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Original Article

Pattern of Joint Involvement, Inflammatory Markers, and Autoantibodies Among Rheumatoid Arthritis Patients Attending Rizgary Teaching Hospital

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Abstract

Background: Rheumatoid arthritis (RA) is a chronic autoimmune disorder characterized by joint inflammation. Early initiation of treatment is essential, and the presence of autoantibodies (RF, anti-CCP) and elevated inflammatory markers (ESR, CRP) plays a central role in diagnosis.
Objective: This study aims to explore the relationship between joint involvement patterns and inflammatory markers (ESR, CRP) and autoantibody profiles (RF, anti-CCP) in newly diagnosed rheumatoid arthritis (RA) patients.
Patients and Methods: A cross-sectional study was conducted from October 2024 to March 2025 at Rizgary Teaching Hospital in Erbil, Iraq. In this study, 60 recently diagnosed patients with RA, aged 18-70 years old, were included based on the criteria reported on the 2010 ACR/EULAR RA criteria. Patients underwent clinical assessments, including joint involvement patterns and disease activity (DAS28), and laboratory tests for ESR, CRP, RF, and anti-CCP levels.
Results: Compared with asymmetrical oligoarthritis, patients with symmetrical polyarthritis had higher ESR (39.08 ± 19.22 vs 27.29 ± 5.82 mm/hr.; p = 0.048) and CRP (11.44 ± 8.81 vs 4.60 ± 2.74 mg/dL; p = 0.047). RF positivity was more frequent in the symmetrical group (42.7%; p = 0.035), while anti-CCP did not differ (p = 0.412). In multivariable logistic regression adjusting for age, sex, BMI, disease duration, and ESR, higher CRP (OR = 1.11; 95% CI: 1.03–1.24; p < 0.001) and RF positivity (OR = 3.80; 95% CI: 2.42–5.64; p < 0.001) independently predicted symmetrical polyarthritis; ESR (p = 0.176) and anti-CCP (p = 0.528) were not independent predictors.
Conclusion: CRP and RF are independent correlates of the symmetrical polyarthritis phenotype in early RA, whereas ESR and anti-CCP were not independently associated after adjustment. These findings support integrating CRP and RF with clinical patterns when assessing early disease activity and phenotype

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Introduction

Rheumatoid arthritis (RA) is one of the common autoimmune diseases characterized by chronic inflammation in most of the organs in the body. Now it is estimated that 0.5% to 1% of the total global population suffers from it, and it tends to be almost thrice as prominent in women as in men. It occurs most frequently

between ages 40 and 50years (1). Despite its precise etiology remaining largely undefined, RA is thought to occur as a result of genetic susceptibility and environmental factors together, which trigger an autoimmune process. RA mainly affects synovial joints, and chronic inflammation results in the erosion of bone and cartilage, which leads to joint deformity (2, 3).

Early diagnosis and prompt initiation of pharmacological treatment are critical to reducing the risk of irreversible joint damage and improving patient outcomes. RA often has an insidious onset, typically presenting as symmetric polyarthritis affecting small joints of the hands and feet. In contrast, large joint involvement (LJI), such as the hips or knees, is less common in the early stages of RA and is generally considered a marker of more advanced stages (4).

The 2010 ACR/EULAR classification criteria focus on small joint disease, particularly in the metacarpophalangeal and proximal interphalangeal joints, to facilitate early recognition. For early RA, which can begin with LJI, this focus may impair the detection of these early RA cases and thereby lead to later diagnosis and more joint deformities. In addition, LJI in early RA has been linked to higher disease activity, radiographic damage in distal joints, and physical disability (5). The starting gold standard features of RA are exact autoantibodies (for instance, anti-citrullinated protein antibodies (ACPA) and rheumatoid factor (RF)). Clinical symptoms typically accompany such biomarkers and correlate with more aggressive disease pathophenotypes. The 2010 ACR/EULAR criteria incorporate anti-CCP to improve diagnostic sensitivity in early disease (6). In addition to joint distribution and serological markers, the criteria also integrate acute-phase reactants such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) to improve diagnostic accuracy (7). Despite the limitations of the availability of data regarding RA in Iraq, the current trial aims to discover the association between joint involvement, markers of inflammation, and autoantibody profiles in newly diagnosed Iraqi RA patients. This cross-sectional study aiming to assess associations between joint involvement patterns and inflammatory markers in newly diagnosed RA patients.

