ORIGINAL ARTICLE

The Function of Platelet-to-lymphocyte Ratio and Neutrophil-to-lymphocyte Ratio in Assessing Disease Activity in Rheumatoid Arthritis Patients

Himanshu Mehta[1], Pooja Dhaon[2*], Sangita Bohara[3], Siddharth Tiwari[4], Dharmendra Uraiya[5], Ruchi Verma[6]

Received: 16 July 2024; *Accepted:* 17 June 2025

Abstract

Aim: To ascertain the function of neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) as biomarkers in evaluation of disease activity in rheumatoid arthritis (RA) patients.

Materials and methods: This cross-sectional research was performed in a hospital and included 381 patients who met the 2010 ACR/EULAR criteria for RA. The clinical disease activity assessment (CDAI) was used to evaluate activity of disease in addition to demographic and disease-related variables. Based on preestablished CDAI cutoff values, the participants were categorized into four groups. For each patient, laboratory analysis included the following: C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and complete blood count (CBC). The conventional procedure was followed in the appropriate computation of PLR and NLR. The four patient groups' NLR and PLR values were compared, and the relation among disease activity indices and NLR and PLR was investigated using Pearson correlation analysis.

Results: In patients, the mean PLR was 132.8 ± 127.7 and the mean NLR was 3.66 ± 2.6. Patients with low disease activity had a substantially lower mean PLR ($p = 0.021$) in comparison to those with higher disease activity. The mean NLR in relation to CDAI was not observed to be statistically significant ($p = 0.69$) across the four groups. While there was a weak positive association between PLR and the physician visual analog scale (VAS) ($r = 0.22$), patient VAS ($r = 0.12$), and CDAI ($r = 0.17$), there was no correlation among CDAI and specific disease indices with NLR, according to Pearson correlation analysis.

Conclusion: PLR, but not NLR, may be an effective biomarker for evaluating the disease activity level in RA patients, particularly higher disease activity.

Journal of The Association of Physicians of India (2025): 10.59556/japi.73.1173

Introduction

Rheumatoid arthritis (RA) is a systemic inflammatory disease with an incidence of 0.75–1% in the Indian population, impacting synovial joints and extra-articular organs.[1] At present, with the treat-to-target strategy, every patient is treated aggressively, aiming at the achievement of remission. Thus, patient assessment is an important part that guides treatment. The predominant methods for evaluating disease activity are composite indices, including the simplified disease activity index (SDAI), disease activity score (DAS), and clinical disease activity assessment (CDAI). These composite indices include joint inspection of tender and swollen joints, laboratory markers like erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), and patient-reported outcomes. But these measurements also have drawbacks, including the unpredictability of physician and patient assessments and the impact of coexisting illnesses on laboratory parameters.[2,3]

There has been a rising demand for innovative biomarkers to assess disease activity in RA. Two indices have attracted attention as potential indicators of inflammation: the neutrophil-to-lymphocyte ratio (NLR) and the platelet-to-lymphocyte ratio (PLR).[4] They are easily collected from complete blood count (CBC) and are inexpensive. Neutrophils are among the first responders to inflammatory sites, causing tissue damage and worsening inflammation, while lymphocytes, particularly T and B cells, are central to autoimmune processes underlying RA.[5] Platelets also are increasingly known for their involvement in inflammation and immune modulation.[6] Increased PLR and NLR have been recognized as markers of systemic inflammation in a number of autoimmune and inflammatory diseases.[7,8]

Data on their clinical utility in RA disease assessment, however, are debatable. Studies with a majority of participants have reported greater NLR and PLR in RA patients than in controls.[9] However, other research that also linked PLR and NLR to the activity of RA produced contradictory findings.[10] There is some Indian data in this regard by Chandrashekara et al., wherein they found that NLR correlates well with disease activity and also serves as an effective measure to predict sustained remission.[11,12] The present research seeks to address this gap by investigating the significance of PLR and NLR in evaluating disease activity in a clearly defined cohort of RA patients. The current work compares these ratios across various disease activity levels and examines their correlation with clinical and laboratory markers in an effort to elucidate their potential as adjuncts to traditional disease activity assessments.

