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# Demographic and clinical associations of autoimmune diseases in rheumatoid arthritis patients: Insights from a tertiary care hospital in Saudi Arabia from 2019 to 2023

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## Abstract

**Background:** Rheumatoid arthritis is a severe inflammatory arthritis that causes irreversible damage to joints and bones, resulting in deformities and disabilities. Population-based studies on the co-occurrence in patients with rheumatoid arthritis are lacking despite shared mechanisms with other autoimmune diseases.

**Objectives:** This study aimed to determine the prevalence and association of autoimmune diseases among patients with rheumatoid arthritis and explore the associations between autoimmune diseases and treatment options for rheumatoid arthritis.

**Method:** This retrospective study was conducted from 2019 to 2023 at King Fahad Armed Forces Hospitals, Jeddah, Saudi Arabia. Data were cleaned in Excel and analyzed using IBM SPSS version 29. The activity of the disease was assessed through clinical manifestations, laboratory findings, and its associations with other autoimmune diseases.

**Results:** Our study included 365 patients with rheumatoid arthritis, predominantly female (89%), and observed diverse demographics and comorbidities. Prevalent conditions included diabetes mellitus (28.2%), hypertension (27.3%), and dyslipidemia (14.7%). Other autoimmune diseases were present in 24.9% of patients, with notable associations with age at rheumatoid arthritis diagnosis and endocrine, rheumatology/dermatology, and pulmonary disorders ($p < 0.001$). Treatment approaches varied, with prednisolone (24.4%) and methotrexate (55.1%) being predominant. No significant associations were observed between autoimmune disorders and specific treatment modalities ($p > 0.05$).

**Conclusion:** Our study provides a thorough overview of rheumatoid arthritis in a large cohort, revealing demographic trends, comorbidities, autoimmune disease prevalence, treatment preferences, and associations. Relationships with age at rheumatoid arthritis diagnosis and other autoimmune diseases were noted. Treatment approaches varied, with no significant associations between autoimmune disorders and specific modalities.

## Keywords

Rheumatoid arthritis, comorbidities, autoimmune diseases

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## Introduction

Rheumatoid arthritis (RA) is a chronic, systemic, inflammatory disorder characterized by persistent synovitis, systemic inflammation, and autoantibodies (particularly rheumatoid factor and citrullinated peptide). Many autoimmune diseases, including RA, share common pathogenic mechanisms,

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cytokine pathways, and a systemic inflammatory cascade. Additionally, a genome-wide association study contributed to the understanding of these shared pathways, their genetic basis (including shared loci), and the common environmental risk factors of autoimmune diseases. Moreover, the misdirected immune response against self that is observed in these diseases involves multiple body systems, frequently causing overlapping syndromes.[1]

The global prevalence of RA is estimated to be 0.24%–1%, but considerably vary globally. Additionally, a variation in RA prevalence is expected across Africa and the Middle East, due to ethnic, climate, and socioeconomic differences. RA was more prevalent among urban than rural populations, consistent with data from other regions.[2]

Several autoimmune diseases are associated with the same human leukocyte antigen (HLA) specificity.[1] In particular, insulin-dependent diabetes mellitus (IDDM), autoimmune thyroid diseases (Graves' disease and Hashimoto's thyroiditis (HT)), myasthenia gravis, systemic lupus erythematosus (SLE), celiac disease, and Addison's disease are associated with HLA-DR3. In addition, HLA-DR4-associated diseases include IDDM, RA, myasthenia gravis, and primary biliary cirrhosis.[3] Clinical and epidemiologic observations that patients with one autoimmune disease and their relatives are more likely to express another autoimmune disease associated with the same HLA-DR specificity than expected from population prevalence data reflected these genetic associations.[4,5]

The presence of other autoimmune diseases in patients with RA increases both disability and mortality. Additionally, RA treatments increase or exacerbate some autoimmune diseases such as SLE and psoriasis.[1] Moreover, various comorbidities complicate the course of RA disease. The most prevalent comorbidities among patients with RA are cardiovascular events, infections, pulmonary diseases, different cancer types, and depression. Moreover, the literature less frequently discussed some of these comorbidities such as hearing loss. RA comorbidities are associated with loss of function, higher rate of hospitalization, and increased mortality rate and socioeconomic burden on the patients and society.[6–9]

On average, patients with RA have two or more comorbid conditions.[1] The association between comorbid diseases and RA is a complex dilemma. Comorbid diseases may present prior, later, or simultaneously. They may be a consequence of RA treatment, such as corticosteroids, or a predisposing factor causing both RA and comorbid diseases, such as smoking.[3,5] Furthermore, RA comorbidities may present due to a shared autoimmune pathology, described as poly autoimmunity or multiple autoimmune syndromes. Comorbidities are frequently underdiagnosed and undertreated. Diagnosing and subsequently treating RA, which is recommended by the European League Against Rheumatism (EULAR), is important considering the importance of comorbid diseases in RA.[10] Additionally, a thorough investigation of comorbid diseases in RA can contribute to the understanding of the common pathological association.

