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Assessment of Rheumatoid Arthritis Disease Activity and Association Factors among Yemeni Patients

Amr A. Saleh [1]*, Anwar K. Al-Madhaji[1], Hassan A. Al-Shamahy[1], Raja M Al-Haimi1[1] and Marwan K. Saeed[2]

[1]**Department of Microbiology and Immunology, Faculty of Medicine and Health Sciences, Sana'a University, Sana'a, Yemen,**
[2]**Department of Microbiology, Faculty of Science, Sana'a University, Sana'a, Yemen.**

*Corresponding author: E-mail: amralhubishi@gmail.com

Abstract

Background: Rheumatoid arthritis is a common autoimmune inflammatory disorder leading to disability and joint deformity. Assessment of rheumatoid arthritis disease activity is a significant step in improving its management.
Aim: To assess the Rheumatoid arthritis disease activity and association factors among Yemeni patients.
Methods: This cross-sectional study included 140 cases of Rheumatoid arthritis at the rheumatology clinic in Sana'a and Ibb cities. Patients were diagnosed according to the American College of Rheumatology and European Alliance of Associations for Rheumatology 2010 and divided into three groups based on the Disease Activity Score-28 joints (low, moderate, and high). Laboratory tests, including CBC, erythrocyte sedimentation rate, rheumatoid factor, and serum anti-cyclic citrullinated peptide levels, were evaluated.
Results: Among 140 RA patients, 115 (82.1%) were female and 25 (17.9%) were male. A total of 86% of patients had moderate to high disease activity (DAS28-ESR $\geq$3.2) with a mean DAS28-ESR score of 4.95±1.03. A significant correlation of tender and swollen joint counts, erythrocyte sedimentation rate, and anti-cyclic citrullinated peptide with DAS28-ESR was observed ($P<0.05$), whereas no correlation was observed between the duration of disease and RF with disease activity.
Conclusion: This study indicates that the majority of patients experience moderate to high disease activity. The results revealed that the factors associated with disease activity were the number of tender and swollen joints, ESR, and anti-cyclic citrullinated peptide levels. These findings underscore the critical importance of early diagnosis and improved access to effective treatment options.

Article Info

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Rheumatoid arthritis, Disease activity, DAS28-ESR, Anti-cyclic citrullinated peptide, Yemen

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1. INTRODUCTION

Rheumatoid arthritis (RA) is a chronic autoimmune inflammatory disease characterized by inflammation of the synovium, leading to joint destruction and disability, impacting 0.2-1% of people worldwide[1].
A characteristic of RA is symmetrical arthritis, which usually affects the hand joints, such as the metacarpophalangeal joints and proximal interphalangeal joints, although it may also affect larger joints, such as the metatarsophalangeal joints, knees, ankles, shoulders, elbows, cervical spine, and temporomandibular joints [2]. Patients commonly experience pain, swelling across multiple joints, and morning stiffness [3].
In 2020, approximately 17.6 million individuals worldwide had RA. Although mortality rates have dropped over the last 30 years, the age-standardized prevalence and years lived with disability continue to increase, with cases expected to rise further by 2050 [4].
The pathogenesis of RA is multifactorial, including immunological dysregulation, environmental factors, and genetic predisposition [5]. Dysregulated immune re-

sponses in the synovium include innate immune cells, autoreactive T and B cells, and complexes that activate synovial cells and leukocytes to release proinflammatory mediators, sustaining inflammation and disease progression [6].

In resource-poor regions, RA treatment is often deprioritized due to the underestimation of the disease burden caused by inadequate diagnosis and overlooking the socioeconomic impact of untreated RA. The inadequate prioritization of RA management compared to other illnesses is due to a lack of knowledge among patients and healthcare providers [7]. The DAS28 is a commonly used composite score in rheumatology that tracks RA disease activity by integrating clinical and patient-reported data. It includes Swollen Joint Count (SJC), Tender Joint Count (TJC), and inflammatory markers such as Erythrocyte Sedimentation Rate (ESR) or C-reactive protein (CRP). It also includes the patient's overall health rating, which is measured on a visual analog scale [8]. One of the first and most thoroughly validated tools for RA assessment, the DAS28-ESR, is still a vital tool for monitoring disease activity [9]. According to the 2010 ACR/EULAR guidelines, joint involvement, serological markers Rheumatoid Factor (RF) and anti-citrullinated protein antibodies (anti-CCP), symptom duration (more or less than six weeks), and CRP and ESR are the four main categories that comprise the diagnostic criteria for RA. Each category has a score. Early diagnosis is necessary to initiate timely treatment, prevent joint damage, and improve patient outcomes[10]. Early RA detection was greatly enhanced by the 2010 ACR/EULAR criteria, which increased sensitivity (62-91%) at the expense of decreased specificity (21-78%). More recent classification schemes for early stage RA aim to strike a balance between sensitivity and specificity, achieving a range of (85-88%). Depending on the disease duration, patient profiles, and research goals, each set of criteria has distinct advantages. Despite these advances, problems still exist, particularly for patients who are seronegative, and integrating imaging methods with novel biomarkers may improve diagnostic precision [11]. Both anti-CCP and RF are included in the 2010 classification criteria for RA established by the ACR/EULAR [12]. RA is one of the most significant autoimmune diseases in Yemen. There is a notable scarcity of studies on this condition, especially in terms of disease severity and associated factors. Thus, the current study aimed to investigate the level of disease severity and identify the factors associated with it among Yemeni patients.

