Section: Miscellaneous

Original Research Article

RHEUMATOID FACTOR AS A PREDICTOR OF DISEASE SEVERITY IN RHEUMATOID ARTHRITIS: A PROSPECTIVE COHORT STUDY

Amol Rebello[1], Kiran Rebello[2], Priyank Verma[3]

[1]*Associate Professor, Department of Orthopaedics, Autonomous State Medical College, Sultanpur Uttar Pradesh, India.*
[2]*Associate Professor, Department of General Surgery, Autonomous State Medical College, Sultanpur Uttar Pradesh, India.*
[3]*Associate Professor, Department of Paediatrics, Autonomous State Medical College, Sultanpur Uttar Pradesh, India.*

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Corresponding Author:
Dr. Amol Rebello,
Associate Professor, Department of Orthopaedics, Autonomous State Medical College, Sultanpur Uttar Pradesh, India.
Email: dramol2002@gmail.com

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ABSTRACT

Background: Rheumatoid arthritis (RA) is a chronic systemic autoimmune inflammatory disorder characterized by persistent synovitis, progressive joint destruction, functional impairment, and extra-articular manifestations. Rheumatoid factor (RF) is an established serological marker used in the classification of RA and may also have prognostic significance. This study aimed to evaluate RF as a predictor of disease severity in patients with rheumatoid arthritis.

Materials and Methods: A hospital-based prospective observational cohort study was conducted among 30 patients with rheumatoid arthritis attending the outpatient department of Autonomous State Medical College, Sultanpur, Uttar Pradesh, from November 2024 to July 2026. Patients aged 20–65 years fulfilling the 2010 ACR/EULAR classification criteria for RA were included. Demographic, clinical, and laboratory parameters were recorded. Quantitative RF, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), tender and swollen joint counts, and Disease Activity Score in 28 joints using ESR (DAS28-ESR) were assessed. Patients were followed prospectively, and RF status and titre were correlated with disease activity.

Results: The mean age of participants was 44.6 ± 11.2 years, and 23 (76.7%) were female. Rheumatoid factor was positive in 21 (70.0%) patients. The mean baseline DAS28-ESR was 5.12 ± 1.08 and decreased to 4.18 ± 1.14 at follow-up. RF-positive patients had significantly higher follow-up DAS28-ESR compared with RF-negative patients (4.55 ± 1.03 vs 3.32 ± 0.88; $p = 0.006$). RF-positive patients also had higher ESR and CRP levels. Quantitative RF titre showed a moderate positive correlation with follow-up DAS28-ESR (Spearman $\rho = 0.58$, $p = 0.001$), ESR ($\rho = 0.61$, $p < 0.001$), and CRP ($\rho = 0.47$, $p = 0.009$).

Conclusion: RF positivity and higher RF titres were associated with greater disease activity and inflammatory burden in patients with rheumatoid arthritis. Quantitative RF may therefore serve as a useful prognostic marker for identifying patients at risk of more severe disease. Larger multicentre studies with longer follow-up are required to confirm these findings.

Keywords: Rheumatoid arthritis, rheumatoid factor, DAS28-ESR, disease severity, disease activity, prognosis.

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic systemic autoimmune inflammatory disease characterized predominantly by persistent synovitis, symmetrical polyarthritis, and progressive destruction of articular cartilage and subchondral bone. The underlying pathogenesis involves complex interactions among genetic susceptibility, environmental factors, adaptive and innate immune responses, autoantibody production, and pro-inflammatory cytokine pathways.[1] Persistent inflammation can result in progressive structural joint damage, deformity, functional impairment, and extra-articular

complications. Consequently, RA represents an important cause of long-term morbidity and impaired quality of life.

RA occurs worldwide, although its prevalence varies considerably among populations and geographical regions. A systematic review and meta-analysis estimated the global prevalence of RA at approximately 0.46%, demonstrating its substantial population-level burden.[2] The clinical course is highly heterogeneous: some patients achieve sustained remission or low disease activity following treatment, whereas others develop persistent inflammatory activity, progressive erosive disease, disability, and systemic complications.[3,4] Identification of patients who are likely to develop a more severe disease course is therefore important for risk stratification, closer monitoring, and timely optimization of disease-modifying therapy.

