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# Exploring rheumatoid arthritis associated interstitial lung disease a retrospective study from two Saudi tertiary care centers

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## Abstract

**Background** Interstitial lung disease (ILD) is an increasingly recognized complication of rheumatoid arthritis (RA) and is associated with significant morbidity and mortality. Many risk factors for RA-related ILD were reported. The current study aims to explore the features and risk factors of Saudi patients with RA-ILD.

**Methods** This is a multicenter, retrospective, observational study of patients with RA-ILD. Clinical and radiological data from patients with RA-ILD were obtained from electronic medical records, including demographics, clinical characteristics, laboratory tests, pulmonary function tests, ECHO, and HRCT images.

**Result** Out of 732 patients, 57 had RA-ILD. The mean age at the time of ILD diagnosis was 61.9 (± 12.2) years. RA-ILD diagnosis was significantly less among females ($p = 0.008$). Patients who ever smoked had significantly more RA-ILD ($p < 0.001$). Patients with RA-ILD were more likely to present with medical comorbidities, namely diabetes ($p < 0.001$), hypertension ($p < 0.001$), ischemic heart disease ($p < 0.001$), and osteoarthritis ($p = 0.030$). The multivariate analysis revealed that the age (OR: 1.035, 95% CI: 48.45–52.86, $p = 0.0001$); gender (OR: 2.581, CI: 1.77–1.86, $p = 0.001$), DM (OR: 2.498, 95% CI: 1.65–1.76, $P = 0.0001$), HTN (OR: 1.975, 95% CI: 1.61–1.74, $P = 0.019$), IHD (OR: 6.043, 95% CI: 1.89–1.93, $P = 0.0001$) have a significant positive association with RA-ILD. No significant differences were observed between seropositive parameters with or without RA-ILD ($p > 0.05$). The most common symptoms of RA-ILD were cough (55.6%) and dyspnea (30.2%), and the most common ILD pattern was Non-specific Interstitial Pneumonia (NSIP) (55.6%) followed by Usual Interstitial Pneumonia (UIP) (38.9%). Traction bronchiectasis (75.5%) and glass ground opacities (73.6%) were also observed. The mean FVC and DLCO at baseline were 64.6% and 53.3%, respectively.

**Conclusion** In this cohort of patients, Saudi RA-ILD patients had a predominant NSIP pattern conversely to what is seen globally. These findings could be explained by the lower rates of smoking in our patient population. Future prospective national studies are needed to confirm the current findings and better evaluate RA-ILD epidemiology and risk factors.

**Keywords** Rheumatoid, Arthritis-, Associated, Interstitial, Lung, Disease

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## Introduction

Rheumatoid arthritis (RA) is an autoimmune disease characterized by progressive, symmetric polyarthritis. The most common extra-articular manifestation is lung involvement, affecting up to 60% of RA patients [1, 2]. However, the true prevalence of RA-associated interstitial lung disease (RA-ILD) is variable [3]. Different studies reported a wide prevalence range of RA-ILD due to applying different methodologies for detecting the disease. Some studies based on clinical detection reported a prevalence ranging from 2 to 8% [2, 4], while other studies reported a higher prevalence rate of 8–20% based on chest images/procedures or billing codes [5–8]. Relying on pharmacy claims, a recent nationwide US study found that RA-ILD prevalence was increasing from 3.2 cases per 100,000 (2003) to 6.0 cases per 100,000 in the general population (2014) [6]. This increase was attributed to many factors, including the recent usage of highly sensitive diagnostic methods.

Classically, patients with RA-ILD are older, male, smokers, and seropositive [9]. The prevalence of seropositivity of circulating rheumatoid factor (RF) and anti-citrullinated peptide antibodies (ACPAs) in RA patients is estimated at 50–80% [10]. Both markers have been linked to ILD development, particularly in high titers [9, 11–16]. Also, a form of reactive lymphoid tissue has been found in patients with RA-ILD, known as inducible bronchus-associated lymphoid tissue. It is associated with the local production of inflammatory cytokines and ACPAs [15]. A study by Ytterberg et al. 2015 examined the protein content in a sample of tissues taken from lung and synovial biopsies of patients with RA and found identical citrullinated vimentin peptides in both sites [12].