At present, few published studies quantify the occurrence of overlapping autoimmune diseases in patients with RA. Most published papers are case reports or clinical hospital studies involving one or a selected few autoimmune diseases.[11–20] No current studies have evaluated the occurrence of multiple autoimmune diseases in patients with RA.[1] Therefore, this study aimed to determine the prevalence and association of co-occurring autoimmune diseases among patients with RA. Moreover, the aim is to quantify the prevalence of other autoimmune diseases, analyze demographics, investigate treatment patterns, and explore the associations between autoimmune diseases and treatment options for RA.

## Material and methods

### Ethics approval

The study was approved by the Research Ethics Committee of Armed Forces Hospitals-Jeddah on 12, June 2023 (approval number: 2023-42). The IRB Committee waived the consent from the patients.

### Study design

This retrospective study aimed to analyze the medical records of 365 patients diagnosed with RA who visited the rheumatology clinic over a 4-year period from 2019 to 2023 at King Fahad Armed Forces Hospitals, Jeddah, Saudi Arabia. The sample size for this study was determined according to available patient records at the hospital, and all eligible patients were included within this timeframe to ensure a comprehensive analysis. A final sample size of 365 patients was deemed sufficient for the study objectives based on these criteria and available patient records. To ensure confidentiality and data protection, each patient was assigned a unique registry code within the database. The inclusion criteria were age $\geqslant$ 18 years, meeting the American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) criteria for the diagnosis of RA,[21] and with or without the presence of other autoimmune diseases. To maintain a clear focus on the adult RA population and to ensure the homogeneity of the study sample, the exclusion criteria were individuals with other autoimmune diseases who did not have RA and those $>$18 years old. This approach allowed for a comprehensive assessment of the RA population within the specified setting that facilitated the examination of various clinical outcomes and characteristics associated with the disease.

A thorough data cleaning process was conducted to ensure data accuracy and reliability, which involved identifying duplicate entries. Missing data were addressed by excluding records with significant missing data. Data points were excluded based on predefined criteria, including patients

who did not meet the ACR/EULAR criteria for RA diagnosis, individuals under 18 years of age, and records with incomplete data.

### Statistical analysis

A comprehensive statistical analysis was conducted on the dataset, encompassing both descriptive and inferential methodologies. First, a descriptive analysis was conducted to summarize the demographic characteristics of the patients, including age, gender, and other parameters. This provided an overview of the study population. Subsequently, inferential analyses, such as chi-square or Fisher's exact tests, were used to investigate the associations between other autoimmune disorders and other parameters. Statistical significance was established at a $p$-value of $\leqslant 0.05$ and a 95% confidence interval. All statistical analyses were executed using IBM Statistical Package for the Social Sciences Software version 29.0.0.

## Results

### Demographic characteristics of the study population

Our study included 365 patients with RA, mostly (89%) female. Age distribution spans various groups, and body mass index (BMI) classifications are as follows: underweight (1.6%), normal (17.2%), overweight (31.5%), and obese classes 1 (30.5%), 2 (12.1%), and 3 (7.1%). The age at RA diagnosis varies. Table 1 shows the demographic characteristics of the patients.

**Table 1.** Demographic characteristics of patients ($n = 365$).

| Variables | Frequency *n* (%) |
|---|---|
| Gender | |
| Male | 40 (11.0) |
| Female | 325 (89.0) |
| Age (years) | |
| <30 | 24 (6.6) |
| 31–40 | 37 (10.1) |
| 41–50 | 70 (19.2) |
| 51–60 | 105 (28.8) |
| 61–70 | 80 (21.9) |
| >70 | 49 (13.4) |
| BMI of patients | |
| Underweight | 6 (1.6) |
| Normal | 63 (17.2) |
| Overweight | 115 (31.5) |
| Class 1 obese | 111 (30.5) |
| Class 2 obese | 44 (12.1) |
| Class 3 obese | 26 (7.1) |
| Age at diagnosis of RA (years) | |
| <20 | 11 (3.0) |
| 20–30 | 45 (12.3) |
| 31–40 | 77 (21.1) |
| 41–50 | 107 (29.3) |
| 51–60 | 83 (22.7) |
| 61–70 | 35 (9.6) |
| >70 | 7 (2.0) |

Frequency: *n*; percentage: %; BMI: body mass index.

### Prevalence of comorbidities

Among the study population, the most prevalent comorbidities included diabetes mellitus (28.2%), hypertension (27.3%), and dyslipidemia (14.7%). Other comorbidities were also noted, as shown in Figure 1, emphasizing the complexity of managing RA patients with multiple health conditions.

