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Correlation of Serological and Inflammatory Markers with Radiographic Findings in Rheumatoid Arthritis Patients

Shivmohan Singh

Assistant Professor, Department of Medical Laboratory Techniques, College of Paramedical Sciences, Teerthanker Mahaveer University, Moradabad, U. P. India, 244001
Correspondence Author Email: *shivbais. thakur10[at]gmail.com*

Abstract: ***Background: Rheumatoid Arthritis is a chronic inflammatory disease characterized by joint damage and systemic complications. This study aimed to investigate the correlation between Rheumatoid Factor, Anti - Cyclic Citrullinated, C - Reactive Protein, and Erythrocyte Sedimentation Rate with radiographic findings in RA patients. Additionally, the association of psychiatric parameters with disease severity was assessed. Methods: A pilot cross - sectional study was conducted on 30 RA patients. Biomarker levels were measured using chemiluminescence and the Westergren method. Radiographic evaluation included joint erosion, joint space narrowing, and osteophyte formation assessed via the Sharp/van der Heijde scoring system. Psychiatric parameters such as depression, anxiety, sleep disturbance, coping difficulties, and cognitive impairment were recorded. Correlation and group comparisons were performed using SPSS. Results: Patients with severe RA had significantly higher RF, Anti - CCP, CRP, and ESR levels than those with mild and moderate disease. Radiographic findings showed progressive joint damage with increasing disease severity. Psychiatric symptoms, particularly anxiety (60%) and depression (53.3%), were more prevalent in severe cases. A strong correlation was observed between inflammatory markers and radiographic severity ($p < 0.05$). Conclusion: Elevated inflammatory biomarkers are associated with worsening radiographic damage in RA patients. Psychiatric comorbidities are prevalent in RA and correlate with disease severity, highlighting the need for a multidisciplinary management approach.***

Keywords: Rheumatoid Arthritis, Inflammatory Biomarkers, Radiographic Severity, Psychiatric Comorbidities, Disease Progression

1. Background

Rheumatoid arthritis (RA) is a chronic, systemic autoimmune disorder characterized by persistent synovial inflammation, which leads to joint destruction, deformity, and functional disability. The pathogenesis of RA involves a complex interplay between genetic predisposition, environmental factors, and immune system dysregulation, which results in the formation of autoantibodies and inflammatory mediators (1) . Over time, chronic inflammation in the synovium leads to the release of proteolytic enzymes and cytokines, causing damage to the cartilage, bone, and surrounding tissues. If left untreated, RA can progress to significant joint deformity and irreversible functional impairment (2).

Beyond its physical manifestations, RA is also associated with substantial psychological distress, including increased rates of anxiety, depression, and cognitive impairment, which further contribute to reduced quality of life and disability (3) . The chronic pain and functional limitations experienced by RA patients often lead to emotional distress, highlighting the need for a multidisciplinary approach that integrates rheumatologic and psychiatric care.

The diagnosis of RA is multi - faceted, incorporating clinical evaluation, laboratory findings, and radiographic imaging. Among the serological markers, rheumatoid factor (RF) and anti - cyclic citrullinated peptide (anti - CCP) antibodies are widely used to aid in the diagnosis of RA and assess disease activity (4). RF, an autoantibody directed against the Fc portion of immunoglobulin G (IgG), is present in a substantial proportion of RA patients but lacks specificity, as it can also be elevated in other autoimmune conditions and infections. Anti - CCP antibodies, however, have demonstrated high specificity for RA and are considered a more reliable biomarker for early diagnosis, particularly in individuals who test negative for RF (5).

Inflammatory markers such as C - reactive protein (CRP) and erythrocyte sedimentation rate (ESR) are acute - phase reactants that are frequently elevated in RA due to the systemic inflammatory response (6).

These markers correlate with disease activity and are used to monitor treatment efficacy, but they lack the specificity required for a definitive diagnosis. CRP is particularly valuable in detecting disease flare - ups and monitoring inflammation levels, while ESR is a general indicator of systemic inflammation (7).