ILD negatively impacts the overall prognosis and utilization of healthcare resources. About 10% of RA patients develop a clinically significant ILD responsible for 10–20% of mortality, with a mean survival of 5–8 years [2, 4, 5, 16]. In addition, approximately one-third of patients have a subclinical disease with varying degrees of functional impairment [17].

Though RA is often diagnosed before the detection of ILD due to the presence of articular disease, patients may present de novo with isolated pulmonary disease; in these cases, a high index of suspicion for RA-ILD is required to distinguish it from Idiopathic Interstitial Pneumonia (IIPs). Similar to the IIPs, patients with RA and ILD most often present with chronic symptoms of dyspnea and cough. A physical examination may reveal inspiratory crackles, and pulmonary function test (PFT) results typically demonstrate restrictive physiology, often with a reduced diffusing capacity. High-Resolution Computed Tomography (HRCT) scanning is generally sufficient to confirm the diagnosis of ILD, although, in a minority of cases, surgical lung biopsy may be required [18].

Four major radiographic patterns have been identified in patients with RA-ILD: usual interstitial pneumonia (UIP) pattern with bilateral subpleural reticulation with or without honeycombing; non-specific interstitial pneumonia (NSIP) pattern with predominant ground-glass opacities; an inflammatory airway disease pattern with centrilobular branching lines with or without bronchial dilatation; and organizing pneumonia (OP) pattern with patchy areas of consolidation [19]. RA-ILD associated with the UIP pattern carries the highest mortality compared to other patterns. Singh et al. 2019 retrospectively reviewed 1256 patients with RA-ILD and 484 total deaths. The relative risk (RR) of death in the UIP RA-ILD pattern was 1.66 compared with other patterns [20]. A recent study by Nieto et al. found that RA-ILD is a life-shortening condition in 10-30% of patients who had died by 3 and 6 years, respectively, after diagnosis of ILD, with a median survival of 8.2 years [21].

Because of the lack of RA-ILD-controlled studies, there is uncertainty about the optimal recommendations for treating RA-ILD. The empirical approach is based mainly on uncontrolled studies. Although the association between pneumonitis and methotrexate (MTX) is generally accepted, a link between the development of full ILD post-MTX exposure has been challenged by the recent findings of a protective effect rather than a causative consequence. Dawson et al. [22] performed chest HRCT and pulmonary function tests in 128 RA patients. The authors found no differences in the dose or duration of MTX therapy among the 28 patients with RA-ILD compared to non-RA-ILD, suggesting no increased risk of ILD related to MTX use.

On the other hand, several biological agents have shown a positive correlation with RA-ILD. In particular, new onsets or exacerbations of ILD have been described by several reports and registry data after administering all anti-tumor necrosis factor alpha (anti-TNFα) agents approved for the treatment of RA (infliximab, etanercept, adalimumab, certolizumab, and golimumab) suggesting a class effect rather than adverse drug events [23–29]. Nakashita and colleagues retrospectively analyzed 163 RA patients treated with biological agents (63 etanercept, 33 infliximab, six adalimumab, 36 tocilizumab, and 25 abatacept). They observed a prevalence of 3% of new ILD events and 24% of ILD worsening with anti-TNFα agents (higher than previously reported [0.5–0.6%] from postmarketing data surveillance). On the contrary, tocilizumab and abatacept did not increase the prevalence of ILD events [30]. Despite previous evidence, the association of anti-TNFα treatment with ILD has been challenged by a retrospective study that included 8,417 patients affected by RA, ankylosing spondylitis, psoriatic arthritis, psoriasis, and inflammatory bowel disease. The study showed no increased risk of ILD in those patients