Rheumatoid factor (RF) is one of the most established serological biomarkers in rheumatoid arthritis. RF represents a group of autoantibodies directed against antigenic determinants on the Fc portion of immunoglobulin G, with IgM-RF being the form most commonly measured in routine clinical practice.[5] Although RF is not specific for RA and may occur in other autoimmune diseases, chronic infections, and occasionally in apparently healthy individuals, it continues to have considerable diagnostic and prognostic relevance when interpreted in an appropriate clinical context.[5,6]

The importance of RF in RA classification is reflected in the 2010 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) classification criteria. These criteria incorporate RF and anti-citrullinated protein antibodies (ACPA), together with joint involvement, acute-phase response, and duration of symptoms, to identify patients with inflammatory synovitis who are at risk of persistent or erosive disease.[7] Importantly, the criteria distinguish low-positive from high-positive serology, supporting the potential clinical significance of autoantibody concentration in addition to simple seropositivity.[7,8]

Beyond its role in diagnosis and classification, RF has long been investigated as a potential marker of disease prognosis. Earlier longitudinal studies demonstrated that patients with seropositive RA may experience greater radiographic progression and functional impairment than some seronegative patients.[9,10] Subsequent investigations have shown associations between RF and/or ACPA and radiographic progression, erosive disease, and extra-articular manifestations.[11,12] In an inception cohort of patients with recent-onset RA, IgM-RF status was among the factors predicting subsequent radiological damage and functional disability.[13] These observations suggest that RF may reflect a disease phenotype characterized by a greater potential for persistent and destructive inflammation.

The prognostic significance of RF, however, should not be considered in isolation. Anti-CCP/ACPA has emerged as another important serological marker associated with RA and structural progression.[13,14] The combination of RF and ACPA may provide additional information regarding disease phenotype and prognosis. Moreover, inflammatory burden, baseline disease activity, duration of disease, existing structural damage, smoking, treatment exposure, and other clinical factors can influence long-term outcome. Thus, assessment of RF in relation to objective measures of disease activity is necessary when examining its potential prognostic role.

Disease activity in rheumatoid arthritis can be quantified using validated composite indices. The Disease Activity Score incorporating 28 joints (DAS28) is one of the most widely used measures in clinical practice and research. It incorporates tender and swollen joint counts together with an acute-phase reactant and patient global assessment, thereby providing a standardized quantitative estimate of inflammatory disease activity. DAS28-based assessment facilitates categorization of patients according to the level of disease activity and enables longitudinal evaluation of response to treatment.[15,16]

Contemporary RA management emphasizes a treat-to-target strategy in which disease activity is assessed regularly and therapy is adjusted with the aim of achieving remission or, where appropriate, low disease activity.[17,18] Current EULAR recommendations also recognize the presence of autoantibodies, high disease activity, and early erosive damage as poor prognostic factors that may influence treatment strategy.[19] This highlights the continuing clinical importance of serological biomarkers in the overall assessment of patients with RA.

RF is particularly attractive as a potential prognostic biomarker in resource-limited clinical settings because the test is relatively inexpensive, widely available, and routinely performed. Quantitative RF measurement may provide more information than simple classification into RF-positive and RF-negative groups. If increasing RF levels are associated with higher subsequent disease activity, quantitative RF could potentially contribute to early risk stratification alongside clinical assessment and inflammatory markers.

Nevertheless, RF positivity should not automatically be equated with severe disease. Modern treatment strategies can substantially modify the natural history of RA, and seronegative patients may also experience clinically significant disease. Systematic evaluation of prognostic factors has demonstrated that RA progression is multifactorial, with disease activity, autoantibodies, imaging abnormalities, and other clinical characteristics contributing to adverse outcomes.[20] Prospective studies are therefore important for determining whether a baseline biomarker predicts subsequent disease activity rather than merely being associated with disease severity at a single point in time.

There is relatively limited prospective evidence from smaller tertiary-care populations in this region regarding the relationship between quantitative RF

levels and subsequent clinical disease activity. Differences in timing of presentation, duration of disease, treatment exposure, access to specialist care, and other demographic and clinical characteristics may influence this relationship.

Therefore, the present prospective cohort study was undertaken among patients with rheumatoid arthritis attending a tertiary care centre in Sultanpur, Uttar Pradesh, to evaluate rheumatoid factor as a predictor of disease severity, with disease activity assessed primarily by DAS28-ESR. The study also aimed to determine the relationship of RF positivity and quantitative RF titre with inflammatory markers and other clinical indicators of rheumatoid arthritis severity.