Materials and Methods

A cross-sectional research was performed at the rheumatology clinic of the department of medicine at the Hind Institute of Medical Sciences from January 2023 to December 2023. The institutional ethics committee approved the informed consent and research procedures. The research encompassed 381 individuals aged 18 and older who satisfied the 2010 American College of Rheumatology (ACR) criteria for RA. Patients with active infections, autoimmune diseases other than RA, significant major organ failure, and abnormalities in the hematocrit were not allowed to take part in the study.

A comprehensive clinical examination, standard laboratory testing, and a full history were used to evaluate each study participant. Disease activity was calculated by utilizing the CDAI. Patients were then classified using predefined CDAI cutoff values (Table 1).[13]

[1]Junior Resident; [2]Professor and Incharge Rheumatology Clinic, Department of Medicine; [3]Professor, Department of Pathology; [4]Senior Resident; [5]Professor, Department of Medicine, Hind Institute of Medical Sciences, Barabanki; [6]Professor, Department of Anesthesia, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, Uttar Pradesh, India; *Corresponding Author

How to cite this article: Mehta H, Dhaon P, Bohara S, *et al.* The Function of Platelet-to-lymphocyte Ratio and Neutrophil-to-lymphocyte Ratio in Assessing Disease Activity in Rheumatoid Arthritis Patients. J Assoc Physicians India 2025;73(10):76–78.

Assessment of Platelet-to-lymphocyte Ratio and Neutrophil-to-lymphocyte Ratio

Peripheral venous blood was obtained at the time of enrollment from each patient, and the total blood count was determined using a BC-5130 auto hematology analyzer. The total and differential WBC counts were subsequently utilized to determine the absolute neutrophil count and the absolute lymphocyte count. The overall platelet count was divided by the total lymphocyte count (TLC) to calculate the PLR, while the total neutrophil count was divided by the TLC to ascertain the NLR.[14]

Statistical Analysis

Statistical Package for the Social Sciences (SPSS) 26th version was utilized for statistical analysis. The quantitative variables were presented as mean and SD, while the qualitative variables were expressed as percentages. The Chi-squared test was utilized for categorical variables, while the *t*-test was employed for continuous variables. Pearson correlation analysis was employed to evaluate the association among NLR, PLR, and disease activity variables related to RA.

Results

Three hundred eighty patients participated in the research, comprising 336 females and 44 males with an average age of 43 ± 11 years. The patients' demographic profile and the core set of variables' mean values are summarized in Table 2. Most patients exhibited moderate to low disease activity, with a mean CDAI of 14.72 ± 11.62. Table 1 presents the patient distribution based on CDAI.

Hematological Indices

The mean NLR in the patients was 3.6 ± 2.1, and the mean NLR in relation to CDAI was as follows: remission, 3.44 ± 2.16; low activity, 3.83 ± 2.82; moderate activity, 3.66 ± 2.05; and high activity, 3.48 ± 1.55. The observed difference in the mean NLR in relation to disease activity was not found to be significant ($p = 0.6$). The mean PLR in the patients was 132.84 ± 127.75, and the mean PLR in relation to CDAI was as follows: remission, 120.35 ± 77.2; low activity, 131.1 ± 60.25; moderate activity, 119.25 ± 57.2; and high activity, 174.6 ± 267.96. The observed difference in the mean PLR in relation to disease activity was found to be significant ($p = 0.021$).

Table 1: Predefined cutoff values for CDAI and distribution of patients according to the level of the disease

*CDAI	*n (%)*
Remission ≤2.8	32 (8.4%)
Low activity >2.8 and ≤10	111 (29.2%)
Moderate activity >10 and ≤22	168 (44.2%)
High activity >22	69 (18.2%)

*Clinical Disease Activity Index

Hematological Parameters and Disease Activity Indices Correlation

Using a Pearson correlation analysis, the association among disease activity indices and hematological indices was investigated. NLR did not correlate with any of the disease activity indicators, though there was a weak positive association—though not a statistically significant one—between PLR and patient visual analog scale (VAS), physician VAS, and CDAI. Table 3 enumerates the details.

Discussion

This study's primary objective was to analyze the role of NLR and PLR in evaluating disease activity in patients with RA, in comparison to conventional disease assessment tools and laboratory markers. PLR specifically correlated with high disease activity in the patients with RA, whereas NLR did not correlate with disease activity.

