

Albumin–Fibrinogen Ratio and C-Reactive Protein–Albumin Ratio as Markers of Disease Activity in Rheumatoid Arthritis: A Cross-Sectional Study

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Abstract

Background: Rheumatoid arthritis (RA) is a chronic systemic inflammatory disease in which accurate assessment of disease activity is essential for treatment monitoring. Conventional inflammatory markers such as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) have recognized limitations. The albumin–fibrinogen ratio (AFR) and CRP–albumin ratio (CAR) combine positive and negative acute-phase reactants and may provide complementary information about inflammatory burden.

Objective: To evaluate AFR and CAR as markers of disease activity in patients with RA and to assess their association with the Disease Activity Score-28 (DAS28).

Methods: This observational cross-sectional study was conducted in the Department of General Medicine at Jaipur Golden Hospital, Rohini, New Delhi. Forty-eight adults fulfilling the ACR/EULAR 2010 classification criteria for RA were included. Disease activity was assessed using DAS28-ESR, and participants were categorized into active disease or remission. Serum albumin, fibrinogen, CRP, ESR and hemoglobin were measured. AFR and CAR were calculated, and group comparisons, correlation analysis, multivariable logistic regression and receiver operating characteristic (ROC) analysis were performed.

Results: Among 48 participants, 24 (50.0%) had active disease and 24 (50.0%) were in remission. AFR was significantly lower in active disease than in remission (8.63 ± 2.05 vs. 12.69 ± 2.92 ; $p < 0.0001$). CAR was significantly higher in active disease [median 0.36 (IQR 0.325–1.044)] than in remission [0.15 (IQR 0.032–0.329); $p = 0.0006$]. AFR showed a significant moderate negative correlation with DAS28 ($r = -0.521$, $p = 0.0002$), whereas CAR showed a significant positive correlation ($r = 0.385$, $p = 0.007$). For discrimination of active disease, AFR had an area under the ROC curve (AUC) of 0.875 (95% CI 0.779–0.971), with 87.5% sensitivity and 75.0% specificity at a cutoff of ≤ 11.1436 . CAR had an AUC of 0.788 (95% CI 0.658–0.918).

Conclusion: In this study population, lower AFR and higher CAR were associated with greater RA disease activity. Both ratios may serve as accessible adjunctive inflammatory indices alongside established clinical disease activity measures. The findings require confirmation in larger, longitudinal studies before routine use as independent disease-activity biomarkers.

Keywords: rheumatoid arthritis, albumin–fibrinogen ratio, CRP–albumin ratio, disease activity, DAS28, inflammation, biomarkers

Introduction

Rheumatoid arthritis is a chronic autoimmune inflammatory disease characterized by persistent synovitis, progressive structural joint damage and a range of extra-articular manifestations. Persistent systemic inflammation is associated with functional impairment and increased cardiovascular and other comorbidity burdens. Assessment of disease activity is therefore central to a treat-to-target approach.

Composite measures such as the Disease Activity Score-28 (DAS28), Simplified Disease Activity Index and Clinical Disease Activity Index are widely used in clinical practice. DAS28 incorporates tender and swollen joint counts, a patient global assessment and an acute-phase reactant, most commonly ESR or CRP. Although ESR and CRP are useful, each is influenced by factors beyond articular inflammation, and discordance between clinical disease activity and laboratory markers may occur.

Albumin is a negative acute-phase reactant whose circulating concentration can fall during systemic inflammation, whereas fibrinogen and CRP are positive acute-phase reactants that generally rise. The AFR therefore combines two proteins that move in opposite directions during inflammation. CAR similarly combines CRP with albumin. The biological rationale for these ratios is that simultaneous changes in positive and negative acute-phase proteins may better represent systemic inflammatory burden than either component alone.

Previous studies cited in the thesis have reported lower AFR and higher CAR in active RA and inverse and positive relationships, respectively, with DAS28. However, evidence remains limited in Indian clinical populations. The present study was undertaken to evaluate AFR and CAR in RA and to examine their relationship with DAS28.

Materials and Methods**Study design and setting**

This was an observational cross-sectional study conducted in the Department of General Medicine at Jaipur Golden Hospital, Rohini, New Delhi, over an 18-month study period.

Participants

Adults aged ≥ 18 years of either sex fulfilling the American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) 2010 classification criteria for rheumatoid arthritis were eligible. Patients with other autoimmune diseases, severe chronic kidney disease, chronic liver disease, concurrent infection or underlying malignancy were excluded.

Clinical and laboratory assessment

A detailed clinical history and examination were performed, including assessment of joint symptoms and treatment history. Disease activity was assessed using DAS28. Laboratory investigations included complete blood count, ESR, liver and kidney function tests, rheumatoid factor, anti-CCP antibody, CRP, serum albumin and serum fibrinogen. The thesis records quantitative CRP estimation using a Mispal i-3 Agappe autoanalyzer, ESR using an Aspen Westergren ESR analyzer, fibrinogen using an Accustar Ceveron Alpha Analyzer, and albumin using a Beckman Coulter AU680 analyzer.