MATERIALS AND METHODS

Study Design and Setting: This hospital-based prospective observational cohort study was conducted at Autonomous State Medical College (ASMC), Sultanpur, Uttar Pradesh, India – 228001, a tertiary care teaching centre. Patients with rheumatoid arthritis (RA) attending the outpatient department were prospectively enrolled and evaluated during the study period from November 2024 to July 2026.

Study Population: The study population comprised adult patients with rheumatoid arthritis attending the outpatient department of ASMC Sultanpur. Patients were screened for eligibility according to predefined inclusion and exclusion criteria. A total of 30 eligible patients were enrolled and followed prospectively.

Study Duration: The study was conducted over a period of 21 months, from November 2024 to July 2026, including patient recruitment, baseline evaluation, prospective follow-up, completion of investigations, data collection, and analysis.

Sample Size and Sampling Technique: A total of 30 patients with rheumatoid arthritis were included in the study. Eligible patients presenting to the outpatient department during the recruitment period were enrolled by consecutive sampling until the required sample size was achieved.

Considering the relatively small sample, the study was designed as an exploratory prospective cohort study, and the results were interpreted with appropriate consideration of the precision of effect estimates.

Inclusion Criteria

1. Age between 20 and 65 years.
2. Diagnosis/classification of rheumatoid arthritis according to the 2010 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) classification criteria.
3. Attendance at the outpatient department of ASMC Sultanpur during the study period.
4. Availability of rheumatoid factor measurement at baseline.
5. Willingness to participate in prospective follow-up.
6. Provision of written informed consent.

Exclusion Criteria

1. Other systemic autoimmune/connective-tissue diseases, including systemic lupus erythematosus, systemic sclerosis, or inflammatory myopathies, that could interfere with assessment of RA.
2. Active severe infection at the time of evaluation.
3. Known active malignancy.
4. Another significant inflammatory disorder likely to independently influence ESR or CRP.
5. Inability or unwillingness to complete the required clinical assessment or follow-up.
6. Missing essential baseline RF or disease activity data.

Data Collection: Data were collected prospectively from all eligible patients using a predesigned case-record form after obtaining written informed consent. Demographic details, disease duration, duration of morning stiffness, comorbidities, smoking/tobacco exposure, extra-articular manifestations, and current treatment were recorded. All patients underwent general and musculoskeletal examination, including 28-joint tender and swollen joint counts and assessment for joint deformities and rheumatoid nodules. Laboratory investigations included complete blood count, ESR, CRP, quantitative rheumatoid factor, and anti-CCP antibody wherever available. Disease activity was assessed using DAS28-ESR at baseline and during follow-up. Baseline RF status and quantitative RF titre were subsequently analysed in relation to follow-up disease activity and other indicators of rheumatoid arthritis severity.

Clinical Examination: All enrolled patients underwent a detailed general physical, systemic, and musculoskeletal examination. The musculoskeletal assessment included examination of 28 joints for tenderness and swelling, comprising bilateral shoulders, elbows, wrists, metacarpophalangeal joints, proximal interphalangeal joints, and knees. Tender joint count (TJC28) and swollen joint count (SJC28) were recorded for calculation of DAS28-ESR. Patients were also examined for features indicating disease severity, including joint deformities, restriction of joint movements, rheumatoid nodules, and extra-articular manifestations of rheumatoid arthritis.

Laboratory Investigations: Venous blood samples were collected from all participants under aseptic precautions. Laboratory investigations included complete blood count, haemoglobin, total leukocyte count, platelet count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and quantitative rheumatoid factor (RF). Anti-cyclic citrullinated peptide (anti-CCP) antibody was assessed wherever available. Rheumatoid factor was recorded both as a quantitative value (IU/mL) and as positive or negative according to the reference range of the institutional laboratory. ESR was used along with clinical parameters for calculation of DAS28-ESR.

All investigations were performed using standard laboratory procedures at the institutional laboratory

Assessment of Rheumatoid Factor: Rheumatoid factor (RF) was assessed in all enrolled patients at baseline and was considered the primary predictor variable of the study. Venous blood samples were collected under aseptic precautions, and quantitative RF levels were measured in the institutional laboratory using standard laboratory procedures. RF values were expressed in IU/mL and classified as positive or negative according to the upper limit of normal specified by the institutional laboratory. Quantitative RF titre was also analysed as a continuous variable to determine its relationship with disease activity and severity, including DAS28-ESR, ESR, CRP, tender joint count, and swollen joint count. Baseline RF status and titre were subsequently compared with disease activity during follow-up.