Patients and Methods

Study Design and Setting

A cross-sectional study was conducted on 60 newly diagnosed RA patients in the outpatient rheumatology clinic of Rizgary Teaching Hospital, Erbil, Kurdistan Region, Iraq, from October 2024 to March 2025. The sample size of 60 patients was determined based on logistical feasibility during the six-month data collection period. The classification of joint involvement patterns into symmetrical polyarthritis and asymmetrical oligoarthritis was based on initial clinical presentation and aimed to differentiate more severe and systemic forms of RA from milder or atypical ones. This approach aligns with the 2010 ACR/EULAR classification criteria, which emphasize symmetrical small joint involvement for early diagnosis (5). Additionally, subgrouping by small, large, and mixed joints was employed to explore whether anatomical distribution correlates with disease activity markers (ESR, CRP) and autoantibody profiles (RF, anti-CCP), Similar distinctions were discussed in the Introduction and supported in the Discussion as potentially meaningful for early diagnosis and disease monitoring. Patients underwent laboratory investigations including ESR, CRP, CBC, RF, and anti-CCP.

Inclusion Criteria

In our study, we only enrolled RA patients who fulfilled the 2010 ACR/EULAR classification standard. Patients were 18-70 years of age with <20 weeks of RA at the 2010 ACR/EULAR criteria (8). In addition, patients had RF and anti-CCP available for testing. Measurable data, such as the profile of joint involvement,

disease activity score, inflammatory markers ESR and CRP were recorded, we included those RA patients who met the criteria according to the 2010 ACR/EULAR classification. Patients were aged 18-70 years and had RA of less than 20 weeks duration by 2010 ACR/EULAR criteria.

Exclusion Criteria

Patients with other autoimmune or other inflammatory joint disease, such as systemic lupus erythematosus and psoriatic arthritis, significant joint trauma, or surgery that might lead to a pattern of joint involvement related to any cause other than RA. Cases with inadequate clinical or laboratory data, including joint involvement, inflammatory markers, and autoantibody profiles, were excluded. We did not include women who were pregnant because the presence of pregnancy could bias disease activity and inflammatory markers. We have also excluded patients with chronic infections (e.g., tuberculosis, HIV) and with active malignancy, which could interfere with inflammatory markers and health status in general. And lastly, patients who were on NSAIDs or steroids within the past two weeks were excluded.

Data Collection

Data collection included both demographic and clinical information. Demographic data encompassed age, gender, and socioeconomic status. Clinical data focused on the duration of recently diagnosed RA and treatment history, including prior and current use of disease-modifying antirheumatic drugs (DMARDs), biologics, and other medications.

Clinical Assessments:

Clinical assessment included a standardized physical examination conducted by attending rheumatologists, using the 28-joint count method to evaluate tenderness and swelling. Based on this evaluation, joint involvement was classified into distinct patterns. Symmetrical polyarthritis was defined as bilateral involvement of the same joints (e.g., both wrists or knees), while asymmetrical oligoarthritis referred to the involvement of fewer than five joints without a mirrored pattern. Additionally, patients were grouped by joint type: small joint involvement (e.g., fingers, wrists), large joint involvement (e.g., knees, shoulders, hips), or mixed joint involvement (a combination of small and large joints).

Laboratory tests

Biochemical parameter tests to assess autoantibody profiles, such as RF anti-CCP antibodies, along with routine tests to evaluate inflammatory biomarkers like ESR, CRP, and CBC.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics v26. Continuous variables were summarized as mean ± standard deviation (SD) or median (9) according to distribution (Shapiro–Wilk). Categorical variables were summarized as n (%). Two-group comparisons (symmetrical vs asymmetrical) used independent-samples t-test for normally distributed variables (e.g., CRP, WBC) and Mann–Whitney U test for non-normal variables (e.g., ESR, Hb, platelets). Categorical variables (RF, anti-CCP) used Chi-square or Fisher's exact test when expected cell counts were <5. For three-group comparisons across joint types (small, large, mixed), one-way ANOVA (normal) or Kruskal–Wallis (non-normal) were applied.