2. MATERIALS AND METHODS

2.1. Study Design and Participants

This cross-sectional study was conducted from April 2024 to March 2025 in Sana'a and Ibb governorates, Yemen, recruiting 140 adults with RA from major tertiary hospitals and various specialized rheumatology clinics. Demographic and clinical data of patients with RA, including age group, sex, residence, disease duration, and disease activity (DAS28-ESR), were recorded. The DAS28-ESR score, including SJC, TJC, ESR, and patient-reported global assessment, evaluated using a visual analog scale (VAS), was used to evaluate disease activity using a DAS28-ESR calculator[13].

According to this score, disease activity was categorized as low (2.6 < DAS28 < 3.2), moderate (3.2 < DAS28 < 5.1), and high (DAS28 $\geq$5.1) [14]. Patients with chronic renal failure, liver disease, or other autoimmune rheumatic diseases were excluded.

2.2. Laboratory tests

Blood samples (5 ml) were collected from all patients with RA. Three milliliters were used for serum separation and stored at -20℃ for serological tests, while 2 mL were placed in tubes containing sodium citrate for the ESR measurement. ESR was measured using the Westergren method. RF was qualitatively detected as positive or negative using latex agglutination kits [RF-Latex, Spinreact,]. Anti-CCP antibodies were quantified using an enzyme-linked immunosorbent assay (ELISA) kit [Elecsys anti-CCP, Roche] following the manufacturer's protocol. Results $\geq$17 IU/mL were considered positive.

Ethical approval for the study was obtained from the Ethics Committee of the College of Medicine and Health Sciences at Sana'a University, and informed consent was obtained from all patients participating in the study.

2.3. Statistical analysis

The data were analyzed using the IBM Statistical Package of Social Science (SPSS) version 26.0 for Windows, Inc., IL, USA. Results are presented as mean±standard deviation (SD), range, or frequencies and percentages, where appropriate. The normality of the data distribution was assessed using the Shapiro–Wilk test. Correlations between laboratory variables were examined using Spearman's correlation test according to the data characteristics. Statistical significance was defined as $p < 0.05$.

3. RESULTS AND DISCUSSION

Table (1) presents the demographic and lifestyle characteristics of the patients with RA in the study. Females represented the majority of the patients (115 [82.1%]), with approximately 81(57.9%) in the 41-60 years age group, followed by 50(35.7%) in the 20-40 years age group, and only 9(6.4%) older than 60 years. Approximately 75(53.6%) participants resided in urban areas, and 65(46.4%) lived in rural areas. Lifestyle habits of the participants included 29(20.7%) smokers and 97(69.3%)

Table 1. Demographic characteristics of Rheumatoid arthritis patients

Variable		Frequency	Percent %
Sex	Male	25	17.9%
	Female	115	82.1%
Age group (years)	20-40	50	35.7%
	41-60	81	57.9%
	60	9	6.4%
Residence	Urban	75	53.6%
	Rural	65	46.4%
Smoking	Yes	29	20.7%
	No	111	79.3%
Qat chewing	Yes	97	69.3%
	No	43	30.7%

Qat chewers. Table (2) shows that the DAS28-ESR score of the RA patients was 4.95±1.03, and the median disease duration was 4 years. A total of 136(97.1%) patients had tender joints, 120(85.7%) had swollen joints, and 103(73.6%) reported morning stiffness. With a mean ESR of 38.43±26.07 mm/hr, Table (2) also shows a high positivity rate for both RF and anti-CCP antibody [113(80.7%) and 122(87.1%)], respectively.