Assessment of Disease Activity: Disease activity was assessed using the Disease Activity Score in 28 joints based on erythrocyte sedimentation rate (DAS28-ESR) at baseline and during follow-up. The DAS28-ESR was calculated using the 28-joint tender joint count (TJC28), 28-joint swollen joint count (SJC28), ESR, and patient global health assessment. Based on the calculated DAS28-ESR score, patients were categorized as being in remission (<2.6), low disease activity (2.6–3.2), moderate disease activity (>3.2–5.1), or high disease activity (>5.1). Follow-up DAS28-ESR was considered the principal measure of disease severity, and its relationship with baseline rheumatoid factor status and quantitative RF titre was analysed.

Follow-up Assessment: All enrolled patients were followed prospectively during the study period and underwent repeat clinical and laboratory assessment at follow-up. Tender joint count, swollen joint count, ESR, patient global health assessment, and DAS28-ESR were reassessed, along with changes in treatment and relevant clinical manifestations. Disease activity at follow-up was categorized as remission, low, moderate, or high according to DAS28-ESR. Baseline rheumatoid factor status and quantitative RF titre were subsequently correlated with follow-up DAS28-ESR and other indicators of disease severity to evaluate the prognostic significance of rheumatoid factor.

Outcome Measures

Primary Outcome Measure: The primary outcome measure was disease severity at follow-up as assessed by DAS28-ESR and its association with baseline rheumatoid factor (RF) status and quantitative RF titre. The difference in follow-up DAS28-ESR between RF-positive and RF-negative patients and the correlation between quantitative RF titre and follow-up DAS28-ESR were evaluated.

Secondary Outcome Measures: The secondary outcome measures included the association of RF status and quantitative RF titre with ESR, CRP, tender joint count, swollen joint count, joint deformities, rheumatoid nodules, extra-articular manifestations, and anti-CCP antibody status, where available. Changes in DAS28-ESR from baseline to follow-up and the distribution of patients according to remission, low, moderate, and high disease activity were also assessed.

Operational Definition of Disease Severity: Disease severity was assessed primarily using the Disease Activity Score in 28 joints based on ESR (DAS28-ESR). A higher DAS28-ESR score was considered indicative of greater disease severity. Patients were categorized as being in remission (DAS28-ESR <2.6), low disease activity (2.6–3.2), moderate disease activity (>3.2–5.1), or high disease activity (>5.1). For the primary analysis, follow-up DAS28-ESR was used as a continuous measure of disease severity. Additional indicators of severe disease included elevated ESR and CRP, higher tender and swollen joint counts, presence of joint deformities, rheumatoid nodules, and extra-articular manifestations.

Ethical Considerations: The study was conducted after obtaining approval from the Institutional Ethics Committee (IEC). Written informed consent was obtained from all participants before enrolment after explaining the purpose and procedures of the study. Participation was voluntary, and participants were free to withdraw from the study at any time without affecting their medical care. Confidentiality and anonymity of participant information were maintained throughout the study, and the collected data were used solely for research purposes. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

Statistical Analysis: Data were entered into Microsoft Excel and analysed using IBM SPSS Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (SD) for normally distributed data and as median with interquartile range (IQR) for non-normally distributed data, while categorical variables were presented as frequencies and percentages. The RF-positive and RF-negative groups were compared using the independent Student's t-test or Mann–Whitney U test for continuous variables and the Chi-square test or Fisher's exact test for categorical variables, as appropriate. Changes in DAS28-ESR between baseline and follow-up were assessed using the paired t-test or Wilcoxon signed-rank test. The relationship between quantitative RF titre and DAS28-ESR, ESR, CRP, tender joint count, and swollen joint count was evaluated using Pearson's or Spearman's correlation coefficient, depending on data distribution. All statistical tests were two-tailed, and a p-value <0.05 was considered statistically significant. Effect estimates with 95% confidence intervals were reported wherever appropriate.

