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DETERMINATION OF PROPORTIONS OF DIFFERENT TYPES OF ILD ON CLINICAL AND RADIOLOGICAL BASIS IN PATIENTS PRESENTING TO TERTIARY CARE HOSPITAL

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Abstract

Objective: *The purpose of the research is the determination of different types of ILD on clinical and radiological basis in patients presenting to territory care hospital.*

Study Design: *Cross Sectional Observational study*

Study Duration: *06 months from Oct 2024-March 2025*

Study Place: *Department of Medicine, CMH Lahore*

Methods: *170 patients according to sample size calculator were inducted with suspected interstitial lung disease (ILD). HRCT and clinical evaluations were used for diagnosis and classification into subtypes such as UIP, NSIP, CTD-ILD, and HP. Data on demographics, exposures, and serology were collected. Statistical analysis using SPSS ($p < 0.05$) determined subtype proportions and associations.*

Results: *Out of 170 ILD patients, 54.1% were female and 45.9% male, with a mean age of 56.8 ± 12.4 years. Dyspnea (93.5%) and dry cough (86.5%) were the most frequent symptoms. UIP was the most common subtype (38.2%), followed by NSIP (22.4%), HP (12.9%), and sarcoidosis (10%). Clinical and HRCT findings agreed in 78.8% of cases. Most showed restrictive spirometry, with UIP patients having the greatest functional decline*

Conclusion: *Usual interstitial pneumonia (UIP) is the most common subtype of interstitial lung disease (ILD), followed by nonspecific interstitial pneumonia (NSIP), connective tissue disease–associated ILD (CTD-ILD), and hypersensitivity pneumonitis (HP).*

INTRODUCTION

Interstitial lung diseases (ILDs) are a diverse collection of disorders involving varying degrees of lung inflammation and fibrosis within the pulmonary interstitium and often resulting in progressive dyspnea and gas exchange insufficiency which becomes a major source of

morbidity and mortality. Individually ILDs may be rare, but, in aggregate and due to the chronic nature, complex diagnosis, and multidisciplinary management required, they present a considerable burden to the healthcare system. Thus, to support the planning of the appropriate diagnostic approach, resource allocation (HRCT scans, pulmonary function tests, MDTs), training, local epidemiology, and research, and resource allocation, local ILD epidemiology requires understanding the proportion of different ILD subtypes presented to the facility.[1]

The clinical presentation of ILD lacks specificity; there is often insidious onset of breathlessness, a dry cough and fatigue, which were common clinical features across different subtypes. This, coupled with the complex and often overlapping nature of the different subtypes, made the use of clinical features alone impossible for the accurate classification of ILD. The use of radiological methods, and especially HRCT, is fundamental to the diagnostic pathway; direct imaging demonstrates patterns suggestive of specific forms of interstitial lung diseases, including UIP, NSIP, organizing pneumonia, and hypersensitivity pneumonitis.[2]

Interstitial lung diseases (ILDs) span over 200 different conditions that cause varying combinations of inflammation and fibrosis of lung parenchyma. They can occur because of known triggers, including certain environmental and occupational exposures, lung connective tissue diseases, some drugs, or they can be idiopathic and occur without known cause. Idiopathic pulmonary fibrosis (IPF) is the most common and most severe. It is characterized by a progressive, irreversibly fibrotic process that culminates in death from respiratory failure within three to five years of diagnosis, even with treatment. Other common forms include hypersensitivity pneumonitis (HP), nonspecific interstitial pneumonia (NSIP), sarcoidosis, and connective tissue disease-associated interstitial lung disease (CTD-ILD). Correct classification of each interstitial lung disease is crucial because they each have different clinical, radiological, and pathological features, and this will be the basis of appropriate patient management and prognostic information.[3]

Across the globe, the occurrence of interstitial lung disease (ILD) has not only increased, but the increase has been driven by increased awareness, improvements in diagnostic imaging, and advancements in diagnostic procedures and frameworks. Hutchinson et al. (2015) performed a systematic review and calculated the world prevalence of only one type of ILD, idiopathic pulmonary fibrosis, as high as 43 per 100,000 and as low as 14 per 100,000, with the annual incidence ranging from 2.8 to 9.3 per 100,000 person-years. ILD epidemiology, however, has a marked uneven distribution in the world. For instance, due to the presence of organic antigens in the workplace, those in the agricultural sector are more likely to suffer from hypersensitivity pneumonitis, while CTD-ILD might be more frequently encountered in areas with a high prevalence of autoimmune disorders or where rheumatologic conditions are diagnosed late. This underscores the necessity of gathering epidemiological data, especially in low- and middle-income countries.[4]