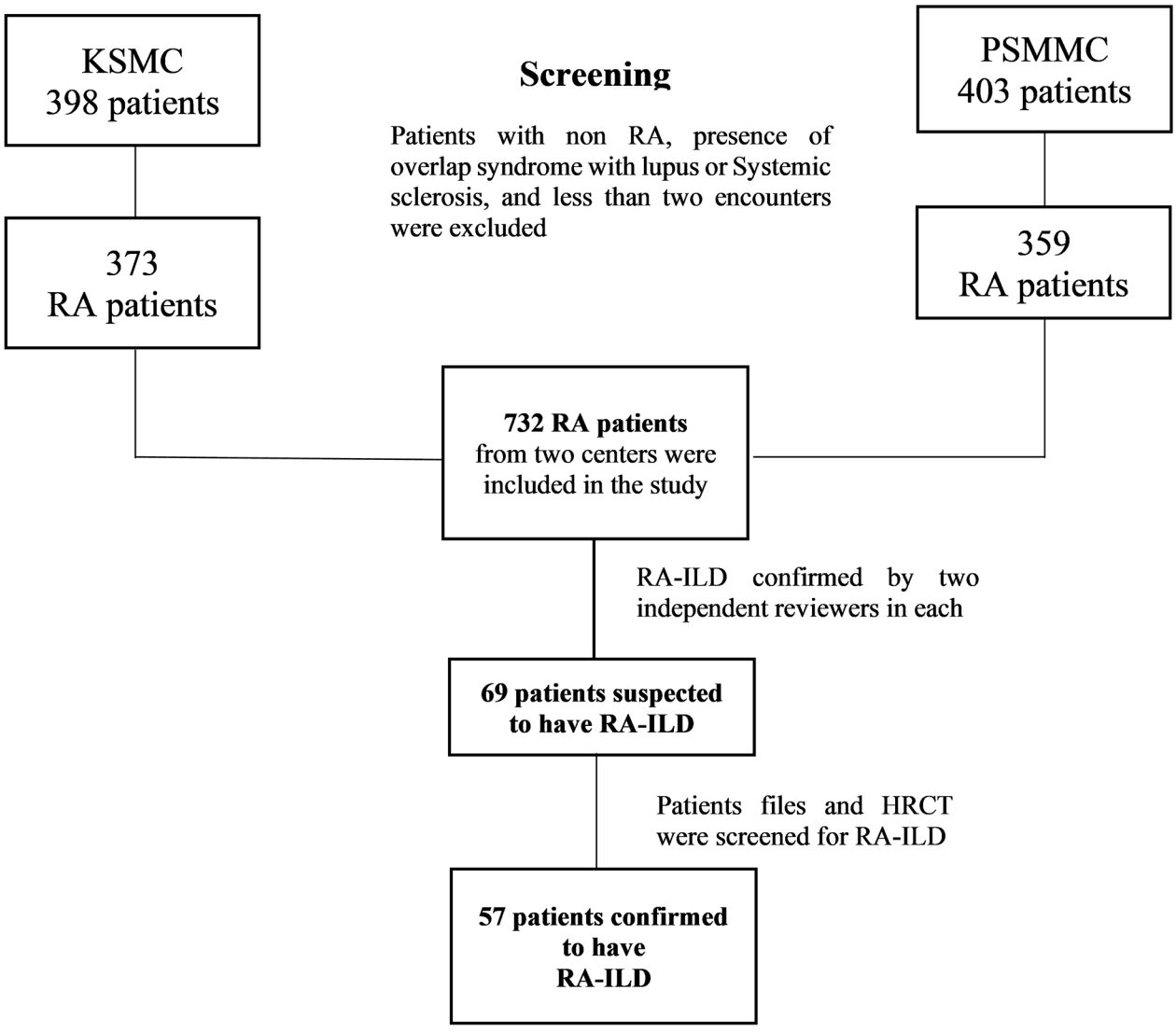


**Fig. 1** Graphical schema of the study database

treated by TNFα compared with those treated with non-biologic drugs (adjusted hazard ratio of 1.03, 95% confidence interval [CI] of 0.51–2.07), with no significant differences among the different anti-TNFα molecules [31].

In Saudi Arabia, no previous reports have studied the RA population's clinical and radiological pattern of ILD. As such, this study aims to describe patients with RA-ILD from two large referral centers.

