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Rheumatoid Arthritis: Patient Characteristics and Disease Activities at Tertiary Hospital in Saudi Arabia

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Abstract **Background:** The systemic autoimmune disease rheumatoid arthritis (RA) is characterized by extra-articular disorders and persistent inflammation of the synovial joints. Rheumatoid factor (RF) and anti-cyclic citrullinated peptide antibody (ACPA) are autoantibodies that are important for diagnosis and prognosis. Treat-to-target guidelines place a strong emphasis on reaching remission or decreased disease activity but they ignore patient characteristics or potential future disease behavior. Aim: To evaluate comparison between RA patients' demographics, medication use and the disease activity at a tertiary hospital in Jeddah, Saudi Arabia. **Materials and Methods:** This retrospective study includes 259 patients with RA aged =18 who meet ACR/EULAR 2010 criteria. Data collected from electronic medical records at King Abdulaziz University hospital (KAUH) between December 2021 and December 2023. Demographics, clinical characteristics, medication history and laboratory data for RF, Anti-Nuclear Antibodies (ANA) and ACPA levels were recorded. Disease activity was assessed using clinical disease activity index (CDAI) or disease activity score in 28 joints (DAS28) -Erythrocyte sedimentation. **Results:** The study involved 259 participants, primarily female, married and college students. There were insignificant differences between disease activity, gender, education, job, marital status, having kids, body mass index (BMI), RF and ACPA. Biologic disease-modifying anti-rheumatic medicines (DMARDs) showed insignificant changes with disease severity but rituximab showed moderate disease severity and infliximab showed more patients with remission. Non-biologic DMARDs, including Leflunomide and Hydrochloroquine, showed low to moderate disease activity. Targeted synthetic DMARDs, notably baricitinib and upadacitinib, dramatically alter disease activity. **Conclusion:** The study revealed that infliximab showed higher remission rates and rituximab showed moderate activity. Leflunomide, hydrochloroquine, baricitinib and upadacitinib exhibited low to moderate disease activity. Medical professionals should evaluate infliximab's efficacy in achieving remission and consider positive ANA. Further research is needed to confirm these findings and investigate additional factors.

Key Words Anti-cyclic citrullinated peptide antibody (ACPA), biologic disease-modifying anti-rheumatic medicines (DMARDs), clinical disease activity index (CDAI), disease activity score in 28 joints (DAS28), demographic characteristics, rheumatoid arthritis, rheumatoid factor, Saudi Arabia, treatment efficacy

INTRODUCTION

The body's defense mechanism against disease and pathogenic microorganisms is the immune system, which is made up of a wide range of chemicals and cells [1]. All autoimmune diseases (AD) are rooted in a failure to distinguish self from non-self, which is a breach of tolerance [2]. Genetic and environmental factors and their interactions all contribute to the development of ADs, even if their pathophysiology and etiology are uncertain [3]. Chronic synovial joint inflammation is a hallmark of rheumatoid arthritis (RA), a systemic inflammatory disease [4]. It also has extra-articular characteristics [5], which include cutaneous, cardiac, pulmonary and renal diseases [6]. Rheumatoid factor (RF) and anti-cyclic citrullinated peptide antibody (ACPA) are autoantibodies that are essential for RA diagnosis and estimation of disease activity [7].

The prevalence of RA has been increasing worldwide, a meta-analysis done between 1980 and 2019 estimated the newly diagnosed cases at 460 per 100,000 people [8]. Treat-to-target (T2T) principles stress the importance of

achieving remission or reduced disease activity [9]. Several practical and safe drugs can reduce inflammation and lead to low disease activity or remission. Among them are oral conventional synthetic disease-modifying anti-rheumatic medicines (DMARDs as methotrexate), injectable biologic DMARDs and oral targeted synthetic DMARDs [9]. However, this therapeutic model did not consider the patient characteristics that could influence a patient's likelihood of returning to minimal disease activity or remission regardless of treatment. Moreover, depending on patient's demographics characteristics and the history of fluctuations in the disease's activity, physicians can predict the future illness behavior [10].

