

FREQUENCY OF IDIOPATHIC AND NON-IDIOPATHIC PULMONARY FIBROSIS IN HIGH-RESOLUTION COMPUTED TOMOGRAPHY PROVEN USUAL INTERSTITIAL PNEUMONIA

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ABSTRACT

Objective: To determine the frequency of idiopathic and non-idiopathic pulmonary fibrosis in high-resolution computed tomography proven usual interstitial pneumonia patients.

Study design: A cross-sectional study.

Settings: Chest Unit, OJHA institute of Chest diseases, Dow University of health sciences, Karachi

Period: November 2024 –April 2025.

Material and Methods: Non-probability consecutive sampling was used to enroll 104 patients aged between 18 and 60 years who had the pattern of usual interstitial pneumonia (UIP) on high-resolution computed tomography (HRCT). Malignant patients or those who did not want to take part in the study were excluded. An SPSS version 25 was used to analyze the data. Chi-square or Fisher exact test was used to evaluate association with a p-value of 0.05 as a statistically significant level.

Results: Among 104 patients, 71 patients were diagnosed as IPF and 33 as Non-IPF. The mean age was 47.6 ± 9.8 years; 59.6% male and 40.4% were females. Dyspnea (85.6%) and dry cough (77.9%) were the most common symptoms. Idiopathic pulmonary fibrosis (68.3) was the most common. Age ($p=0.041$) and smoking ($p=0.032$) were significantly related to IPF. Age group ($p=0.041$) and smoking ($p=0.032$) showed significant associations with IPF. There was no

difference between groups in terms of clinical features, but systemic symptoms were more common in non-IPF. Among non-IPF causes the most common was CTD-ILD, particularly ILD related to rheumatoid arthritis (33.3%).

Conclusion: The most common subtype among the patients with usual interstitial pneumonia proved by HRCT was idiopathic pulmonary fibrosis.

INTRODUCTION

Idiopathic pulmonary fibrosis (IPF) is a progressive, chronic fibrosing interstitial lung disease, typified by deteriorating pulmonary functionality, aggravating dyspnea and terrible prognosis. It is the most prevalent type of idiopathic interstitial pneumonia and its median survival is about 35 years after onset despite the improvements in the supportive care and antifibrotic therapy. Prognostication and proper management of affected patients requires early and accurate diagnosis [1]. High-resolution computed tomography (HRCT) is a key step in diagnosis of interstitial lung diseases, especially in determining the common interstitial pneumonia (UIP) pattern which is regarded to be the radiological pattern of IPF. Chen et al. have provided the results of a real-world cohort study including 179 patients with suspected IPF in which the use of HRCT showed definite UIP in 44.1% and probable UIP in 32.4% cases [2], which indicates the diagnostic significance of imaging patterns in clinical analysis.

Other imaging modalities have also been examined to monitor fibrosing lung diseases other than HRCT, including lung ultrasound. Milad et al. compared 82 patients with the UIP and non-specific interstitial pneumonia (NSIP) and showed that lung ultrasound results were significantly associated with HRCT scores and parameters of pulmonary functions that justify the use of imaging to determine the disease progression in the patient [3]. The degree of fibrotic activity on HRCT has also been demonstrated to have prognostic consequences. The ILD-PRO registry data of 395 patients with progressive pulmonary fibrosis showed that the level of lung fibrosis on HRCT was a more potent predictor of mortality than the individual pattern of HRCT, which showed clinical significance of radiological assessment [4].

The prognostic assessment of IPF has also been improved due to quantitative HRCT evaluation. Du et al. reported in a cohort of 106 IPF patients that fibrotic lung volume on HRCT was highly predictive of disease progression and long-term mortality and higher fibrotic volume was associated with worse outcomes [5]. Various patterns of HRCT also have effects on survival of pulmonary fibrosis. In a follow-up study, 129 IPF patients were assessed and the authors noted that patients with classical UIP patterns were more aggressive and less likely to survive than other fibrotic patterns seen in HRCT [6].

Pulmonary fibrosis can also accompany the autoimmune disease that is systemic in nature. As an example, Manfredi et al. established that progressive fibrosing interstitial lung disease developed in about 24% of patients with primary Sjogren syndrome, and this shows that fibrotic lung disease can also be as a result of non-idiopathic etiologies [7]. The distinction between UIP and other patterns of fibrosing interstitial lung disease patterns like NSIP is important radiologically, as the treatment interventions and the prognosis of the two are very different. According to Karaman, the most common UIP radiographical appearances on the HRCT are basal and sub pleural reticulation, which dominates, honeycombing, as well as traction bronchiectasis features, which differentiate UIP and other fibrotic lung disorders [8].