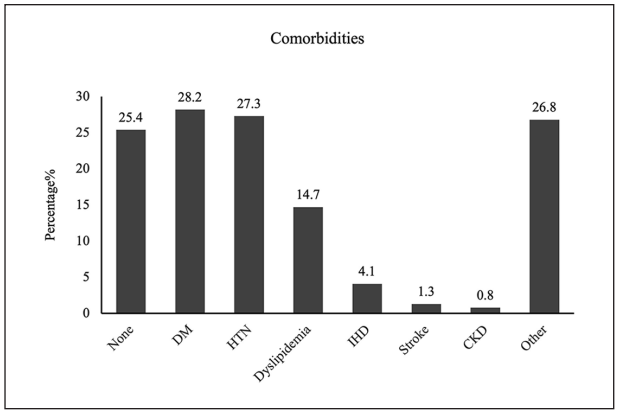


**Figure 1.** Bar chart showing the prevalence of various comorbidities among 365 patients diagnosed with RA. The most prevalent conditions were diabetes mellitus (DM), hypertension (HTN), and dyslipidemia (DM). Other notable comorbidities included ischemic heart disease (IHD), stroke, and chronic kidney disease (CKD). Other patients reported other comorbidities, whereas some had none.

### Prevalence of other autoimmune diseases

The prevalence of other autoimmune diseases in 365 patients with RA is shown in Table 2. Of these, 24.9% had other autoimmune diseases. The age of diagnosis for these diseases ranged from <20 to 61–70 years, with the 41–50 age group being the most prevalent (28.6%). Rheumatoid factor was positive in 85.2%, and anti-CCP was positive in 81.9%. Endocrine disorders included HT or autoimmune (19.2%), and rheumatological or dermatological disorders encompassed SLE (1.9%). Pulmonary disorders, such as interstitial lung disease (4.4%), gastrointestinal tract disorders, hematological disorders, and neurological disorders had varying prevalence.

### Treatment approaches

The treatment options for patients with RA are shown in Table 3. Prednisolone is used by 24.4% of patients,

**Table 2.** Prevalence of other autoimmune diseases with different system involvement and other serological factors (n = 365).

| Variables | Frequency *n* (%) |
|---|---|
| Other autoimmune disease | |
| No | 274 (75.1) |
| Yes | 91 (24.9) |
| Age of diagnosis of other autoimmune disease (*n* = 91, 24.9%) | |
| <20 years | 6 (6.6) |
| 20–30 years | 14 (15.4) |
| 31–40 years | 25 (27.5) |
| 41–50 years | 26 (28.6) |
| 51–60 years | 12 (13.2) |
| 61–70 years | 8 (8.8) |
| Rheumatoid factor | |
| Negative | 54 (14.8) |
| Positive | 311 (85.2) |
| Anti-CCP | |
| Negative | 66 (18.1) |
| Positive | 299 (81.9) |
| Endocrine disorders | |
| Graves' disease | 2 (0.5) |
| Hashimoto's/autoimmune | 70 (19.2) |
| Type 1 DM | 4 (1.1) |
| Rheumatological/dermatological disorders | |
| Ankylosing spondylitis | 1 (0.3) |
| Giant cell arteritis | 1 (0.3) |
| Psoriasis | 1 (0.3) |
| Psoriatic arthritis | 1 (0.3) |
| Sjögren's/sicca syndrome | 3 (0.8) |
| SLE | 7 (1.9) |
| Pulmonary disorders | |
| ILD/pulmonary fibrosis | 16 (4.4) |
| GIT disorders | |
| Celiac disease | 1 (0.3) |
| Hematological disorders | |
| Hemolytic anemia | 1 (0.3) |
| Neurological disorders | |
| None | 365 (100) |

Frequency: *n*; percentage: %; DM: diabetes mellitus; GIT: gastrointestinal tract; SLE: systemic lupus erythematosus; ILD: interstitial lung disease; anti-CCP: anti-cyclic citrullinated peptide.

predominantly at 5 mg (88.8%). Methotrexate was the most predominant conventional synthetic disease-modifying antirheumatic drugs (DMARDs) (55.1%), with various combinations used. Targeted synthetic DMARDs and biologics were less frequently prescribed, with upadacitinib (3.6%), adalimumab (10.2%), and rituximab (7.4%) having the highest representation. Notably, a majority had no usage in targeted synthetic DMARDs (95.9%) and biologic DMARDs (antitumor necrosis factor (TNF), 80.5% and non-TNF (85.8%)) categories, indicating diverse treatment approaches and potential preferences in RA management.