RA imposes a significant socioeconomic burden on patients and healthcare systems in Saudi Arabia. A study at King Saud University Medical City estimated the average annual direct medical cost per RA patient to be 38,596 SAR (±3,055). Costs increased to 75,097 SAR for patients undergoing knee replacement procedures. The primary cost driver was biologic disease-modifying antirheumatic drugs (DMARDs), accounting for 84% of expenses [11]. Research comparing tocilizumab to adalimumab and etanercept among RA patients in Saudi Arabia highlighted the need for cost-effectiveness analyses to inform treatment decisions, given the high costs associated with biologic DMARDs [12]. RA treatment in Saudi Arabia presents a substantial economic burden, mainly due to the high costs of biologic therapies. Addressing these challenges requires strategies to improve insurance coverage, enhance cost-effectiveness of treatments and support patients financially to ensure access to necessary care.

Recent advancements in RA management have revolutionized treatment approaches, leading to improved disease control, reduced joint damage and better patient outcomes. Key innovations include early aggressive treatment strategies, targeted biologic therapies and personalized medicine. Modern RA management emphasizes early diagnosis and aggressive pharmacological intervention to prevent disease progression [13]. The "treat-to-target" strategy focuses on tight disease control using composite disease activity measures [14]. Advances in biologics include TNF inhibitors (etanercept, infliximab), IL-6 inhibitors (sarilumab, tocilizumab) and B-cell therapies (rituximab), which provide targeted suppression of inflammatory pathways. Janus kinase (JAK) inhibitors such as tofacitinib and filgotinib offer an oral alternative to biologics with promising efficacy [4]. The past decade has seen a shift from traditional DMARD monotherapy toward targeted biologics, JAK inhibitors and personalized combination therapies. These advancements have significantly improved patient outcomes, though cost, safety and accessibility remain challenges. Future research aims to refine treatment strategies for higher remission rates and fewer side effects [15].

According to research done in Ecuador in 2019, women are more likely than males to have the disease, which results in greater impairment and more severe symptoms [16]. A 2020 study conducted in Mexico revealed a strong positive correlation between having a high body mass index (BMI) and number of swollen joints [17]. Additionally, a study conducted in Mexico in 2022 revealed that individuals with positive antibody tests have higher joint damage based on their ACPA and RF status, especially in the metacarpophalangeal (MCP) joints [18]. Leflunomide therapy at prescribed dosages enhances clinical improvement, according to a 2019 Polish study [19]. In addition, a study done in Germany in 2015 concluded that patients with chronically high disease activity have a higher mortality risk that reduced by efficient management of disease activity [20]. Additionally, a Japanese study has shown that increased use of biological DMARDs (bDMARDs) and targeted synthetic DMARDs (tsDMARDs) improved the disease activity and functional impairment measures of RA patients over ten years [21].

There are few studies done in Saudi Arabia to assess the disease activity with other factors. This study aimed to evaluate comparison between RA patients' demographics, medication use and the disease activity at a tertiary hospital in Jeddah, Saudi Arabia.

METHODS

Study Design and Settings

This retrospective study was conducted at King Abdulaziz University Hospital (KAUH), a tertiary care facility in Jeddah, Saudi Arabia.

Study Participants and Ethical Considerations

The study included 259 patients diagnosed with RA by a rheumatologist and met the ACR/EULAR 2010 categorization criteria for RA diagnoses aged ≥18 years during the study period [22]. Excluded from the study were patients did not meet the ACR/EULAR 2010 categorization criteria for RA diagnoses and those under 18. Data was collected from the internal medicine department's electronic medical records (EMR) at KAUH during period from December 2021 to December 2023. The study received approval from the Institutional Review Board (IRB) of KAUH (Reference Number 744-23).

