JOURNAL OF HEALTHCARE SCIENCES

Volume 5 Issue 12 2025, Article ID: JOHS2025001107

http://dx.doi.org/10.52533/JOHS.2025.51215

e-ISSN: 1658-8967

Review

Silent Interstitial Lung Disease in Early Autoimmune Disorders: A Systematic Review

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Received: 29 September 2025, Accepted: 18 December 2025, Published: 22 December 2025.

Abstract

Silent or subclinical interstitial lung disease (ILD) is increasingly recognized in patients with early-stage autoimmune disorders, often preceding clinically apparent symptoms. While ILD is a well-documented complication of systemic autoimmune diseases such as rheumatoid arthritis (RA), systemic sclerosis (SSc), and idiopathic inflammatory myopathies (IIM), its asymptomatic form remains underdiagnosed and poorly characterized. This systematic review aimed to systematically review and synthesize current evidence on the prevalence, diagnostic features, radiologic and pulmonary function findings, associated risk factors, and clinical implications of silent ILD in patients with early autoimmune diseases. Following PRISMA guidelines, a comprehensive literature search was conducted across PubMed, ScienceDirect, Scopus, and Web of Science databases from 2014 to 2025. Studies were included if they investigated asymptomatic ILD in patients diagnosed with autoimmune disease within five years, using high-resolution computed tomography (HRCT) or pulmonary function tests (PFTs). Quality assessment was conducted using the Newcastle-Ottawa Scale (NOS). Nine studies met the inclusion criteria, with reported prevalence of silent ILD ranging from 1.9% to 19.3%. HRCT frequently revealed subpleural fibrosis, traction bronchiectasis, and usual interstitial pneumonia (UIP) patterns in asymptomatic patients. Diffusing capacity of the lungs for carbon monoxide (DLCO) was consistently reduced, even when spirometry values remained within normal ranges, indicating early alveolar-capillary dysfunction. Subpleural distribution and fibrotic HRCT patterns were associated with higher progression risk. Despite the absence of symptoms, many patients exhibited structural and functional evidence of early lung involvement. Silent ILD is a prevalent and clinically significant manifestation in early autoimmune disease, often detectable only through imaging and gas exchange testing. Its presence correlates with radiologic patterns predictive of disease progression, underscoring the need for routine screening in high-risk populations. Standardized diagnostic criteria and prospective studies are urgently needed to guide early identification, monitoring strategies, and intervention timing to mitigate long-term pulmonary complications.

Keywords: *Silent ILD, subclinical ILD, autoimmune disease, rheumatoid arthritis, systemic sclerosis, interstitial lung abnormalities, early detection*

Introduction

Interstitial lung diseases (ILDs) are a group of conditions that primarily affect the lung parenchyma. Their development, symptoms, and prognosis vary widely depending on the specific underlying cause (1).

ILDs represent a broad and diverse category of lung disorders that affect the lung parenchyma. This group includes both idiopathic interstitial pneumonias (IIPs), which have no identifiable cause, and ILDs linked to underlying diseases or environmental exposures. Among these, idiopathic pulmonary fibrosis (IPF) is the most thoroughly researched subtype. IPF primarily affects individuals over the age of 60 and is marked by progressive lung scarring, deteriorating respiratory function, and a high mortality rate (2, 3).

A multidisciplinary task force from the American Thoracic Society (ATS) and the European Respiratory Society (ERS) recently introduced an updated classification system for ILDs, which incorporates clinical, imaging, and histopathological characteristics (4). The frequency and progression of ILDs differ significantly based on the disease subtype. For instance, in the United States, IPF has an estimated incidence of 6.8 to 16.3 cases per 100,000 person-years (5) and becomes more common with increasing age. The median survival following an IPF diagnosis ranges between 2 and 5 years. Conversely, cryptogenic organizing pneumonia is less common, with an annual incidence of approximately 2.0 per 100,000 person-years and has a longer median survival of about 8 years from diagnosis (6, 7).

ILD frequently occurs in individuals with systemic autoimmune conditions and is a major contributor to mortality in this population. In some cases, autoimmune-related ILD progresses to a fibrosing phenotype, marked by increased fibrosis visible on high-resolution computed tomography (HRCT), declining lung function, and a heightened risk of early death (8). Although the clinical progression of autoimmune ILD varies among patients, with some not needing immediate therapy, all affected individuals must be regularly monitored for signs of disease progression (9).

Symptoms such as cough, shortness of breath (dyspnea), and fatigue, common in ILD, can significantly reduce the quality of life for individuals with systemic autoimmune disorders. In a survey conducted at a U.S. center involving 50 patients with rheumatoid arthritis-associated ILD (RA-ILD), it was found that fatigue and dyspnea were the most influential factors contributing to declines in physical health. Additionally, the combination of cough, fatigue, and dyspnea was identified as the most significant predictor of reduced mental health (10).

The unexpected identification of early-stage ILD has given rise to the term interstitial lung abnormalities (ILA) or silent, preclinical or subclinical ILD, a radiologic classification referring to incidental findings on HRCT scans that involve more than 5% of any lung zone. Recently, two key publications have updated the definition of ILA and emphasized the importance of monitoring individuals with these findings, particularly those at higher risk of disease progression (11).