**Table 3.** Different treatment alternatives in patients with RA (*n* = 365).

| Variables | Frequency (*n* = 365) |
|---|---|
| Use prednisolone for treatment of RA | |
| No | 276 (75.6) |
| Yes | 89 (24.4) |
| Dose of prednisolone (*n* = 89, %) | |
| 2.5 mg | 6 (6.7) |
| 5 mg | 79 (88.8) |
| 10 mg | 3 (3.4) |
| 20 mg | 1 (1.1) |
| Conventional synthetic DMARDs | |
| Methotrexate | 201 (55.1) |
| Hydroxychloroquine | 43 (11.8) |
| Methotrexate + hydroxychloroquine | 38 (10.4) |
| Sulfasalazine + hydroxychloroquine | 16 (4.4) |
| Other combination | 27 (7.3) |
| N/A | 40 (11.0) |
| Targeted synthetic DMARDs | |
| Tofacitinib | 2 (0.5) |
| Upadacitinib | 13 (3.6) |
| N/A | 350 (95.9) |
| Biologic DMARDs (anti-TNF) | |
| Adalimumab | 37 (10.2) |
| Certolizumab | 2 (0.5) |
| Etanercept | 32 (8.8) |
| N/A | 294 (80.5) |
| Biologic DMARDs (non-TNF) | |
| Abatacept | 17 (4.7) |
| Rituximab | 27 (7.4) |
| Tocilizumab | 8 (2.1) |
| N/A | 313 (85.8) |

Frequency: *n*; Percentage: %; DMARDs: disease-modifying antirheumatic drugs; TNF: tumor necrotic factor; RA: rheumatoid arthritis.

## *Associations between autoimmune diseases and demographic/clinical factors*

The prevalence of autoimmune disorders in patients with RA, showing associations with various factors, is shown in Table 4. Noteworthy results include a significant association between autoimmune disease and age at RA diagnosis showing that other autoimmune disorders in RA are most prevalent 41–50-year age group (32.7%) ($p = 0.041$), the presence of endocrine disorders (93.4%) ($p < 0.001$), rheumatology/dermatology disorders (78.6%) ($p < 0.001$), and pulmonary disorders (81.2%) ($p < 0.001$).

## *Associations between autoimmune diseases and treatment modalities*

The association between autoimmune disorders and treatment modalities in patients with RA is shown in Table 5. No significant association was found between the presence of

**Table 4.** Prevalence of autoimmune disorders and their association with different factors and other system diseases.

| Variables | Presence of autoimmune disease in patients with RA | | Sig. value |
|---|---|---|---|
| | No, *n* (%) | Yes, *n* (%) | |
| Gender | | | |
| Male | 35 (87.5) | 5 (12.5) | 0.054[a] |
| Female | 239 (73.5) | 86 (26.5) | |
| Age | | | |
| <30 years | 21 (87.5) | 3 (12.5) | 0.694[a] |
| 31–40 years | 29 (78.4) | 8 (21.6) | |
| 41–50 years | 53 (75.7) | 17 (24.3) | |
| 51–60 years | 75 (71.4) | 30 (28.6) | |
| 61–70 years | 59 (73.8) | 21 (26.3) | |
| >70 years | 37 (75.5) | 12 (24.5) | |
| BMI | | | |
| Underweight | 4 (66.7) | 2 (33.3) | 0.849[b] |
| Normal | 51 (81.0) | 12 (19.0) | |
| Overweight | 86 (74.8) | 29 (25.2) | |
| Class 1 obese | 81 (73.0) | 30 (27.0) | |
| Class 2 obese | 32 (72.7) | 12 (27.3) | |
| Class 3 obese | 20 (76.9) | 6 (23.1) | |
| Age at diagnosis of RA | | | |
| <20 years | 9 (81.8) | 2 (18.2) | *0.041*[b] |
| 20–30 years | 40 (88.9) | 5 (11.1) | |
| 31–40 years | 52 (67.5) | 25 (32.5) | |
| 41–50 years | 72 (67.3) | 35 (32.7) | |
| 51–60 years | 67 (80.7) | 16 (19.3) | |
| 61–70 years | 28 (80.0) | 7 (20.0) | |
| >70 years | 6 (85.7) | 1 (14.3) | |
| RA factor | | | |
| Negative | 41 (75.9) | 13 (24.1) | 0.875[a] |
| Positive | 233 (74.9) | 78 (25.1) | |
| Anti-CCP | | | |
| Negative | 45 (68.2) | 21 (31.8) | 0.153[a] |
| Positive | 229 (76.6) | 70 (23.4) | |
| Endocrine disorders | | | |
| No | 269 (93.1) | 20 (6.9) | *<0.001*[a] |
| Yes | 5 (6.6) | 71 (93.4) | |
| Rheumatology/derma disorders | | | |
| No | 271 (77.2) | 80 (22.8) | *<0.001*[b] |
| Yes | 3 (21.4) | 11 (78.6) | |
| Pulmonary disorders | | | |
| No | 271 (77.7) | 9 (22.3) | *<0.001*[b] |
| Yes | 3 (18.8) | 18 (81.2) | |