To identify variables independently associated with joint involvement pattern, we fitted a binary logistic regression with outcome coded as symmetrical polyarthritis = 1 vs asymmetrical oligoarthritis = 0. A priori covariates were age, sex, BMI, disease duration, ESR, CRP, RF (positive/negative), and anti-CCP (positive/negative). Results are reported as odds ratios (OR) with 95% confidence intervals (CI) and p-values.

Ethical Consideration

The study obtained permission from the Ethical Committee of the College of Medicine, Erbil University, Erbil, Kurdistan Region, Iraq (Approval No: 47; Date: 8/8/2024).

Results

Sociodemographic Characteristics of Rheumatoid Arthritis Patients

The current data included 60 patients (total) diagnosed with RA, with a mean age of 47.33 ± 14.10 years, and a 95% confidence interval ranging from 43.69 to 50.98 years. Of the patients, the majority were female (78.3%, n = 47), with males representing only 21.7% (n = 13), resulting in a female-to-male ratio of 3.3:1. In terms of residency, most patients resided inside the city (78.3%, n = 47), while a smaller proportion (21.7%, n = 13) lived outside the city. The patients were predominantly Kurdish, accounting for 91.7% (n = 55), with a small percentage (8.3%, n = 5) identifying as Arabic. Regarding marital status, most patients were married (90.0%, n = 54), with fewer individuals being single (8.3%, n = 5) or widowed (1.7%, n = 1). Additionally, the smoking status of the patients indicated that a large proportion were non-smokers (75.0%, n = 45), whereas 13.3% (n = 8) were current smokers, and 11.7% (n = 7) were former smokers. As shown in Table 1.

Table 1. Sociodemographic Characteristics of RA Patients.

Sociodemographic Characteristics		Values
Age (year)	Mean ± SD	47.33 ± 14.10
	CI 95%	43.69 – 50.98
Gender	Female, n (%)	47 (78.3%)
	Male, n (%)	13 (21.7%)
	Female: Male ratio	3.3:1
Residency	Inside the city, n (%)	47 (78.3%)
	Outside the city, n (%)	13 (21.7%)
Nationality	Kurdish, n (%)	55 (91.7%)
	Arabic, n (%)	5 (8.3%)
Marital state	Single, n (%)	5 (8.3%)
	Married, n (%)	54 (90.0%)
	Widow, n (%)	1 (1.7%)
Smoking status	Nonsmoker, n (%)	45 (75.0%)
	Current smoker, n (%)	8 (13.3%)
	Former smoker, n (%)	7 (11.7%)

N: number; %: percentage; SD: standard deviation; CI: confidence interval

Clinical Characteristics of Rheumatoid Arthritis Patients

Patients in this study had a mean BMI of 31.71 ± 6.15 kg/m², with a 95% confidence interval ranging from 30.12 to 33.30. The mean Disease Activity Score (DAS 28) was 5.24 ± 0.93, with a 95% confidence interval between 5.0 and 5.48, indicating moderate disease activity. The average duration of symptoms before diagnosis was 6.24 ± 3.24 months, with a 95% confidence interval of 5.39 to 7.04 months.

Regarding extra-articular manifestations, the majority of patients (65.0%, n = 39) did not present any such manifestations, while 35.0% (n = 21) experienced them. In terms of family history, 45.0% (n = 27) of patients reported a family history of rheumatoid arthritis, whereas 55.0% (n = 33) did not. A significant proportion of patients (86.7%, n = 52) had no history of other autoimmune diseases, while 13.3% (n = 8) reported such a history. Furthermore, 68.3% (n = 41) of patients had no other comorbidities, while 31.7% (n = 19) had

one or more comorbid conditions. These sociodemographic and clinical characteristics provide valuable context for understanding the relationship between joint involvement, inflammatory markers, and autoantibodies among the RA patients in this study; all of these are listed in Table 2.