Table 2. Clinical and laboratory characteristics of RA patients

Variable (n=140)		Frequency	Percent %
Clinical characteristics			
Tender joint	Yes	136	97.1%
	No	4	2.9%
Swelling joint	Yes	120	85.7%
	No	20	14.3%
Morning stiffness	Yes	103	73.6%
	No	37	26.4%
Disease duration (years) Median (IQR)		4(4)	
DAS28-ESR (Mean±SD)		4.95±1.03	
Laboratory tests			
ESR (Mean±SD)		38.43±26.07	
RF	Positive	113	80.7%
	Negative	27	19.3%
Anti-CCP	Positive	122	87.1%
	Negative	18	12.9%

Figure 1 shows the disease activity distribution among the participants based on DAS28-ESR. The results

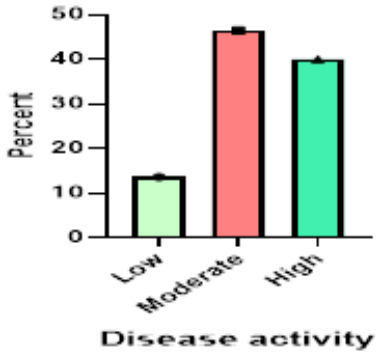


Figure 1. Disease activity distribution among participants based on DAS28-ESR.

showed that the majority of participants presented with moderate to high disease severity (46.4% and 40.0%, respectively), whereas (13.6%) with low severity.

The bar chart illustrates the percentage of patients categorized into three disease activity groups: Low, Moderate, and High.

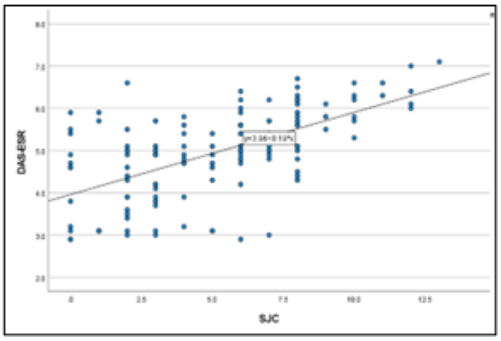
Table (3) shows the distribution of disease activity levels among patients with RA according to demographic and lifestyle factors. The highest proportion of high disease activity was observed in the 41-60 (43.2%) age group and those over 60 years (44.4%). Moderate disease activity was the most common across most categories, especially in rural residents (52.3%) and women (45.2%). No statistically significant associations were observed between disease activity and age (p=0.755), sex (p=0.663), residence (p=0.429), smoking status (p=0.779), or qat chewing (p=0.474).

Table (4) and figure 2 (a-d) show significant positive correlations between disease activity measured by DAS28-ESR and clinical parameters such as SJC (r=0.603, p<0.001), TJC (r=0.596, p<0.001), ESR (r=0.475, p<0.001), and anti-CCP (r=0.304, p <0.001). Age was also weakly positively correlated with disease activity (r=0.134, P=0.030), whereas disease duration and RF did not show significant correlations with disease activity (p=0.264 and p=0.306, respectively). These results indicate that joint pain and swelling, the inflammation marker ESR, and anti-CCP antibody levels are strongly associated with disease activity in patients with RA.

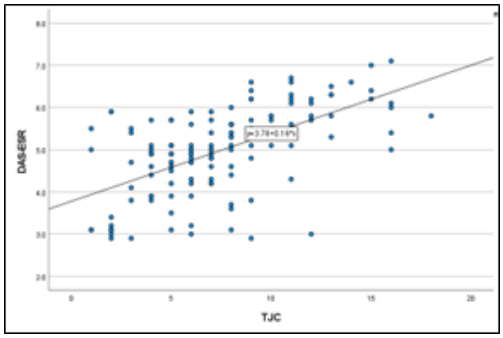
4. DISCUSSION

RA is a chronic, inflammatory, and debilitating disease that can cause irreversible joint damage and lasting disability. Initial diagnosis and therapeutic management are essential for preventing irreversible damage and subsequent loss of essential bodily functions [15].

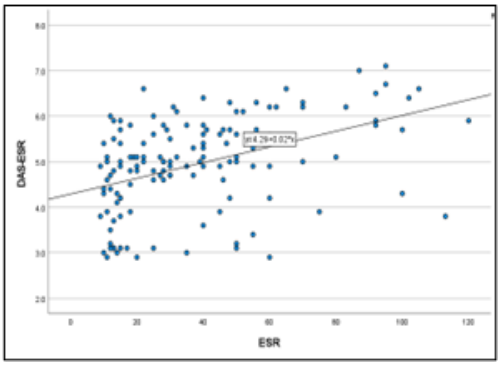
The findings revealed that most participants were female (82.1%). Similar results were reported by Alanazi et al. (2024) in Saudi Arabia (84.8%) [16] and Albiss et



