arthritis patients and ascertain their value as stand-in indicators of systemic inflammation. ***Methods:*** Between January 2019 and June 2020, 164 rheumatoid arthritis patients who were hospitalised in the Department of General Medicine at ESIC Medical College and PGIMSR Model Hospital in Bengaluru participated in a hospital-based correlational study. Following informed agreement, patients were chosen in accordance with the American College of Rheumatology's (ACR) standards. A pre-made proforma was used to record clinical information and laboratory tests. DAS-28 was used to measure disease activity, and standard haematological parameters were used to compute NLR and PLR. Correlation analysis was performed to determine the relationship between these biomarkers and DAS-28 scores. ***Results:*** Patients with rheumatoid arthritis demonstrated significantly elevated NLR and PLR values. Both biomarkers showed a significant positive correlation with DAS-28 ESR scores, indicating that higher NLR and PLR were associated with increased disease activity and systemic inflammation. ***Conclusion:*** NLR and PLR are simple, cost-effective, and readily available biomarkers that correlate significantly with disease activity in rheumatoid arthritis. These indices may serve as reliable adjuncts to DAS-28 for assessing systemic inflammation and monitoring disease activity, particularly in resource-limited settings.

Keywords: Rheumatoid Arthritis, Neutrophil-to-Lymphocyte Ratio (NLR), Platelet-to-Lymphocyte Ratio (PLR), Disease Activity Score-28 (DAS-28), Systemic Inflammation.

INTRODUCTION

Persistent synovial inflammation, increasing cartilage degradation, bone erosion, and extra-articular symptoms are the hallmarks of RA (Rheumatoid Arthritis), a chronic, systemic autoimmune inflammatory disease that eventually causes functional impairment and a lower quality of life.[1] It is more prevalent in women than in men and affects 0.5–1% of adults globally.[1,2] Genetic predisposition, environmental variables, and dysregulated innate and adaptive immune responses interact intricately in the development of RA, resulting in chronic inflammation and irreparable joint destruction if treatment is not received.[1,3] In individuals with RA, early diagnosis and timely use of disease-modifying antirheumatic medications (DMARDs) using a treat-to-target approach have greatly improved clinical results and decreased long-term disability.[1,4]

For the purpose of making therapeutic decisions and tracking therapy response in RA, accurate evaluation of disease activity is crucial.[4] In ordinary clinical practice and research, composite disease activity indicators including the Disease Activity Score in 28 joints (DAS28), SDAI (Simplified Disease Activity Index), and CDAI (Clinical Disease Activity Index) are frequently utilised.[4] Despite the fact that these indices offer accurate indicators of disease activity, they necessitate thorough clinical examination and laboratory tests like ESR (Erythrocyte Sedimentation Rate) or CRP (C-Reactive Protein), which are not always easily accessible, especially in healthcare settings with limited resources.[4]

Inflammation in RA is associated with characteristic alterations in peripheral blood cell counts, including neutrophilia, relative lymphopenia, and thrombocytosis.[3,5] Calculated from standard complete blood count values, the NLR (Neutrophil-to-Lymphocyte Ratio) and PLR (Platelet-to-Lymphocyte Ratio) have become new inflammatory biomarkers that indicate systemic immunological activity.[5,6] Because these indices are inexpensive, reproducible, and universally available, they have gained increasing attention in the assessment of various inflammatory, cardiovascular, malignant, and autoimmune disorders.[5,6]

Several studies have demonstrated significantly higher NLR and PLR values in patients with active RA compared with those in remission or with low disease activity, and both indices have shown positive correlations with DAS28, ESR, and CRP.[6-8] A recent systematic review and meta-analysis involving more than 3,000 patients concluded that elevated NLR and PLR effectively discriminate active from inactive RA, suggesting their potential utility as adjunctive markers of disease activity.[5] Furthermore, recent evidence has demonstrated acceptable diagnostic accuracy of NLR and PLR in identifying active RA, although these biomarkers should complement rather than replace established clinical assessment tools.[7]

AIMS AND OBJECTIVES

The present study aims to assess the severity of rheumatoid arthritis in patients by evaluating disease activity using the Disease Activity Score-28 (DAS-28) and to determine the relationship between systemic inflammatory markers, namely the NLR and PLR, and disease activity. The specific objectives are to assess the severity of rheumatoid arthritis using the DAS-28 clinical scoring system and to study the correlation of NLR and PLR with DAS-28 for assessing of systemic inflammation and disease activity in patients with rheumatoid arthritis.

MATERIALS AND METHODS

Study Design

This observational cross-sectional study was carried out in the general medicine department of ESIC Medical College & PGIMSR Model Hospital in Bengaluru. During the course of the trial, 164 rheumatoid arthritis patients who met the inclusion criteria were enrolled one after the other. The Disease Activity Score-28 (DAS-28) was used for clinical evaluation of disease activity.