While ILD is a known complication of systemic autoimmune disorders, the silent or asymptomatic form, often detectable only by imaging or pulmonary function tests, remains under-recognized, especially in the early stages of disease. Existing studies primarily focus on clinically evident ILD, with limited attention to subclinical or incidentally detected cases. There is a lack of consolidated evidence regarding the prevalence, diagnostic methods, risk of progression, and clinical outcomes of silent ILD in early autoimmune disorders.

The current systematic review aimed to systematically review and synthesize current evidence on the prevalence, radiologic and functional diagnostic criteria, associated risk factors, and clinical outcomes of silent ILD in individuals with early autoimmune diseases, to guide early detection and management strategies.

http://dx.doi.org/10.52533/JOHS.2025.51215

Material and methods

The systematic review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Definition of outcomes and inclusion criteria

The prevalence of silent ILD was the primary outcome of interest. Secondary outcomes included radiologic and functional diagnostic characteristics, associated risk factors, and clinical outcomes of silent ILD. Radiologic outcomes comprised HRCT findings, including the presence of fibrotic and non-fibrotic abnormalities, specific imaging features, and HRCT patterns such as usual interstitial pneumonia (UIP), probable UIP, indeterminate UIP, non-specific interstitial pneumonia (NSIP), or mixed patterns. Functional outcomes included pulmonary function test parameters, such as forced vital capacity (FVC), forced expiratory volume in one second (FEV1), FEV1/FVC ratio, diffusing capacity of the lung for carbon monoxide (DLCO), and other reported spirometric indices.

Furthermore, we identified markers linked to disease occurrence or advancement, encompassing inflammatory and hematologic indices, autoantibody status, and oxygenation metrics when accessible.

Studies were included in this systematic review if they met the following criteria: (1) original research articles, including observational cohort studies, case-control studies, and cross-sectional studies; (2) studies involving patients with early-stage autoimmune diseases such as rheumatoid arthritis (RA), systemic sclerosis (SSc), or idiopathic inflammatory myopathies (IIM); (3) studies specifically addressing the presence of silent or asymptomatic ILD identified via HRCT or pulmonary function tests (PFTs); and (4) articles published in peer-reviewed journals in English. Early autoimmune disease was defined as within five years of symptom onset or diagnosis, as specified by the study authors.

Exclusion criteria included: (1) case reports, conference abstracts, editorials, reviews, or expert opinions; (2) studies focusing on symptomatic ILD or advanced stages of autoimmune diseases; (3) studies involving pediatric populations or non-autoimmune-related causes of ILD; (4) animal studies or in vitro experiments; and (5) non-English language publications. Studies that did not clearly distinguish between symptomatic and silent ILD or failed to provide specific diagnostic criteria for ILD were also excluded.

Search Strategy

A comprehensive literature search was conducted in the following electronic databases: PubMed, ScienceDirect, Scopus, and Web of Science, from inception through [2014-2025]. The search strategy combined terms related to autoimmune diseases, interstitial lung disease, and asymptomatic presentations. Key search terms included: (“interstitial lung disease” OR “ILD”) AND (“asymptomatic” OR “silent” OR “subclinical” OR “preclinical”) AND (“autoimmune disease” OR “connective tissue disease” OR “systemic sclerosis” OR “rheumatoid arthritis” OR “inflammatory myopathy”). Medical Subject Headings (MeSH) terms and synonyms were used to maximize sensitivity.

Screening and extraction

Articles with irrelevant titles were excluded from consideration. In the subsequent phase, both the full text and abstracts of the papers were meticulously reviewed to determine their compliance with the inclusion criteria. To streamline the process, titles and abstracts were organized, assessed, and scrutinized for any duplicate entries using reference management software (EndNote X8). To ensure the highest quality of selection, a dual screening approach was adopted, involving one screening for the evaluation of titles and abstracts, and another for the comprehensive examination of the entire texts. Once all relevant articles were identified, a structured extraction sheet was created to capture pertinent information aligned with our specific objectives. Two separate researchers conducted the data extraction process independently. The gathered information included various study attributes like the author's name, publication year, country of origin, study design, sample size, participants' age

http://dx.doi.org/10.52533/JOHS.2025.51215

and gender, adherence rates, symptom control, asthma exacerbations, and healthcare costs.

Quality Assessment

In our systematic review, we employed the Newcastle-Ottawa Scale (NOS) as a critical tool for assessing the quality of non-randomized studies included in our analysis. The NOS is widely recognized for its utility in evaluating the methodological quality and risk of bias in observational studies, including cohort and case-control studies. It provides a structured framework for evaluating key aspects of study design, including selection of study groups, comparability, and ascertainment of outcomes.