RESULTS

A total of 30 patients with rheumatoid arthritis were included in the study and analysed. The mean age of

the study population was 44.6 ± 11.2 years. The majority of participants were female, with 23 (76.7%) females and 7 (23.3%) males. The mean duration of rheumatoid arthritis was 5.1 ± 3.4 years. Morning stiffness lasting more than 30 minutes was reported by 21 (70.0%) patients. Joint deformities were present in 8 (26.7%), rheumatoid nodules in 4 (13.3%), and extra-articular manifestations in 6 (20.0%) patients. The baseline demographic and clinical characteristics of the study population are summarized in [Table 1].

Table 1: Baseline demographic and clinical characteristics of the study participants

Characteristics	Value (n=30)
Age, years	44.6 ± 11.2
Female, n (%)	23 (76.7)
Male, n (%)	7 (23.3)
Disease duration, years	5.1 ± 3.4
Morning stiffness >30 minutes, n (%)	21 (70.0)
Tender joint count	8.6 ± 4.3
Swollen joint count	5.4 ± 3.1
Joint deformities, n (%)	8 (26.7)
Rheumatoid nodules, n (%)	4 (13.3)
Extra-articular manifestations, n (%)	6 (20.0)
Methotrexate use, n (%)	24 (80.0)
Corticosteroid use, n (%)	13 (43.3)

Table note: Data are presented as mean ± standard deviation (SD) or number (percentage), as appropriate. TJC = tender joint count; SJC = swollen joint count.

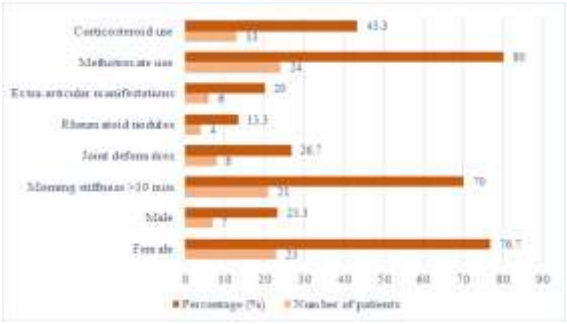

Figure 1: Distribution of Baseline Clinical Characteristics Among Patients with Rheumatoid Arthritis

Figure note: The bar chart shows the percentage distribution of selected baseline clinical characteristics among the study participants (n=30), including sex, morning stiffness lasting >30 minutes, joint deformities, rheumatoid nodules, extra-articular manifestations, methotrexate use, and corticosteroid use. Values are expressed as percentages of the total study population.

Laboratory Profile: Rheumatoid factor was positive in 21 (70.0%) patients and negative in 9 (30.0%) patients. The median quantitative RF titre was 86 IU/mL (IQR: 42–168 IU/mL). The mean ESR was 48.7 ± 21.5 mm/hour, while the median CRP concentration was 13.4 mg/L (IQR: 6.8–24.6 mg/L). The mean haemoglobin concentration was 10.9 ± 1.6 g/dL. Anti-CCP results were available for 26 patients, of whom 19 (73.1%) were positive. The laboratory profile of the participants is presented in Table 2.

Table 2: Laboratory characteristics of the study participants

Laboratory parameter	Value
RF positive, n (%)	21 (70.0)
RF negative, n (%)	9 (30.0)
RF titre, IU/mL	86 (42–168)
ESR, mm/hour	48.7 ± 21.5
CRP, mg/L	13.4 (6.8–24.6)
Haemoglobin, g/dL	10.9 ± 1.6
Total leukocyte count, cells/mm³	7,860 ± 1,940
Platelet count, ×10³/mm³	312 ± 78
Anti-CCP positive, n/N (%)	19/26 (73.1)

Table note: Normally distributed continuous variables are presented as mean ± SD, skewed variables as median (IQR), and categorical variables as n (%). Anti-CCP testing was available in 26 of 30 participants. RF = rheumatoid factor; ESR = erythrocyte sedimentation rate; CRP = C-reactive protein; anti-CCP = anti-cyclic citrullinated peptide antibody; SD = standard deviation; IQR = interquartile range.

Disease Activity at Baseline and Follow-up: At baseline, the mean DAS28-ESR was 5.12 ± 1.08. High disease activity was observed in 12 (40.0%) patients, moderate disease activity in 13 (43.3%), low disease activity in 3 (10.0%), and remission in 2 (6.7%) patients.