## Methods

### Patients and setting

RA patients aged ≥ 18 years and fulfilling the 2010 American College of Rheumatology/European League Against Rheumatism classification criteria with a ≥ 6-month disease duration were included. ILD was confirmed by the clinical, physiological, and radiological evaluation. Patients were recruited from Prince Sultan Military Medical City (PSMMC) and King Saud Medical City (KSMC) in Riyadh, KSA. Verbal consent was obtained from all patients. A total of 732 RA patients were reviewed. The clinical and radiological information of RA-ILD patients were obtained from the electronic medical records that included demographics, clinical characteristics, laboratory tests, pulmonary function tests, ECHO, and HRCT images. Two independent reviewers in both centers reviewed HRCT films, and all patients in this study were discussed in multidisciplinary meetings, including a pulmonologist, rheumatologist, chest radiologist, and histopathologist. None of the patients needed a biopsy to confirm the diagnosis. Patients with overlapping systemic sclerosis, inflammatory myopathy, mixed connective tissue disease, and systemic lupus erythematosus or underlying ILD, such as occupational dust exposure, infection

**Table 1** Baseline characteristics of the patients with or without the presence of RA-ILD *(n=732)*

| Study Data | RA-ILD *N* (%) *(n=54)* | RA *N* (%) *(n=678)* | *P*-value [§] |
|---|---|---|---|
| Age at diagnosis of RA (mean ± SD) | 56.5 ± 13.7 | 46.4 ± 15.4 | **< 0.001** ** |
| Age at diagnosis of RA-ILD (mean ± SD) | 61.9 ± 12.2 | -- | -- |
| Female gender | 42 (77.8%) | 608 (89.7%) | **0.008** ** |
| Male gender | 12 (22.2%) | 70 (10.3%) | |
| Smoking | | | |
| • Ever smoked | 09 (16.7%) | 20 (2.9%) | **< 0.001** ** |
| • Never smoked | 45 (83.3%) | 658 (97.1%) | |
| Comorbidities | | | |
| • DM | 23 (42.6%) | 130 (19.2%) | **< 0.001** ** |
| • HTN | 26 (48.1%) | 171 (25.3%) | **< 0.001** ** |
| • DLP | 04 (07.4%) | 57 (08.4%) | 0.793 |
| • Hypothyroidism | 11 (20.4%) | 91 (13.5%) | 0.159 |
| • IHD | 08 (14.8%) | 12 (01.8%) | **< 0.001** ** |
| • OA | 10 (18.5%) | 63 (09.3%) | **0.030** ** |
| • Osteoporosis | 07 (13.0%) | 52 (07.7%) | 0.171 |
| • Others | 17 (56.7%) | 175 (68.6%) | 0.186 |
| Seropositive | | | |
| • RF | 35 (71.4%) | 356 (59.9%) | 0.113 |
| • Anti-CCP | 31 (66.0%) | 334 (58.2%) | 0.298 |
| • Double positive | 03 (09.1%) | 50 (16.3%) | 0.279 |
| • Seronegative | 01 (03.0%) | 21 (06.8%) | 0.400 |
| • Antinuclear Antibody (ANA) | 24 (60.0%) | 332 (67.9%) | 0.306 |

DM- Diabetes; HTN- Hypertension; DLP- Dyslipidemia; IHD- Ischemic heart disease; OA- Osteoarthritis

[§] *P*-value has been calculated using Chi-square test

** Significant at $p < 0.05$ level

(such as pneumocystis carinii pneumonia or Coronavirus disease (COVID-19)), drugs (such as bleomycin), and radiation exposure were excluded from the analysis. A total of 57 out of 732 RA patients were confirmed to have RA-ILD. HRCT, PFT, 6-minute walk test, and echocardiogram were only performed in patients with ILD and a minority of patients who presented with dyspnea. These tests were done at the onset of ILD-RA diagnosis. The study database scheme is shown in Fig. 1.