Data Collection

Demographic data, including gender, marital status, whether they have children, education and occupation, were recorded. Clinical characteristics, including the disease duration and BMI, were collected. Data was also gathered regarding past and current medications including Non-steroidal Anti-inflammatory Drugs (NSAIDs), corticosteroids, DMARDs and other medications. RF, anti-nuclear antibody (ANA) and ACPA levels were obtained by accessing laboratory data from the patient's file. Two methods were used to measure disease activity: the disease activity score in 28 joints (DAS28) or the clinical disease activity index (CDAI) [23,24].

Total Joint Count (TJC), Swollen Joint Count (SJC), provider global assessment and patient global assessment were used to calculate CDAI. Remission (CDAI $\leq$ 2.8), mild disease activity (CDAI >2.8 and $\leq$10), moderate disease activity (CDAI >10 and $\leq$22) and severe disease activity (CDAI >22) were the four categories of disease activity according to the CDAI [23]. TJC, SJC, an Erythrocyte Sedimentation Rate (ESR) and a visual analog scale were used to determine DAS28. A patient is in remission if their DAS28-ESR score is less than 2.6; low activity is suggested by a score higher than or equal to 2.6 and less than 3.1; moderate activity is indicated by a score greater than or equal to 3.1 and less than 5.1; and high activity is indicated by a score of 5.1 or more [24].

Data Analysis

Data were collected and stored throughout Microsoft Spreadsheet Version 20 and Statistical analysis was done using Statistical Package of Social Science (SPSS) version 21. A p-value less than 0.05 was considered significant. Categorical data has been stated according to the drug class and disease activity. Pearson Chi-Square (χ^2) Test used to assess comparison between disease activity and different drug classes. Quantitative and demographic variables have been visualized in compound bar charts.

RESULTS

In this retrospective record study 259 RA patients were included, most of them were females (N = 230), married (N = 205) and had children (n = 206). Also, most subjects who participated in the study were college students (N = 116) and were unemployed (N = 238). ANA, RF and anti-CCP were positive in 90, 109 and 103 patients, respectively. There were 232 patients on treatment and 27 did not receive treatment. There were insignificant different between treated and untreated patients regarding gender (p = 0.998), marital status (p = 0.809), having children (p = 0.780), education (p = 0.977), job (p = 0.672) as well as status of ANA (p = 0.587), RF (p = 0.998) and Anti-CCP (p = 0.748) (Table 1). The distribution of the illness duration is represented in Figure 1.

Regarding the disease activity, patients on treatment are categorized achieve remission (N = 30, 12.9%), low disease activity (N = 104, 44.8%) moderate disease activity (N = 93, 40.1%) and high disease activity (N = 5, 2.1%) (Figure 2).

Disease Activity among Subjects Using Different Therapeutic Modalities

In patients using Non-Biologic DMARDs, the diseased activity was mostly low (43.7%), then moderate (40%), remission (11.3%) and lastly high (3.7%), with significant difference between them (p = 0.020). In patients using

Table 1: Subject's demographic characteristics and laboratory data according to treatment status

	Treatment status				
	No treatment (n = 27)		On treatment (n = 232)		
Characteristics	No.	Percentage	No.	Percentage	p-value
Gender					
Female (n = 230)	24	88.9	206	88.8	0.998
Male (n = 29)	3	11.1	26	11.2	
Marital status					
Single (n = 38)	4	15.4	34	15.0	0.809
Married (n = 205)	21	80.8	184	81.4	
Divorced (n = 4)	0	0.0	4	1.8	
Widow (n = 5)	1	3.8	4	1.8	
Kids					
Yes (n = 206)	21	80.8	185	83.0	0.780
No (n = 43)	5	19.2	38	17.0	
Education					
Primary (n = 31)	5	21.7	26	12.0	0.977
Intermediate (n = 60)	4	17.4	56	25.9	
High School (n = 20)	2	8.7	16	7.4	
Collage (n = 116)	8	34.8	98	45.4	
Diploma (n = 4)	0	0.0	4	1.9	
Post-graduate (n = 11)	4	17.4	7	3.2	
Illiterate (n = 9)	0	0.0	9	4.2	
Job					
Employed (n = 48)	6	23.1	42	19.2	0.672
Unemployed (n = 238)	18	69.2	167	76.3	
Retired (n = 12)	2	7.7	10	4.6	
ANA					
Positive (n = 90)	10	55.6	80	60.6	0.587
Negative (n = 60)	8	44.4	52	39.4	
RF					
Positive (n = 109)	13	54.2	96	49.2	0.998
Negative (n = 110)	11	45.8	99	50.8	
Anti-CCP					
Positive (n = 103)	10	50.0	93	56.4	0.748
Negative (n = 82)	10	50.0	72	43.6	