Although previous research suggests NLR to be a good inflammatory marker for RA, the present study did not find any relation of NLR with CDAI-defined disease activity groups or with any individual indices.[4,9] The variability in NLR may be due to various confounders that were not adjusted during analysis, such as age, obesity, and medications the patients were taking for RA that may affect neutrophil

Table 2: Demographic data of patients and core set of disease variables

Parameter (n = 380)	*Value*
Age in years (mean ± SD)	43 ± 11.5
BMI (kg/m^2)	24.24 ± 1.93
Males *n* (%)	44 (11.6%)
Females *n* (%)	336 (88.4%)
Postmenopausal females *n* (%)	170 (49.4%)
Positive rheumatoid factor *n* (%)	284 (75%)
Positive anticyclic citrullinated peptide *n* (%)	309 (81%)
Duration of disease in months (mean ± SD)	42.6 ± 54
Disease activity indices (mean ± SD)	
Tender joint count (0–28)	4.99 ± 5.47
Swollen joint count (0–28)	2.19 ± 3.90
Physician VAS (0–10)	4.20 ± 2.25
Patient VAS (0–10)	3.32 ± 2.13
CDAI (0–76)	14.72 ± 11.62
ESR (in mm/hour)	35.64 ± 27.74
CRP (mg/dL)	5.29 ± 12.80

Table 3: Hematological and disease activity parameters in RA are correlation

	Hematological indices			
Disease activity indices	*NLR*		*PLR*	
	r	*p*	*r*	*p*
Individual indices				
ESR	0.025	0.62	0.02	0.61
CRP	0.04	0.43	0.002	0.9
TJC	0.05	0.3	0.03	0.5
SJC	0.02	0.6	0.08	0.11
Physician VAS	0.01	0.7	0.12	0.01
Patient VAS	0.04	0.3	0.12	0.01
Composite indices				
CDAI	0.04	0.376	0.09	0.07

By using a Pearson correlation analysis, *p*-values were determined. Data have a correlation coefficient assigned to them (*r*). A few examples of abbreviations are: CDAI, clinical disease activity index; TJC, tender joint count; PLR, platelet-to-lymphocyte ratio; NLR, neutrophil-to-lymphocyte ratio; and VAS, visual analog scale

and lymphocyte counts independently of RA disease activity.[15]

On the other hand, PLR did correlate with CDAI-defined activity state and mainly with high disease state, suggesting that PLR is associated with severe disease. This supports the knowledge that platelets have been linked with immunological response and inflammation.[16]

Previous studies have reported that high platelet count and reduced lymphocyte count indicate high disease activity in RA patients.[17,18] Although the correlation of PLR with physician and patient VAS was weak, PLR can be used along with existing standard biomarkers in regular disease assessment in patients with RA. Similarly, with CDAI, PLR also had a modest correlation; thus, PLR could be integrated along with routine evaluations to provide a more comprehensive picture of disease activity.[18]

Clinical Implications

The outcomes of the research proposed that NLR might not be a helpful marker in disease assessment, but PLR can be used to assess patients, and high PLR does indicate high disease activity, which helps in putting patients on more aggressive treatment from the beginning. Also, PLR is a cheap biomarker and can be calculated easily using the standard medical tests done for regular evaluation of patients with RA.

Limitations

It is necessary to recognize that the study has several limitations. It is challenging to determine a causal association between NLR, PLR, and RA disease activity because this study is cross-sectional. A longitudinal study is required to verify these findings and the relation of these markers with time. Also, the results may have been affected by confounders such as age, weight, medication use, and concomitant diseases, which were not adjusted during analysis.

Conclusion

The study's findings indicate that PLR, but not NLR, has the potential to be a biomarker for determining the RA patient's disease activity. PLR's usefulness in clinical practice is highlighted by its strong connection with clinical assessments and considerable link with high disease activity. Subsequent investigations ought to concentrate on long-term studies to confirm PLR's function and explore its predictive significance in the handling of RA.

Author Contributions

All the authors contributed equally to the manuscript, compiling, writing, and collection of data.

