

Prevalence and Clinical Characteristics of Rheumatoid Arthritis-Associated Interstitial Lung Disease at Srinagarind Hospital: A Retrospective Cross-sectional Study

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Background: Interstitial lung disease (ILD) is a severe extra-articular manifestation of rheumatoid arthritis (RA) associated with increased mortality. Data characterizing RA-associated ILD (RA-ILD) in Thailand remain limited. This study aimed to estimate the prevalence of clinically recognized, HRCT-confirmed RA-ILD and describe the clinical, serological, radiological, and functional characteristics of affected patients at Srinagarind Hospital.

Methods: We conducted a retrospective cross-sectional study of adult patients with RA who attended Srinagarind Hospital, Khon Kaen University, from 2020 to 2024. RA-ILD was confirmed by high-resolution computed tomography (HRCT). The prevalence of clinically recognized, HRCT-confirmed RA-ILD was calculated using all identified patients with RA as the denominator. Characteristics of patients with RA-ILD were summarized using descriptive statistics.

Results: Among 1,054 patients with RA, 21 had clinically recognized, HRCT-confirmed RA-ILD, corresponding to a prevalence of 2.0% (95% CI 1.3–3.0%). The mean age of patients with RA-ILD was 62.8 ± 10.9 years, 81.0% were female, and 4.8% had a smoking history. Mean RA duration was 13.5 ± 8.9 years, and 76.2% had low disease activity or remission when ILD was identified. All patients were rheumatoid factor positive and had radiographic bone erosion, whereas 47.6% were anti-CCP positive. The usual interstitial pneumonia (UIP) pattern was the most common HRCT finding (52.4%), followed by non-specific interstitial pneumonia (NSIP; 38.1%). FVC impairment was recorded in 81.0%.

Conclusion: Clinically recognized, HRCT-confirmed RA-ILD affected 2.0% of patients with RA at Srinagarind Hospital. Patients with RA-ILD commonly had long-standing RA, RF positivity, radiographic bone erosion, a UIP pattern, and impaired FVC. Because this descriptive study did not include a non-ILD comparison group, the observed characteristics should not be interpreted as independent risk factors.

Keywords: Rheumatoid arthritis; Interstitial lung disease; HRCT; Seropositivity; Bone erosion; Thailand

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Introduction

Rheumatoid arthritis (RA) is a chronic, systemic autoimmune disorder characterized primarily by symmetrical polyarthritis and progressive joint destruction¹, affecting approximately 0.46–1% of the population worldwide.^{2,3} In 2020, the prevalence of seropositive RA in Thailand was 99.2 per 100,000 population, increasing to 127.8 per 100,000 in the Northeastern region.⁴ Beyond its articular hallmark, RA carries a substantial burden of extra-articular disease that drives excess morbidity and mortality. Pulmonary involvement is the most common extra-articular manifestation, occurring in up to 60% of patients over the disease course², and interstitial lung disease (ILD) represents its most severe form. Rheumatoid arthritis-associated ILD (RA-ILD) accounts for an estimated 10–20% of RA-related deaths, and patients with a usual interstitial pneumonia (UIP) pattern on high-resolution computed tomography (HRCT) have a median survival of only 3–7 years — comparable to idiopathic pulmonary fibrosis.^{1,5} Reported RA-ILD prevalence varies widely across the literature (1–58%)⁶, reflecting differences in diagnostic modality, case definition, and screening strategy; recent meta-analyses estimate a global pooled prevalence of roughly 18.7–21.4%^{7,8}, with HRCT-based screening studies consistently yielding higher rates than symptom- or radiograph-based ascertainment.^{6,8} Asian cohorts report a prevalence of approximately 17.8%, though with considerable heterogeneity.⁸ Despite the relatively high prevalence of seropositive RA in Northeastern Thailand, local data on RA-ILD remain limited. A previous single-center study conducted in Bangkok reported an RA-ILD prevalence of 4.5%, suggesting that ethnicity, geography, environmental exposures, and case-ascertainment methods may influence the observed disease burden.³ Established risk factors for RA-ILD include older age, male sex, cigarette smoking (particularly beyond 30 pack-years)^{8–10}, high titers of rheumatoid factor (RF) and anti-cyclic citrullinated peptide antibody (anti-CCP)^{2,8}, and high RA disease activity.^{8,9} These associations point to a pathogenesis driven by both systemic autoimmune inflammation and environmental lung injury. However, most available epidemiological data derive from Western or East Asian¹¹ registries that may not generalize to Southeast Asian populations, and evidence from Northeastern Thailand specifically is lacking. Determining the local prevalence and clinical characteristics of RA-ILD is a necessary first step toward developing context-specific screening strategies.¹² We therefore conducted a retrospective cross-sectional study to estimate the prevalence of clinically recognized, HRCT-confirmed RA-ILD among patients attending Srinagarind Hospital and to describe the demographic, clinical, serological, radiological, and functional characteristics of affected patients.