The histopathological studies have also revealed the differences between idiopathic and secondary pulmonary fibrosis. Wazir et al. contrasted lung tissue samples of idiopathic and occupation related fibrosis in lung disease and found that there are different patterns of collagen deposition, and inflammatory cell infiltration, which confirms the heterogeneity of fibrotic lung diseases [9]. In Pakistan, a survey of the National Registry of Interstitial Lung Disease involving 744 cases revealed that IPF constituted about 38 percent of

interstitial lung disease cases, with connective tissue disease related ILD, and hypersensitivity pneumonitis ranking next leading to the high burden of fibrotic lung diseases in Pakistan [10]. Since the etiologies and clinical implications of pulmonary fibrosis are varied, a distinction between idiopathic and non-idiopathic etiologies in the patient who has a UIP pattern of HRCT is of significant clinical interest. Nevertheless, local data are scarce on the comparative incidence of idiopathic and secondary pulmonary fibrosis in patients who's UIP has been confirmed using the HRCT. Thus, the current research will establish the prevalence of idiopathic and non-idiopathic pulmonary fibrosis among the patients with HRCT-proven usual interstitial pneumonia that could aid in clinical practice in enhanced diagnostic subdivision and treatment methods.

MATERIAL AND METHODS

The study was cross-sectional and was carried out in the inpatient and outpatient units of the Chest Unit, OJHA institute of Chest diseases, Dow University of health sciences, Karachi. The research was conducted within a span of six months from November 2024 - April 2025 after obtaining the research synopsis approval by the College of Physicians and Surgeons Pakistan (CPSP). The study was conducted with the institutional ethical guidelines, and ethical approval of the study was obtained through the Research Evaluation Unit of the College of Physicians and Surgeons Pakistan (**Ref No: CPSP/REU/PUL-2023-212-902**) and approved by institutional review board of Dow University of health sciences, Karachi. All participants provided written informed consent before participating in the study.

The sample was estimated in the OpenEpi software of estimation of sample size, based on the proportion of 67.8% of the patient population who have been reported to have idiopathic pulmonary fibrosis with a usual interstitial pneumonia (UIP) pattern on high-resolution computed tomography (HRCT), using a 95% confidence interval and a margin of error of 9 resulting in a required sample size of 104 patients.

The recruitment of the patients was done using a non-probability consecutive sampling method.

The study involved patients of both genders between 18 and 60 years old with usual interstitial pneumonia that was demonstrated by HRCT. The study eliminated patients with malignant diseases that were concomitant and those who were not willing to participate.

The study was conducted by enrolling patients to the study after taking informed consent and permission of the Research Evaluation Unit (REU) of the College of Physicians and Surgeons Pakistan and fulfilled the inclusion criteria comprised of patients visiting the outpatient department or admitted to the Chest Unit of OJHA Institute of Chest Diseases. Demographic information such as age and gender was captured. The anthropometrics measurements were done recording weight in digital weighing scale and height in stadiometer with the patient wearing light clothes and without shoes. The formula $BMI = \text{weight (kg)} / \text{height (m}^2\text{)}$ was used to determine the body mass index. Data on comorbidities like diabetes mellitus, hypertension, history of family members with interstitial lung disease and smoking status (past medical history) were collected. The clinical features were given such as dry cough, dyspnea, fatigue, weight loss, oral ulcers, photosensitivity, rash, and muscle/joint pains. A physical examination was done in detail to evaluate the existence of fine inspiratory crackles and digital clubbing. Every patient, who was enrolled, had high-resolution computed tomography (HRCT) of the chest done to ensure the normal pattern of interstitial pneumonia. Moreover, the blood samples were taken in aseptic conditions and were referred to the laboratory where the autoimmune serology such as anti-cyclic citrullinated peptide (anti-CCP), rheumatoid factor (RF), extractable nuclear antigen (ENA) and Anti-Nuclear Antigen (ANA) profile were done to distinguish between idiopathic and non-idiopathic pulmonary fibrosis. The principal investigator admitted all of the findings on a structured proforma.

The analysis of the data was conducted with the help of Statistical Package of Social Sciences (SPSS) 25. Quantitative variables such as age,

height, weight, BMI, and laboratory data were reported as mean and standard deviation when the data was normally distributed and in the non-normally distributed data, it was reported as median and interquartile range (IQR). Qualitative variables that included gender, age, BMI category, comorbidities (diabetes mellitus, hypertension, family history of interstitial lung disease, and smoking), clinical findings and symptoms, and outcomes of the study (idiopathic and non-idiopathic pulmonary fibrosis) were displayed in frequencies and percentages. Age groups, gender, BMI classification and comorbidities are the effect modifiers that were controlled using stratification. Chi-square test was used to evaluate the associations and a p-value of 0.05 was taken to be statistically significant. In case the expected cell frequency was under 5, the Fisher exact test was used.