Definitions and calculations

Participants were categorized as having remission when DAS28 was < 2.6 ; those with DAS28 ≥ 2.6 were classified as having active disease for the study analysis. AFR was calculated as serum albumin divided by serum fibrinogen, and CAR as CRP divided by serum albumin, using the laboratory units recorded in the study.

Statistical analysis

Categorical variables were summarized as number and percentage. Quantitative variables were summarized as mean $\pm$ standard deviation or median with interquartile range, according to distribution. Normality was assessed using the Shapiro–Wilk test. Independent-samples t test or Mann–Whitney test was used for continuous variables as appropriate, and chi-square or Fisher exact test for categorical variables. Multivariable logistic regression was used to explore independent factors associated with active disease. ROC analysis was performed to estimate cutoff values, sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy. A p value <0.05 was considered statistically significant. Statistical analysis was performed using IBM SPSS Statistics version 25.0.

Ethical considerations

The thesis records that written informed consent was obtained from participating patients and that ethical clearance was to be obtained from the Institutional Ethics Committee. The thesis material available for manuscript preparation does not provide an ethics committee approval number or approval date; these details should be inserted from the original ethics approval letter before journal submission.

Results

Participant characteristics

A total of 48 patients with RA were included. The mean age was 48.31 ± 15.90 years, with a median age of 46.5 years (IQR 37.25–62.25) and a range of 21–74 years. Thirty-two participants (66.67%) were female and 16 (33.33%) were male. Mean disease duration was 107.48 ± 67.94 months, with a median of 103 months (IQR 41.25–161).

Characteristic	Value
Age, mean $\pm$ SD (years)	48.31 ± 15.90
Age, median (IQR), years	46.5 (37.25–62.25)
Female sex, n (%)	32 (66.67%)
Male sex, n (%)	16 (33.33%)
Disease duration, mean $\pm$ SD (months)	107.48 ± 67.94
Active disease, n (%)	24 (50.00%)
Remission, n (%)	24 (50.00%)

Laboratory parameters

Parameter	Overall (n=48)
Albumin, g/dL, mean $\pm$ SD	3.74 ± 0.50
Fibrinogen, mg/dL, mean $\pm$ SD	369.82 ± 72.94
CRP, mg/L, mean $\pm$ SD	13.41 ± 13.24
ESR, mm/hour, mean $\pm$ SD	28.15 ± 21.29
Hemoglobin, g/dL, mean $\pm$ SD	12.19 ± 1.53
AFR, mean $\pm$ SD	10.66 ± 3.18
CAR, mean $\pm$ SD	0.38 ± 0.40
DAS28, mean $\pm$ SD	3.17 ± 1.26

Comparison between active disease and remission

Parameter	Active disease (n=24)	Remission (n=24)	p value
Albumin, g/dL	3.37 ± 0.38	4.10 ± 0.44	<0.0001
Fibrinogen, mg/dL	402.48 ± 59.35	337.16 ± 71.59	<0.001
CRP, mg/L, median (IQR)	11.9 (10.225–35.525)	5.85 (1.45–11.9)	<0.05
ESR, mm/hour, median (IQR)	44.5 (32.75–56.25)	11 (6–17.25)	<0.001
Hemoglobin, g/dL	10.93 ± 1.06	13.45 ± 0.59	<0.0001
AFR, mean ± SD	8.63 ± 2.05	12.69 ± 2.92	<0.0001
CAR, median (IQR)	0.36 (0.325–1.044)	0.15 (0.032–0.329)	0.0006
DAS28, mean ± SD	4.32 ± 0.68	2.03 ± 0.19	<0.0001

Age and sex distribution were comparable between the active and remission groups. The active group had lower albumin and hemoglobin, higher fibrinogen, CRP and ESR, lower AFR and higher CAR. The mean DAS28 was 4.32 ± 0.68 in active disease compared with 2.03 ± 0.19 in remission ($p < 0.0001$).

Correlation with DAS28

Marker	Correlation with DAS28	p value
AFR	$r = -0.521$	0.0002
CAR	$r = 0.385$	0.007

AFR demonstrated a statistically significant moderate inverse correlation with DAS28, indicating that lower AFR values were associated with higher disease activity. CAR demonstrated a statistically significant positive correlation with DAS28.