Methods

Study design and setting

This was a retrospective cross-sectional study conducted at Srinagarind Hospital, a university-affiliated tertiary care center in Khon Kaen, Northeastern Thailand. Data were retrieved from the rheumatology outpatient clinic for patients attending between 2020 and 2024.

Participants

Adult patients (≥18 years) with a documented diagnosis of RA meeting the 2010 ACR/EULAR classification criteria¹³ were identified from the hospital medical record system. Potential RA-ILD cases were identified through review of chest HRCT reports in the radiology database, cross-referenced with the RA patient registry maintained by the Division of Rheumatology. Patients were included in the RA-ILD group if they had at least one chest HRCT demonstrating interstitial abnormality, confirmed on radiologist

re-review, and sufficient medical record data for analysis. Patients were excluded if they had an alternative or overlapping diagnosis better accounting for the interstitial lung disease (idiopathic inflammatory myopathy-associated ILD, mixed connective tissue disease-associated ILD, systemic sclerosis, systemic lupus erythematosus), no confirmed interstitial abnormality on HRCT re-review, active pulmonary infection, pre-existing chronic lung disease not attributable to RA-ILD (e.g., chronic obstructive pulmonary disease with asthma overlap, COPD GOLD stage ≥ 3), heart failure with pulmonary edema, active malignancy within 5 years, or pregnancy at the time of ILD diagnosis.

Definitions

ILD was defined as characteristic interstitial abnormality on HRCT reported by a board-certified radiologist, classified according to the 2022 ATS/ERS/JRS/ALAT criteria¹⁴ as UIP, probable UIP, non-specific interstitial pneumonia (NSIP), organizing pneumonia (OP), or unclassifiable ILD; findings attributable solely to infection, heart failure, or malignancy were excluded. RA-ILD was defined as ILD occurring in a patient meeting RA criteria after exclusion of alternative causes. Disease activity was assessed using the DAS28-ESR and categorized as remission (<2.6), low disease activity ($2.6-3.2$), moderate disease activity ($>3.2-5.1$), or high disease activity (>5.1).^{15,16} For the purposes of this study, FVC impairment was operationally defined as FVC $<80\%$ predicted. Percent-predicted values were calculated using the Global Lung Function Initiative 2012 reference equations for the South East Asian population. The index date was defined as the date of the chest HRCT establishing the diagnosis of RA-ILD. DAS28 and pulmonary function test (PFT) values reported in this study represent the first available measurement obtained after the index HRCT; complete DAS28 and PFT data defined in this way were available for all 21 included patients (100%).¹⁷

Data collection

Clinical data were abstracted from electronic and paper medical records using a structured case-report form covering demographics, smoking history, comorbidities, RA disease duration and activity, respiratory symptoms and signs, serology (RF, anti-CCP), treatment history (DMARDs, biologics, corticosteroids, antifibrotics), HRCT pattern, and pulmonary function. No formal sample size calculation was performed given the retrospective design and the rarity of RA-ILD; all eligible patients identified during the study period were included.

Statistical analysis

Data were analyzed using IBM SPSS Statistics for Windows, Version 28.0 (IBM Corp., Armonk, NY, USA). Continuous variables are presented as mean $\pm$ standard deviation (SD) or median with interquartile range, as appropriate, and categorical variables as frequencies and percentages. The prevalence of clinically recognized, HRCT-confirmed RA-ILD was calculated using the number of identified RA-ILD cases as the numerator and all eligible patients with RA during the study period as the denominator; a 95% confidence interval (CI) was calculated using the Wilson method. No comparative or regression analyses were performed.