RESULTS

A total of 104 patients with high-resolution computed tomography (HRCT) proven usual interstitial pneumonia were included in the study. The baseline demographic characteristics and comorbidities of the study participants are presented in **Table 1**. The mean age of the patients was 47.6 ± 9.8 years, with most participants belonging to the 46–60year age group, indicating a predominance of middle-aged adults. Male patients were slightly more common than females. With regard to body mass index, a considerable proportion of patients were overweight or obese. Among comorbid conditions, diabetes mellitus and hypertension were frequently observed, while a smaller proportion reported family history of interstitial lung disease and smoking history.

Table 1: Demographic Characteristics and Comorbidities of Study Participants (n=104)

Variables	n (%)
Age Group (years)	
18–30	23 (22.1)
31–45	35 (33.7)
46–60	46 (44.2)
Gender	
Male	62 (59.6)
Female	42 (40.4)
BMI Classification	
Normal	39 (37.5)
Overweight	41 (39.4)
Obese	24 (23.1)
Comorbidities	
Diabetes Mellitus	34 (32.7)
Hypertension	29 (27.9)
Family History of ILD	12 (11.5)
Smoking	37 (35.6)

The clinical symptoms and physical examination findings of the participants are summarized in **Table 2**. Dyspnea and dry cough were the most common presenting symptoms, reflecting the typical clinical presentation of usual interstitial pneumonia. Other symptoms such as tiredness and weight loss were also observed in a substantial

number of patients, whereas oral ulcers, photosensitivity, rash, and musculoskeletal symptoms were less frequently reported. On physical examination, fine inspiratory crackles were the most frequent finding, while digital clubbing was present in approximately one-third of the patients.

Table 2: Clinical Presentation and Physical Examination Findings (n=104)

Clinical Variables	n (%)
Symptoms	
Dry cough	81 (77.9)
Dyspnea	89 (85.6)
Tiredness	54 (51.9)
Weight loss	32 (30.8)
Oral ulcers	11 (10.6)
Photosensitivity	14 (13.5)
Rash	9 (8.7)
Muscle / joint pain	21 (20.2)
Physical Examination	
Fine inspiratory crackles	92 (88.5)
Clubbing	38 (36.5)

The frequency of idiopathic and non-idiopathic pulmonary fibrosis and their association with demographic and clinical variables are presented in **Table 3**. Idiopathic pulmonary fibrosis constituted the majority of cases in the study population. Stratification analysis demonstrated a

statistically significant association between age group and smoking history with idiopathic pulmonary fibrosis. In contrast, gender, BMI classification, diabetes mellitus, and hypertension did not show significant associations with the disease subtype.

Table 3: Stratification of Idiopathic and Non-Idiopathic Pulmonary Fibrosis with Demographic Variables (n=104)

Variables	Idiopathic PF n (%) (n=71)	Non-Idiopathic PF n (%) (n=33)	p-value
Age Group (years)			0.041
18-30	12 (16.9)	11 (33.3)	
31-45	24 (33.8)	11 (33.3)	
46-60	35 (49.3)	11 (33.3)	
Gender			0.287
Male	45 (63.4)	17 (51.5)	
Female	26 (36.6)	16 (48.5)	
BMI Classification			0.521
Normal	25 (35.2)	14 (42.4)	
Overweight	29 (40.8)	12 (36.4)	
Obese	17 (23.9)	7 (21.2)	
Smoking			0.032
Yes	30 (42.3)	7 (21.2)	
No	41 (57.7)	26 (78.8)	
Diabetes Mellitus			0.618
Yes	24 (33.8)	10 (30.3)	
No	47 (66.2)	23 (69.7)	
Hypertension			0.704
Yes	21 (29.6)	8 (24.2)	
No	50 (70.4)	25 (75.8)	

A comparative analysis of clinical symptoms between IPF and non-IPF patients is presented in **Table 4**. Dyspnea and dry cough were highly prevalent in both groups, with slightly higher frequencies in IPF patients. Systemic and

autoimmune-related symptoms, including oral ulcers, photosensitivity, rash, and musculoskeletal complaints, were more commonly observed in non-IPF patients. However, these differences did not reach statistical significance ($p>0.05$).

Table 4: Comparison of Clinical Symptoms Between IPF and Non-IPF Patients (n=104)

Symptoms	IPF n (%) (n=71)	Non-IPF n (%) (n=33)	p-value
Dry cough	58 (81.7)	23 (69.7)	0.182
Dyspnea	63 (88.7)	26 (78.8)	0.201
Tiredness	34 (47.9)	20 (60.6)	0.218
Weight loss	20 (28.2)	12 (36.4)	0.392
Oral ulcers	5 (7.0)	6 (18.2)	0.082
Photosensitivity	7 (9.9)	7 (21.2)	0.109
Rash	4 (5.6)	5 (15.2)	0.094
Muscle/joint pain	11 (15.5)	10 (30.3)	0.071

Further evaluation of non-IPF cases (n=33) revealed that connective tissue disease-associated interstitial lung disease (CTD-ILD) was the most common underlying etiology. Rheumatoid arthritis-associated ILD was the leading cause, followed by systemic lupus erythematosus and

mixed connective tissue disease. Other causes included ANCA-Vasculitis, drug-induced ILD, and occupational/environmental exposure-related ILD (**Table 5**).