At follow-up, the mean DAS28-ESR decreased to 4.18 ± 1.14. High disease activity was present in 6 (20.0%) patients, moderate disease activity in 14 (46.7%), low disease activity in 6 (20.0%), and remission in 4 (13.3%) patients. The reduction in mean DAS28-ESR from baseline to follow-up was statistically significant (5.12 ± 1.08 vs. 4.18 ± 1.14; p=0.002). The distribution of disease activity categories at baseline and follow-up is shown in [Table 3].

Table 3. Distribution of disease activity according to DAS28-ESR at baseline and follow-up

DAS28-ESR category	Baseline, n (%)	Follow-up, n (%)
Remission	2 (6.7)	4 (13.3)
Low disease activity	3 (10.0)	6 (20.0)
Moderate disease activity	13 (43.3)	14 (46.7)
High disease activity	12 (40.0)	6 (20.0)
Total	30 (100.0)	30 (100.0)

Table note: Disease activity was categorized according to DAS28-ESR as remission (<2.6), low disease activity (2.6–3.2), moderate disease activity (>3.2–5.1), and high disease activity (>5.1). DAS28-ESR = Disease Activity Score in 28 joints using erythrocyte sedimentation rate.

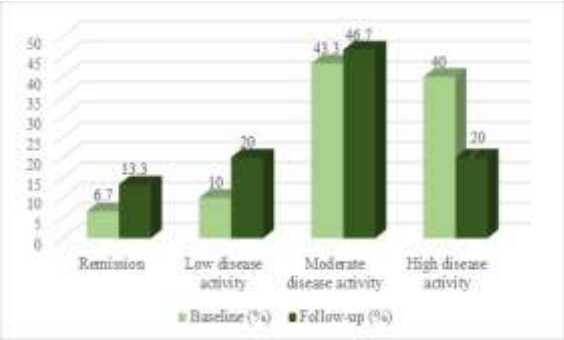

Figure 2: Comparison of Disease Activity Categories at Baseline and Follow-up According to DAS28-ESR

Figure note: The bar chart illustrates the distribution of rheumatoid arthritis disease activity at baseline and follow-up among the study participants (n=30). Disease activity was classified according to DAS28-ESR as remission (<2.6), low disease activity (2.6–3.2), moderate disease activity (>3.2–5.1), and high disease activity (>5.1). Values are expressed as percentages. The proportion of patients with high disease activity decreased from 40.0% at baseline to 20.0% at follow-up, while the proportion in remission increased from 6.7% to 13.3%.

Association of Rheumatoid Factor With Disease Severity: RF-positive patients demonstrated greater disease activity than RF-negative patients. The mean baseline DAS28-ESR was significantly higher among RF-positive patients than among RF-negative patients (5.43 ± 0.96 vs. 4.39 ± 1.03; p=0.012). At follow-up, RF-positive patients continued to have significantly greater disease activity (4.55 ± 1.03 vs. 3.32 ± 0.88; p=0.006).

Inflammatory markers were also higher in the RF-positive group. Mean ESR was 55.2 ± 20.6 mm/hour among RF-positive patients compared with 33.4 ± 15.0 mm/hour among RF-negative patients (p=0.008). Median CRP was 16.2 mg/L and 7.8 mg/L, respectively (p=0.014). Joint deformities were observed in 8 (38.1%) RF-positive patients and none of the RF-negative patients (p=0.036). Detailed comparisons between the RF-positive and RF-negative groups are presented in [Table 4].

Table 4: Comparison of clinical and laboratory parameters between RF-positive and RF-negative patients

Parameter	RF-positive (n=21)	RF-negative (n=9)	p-value
Age, years	45.8 ± 10.8	41.8 ± 12.0	0.370
Disease duration, years	5.8 ± 3.5	3.6 ± 2.7	0.100
ESR, mm/hour	55.2 ± 20.6	33.4 ± 15.0	0.008
CRP, mg/L, median	16.2	7.8	0.014
Baseline DAS28-ESR	5.43 ± 0.96	4.39 ± 1.03	0.012
Follow-up DAS28-ESR	4.55 ± 1.03	3.32 ± 0.88	0.006
Joint deformities, n (%)	8 (38.1)	0 (0.0)	0.036
Rheumatoid nodules, n (%)	4 (19.0)	0 (0.0)	0.290
Anti-CCP positive, n/N (%)	17/19 (89.5)	2/7 (28.6)	0.004

Table note: Continuous variables are presented as mean ± SD unless otherwise specified; categorical variables are presented as n (%). Independent-samples Student's t-test or Mann–Whitney U test was used for continuous variables, while the Chi-square test or Fisher's exact test was used for categorical variables, as appropriate. A p-value <0.05 was considered statistically significant. RF = rheumatoid factor; ESR = erythrocyte sedimentation rate; CRP = C-reactive protein; DAS28-ESR = Disease Activity Score in 28 joints using ESR; anti-CCP = anti-cyclic citrullinated peptide antibody; SD = standard deviation.