Ethical approval

This study did not involve direct patient contact and used only retrospectively collected medical record data. The study protocol was approved by the Khon Kaen University Ethics Committee (approval number HE681620), with institutional permission obtained from Srinagarind Hospital prior to data collection.

Results

Study population

Among 1,054 patients with RA attending Srinagarind Hospital during the study period, 36 were initially identified as having possible RA-ILD through cross-referencing of chest HRCT reports in the radiology database with the RA patient registry. Of these, 15 were subsequently excluded because an alternative or overlapping diagnosis better accounted for the interstitial lung disease (idiopathic inflammatory myopathy-associated ILD or mixed connective tissue disease-associated ILD), because no interstitial abnormality was confirmed on HRCT re-review (RA without ILD), or because of chronic obstructive pulmonary disease with asthma overlap (Figure 1). After exclusions, 21 patients had clinically recognized, HRCT-confirmed RA-ILD, corresponding to a prevalence of 2.0% (95% CI 1.3–3.0%).

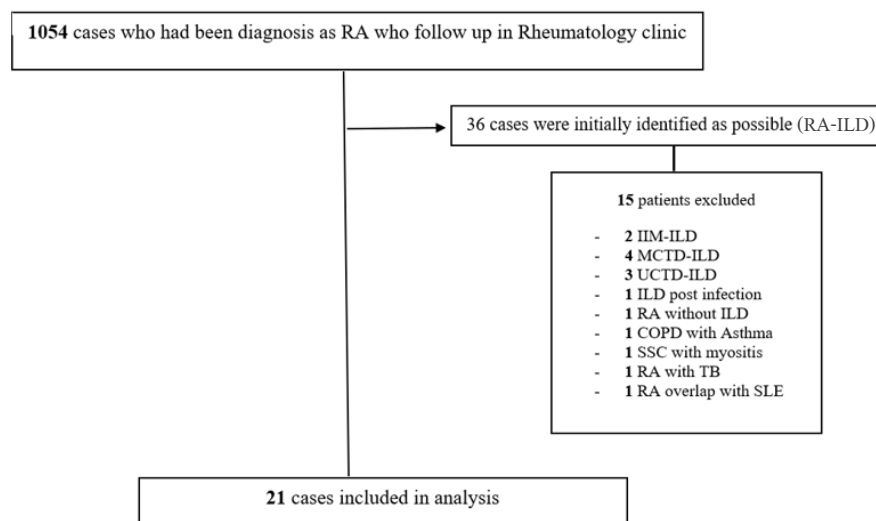


Figure 1 Study flow diagram showing case ascertainment, exclusions, and the final RA-ILD cohort.

Demographic characteristics

The cohort had a mean age of 62.8 ± 10.9 years (range 45–96), with the largest subgroup aged 50–59 years (38.1%). Patients were predominantly female (81.0%), and 95.2% were never-smokers, with only one patient (4.8%) reporting a smoking history (Table 1).

Table 1 Demographic characteristics of patients with RA-ILD

Characteristic	n = 21	%
Age group, years		
<50	2	9.5
50–59	8	38.1
60–69	5	23.8
>70	6	28.6
Sex		
Female	17	81.0
Male	4	19.0
Smoking history		
Never smoker	20	95.2
Former smoker	1	4.8

Clinical characteristics

Mean RA disease duration was 13.5 ± 8.9 years. Despite this long-standing disease, 76.2% of patients had low disease activity (52.4%) or remission (23.8%) by DAS28 at the time ILD was identified, while 19.0% had moderate and 4.8% had high disease activity. Cough was the most common respiratory symptom (81.0%), followed by dyspnea (28.6%) and fatigue (23.8%); lung crackles were audible on auscultation in 66.7% of patients (Table 2).

