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**Clinical spectrum and profile of interstitial lung disease:
an ambispective study from a tertiary center in North India**

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Patient consent for publication: written informed consent was obtained from a legally authorized representative(s) for anonymized patient information to be published in this article. The manuscript does not contain any individual person's data in any form.

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Abstract

Interstitial lung diseases (ILDs) comprise a heterogeneous group of disorders characterized by varying degrees of inflammation and fibrosis, necessitating precise epidemiological characterization. This ambispective observational study evaluated the clinical spectrum and diagnostic distribution of 1201 patients at a tertiary center in North India, utilizing a multidisciplinary discussion (MDD) framework for final diagnostic consensus. The mean age of the cohort was 52.7 (± 13.04) years, with a female predominance of 55.6%. Idiopathic interstitial pneumonia (IIP) was the most prevalent diagnosis (48.8%), followed by connective tissue disease-associated ILD (CTD-ILD; 19.8%) and hypersensitivity pneumonitis (14.6%). Within the IIP subgroup, idiopathic pulmonary fibrosis predominated (49.7%), followed by nonspecific interstitial pneumonia (39.2%). Statistical analysis identified tobacco use as a significant driver for IIP phenotypes (odds ratio: 3.36; 95% confidence interval: 2.37-4.75; $p < 0.01$). Physiological assessment revealed a restrictive ventilatory defect in 83.9% of the cohort. Patients with sarcoidosis (13.4%) exhibited significantly higher functional reserve (mean forced vital capacity %: $74.1 \pm 17.9\%$) compared to more fibrotic subtypes ($p < 0.01$), and demonstrated superior exercise capacity (mean 6-minute walk distance: 392.4 ± 85.6 m vs. 347.7 ± 90.1 m in CTD-ILD; $p < 0.01$). These findings establish that fibrotic IIPs constitute the primary disease burden in North India, highlighting the clinical necessity of standardized, MDD-based pathways to ensure accurate phenotype differentiation and timely initiation of targeted therapies in a region characterized by complex environmental triggers.

Key words: IPF, ambispective, ILD registry, multidisciplinary discussion.

Introduction

Interstitial lung diseases (ILDs) comprise a heterogeneous group of diffuse parenchymal lung diseases characterized by varying degrees of inflammation and fibrosis. These conditions may be associated with known underlying diseases, environmental triggers, or a lack of any discernible cause, posing significant diagnostic and therapeutic challenges to clinicians. A majority of these disorders are defined by progressively worsening fibrosis and are associated with substantial morbidity and mortality despite the implementation of contemporary standard-of-care therapies [1]. Consequently, accurate differentiation between ILD subtypes is imperative, as risk factors, etiology, therapeutic requirements, and clinical outcomes vary considerably across the disease spectrum.

Multiple international studies have characterized the prevalence and relative frequency of ILDs. Regrettably, many of these historical reports failed to utilize the updated classification system proposed in the 2002 ATS/ERS consensus statement and its 2013 revision [2]. Furthermore, much of the existing global research originates from industrialized nations, which may differ markedly from developing countries regarding genetic susceptibility, environmental pollutants, occupational hazards, smoking prevalence, and traditional agricultural practices.

India, and particularly North India, presents a unique epidemiological landscape shaped by distinct climatic conditions, high biomass fuel exposure, and specific industrial or agricultural environments, alongside restricted diagnostic accessibility. Although several studies have explored the clinical spectrum of ILD in India, results remain inconsistent and often contradictory, particularly regarding the distribution of specific subtypes. Given these ambiguities, there is a clear necessity for rigorous regional epidemiological data to better define the characteristics of ILD in this population. By providing a comprehensive assessment of ILD subtypes and associated risk factors within a tertiary care setting, this study seeks to address these existing knowledge gaps.