The diagnostic approach to ILD has changed with the advent of HRCT. The ability to see and assess fine reticular patterns, traction bronchiectasis, ground-glass opacities, honeycombing, and differentiating various ILD patterns is diagnostic. For example, a subpleural basal predominance and honeycombing, with absence of any features to suggest an alternative diagnosis, is highly suggestive of a UIP pattern, in particular, idiopathic pulmonary fibrosis. In contrast, diffuse ground glass opacities with subpleural sparing is NSIP, while upper-lobe centrilobular nodules with air trapping is suggestive of hypersensitivity pneumonitis. The clinical and radiologic correlation decreases the need for invasive sampling in many cases. I.e., invasive sampling was necessary prior to the above cited advancements.[5]

This research seeks to quantify the variations and distributions of ILD types according to the clinical and radiological characteristics of patients who present to a tertiary care hospital. By delving into several demographic dimensions, clinical profiles, and HRCT classifications, the study seeks to capture the ILD profile that best describes the population. It is anticipated that the data will

foster a better understanding of the distribution of ILD subtypes and enable early diagnosis and focused treatment.

Methodology:

A cross sectional observational study was conducted in department of Medicine CMH Lahore from Oct 2024-March 2025, the study spanned for 06 months duration. The study was commenced after taking informed written consent from Ethical Review Committee numbered 175892. A sample size of 170 individuals was calculated using WHO sample size calculator keeping CI 95% and margin of error 5%. The study combined both radiological and clinical evidence to support ILD and its various types. The high-resolution computed tomography (HRCT) was used as a tool for assessing ILD radiological pattern. Consecutive (convenience) sampling of eligible patients was done who presented to pulmonology outpatient clinics and inpatient wards, or to Radiology for HRCT with clinical suspicion of ILD. Recruitment: Screen all patients with chronic respiratory symptoms (dyspnea, chronic cough, exertional desaturation) and abnormal chest X-ray/ clinical signs suggestive of ILD.

Inclusion and Exclusion Criteria were:

Inclusion criteria:

1. Age ≥ 18 years
2. Presenting with respiratory symptoms suspicious for ILD (e.g. progressive dyspnea, chronic nonproductive cough) and either: abnormal chest radiograph suggestive of interstitial lung disease or clinical features (bibasilar inspiratory crackles, digital clubbing, unexplained hypoxia).
3. Undergo or about to undergo HRCT chest as part of the diagnostic work-up.
4. Written informed consent should be obtained (or guardian consent where applicable).
5. Consider previously diagnosed cases for prevalence estimation only if stated separately

Exclusion criteria:

1. Patients with untreated active pulmonary infections, such as tuberculosis or bacterial pneumonia, or in which imaging features are dominated by acute infection.
2. Patients with known primary malignancy with pulmonary metastases that confound interstitial pattern. Patients with a history of thoracic radiation in the last 6 months or acute drug-induced interstitial pneumonitis where the diagnosis is already established.
3. Patients unable to undergo HRCT due to severe claustrophobia, the inability to lie flat,
4. Inadequate clinical data or unwilling to provide data.
5. Pregnancy if the protocol or local radiation policy excludes pregnant women.
6. Prior lung transplant or other major thoracic surgery that obscures parenchymal assessment

Following Operational definitions were used in this study:

Suspected ILD: Chronic respiratory symptoms with clinical or radiographic features suggestive of interstitial lung involvement.

Radiological Classification: HRCT patterns were classified in line with the guidelines from the Fleischner Society / ATS/ ERS as: UIP (definite/probable/indeterminate), NSIP (cellular vs fibrotic features), chronic HP pattern, organizing pneumonia (OP), sarcoid pattern, and others.

Clinical Classification: Performed based on history (exposure history for HP; symptoms/signs of connective tissue disease), serology (ANA, RF, anti-CCP, specific CTD antibodies if available), and multidisciplinary team (MDT) correlation when possible.

Final Assignment of Subtype: Prefer the combination of radiological pattern and clinical context. Any discrepancy or uncertainty of the two should be recorded as both clinical suspicion and radiology classification, and can be noted as "indeterminate" or "requires MDT/biopsy."