ROC analysis

Parameter	AUC (95% CI)	Cutoff	Sensitivity	Specificity	Diagnostic accuracy
AFR	0.875 (0.779–0.971)	≤ 11.1436	87.5%	75.0%	81.25%
CAR	0.788 (0.658–0.918)	> 0.2591	83.33%	66.67%	72.92%

Both AFR and CAR demonstrated statistically significant discrimination for active disease. For AFR, the AUC was 0.875 (95% CI 0.779–0.971; $p < 0.0001$), with sensitivity 87.5% and specificity 75.0% at a cutoff of ≤ 11.1436 . CAR had an AUC of 0.788 (95% CI 0.658–0.918; $p < 0.0001$), with sensitivity 83.33% and specificity 66.67% at a cutoff of > 0.2591 .

Multivariable logistic regression did not identify an individual parameter as an independent statistically significant risk factor for active disease in the study model.

Discussion

The present cross-sectional study evaluated two composite inflammatory indices, AFR and CAR, in 48 patients with RA categorized according to DAS28. The principal findings were that AFR was significantly lower and CAR significantly higher in active disease than in remission, and that AFR and CAR showed inverse and positive correlations, respectively, with DAS28.

The biological direction of these findings is consistent with the acute-phase response. Albumin behaves as a negative acute-phase reactant and may decline with systemic inflammation, while fibrinogen and CRP increase as positive acute-phase reactants. Consequently, active inflammatory disease may produce a lower albumin-to-fibrinogen ratio and a higher CRP-to-albumin ratio.

The findings are consistent with the study by Yang et al., which evaluated AFR and CAR in RA and reported lower AFR and higher CAR in active disease, together with inverse and positive correlations with DAS28-ESR, respectively. The present study also agrees directionally with the observations of He et al., who reported reduced AFR and elevated CAR in RA and relationships with inflammatory and immunological parameters.

Afifi et al. reported inverse correlation between AFR and DAS28-ESR and positive correlation between CAR and disease activity, with good ROC performance for both ratios. In the present study, AFR showed an AUC of 0.875 and CAR an AUC of 0.788. Differences in sample size, study population, design and clinical characteristics may contribute to differences in observed effect sizes and discriminatory performance.

The present study also showed substantial differences in albumin, fibrinogen, CRP and ESR between active disease and remission. These findings support the biological plausibility of AFR and CAR as composite indices, while also emphasizing that the ratios remain influenced by their component variables and therefore should not be interpreted independently of clinical assessment.

An important observation was that multivariable logistic regression did not identify an independent predictor of active disease. This may reflect the limited sample size and interrelationship among inflammatory variables. ROC analysis nevertheless demonstrated significant discrimination, particularly for AFR. These results support the potential use of AFR and CAR as adjunctive markers rather than replacements for validated clinical disease-activity instruments.

Clinical implications

AFR and CAR are calculated from laboratory parameters that are commonly available in routine clinical practice. Their association with DAS28 suggests that they may provide additional information when interpreted alongside joint examination, patient assessment and conventional inflammatory markers. However, the cross-sectional design and modest sample size preclude conclusions about longitudinal treatment response, prognosis or causality.

Limitations

- The sample size was modest (48 participants), which limits statistical power and precision of subgroup analyses.
- The cross-sectional design prevents assessment of temporal relationships and treatment responsiveness.
- Participants were recruited from a single hospital, limiting generalizability to other populations and healthcare settings.

- AFR and CAR can be influenced by factors affecting albumin, fibrinogen or CRP beyond RA activity; the study excluded several major comorbid conditions but residual confounding cannot be excluded.
- The study used DAS28-based categorization as the reference for disease activity; independent validation against other composite indices or imaging measures was not performed.

Conclusion

In this cohort of patients with rheumatoid arthritis, active disease was characterized by significantly lower AFR and higher CAR compared with remission. AFR showed a significant inverse correlation with DAS28 and demonstrated an AUC of 0.875 for discrimination of active disease, while CAR showed a significant positive correlation and an AUC of 0.788. These findings indicate that AFR and CAR may be useful, accessible adjunctive inflammatory indices in RA disease-activity assessment. Larger prospective multicenter studies with longitudinal follow-up are required to determine their reproducibility, treatment responsiveness and prognostic value.

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Author contributions

The thesis identifies Dr. Dhruv Roopkishore Pathak as the investigator and author of the work, under the guidance and supervision of Dr. Rajesh Ranjan and Dr. Paras Passi. For journal submission, the final author-contribution statement should be revised to reflect the actual contributions of all individuals who qualify for authorship under the target journal's authorship policy.

Ethics statement

Written informed consent was obtained from study participants according to the thesis methodology. The available thesis text states that ethical clearance was to be obtained from the Institutional Ethics Committee. The ethics approval number/date is not present in the material used to prepare this manuscript and should be added from the original approval document before submission.

Data availability

The underlying patient-level dataset was not included in the thesis document provided for manuscript preparation. The corresponding author should provide a data-availability statement consistent with institutional policy and the target journal's requirements.

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