Frequency: *n*; Percentage: %; RA: rheumatoid arthritis; anti-CCP: anticyclic citrullinated peptide; BMI: body mass index.
[a]Chi-square test.
[b]Fisher's exact test.

autoimmune diseases and the use of prednisolone in RA ($p = 0.537$) or its dosage ($p = 0.546$). Similarly, no significant correlations emerge between autoimmune disorders and the use of targeted synthetic or biologic DMARDs (both anti-TNF and non-TNF) ($p > 0.05$).

**Table 5.** Prevalence of autoimmune disorders and their association with different treatment options for RA.

| Variables | Presence of autoimmune disease in RA patients | | Sig. value |
|---|---|---|---|
| | No (*n*, %) | Yes (*n*, %) | |
| Use of prednisolone in RA | | | |
| No | 205 (74.3) | 71 (25.7) | 0.537[a] |
| Yes | 69 (77.5) | 20 (22.5) | |
| Dosage of prednisolone | | | |
| 2.5 mg | 6 (100) | 0 (0) | 0.546[b] |
| 5 mg | 60 (75.9) | 19 (24.1) | |
| 10 mg | 2 (66.7) | 1 (33.3) | |
| 20 mg | 1 (100) | 0 (0) | |
| Targeted synthetic DMARDs | | | |
| Tofacitinib | 1 (50.0) | 1 (50.0) | 0.476[b] |
| Upadacitinib | 10 (76.9) | 3 (23.1) | |
| Biologic DMARDs (anti-TNF) | | | |
| Adalimumab | 34 (91.9) | 3 (8.1) | 0.263[b] |
| Certolizumab | 2 (100.0) | 0 (0.0) | |
| Etanercept | 25 (78.1) | 7 (21.9) | |
| Biologic DMARDs (non-TNF) | | | |
| Abatacept | 13 (76.5) | 4 (23.5) | 0.829[b] |
| Rituximab | 20 (74.1) | 7 (25.9) | |
| Tocilizumab | 5 (62.5) | 3 (37.5) | |

Frequency: *n*; Percentage: %; DMARDs: disease-modifying antirheumatic drugs; RA: rheumatoid arthritis; TNF: tumor necrotic factor.
[a]Chi-square test.
[b]Fisher's exact test.

## Discussion

RA is a severe inflammatory arthritis causing irreversible damage to tendons, joints, and bones. Our study provides comprehensive insights into the demographic distribution, comorbidities, associations with other autoimmune diseases, and treatment options among patients suffering from RA. Here, we discuss the implications and potential avenues for further investigation based on the study results.

The predominance of the female population (89%) aligns with the established higher prevalence of RA in females as evident in previous studies revealing a female-to-male ratio of 3:1.[16] The age distribution reveals a spectrum of RA onset, with a substantial representation in the 41–60-year age groups. This is congruent with the existing knowledge of RA onset in middle age, as a study by Zhang et al.[17] reveals that the mean age in patients with RA is 51.8 years.

Similarly, the BMI classification distribution emphasizes the importance of considering weight management in patients with RA, with notable percentages falling into overweight and obese categories, as a study by Feng et al.[18] reveals that increased BMI was associated with an increased risk for RA.

The prevalence of several comorbidities emphasizes the need for a holistic approach to patient care. DM,[19] hypertension,[20] and dyslipidemia[22] are prevalent, requiring integrated

management strategies. The significant percentage with other comorbidities highlights the complexity of RA management, warranting a personalized approach.

Apart from joint issues, RA demonstrates extra-articular manifestations in other organs that correlate with high morbidity and mortality rates. The prevalence of other autoimmune diseases in patients with RA indicates a multifaceted autoimmune landscape. The high percentage (24.9%) of patients with additional autoimmune conditions indicates the need for vigilance in monitoring and managing these overlapping disorders. The positive rates of rheumatoid factor (85.2%) and anti-CCP (81.9%) highlight the typical immunological profile associated with RA.[23] Concerning the correlations between other autoimmune disorders and diverse factors in patients with RA, the significant associations observed with age at RA diagnosis and endocrine, rheumatology/dermatology, and pulmonary disorders provide valuable insights. The noteworthy finding of heightened prevalence of other autoimmune diseases in the 41–50-year age group resonates with the recognized spectrum of autoimmune conditions spanning various age categories. The associations emphasize the nuanced association between age and autoimmune comorbidities in RA. Amador et al.[24] reveal that age demonstrated some effect on autoimmune disorders and age at onset varies among ADs and thus their manifestations and outcomes. Moreover, the determined prevalence of endocrine, rheumatology/dermatology, and pulmonary disorders accentuates the systemic effect of RA on multiple organ systems. Wu et al.[25] reveal that the systemic autoimmune disease RA usually causes damage not only to joints, but also to other tissues and organs, including the heart, kidneys, lungs, digestive system, eyes, skin, and nervous system. This analysis contributes to a deeper understanding of the intricate connections between autoimmune disorders and specific factors in patients with RA, fostering awareness of the diverse clinical manifestations across different age cohorts.