Materials and Methods

Study setting and design

This investigation was conducted at the Department of Pulmonary, Critical Care, and Sleep Medicine at the All India Institute of Medical Sciences (AIIMS) in New Delhi, India. The study followed an ambispective observational design, incorporating all patients diagnosed with interstitial lung disease (ILD) who attended the specialized tertiary ILD clinic. Prospective recruitment occurred between October 2019 and July 2021, while retrospective data were meticulously extracted from institutional medical record files covering the period from January 2015 to September 2019. The study protocol received

approval from the Institute's Ethics Committee (IECPG-586/24.10.2019), and written informed consent was obtained from all prospectively enrolled participants or their legal guardians.

Patient selection criteria

Adult patients aged 18 years or older presenting with clinical symptoms and a computed tomography (CT) diagnosis of diffuse parenchymal lung disease (DPLD) were eligible for inclusion. We strictly excluded individuals with alternative diagnoses that could mimic ILD features, such as active pulmonary infections, tuberculosis, or malignancy. All participants exhibited a clinical history consistent with ILD, primarily characterized by chronic non-productive cough and exertional breathlessness.

Diagnostic protocol and evaluation

Radiological assessment involved high-resolution computed tomography (HRCT) of the chest, interpreted according to the 2013 ATS/ERS consensus statement on idiopathic interstitial pneumonias (IIP). Standardized biochemical evaluations, including rheumatoid factor, antinuclear antibody (ANA), antineutrophil cytoplasmic antibodies (ANCA), and extractable nuclear antigen (ENA) profiles, were performed to identify connective tissue diseases (CTD) and other secondary etiologies. Comprehensive imaging data from both chest X-rays and HRCT were documented for each patient. Final diagnoses were established through collaborative clinical and radiological review in accordance with the 2013 international guidelines.

If a definitive diagnosis could not be reached via non-invasive means, every effort was made to secure a histopathological diagnosis [3-5]. Depending on clinical indication and patient fitness, bronchoscopic procedures—including bronchoalveolar lavage (BAL), transbronchial needle aspiration (TBNA), transbronchial lung biopsy (TBLB), or cryobiopsy—were utilized, with surgical lung biopsy reserved for selected cases following established protocols. These findings were then integrated into a formal multidisciplinary discussion (MDD) involving expert pulmonologists, dedicated thoracic radiologists, and specialized pathologists. Sarcoidosis was diagnosed based on consistent clinico-radiological patterns and the identification of non-caseating granulomatous inflammation after excluding alternate causes like tuberculosis. In the absence of tissue specimens, the MDD utilized HRCT findings and ancillary tests, such as serum ACE levels or specific auto-antibodies. Cases failing to meet specific diagnostic criteria despite comprehensive evaluation were categorized as unclassifiable ILD.

Detailed clinical histories were recorded, including demographics, smoking status, and various occupational or environmental exposures. Physical examinations and anthropometric measurements were systematically documented using a standardized proforma. Patients underwent thorough physiological testing, encompassing spirometry, diffusion capacity for carbon monoxide (DLCO), and a 6-minute walk test (6MWT).

Statistical analysis

Study data were managed using Microsoft Excel and subjected to rigorous quality control to minimize entry errors. Categorical variables are presented as frequencies and percentages. Continuous variables are expressed as mean (\pm SD) or median (range) depending on the normality of distribution. Fisher's exact test was employed for categorical comparisons, while Student's t-test or Wilcoxon rank-sum tests were used for two-group comparisons of means or medians, respectively. Analysis of variance (ANOVA) or Kruskal-Wallis tests were utilized for multigroup comparisons. Statistical analyses were performed using Stata version 14.0, with a p-value of <0.05 considered statistically significant. Missing values in physiological data were addressed using a complete case analysis approach to ensure the integrity of functional correlations.

Results

A total of 1,201 patients were finalized for inclusion in this study, comprising 1,008 retrospective and 193 prospective subjects. The comprehensive pathway for screening, referral, and enrollment is delineated in the STROBE flow diagram (Figure 1). The cohort's mean age was 52.7 (\pm 13.04) years (range: 18–90 years). Age distribution analysis revealed that 53.0% of the cohort belonged to the 46–65 years age group, followed by the 26–45 years category (26.7%). A female predominance was noted, accounting for 668 (55.6%) of the total subjects. Regarding tobacco use, 244 (20.3%) patients had a history of smoking; of these, 46.7% were bidi smokers and 36.1% used cigarettes. The comorbidity profile showed that 59.4% of patients had no underlying chronic conditions. Among those with comorbidities, systemic hypertension predominated followed by diabetes mellitus. The hallmark clinical presentations were cough (84.7%) and exertional dyspnea (78.1%). Sputum expectoration and hemoptysis were less frequent, reported by 21.5% and 2.1% of subjects, respectively. At the time of presentation to our tertiary center, 51.4% were diagnosis-naïve, while 48.6% had a pre-existing diagnosis of ILD (*Supplementary Table 1*).