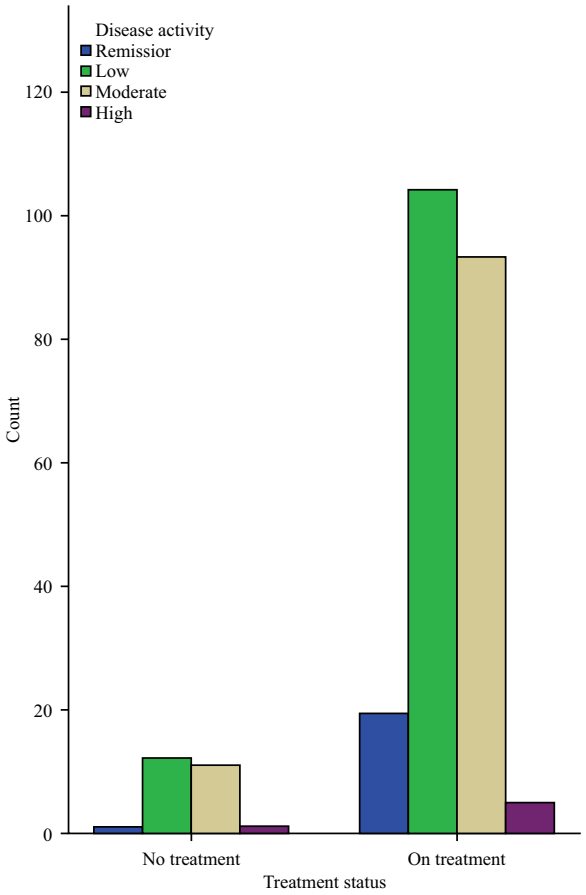

Figure 1: The distribution chart shows the duration of illness according to treatment status

Table 2: Disease activity among subjects using different therapeutic modalities

	Remission		Low		Moderate		High		
Disease activity	No.	Percentage	No.	Percentage	No.	Percentage	No.	Percentage	p-value
Non-biologic DMARDs	33	11.3	127	43.7	119	40.0	11	3.7	0.020
Biologic DMARDs	5	8.5	31	51.6	21	35	3	5	0.058
tsDMARDs	2	9.09	8	36.3	12	54.5	0	0	0.034
NSAIDs	0	0	6	66.66	3	33.33	0	0	0.590
Corticosteroids	4	17.3	8	34.7	10	43.4	1	4.3	0.274

tsDMARDs, the diseased activity was mostly moderate (54.5%), then low (36.3%) and lastly remission (9.09%), with significant difference between them (p = 0.034). Meanwhile, there were insignificant changes of disease activity in patients used Biologic DMARDs (p = 0.058), NSAIDs (p = 0.590) and corticosteroids (p = 0.274) (Table 2).

Comparison of Disease Activity According to Subjects' Demographics Characteristics

Pearson Chi-square test (χ^2) was done between demographic parameters and disease activity. Overall, there were no statistically significant differences between disease activity and gender (p = 0.703), education (p = 0.175), Job (p = 0.904), marital Status (p = 0.909) and having kids (p = 0.945) (Table 3).