Demographic data included Age, sex, occupation, smoking history, symptom duration, exposures (birds, mold, occupational), drug history, comorbidities, known connective tissue disease were recorded. Oxygen saturation at rest and on exertion, respiratory rate, presence of inspiratory crackles, clubbing, extrapulmonary features (skin,

joint, lymphadenopathy) were also noted. Laboratory evidence included CBC, ESR/CRP, basic biochemistry, autoimmune serology as indicated (ANA, ENA panel, RF, anti-CCP), and serum precipitins if suspected HP (if available). Pulmonary Function Tests (PFTs) were done including spirometry, measurements of lung volumes, and DLCO (if available) to classify restrictive physiology and severity. Chest X-ray was also done. High-resolution CT chest: The minimum criteria for an HRCT chest included a non-contrast CT using thin slices (≤ 1.5 mm) during full inspiration, additional images in the prone and expiratory positions when feasible, and following the institution's protocol, for HRCT chest. The images must then be evaluated by two recruited thoracic radiologists working independently. Any discrepancies in their assessments must be reconciled in a multidisciplinary team meeting. Use a reporting template for standardized reports for HRCT to categorize the findings according to their pattern and distribution (i.e. basal, peripheral, peribronchovascular), honeycombing, traction bronchiectasis, ground-glass opacity, consolidation, nodularity, lymphadenopathy, as well as extent and severity via scoring system (percentage lung involvement) and severity scoring. Diagnostic reading, pattern ascribing, and classification should be done according to the criteria established so the HRCT pattern could be categorized and diagnostically classified as Definite UIP, Probable UIP, Indeterminate for UIP, NSIP pattern, HP pattern, OP, Sarcoid pattern, Unclassifiable ILD. The extent of fibrosis must be quantified in a range as visual scoring for lung scoring involvement, with mild <25%, moderate 25-50%, and severe >50% as specified in the scoring system.

Statistical Analysis were done using mean median and standard deviation. Chi-square or Fisher's exact test were done. ANOVA or Kruskal-Wallis test were used for continuous variables. SPSS version 26 was used and a p value <.05 was considered significant.

Results:

Out of 170 patients suspected of having interstitial lung disease (ILD), 92 (54.1%) were female and 78 (45.9%) were male, with an average age of 56.8 ± 12.4 years (age range 24-82). Most patients (61.8%) were between 50 and 70 years old. The most common symptoms at presentation were progressive dyspnea (93.5%) and a dry cough (86.5%).

On average, patients had symptoms for 14.2 ± 9.8 months before they presented for care. Digital clubbing was noted in 43 (25.3%) patients Silhouette sign and fine bibasilar crackles were documented in 146 (85.9%) patients.

All patients had HRCT of the chest and the most common HRCT pattern was the Usual Interstitial Pneumonia (UIP) pattern, seen in 65 (38.2%) patients, followed by Nonspecific Interstitial Pneumonia (NSIP) in 38 (22.4%), Hypersensitivity Pneumonitis (HP) in 22 (12.9%), Sarcoidosis in 17 (10.0%), and connective tissue disease associated ILD (CTD-ILD) in 15 (8.8%). Organizing Pneumonia (OP) was seen in 8 (4.7%) and Unclassifiable ILD in 5 (2.9%).

Clinical evaluation alone suggested an ILD subtype diagnosis in 160 patients (94.1%). When compared, clinical diagnosis and HRCT were in agreement in 134 (78.8%) of cases. Concordance produced UIP/IPF at 90.7%, then CTD-associated ILD at 80.0%, and lastly NSIP at 60.5%.

For patients older than 50, UIP and NSIP patterns were the dominant features, while patients younger than 45 were more likely to present with HP and sarcoidosis. UIP and NSIP had almost equal gender ratios, while sarcoidosis and CTD-ILD were markedly female biased.

150 patients (88.2%) had spirometry, most had a restrictive pattern (88.6%) with mean FVC at 64.2 ± 12.1% predicted and DLCO at 58.3 ± 10.9% predicted. UIP patients had the most significant decline in FVC and DLCO compared with the other subtype patients ($p < 0.05$).