Inclusion and Exclusion Criteria

The study included male and female patients aged 18 years and above who had been previously diagnosed with rheumatoid arthritis according to the EULAR (European League Against Rheumatism) classification criteria and who were willing to participate in the study by providing informed consent. Patients who did not provide informed consent and those with inflammatory diseases other than rheumatoid arthritis were excluded from the study.

Sample Size Calculation

On the basis of mean value of PLR in RA patients, from previous literature, sample size was calculated.
t tests - Means: Difference between two independent means (two groups)
Analysis: A priori: Compute required sample size
Input: Tail(s) = Two Effect size d = 0.4415000
α err prob = 0.05
Power (1-β err prob) = 0.80
Allocation ratio N2/N1 = 1
Output: Noncentrality parameter δ = 2.8269794

Critical t		1.9747158
Df		162
Total sample size	=	164
Actual power	=	0.8023992

Data Collection Procedure

Written informed consent was obtained from all patients before their enrollment in the study. Relevant demographic, clinical, and laboratory data were collected using a predesigned proforma. Patients were selected based on detailed clinical examination, fulfillment of the American College of Rheumatology (ACR)/EULAR classification criteria for rheumatoid arthritis, and relevant biochemical investigations.

Statistical Analysis

The Statistical Package for the Social Sciences (SPSS) program was used to enter and analyse the data. The study variables were summarised using descriptive statistics, such as frequency, percentage, mean, and standard deviation. Statistical

significance was defined as a p-value of less than 0.05 ($p < 0.05$). The independent sample t-test was utilised to compare the mean values between two independent groups, and the chi-square test was utilised to evaluate the relationship between categorical variables. Additional appropriate statistical tests were employed wherever necessary, depending on the nature and distribution of the data.

RESULTS

Table 1. Distribution of Study Participants by Sex

Sex	n	%
Female	135	82.3
Male	29	17.7
Total	164	100

Table 1 illustrates the sex distribution of the study participants. Females constituted the majority of the study population (82.3%), while males accounted for 17.7%, indicating the higher prevalence of rheumatoid arthritis among women.

Table 2. Distribution of Rheumatoid Factor Positivity

RA Factor	N	%
Positive	121	73.8
Negative	43	26.2
Total	164	100

Table 2 shows that 73.8% of patients were rheumatoid factor positive, whereas 26.2% were rheumatoid factor negative.

Table 3. Distribution by Age Group

Age Group (in years)	n
18–20	0
21–30	13
31–40	44
41–50	61
51–60	34
≥61	12
Total	164

Table 3 depicts the age-wise distribution of study participants. Most patients belonged to the 41–50 years age group.

Table 4. Mean Inflammatory Markers

Variable	Mean
Platelet-to-Lymphocyte Ratio (PLR)	226.0
Neutrophil-to-Lymphocyte Ratio (NLR)	4.03
DAS28 score	4.43

Table 4 summarizes the mean values of PLR, NLR and DAS28 among the study population.

Table 5. Distribution According to DAS28 Disease Activity

DAS28 Category	N	%
Remission (<2.8)	6	3.7
Low (2.8–3.2)	14	8.5
Moderate (3.2–5.1)	96	58.5
High (>5.1)	49	29.9

Table 5 demonstrates that the majority of patients had moderate disease activity, followed by high disease activity.

Table 6. Gender Distribution According to DAS28 Category

DAS28 category	Female	Male
<2.8	5	1
2.8–3.2	14	0
3.2–5.1	80	16
>5.1	37	12

Table 6 presents the distribution of disease activity by gender. Females predominated across all disease activity categories.

Table 7. Correlation of Inflammatory Markers with Disease Activity

Parameter	Observation
PLR vs DAS28	Positive correlation
NLR vs DAS28	Positive correlation
NLR vs ESR	Positive correlation
PLR vs ESR	Positive correlation

Table 7 summarizes the correlation analysis, demonstrating positive correlations of NLR and PLR with DAS28 and ESR, indicating that both biomarkers reflect disease activity.

DISCUSSION

Sex Distribution

In the present study, females constituted 82.3% (n = 135) of participants, giving a female-to-male ratio of approximately 4.6:1. This female preponderance is consistent with the well-established sex bias in rheumatoid arthritis (RA), generally quoted as a female-to-male ratio of about 3:1 since RA is a chronic inflammatory disease affecting mostly women with a female/male ratio of 3:1 (Maranini B).[9] The ratio observed here is closer to that reported by Chopra et al. (2012)[10] in an Indian COPCORD-based community study, in which 198 patients classified as clinical RA were 83% women, giving an overall female-to-male ratio of 5:1. Similarly high female representation has been reported by Intriago et al. (2019)[11] in an Ecuadorian hospital-based cohort, supporting a consistent cross-population gender skew in RA.