Comparison of Disease Activity According to BMI

Pearson Chi-square test (χ^2) has been done for comparison between BMI and disease activity. There were insignificant changes of disease activity and whether the patient is of normal weight (Remission N = 7, Low N = 25, Moderate N = 18, High N = 0, p = 0.547), underweight weight (Remission N = 0, Low N = 2, Moderate N = 2, High N = 0, p = 0.610) overweight weight (Remission N = 6, Low N = 31, Moderate N = 26, High N = 3, p = 0.698) or obese (Remission N = 7, Low N = 58, Moderate N = 58, High N = 3, p = 0.966) (Table 4).

Comparison of Disease Activity and Subjects' Treatment Options

Pearson Chi-square test (χ^2) compared pharmacological therapy options and disease activity. Biological DMARDs

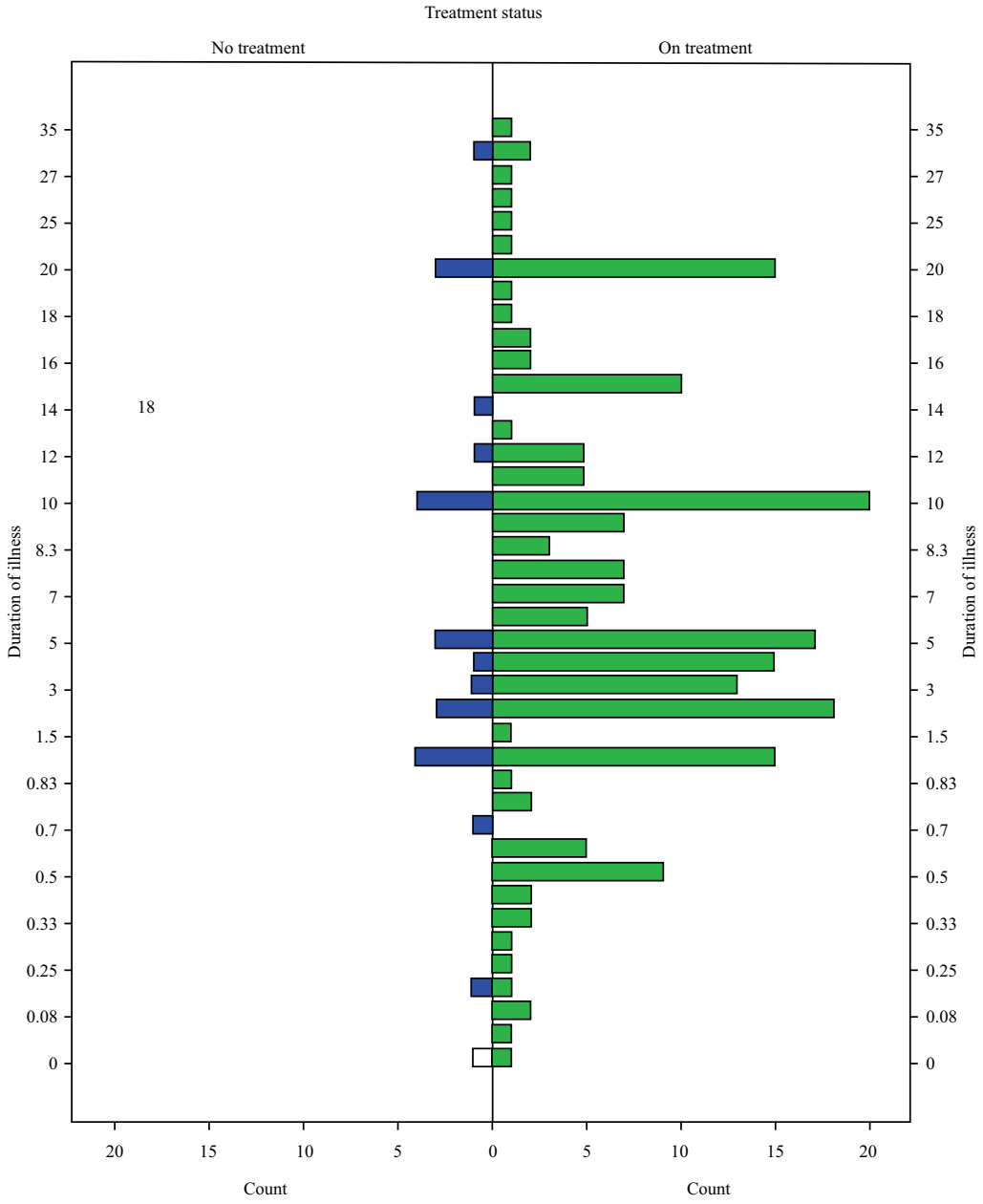

Figure 2: The stacked bar chart shows disease activity among subjects according to different therapeutic modalities

show a statistically non-significant correlation between decreased disease activity and the use of the drug class as Adalimumab (p = 0.211), Etanercept (p = 0.576), Tocilizumab (p = 0.891) and Certolizumab (p = 0.77). Patients treated with infliximab show more remission rates (40%, p = 0.013) while patients treated with rituximab shows high and moderate disease severity in comparison to subjects who did not take it (33.3 and 9.5%, p = 0.003), as shown in Table 5.

On the contrary, the use of non-biologic DMARDs shows statistically significant differences between decreased disease activity and the use of the drug class. Specifically, patients treated with leflunomide and hydroxychloroquine had low disease activity when compared to other drug classes (p = 0.040 and p = 0.024, respectively), as depicted in Table 6.

Also, using Targeted Synthetic DMARDs as monotherapy shows a statistically significant change in disease activity, more prominently with Baricitinib and Upadacitinib showed low to moderate disease activity compared to other drug classes (p = 0.047 and p = 0.036, respectively), as shown in Table 7.