The exact mechanism underlying the association between RA and other autoimmune diseases remains unclear, but several theories have been proposed. One of the most common theories is genetic susceptibility, which increases the risk of developing multiple autoimmune diseases. One example is HLA-DRB1, which is associated with both RA and SLE.[26] Another mechanism is environmental factors, such as infections, smoking, and diet, which trigger the autoimmune response in susceptible patients. In particular, infections may trigger autoimmune diseases through molecular mimicry. Additionally, epigenetic factors, including DNA methylation and histone modification, influence and contribute to autoimmune disease development.[27] RA frequently coexists with other autoimmune diseases, also known as the clustering phenomenon. The association can be associated with rheumatic or non-rheumatic autoimmune diseases. For example, Sjogren's syndrome affects 10%–20% of the RA population, followed by SLE and psoriasis. Autoimmune thyroid disease is observed in 10% of patients with RA. Inflammatory bowel diseases, such as Crohn's disease and ulcerative colitis, demonstrated a lower rate of association, which was observed in 1%–2% cases.[28]

Prednisolone and methotrexate are predominantly used, in line with conventional approaches.[29,30] However, the lower utilization of targeted synthetic DMARDs and biologics indicates potential variations in treatment preferences or limited access. The prevalence of no use in certain categories (e.g., 95.9% for targeted synthetic DMARDs) underscores the diverse approaches used in RA management. Early diagnosis and treatment initiation are crucial for patients with RA to prevent irreversible joint deterioration. Over the past few decades, care for RA has exhibited a substantial shift, which has improved patient outcomes and quality of life. The effective determination of many pathways implicated in the pathophysiology of RA has made this possible.[31] Commonly used to treat RA, DMARDs include methotrexate, leflunomide, hydroxychloroquine, and sulfasalazine. Etanercept, infliximab, adalimumab, golimumab, and certolizumab pegol are examples of anti-TNF-alpha drugs. T-cell costimulation inhibitors, such as abatacept (CTLA4-Ig), interleukin (IL) 6 inhibitors, including tocilizumab and sarilumab, and anti-CD20 B-cell depleting monoclonal antibodies, such as rituximab, are examples of additional biologic DMARDs. Janus kinases (JAK) inhibitors, such as tofacitinib, baricitinib, and upadacitinib, are types of targeted synthetic DMARDs.[32] Treatment selection should start first with factors, such as the presence of comorbid diseases, structural joint damage, patient age, and the presence or absence of poor prognostic factors. The treatment should aim to achieve disease remission or at least low disease activity.[33] Methotrexate is the cornerstone therapy for patients with RA due to its efficacy and safety profile. Sulfasalazine and leflunomide are considered in patients who are contraindicated for methotrexate and have no poor prognostic factors. Biological DMARDs are expanding, and several medications have been introduced. All biological DMARDs are administered intravenously or subcutaneously except for JAK inhibitors, which are oral medications.[33] Steroid therapy can be used for short-term relief, and their use should be minimized and tapered as soon as possible.[33]

The interplay between autoimmune disorders and treatment options demonstrates that the lack of significant associations with prednisolone usage or dosage indicates a degree of independence in prescribing decisions. However, considering the high association between RA and comorbidities, such as DM, hypertension, and dyslipidemia, and the effects of steroids on comorbidities, steroid therapy should be minimized as soon as possible to avoid long-term side effects. Moreover, the association between lung diseases and RA limits the use of some medications due to lung toxicity, such as methotrexate. The relatively low use of targeted synthetic DMARDs and biologics may prompt further investigation into factors affecting treatment choices, such as patient preferences, cost considerations, or perceived efficacy. Furthermore, some biologic medications mask other autoimmune diseases.[9]