### Statistical analysis

Categorical variables were shown as numbers and percentages (%), while continuous variables were summarized as mean and standard deviation. The relationship between the evidence of RA-ILD among the baseline characteristics and the echo findings was conducted using the Chi-square test. Furthermore, univariate and multivariate analysis was used to assess demographic characteristics and comorbidities associated with risk factors for RA-ILD. A $p$-value < 0.05 was considered statistically significant. Finally, two-tailed analyses with $p < 0.05$ indicated statistical significance. All data analyses were performed using the statistical package for social sciences, version 26 (SPSS, Armonk, NY: IBM Corp, USA).

## Results

A total of 732 patients who were diagnosed with RA, were evaluated. Table 1 presents the baseline characteristics of the patients with or without ILD. The mean age at RA diagnosis was significantly higher among those with associated ILD ($p < 0.001$). The mean age of RA-ILD patients at diagnosis was 61.9 (SD 12.2). RA-ILD diagnosis was

**Table 2** Univariate analysis of comorbidities in rheumatoid arthritis with or without interstitial lung disease

| | OR (95% CI) | *P*- Value |
|---|---|---|
| Age (years) | 1.035 (45.265–59.069) | 0.0001** |
| Gender | 2.581 (1.478–4.509) | 0.002** |
| **Comorbidities** | | |
| DM | 2.498 (1.517–4.113) | 0.001** |
| HTN | 1.975 (1.198–3.256) | 0.007** |
| DLP | 0.801 (0.300–2.142) | 0.444 |
| Hypothyroidism | 1.285 (0.671–2.462) | 0.281 |
| IHD | 6.043 (3.411–10.703) | 0.0001** |
| OA | 1.864 (0.983–3.533) | 0.055 |
| Osteoporosis | 1.540 (0.730–3.248) | 0.187 |

DM- Diabetes; HTN- Hypertension; DLP- Dyslipidemia; IHD- ischemic heart disease; OA- Osteoarthritis

OR: odd's ratio, 95% CI: 95% confidence interval

** Significant at $p < 0.05$ level

significantly less among females ($p=0.008$) and significantly more among smokers ($p<0.001$). Patients with RA-ILD were more likely to present with medical comorbidities, namely diabetes ($p<0.001$), hypertension ($p<0.001$), ischemic heart disease ($p<0.001$), and osteoarthritis ($p=0.030$). No significant differences were observed between seropositive parameters with or without RA-ILD ($p>0.05$).

Univariate analysis of factors in RA with and without ILD revealed that the following factors were found to have a significant positive association with RA-ILD: age (OR: 1.035, 95% CI: 45.265–59.069, $p=0.0001$); gender (OR: 2.581, CI: 1.478–4.509, $p=0.002$), DM (OR: 2.498, 95% Cl: 1.517–4.113, $P=0.001$), HTN (OR: 1.975, 95% Cl: 1.198–3.256, $P=0.007$), IHD (OR: 6.043, 95% Cl: 3.411–10.703, $P=0.0001$) (Table 2).

Multivariate analysis of factors in RA with and without ILD revealed that the following factors were found to have a significant positive association with RA-ILD: age (OR: 1.035, 95% CI: 48.45–52.86, $p=0.0001$); gender (OR: 2.581, CI: 1.77–1.86, $p=0.001$), DM (OR: 2.498, 95% Cl: 1.65–1.76, $P=0.0001$), HTN (OR: 1.975, 95% Cl: 1.61–1.74, $P=0.019$), IHD (OR: 6.043, 95% Cl: 1.89–1.93, $P=0.0001$) (Table 3).

The characteristics of RA-ILD patients are given in Table 4. The most commonly known symptoms of RA-ILD were cough (55.6%) and dyspnea (30.2%), while the most common ILD pattern was NSIP (55.6%) followed by UIP (38.9%) (see also Fig. 2). Traction bronchiectasis (75.5%) and glass ground opacities (73.6%) were two of the major HCRT findings. The mean FVC and DLco were 64.6% and 53.3%, respectively. The mean 6-minute walk distance was 267.7, and the mean 6-minute pre and post-oxygen saturation (%) were 95.1% and 83.4%, respectively.