Table 2 Clinical characteristics, respiratory symptoms, and physical signs

Variable	n = 21	%
RA duration, years (mean $\pm$ SD)	13.5 $\pm$ 8.9	
DAS28 status		
Remission	5	23.8
Low disease activity	11	52.4
Moderate disease activity	4	19.0
High disease activity	1	4.8
Respiratory symptoms		
Cough	17	81.0
Dyspnea	6	28.6
Fatigue	5	23.8
Physical examination		
Lung crackles	14	66.7

Serological and radiological profile

Rheumatoid factor was positive in all 21 patients (100%), and radiographic bone erosion was likewise universal (100%). Anti-CCP antibody was positive in 47.6% of patients (Table 3).

Table 3 Serological and radiographic erosion profile

Variable	n = 21	%
Rheumatoid factor positive	21	100.0
Anti-CCP positive	10	47.6
Radiographic bone erosion present	21	100.0

Treatment exposure

Prednisolone was the most frequently recorded medication (71.4%). Among conventional synthetic DMARDs, sulfasalazine was most common (42.9%), followed by methotrexate (33.3%), cyclosporine (28.6%), leflunomide (23.8%), azathioprine (23.8%), and hydroxychloroquine (14.3%). Other recorded immunosuppressive, biologic, and antifibrotic therapies included mycophenolate mofetil (28.6%), cyclophosphamide (14.3%), rituximab (9.5%), anti-TNF therapy (4.8%), and nintedanib (4.8%). These medications represent any treatment received during the RA disease course up to and including the time of RA-ILD identification; the retrospective dataset did not allow reliable distinction between treatment preceding RA-ILD identification and treatment subsequently initiated for ILD. Percentages exceed 100% because patients could have received more than one treatment (Table 4).

Table 4 Treatment characteristics of patients with RA-ILD

Medication	n = 21	%
Corticosteroid (prednisolone)	15	71.4
Conventional synthetic DMARDs		
Sulfasalazine	9	42.9
Methotrexate	7	33.3
Cyclosporine	6	28.6
Leflunomide	5	23.8
Azathioprine	5	23.8
Hydroxychloroquine	3	14.3
Other immunosuppressive, biologic, and antifibrotic therapies		
Mycophenolate mofetil	6	28.6
Cyclophosphamide	3	14.3
Rituximab	2	9.5
Anti-TNF	1	4.8
Nintedanib	1	4.8

Radiological patterns

HRCT revealed a UIP pattern in 52.4% of patients, an NSIP pattern in 38.1%, and other or mixed patterns in 9.5%; no patient had isolated organizing pneumonia (Table 5).

Table 5 HRCT radiological patterns in RA-ILD

HRCT pattern	n = 21	%
Usual interstitial pneumonia (UIP)	11	52.4
Non-specific interstitial pneumonia (NSIP)	8	38.1
Other / mixed pattern	2	9.5
Organizing pneumonia	0	0.0

Pulmonary function

FVC impairment was present in 81.0% of patients (Table 6). Data on FEV1, FEV1/FVC ratio, and DLCO were not consistently recorded in this retrospective cohort and are not reported.

Table 6 Pulmonary function characteristics (FVC impairment)

FVC status	n = 21	%
FVC impairment present	17	81.0
FVC impairment absent	4	19.0

Discussion

This study characterizes the prevalence and clinical profile of RA-ILD among patients at a major tertiary referral center in Northeastern Thailand. Patients with RA-ILD in this population commonly had a long-standing, seropositive, and erosive disease phenotype, occurring largely independent of smoking.

Prevalence of ILD among RA patients

The prevalence of clinically recognized, HRCT-confirmed RA-ILD in our cohort was 2.0% (21/1,054), lower than global pooled estimates of 18.7–21.4% and the 17.8% reported for Asian populations, most of which derive from systematically screened cohorts^{7,8}, and somewhat below the 4.5% previously reported at Siriraj Hospital in Bangkok.³ This discrepancy likely reflects our retrospective design, which captured only clinically apparent cases identified by symptom-triggered HRCT rather than systematic screening; studies using universal HRCT screening report substantially higher rates, up to 40%, by detecting subclinical disease.^{2,18} This suggests the true burden of RA-ILD in Thai patients may be underestimated and supports a more proactive screening approach.