Comparison of Disease Activity and Subjects' Auto-antibodies

Subjects with positive ANA show more likelihood of having mild to moderate disease activity (p = 0.048). Meanwhile, there were insignificant changes in the disease activity in relation to status of RF (p = 0.921) and ACPA (p = 0.816), as shown in Table 8.

DISCUSSION

The purpose of this study was to evaluate the level of disease activity in RA patients as well as the relationship between disease activity and variables related to demographic and clinical characteristics as well as treatment modalities. Leflunomide and hydroxychloroquine, two non-biological DMARDs, were more frequently administered to individuals in this research who had low to moderate disease activity. Due to their effectiveness and cheaper cost, these medications have formed the cornerstone of RA treatment since the disease's identification [25]. Due to its superior risk profile and tolerance in RA patients, hydroxychloroquine has been suggested conditionally by the American College of

Table 3: Disease activity according to different demographic characteristics

	Disease activity				
	Remission N	Low N	Moderate N	High N	p-value
Gender					
Female	18	101	94	6	0.703
Male	2	15	10	0	
Education					
Primary	1	16	13	0	0.175
Intermediate	4	27	24	1	
High school	0	11	6	1	
Collage	10	47	43	1	
Diploma	2	1	1	0	
Post-graduate	0	7	3	1	
Illiterate	0	4	5	0	
Job					
Employed	4	21	21	1	0.904
Unemployed	14	84	73	4	
Retired	1	8	3	0	
Marital status					
Single	4	17	15	1	0.909
Married	15	95	81	4	
Divorced	0	2	2	0	
Widow	0	1	4	0	
Kids					
Yes	14	92	85	4	0.945
No	4	21	17	1	

Table 4: Disease activity according to body mass index (BMI)

	Disease activity								
	Remission		Low		Moderate		High		
BMI	No.	Percentage	No.	Percentage	No.	Percentage	No.	Percentage	p-value
Underweight	0	0.0	2	1.7	2	1.9	0	0.0	0.610
Normal	7	35.0	25	21.6	18	17.3	0	0.0	0.547
Overweight	6	30.0	31	26.7	26	25.0	3	50.0	0.698
Obese	7	35.0	58	50.0	58	55.8	3	50.0	0.966