High-resolution computed tomography (HRCT) was performed for the entire cohort and subjected to formal multidisciplinary discussion (MDD). The predominant radiological signatures identified were interlobular (63.7%) and intralobular (55.95%) septal thickening.

These findings, alongside a high prevalence of traction bronchiectasis, provide a morphological basis for the observed restrictive physiological defects, indicating a significant burden of established architectural distortion and fibrotic remodeling. Mediastinal lymphadenopathy was identified in 89 patients, 56.1% of these individuals (n=50) exhibited "significant" lymphadenopathy (short-axis diameter >10 mm). This necessitates a rigorous diagnostic distinction between sarcoidosis, occupational exposures (e.g., silicosis), and reactive nodal hyperplasia secondary to fibrosis. Conversely, the rarity of centrilobular nodules (3.1%) suggests the cohort was primarily characterized by advanced fibrotic processes rather than early cellular inflammatory patterns seen in acute hypersensitivity pneumonitis.

Lung function assessment was successfully performed in 1,059 subjects (88.2%; *Supplementary Table 2*). Testing was deferred in others due to clinical contraindications (e.g., recent myocardial infarction, uncontrolled pulmonary hypertension) or COVID-19 logistical constraints. A restrictive ventilatory defect was the hallmark impairment, identified in 83.9% of patients, (Figure 2) serving as a functional correlate to the extensive parenchymal fibrosis seen on HRCT. An obstructive pattern was identified in only 6.9% of cases. Stratification by ILD subtype revealed a higher functional reserve in sarcoidosis patients (mean FVC 2.4 ± 0.9 L; $74.1 \pm 17.9\%$ predicted) compared to fibrotic subtypes ($P < 0.01$). Functional exercise capacity, measured by the 6-minute walk distance (6MWD), further highlighted these disparities (*Supplementary Table 3*). Sarcoidosis patients achieved a mean distance of 392.4 ± 85.6 meters, significantly exceeding the 347.7 ± 90.1 meters recorded for CTD-ILD patients ($P < 0.01$). This suggests that CTD-ILD patients suffer from higher exertional limitation, likely due to combined pulmonary restriction and systemic musculoskeletal or cardiac involvement.

Following MDD consensus, the cohort was categorized into distinct subtypes (Figure 3). The most prevalent category was idiopathic interstitial pneumonia (IIP; 48.8%), followed by connective tissue disease-associated ILD (CTD-ILD; 19.8%) and hypersensitivity pneumonitis (HP; 14.6%). Sarcoidosis and idiopathic pneumonia with autoimmune features (IPAF) accounted for 13.4% and 1.6%, respectively. Within the IIP subgroup, idiopathic pulmonary fibrosis (IPF) was the dominant phenotype (49.7%), followed by idiopathic nonspecific interstitial pneumonia (iNSIP; 39.2%) and cryptogenic organizing pneumonia (4.4%; Table 1). Among the 238 CTD-ILD patients (19.8%), systemic sclerosis (SSc) was the most frequent condition (49.2%), followed by rheumatoid arthritis (RA; 26.9%). Morphological patterns differed significantly: in RA-ILD, the usual interstitial pneumonia (UIP) pattern was most frequent (50.0%), while in SSc-ILD, the NSIP pattern predominated (47.3%), followed closely

by the UIP pattern (42.1%). This divergence underscores the necessity of differentiating lung injury patterns to guide prognosis in connective tissue disorders.