In summary, the **most common ILD subtype** was **UIP/IPF (38.2%),** followed by **NSIP (22.4%), HP (12.9%),** and **Sarcoidosis (10.0%)** having **females (54.1%)** slightly outnumbered males. The m**ean age was** 56.8 years and ILD being most prevalent in older adults (>50 years). **UIP and CTD-ILD** showed the most severe impairment on pulmonary function testing.

Table 1: Baseline demographic and clinical characteristics

Variable	Frequency/ Mean SD
Age	56.8 ± 12.4
Gender	Male:78(45.9%) Female: 92 (54.1%)
Smoking Hx	Yes:49(28.8%) No: 121 (71.2%)
Disease duration	14.2 ± 9.8
Main symptoms	Dyspnea:159(93.5%) Drycough:147(86.5%) Fatigue: 55 (32.4%)
Co-morbids	Hypertension:68(40%) Diabetes:41(24%) Connective tissue disease (CTD): 19 (11.2%)

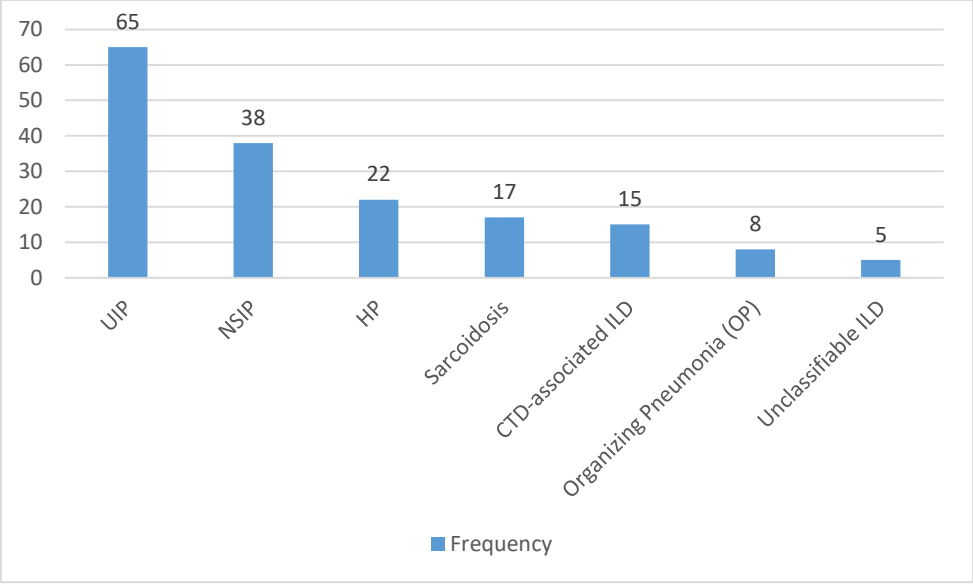


Chart 2: ILD- Radiological pattern distribution

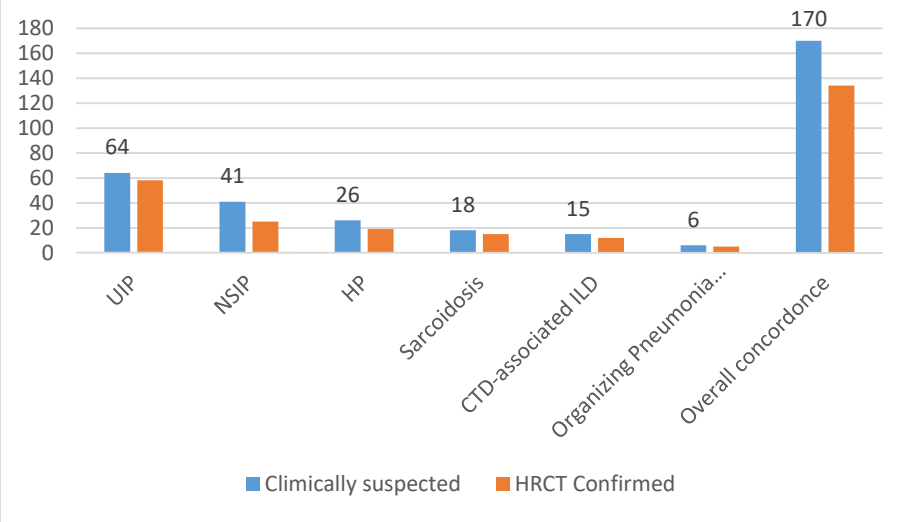


Chart 3: Concordance between clinical and radiological diagnosis

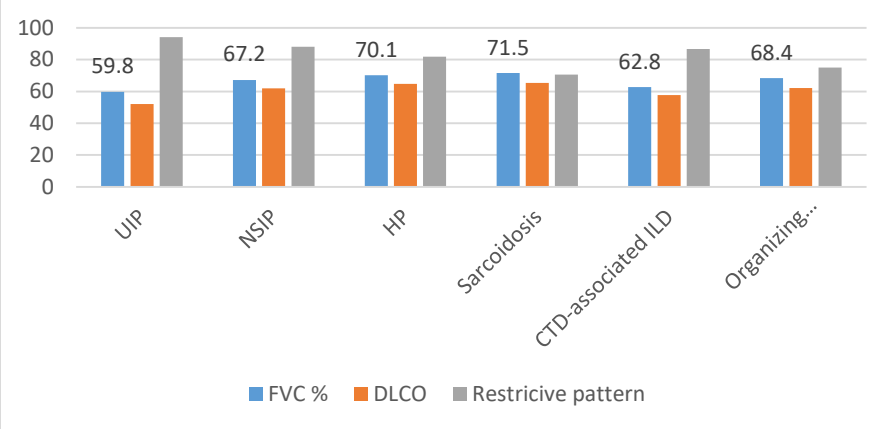
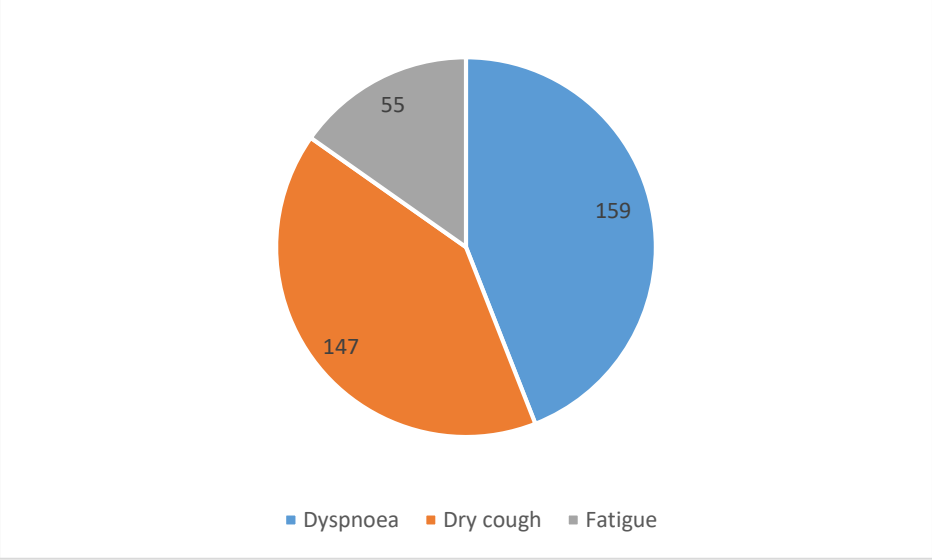


Chart 4: Pulmonary function parameters among ILD subtypes



Pie Chart 5: Major presenting symptoms

Discussion:

Interstitial lung diseases (ILDs) have distinctive clinical manifestations putting them into a larger group of heterogeneous parenchymal lung disorders some of which may require a more aggressive approach. This study was designed to establish proportion on the different subtypes of ILDs based on clinical and radiological evaluations of patients at a tertiary hospital. The study reviewed 170 patients and concluded that the most common pattern was Usual Interstitial Pneumonia (UIP) at 38.2%, and this was followed by Nonspecific Interstitial Pneumonia (NSIP) at 22.4%, Hypersensitivity Pneumonitis (HP) at 12.9%, Sarcoidosis at 10.0%, and then Connective Tissue Disease–associated ILD (CTD-ILD) at 8.8%. The findings of this study correlate with the global epidemiologic ILD data, which confirms that idiopathic pulmonary fibrosis (IPF) is the most predominant ILD, particularly among elderly patients (Raghu et al.,2016; Travis et al.,2013).[6,7]