Table 2. Clinical Characteristics of Rheumatoid Arthritis Patients

Clinical Characteristics		Values
BMI (kg/m2)	Mean ± SD	31.71 ± 6.15
	CI 95%	30.12 – 33.30
DAS 28	Mean ± SD	5.24 ± 0.93
	CI 95%	5.0 – 5.48
Duration of symptom before diagnosis (month)	Mean ± SD	6.24 ± 3.24
	CI 95%	5.39 – 7.04
Extra-articular manifestation	No, n (%)	39 (65.0%)
	Yes, n (%)	21 (35.0%)
Family history of RA	No, n (%)	33 (55.0%)
	Yes, n (%)	27 (45.0%)
History of other autoimmune diseases	No, n (%)	52 (86.7%)
	Yes, n (%)	8 (13.3%)
Other comorbidity	No, n (%)	41 (68.3%)
	Yes, n (%)	19 (31.7%)

N: number; %: percentage; SD: standard deviation; CI: confidence interval; BMI: body mass index; DAS 28: Disease Activity Score using 28 joint counts; RA: Rheumatoid arthritis; kg: kilogram; m: meter.

Laboratory Findings in Patients with Asymmetrical Oligoarthritis and Symmetrical Polyarthritis

The biochemical results revealed notable variation among patients with asymmetrical oligoarthritis and those with symmetrical polyarthritis, as shown in Table 3. The ESR was significantly lower in the asymmetrical group (27.29 ± 5.82 mm/hr) compared to the symmetrical group (39.08 ± 19.22 mm/hr), with a p-value of 0.048. Similarly, C-reactive protein (CRP) levels were significantly lower in the asymmetrical group (4.60 ± 2.74 mg/dL) compared to the symmetrical group (11.44 ± 8.81 mg/dL), with a p-value of 0.047. In contrast, white blood cell count (WBC) (6.41 ± 2.24 vs 7.54 ± 2.14, p = 0.295), hemoglobin (Hb) (12.43 ± 1.52 vs 12.60 ± 1.31, p = 0.718), and platelet count (255.14 ± 42.63 vs 269.04 ± 75.56, p = 0.991) showed no considerable changes among the other two groups.

Regarding autoantibodies, rheumatoid factor (RF) was significantly more common in the symmetrical polyarthritis group (42.7%) compared to the asymmetrical group (0%), with a p-value of 0.035. However, anti-citrullinated peptide antibody (anti-CCP) positivity was similar between the two groups (57.1% vs 35.8%, p = 0.412). These results highlight that RF and CRP may serve as distinguishing markers between the two joint involvement patterns in RA.

Table 3. Laboratory Findings in Patients with Asymmetrical Oligoarthritis and Symmetrical Polyarthritis

Laboratory Tests	Pattern of Joint Involvement			P value
	Asymmetrical oligoarthritis N=7, 11.7%	**Symmetrical polyarthritis N=53, 88.3%**	**Total N=60, 100.0%**	
Inflammatory and hematological profile, mean ± SD				
ESR, mm/hr.	27.29 ±5.82	39.08 ± 19.22	37.70 ± 19.31	0.048 *

CRP, mg/dL	4.60 ± 2.74	11.44 ± 8.81	10.87 ± 12.76	0.047 *
WBC, $\times 10^9$/L	6.41 ± 2.24	7.54 ± 2.14	7.41 ± 2.16	0.295 ns
Hb, g/dL	12.43 ± 1.52	12.60 ± 1.31	12.58 ± 1.32	0.718 ns
Platelet, $\times 10^9$/L	255.14 ± 42.63	269.04 ± 75.56	267.39 ± 72.31	0.991 ns
Autoantibody profiles, n (%)				
RF, Negative	7 (100.0%)	28 (52.8%)	35 (58.3%)	0.035 *
RF, Positive	0 (0.0%)	25 (42.7%)	25 (41.7%)	
Anti-CCP, Negative	3 (42.9%)	34 (64.2%)	37 (61.7%)	0.412 *
Anti-CCP, Positive	4 (57.1%)	19 (35.8%)	23 (38.3%)	

N: number; %: percentage; SD: standard deviation; millimeter; hr.: hour; L: litter; g: gram; dL: deciliter; mg: milligram; ESR: erythrocyte sedimentation rate; CRP: c reactive protein; WBC: white blood cell; Hg: Hemoglobin; RF: Rheumatoid factor; Anti-CCP: anti-citrullinated peptide antibody; ns: no significant difference; *: significant difference. The data were analyzed using an independent sample t-test (CRP and WBC), Mann-Whiney U test (ESR, Hb, and platelets), and Fisher's exact test (RF and anti-CCP).