In most cases (78.7%), a final diagnosis was established through clinical and radiological integration within the MDD framework (Table 2). The remaining 21.3% required histopathological confirmation. Invasive procedures were deferred for definitive UIP patterns on HRCT, established CTD-ILD, or in patients clinically unfit for biopsy. The yields of transbronchial lung biopsy (TBLB), cryobiopsy, and surgical lung biopsy are detailed in *Supplementary Table 4*. Statistical analysis revealed a profound association between tobacco use and IIP development. The correlation between smoking status and IIP versus non-IIP subtypes was highly significant ($X^2 = 63.96$, $P < 0.01$). Smokers faced a 3.36-fold increased risk of IIP (OR = 3.36; 95% CI: 2.37–4.75; $P < 0.01$), suggesting smoking is a primary driver of idiopathic fibrotic phenotypes. Furthermore, environmental and domestic exposures played a decisive role in HP pathogenesis. A significant correlation ($P < 0.01$) was identified between HP and exposure to domestic molds, air conditioning systems, pigeons, and farm animals. These findings emphasize that regional environmental factors and domestic practices are primary contributors to the HP burden in this cohort.

Discussion

The current study represents one of the largest single-center ILD cohorts in North India (n=1,201). The novelty of this data lies in its granular depiction of the evolving ILD landscape in a region characterized by high environmental exposure and a significant burden of infectious mimics, specifically tuberculosis. Our findings provide a critical cross-sectional analysis of diagnostic and therapeutic trends that differ significantly from Western cohorts.

A striking observation was that 95.5% of patients were receiving corticosteroids prior to referral, regardless of ILD subtype. This high prevalence suggests a systemic reliance on broad-spectrum anti-inflammatory treatment at primary care levels. Mechanistically, this likely reflects limited early access to Multidisciplinary Discussion (MDD) and HRCT, leading clinicians to treat ILD as a generic inflammatory condition or obstructive airway disease. Clinically, this is concerning for Idiopathic Pulmonary Fibrosis (IPF) patients, where steroid monotherapy may exacerbate disease progression and increase morbidity.

The female predominance (55.6%) observed aligns with other major Indian registries [6,7]. This pattern warrants a socio-environmental hypothesis: in North India, women are disproportionately exposed to domestic triggers, including biomass fuel smoke and organic dust, which may prime the lung parenchyma for interstitial injury. Furthermore, the 16.1% prevalence of tuberculosis underscores a unique diagnostic challenge. The "TB-first" mindset

often leads to repeated courses of anti-tubercular therapy (ATT) in ILD patients, resulting in delayed diagnosis and irreversible fibrosis.

Physiologically, 83.9% of subjects exhibited a restrictive defect, significantly higher than the 58.6% reported by Dhooria et al. [6]. This disparity is likely due to cohort composition; while Dhooria et al. reported high sarcoidosis prevalence (often presenting with preserved volumes), our cohort was dominated by fibrotic phenotypes (IPF and f-NSIP) characterized by severe architectural distortion. This highlights that North Indian tertiary centers are increasingly seeing "late-stage" referrals with profound restrictive defects.

The distribution of ILD subtypes—predominated by IIP (48.8%)—aligns more closely with Western registries than with previous multi-centric Indian data [6-9]. This challenges the narrative that hypersensitivity pneumonitis (HP) is the most common ILD in India. We hypothesize that high IIP prevalence (24.3% IPF) is driven by urbanization and particulate exposure, where rising ambient pollution acts as a chronic alveolar trigger in aging populations. Additionally, as a tertiary center receiving "diagnostic dilemmas," our high IIP rate suggests that once infectious mimics are excluded, the underlying burden of primary fibrotic disease is higher than previously estimated.

A major departure from the landmark Indian ILD registry (which reported HP at 47.3%) is our significantly lower HP prevalence of 14.6% [7]. This discrepancy provides insight into potential "over-diagnosis" of HP in India. Previous registries relied on non-consecutive enrollment and lacked "cause-and-effect" validation for exposures like evaporative "air coolers." Mechanistically, our study suggests regional HP is more likely linked to avian exposure (pigeons) and domestic molds. By utilizing MDD and histopathology in 21.3% of cases, we likely reclassified "suspected HP" into IIP or CTD-ILD categories. This underscores a vital clinical implication: without standardized MDD-driven validation, there is a risk of mislabeling fibrotic IIPs as HP, leading to inappropriate avoidance strategies and delayed antifibrotic therapy.