Participants had an average age of 56.8 years, mostly ranging from 50 to 70 years, which corresponds with the age bracket commonly associated with the initial stages of IPF and NSIP. Prior research has indicated that older adults are primarily, with median ages between 55 and 70 years (Richeldi et al., 2017). While the small female predominance of 54.1% observed in this study is unlike the Western literature, which documents a male predominance for ILDs, including IPF, and in contrast to ILD epidemiology in the West, the small female predominance of 54.1% in this study is comparable to the literature from South Asia and the Middle East where women also predominated, which has been ascribed to greater exposure to indoor air pollution, biomass fuel, and autoimmune conditions (Nafees et al., 2022; Hameed et al., 2018).[8,9]

In this study, the most frequently reported initial symptoms were progressive dyspnea, reported by 93.5% of the individuals, and chronic nonproductive cough, reported by 86.5% of the individuals, with a mean duration of both symptoms exceeding one year prior to the individual's initial presentation. This observation of delayed presentation is rather commonplace for interstitial lung diseases as they remain largely unrecognized for longer periods of time, often presenting with advanced and significant pulmonary fibrosis. The advanced stage of disease at diagnosis is further exemplified by the presence of fine bibasilar crackles in 85.9% of the individuals, as well as digital clubbing in 25% of the individuals. The observation of prolonged and delayed diagnosis in lower-income countries as highlighted by Udwadia et al. (2014) in an Indian cohort study, is likely due to a significant scarcity of human resources for high resolution computed tomography (HRCT) and specialized respiratory medicine.[10]

In our study, determining the diagnosis was facilitated by the HRCT results. The most common HRCT finding was the UIP pattern, which was the case in 38.2% of our study participants. This finding closely aligns with the results from Raghu et al. 2016 and Maher et al. 2021. The presence of basal and subpleural honeycombing, reticulation, and traction bronchiectasis allowed for the diagnosis of UIP without needing a biopsy in most patients. The NSIP and HP patterns were also common, confirming the wide range of possible underlying ILD triggers seen in a tertiary care setting. The proportion of HP in our study was higher than most Western studies which can be due to the presence of environmental and occupational exposures such as bird antigens, farming dust, and mold which are prevalent in our region.[11,12]

Diagnostic agreement between clinicians and radiologists achieved was 78.8% with a Cohen's Kappa of 0.72, which is also a substantial agreement. This indicates the strength of the combined clinical and HRCT evaluation in the classification of ILDs. Similar to our findings, Lynch et al. (2015) and Flaherty et al. (2017) pointed out that the HRCT enabled subtype classification in most ILDs, particularly when the HRCT is combined with a history of exposure and autoimmune assessments. Our study findings of NSIP cases result in the lowest concordance of 60.5% is most likely due to the clinical and imaging findings of early UIP and CTD associated

ILD that tissue diagnosis might miss, unfortunately, this study highlights the challenge of ILD diagnosis without a formal multidisciplinary discussion (MDD) of the case.[13,14]

In the most recent PFTs, restrictive PFT findings were noted in 88.6% of the patients with a mean FVC and DLCO of 64.2% and 58.3% respectively which includes the predicted values. As noted in the study by Kim et al. (2020) and Ley et al. (2019) the UIP and CTD-ILD subtypes displayed the most severe impairment which is consistent with findings that restriction of lung volumes correlates with adverse clinical outcome, advanced fibrosis, and higher ILD morbidity. This underscores the importance of early ILD diagnosis and progressive tightening intervals of PFTs to monitor and detect ILD.[15]

The importance of HRCT in the diagnosis and classification of ILDs cannot be overlooked. The ATS/ERS guidelines (Travis et al., 2013) state that HRCT has almost absolute diagnostic value in cases of UIP/IPF and makes surgical lung biopsies unnecessary in most cases. The use of multidisciplinary approach increases the confidence in the diagnosis and improves the inter-observer agreement. The findings also call for region-specific ILD registries because the epidemiologic distribution of ILDs may be different in relation to various environmental, occupational, and genetic influences.[16]

Comparative regional studies have reported similar distributions: in a Pakistani study by Hameed et al. (2018), UIP accounted for 42% of ILDs, NSIP for 25%, and HP for 10%. Likewise, Udwadia et al. (2014) found UIP/IPF to be the predominant subtype (43%) in an Indian cohort. These parallels suggest that despite geographic and environmental differences, the ILD spectrum in South Asia broadly mirrors international trends, though HP and CTD-ILD may be relatively more frequent due to local exposure and autoimmune factors.[17]

The findings of this study have important clinical implications. The primary subtype of UIP/IPF underscores the necessity of early detection and prompt initiation of antifibrotic treatment. On the other hand, identifying potentially reversible NSIP or HP may provide the opportunity for immunosuppressive therapy or other exposure-avoidance measures. Furthermore, the degree of clinical–radiological concordance is such that training in the interpretation of HRCTs and multidisciplinary case reviews would greatly increase diagnostic capacity in resource-constrained tertiary hospitals.