Results

Search Results

We executed the search methodologies outlined previously, resulting in the identification of a total of 441 citations, subsequently reduced to 318 following the removal of duplicates. Upon screening titles and abstracts, only 122 citations met the eligibility criteria for further consideration. Through full-text screening, this number was further refined to 9 articles aligning with our inclusion and exclusion criteria (12-20). **Figure 1** provides an in-depth depiction of the search strategy and screening process.

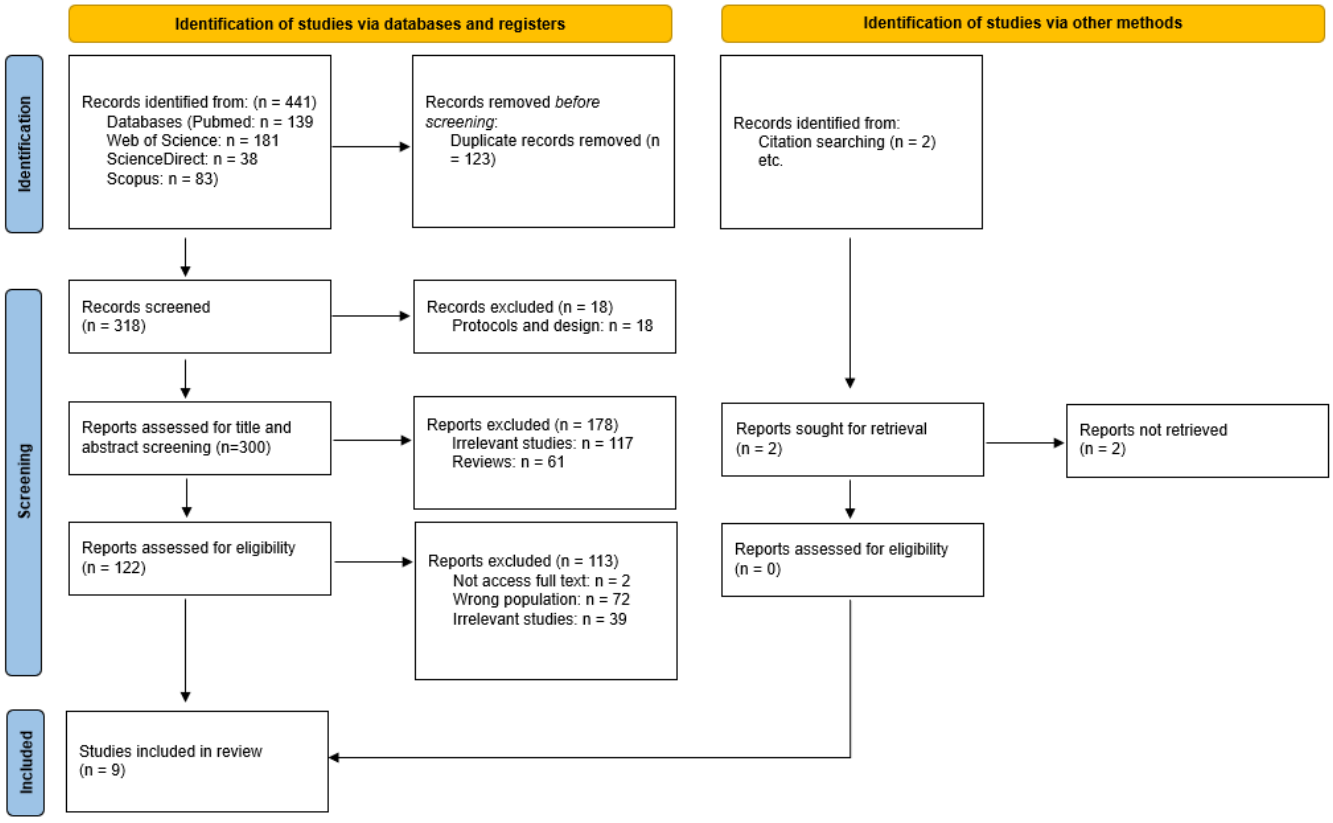

Figure 1: PRISMA Flowchart

Results of Quality Assessment

The methodological quality of six retrospective cohort studies was assessed using the NOS, a standardized tool for evaluating non-randomized studies based on three key domains: selection of study groups, comparability of cohorts, and outcome assessment. Across the studies, most criteria were consistently met, indicating generally strong study designs.

Roca et al. (2017) (13), Kawano-Dourado et al. (2020) (14), Lin et al. (2022) (12), and Chai et al. (2023) (19) met all or nearly all NOS criteria,

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reflecting high levels of methodological rigor. Notably, Lin et al. (12) and Chai et al. (19) were awarded two stars in the comparability domain, highlighting their strong control of potential confounding variables. Yamakawa et al. (2019) (18) lacked a star for the selection of the non-exposed cohort, suggesting a possible source of selection bias. Mori et al. (2025) (17) fulfilled most quality criteria but did not receive a star for the adequacy of follow-up, which may indicate limitations in follow-up completeness or duration.

Overall, the consistent fulfillment of NOS criteria across these studies supports their reliability and strengthens the validity of their conclusions within retrospective cohort research **(Table 1).**

The methodological quality of three cross-sectional studies was evaluated using the NOS adapted for cross-sectional designs. This version of the NOS assesses studies across three domains: selection of participants, comparability (control of confounding factors), and outcome assessment. Each domain includes several criteria, with a maximum total score of 10 stars.