Echocardiographic evaluation showed no significant differences observed in right ventricular size ($p=0.152$), tricuspid regurgitation ($p=0.625$), left ventricular ejection fraction ($p=0.456$), and pulmonary artery systolic pressure ($p=0.686$) between RA-ILD and non-RA-ILD patients (Table 5).

The potential association/causation between the immunosuppression therapy and RA-ILD is illustrated in Table 6. Only MTX showed a significant difference between pre-and post-ILD diagnoses, whereas post-ILD diagnosis was more associated with less use of MTX ($p=0.002$).

**Table 3** Multivariate analysis of comorbidities in rheumatoid arthritis with or without interstitial lung disease

| | OR (95% CI) | *P*- Value |
|---|---|---|
| Age (years) | 1.035 (48.45–52.086) | 0.0001** |
| Gender | 2.581 (1.77–1.86) | 0.001** |
| **Comorbidities** | | |
| DM | 2.498 (1.65–1.76) | 0.0001** |
| HTN | 1.975 (1.61–1.74) | 0.019** |
| DLP | 0.801 (1.88–1.96) | 0.967 |
| Hypothyroidism | 1.285 (1.78–1.88) | 0.241 |
| IHD | 6.043 (1.89–1.93) | 0.0001** |
| OA | 1.864 (1.84–1.92) | 0.066 |
| Osteoporosis | 1.540 (1.86–1.94) | 0.258 |

DM- Diabetes; HTN- Hypertension; DLP- Dyslipidemia; IHD- ischemic heart disease; OA- Osteoarthritis

OR: odd's ratio, 95% CI: 95% confidence interval

** Significant at $p<0.05$ level

**Table 4** Characteristics of patients with RA-ILD at baseline $^{(n=54)}$

| Characteristics | *N* (%) |
|---|---|
| Symptoms | |
| Dyspnea | 16 (30.2%) |
| Cough | 30 (55.6%) |
| Chest pain | 06 (11.5%) |
| ILD pattern | |
| UIP | 21 (38.9%) |
| NSIP | 30 (55.6%) |
| HRCT findings | |
| Traction bronchiectasis | 40 (75.5%) |
| Glass ground opacities | 39 (73.6%) |
| Peripheral reticulation | 33 (62.3%) |
| Honeycombing | 24 (45.3%) |
| Basal predominance | 20 (37.7%) |
| Lung nodules | 10 (18.9%) |
| **PFT** | |
| Spirometry pattern | |
| • Normal | 0 |
| • Restrictive | 42 (100%) |
| • Obstructive | 0 |
| Mean FVC, % predicted | 64.6 ± 20.7 |
| Mean DLCO, % predicted | 53.3 ± 19.7 |
| 6-min walk distance | 267.7 ± 53.7 |
| 6-min walk sat % pre | 95.1 ± 1.19 |
| 6-min walk sat % post | 83.4 ± 6.66 |

UIP- Usual interstitial pneumonia; NSIP- Nonspecific interstitial pneumonia; OP-Organizing pneumonia

## Discussion

The current study explores the characteristics, risk factors, and patterns of RA-ILD in Saudi patients. UIP was long considered the most common subtype related to RA [18, 32, 33] from the United States [34], Europe [35], and China [36]. However, we found that the most common pattern in our cohort was NSIP (55.6%), followed by UIP (38.9%) and organizing pneumonia (5.6%). This difference might be explained by ethnicity, genetic background, or environmental factors. Also, our population differed from others as the female gender was higher than other ethnicities [34, 36, 37], and the rate of smokers was significantly lower than the reported data from the United States and China [34, 36]. Finally, the rate of Antinuclear Antibody (ANA) positivity in our study was higher than what has been reported in some studies, such as Nurmi