Demographic, clinical, and serological characteristics

All patients with RA-ILD in this cohort were RF positive and had radiographic bone erosion, whereas 47.6% were anti-CCP positive. Previous studies have reported associations between autoantibodies and pulmonary involvement. One proposed mechanism is a “mucosal origin” hypothesis, whereby environmental or genetic lung injury promotes protein citrullination and generates neoantigens that trigger autoantibody production before articular symptoms emerge.^{2,19} However, because the present study did not include patients with RA without ILD as a comparison group, it cannot determine whether RF positivity or bone erosion independently increases the risk of ILD.

Radiological and pulmonary function characteristics

UIP was the predominant HRCT pattern (52.4%), consistent with global reports identifying UIP as a common RA-ILD phenotype, although this contrasts with a prior Thai cohort in which NSIP predominated (69.2%).³ FVC impairment was recorded in 81.0% of patients. This finding demonstrates substantial physiological involvement among recognized cases, although this descriptive cross-sectional study does not itself evaluate the utility of pulmonary function testing as a screening or monitoring strategy.

RA disease activity, duration, and treatment

Patients had long-standing RA (mean 13.5 years), and 76.2% were in low disease activity or remission when ILD was identified. Although high RA disease activity has been associated with incident RA-ILD, the cross-sectional data in this study do not establish whether ILD developed or progressed while articular disease was controlled. Prednisolone was the most frequently recorded agent (71.4%), and sulfasalazine was the most frequently recorded conventional DMARD (42.9%), followed by methotrexate (33.3%). Contemporary studies indicate that methotrexate is not associated with chronic fibrotic RA-ILD

and may delay its onset.^{20,21} Several patients had received immunosuppressive or biologic therapies, including mycophenolate mofetil, cyclophosphamide, rituximab, or anti-TNF therapy. Because treatment timing and indication were not analyzed, these data should be interpreted as treatment exposure rather than comparative effectiveness.

Clinical implications

The predominance of UIP and the frequent FVC impairment in this cohort emphasize the need for careful pulmonary assessment and follow-up after RA-ILD has been identified. Whether RF positivity or erosive disease can be used to select asymptomatic patients for HRCT screening requires confirmation in comparative prospective studies.

Strengths and limitations

This study provides real-world data from a tertiary academic center in Thailand, using a large denominator of patients with RA (N = 1,054). All identified RA-ILD cases were confirmed by HRCT, and serological, joint-imaging, HRCT, and pulmonary-function data allowed a multidimensional description of the recognized cases.

Several limitations should be noted. The retrospective, single-center design relied on the completeness of historical records; quantitative DLCO values and some disease-activity scores were not consistently available. The small number of RA-ILD cases (n = 21), together with the absence of a non-ILD comparison group, precluded analysis of factors associated with RA-ILD. The tertiary referral setting may have introduced selection bias toward more severe or symptomatic disease, limiting generalizability. Because HRCT was performed on clinical suspicion rather than as universal screening, subclinical RA-ILD was likely underestimated. The cross-sectional design also precluded causal inference and assessment of longitudinal disease course. Finally, nintedanib use was recorded in only one patient. Because longitudinal physiological and radiological progression was not systematically assessed, this study could not determine the frequency of progressive pulmonary fibrosis or evaluate treatment effectiveness.

Conclusion

Clinically recognized, HRCT-confirmed RA-ILD was identified in 2.0% of patients with RA at Srinagarind Hospital. The affected patients commonly had long-standing RA, RF positivity, radiographic bone erosion, a UIP pattern on HRCT, and impaired FVC. These findings describe the phenotype of recognized RA-ILD at this center but do not establish independent risk factors. Comparative and prospective studies are needed to define locally relevant screening strategies and longitudinal outcomes.

Declarations

- **Ethics approval and consent to participate:** This study was approved by the Khon Kaen University Ethics Committee (approval number HE681620). As a retrospective medical record review with no direct patient contact, the ethics committee waived the requirement for individual informed consent.
- **Consent for publication:** Not applicable.

- **Availability of data and materials:** The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.
- **Competing interests:** The authors declare that they have no competing interests.
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- **Authors' contributions:** AK conceived the study, collected and analyzed data, and drafted the manuscript. AM contributed to study design, methodology, and manuscript revision. SS, CF, PP, and TO contributed to patient identification, clinical data interpretation, and critical revision of the manuscript. All authors read and approved the final manuscript.
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