Multivariable Logistic Regression of Inflammatory Markers and Autoantibodies in RA

In the adjusted logistic regression model, age (OR = 0.987, 95% CI: 0.955–1.026, p = 0.557), sex (female vs. male; OR = 1.517, 95% CI: 0.923–2.743, p = 0.094), BMI (OR = 0.941, 95% CI: 0.866–1.003, p = 0.064), disease duration (OR = 1.738, 95% CI: 0.780–2.871, p = 0.172), and ESR (OR = 1.004, 95% CI: 0.997–1.014, p = 0.176) were not significantly associated with joint involvement pattern. By contrast, higher CRP levels (OR = 1.11, 95% CI: 1.029–1.242, p < 0.001) and RF positivity (OR = 3.802, 95% CI: 2.421–5.642, p < 0.001) were strong independent predictors of symmetrical polyarthritis. Anti-CCP positivity showed no significant effect (OR = 0.769, 95% CI: 0.346–1.805, p = 0.528). These findings indicate that CRP and RF, but not ESR or anti-CCP, independently distinguish symmetrical from asymmetrical RA after adjustment for demographic and clinical confounders. As shown in Table 4.

Table 4. Multivariable Logistic Regression (Adjusted: age, sex, BMI, duration).

Laboratory Tests	**Pattern of Joint Involvement**			
	Adjusted OR	**95% CI lower**	**95% CI upper**	**P value**
Age	0.987	0.955	1.026	0.557
Gender (Female vs male)	1.517	0.923	2.743	0.094
BMI	0.941	0.866	1.003	0.064
Disease duration	1.738	0.78	2.871	0.172
ESR	1.004	0.997	1.014	0.176
CRP	1.11	1.029	1.242	<0.001
RF (positive vs negative)	3.802	2.421	5.642	<0.001
Anti-CCP (Positive vs Negative)	0.769	0.346	1.805	0.528

Laboratory Findings in Patients with Different Patterns of Joint Involvement

The biochemical results with variable patterns of joint involvement (small joint, large joint, and mixed joint) did not show significant differences in most markers. The erythrocyte sedimentation rate (ESR) was 42.80 ± 20.32 mm/hr for small joint involvement, 35.83 ± 17.76 mm/hr for large joint involvement, and 37.41 ± 19.69 mm/hr for mixed joint involvement, with no significant difference (p = 0.760). Similarly, C-reactive protein (CRP)

levels were 13.58 ± 11.09 mg/dL for small joint involvement, 9.80 ± 15.09 mg/dL for large joint involvement, and 10.73 ± 12.86 mg/dL for mixed joint involvement, with no significant difference (p = 0.876).

For white blood cell count (WBC), the values were 6.34 ± 2.08 × 10⁹/L for small joints, 7.30 ± 2.75 × 10⁹/L for large joints, and 7.53 ± 2.11 × 10⁹/L for mixed joints, with no significant difference (p = 0.507). The hemoglobin (Hb) levels were 12.48 ± 1.11 g/dL for small joints, 13.50 ± 1.04 g/dL for large joints, and 12.48 ± 1.35 g/dL for mixed joints, with no significant difference (p = 0.120). The platelet count was 263.20 ± 75.08 × 10⁹/L for small joints, 293.83 ± 85.54 × 10⁹/L for large joints, and 264.52 ± 71.37 × 10⁹/L for mixed joints, with no significant difference (p = 0.737).

Regarding autoantibodies, rheumatoid factor (RF) was negative in 60.0% of patients with small joint involvement, 66.7% with large joint involvement, and 57.1% with mixed joint involvement (p = 0.902), with no significant differences. For anti-citrullinated peptide antibody (anti-CCP), 60.0% of small joint patients, 33.3% of large joint patients, and 36.7% of mixed joint patients tested positive, but again, no significant difference was found (p = 0.574). As shown in Table 5.

Table 5. Laboratory Findings in Patients with Different Patterns of Joint Involvement.

