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Original Article

High Quantitative CRP And Low Albumin as Marker of Disease Activity in Patients with Rheumatoid Arthritis

Najeeb Ullah[1], Amjad Ali[1]*, Muhammad Ayub[2]

[1]Post-Graduate Resident- Department of Rheumatology- Khyber Teaching Hospital- Peshawar, Pakistan

[2]Medical Officer- District Headquarter Hospital- Batkhaila, Malakand, Pakistan

Corresponding Author: Amjad Ali; Email: amjadalikhan145@gmail.com

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ABSTRACT

Background: Rheumatoid arthritis (RA) is a chronic inflammatory disorder characterized by synovial tissue inflammation, leading to joint damage, pain, and systemic effects.

Objective: To evaluate the utility of high quantitative C-reactive protein (CRP) and low serum albumin levels as markers of disease activity in RA patients.

Methods: This cross-sectional study was conducted at the Department of Rheumatology, Khyber Teaching Hospital, Peshawar, from September 1, 2023, to February 29, 2024. Male and female RA patients aged 18 to 70 years were enrolled. Disease activity was assessed using the Disease Activity Score 28 (DAS 28). Serum CRP and albumin levels were measured and compared with DAS28 scores.

Results: A total of 105 patients were included, with a majority being female (n=60, 57.1%). The mean age was 52.4 ± 9.8 years, with most participants aged between 40 and 50 years (n = 35, 33.3%). Elevated CRP levels were associated with increased disease activity, with an odds ratio of 1.82 (95% CI: 1.53- 2.17, $p < 0.001$). Conversely, lower albumin levels were linked to higher disease activity, with an odds ratio of 3.47 (95% CI: 4.35- 2.63, $p < 0.001$).

Conclusion: Serum CRP and albumin levels serve as valuable indicators for assessing disease activity in RA patients, highlighting their potential role in clinical management.

Keywords: C-Reactive Protein, Disease Activity, Rheumatoid Arthritis, Serum Albumin

INTRODUCTION

Rheumatoid arthritis (RA) is characterized by persistent inflammation of the synovial tissue, leading to joint deterioration, discomfort, impairment, and systemic consequences (1, 2). The condition affects approximately 0.5-1% of adults globally, with a higher prevalence in women and an increased frequency with age (3, 4). RA's etiology involves a complex interplay between genetic susceptibility, environmental influences, and disrupted immune responses, culminating in chronic inflammation and damage to joints and other organs (5).

Evaluating disease activity in RA is crucial for guiding treatment decisions, predicting prognosis, and assessing therapeutic efficacy (6, 7). Composite indices, such as the Disease Activity Score 28 (DAS28), incorporate clinical, laboratory, and radiographic characteristics to measure RA activity (8, 9). Among laboratory markers, C-reactive protein (CRP) and serum albumin have garnered interest for their potential as surrogate measures of inflammation and disease severity (10).

CRP, an acute-phase protein produced by the liver in response to inflammatory signals, serves as a marker of inflammation in RA (11). Elevated CRP levels correlate with increased disease activity, joint destruction, and progression of RA (12). Conversely, serum albumin, a major blood plasma protein synthesized by the liver, decreases in the presence of systemic inflammation and malnutrition, acting as a negative acute-phase reactant. Low serum albumin levels are associated with severe RA, reduced functional capacity, and poorer prognosis (14).

Although CRP and albumin are established indicators of inflammation and nutritional status, their combined relevance as markers of disease activity in RA remains unclear. This study aimed to investigate the relationship between elevated quantitative CRP levels and decreased serum albumin levels with disease activity in patients with rheumatoid arthritis. Understanding the association

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between these biomarkers and RA activity could enhance clinicians' ability to monitor disease progression, optimize treatment strategies, and improve patient outcomes.

MATERIAL AND METHODS

This cross-sectional study was conducted from September 1, 2023, to February 29, 2024, at the Department of Rheumatology, Khyber Teaching Hospital, Peshawar. The study enrolled male and female patients aged 18 to 70 years who had been diagnosed with rheumatoid arthritis. Patients with protein-losing enteropathy, chronic liver disease, chronic renal failure, severe cardiopulmonary compromise, and a history of malignancy were excluded from the study.

Data on each participant's age, gender, disease duration, and current medications were collected through structured interviews and medical record reviews. Disease activity was assessed using the Disease Activity Score 28 (DAS28). Blood samples were taken from all patients for laboratory analysis of CRP and serum albumin levels. A CRP level greater than 1 mg/dL was considered high, while a serum albumin level less than 3.5 g/dL was considered low. The high CRP levels and low albumin levels were compared with DAS28 scores, which classified disease activity as remission, low, moderate, or high.