All three studies: Mohanty et al. (2019) (16), Paulin et al. (2021) (15), and Palalane et al. (2022) (20), achieved moderate to high-quality ratings. Paulin et al. (15) and Palalane et al. (20) both received 8 out of 10 stars, reflecting strong methodological practices, particularly in controlling for confounding variables and robust outcome assessment. In contrast, Mohanty et al. (16) received a total of 6 stars. While it met the criteria for representativeness, exposure ascertainment, outcome assessment, and use of appropriate statistical tests, it lacked points for sample size justification, response rate reporting, and adjustment for confounding factors, which may affect the study's internal validity.

Overall, while all studies demonstrated acceptable quality, those by Paulin and Palalane stand out for their more comprehensive methodological rigor, especially in accounting for confounders and applying reliable outcome assessment methods **(Table 2)**.

Table 1: Quality assessment of Newcastle–Ottawa scale (NOS) for retrospective cohort studies

Study	Year	Representativeness of the exposed cohort (★)	Selection of the non-exposed cohort (★)	Ascertainment of exposure (★)	Demonstration that outcome of interest was not present at start of study (★)	Comparability of cohorts based on the design or analysis (max★★)	Assessment of outcome (★)	Was follow-up long enough for outcomes to occur? (★)	Adequacy of follow up of cohorts (★)
Roca et al., 2016 (13)	2017	★	★	★	★	★	★	★	★
Yamakawa et al., (18)	2019	★	-	★	★	★	★	★	★
Kawano-Dourado et al., (14)	2020	★	★	★	★	★	★	★	★
Lin et al., (12)	2022	★	★	★	★	★★	★	★	★
Chai et al., (19)	2023	★	★	★	★	★★	★	★	★
Mori et al., (17)	2025	★	★	★	★	★★	★	★	

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Table 2: Quality assessment of Newcastle–Ottawa scale (NOS) for cross-sectional studies

Study	Year	Selection				Comparability	Outcome		Total
		Representativeness of sample (★)	Sample size (★)	Non respondents (★)	Ascertainment of exposure (★★)	Confounding factors controlled (max★★)	Assessment of outcome (★★)	Statistical test (★)	
Mohanty et al., 2019 (16)	2019	★	-	-	★★	-	★★	★	6
Paulin et al., 2021 (15)	2021	★	-	-	★★	★★	★★	★	8
Palalane, et al., (20)	2022	★	-	-	★★	★★	★★	★	8

Demographic characteristics of the included studies

This systematic review included nine studies spanning a range of countries, study designs, and patient populations, offering a comprehensive overview of the prevalence and characteristics of subclinical ILD in the context of systemic autoimmune disorders **(Table 3)**.

The majority of studies were retrospective in design, with only a few employing cross-sectional methodologies. These studies were conducted across diverse geographic locations, including France, Japan, China, India, Brazil, and South Africa, reflecting a global interest in the early detection of ILD among patients with autoimmune conditions.

Participant numbers varied widely from as few as 72 (Mohanty et al., 2019) (16) to as many as 781 (Mori et al., 2025) (17), with mean or median ages typically in the middle-aged to elderly range. Notably, there was a consistent predominance of female participants across all studies, aligning with the known gender distribution of systemic autoimmune diseases such as rheumatoid arthritis (RA) and Sjögren's syndrome (SS).

The autoimmune diagnoses investigated were primarily RA, but also included primary Sjögren's syndrome (pSS), systemic sclerosis (SSc), and other connective tissue diseases (OCTD). Several studies, such as those by Kawano-Dourado et al. (14) and Lin et al., (12) provided focused insights into ILD or ILA among these populations. For instance, Kawano-Dourado et al. (2020) (14) provided stratified data comparing patients with ILA/ILD, no ILA, and indeterminate ILA, offering a nuanced view of disease presence and progression.

http://dx.doi.org/10.52533/JOHS.2025.51215

Table 3: Baseline characteristics of included studies

Study	Country	Published Year	Study Period	Study Design	Total Participants	Mean/median age of total participants (Years)	Gender (M/F) %	Diagnosis Of Systemic Autoimmune Disorders
Roca et al., 2016 (13)	France	2017	1996-2012	Retrospective	263	63	11.98 %/88.02%	SS
Mohanty et al., 2019 (16)	India	2019	NR	Descriptive cross sectional	72	37.5	76.39 %/23.61%	RA
Yamakawa et al., 2019 (18)	Japan	2019	2012 -2017	Retrospective cohort	96	69.0±10.3	39%/61%	RA
Kawano-Dourado et al., 2020 (14)	Brazil	2020	2014 – 2016	Retrospective	Total=293, ILA/ILD =64 No ILA=204 Indeterminate ILA=25	ILA/ILD =65.6± 9.9 No ILA= 59.5 ±10.9	17.54 %/82.46%	RA
Paulin et al., 2021 (15)	NR	2021	2017-2020	Cross-sectional	83	46.49 ±17.09	83%/17%	RA
Lin et al., 2022 (12)	China	2022	2016-2019	Retrospective	333	54	6.91%/ 93.09 %	pSS
Palalane et al., 2022 (20)	South Africa	2022	2018-2019	Cross-sectional	124	45	13.7% /86.3%	RA, SSc, OCTD
Chai et al., 2023 (19)	China	2023	2017-2021	Retrospective cohort	371	62	30.7%/ 69.3%	RA
Mori et al., 2025 (17)	Japan	2025	2001-2023	Retrospective	781	63.2 ±12.8	25.9%/ 74.1%	RA