Radiographic imaging, especially X - rays, plays a crucial role in both the diagnosis and monitoring of disease progression in RA. Early radiographic findings may be subtle, but as the disease progresses, characteristic changes become evident. Joint erosions, joint space narrowing, and periarticular osteopenia are considered hallmarks of RA on X - ray. Joint erosions, particularly in the hands and feet, result from the inflammatory destruction of bone and cartilage, while narrowing of joint spaces reflects cartilage loss (1) . Periarticular osteopenia, the reduction in bone mineral density around the affected joints, is an early sign of inflammatory activity and is often seen prior to the appearance of erosions. In advanced stages, X - rays may reveal joint deformities, ankylosis, and bony remodelling.

This study aims to explore the correlation between RF, anti - CCP antibodies, inflammatory markers (CRP and ESR), and radiographic findings in patients with RA. By investigating

these associations, the study seeks to provide a more comprehensive understanding of how laboratory and radiographic markers interact to reflect disease severity and progression. Given the growing recognition of the psychological burden associated with RA, this research also underscores the importance of integrating psychiatric rehabilitation into routine care. Addressing the mental health challenges faced by RA patients—such as depression, anxiety, and coping difficulties—can enhance treatment adherence, improve overall well - being, and optimize rehabilitation outcomes. Ultimately, this study aims to contribute to a holistic approach to RA management that considers both physical and psychological aspects of the disease.

2. Materials and Methods

2.1 Study Design and Site

This study was a correlational observational study with a cross - sectional design, conducted at the Orthopaedic Department of Teerthanker Mahaveer Hospital and Research Center, Moradabad, Uttar Pradesh, India. The study adhered to ethical guidelines, and written informed consent was obtained from all participants before enrollment.

2.2 Study Population

Study population selected on the basis of inclusion and exclusion criteria.

2.2.1 Inclusion Criteria

- Patients aged 18–70 years with a confirmed diagnosis of Rheumatoid Arthritis (RA) based on the 2010 American College of Rheumatology (ACR) /European League Against Rheumatism (EULAR) classification criteria.
- Patients presenting with active disease, defined by elevated levels of C - reactive protein (CRP) and erythrocyte sedimentation rate (ESR).
- Patients who given informed consent form.

2.2.2 Exclusion Criteria

- Patients diagnosed with other autoimmune diseases.
- Patients with systemic inflammatory conditions.
- Patients who had undergone joint replacement surgery or any invasive joint intervention prior to the study.
- Patients with chronic infections or malignancies.
- Patients who do not give informed consent form.

2.3 Data collections

Blood samples were collected from 30 RA patients under aseptic conditions. For ESR analysis, blood was drawn into an EDTA vial, while serum samples for RF (IU/mL), Anti - CCP (U/mL), and CRP (mg/L) were collected in plain vials, centrifuged, and analyzed using a fully automated analyzer. Radiographic assessment of the hands, wrists, and feet was performed using X - ray imaging, evaluated based on the Sharp/van der Heijde scoring system, which includes Joint Erosion Score, Joint Space Narrowing, and Osteophyte formation.

Demographic and clinical parameters such as age, gender, disease duration, and RA severity were recorded. Additionally, psychosocial factors including depression, anxiety, and coping difficulties were assessed due to their relevance in RA disease progression and patient quality of life.

2.4 Statistical Analysis

Data were analyzed using **SPSS**. Continuous variables were compared using **one - way ANOVA or Kruskal - Wallis test**, with **Bonferroni correction** for post - hoc analysis. **Chi - square test** assessed psychiatric symptoms across RA severity groups. **Pearson's correlation** evaluated associations between biomarkers and radiographic findings. A **p - value < 0.05** was considered significant.

3. Result

Table 1 presents the age distribution by gender among the 30 RA patients included in this study. The mean age was 52.3 ± 9.8 years, with males having a higher mean age (54.2 ± 8.5 years) than females (49.6 ± 10.2 years).

Table 1: Age Distribution of RA Patients by Gender

Gender	Mean Age (Years) ± SD
Male (n=18)	54.2 ± 8.5
Female (n=12)	49.6 ± 10.2
Total (n=30)	52.3 ± 9.8

All values were mean and standard deviation (SD) of the age distribution in male and female RA patients. The majority of the patients were males, and the overall mean age was 52.3 ± 9.8 years.

Table 2 illustrates the gender distribution, showing a male predominance with 60.0% (n=18) of the participants being male and 40.0% (n=12) being female.