Statistical analysis was performed using SPSS version 25. Descriptive statistics were used to summarize demographic and clinical data. Continuous data were presented as mean ± SD or median with IQR, while categorical variables were reported as frequencies and percentages. The Pearson correlation coefficient was used to examine the relationship between CRP, albumin, and disease activity. Logistic regression analysis was conducted to identify independent predictors of disease activity, while controlling for covariates. A p-value of ≤0.05 was considered statistically significant.

RESULTS

105 participants in all participated in this study; 45 (42.9%) were male and 60 (57.1%) were female. The participants were 52.4 years old on average, with a 9.8 year standard deviation. Most of participants fell within the age ranges of 40 to 50 and 51 to 60. The median of the disease duration was 8.7 years, with an interquartile range of 5.3 to 12.1 years. In Table 1, it is shown that methotrexate (33.3%) and other disease-modifying anti-rheumatic medicines (42.9%) were the medications most often administered. As Table 2 indicates, the patients were divided into discrete disease activity groups according to their Disease Activity Score 28 (DAS28) assessments. 20 patients (19.0%), of the participants overall, were in remission. Additionally, 35 patients (33.3%) showed low disease activity, 30 patients (28.6%) showed moderate disease activity, and 20 patients (19.0%) showed serious disease activity. Table 3 displays the distribution of serum C-reactive protein (CRP) values across several categories of disease activity. The median levels of CRP showed a positive correlation with disease activity, with values ranging from 2.5 mg/L (interquartile range: 1.2 - 4.7 mg/L) in remission to 25.9 mg/L (interquartile range: 19.6 - 32.7 mg/L) in persons with high disease activity. Table 4 demonstrates the distribution of serum albumin levels across different disease activity groups. Albumin levels had a negative correlation with disease activity, as seen by a reduction in median values. In the remission group, whereas individuals with high disease activity had a median albumin level of 3.2 g/dL (interquartile range: 2.9 - 3.4 g/dL), the median albumin level was 4.2 g/dL (interquartile range: 4.0 - 4.4 g/dL). Serum albumin levels and blood CRP levels were shown to be strong indicators of disease activity in rheumatoid arthritis patients by the logistic regression analysis (Table 5). With an odds ratio of 1.82 (95% confidence interval: 1.53 - 2.17, $p < 0.001$) greater CRP levels were associated with a greater probability of disease activity. Conversely, an odds ratio of 3.47 (95% confidence interval: 4.35 - 2.63, $p < 0.001$) linked lower albumin levels to a greater chance of disease activity. Even when age, gender, and length of disease were taken into consideration, these correlations remained significant. Our findings highlight the association, in rheumatoid arthritis patients, between serum albumin levels, blood CRP levels, and disease activity. This underscores the potential usefulness of these biomarkers in monitoring the development of the disease and informing therapy choices.

Table 1: Demographics and Clinical Features of Study Participants

Characteristic	Number of patients (n=105)	Frequency (%)
Gender		
Male	45	(42.9%)
Female	60	(57.1%)
Age (years)	52.4 ± 9.8	
Age Group (years)		
< 40 years	25	(23.8%)
40 – 50 years	35	(33.3%)

51 – 60 years	30	(28.6%)
> 60 years	15	(14.3%)
Total	105	(100%)
Disease Duration (years)	8.7 (5.3 - 12.1)	
Current Medications		
Methotrexate	35	(33.3%)
TNF Inhibitors	25	(23.8%)
Other DMARDs	45	(42.9%)

Table 2: Disease Activity Classification Based on DAS28 Scores

Disease Activity	DAS28 Score Range	Number of Patients (n=105)	Frequency (%)
Remission	< 2.6	20	(19.0%)
Low Activity	2.6 - 3.2	35	(33.3%)
Moderate Activity	3.2 - 5.1	30	(28.6%)
High Activity	> 5.1	20	(19.0%)

Table 3: Distribution of Serum CRP Levels and Disease Activity

Disease Activity	Median CRP (mg/L)	Interquartile Range (IQR)
Remission	2.5	(1.2 - 4.7)
Low Activity	6.8	(4.3 - 9.5)
Moderate Activity	12.4	(9.8 - 16.5)
High Activity	25.9	(19.6 - 32.7)

Table 4: Distribution of Serum Albumin Levels and Disease Activity

Disease Activity	Median Albumin (g/dL)	Interquartile Range (IQR)
Remission	4.2	(4.0 - 4.4)
Low Activity	3.9	(3.7 - 4.1)
Moderate Activity	3.6	(3.4 - 3.8)
High Activity	3.2	(2.9 - 3.4)