Our HP prevalence (14.6%) mirrors German registries (13%) but remains higher than Mediterranean cohorts (2.6–7%) [10-13]. This variation highlights a socio-environmental contributor: the high density of avian exposure and specific domestic practices in North India creates a unique "antigenic load." Furthermore, variation between Indian studies reflects the lack of uniform diagnostic protocols [6,14]. Our findings advocate for the MDD approach as the "gold standard" to prevent inaccuracies inherent in registry-based studies.

In our cohort, 21.3% underwent histopathological sampling, situated between the 7.5% in the Indian registry [7], and 49.9% reported by Dhooria et al. [6]. The "unwillingness" to undergo biopsy often stems from high out-of-pocket expenses and fear of invasive procedures. Mechanistically, our lower biopsy rate compared to Dhooria et al. reflects

increasing diagnostic confidence in HRCT. Within an MDD framework, definitive "UIP patterns" or clear "CTD-ILD" profiles allow high-confidence diagnosis without biopsy morbidity. In resource-limited settings, strengthening MDD protocols is more pragmatic than mandating invasive biopsies.

The primary strength of this study is its single-center, protocol-driven design. Unlike multi-centric registries prone to selection bias and heterogeneous standards, our study ensures all 1,201 patients were evaluated through a uniform algorithm [8]. This provides a level of data "purity" novel to the Indian context. By maintaining consistent MDD members, we minimized inter-observer variability, allowing us to conclude with confidence that our observed patterns reflect the true regional disease burden.

Limitations

Several limitations warrant acknowledgment. As a single-center, tertiary study, an inherent referral and selection bias likely resulted in an overrepresentation of advanced fibrotic cases. This potentially inflated the prevalence of IPF and IIPs compared to community settings, where early-stage or milder phenotypes might predominate. The retrospective nature of a portion of the cohort introduced data completeness challenges; specifically, the absence of HRQoL metrics (K-BILD/SGRQ) prevents a correlation between physiological decline and patient-reported outcomes, likely under-capturing the true symptomatic and psychological burden in this population.

Regarding diagnostic certainty, the limited histopathology rate (21.3%) necessitated a heavy reliance on radiological patterns. This increased the risk of misclassifying "occult" hypersensitivity pneumonitis (HP) or NSIP variants that mimic the UIP pattern. Furthermore, inconsistent serological evaluation for specific antigens meant many HP diagnoses remained "probable" rather than "proven," limiting our ability to establish definitive cause-and-effect relationships for regional environmental triggers. Finally, the COVID-19 pandemic severely disrupted longitudinal follow-up and prospective enrollment. This interruption restricted our ability to perform repeated HRCT fibrosis scoring and limited the analysis of antifibrotic efficacy and long-term survival, potentially leading to an underestimation of disease progression rates during the study period.

Conclusions

This large-scale study establishes a contemporary clinical profile of ILD in North India, identifying idiopathic interstitial pneumonias (IIP) as the dominant disease burden. By utilizing a rigorous, multidisciplinary diagnostic (MDD) framework, these findings challenge previous regional assumptions that hypersensitivity pneumonitis is the most prevalent

subtype, highlighting the risk of diagnostic misclassification in the absence of standardized protocols.

The clinical implications are significant for regional practice. The high prevalence of advanced fibrosis at presentation suggests that the "TB-first" diagnostic mindset and empiric steroid use at the primary care level frequently delay specialized intervention. Our results advocate for a paradigm shift toward early tertiary referral and phenotype-specific management. By aligning regional data with international standards, this study provides a pragmatic blueprint for standardizing ILD care in India, ensuring that patients with progressive fibrotic disease receive timely, evidence-based therapy.