Table 2: Gender Distribution of RA Patients

Gender	Number (%)
Male	18 (60.0%)
Female	12 (40.0%)

Table presents the gender distribution of the study population. The sample had a higher proportion of males (60.0%) compared to females (40.0%).

Table 3 categorizes the severity of Rheumatoid Arthritis (RA) based on the Disease Activity Score 28 (DAS28). Among the patients, 20.0% had mild disease activity, 46.7% exhibited moderate disease severity, and 33.3% were classified as having severe RA.

Table 3: Severity of Rheumatoid Arthritis Based on DAS28

Severity Category	Number (%)
Mild (DAS28 < 3.2)	6 (20.0%)
Moderate (DAS28: 3.2–5.1)	14 (46.7%)
Severe (DAS28 > 5.1)	10 (33.3%)

The table classifies RA severity according to the Disease Activity Score 28 (DAS28). The majority of patients (46.7%) had moderate disease activity, while 33.3% had severe RA.

The study participants exhibited elevated levels of RF (mean = 60.0 ± 18.2 IU/mL) and Anti - CCP (mean = 335.5 ± 65.4

U/mL), consistent with moderate to high disease activity. Elevated levels of CRP (mean = 26.1 ± 7.5 mg/L) and ESR (mean = 39.1 ± 9.6 mm/h) were also observed, indicating active inflammation in the RA patients. Radiographic findings revealed moderate joint damage, with a mean joint erosion score of 3.8 ± 1.0, a mean joint space narrowing score of 2.6 ± 0.7, and a mean osteophyte score of 2.3 ± 0.7, suggesting moderate disease progression.

Table 4: Rheumatoid Arthritis Biomarkers and Radiographic Findings

	RF (IU/mL)	Anti - CCP (U/mL)	CRP (mg/L)	ESR (mm/h)	X - ray		
					Joint Erosion Score	Joint Space Narrowing	Osteophytes
Mean	60	335.5	26.1	39.1	3.8	2.6	2.3
SD	18.2	65.4	7.5	9.6	1.0	0.7	0.7

The table presents the mean and standard deviation (SD) values of Rheumatoid Factor (RF), Anti - Cyclic Citrullinated Peptide (Anti - CCP), C - Reactive Protein (CRP), Erythrocyte Sedimentation Rate (ESR), and radiographic findings (joint erosion score, joint space narrowing score, and osteophyte score) in the study sample. Elevated levels of RF, Anti - CCP, CRP, and ESR indicate moderate to high disease activity and active inflammation in RA patients. Radiographic findings suggest moderate joint damage and disease progression.

The psychiatric symptoms observed in RA patients. Depression was reported in **53.3%** of the participants, while **60.0%** experienced anxiety. Sleep disturbances were prevalent in **46.7%**, and **40.0%** had difficulty coping with daily activities. Additionally, **30.0%** of the patients exhibited signs of cognitive impairment.

Table 5: Psychiatric Symptoms in RA Patients

Psychiatric Parameter	Number (%)
Depression	16 (53.3%)
Anxiety	18 (60.0%)
Sleep Disturbance	14 (46.7%)
Coping Difficulties	12 (40.0%)
Cognitive Impairment	9 (30.0%)

Table presents the prevalence of psychiatric symptoms in RA patients. Depression (53.3%) and anxiety (60.0%) were the most common psychiatric conditions, followed by sleep disturbances, coping difficulties, and cognitive impairment. These findings highlight the psychological burden associated with RA.

A one - way ANOVA (or Kruskal - Wallis test for non - normally distributed data) was used to compare biomarker levels among mild (n=6), moderate (n=14), and severe (n=10) RA groups.

Table 6: Comparison of Biomarker Levels Across RA Severity Groups

Parameter	Mild RA (n=6)	Moderate RA (n=14)	Severe RA (n=10)	p - value
RF (IU/mL)	42.8 ± 9.6	56.7 ± 11.5	75.3 ± 14.9	< 0.01
Anti - CCP (U/mL)	270.2 ± 51.3	330.8 ± 64.7	405.2 ± 69.8	< 0.01
CRP (mg/L)	18.0 ± 4.9	25.4 ± 7.2	34.9 ± 8.7	< 0.01
ESR (mm/h)	29.6 ± 6.8	38.4 ± 9.2	47.8 ± 10.9	< 0.01
Joint Erosion Score	2.3 ± 0.5	3.7 ± 0.9	5.0 ± 1.2	< 0.01
Joint Space Narrowing	1.7 ± 0.4	2.5 ± 0.6	3.4 ± 0.8	< 0.01
Osteophytes	1.5 ± 0.3	2.2 ± 0.6	3.0 ± 0.7	< 0.01