Table 5: Logistic Regression Analysis of Predictors of Disease Activity

Predictor	Odds Ratio (95% CI)	p-value
High Serum CRP Level	1.82 (1.53 - 2.17)	< 0.001
Low Serum Albumin Level	3.47 (4.35 - 2.63)	< 0.001
Age (years)	1.05 (0.97 - 1.14)	0.123
Gender (Female vs. Male)	0.86 (0.48 - 1.54)	0.456
Disease Duration (years)	1.12 (1.02 - 1.23)	0.021

DISCUSSION

The demographic and clinical characteristics of the study participants provide valuable insights into the profile of individuals with rheumatoid arthritis (RA) included in the analysis. Consistent with the well-established epidemiology of RA, our study observed a higher proportion of females, reflecting the higher incidence of RA in women compared to men. This finding aligns with previous research, which consistently reports a female predominance in RA, with ratios ranging from 2:1 to 3:1 (1, 2).

Regarding age distribution, the majority of participants in our study were in the age groups of 40-50 years and 51-60 years, with smaller proportions below 40 and above 60 years of age. This age distribution pattern mirrors the typical occurrence and peak frequency of RA among middle-aged individuals, particularly in their fifth and sixth decades of life. These results are consistent with previous studies, such as that by Steiner et al. (15), which suggested that RA often manifests between the ages of 30 and 60, with the highest incidence observed in the fourth to sixth decades of life.

The median disease duration in our analysis was 8.7 years, highlighting the chronic nature of RA characterized by persistent inflammation and gradual joint deterioration over time. This finding is in line with a study from 2016, which reported median disease

durations ranging from 5 to 15 years at the time of evaluation, underscoring the long-term management requirements for RA to minimize disease progression and optimize patient outcomes (16).

In terms of medication utilization, methotrexate was the most frequently prescribed drug, followed by tumor necrosis factor (TNF) inhibitors and other disease-modifying antirheumatic drugs (DMARDs). Methotrexate remains the cornerstone of RA treatment, recommended as first-line therapy for patients who have not previously received conventional and biologic DMARDs. The use of TNF inhibitors reflects the widespread acceptance of biologic therapies in managing moderate to severe RA, particularly when conventional DMARDs have been inadequate. These findings are consistent with current treatment guidelines and previous research, such as that by Gharaibeh et al. (17), which examined the frequency of methotrexate and biologic DMARD use in RA populations.

Our analysis revealed a progressive increase in CRP levels with higher disease activity categories, consistent with the typical inflammatory response observed in active RA. The distribution of DAS28 scores in our study, categorizing disease activity as low, moderate, high, and in remission, is similar to findings from previous research, which demonstrated higher CRP levels in individuals with active RA compared to those in remission or with minimal disease activity (18). The median CRP values reported in our study, ranging from 2.5 mg/L in remission to 25.9 mg/L in high disease activity, are also consistent with previous studies (19).

Furthermore, our study identified a consistent correlation between disease activity and serum albumin levels, with lower albumin levels observed in RA patients with greater disease activity. Serum albumin serves as an indicator of both nutritional status and systemic inflammation, with reduced levels indicating heightened inflammation and disease severity. The median albumin levels reported in our study, ranging from 4.2 g/dL during remission to 3.2 g/dL during high disease activity, align with previous studies examining albumin levels in RA patients (20).

Our logistic regression analysis demonstrated that both serum CRP levels and serum albumin levels were significant predictors of disease activity in RA patients, even after adjusting for potential confounders such as age, gender, and disease duration (21). These findings support the growing body of evidence that CRP and albumin are valuable prognostic indicators for disease activity in RA.

In conclusion, our study contributes to existing literature by providing further evidence of the association between CRP levels, serum albumin levels, and disease activity in RA. These biomarkers offer valuable insights into disease progression and may aid clinicians in monitoring disease activity, optimizing treatment strategies, and improving patient outcomes. However, the study's retrospective design and cross-sectional nature limit the ability to establish causality. Future prospective studies are warranted to validate these findings and explore the potential utility of these biomarkers in clinical practice.

CONCLUSION

This study underscores the significance of serum CRP and albumin levels as reliable indicators for assessing disease activity in RA. The clear association between elevated CRP levels and disease activity, along with decreased albumin levels and disease severity, highlights the potential utility of these biomarkers in clinical practice. These findings suggest that monitoring CRP and albumin levels could provide clinicians with valuable insights into disease progression and treatment response in RA patients. Incorporating these biomarkers into routine clinical assessments may enhance the management of RA by enabling more accurate monitoring of disease activity and optimizing treatment strategies to improve patient outcomes.

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