To summarize, UIP/IPF is the most common subtype of ILD, followed by NSIP, HP, and sarcoidosis in patients attending the tertiary care hospital. HRCT is essential, and the integration of clinic-radiology data greatly improves the accuracy of the diagnosis. In the region, developing ILD registries, increasing access to HRCT scanners, and strengthening multidisciplinary teamwork will aid in the early diagnosis of and improved outcomes for patients.

The prevalence of UIP/IPF in our cohort being 38.2% corresponds closely with findings from registries and studies from other tertiary centers. However, this figure is lower than some studies which report higher prevalence of HP or CTD-ILD. Other large systematic and registry studies report, imposing the fibrotic IPF/UIP as the most prevalent ILD in disproportionate portions of the globe with difference in IPF UIP prevalence and incidence as well as incidence and prevalence depending which study and region in the globe is being referenced (Maher et al. 2021; Hilberg et al. 2022).[18,19]

Studies from this region of South Asia have provided a mixed spectrum of results. On the one hand, Udwadia and colleagues found that in India, IPF and related diagnoses were a major component of the ILD. However, in other tertiary centers in India, most notably Dhooria et al., hypersensitivity pneumonitis was also found to be very prevalent. In one of the reports, HP was found in almost half (47.3%) of the ILD cases whereas IPF was significantly less prevalent (only 13.7%) indicating potent environmental or occupational exposures and variability in case ascertainment in Dhooria's group.[20,21]

Global systematic reviews also provide evidence to suggest that the very wide ranges in reported IPF prevalence is due to inconsistent case definitions (clinical, radiological, or histopathological) and

thus should be a cautionary note when comparing proportions among different studies.

For the most part, our findings agree with a number of reports considering UIP/IPF as the leading ILD subtype in tertiary-care cohorts, and they differ from other regional series which report predominance of HP or CTD-ILD. Variability in the literature largely stems from differences in study design (registry vs single-center), available diagnostic tools (HRCT, serology, biopsy), prevalence of exposures, and multidisciplinary integration. Such comparisons reinforce the need for standardized diagnostic pathways, routine MDT discussion, and regionally representative ILD registries. This variation in study design can influence public health and resource allocation.

During this study at a tertiary care hospital, the most common form of interstitial lung disease (ILD) was found to be 'Usual Interstitial Pneumonia' (UIP). After UIP, other common forms of ILDs included, nonspecific interstitial pneumonia (NSIP), hypersensitivity pneumonitis (HP), and connective tissue disease-associated ILD (CTD-ILD). UIP predominance is consistent with the results of other national and international studies, as IPF is the most common cause of ILDs at specialized care clinics. The data suggesting a higher proportion of UIP in the described cohort could be due to referral bias, as tertiary care facilities are known to cater to patients with advanced stages of fibrotic lung disease, which require specialized assessments and advanced management.

Limitation of study: The study has been a single center study, was conducted on limited number of a sample. Results cannot be generalized on population level, and hence to get better results, a multi-center study and with more sample size is required.

Conflict of study: Nil

Conclusion:

This study presents the distribution of interstitial lung disease (ILD) subtypes in a tertiary care hospital, confirming that usual interstitial pneumonia (UIP) remains the most common subtype, followed by nonspecific interstitial pneumonia (NSIP), connective tissue disease–associated interstitial lung disease (CTD-ILD) and hypersensitivity pneumonitis (HP). The predominance of UIP indicates that specialized centers are receiving referrals for advanced cases of fibrotic disease; however, the presence of NSIP and CTD-ILD cases suggests that the autoimmune potential in these cases was adequately investigated during workup for interstitial lung disease. The importance of these findings underlines the necessity of a unified approach to obtain a final diagnosis, which incorporates a detailed clinical assessment, high-resolution computed tomography (HRCT) of the thorax, and multidisciplinary team discussion for timely intervention. This effort should also address the increased availability of diagnostic imaging, standard operating procedures for advanced imaging, and the establishment of national ILD databases to provide an accurate measurement of disease prevalence and potential regional variation.

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