Data are presented as mean ± standard deviation (SD). A one - way ANOVA was used for normally distributed data, and the Kruskal - Wallis test was used for non - normally distributed variables. Post - hoc pairwise comparisons were performed using Bonferroni correction. A p - value < 0.05 was considered statistically significant. Rheumatoid Factor (RF), Anti - Cyclic Citrullinated Peptide (Anti - CCP), C - Reactive Protein (CRP), Erythrocyte Sedimentation Rate (ESR), and radiographic findings (joint erosion score, joint space narrowing score, and osteophyte score).

A Chi - square test was performed to compare psychiatric symptoms among RA patients. A high prevalence of psychiatric symptoms was observed in RA patients, with anxiety (60%) and depression (53.3%) being the most common. Other symptoms, such as sleep disturbances (46.7%), coping difficulties (40%), and cognitive impairment (30%), were also notable.

Table 7: Psychiatric Symptoms in RA Patients

Psychiatric Parameter	Number (%)	p - value
Depression	16 (53.3%)	0.02
Anxiety	18 (60.0%)	< 0.01
Sleep Disturbance	14 (46.7%)	0.03
Coping Difficulties	12 (40.0%)	0.04
Cognitive Impairment	9 (30.0%)	0.05

Data are presented as number (percentage). The p - value was obtained using the Chi - square test. A significant association was found between psychiatric symptoms and RA severity (p < 0.05).

4. Discussion

The findings of this study provide valuable insights into the demographic, clinical, and psychiatric characteristics of patients with rheumatoid arthritis (RA). The data reveal a higher prevalence of RA in males (60%) compared to females (40%), with a mean age of 52.3 years, which is consistent with previous studies suggesting that RA onset typically occurs in middle age (**Mutalipova et al., 2024)** (8) **.** The gender distribution aligns with global trends, where RA is more commonly diagnosed in women, but the male predominance

in this cohort may reflect regional or sampling variations (**Yu et al., 2020)** (9)**.**

The severity of RA, as assessed by the DAS28 score, showed that the majority of patients (46.7%) had moderate disease activity, while 33.3% had severe disease. This distribution is comparable to findings by (**Toledano et al.2021)** (10)**,** who reported that moderate disease activity is the most common presentation in RA patients. The significant increase in RF, anti - CCP, CRP, and ESR levels with disease severity ($p < 0.01$) further supports the association between these biomarkers and RA progression, as highlighted in prior research (**Shapiro et al., 2021)** (11)**.** The radiographic findings, including joint erosion, joint space narrowing, and osteophytes, also correlated strongly with disease severity, consistent with the work of (**Scott et al.2004)** (12)**,** who emphasized the role of imaging in assessing RA progression.

Psychiatric symptoms were prevalent in this cohort, with anxiety (60%) and depression (53.3%) being the most common. These findings align with studies by (**Matchamet al.2016),** who reported that RA patients are at a higher risk of developing mental health disorders due to the chronic nature of the disease and its impact on quality of life (13) . The significant p - values for depression ($p = 0.02$), anxiety ($p < 0.01$), and sleep disturbance ($p = 0.03$) underscore the need for integrated care addressing both physical and mental health in RA management.

The elevated levels of RF and anti - CCP in severe RA patients are consistent with the findings of (**Sokolova et al.2022),** who demonstrated that these biomarkers are strong predictors of disease severity and joint damage (14) . Similarly, the progressive increase in CRP and ESR levels across severity groups supports their utility as indicators of systemic inflammation, as noted by (**Matteoet al.2025)** (15)**.**

5. Conclusion

In conclusion, this study highlights the interplay between demographic factors, disease severity, biomarkers, and psychiatric symptoms in RA patients. The findings align with existing literature and emphasize the importance of a multidisciplinary approach to RA management, incorporating both physical and mental health interventions. Future research should focus on longitudinal studies to better understand the causal relationships between these factors and to develop targeted therapeutic strategies.

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Conflict of Interest
The authors declare no conflict of interest.

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