Table 5: Causes of Non-Idiopathic Pulmonary Fibrosis (n=33)

Causes of Non-IPF	n (%)
Rheumatoid arthritis-associated ILD	11 (33.3)
Systemic lupus erythematosus-associated ILD	7 (21.2)
Mixed connective tissue disease	5 (15.2)
ANCA-Vasculitis	4 (12.1)
Drug-induced ILD	3 (9.1)
Occupational/environmental exposure	3 (9.1)

DISCUSSION

Fibrosing interstitial lung diseases (ILDs), especially usual interstitial pneumonia (UIP) and idiopathic pulmonary fibrosis (IPF) have continued to be a significant cause of chronic respiratory morbidity in the world. The high-resolution computed tomography (HRCT) has made significant progress and is useful in the diagnostic assessment of these conditions without the need to use invasive procedures. New methods like quantitative CT texture analysis and automated airway evaluation also contribute to the improvement of diagnostic accuracy and prognostic stratification, which is a developing

trend in the study of ILD [11,12]. In this framework, the current research examined demographic profile, clinical characteristics and stratification of idiopathic and non-idiopathic pulmonary fibrosis among the patients with the HRCT-confirmed UIP.

The study population was predominantly middle-aged, with a mean age of 47.6 ± 9.8 years and the highest proportion in the 46–60-year group. This is in line with well-established epidemiological trends that show a rising incidence and prevalence of IPF in older years, and especially after the fifth decade [13,14]. The observed minor male dominance (59.6) is also in line with other

available literature since increased exposure to environmental and occupational risk factor as well as lifestyle variations (such as smoking) have been implicated [15,16]. Even though gender was not a significant association in this study that indicated disease subtype, the distribution is representative of what is broadly reported demographics.

A large percentage of patients were obese or overweight. Obesity is not a direct etiological agent of pulmonary fibrosis, but it could contribute to respiratory compromise by altering lung mechanics and decreasing functional capacity. Also, the comorbidity of metabolic abnormalities can affect the severity and progression of the disease as implied in earlier research [17].

Comorbid conditions, especially diabetes mellitus and hypertension, were commonly seen. These results are compatible with the available data that suggests that ILD patients often have comorbid systemic diseases, making them more prone to morbidity and healthcare burden. These comorbidities need to be managed effectively to provide comprehensive care to the patient, and this might affect overall outcomes [18].

The most common symptoms were dyspnea and dry cough, which are the typical characteristics of fibrosing lung disease with progressive restriction and poor gas exchange. These results are similar to the previous ones in that chronic exertional dyspnea and non-productive cough are considered to be cardinal manifestations of IPF and other ILDs [19]. When examined, fine inspiratory (Velcro-like) crackles were predominantly found with digital clubbing coming second. These are typical markers of interstitial fibrosis and clubbing is usually linked to a more progressive or chronic illness [20].

Altogether, the results of the present research support current data on the demographic and clinical features of UIP and IPF and underline the importance of HRCT in the diagnosis. The initial identification of typical characteristics, as well as the determination of risk factors and etiologies, are essential to make a timely diagnosis, relevant categorization, and effective treatment of fibrosing interstitial lung diseases.

Limitations of study: There are a number of limitations in this study. To begin with, the study was carried out in one facility and the sample size was relatively small which could restrict the ability to generalize the results to large populations. Second, the cross-sectional design cannot be used to measure disease progression, response to treatment, or long-term survival. Third, other diagnostic methods like pulmonary function testing, histopathological confirmation or longitudinal follow-up radiology were not encompassed in the analysis. It is advisable that future multicenter prospective studies that will involve larger sample sizes and more detailed clinical examinations should be used to substantiate and build on these findings.

CONCLUSION

In patients with UIP pattern on high-resolution computed tomography (HRCT) of the chest, idiopathic pulmonary fibrosis (IPF) was the most common diagnosis and was significantly associated with increasing age and smoking. Non-idiopathic pulmonary fibrosis (PNF)-related interstitial lung disease (ILD) most commonly occurred as a result of rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE). Early recognition of characteristic clinical and radiological patterns and a careful assessment of underlying etiologies, is essential for accurate diagnosis of fibrosing ILD. It is crucial that these conditions are identified in a timely manner and appropriately classified in order to manage the patient optimally and achieve the best clinical result.

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