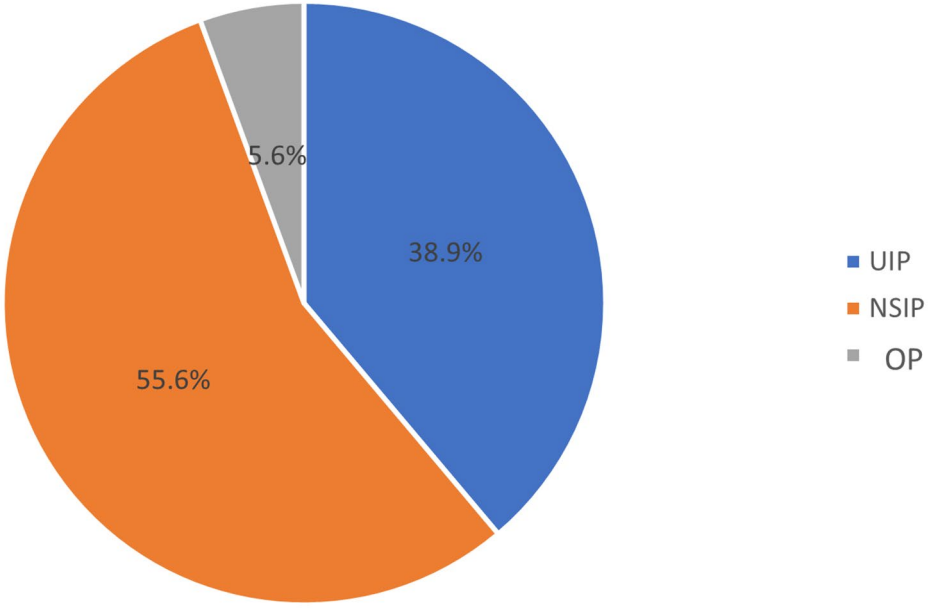


**Fig. 2** Rheumatoid arthritis-associated Interstitial lung disease pattern. UIP- Usual interstitial pneumonia; NSIP- Nonspecific interstitial pneumonia; OP- Organizing pneumonia

et al. (17.8%) [35], which may suggest a different autoimmune phenotype.

In our cohort, we observed a higher prevalence of comorbidities in RA-ILD, specifically DM, HTN, and IHD. This finding could be confounded by the older age in the RA-ILD group. Furthermore, patients with RA-ILD were significantly more likely to have a positive RF, ACPA, and ANA compared to non-RA-ILD patients. Dyspnea on exertion and cough were the most common symptoms of ILD, with cough being the most prevalent. These findings were consistent with the other published descriptive studies of RA-ILD.

Our physiological findings were compatible with the study published by Solomon et al. [34] that found a significant reduction in the forced vital capacity (FVC) (69.3 ± 19.2 of predicted) and transfer factor (DLco) (48.9 ± 17.8).

Finally, we discovered that patients with RA-ILD had significant desaturation during the 6-minute walk. Echocardiography, an effective screening method for pulmonary hypertension (PH), showed no statistically significant differences in ejection fraction (EF), Pulmonary arterial systolic pressure (PASP), right ventricle (RV) size, or tricuspid regurgitation TR between RA and RA-ILD patients.

No high-quality randomized clinical trials have been conducted to identify the optimal treatment strategy for patients. Regardless of the ILD pattern, immunosuppressive drugs are frequently prescribed. Additional studies and research are required to determine if this is the optimal treatment strategy. Corticosteroids are still considered the backbone of RA-ILD treatment, especially in cases of NSIP or OP. Different types of DMARDs are used in the management of RA, including csDMARDs, anti-TNF bDMARDs, non-TNF bDMARDs, and tsDMARDs.