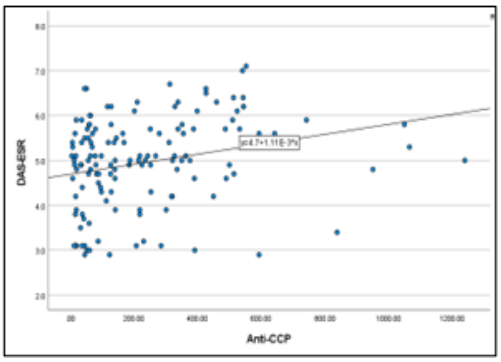
(a) Correlation between SJC and DAS-ESR



(b) Correlation between TJC and DAS-ESR



(c) Correlation between ESR and DAS-ESR



(d) Correlation between Anti-CCP and DAS-ESR

Figure 2. Correlation between DAS-ESR and SJC (a), TJC (b), ESR (c), and Anti-CCP (d) in rheumatoid arthritis patients.

Table 3. Association between demographic/ lifestyle factors and disease activity (das28-esr) in Rheumatoid arthritis patients.

Variable		DAS28-ESR			X^2	P value
		Low	Moderate	High		
Age group	**20-40** (n=50)	6(12.0%)	27(54.0%)	17(34.0%)	1.897	0.755
	41-60 (n=81)	12(14.8%)	34(42.0%)	35(43.2%)		
	>60 (n=9)	1(11.1%)	4(44.4%)	4(44.4%)		
Sex	Male	4(16.0%)	13(52.0%)	8(32.0%)	0.823	0.663
	Female	15(13.0%)	52(45.2%)	48(41.7%)		
Residence	Urban	11(14.7%)	31(41.3%)	33(44.0%)	1.692	0.429
	Rural	8(12.3%)	34(52.3%)	23(35.4%)		
Smoking	Yes	4(13.8%)	15(51.7%)	10(34.5%)	0.501	0.779
	No	15(13.5%)	50(45.0%)	46(41.4%)		
Qat chewing	Yes	12(12.4%)	43(44.3%)	42(43.3%)	1.494	0.474
	No	7(16.3%)	22(51.2%)	14(32.6%)		

al. (2025) in Jordan (86%) [17]. As shown by global epidemiological data, the prevalence of RA is 1:3 in women and men.

In this study, 57.9% of patients with RA were in the 41-60 year age group, whereas 35.7% were in the 20-40 year age group. According to global data, RA usually develops in middle age, with a reported mean age of onset of approximately 51.8 years [18]. This observation highlights the necessity of early diagnosis and appropriate interventions in this group of individuals.

The study found that 53.6% of RA patients were from urban regions, and 46.4% from rural regions, suggesting that a significant proportion came from urban regions. According to a study by [19], people in urban areas have better access to specialized rheumatology services than those in rural regions, who often depend on primary care because fewer specialists are available.

In this study, the mean duration of RA was 4 years, which closely corresponds with the findings of a similar study conducted in Egypt that reported a median disease duration of 4 years [20]. In contrast to these findings, Kuwait [21], the Emirates [22], and Saudi Arabia [23] reported longer disease durations.

The findings of the present study revealed a substantial prevalence of morning stiffness (MS), observed in 73.6%. This high rate substantiates that the examined participants were characterized by active inflammatory disease. Supporting this observation, the literature confirms that MS is a recognized characteristic of RA and

Table 4. text**Correlations between clinical and laboratory parameters and disease activity (DAS28-ESR) in Rheumatoid arthritis patients.**

Variable	DAS28-ESR	
	Correlation coefficient	*P* value
Age	0.134	0.030*
Disease duration	0.006	0.499
SJC	0.603	<0.001*
TJC	0.596	<0.001*
ESR	0.475	<0.001*
RF	0.087	0.306
Anti-CCP	0.304	<0.001*

has been shown to correlate with signs of local and systemic inflammation in affected patients [24].

The mean DAS28-ESR score in this study was 4.95±1.03, which was higher than that in Saudi Arabia (3.6±1.02) [25] and Lebanon (3.75±2.28) [26], suggesting relatively higher values with suboptimal disease control within this population. In contrast, studies from Iraq have reported a mean DAS-28 of 5.7 ± 1.2[27], and most patients had moderately active disease.