NR: not reported; SS: Sjogren's syndrome; pSS: primary Sjogren's syndrome; RA: rheumatoid arthritis; SSc: systemic sclerosis; OCTD = other connective tissue diseases

Outcomes within the included studies

The included studies assessed the prevalence of silent ILD, radiologic and functional diagnostic characteristics, associated risk factors, and clinical outcomes of silent ILD **(Table 4)**.

The prevalence of silent ILD in patients with autoimmune disorders

The prevalence of silent ILD in patients with autoimmune disorders varies considerably across studies, ranging from as low as 1.9% to as high as 19.3%. For instance, Chai et al. (2023) (19) reported the highest prevalence at 19.3%, indicating that nearly one in five individuals with autoimmune disease may develop ILD. In contrast, Roca et al. (2016) (13) found a much lower prevalence of only 1.9%. Several other studies, including those by Lin et al. (2022) (12), Kawano-Dourado et al. (2020) (14), Paulin et al. (2021) (15), Mohanty et al. (2019) (16), Mori et al. (2025) (17), and Palalane et al. (2022) (20), reported ILD prevalence between approximately 7% and 11%, suggesting a consistent moderate presence of ILD in this population. Notably, Yamakawa et al. (2019) (18) observed that more than half of the 96 patients with ILD were asymptomatic, emphasizing the silent nature of ILD in many autoimmune cases. These findings highlight not only the variable but potentially underestimated burden of ILD in autoimmune diseases, especially in its subclinical form, thereby

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underlining the importance of early detection and monitoring in at-risk patients.

Pulmonary functions in silent ILD patients with autoimmune disorders

Pulmonary function data were reported in two studies, with most lacking detailed respiratory assessments. Mori et al. (2025) (17) provided comprehensive PFT data, showing that among 70 patients with autoimmune-related ILD, the mean FVC was 95.3% of predicted, and the forced expiratory volume in one second (FEV1) was 113.6% of predicted. Interestingly, the FEV1/FVC ratio was notably elevated at 125.5%, which may reflect a restrictive pattern or measurement variability. Maximal mid-expiratory flow (MMF) was reduced to 70.4% of predicted, and diffusing capacity for carbon monoxide (DLCO), a sensitive marker of gas exchange, was moderately impaired at 83.2% of predicted. Chai et al. (2023) (19) similarly reported preserved FVC (103.7±20.1%) but a more pronounced reduction in DLCO (70.7±13.6%), indicating early impairment in alveolar-capillary gas transfer. Additionally, arterial oxygen pressure (PaO2) at rest on room air averaged 84.3 mmHg, suggesting some degree of hypoxemia in certain patients. These findings imply that while spirometric values like FVC and FEV1 may remain within normal limits in early or silent ILD, abnormalities in DLCO and gas exchange may serve as early indicators of pulmonary involvement in autoimmune diseases.

Table 4: Outcomes of included studies

Study	Prevalence of silent ILD n (%)	Pulmonary function	HRCT findings	HRCT pattern	Markers
Lin et al., 2022 (12)	24 (7.21)	-	-	-	-
Kawano-Dourado et al., 2020 (14)	21 (7.17)		Pulmonary indications: Progressors: 3 (50%) Non-progressors: 9 (60%) Non-pulmonary/Other: Progressors: 3 (50%) Non-progressors: 6 (40%	Subpleural pattern: Progressors: 6 (100%) Non-progressors: 8 (53%) P = .06 (borderline association with progression) Centrilobular pattern: Progressors: 0 (0%) Non-progressors: 5 (33%) pattern: Progressors: 0 (0%) Non-progressors: 2 (14%)	-
Paulin et al., 2021 (15)	6 (7.5)	-	-	-	-
Mohanty et al., 2019 (16)	8 (11.1)	-	-	-	-
Mori et al., 2025 (17)	77 (9.86)	FVC, % predicted (n = 70) 95.3 (19.0) FEV1, % predicted (n = 70) 113.6 (12.6) FEV1/FVC ratio (n = 70) 125.5 (35.8) MMF, % predicted (n = 70) 70.4 (30.0)	Honeycombing 39 (50) Traction bronchiectasis 62 (79.5) Emphysema 36 (46.2	Definite UIP pattern 29 (37.2) Probable UIP pattern 14 (17.9) Indeterminate for UIP pattern 26 (33.3) Early UIP 5 (6.4) NSIP/UIP 21 (26.9) NSIP 9 (11.5)	