Rheumatoid Factor (RF) Positivity

RF positivity in the present cohort was 73.8%. This is comparable to the figure reported in an Indian multicentric diagnostic-utility study, where of 803 patients, RF was positive in 566 (70.5%) (Kumar A et al).[12] It is somewhat higher than the seropositivity reported by Handa et al. (2016)[13] in their review of Indian RA literature, where 62% of clinically diagnosed RA cases in a Pune-based cohort were seropositive for RF, while all were seropositive for anti-CCP antibody. The slightly higher RF-positivity in the present study compared with Handa et al. (2016)[13] but close agreement with the 70.5% reported in Kumar et al.,[12] may reflect differences in disease duration, assay method, or referral bias toward more established seropositive disease.

Age Distribution

The majority of participants were in the 41–50 age range, with the 31–40 age group coming in second. The peak age of RA onset has progressively moved from the fourth decade of life in the 1930s to the sixth and even seventh decade in recent decades, according to traditional epidemiological accounts of RA start (Slobodin, G., 2020).[14] It is also broadly consistent with general epidemiological statements that RA rates are more common among individuals aged 40–65 years. Chopra et al. (2012)[10] similarly found 42% of patients in the 25–44-year band and 40% in the 45–64-year band, closely paralleling the peak age distribution seen in the present study.

PLR, NLR and DAS28 (Mean Values)

The mean PLR (226.0), NLR (4.03) and DAS28 (4.43) in the present cohort suggest moderately active disease. In an Egyptian case–control study, active RA patients showed an NLR of 3.27 ± 2.81, with NLR and PLR significantly correlating with DAS28 ($p = .001$ and $p = .03$, respectively)[15] - a similar direction of association to the present findings, though the present NLR/DAS28 values are somewhat higher. Sargin et al. (2018)[16] likewise found that NLR and PLR were higher in RA patients than controls and correlated significantly with DAS28-ESR. A large retrospective Chinese Cohort Shen et al.,[17] reported that DAS28-ESR was positively associated with PLR, along with ESR, CRP, platelet and neutrophil counts, reinforcing the biomarker–activity relationship reported here.

DAS28-based Disease Activity Distribution

The majority of patients in this study had moderate disease activity (58.5%), followed by high disease activity (29.9%), with only 3.7% in remission. A Saudi cross-sectional study on Abdulaziz, S RAPID3/DAS28 correlation (2023)[18] similarly reported a mean DAS28-ESR of 4.16, categorised as moderate disease activity, in a predominantly female cohort (89%) - figures close to the present study's mean DAS28 of 4.43 in an 82.3% female cohort. This convergence suggests that clinic-based RA cohorts, as opposed to tightly monitored trial populations, often present with inadequately controlled disease activity.

Gender and DAS28 Category

Females predominated across all DAS28 categories in the present study, including high disease activity. This is consistent with the large multinational QUEST-RA cohort study (Sokka et al.)[19] where women had statistically significantly higher mean values on nearly all disease-activity measures compared with men, and met DAS28 remission less often, with a mean DAS28 of 4.3 in females versus 3.8 in males. Intriago et al. (2019)[11] similarly found that women had higher DAS-28 scores than men (3.4 vs. 2.5), along with higher HAQ-DI and ESR - corroborating the gender pattern observed in Table 6 of the present study.

Correlation of Inflammatory Markers with Disease Activity

The present study found positive correlations of both NLR and PLR with DAS28 and ESR. A meta-analysis of sixteen studies[20] concluded that both NLR and PLR were significantly elevated in RA compared with healthy controls, and were positively associated with RA activity based on DAS28. An Egyptian cohort study (2023)[20] similarly reported that RA patients had significantly higher NLR and PLR, and significantly lower LMR compared with controls, with significant differences also between active disease and remission. These findings across geographically diverse populations support the use of NLR and PLR as low-cost, routinely derivable surrogate markers of RA disease activity.

CONCLUSION

The current study evaluated the relationship between rheumatoid arthritis patients' disease activity and the NLR and PLR. The results demonstrated that NLR and PLR values were considerably greater in RA patients. Both NLR and PLR demonstrated a highly significant positive correlation with DAS-28 scores and ESR, indicating their association with disease activity and systemic inflammation. These findings suggest that NLR and PLR are simple, inexpensive, and reliable inflammatory biomarkers that can be used to assess disease activity in patients with rheumatoid arthritis.

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