## Limitations

Despite the valuable insights provided by this study, we acknowledge its limitations. The study utilized retrospective data from a single tertiary care hospital, which presents several constraints. For instance, the demographic and clinical characteristics of patients, as well as the treatment approaches at one territory center, may not fully represent those in other regions or healthcare settings. This limitation may restrict the generalizability of our findings. Another limitation is the absence of a power analysis to determine the sample size. While we included all eligible patients within the specified timeframe to ensure a comprehensive analysis, it is important to note that this is a retrospective study with a limited number of patient records. The lack of a priori power calculation means that the study may not be adequately powered to detect certain associations, particularly for less common autoimmune diseases. To overcome these limitations in future studies, it is recommended that a multicenter study be conducted to provide a more representative view of RA in diverse patient populations from different regions to improve generalizability. Also, larger sample sizes in future studies could provide more robust data and enhance the statistical power of the results. Future studies should incorporate a power analysis during the design phase to ensure that the sample size is adequate to detect meaningful associations. Another limitation is that the study did not capture detailed information on treatment duration. Future studies should include more comprehensive treatment data to better understand the effects of different therapies. Moreover, the study did not evaluate other factors, such as diet and smoking, which could affect the prevalence and management of comorbidities. Therefore, future research should include these factors to provide a view of patient health and management of RA.

## Conclusion and clinical implications

Our study provides a comprehensive snapshot of RA in a sizable cohort. The results elucidate demographic patterns, comorbidities, other autoimmune disease prevalence, treatment preferences, and associations with autoimmune disorders. The nuanced understanding gained from our study informs clinicians, researchers, and policymakers in tailoring strategies for RA management. Future research endeavors should investigate deeper into the identified associations, explore treatment decision-making processes, and evaluate the long-term effect of personalized approaches on patient outcomes.

Our study's clinical implications are manifold. First, the high prevalence of comorbidities emphasizes the importance of a holistic approach to RA management, thereby addressing not only joint symptoms but also associated conditions. Second, the diverse treatment patterns highlight the requirement for personalized therapeutic strategies, considering patient-specific factors and preferences. The associations with autoimmune disorders emphasize the interconnected nature of autoimmune conditions, necessitating a comprehensive evaluation of patients with RA. Additionally, careful consideration of different factors and associations is important in managing patients with RA. Considering comorbidity associations and treatment side effects will guide the treatment strategy for the patients.

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### Author contributions

TA, NA and A. Alhazmi contributed to the study's conception and design. The clinical documentation and practice involved in the study were carried out by TA, NA, A. Aladnani, A. Alhazmi, SI, and SA. Data collection and analysis were performed by GS, A. Aladnani, and A. Alfarsi. AZ wrote and reviewed the manuscript. All authors read and approved the final manuscript.

### Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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### Ethical approval

The study was approved by the Research Ethics Committee of Armed Forces Hospitals-Jeddah on 12 June 2023 (approval number: 2023-42).

### Informed consent

The IRB Committee waived the consent from the patients.

### Trial registration

Not applicable.

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### References

1. Simon TA, Kawabata H, Ray N, et al. Prevalence of co-existing autoimmune disease in rheumatoid arthritis: a cross-sectional study. *Adv Ther* 2017; 34: 2481–2490.
2. Harrison SR, Li D, Jeffery LE, et al. Vitamin D, autoimmune disease and rheumatoid arthritis. *Calcif Tissue Int* 2020; 106: 58–75.
3. Hemminki K, Li X, Sundquist J, et al. Familial associations of rheumatoid arthritis with autoimmune diseases and related conditions. *Arthritis Rheum* 2009; 60: 661–668.
4. Michou L, Rat AC, Lasbleiz S, et al. Prevalence and distribution of autoimmune diseases in 368 rheumatoid arthritis families. *J Rheumatol* 2008; 35: 790–796.