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		DLCO, % predicted (n = 64) 83.2 (20.3)			
Palalane et al., 2022 (20)	13 (10)	-	-	-	-
Chai et al., 2023 (19)	73 (19.3)	FVC, %predicted 103.7±20.1 DLCO, %predicted 70.7±13.6 PaO2, mmHg (room air, at rest) 84.3(77.0-91.5)	HRCT score: 4.0(3.0-7.5)	Among the 73 patients with RA-pILD: 53.4% had subpleural non-fibrotic abnormalities. Among the progressors RA-pILD: 63.6% (14 out of 22) had subpleural fibrosis. 67.9% (19 out of 28) exhibited a usual interstitial pneumonia (UIP) pattern.	NLR 3.0 (2.0–4.1) MLR 0.3 (0.2–0.4) PLR 143.8 (105.0–211.9) SII 765.0 (378.8–1031.8) SIRI 1.4 (0.8–2.2) AISI 346.7 (122.4–547.6) Anti-CCP positivity, n (%) 64(87.7) Anti-CCP titer, IU/ml 865.6(293.5-2753.5)
Yamakawa et al., 2019 (18)	Over half of the 96 patients with ILD may have experienced the condition without showing any symptoms.	-	-	-	-
Roca et al., 2016 (13)	5 (1.9)	-	-	-	-

HRCT findings

HRCT findings were reported in three studies, yet they provide important insight into the structural lung changes associated with early or silent ILD in autoimmune disorders. Mori et al. (2025) (17) identified key radiologic features, with traction bronchiectasis observed in 79.5% of cases, honeycombing in 50%, and emphysema in 46.2%, reflecting substantial fibrotic and structural abnormalities even in potentially asymptomatic patients. Chai et al. (2023) (19) quantified disease burden using a semi-quantitative HRCT scoring system, reporting a median score of 4.0 (IQR: 3.0–7.5), indicating mild to moderate radiographic involvement. Kawano-Dourado et al. (2020) (14) explored the clinical context of HRCT use, noting that in both progressor and non-progressor groups, CT scans were often initiated for non-pulmonary or

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incidental findings as well as for pulmonary symptoms, highlighting that silent ILD may be detected during evaluations for unrelated issues. These findings underscore the importance of imaging in uncovering subclinical ILD in autoimmune patients and suggest that significant radiographic abnormalities can exist even in the absence of symptoms.

HRCT pattern analysis

HRCT pattern analysis revealed distinct radiologic features associated with disease progression in patients with early or silent ILD related to autoimmune disorders. Kawano-Dourado et al. (2020) (14) reported a subpleural pattern in all progressor patients (100%) compared to 53% in non-progressors, suggesting a borderline association with disease progression (P = .06). In contrast, centrilobular and mixed patterns were observed only among non-progressors, potentially indicating less aggressive disease forms. Mori et al. (2025) (17) provided a more detailed classification of ILD patterns, identifying a definite usual UIP pattern in 37.2% of cases, probable UIP in 17.9%, and indeterminate patterns in 33.3%. Additionally, 6.4% showed early UIP, while NSIP features were found either in isolation (11.5%) or mixed with UIP (26.9%), reflecting significant heterogeneity in radiologic patterns even in pre-symptomatic stages.

Chai et al. (2023) (19) specifically examined patients with rheumatoid arthritis-associated preclinical ILD (RA-pILD), reporting that 53.4% had subpleural, non-fibrotic abnormalities. Among those who progressed, 63.6% had subpleural fibrosis and 67.9% exhibited a UIP pattern, both of which are known to correlate with worse prognosis. Collectively, these findings underscore that subpleural distribution and UIP patterns on HRCT may serve as early radiologic indicators of progression in autoimmune-associated ILD, supporting their role in risk stratification and guiding surveillance strategies.

Discussion

Summary of findings

This comprehensive review consolidates existing knowledge about the frequency, diagnostic characteristics, and clinical ramifications of silent interstitial lung disease in individuals with early-stage autoimmune illnesses. The findings highlight that subclinical or asymptomatic ILD is a very common yet underappreciated presentation in this population, with significant diagnostic and prognostic consequences.

The reported prevalence of silent ILD in patients with autoimmune disorders varied from 1.9% to 19.3%, highlighting the variability of study populations and possible inconsistencies in screening and diagnostic methodologies. Chai et al. (2023) observed a prevalence of 19.3%, indicating that nearly one in five individuals may exhibit subclinical pulmonary disease. Conversely, research conducted by Roca et al. (2016) (13) revealed far lower rates (1.9%), presumably due to variations in imaging thresholds, patient selection criteria, and definitions of "early" autoimmune illness. This diversity raises significant concerns about the underdiagnosis of ILD in asymptomatic individuals. The actual prevalence of silent ILD may be considerably underestimated, as numerous cases are identified unintentionally during HRCT scans conducted for unrelated purposes. This underscores the necessity for proactive screening measures, particularly in patients with established risk factors such as RA, SSc, or ILM. Garrote Corral et al. conducted a systematic review indicating that the prevalence of ILM varies by cohort and study methodology, ranging from 5% to 61%. This prevalence range exceeds our included studies. Their study determined that between 5% and 55% of cases are considered asymptomatic (21). One of the biggest challenges in estimating the incidence and prevalence of ILD is underdiagnosis. The 2020 EULAR guidelines recommend screening for asymptomatic ILD in certain patients, particularly those with systemic sclerosis, myositis, and mixed connective tissue disease (22).