Laboratory Tests	Joint involvement				P value
	Small joint N=5, (8.3%)	Large joint N=6, (10.0%)	Mixed joint N=49, (81.7%)	Total N=60, 100.0%)	
Inflammatory and hematological profile, mean ± SD					
ESR, mm/hr.	42.80 ± 20.32	35.83 ±17.76	37.41 ± 19.69	37.70 ± 19.31	0.760 ns
CRP, mg/dL	13.58 ± 11.09	9.80 ± 15.09	10.73 ± 12.86	10.87 ± 12.76	0.876 ns
WBC, $\times 10^9$/L	6.34 ± 2.08	7.30 ± 2.75	7.53 ± 2.11	7.41 ± 2.16	0.507 ns
Hb, g/dL	12.48 ± 1.11	13.50 ± 1.04	12.48 ± 1.35	12.58 ± 1.32	0.120 ns
Platelet, $\times 10^9$/L	263.20 ± 75.08	293.83 ± 85.54	264.52 ± 71.37	267.39 ± 72.31	0.737 ns
Autoantibody profiles, n (%)					
RF, Negative	3 (60.0%)	4 (66.7%)	28 (57.1%)	35 (58.3%)	0.902 ns
RF, Positive	2 (40.0%)	2 (33.3%)	21 (42.9%)	25 (41.7%)	
Anti-CCP, Negative	2 (40.0%)	4 (66.7%)	31 (63.3%)	37 (61.7%)	0.574 ns
Anti-CCP, Positive	3 (60.0%)	2 (33.3%)	18 (36.7%)	23 (38.3%)	

N: number; %: percentage; SD: standard deviation; millimeter; hr.: hour; L: liter; g: gram; dL: deciliter; mg: milligram; ESR: erythrocyte sedimentation rate; CRP: C reactive protein; WBC: white blood cell; Hb: Hemoglobin; RF: Rheumatoid factor; Anti-CCP: anti-citrullin inactivated peptide antibody; ns: no significant difference. The data were analyzed using ANOVA (CRP and WBC), Kruskal-Wallis test (ESR, Hb, and platelets), and Chi-square test (RF and anti-CCP).

Discussion

Rheumatoid arthritis (RA) is a clinically heterogeneous autoimmune disease in which patterns of joint involvement and serological markers play a pivotal role in defining disease phenotype and prognosis. Previous studies highlight that symmetrical polyarthritis, elevated inflammatory markers, and autoantibody positivity are closely linked to more aggressive disease courses (3).

The sociodemographic profile of the RA patients in this study revealed several key characteristics. The mean age of the patients was 47.33 ± 14.10 years, which aligns with the typical age of RA onset, generally reported to be between 30 and 60 years (10). Innala et al. 2014 conducted a prospective study on early RA and stratified patients into young-onset and late-onset groups. They defined young-onset RA (YORA) as onset below the median age of

58, with many patients developing symptoms between 25 and 45 years. This group showed distinct immunological and treatment response profiles (11)This variability highlights the broad age spectrum at which RA can manifest. Regarding the gender of patients about 78.3% of patients are female while the other is male, and this result agree with the results of wide ranges of studies which done previously which found that most of the cases of RA are females, for instance, a comprehensive analysis from the Global Burden of Disease Study 2021 confirmed that females dependably showed higher level of age-standardized occurrence and higher rates of RA across all regions and age groups, underscoring a persistent gender disparity in disease burden (12).

Additionally, a result of a systematic review and meta-analysis by Namavari et al. (2024) emphasized that a higher odds of developing RA occur in women in post-menopausal, especially in early menopause, which may be related to a potential hormonal change and its effect on RA(13).

Regarding smoking status, 75.0% of the patients were non-smokers, while 13.3% were current smokers and 11.7% were former smokers. A well-recognized risk factor for RA is smoking, and is linked with an advanced state of disease activity and joint damage, which is supported by the results of by van Wesemael et al. (2008), who found that smoking was predominantly associated with IgA autoantibody isotypes, including RF-IgA and ACPA-IgA, suggesting a mucosal origin of autoimmunity in smokers with RA (14).