Orcid

Pooja Dhaon https://orcid.org/0000-0002-5516-2555

References

1. Malaviya AN, Kapoor SK, Singh RR, et al. Prevalence of rheumatoid arthritis in the adult Indian population. Rheumatol Int 1993;13(4):131–134.
2. Salaffi F, Di Carlo M, Farah S, et al. Rheumatoid arthritis disease activity assessment in routine care: performance of the most widely used composite disease activity indices and patient-reported outcome measures. Acta Biomed 2021;92(4):e2021238.
3. Prevoo ML, van 't Hof MA, Kuper HH, et al. Modified disease activity scores that include twenty-eight-joint counts. Development and validation in a prospective longitudinal study of patients with rheumatoid arthritis. Arthritis Rheum 1995;38(1):44–48.
4. Chandrashekara S, Mukhtar Ahmad M. The basal ratio of platelet count to lymphocyte count and neutrophil count to lymphocyte count can predict the clinical response at three months in patients with rheumatoid arthritis on conventional synthetic disease-modifying antirheumatic drugs. J Clin Rheumatol 2017;23(4):145–150.
5. Biswas M, Suvarna R, Krishnan SV, et al. The mechanistic role of neutrophil lymphocyte ratio perturbations in the leading noncommunicable lifestyle diseases. F1000Res 2022;11:960.
6. Scherlinger M, Richez C, Tsokos GC, et al. The role of platelets in immune-mediated inflammatory diseases. Nat Rev Immunol 2023;23:495–510.
7. Imtiaz F, Shafique K, Mirza SS, et al. Neutrophil lymphocyte ratio as a measure of systemic inflammation in prevalent chronic diseases in Asian population. Int Arch Med 2012;5(1):2.
8. Zhang J, Huang SH, Li HW, et al. Usefulness of neutrophil to lymphocyte ratio and platelet to lymphocyte ratio in evaluating disease activity and severity of systemic lupus erythematosus. Clin Rheumatol 2019;38(10):2701–2709.
9. Erre GL, Paliogiannis P, Castagna F, et al. Meta-analysis of neutrophil-to-lymphocyte and platelet-to-lymphocyte ratio in rheumatoid arthritis. Eur J Clin Invest 2019;49(1):e13037.
10. Zinellu A, Mangoni AA. Neutrophil-to-lymphocyte and platelet-to-lymphocyte ratio and disease activity in rheumatoid arthritis: a systematic review and meta-analysis. Eur J Clin Invest 2023;53(2):e13877.
11. Chandrashekara S, Mukhtar Ahmad M, Renuka P, et al. Characterization of neutrophil-to-lymphocyte ratio as a measure of inflammation in rheumatoid arthritis. Int J Rheum Dis 2017;20(10):1457–1467.
12. Chandrashekara S, Rajendran A, Bai Jaganath A, et al. Neutrophil-lymphocyte ratio, pain perception, and disease activity score may serve as important predictive markers for sustained remission in rheumatoid arthritis. Reumatismo 2015;67(3):109–115.
13. Aletaha D, Smolen JS. The Simplified Disease Activity Index (SDAI) and Clinical Disease Activity Index (CDAI) to monitor patients in standard clinical care. Best Pract Res Clin Rheumatol 2007;21(4):663–675.
14. Moosazadeh M, Maleki I, Alizadeh-Navaei R, et al. Normal values of neutrophil-to-lymphocyte ratio, lymphocyte-to-monocyte ratio and platelet-to-lymphocyte ratio among Iranian population: results of Tabari cohort. Caspian J Intern Med 2019;10(3):320–325.
15. Buonacera A, Stancanelli B, Colaci M, et al. Neutrophil to lymphocyte ratio: an emerging marker of the relationships between the immune system and diseases. Int J Mol Sci 2022;23(7):3636.
16. Sonmez O, Sonmez M. Role of platelets in immune system and inflammation. Porto Biomed J 2017;2(6):311–314.
17. Zha Q, He Y, Lu Y, et al. Relationship between platelet counts and cartilage erosion in 436 cases of rheumatoid arthritis. Clin Chim Acta 2006;371:194–195.
18. Elsayed SA, Basily SM, Esmail MA, et al. Platelet/lymphocyte, neutrophil/lymphocyte, and lymphocyte/monocyte ratios as biomarkers for rheumatoid arthritis: correlation with disease activity. Egypt Rheumatol Rehabil 2023;50:37.