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Prior studies have reported that while FVC is a well-known parameter for ILD severity and progression assessment, the DLCO is more sensitive for detecting early interstitial changes and monitoring progression (23). This aligns with the findings of the present systematic review, which explained that PFTs showed subtle yet clinically meaningful impairments in gas exchange. Specifically, DLCO was often diminished, even in patients with normal or near-normal FVC and FEV1. This indicates that gas transport anomalies may occur prior to evident restrictive deficiencies, acting as an early physiological indicator of interstitial involvement. Mori et al. (2025) (17) and Chai et al. (2023) (19) both reported relatively intact spirometry results with moderately diminished DLCO values, suggesting early impairment of the alveolar-capillary membrane despite maintained lung volumes. Furthermore, evidence of resting hypoxemia was noted, reinforcing the notion of early pulmonary compromise. These findings advocate the use of DLCO and arterial blood gas assessments in the routine monitoring of patients with early autoimmune illness, regardless of symptom presence.

Radiologic imaging, particularly HRCT, was essential in detecting structural problems in asymptomatic cases, even when a person has no respiratory symptoms, which supports the need for early screening in at-risk individuals. For the diagnosis and prognosis, severity assessment, pattern recognition, and therapeutic monitoring of ILD, it is the gold standard imaging method (24). Significant observations, including traction bronchiectasis, subpleural reticulations, honeycombing, and emphysema, were documented in multiple studies, particularly by Mori et al. (2025) (17) and Chai et al. (2023) (19). These alterations, however, are frequently nuanced, signify the onset of early fibrotic remodeling. Furthermore, the examination of HRCT pattern distributions indicated that specific imaging phenotypes, including subpleural fibrosis and UIP pattern, were more prevalent in patients who underwent radiographic or clinical progression. Kawano-Dourado et al. (2020) (14) identified a 100% prevalence of subpleural patterns among progressors, in contrast to 53% in non-progressors, indicating a robust correlation between HRCT patterns and disease progression. These observations endorse the application of HRCT not only as a diagnostic instrument but also as a prognostic tool to discern patients at elevated risk of ILD progression. However, its regular use is considerably restricted because of its high cost, limited availability in non-tertiary healthcare facilities, lengthy wait times in certain places, and ionizing radiation (25).

Clinical implications

The findings of this systematic review carry several significant clinical implications, particularly in the context of early detection, risk stratification, and long-term management of patients with autoimmune disorders who may develop silent or subclinical ILD. Although asymptomatic, silent ILD can precede clinically apparent disease and contribute to irreversible fibrotic changes and compromised pulmonary function. The following key implications should guide future clinical practice: Routine screening in high-risk populations, as one of the most striking findings is the relatively high prevalence of silent ILD in early autoimmune diseases such as RA, SSc, and IIM. The detection of ILD in up to 19.3% of patients, even in the absence of respiratory symptoms, warrants the consideration of routine screening protocols in newly diagnosed autoimmune disease patients, particularly those with established risk factors (e.g., older age, male sex, anti-CCP positivity in RA, or anti-synthetase antibodies in myositis) (26, 27). HRCT and DLCO should be incorporated as part of the baseline workup in selected patients, especially when lung auscultation, serological markers, or clinical history raise suspicion, even if subclinical (28).

Our study findings strengthen the American College of Rheumatology (ACR) 2023 guidelines, which recommend proactive screening and monitoring for ILD in patients with systemic autoimmune rheumatic diseases. The finding emphasizes that this proactive approach is clinically relevant because early detection of subclinical ILD can

http://dx.doi.org/10.52533/JOHS.2025.51215

allow for intervention before the disease progresses to irreversible lung fibrosis (29).

The assumption that asymptomatic ILD may remain non-progressive is not supported by the reviewed data. Structural abnormalities detected on HRCT such as subpleural fibrosis, traction bronchiectasis, and honeycombing can exist well before symptom onset. These radiologic features, particularly when consistent with UIP or when distributed in a subpleural fashion, may predict eventual disease progression and functional decline. This challenges the traditional "watch-and-wait" approach and reinforces the need for early identification and longitudinal monitoring, even in the absence of overt symptoms (30).

Specific HRCT patterns (e.g., definite or probable UIP) are associated with worse outcomes and higher risk of fibrosis progression. Subpleural and fibrotic changes when present at baseline may help identify patients who are likely to benefit from early pulmonary referral, closer surveillance intervals, or preemptive therapeutic strategies. A structured HRCT evaluation using validated scoring systems or radiologic classification frameworks can aid in developing a risk stratification algorithm for clinical use. This can help determine which patients may benefit from closer follow-up or early therapeutic intervention, such as antifibrotics or immunomodulatory therapies (31).