Interestingly, many studies have failed to show a positive correlation between the efficacy of DMARDs and the progression of ILD in RA patients. MTX, which is known to cause hypersensitivity pneumonitis during the initial months of treatment, does not seem to have an increased risk of developing ILD in RA patients [38, 39]. Despite this, half of the patients in our cohort who were using MTX before the ILD diagnosis discontinued its use. Finally, it is noteworthy that only four patients in our

**Table 5** Comparison of ECHO findings in RA-ILD and non-RA-ILD

| ECHO | RA-ILD *N* (%) | RA *N* (%) | *P*-value [§] |
|---|---|---|---|
| RV size | | | |
| • Normal | 42 (89.4%) | 204 (94.9%) | 0.152 |
| • Dilated | 05 (10.6%) | 11 (05.1%) | |
| TR | | | |
| • Normal | 27 (57.4%) | 113 (54.1%) | 0.625 |
| • Mild | 17 (36.2%) | 78 (37.3%) | |
| • Moderate | 01 (02.1%) | 13 (06.2%) | |
| • Severe | 02 (04.3%) | 05 (02.4%) | |
| | **Mean ± SD** | **Mean ± SD** | **P-value[‡]** |
| LVEF | 56.2 ± 9.68 | 56.6 ± 3.31 | 0.456 |
| PASP | 36.1 ± 8.39 | 35.8 ± 4.95 | 0.686 |

RV- Right ventricle; TR- Tricuspid regurgitation; LVEF- Left ventricular ejection fraction; PASP- Pulmonary arterial systolic pressure

[§] *P*-value has been calculated using the Chi-square test

**Table 6** Treatments before and after the ILD diagnosis *(n=54)*

| Medications | Before ILD Diagnosis *N* (%) | Post ILD diagnosis *N* (%) | *P*-value [§] |
|---|---|---|---|
| Prednisolone use | 19 (35.8%) | 18 (35.3%) | 1.000 |
| Methotrexate | 27 (50.9%) | 14 (28.0%) | **0.002** ** |
| Other csDMARDs | 22 (41.5%) | 25 (49.0%) | 0.742 |
| bDMARDs | | | |
| • Anti-TNF | 07 (13.0%) | 09 (17.6%) | 0.485 |
| • Non-TNF | 11 (20.8%) | 10 (19.6%) | 0.742 |
| tsDMARDs | 07 (13.0%) | 14 (27.5%) | 0.051 |
| Rituximab | 07 (13.0%) | 10 (20.0%) | 0.322 |
| Cyclophosphamide | 01 (01.9%) | -- | -- |
| Anti-fibrotic | -- | 04 (07.8%) | -- |

csDMARDs- conventional synthetic disease-modifying antirheumatic drugs; bDMARDs- biologic disease-modifying antirheumatic drugs; tsDMARDs- targeted synthetic disease-modifying antirheumatic drugs

[§] *P*-value has been calculated using paired sample t-test

** Significant at $p < 0.05$ level

study were treated with anti-fibrotics; two received nintedanib, and the other two received pirfenidone.

Limitations of our study include its retrospective design, missing data, and selection bias. Nevertheless, our study is the first to explore RA-ILD in Saudi patients. It paves the way for a more extensive nationwide study to confirm our findings and explore genetic risk factors and long-term treatment outcomes. Currently, we are working on a second paper studying the physiological, radiological, mortality, and morbidity of RA-ILD in the Saudi population.

## Conclusion

The most common pattern of ILD in the Saudi population with RA was NSIP, followed by UIP and OP. Diabetes, hypertension, ischemic heart disease, and osteoarthritis were the common comorbidities associated with RA-ILD patients. All patients were observed to have restrictive spirometry patterns.

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**Author contributions**
AMB, MAA, HMA, and FAA have contributed substantially to conceptualization and methodology. RGA, KGB, and NYA have made a substantial contribution to both investigation and data collection. MMI, NNA, EHA, and NHA have made substantial contributions to review images. AMB has made a substantial contribution to writing the original draft. MMI and MAO have made a substantial contribution to reviewing & editing the manuscript. All authors have given final approval for the version to be published.

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**Data availability**
Data of the study are available upon request to the corresponding author.

## Declarations

**Ethics approval and consent to participate**
This was a retrospective study of patients who had previously been diagnosed and treated in the Departments of Rheumatology and Pulmonology of PSMMC and KSMC, and informed consent was obtained from all subjects and/or their legal guardians. The study was approved by the Ethics Committee of Prince Sultan Military Medical City Scientific Research Center (No. E-2161).

**Consent for publication**
Not applicable.

**Competing interests**
The authors declare no competing interests.

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