The results of the current study regarding RA patients provide further insights into the disease presentation. The mean body-mass index (BMI) of 31.71 ± 6.15 kg/m² shows the average patient population is classified as obese. This finding is important because of the risk of developing RA in individuals with high BMI, and that worse RA symptoms due to a heavy weight could render some medications ineffective. Higher BMI is a risk factor for RA in several studies, with, again, a stronger association in females (Asimakopoulou et al. Meta-analysis in 2015 (Qin et al.) showed obese individuals had about 25% higher risk of RA subsequently (15).

The DAS28 is one of the most commonly employed composite scores for RA disease activity, consisting of tender and swollen joint counts, patient global assessment, and an acute phase reactant (ESR or CRP). A score of 5.24 usually represents active disease needing treatment. Van Riel et al. (2016) support this interpretation. A DAS28 >5.1 is an important threshold for starting biologicals, which has been pointed out as important both in clinical practice and in trials (16).

The mean duration of symptoms before diagnosis was 6.24 ± 3.24 months. Early identification and treatment in RA are essential to diminish permanent joint injury and improve long-term outcomes, but symptoms may develop over a period of weeks to months. Inflammation lasting longer than six months is considered chronic. Inflammation persisting >6 months can progress to structural joint damage of the joints, if not treated properly. As Kim and Suh (2020) pointed out, untreated inflammation lasting more than six months results in permanent damage to joints, organs, and also leads to systemic complications, thus emphasizing the immediate need for diagnosis (17).

Of the patients, 35.0% had extra-articular manifestations (EAMs). Since RA is a systemic disease affecting many organ systems, EAMs can occur at any stage of the disease [7,8]. Extra-articular manifestations (EAMs) are part and parcel of rheumatoid arthritis (RA) due to its systemic inflammatory nature. This study reported EAMs in 35.0% of patients, which agrees with the results of a large number of cohort studies. According to the findings of a study, the overall prevalence of EAMs is 23.4%, as well as a positive correlation with the long-lasting duration of diseases and a high level of disease activity,

and seropositivity. Such indicators can be linked with impaired quality of life and poor prognosis among patients.

About 45% of the RA patients have a link with familial history, and may increase the risk of RA genetic predisposition is an identified risk factor for RA. A large case–control study by Kronzer et al. (2021) found that a family history of rheumatic autoimmune diseases was associated with an 89% increased risk of developing RA (adjusted OR 1.89, 95% CI 1.41–2.52). The study also emphasized that first-degree relatives of RA patients exhibited higher levels of inflammatory markers and autoantibody reactivity, reinforcing the role of genetic predisposition in RA pathogenesis (18).

Furthermore, 31.7% of patients had one or more comorbid conditions, while 13.3% reported a history of other autoimmune diseases, and this agrees with results from Vicente et al. (2021, who reported that over 60% of RA patients had at least one cardiovascular comorbidity, with hypertension being the most prevalent (19). Jagpal and Navarro-Millán further noted that RA patients face a markedly elevated risk of cardiovascular disease (CVD) as a result of both traditional risk factors and chronic systemic inflammation. They recommend the management of CVD risk factors alongside RA disease control (20).

Patients with asymmetrical oligoarthritis differed significantly from patients with symmetrical polyarthritis regarding biochemical findings. Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were also significantly lower in the asymmetrical group (p=0.048 and p=0.047, respectively). ESR and CRP are both common markers of inflammation in RA; raised levels of both tests indicate greater disease activity. This result is consistent with that of Masoumi et al. (2024), with the results of the present study, which reported higher ESR and CRP levels for active RA, high enough to be used for diagnosis of active disease versus remission (21). In addition, Youssef et al. They observed a statistically significant association between ESR levels and DAS28 scores and tender joint and swollen joint counts in rheumatoid arthritis patients in their report (22).

About autoantibodies, positive RF was more common in the symmetrical polyarthritis group (42.7%) than the asymmetrical group (0%) (p = 0.035). This is consistent with previous reports. For instance, van der Helm-van Mil et al. baseline symmetrical joints in early inflammatory arthritis at baseline, were significantly associated with increased odds of RF and anti-CCP positivity, and faster radiographic progression with time. Their research underscored that symmetry in the involvement of joints is a recognized diagnostic feature of RA and may be associated with more active or seropositive disease presentations, although longitudinal data are needed to confirm prognostic implications (23).