PFTs, particularly DLCO, are sensitive early indicators of subclinical pulmonary involvement and should not be overlooked in patients with autoimmune disease, even when FVC and FEV1 are normal. Abnormal gas exchange or early desaturation on exertion may indicate functional compromise and warrant further imaging or specialist evaluation. Serial PFTs, including DLCO, should be used to track disease trajectory and detect early signs of progression. In practice, a combination of HRCT and DLCO offers complementary insights into structural and functional lung integrity (31, 32).

The complexity of silent ILD detection and management in autoimmune disease necessitates a multidisciplinary approach, involving rheumatologists, pulmonologists, and radiologists. Early engagement with ILD specialists allows for accurate interpretation of subtle imaging findings, appropriate risk stratification, and guidance on monitoring intervals. Multidisciplinary team (MDT) discussions are particularly important in cases where HRCT findings are indeterminate or where clinical decision-making (e.g., initiation of immunosuppression or antifibrotic therapy) may hinge on nuanced interpretation (33).

Although none of the reviewed studies directly addressed therapeutic outcomes in silent ILD, the presence of fibrotic patterns and early functional decline suggests that some patients may benefit from earlier intervention. Current clinical trials and observational data in symptomatic ILD show promise for antifibrotic agents (e.g., nintedanib) in slowing progression, even in non-idiopathic fibrosing ILD. In the future, preemptive treatment strategies for high-risk silent ILD patients may evolve as evidence accumulates. Clinical trials specifically targeting subclinical ILD in autoimmune disease are needed to determine the efficacy, safety, and timing of such interventions (34).

This review also highlights the urgent need for standardized definitions and diagnostic criteria for silent or subclinical ILD. Inconsistent terminology and variable thresholds for imaging abnormalities hinder comparison across studies and limit the development of evidence-based guidelines. Professional societies should work toward consensus criteria that define the extent, distribution, and severity of ILD necessary to warrant the label of “silent” or “subclinical” ILD, and outline evidence-based pathways for management.

Limitations and recommendations

This systematic review, while providing useful insights, is constrained by various constraints that may affect the interpretation and generalizability of its findings. The included studies demonstrated considerable variability in research design, population characteristics, and diagnostic criteria for silent ILD. The discrepancies in the definitions

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of "silent" or "asymptomatic" ILD, along with the absence of uniform imaging or functional criteria, hinder comparability among research. Secondly, the majority of the existing evidence originates from retrospective observational studies characterized by very small sample sizes and restricted geographic variety, potentially introducing selection bias and undermining the reliability of prevalence estimates. Moreover, only a limited number of studies offered longitudinal follow-up data, complicating the determination of the authentic natural history or development patterns of subclinical ILD. The inadequate reporting of pulmonary function metrics and the variable application of HRCT scoring systems further limit the capacity to establish definitive findings on structure-function links. The lack of randomized controlled studies assessing early therapies in this population limits the formulation of evidence-based treatment options.

Based on the existing evidence, multiple clinical and research suggestions may be formulated. Clinicians ought to implement routine screening for ILD in patients with early autoimmune disorders, especially those exhibiting risk factors or serological markers indicative of pulmonary involvement, utilizing HRCT and DLCO as components of the baseline evaluation. Moreover, the establishment of consistent diagnostic criteria and categorization methods for silent ILD is crucial to unify future research and clinical practice. Radiologic characteristics, including subpleural distribution and UIP patterns, along with functional deficits such as diminished DLCO, ought to be integrated into risk stratification models to inform monitoring intervals and treatment choices. Longitudinal cohort studies are necessary to clarify progression rates, discover predictive biomarkers, and assess the long-term effects of early detection. Interventional trials evaluating the timing and efficacy of antifibrotic or immunomodulatory treatments in asymptomatic ILD patients are urgently needed to guide evidence-based therapy choices.

Conclusion

Asymptomatic ILD in the initial stages of autoimmune illnesses constitutes a clinically important yet underappreciated syndrome that may precede symptomatic and progressive lung fibrosis. This comprehensive review highlights the diversity in reported prevalence, the significance of imaging and pulmonary function tests in early diagnosis, and the prognostic impact of particular radiologic patterns. Although some individuals are asymptomatic at the time of diagnosis, structural and functional problems frequently exist, underscoring the necessity for proactive screening and vigilant monitoring. Enhancing early detection, standardizing diagnostic criteria, and conducting targeted research would enable doctors to get a deeper understanding of the natural history of silent ILD and potentially reduce long-term respiratory morbidity and mortality in affected individuals. The amalgamation of diverse knowledge and patient-centered monitoring systems will be essential for progressing care in the developing field of autoimmune pulmonary medicine.

Disclosure

Conflict of interest

There is no conflict of interest.

Funding

No funding.

Ethical consideration

Non applicable.

Data availability

All data are available within the manuscript.

Author contribution

All authors contributed to conceptualizing, data drafting, collection and final writing of the manuscript.

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