Table 5: Disease activity according to Biologic DMARDs

	Disease activity								
	Remission		Low		Moderate		High		
bDMARDs	No.	Percentage	No.	Percentage	No.	Percentage	No.	Percentage	p-value
Adalimumab	1	20.0	18	60.0	11	52.4	2	66.7	0.211
Etanercept	2	40.0	10	33.3	5	23.8	0	0.0	0.576
Tocilizumab	0	0.0	2	6.7	1	4.8	0	0.0	0.891
Rituximab	0	0.0	0	0.0	2	9.5	1	33.3	0.003
Infliximab	2	40.0	0	0.0	2	9.5	0	0.0	0.013
Certolizumab	0	0.0	1	3.3	0	0.0	0	0.0	0.771

Table 6: Disease activity according to non-biologic DMARDs

	Disease activity								
	Remission		Low		Moderate		High		
Non-Biologic DMARDs	No.	Percentage	No.	Percentage	No.	Percentage	No.	Percentage	p-value
Leflunomide	13	39.4	45	35.4	36	30.3	4	36.4	0.040
Methotrexate	8	24.2	42	33.1	49	41.2	2	18.2	0.113
Hydroxychloroquine	11	33.3	34	26.8	29	24.4	4	36.4	0.024
Azathioprine	0	0.0	1	1.1	2	1.7	0	0.0	0.832
Sulfasalazine	1	3.0	5	0.8	3	2.5	1	9.1	0.411

Table 7: Disease activity according to Targeted Synthetics DMARDs

	Disease activity								
	Remission		Low		Moderate		High		
Targeted synthetic DMARDs	No.	Percentage	No.	Percentage	No.	Percentage	No.	Percentage	p-value
Baricitinib	0	0.0	3	37.5	3	25.0	0	0.0	0.047
Upadacitinib	2	100.0	2	25.0	8	66.7	0	0.0	0.036
Tofacitinib	0	0.0	3	37.5	1	8.3	0	0.0	0.709

Table 8: Disease activity according to different autoantibodies

	Disease activity				
Autoantibodies	Remission Count	Low Count	Moderate Count	High Count	p-value
ANA					
Positive	9	30	42	4	0.048
Negative	4	33	22	0	
RF					
Positive	10	46	41	3	0.921
Negative	9	51	46	2	
ACPA					
Positive	10	48	34	2	0.816
Negative	6	41	33	1	

Rheumatology for individuals with modest disease activity. Since most of our patients fall into the low-disease activity group, they have shown a good response. However, their guidelines recommend methotrexate against leflunomide due to greater dosing flexibility and lower cost. Nonetheless, the findings of this study go well with the findings of the Polish study, which discussed better clinical outcomes when leflunomide is used with the recommended dosing [19,26]. With regards to moderate to high disease activity, methotrexate is the drug that is strongly recommended for use as monotherapy against hydroxychloroquine and leflunomide in moderate-high disease activity. Nevertheless, this recommendation comes with a low certainty of evidence regarding hydroxychloroquine and leflunomide [26-28].

On the contrary, bDMARDs have shown a non-significant correlation with disease activity. A research conducted in Saudi Arabia considered that one of the most critical variables of increased remission rates after a year of follow-up is effective referral networks that facilitate access to biologics [8]. This result is the opposite of what we find. However, it is essential to note that infliximab has shown more patients with remission and this comes in agreement with a previous study evaluating the use of this drug in patients with RA, which associated infliximab with a better health-related quality of life. Also, another retrospective study conducted in France mentioned that one of their infliximab-treated patients achieved prolonged remission [29,30]. Rituximab has shown moderate disease activity in our sample and a systematic review associated it with a reduction in disease activity, especially when combined with methotrexate; furthermore, this drug has shown reduced joint damage and improved pain and function [31]. These results may be explained by selecting the disease activity at one point in time only, which could be a high disease activity and no follow-up measurements; therefore, this result should not be relied upon definitively, especially since previous studies indicate that biological treatments are more effective compared to traditional treatments [26].