Anti-CCP positivity, however, was not significantly different in the 2 groups (57.1% vs 35.8%, p=0.412). This is in line with the literature. As an example, a study by Rahali. et al. highlighted that anti-CCP antibodies are helpful in the early diagnosis of RA and in predicting joint erosions, although they are not exclusive to a specific clinical phenotype, such as symmetric or asymmetric arthritis (24).

Our findings of elevated ESR, CRP, and RF in patients with symmetrical polyarthritis are consistent with established literature indicating a more active and seropositive disease phenotype in such presentations. This aligns with van der Helm-van Mil et al., who reported that symmetry in joint involvement was associated with increased odds of RF and anti-CCP positivity, as well as accelerated radiographic progression (23).. Similarly, a recent meta-analysis by Qin et al.(2015) (15). emphasized the influence of clinical and metabolic factors such as BMI on RA activity and progression. Our data also resonates with

the Global Burden of Disease Study (12), which outlines a significant increase in RA burden among seropositive patients, particularly females, worldwide. Furthermore, the study by Masoumi et al. (21). which evaluated over 300 RA patients, concluded that ESR and CRP are consistently elevated in more severe or active RA, regardless of joint type, thus supporting our observation that inflammatory markers are more reflective of disease severity than anatomical distribution alone.

It is important to emphasize that the cross-sectional design of this study inherently limits our ability to infer causality between the pattern of joint involvement and the levels of inflammatory or serological markers. While we observed statistically significant associations, particularly among patients with symmetrical polyarthritis, these relationships represent correlations at a single point in time. The dynamic nature of rheumatoid arthritis progression, including fluctuations in disease activity and biomarker expression, necessitates longitudinal or cohort-based studies to establish temporal sequences and potential causal pathways. Future prospective investigations incorporating serial measurements and radiographic data will be essential to validate and expand upon our findings.

Further analysis of laboratory findings in patients with different patterns of joint involvement (small joint, large joint, and mixed joint) did not reveal significant differences in most markers, including ESR, CRP, WBC, Hb, and platelet count. This suggests that while overall inflammation markers (ESR, CRP) are important for assessing disease activity, their levels may not significantly vary across different joints. This observation aligns with findings from recent studies, for instance, a 2024 study by Masoumi et al (2024). evaluated over 300 RA patients and found that while ESR and CRP were elevated in active disease, their levels did not consistently correlate with the anatomical pattern of joint involvement (e.g., small vs. large joints). Instead, these markers were more reflective of overall disease activity rather than specific joint subsets (21). Similarly, Pan et al. (2023) reported that hematological indices such as WBC, Hb, and platelet count showed modest correlations with acute-phase reactants like CRP and ESR, but these associations were not significantly influenced by the type of joint involvement. Their retrospective cohort analysis emphasized that systemic inflammation in RA may manifest independently of joint size or location, particularly in patients receiving DMARDs (25).

Conclusions

In this study, we examined patterns of joint involvement, inflammatory markers, and autoantibody profiles in early RA. Patients with symmetrical polyarthritis also had significantly elevated levels of ESR, CRP, and RF, which may reflect higher disease activity at the time of assessment, though this cannot establish severity or prognosis due to the cross-sectional design. No significant differences were found in inflammatory markers according to the pattern of joint involvement, although these biomarkers are useful for assessing disease activity and treatment strategy. Although our findings suggest a significant association between symmetrical joint involvement and elevated inflammatory markers and RF positivity, the cross-sectional nature of the study precludes any causal inference. Future longitudinal studies are warranted to explore these associations over time and assess their predictive value for disease progression.

Recommendations

Clinicians may consider ESR, CRP, and autoantibodies like RF and anti-CCP as supportive markers for disease activity assessment in early RA, while acknowledging

that prognostic conclusions require longitudinal follow-up. Further research with larger sample sizes and long-term follow-ups is needed to better understand the role of these markers in RA progression and treatment response.

Limitations

The study's cross-sectional design and small sample size limit its ability to establish causal relationships. Excluding patients with other autoimmune diseases and relying on self-reported data may introduce bias. Additionally, the lack of long-term outcome data calls for further prospective studies to validate these findings.

Conflict of Interest Statement:

The authors declare no conflict of interest concerning the authorship and/or publication of this article.

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