5. Cárdenas Roldán J, Amaya-Amaya J, Castellanos-de la Hoz J, et al. Autoimmune thyroid disease in rheumatoid arthritis: a global perspective. *Arthritis* 2012; 2012: 864907.
6. Emamifar A and Jensen Hansen IM. The influence of thyroid diseases, diabetes mellitus, primary hyperparathyroidism, vitamin B12 deficiency and other comorbid autoimmune diseases on treatment outcome in patients with rheumatoid arthritis: an exploratory cohort study. *Med (Baltim)* 2018; 97: e10865.
7. Ordoñez-Cañizares MC, Mena-Vázquez N, Redondo-Rodriguez R, et al. Frequency of polyautoimmunity in patients with rheumatoid arthritis and systemic lupus erythematosus. *J Clin Rheumatol* 2022; 28: e38–e43.
8. Harrold LR, Shan Y, Rebello S, et al. Prevalence of Sjögren's syndrome associated with rheumatoid arthritis in the USA: an observational study from the Corrona registry. *Clin Rheumatol* 2020; 39: 1899–1905.
9. Lazúrová I, Jochmanová I, Benhatchi K, et al. Autoimmune thyroid disease and rheumatoid arthritis: relationship and the role of genetics. *Immunol Res* 2014; 60: 193–200.
10. Jonkers IH and Wijmenga C. Context-specific effects of genetic variants associated with autoimmune disease. *Hum Mol Genet* 2017; 26: R185–R192.
11. Parameswaran A, Attwood K, Sato R, et al. Identification of a new disease cluster of pemphigus vulgaris with autoimmune thyroid disease, rheumatoid arthritis and type I diabetes. *Br J Dermatol* 2015; 172: 729–738.
12. Przygodzka M and Filipowicz-Sosnowska A. Prevalence of thyroid diseases and antithyroid antibodies in women with rheumatoid arthritis. *Pol Arch Med Wewn* 2009; 119: 39–43.
13. Wu D, Xian W, Hong S, et al. Graves' disease and rheumatoid arthritis: a bidirectional Mendelian randomization study. *Front Endocrinol (Lausanne)* 2021; 12: 702482.
14. Conigliaro P, D'Antonio A, Pinto S, et al. Autoimmune thyroid disorders and rheumatoid arthritis: a bidirectional interplay. *Autoimmun Rev* 2020; 19: 102529.
15. Francis J, Carty JE and Scott BB. The prevalence of coeliac disease in rheumatoid arthritis. *Eur J Gastroenterol Hepatol* 2002; 14: 1355–1356.
16. Maranini B, Bortoluzzi A, Silvagni E, et al. Focus on sex and gender: what we need to know in the management of rheumatoid arthritis. *J Pers Med* 2022; 12: 499.
17. Zhang Q, Liu Q, Lin C, et al. The prevalence of rheumatoid arthritis in middle-aged and elderly people living in Naqu City, Tibet, Autonomous Region of China. *J Orthop Surg Res* 2020; 15: 338.
18. Feng X, Xu X, Shi Y, et al. Body mass index and the risk of rheumatoid arthritis: an updated dose-response meta-analysis. *BioMed Res Int* 2019; 2019: 3579081.
19. Tian Z, McLaughlin J, Verma A, et al. The relationship between rheumatoid arthritis and diabetes mellitus: a systematic review and meta-analysis. *Cardiovasc Endocrinol Metab* 2021; 10: 125–131.
20. Manavathongchai S, Bian A, Rho YH, et al. Inflammation and hypertension in rheumatoid arthritis. *J Rheumatol* 2013; 40: 1806–1811.
21. Kay J and Upchurch KS. ACR/EULAR 2010 rheumatoid arthritis classification criteria. *Rheumatology* 2012; 51(suppl 6): vi5–vi9.
22. Erum U, Ahsan T and Khowaja D. Lipid abnormalities in patients with rheumatoid arthritis. *Pak J Med Sci* 2017; 33: 227–230.
23. Lee AN, Beck CE and Hall M. Rheumatoid factor and anti-CCP autoantibodies in rheumatoid arthritis: a review. *Clin Lab Sci* 2008; 21: 15–18.
24. Amador-Patarroyo MJ, Rodriguez-Rodriguez A and Montoya-Ortiz G. How does age at onset influence the outcome of autoimmune diseases? *Autoimmune Dis* 2012; 2012: 251730.
25. Wu D, Luo Y, Li T, et al. Systemic complications of rheumatoid arthritis: focus on pathogenesis and treatment. *Front Immunol* 2022; 13: 1051082.
26. Cruz-Tapias P, Castiblanco J and Anaya JM. HLA association with autoimmune diseases. In: Anaya JM, Shoenfeld Y, Rojas-Villarraga A, et al. (eds.) *Autoimmunity: from bench to bedside*. Bogota, Colombia: El Rosario University Press, 2013, pp. 271–285.
27. Doria A, Zen M, Bettio S, et al. Autoinflammation and autoimmunity: bridging the divide. *Autoimmun Rev* 2012; 12: 22–30.
28. Smolen JS, Landewé RBM, Bijlsma JWJ, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2019 update. *Ann Rheum Dis* 2020; 79: 685–699.
29. Lopez-Olivo MA, Siddhanamatha HR, Shea B, et al. Methotrexate for treating rheumatoid arthritis. *Cochrane Database Syst Rev* 2014; 2014: CD000957.
30. Stacy JM, Greenmyer JR, Beal JR, et al. The efficacy of low dose short-term prednisone therapy for remission induction in newly diagnosed rheumatoid arthritis patients. *Adv Rheumatol* 2021; 61: 50.
31. Radu AF and Bungau SG. Management of rheumatoid arthritis: an overview. *Cells* 2021; 10: 2857.
32. Chauhan K, Jandu JS, Brent LH, et al. Rheumatoid arthritis. In: *StatPearls* [Internet]. Treasure Island, FL: StatPearls Publishing, 2023, p. 2024.
33. Smolen JS, Landewé R, Breedveld FC, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs. *Ann Rheum Dis* 2010; 69: 964–975.