In this investigation, tsDMARDs, which consist of the Janus kinase (JAK) inhibitors, had a considerable influence on lowering disease activity, primarily Baricitinib and Upadacitinib. A Japanese study indicates that JAKi's efficacy is superior for challenging and very difficult-to-treat RA patients, mainly when they are not treated with glucocorticoid or MTX [5]. The finding emphasizes the role of tsDMARDs in reducing disease activity in RA patients, which is consistent the finding of this research.

Concerning inflammatory markers, neither the rheumatoid factor nor ACPA were considered significant, even though ACPA was specifically considered highly predictive of disease severity [32]. On the other hand, the marker associated with a higher likelihood of developing mild to moderate disease was ANA but this marker is not specific to RA. It can be linked with many other diseases, which may help identify overlapping syndromes or other autoimmune conditions [33].

BMI showed insignificance difference with the disease activity; however, there has been an increasing body of evidence implicating the impact of obesity on disease remission, as a meta-analysis reported that obese patients had 40% lower odds of attaining disease remission. Nonetheless, no clear hypothesis has suggested the exact mechanism of the impact of obesity; therefore, geographical differences might come into play, especially about dietary differences. For example, it is well known that the Mediterranean diet has been highly recommended for RA due to its potent anti-inflammatory and antioxidant characteristics [34,35].

RA treatment response varies significantly among patients due to genetic, biological, environmental and psychological factors. Understanding these factors can help optimize treatment strategies, improve patient outcomes and reduce healthcare costs. Genetic markers, such as HLA-DRB1, TRAF1 and PSORS1C1, influence disease severity and response to treatment [36]. Studies suggest that genome-wide association studies (GWAS) can identify genetic predictors for response to biologic therapies like tocilizumab [37]. Cytokine imbalances (e.g., TNF-α, IL-6, IL-1) are key drivers of RA inflammation and influence drug efficacy [38]. Variability in the immune response affects treatment success, especially with biologics [39]. Dietary factors such as adherence to a Mediterranean diet may have beneficial effects on treatment response [36]. Depression and anxiety are linked to poorer treatment outcomes and increased disease activity [40]. Omics approaches (genomics, transcriptomics, proteomics) help identify biomarkers to predict treatment response [41]. Pharmacogenomics is emerging as a tool for optimizing TNF inhibitor therapy [42].

Limitations

This study's limitations include its retrospective design, which resulted in missing data; additionally, evaluating the disease activity at a specific point in time is a crucial limitation. Furthermore, the reason for their marginally nonsignificant association with disease activity could be attributed to a small sample size of patients on bDMARDs. Treatment duration, including biologics, was not included, which could have resulted in an incorrect disease activity score. The data was collected from a single tertiary center in the western region of Saudi Arabia; therefore, multicenter studies across the nation are required to assess patient characteristics and their association with disease activity.

CONCLUSION

The study evaluated the relationship between the disease activity and factors related to the patient's demographic and clinical characteristics as well as treatment modalities. This study found insignificance difference between disease activity and gender, education, job, marital status, having kids, or BMI. However, among those who take different types of medication, remission was more in the patients taking infliximab. Moreover, Leflunomide and Hydrochloroquine showed low to moderate disease activity. Additionally, low to moderate disease activity was observed with baricitinib and upadacitinib. Concerning the laboratory data, patients with positive ANA demonstrated a higher probability of having mild to moderate disease activity. This study recommends that medical professionals assess the efficacy of different medications, particularly infliximab, in achieving disease remission. Furthermore, while analyzing the patient's disease activity, a positive ANA must be considered. We further suggest that creating a local, national cohort will be helpful in better understanding the disease activity associations with specific demographics, knowing the response rate and highly effective medications for our population to help us for future development of local guidelines and better cost-effective management.

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