References

1. Raghu G, Mehta S. Interstitial lung disease (ILD) in India: insights and lessons from the prospective, landmark ILD-India registry. *Lung India* 2016;33:589-91.
2. Travis WD, Costabel U, Hansell DM, et al. An official American Thoracic Society/European Respiratory Society statement: update of the international multidisciplinary classification of the idiopathic interstitial pneumonias. *Am J Respir Crit Care Med* 2013;188:733-48.
3. Raghu G, Collard HR, Egan JJ, et al. An official ATS/ERS/JRS/ALAT statement: Idiopathic pulmonary fibrosis: evidence-based guidelines for diagnosis and management. *Am J Respir Crit Care Med* 2011;183:788-824.
4. American Thoracic Society; European Respiratory Society. American Thoracic Society/European Respiratory Society International Multidisciplinary Consensus Classification of the Idiopathic Interstitial Pneumonias. This joint statement of the American Thoracic Society (ATS), and the European Respiratory Society (ERS) was adopted by the ATS board of directors, June 2001 and by the ERS Executive Committee, June 2001. *Am J Respir Crit Care Med* 2002;165:277-304.
5. Fischer A, Antoniou KM, Brown KK, et al. An official European Respiratory Society/American Thoracic Society research statement: interstitial pneumonia with autoimmune features. *Eur Respir J* 2015;46:976-87.
6. Dhooria S, Agarwal R, Sehgal IS, et al. Spectrum of interstitial lung diseases at a tertiary center in a developing country: a study of 803 subjects. *PLoS One* 2018;13:e0191938.
7. Singh S, Collins BF, Sharma BB, et al. Interstitial lung disease in India results of a prospective registry. *Am J Respir Crit Care Med* 2017;195:801-13.

8. López-Campos JL, Rodríguez-Becerra E, The Neumosur Task Group of the Registry of Interstitial Lung Diseases (RENIA). Incidence of interstitial lung diseases in the south of Spain 1998-2000: the RENIA study. *Eur J Epidemiol* 2004;19:155-61.
9. Coultas DB, Zumwalt RE, Black WC, Sobonya RE. The epidemiology of interstitial lung diseases. *Am J Respir Crit Care Med* 1994;150:967-72.
10. Tinelli C, De Silvestri A, Richeldi L, Oggioni T. The Italian register for diffuse infiltrative lung disorders (RIPID): a four-year report. *Sarcoidosis Vasc Diffus Lung Dis* 2005;22:S4-8.
11. Karakatsani A, Papakosta D, Rapti A, et al. Epidemiology of interstitial lung diseases in Greece. *Respir Med* 2009;103:1122-9.
12. Hyldgaard C, Hilberg O, Muller A, Bendstrup E. A cohort study of interstitial lung diseases in central Denmark. *Respir Med* 2014;108:793-9.
13. Schweisfurth H, Kieslich C, Satake N, et al. How are interstitial lung diseases diagnosed in Germany? Results of the scientific registry for the exploration of interstitial lung diseases ("Fibrosis registry") of the WATL. *Pneumologie* 2003;57:373-82. [Article in German].
14. Kumar R, Gupta N, Goel N. Spectrum of interstitial lung disease at a tertiary care centre in India. *Pneumonol Alergol Pol* 2014;82:218-26.

Online supplementary material

Supplementary Table 1. Baseline characteristics of patients included in the study (n=1201).

Supplementary Table 2. Spirometric abnormalities in included subjects (n=1059).

Supplementary Table 3. Correlation between lung function tests and 6-minute walk distance among various subtypes of interstitial lung diseases (n=1059).

Supplementary Table 4. Yield of different methods for the diagnosis of interstitial lung disease in included patients (n=256/1201).

Table 1. Final diagnosis of study subjects (n=1201) after MDD.