In this study, 46% of patients with RA showed moderate disease activity, with 40% having high activity levels. This is notably higher than what was reported in Lebanon, where 36.8% of patients had moderate and 32.2% had high disease activity [26]. However, these findings are closer to those from Jordan, where 51% of patients with RA showed high disease activity [28]. The difference in disease activity may be due to delayed presentation to rheumatologists and limited healthcare access in Yemen, which likely contributes to higher disease activity.

These results showed that 80.7% of patients with RA were RF positivity and 87.1% were anti-CCP-positive. These results are in agreement with a recent study in Saudi Arabia by Alshahrani et al.[29], who reported RF and anti-CCP positivity at 85.2% and 81.9%, respectively. In contrast, a study from Egypt [30] found lower positivity rates of 73.7% for RF and 66.7% for anti-CCP.

The present study found no significant relationships between sex, residence, and disease severity. This finding aligns with that of a study by Nishino *et al.* . (2023), who found a non-significant relationship between sex and disease severity [31].

Regarding smoking, our findings were consistent with those of Masoudi *et al.*. (2025) [32] and Kurniari *et al.* (2021) [33], who did not find a relationship between smoking and disease severity. However, several studies conducted by Alfredsson *et al.* (2023) [34] and Safy *et al.* (2018) [35] found a strong relationship between increased disease activity and smoking. The variance in this finding could be linked to the smaller number of participants who smoked.

The clinical appearance of the disease may differ, but the most common observation is symmetrical pain and swelling of the small joints, along with signs of fatigue and weight loss. In addition to these clinical symptoms, there may be abnormal laboratory results, including elevated CRP and ESR levels [33].

The central role of SJC and TJC as direct measures of inflammatory burden and key drivers of disease activity scores is well established. A EULAR-endorsed study published in the Annals of the Rheumatic Diseases reinforces that these clinical measures of synovitis are fundamental in defining disease activity states and guiding treatment decisions [36].

This study revealed a moderate to strong significant positive correlation between disease activity measured by DAS28-ESR and SJC (r=0.603, p<0.001) and TJC (r=0.596, p<0.001). Similar results were observed in the study by Naser *et al.* (2022) [37]. Elevated ESR and anti-CCP levels were also positively correlated with disease severity (r=0.475, p<0.001; r=0.304, p<0.001, respectively). This finding is in agreement with former studies conducted by Kurniari *et al.* (2021) [33] and Orr *et al.* (2018) [38], which showed a correlation between ESR and disease severity. Masoumi *et al.* (2024) [14] also demonstrated that ESR and CRP levels are elevated in patients with active RA.

These results are contrary to those of Moel *et al.* . (2019) [39] and Sobhy *et al.* (2022) [40] for anti-CCP and disease activity levels, respectively. These findings indicate that although these autoantibodies are important serological markers, their predictive value for disease severity requires cautious interpretation.

The results of the present study indicated that there was no significant correlation between disease duration and disease activity (r=0.006, p=0.499). These results indicate that disease duration did not influence the DAS28-ESR score. Karakas *et al.* (2025) [41] also found no significant association between disease duration and severity. In contrast, a study conducted by Masoudi *et al.*. (2025) [32] found a significant correlation between disease duration and severity. The differences in this finding may be attributed to delayed access to rheumatological care, and patients in this setting may present with considerably worsened symptoms even at earlier stages; therefore, the expected relationship between duration and cumulative disease burden may not be observed.

Similarly, RF did not show significant correlations with the disease activity indices (p = 0.264 and p = 0.306). This finding might be attributed to the use of the latex agglutination test rather than a quantitative turbidimetric assay, which may limit the analytical sensitivity and reduce the ability to detect subtle correlations with DAS28 scores.

5. STUDY LIMITATIONS

This study has some limitations that need to be considered. First, the study's data collection was restricted to a single assessment point, and further follow-up measurements could not be performed because of logistical and resource limitations. Second, the lack of adjustment for clinical covariates, such as medication protocols, treatment adherence, and comorbid conditions, may have influenced the observed associations. Third, the study relied on a relatively small sample size owing to data availability constraints, which may limit the statistical power and generalizability of the results to the broader RA population. Fourth, the use of qualitative rather than quantitative RF testing may have limited a more detailed analysis of its correlation with disease activity in our study. Therefore, future longitudinal studies incorporating these clinical factors are recommended.

6. CONCLUSION

The findings of this study indicate that the majority of patients experience moderate to high disease activity, which may be attributed to delayed diagnosis and difficulty in accessing appropriate treatment. The results also revealed a statistically significant association between disease activity and TJC, SJC, ESR, and anti-CCP levels. These findings underscore the critical importance of early diagnosis and improved access to effective therapeutic options, including biological agents, given their pivotal role in improving patient clinical outcomes and overall quality of life.

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