Correlation Between Quantitative RF Titre and Disease Severity: Quantitative RF titre demonstrated a moderate positive correlation with follow-up DAS28-ESR (Spearman's ρ=0.58, p=0.001), indicating that higher RF titres were associated with greater disease activity during follow-up. RF titre was also significantly correlated with baseline DAS28-ESR (ρ=0.52, p=0.003), ESR (ρ=0.61, p<0.001), CRP (ρ=0.47, p=0.009), tender joint count (ρ=0.44, p=0.015), and swollen joint count (ρ=0.49, p=0.006). The correlations between quantitative RF titre and different indicators of disease severity are summarized in [Table 5].

Table 5: Correlation of quantitative rheumatoid factor titre with indicators of disease severity

Parameter	Spearman's ρ	p-value
Baseline DAS28-ESR	0.52	0.003
Follow-up DAS28-ESR	0.58	0.001

ESR	0.61	<0.001
CRP	0.47	0.009
Tender joint count	0.44	0.015
Swollen joint count	0.49	0.006

Table note: Correlations were assessed using Spearman's rank correlation coefficient (ρ). Positive values indicate that higher RF titres were associated with higher values of the respective disease severity parameter. A p-value <0.05 was considered statistically significant. RF = rheumatoid factor; DAS28-ESR = Disease Activity Score in 28 joints using erythrocyte sedimentation rate; ESR = erythrocyte sedimentation rate; CRP = C-reactive protein.

DISCUSSION

Rheumatoid arthritis (RA) is a chronic systemic autoimmune disease characterized by persistent synovial inflammation, progressive joint destruction, and functional impairment. Its pathogenesis involves complex interactions between genetic susceptibility, environmental factors, autoantibody production, and dysregulated immune responses.[1] RA contributes substantially to global morbidity, with considerable variation in prevalence across populations and a consistent predominance among women.[2] Persistent inflammatory activity may lead to progressive radiographic damage and irreversible disability,[3] making early identification of patients at risk of severe disease an important component of clinical management.[4]

In the present study, the mean age of patients was 44.6 ± 11.2 years, with females accounting for 76.7% of the study population. Rheumatoid factor (RF) was positive in 70.0% of patients. RF remains an important and widely available serological marker in RA, with established diagnostic as well as potential prognostic applications.[5] Although RF is not specific for RA, its diagnostic utility, particularly when interpreted along with anti-cyclic citrullinated peptide (anti-CCP) antibodies and clinical findings, has been well established.[6] Its importance is also reflected in the 2010 ACR/EULAR classification criteria,[7] in which higher RF or ACPA levels receive greater weighting than low-positive results.[8]

The principal finding of the present study was that RF-positive patients had significantly greater disease activity than RF-negative patients. The mean baseline DAS28-ESR was significantly higher in RF-positive patients than in RF-negative patients (5.43 ± 0.96 vs. 4.39 ± 1.03; p=0.012). This difference persisted at follow-up (4.55 ± 1.03 vs. 3.32 ± 0.88; p=0.006). Previous studies have identified serological status and inflammatory disease activity as important factors associated with radiographic damage and physical disability in early RA.[9] Long-term observations have similarly demonstrated that persistent RA may result in substantial structural and functional deterioration.[10]

An important observation was the significant relationship between quantitative RF titre and disease activity. RF titre correlated positively with both baseline DAS28-ESR (ρ=0.52, p=0.003) and follow-up DAS28-ESR (ρ=0.58, p=0.001). These findings suggest that quantitative RF levels may provide additional prognostic information beyond simple RF-positive or RF-negative classification. De Rycke et al. reported associations between RF, anticitrullinated protein antibodies, radiological progression, and extra-articular manifestations,[11] while specific RF isotypes have also been associated with extra-articular disease.[12]

RF titre also demonstrated significant positive correlations with ESR (ρ=0.61), CRP (ρ=0.47), tender joint count (ρ=0.44), and swollen joint count (ρ=0.49). These associations suggest that higher RF levels may accompany a greater inflammatory burden. However, RF should not be regarded as a direct marker of current inflammation because disease activity is influenced by multiple clinical and biological factors.