Type of ILD	N (%)
Idiopathic interstitial pneumonia	587 (48.8%)
Idiopathic pulmonary fibrosis	292(49.7%)
Idiopathic NSIP	230(39.2%)
Cryptogenic Organising Pneumonia	26(4.4%)
RB-ILD	13(2.2%)
Desquamative interstitial pneumonia	20(3.4%)
Lymphocytic interstitial pneumonia	05(0.9%)
AIP	01(0.2%)
CTD ILD	238(19.8%)
Systemic sclerosis	117(49.2%)
Rheumatoid arthritis	64(26.9%)
Sjogren's syndrome	14(5.9%)
Dermatomyositis	11(4.6%)
Polymyositis	10(4.2%)
MCTD	11(4.6%)
SLE	08(3.4%)
Overlap	03(1.3%)
IPAF	20(1.6%)
Sarcoidosis	161(13.4%)
Hypersensitivity pneumonitis	176(14.6%)
Idiopathic pulmonary hemosiderosis	03(0.2%)
Unclassifiable ILD	06(0.5%)
Pneumoconiosis	9(0.7%)
Chronic eosinophilic pneumonia	01(0.08%)

Table 2. Mode of diagnosis of ILD in included patients (n=256/1201).

Methods of MDD Diagnosis	N (%)
Clinico-radiological discussion	945(78.7%)
Clinico-radiological and histopathological discussion	256(21.3%)
Histopathologic Diagnosis	
Sarcoidosis	125(48.8%)
Hypersensitivity pneumonitis	51(19.9%)
Idiopathic pulmonary fibrosis	27(10.5%)
Nonspecific interstitial pneumonia	46(17.9%)
Cryptogenic organizing pneumonia	07(2.7%)

Study Population Recruitment

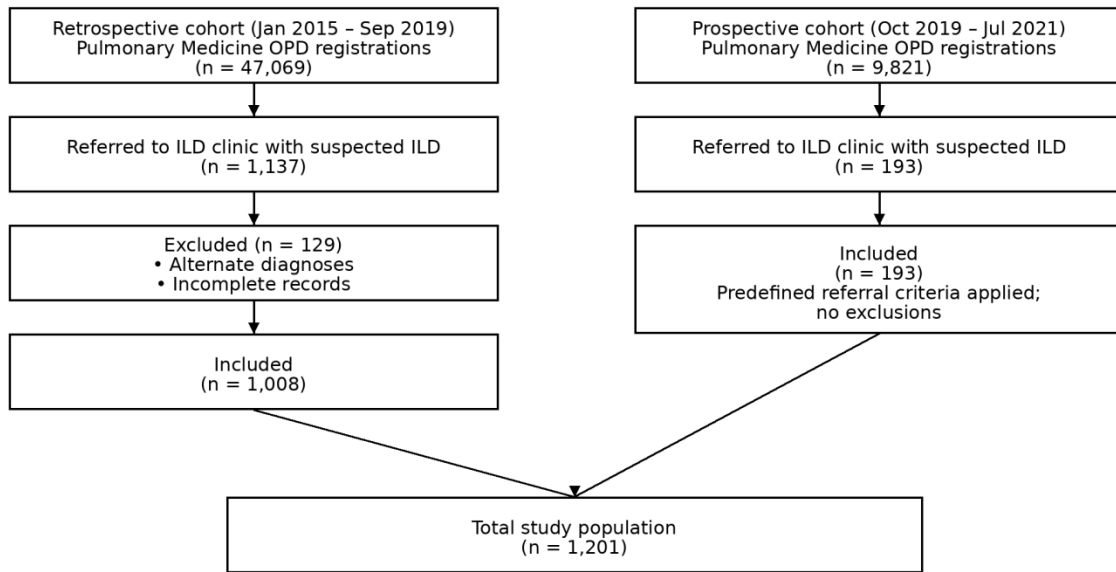
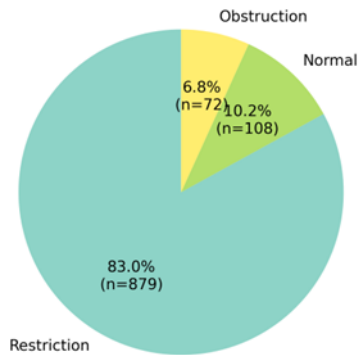


Figure 1. Study population recruitment.