Anti-CCP positivity was more frequent among RF-positive patients. Anti-CCP antibodies have been associated with subsequent radiographic damage and adverse disease outcomes,[13] and their diagnostic and prognostic significance in RA is well established.[14] Therefore, the frequent coexistence of RF and anti-CCP should be considered when interpreting the independent prognostic role of RF.

Disease activity was evaluated using DAS28-ESR, a validated composite measure incorporating tender and swollen joint counts, ESR, and patient global assessment.[15] Consistent use of DAS28-ESR during follow-up is important because differences have been demonstrated between DAS28 calculated using ESR and CRP.[16] In the present study, mean DAS28-ESR decreased significantly from 5.12 ± 1.08 at baseline to 4.18 ± 1.14 at follow-up (p=0.002). The proportion of patients with high disease activity also decreased from 40.0% to 20.0%. This improvement may reflect ongoing treatment and regular clinical follow-up.

These observations are relevant to the contemporary treat-to-target approach, which recommends regular assessment of disease activity and modification of therapy to achieve remission or low disease activity.[17] Updated treat-to-target recommendations further emphasize sustained disease control to minimize structural damage and disability.[18] Current EULAR recommendations also recognize autoantibody positivity and high disease activity among factors indicating an unfavourable prognosis.[19]

Joint deformities were more frequent among RF-positive patients in the present cohort. Nevertheless, structural damage in RA is multifactorial and may be influenced by disease duration, cumulative inflammatory burden, delayed treatment, autoantibody status, and therapeutic response. Systematic evidence indicates that prediction of poor outcomes requires consideration of multiple clinical,

laboratory, and imaging characteristics rather than reliance on a single biomarker.[20]

The present study has clinical relevance because RF is inexpensive, readily available, and routinely measured in patients with RA. Quantitative RF assessment may therefore contribute to risk stratification, particularly in resource-limited settings. The prospective design and evaluation of RF as both a categorical and continuous variable were strengths of the study. However, the small sample size, single-centre design, variation in treatment exposure, incomplete anti-CCP testing, absence of standardized radiographic assessment, and limited follow-up restrict the generalizability of the findings. In conclusion, RF positivity and higher quantitative RF titres were associated with greater disease activity and inflammatory burden in RA. The correlation of RF titre with follow-up DAS28-ESR and other measures of inflammatory activity suggests a potential prognostic role for quantitative RF. Nevertheless, RF should be interpreted as part of a comprehensive assessment rather than as an isolated predictor. Larger multicentre prospective studies with longer follow-up are required to confirm its independent predictive value.

Limitations: The present study has several limitations. First, the relatively small sample size of 30 patients limits the statistical power and precision of the findings. Second, this was a single-centre study conducted in a tertiary care setting, which may limit the generalizability of the results to the wider rheumatoid arthritis population. Third, variations in disease duration, previous treatment, and ongoing use of DMARDs and corticosteroids may have influenced disease activity and inflammatory markers during follow-up. Anti-CCP testing was not available for all participants, and standardized radiographic assessment of structural joint damage was not included as a primary outcome. The relatively short follow-up period limited the evaluation of long-term outcomes such as radiographic progression and permanent functional disability. Furthermore, the small sample size restricted robust multivariable adjustment for potential confounding factors. Therefore, larger multicentre prospective studies with longer follow-up are required to confirm the independent prognostic value of rheumatoid factor in predicting rheumatoid arthritis severity.

CONCLUSION

The present study demonstrated that rheumatoid factor positivity and higher quantitative RF titres were associated with greater disease activity in patients with rheumatoid arthritis. RF-positive patients had higher DAS28-ESR scores and inflammatory markers compared with RF-negative patients, while increasing RF titres showed significant positive correlations with DAS28-ESR, ESR, CRP, tender joint count, and swollen joint count. These findings suggest that quantitative RF may have prognostic value in addition to its established diagnostic and classification role. However, rheumatoid arthritis severity is multifactorial, and RF should be interpreted together with clinical disease activity, inflammatory markers, other serological markers, and treatment response. Larger prospective multicentre studies with longer follow-up are needed to confirm the independent predictive value of RF for disease severity.

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