A. Spirometric abnormality pattern (N = 1059)



B. Severity of restriction based on FVC (N = 889)

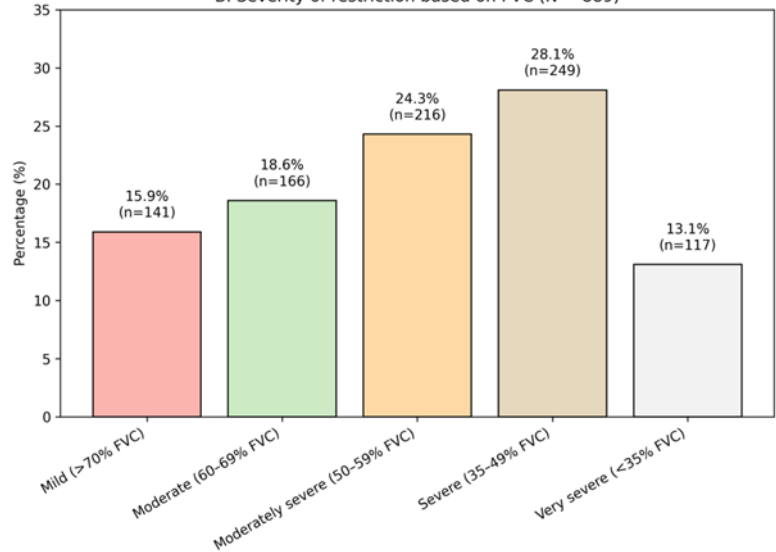


Figure 2. Spirometric abnormality patterns and severity of restrictive defect among patients with interstitial lung disease. Panel A shows spirometric patterns among patients who underwent pulmonary function testing (n=1059). Panel B shows the severity of restrictive defect among patients with restrictive spirometry (n=889). Percentages are shown with absolute numbers (n).

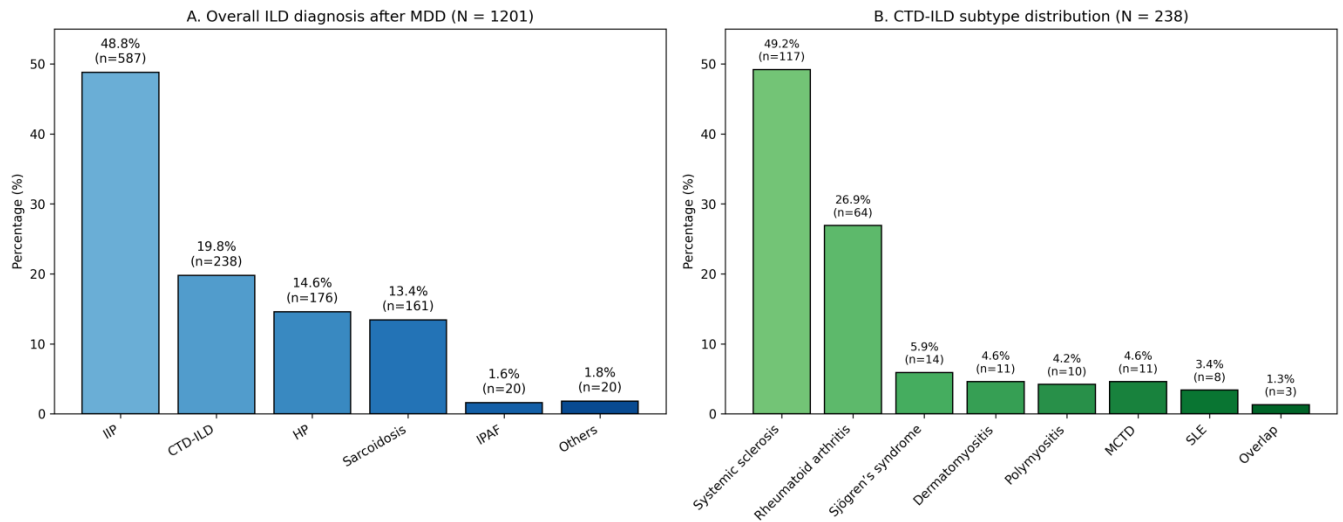


Figure 3. Distribution of interstitial lung disease diagnoses after multidisciplinary discussion. Panel A shows the overall ILD spectrum, and Panel B shows the distribution of connective tissue disease–associated ILD subtypes.