

# An Observational Cross Sectional Study on the Diagnosis of Possible Interstitial Lung Disease Through Imaging and Clinical Findings in and Around Prayagraj

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**Abstract:** **Background:** The term interstitial lung diseases is an broad term for large group of lung diseases rather than a specific disease entity. The interstitium includes the space between epithelium and endothelial basement membranes, it is the primary site of injury in ILD. However, these disorders not only affects interstitium but also airspaces and vessels, peripheral airways. **Objectives:** To find out the distribution of various types of ILD in and around Prayagraj. **Methods:** A Observational study was conducted between October 2022 and January 2024 in MLN Medical college Prayagraj. Baseline demographic details, clinical symptoms, signs, radiological findings (chest radiograph and HRCT Thorax), serology and Lung function test were performed and diagnosis of type of interstitial lung disease was made using multidisciplinary discussion. **Results:** A total of 140 patients were recruited of which 70.5% were females. Most common ILD subtype in our study was connective tissue disease associated ILD - 76 patients. Most common type of CTD ILD observed in our study was Rheumatoid-ILD (51 patients) and most common HRCT finding was UIP pattern (80.3%) and most commonly observed Lung function abnormality was moderate restriction. **Conclusion:** Connective tissue disease-associated ILD was the most common ILD found in our study around prayagraj. This suggests that the distribution of ILD would vary depending on the geographical area and the environmental exposure, occupation, and smoking habits which is different with the Indian ILD registry. (Keywords: ILD- Interstitium lung disease; IPF- Idiopathic pulmonary fibrosis).

**Keywords:** connective tissue disease, interstitial lung disease, rheumatoid ILD, HRCT thorax, Prayagraj study

## 1. Introduction

INTERSTITIAL LUNG DISEASE (ILD) describes a heterogeneous group of disease resulting from damage to the lung parenchyma by varying patterns of inflammation and fibrosis. The interstitium includes the space between epithelium and endothelial basement membranes, it is the primary site of injury in ILD. However, these disorders not only affects interstitium but also airspaces and vessels, peripheral airways (1). In world the prevalence and incidence lies between 5.6-82.4 and 1-70.1 per 100,000 population. In india the prevalence and incidence lies between 6.27- 97.9 and 10.1- 60.7 per 100,000 population respectively (2,3,4,5). In India ILD Registry, the mean age of participants was 55.3 years . HP was the final diagnosis in a majority of cases (47.3%), followed by CTD-ILD/ (13.9%), IPF (13.7%), sarcoidosis (7.8%), and pneumoconiosis (3%). Among patients with HP, 48.1% had been exposed to air coolers, 26.3% to air conditioners, 21.4% to birds and 20.7% to mold in their homes. RA was the most common type of CTD-ILD (38.4%) followed by scleroderma (22.5%) (6,7,8). ALVEOLAR EPITHELIAL INJURY is one of the primary initiating mechanism of pulmonary fibrosis, but activated fibroblasts are the primary effector of the disease (9)

## 2. Materials and Methods

- 1) It was a cross-sectional, observational and comparative study, carried out at the Department of Pulmonary Medicine, SRN Hospital, MLN Medical College, Prayagraj. After obtaining approval from the institutional ethics committee, patients were recruited from October 2023 to January 2024 after obtaining an informed consent. Patients suspected to have ILD by history, clinical examination, and chest radiography were consecutively selected for the study.
- 2) Patients will be enrolled in this study as per inclusion and exclusion criteria.
- 3) Diagnosis of ILD through multidisciplinary discussion.

### Inclusion criteria:

- 1) Age greater than 18 years.
- 2) Patients with respiratory symptoms like shortness of breath and cough, chest pain etc.
- 3) Bilateral abnormality in chest x ray/ High resolution Computed tomography thorax.

### Exclusion criteria:

- 1) Patients not giving consent.
- 2) Age less than 18 years.

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- 3) Patients with clinical suspicion of recent or active infection, those who are sputum positive for AFB.
- 4) Patients with any malignant disease.

### 3. Study Procedure

After obtaining written informed consent, patient qualifying inclusion criteria will be assessed as follows:

- Recording of semi structured socio-demographic proforma.
- All patient were subjected to detailed clinical history (including work environment and occupational history) followed by general and systemic examination.
- Routine blood tests like CBC, LFT, RFT, Serum electrolytes, Urine analysis, HbA1c, Chest x ray (PA View) to rule out any infections.
- HRCT chest and Contrast also done if mediastinal lymphadenopathy suspected.
- Serological tests like ANA (by immunofluorescence), RA factor (by nephelometry) were done for all cases, other tests such as Anti CCP Ab, Anti-Ro Ab, Anti-La Ab, Anti SCL 70 Ab, Anti Centromere Ab, Anti Ds DNA Ab, Anti Smith Ab, Anti U1 RNP Ab, S.ACE also and 24 hr urinary calcium also done wherever indicated.
- 6 Minute walk test.
- 2D ECHO.
- Spirometry

### 4. Diagnostic Criteria

For the diagnosis of IPF, the ATS/ERS guidelines were followed (10). For the diagnosis of other IIPs, the ATS/ERS MDD Consensus Classification of the IIPs was followed (11,12). A diagnosis of sarcoidosis was made on the basis of consistent clinical and radiological findings, in the absence of other known causes such as tuberculosis (13). A diagnosis of HP was made based on a history of exposure to organic dusts, typical HRCT appearance (any combination of GGOs, septal thickening, mosaic attenuation and honeycombing). A diagnosis of a CTD related ILD the subjects was diagnosed based on standard criteria using the ATS/ERS research statement (14).

### 5. Results

A total of 140 cases of interstitial lung disease patients aged between 29 to 80 years were enrolled over a period of 1-1.5 years. There was 64 (45.7%) males and females 76 (54.2%). The mean age of presentation of ILD Patients was 50.06±14.91 years. 80 Patients were from Rural background (57.1%) and 60 were from Urban area (42.8%).

In this study, the percentage of smokers and non-smokers were 34.2%, 65.7%. The disease wise details are given table-1.

**Table 1: Shows Various Clinico-Radiological Parameters**

S. No	Parameter	IPF	Sarcoidosis	HP	NSIP	CTD-ILD	Silico-Pneumoconiosis	Total	
1.	Mean age	68 ± 9.40	67.5 ± 1.91	68.70 ± 9.57	45 ± 5.89	40.08 ± 4.97	41.29 ± 3.40	50.06 ± 14.91	
2.	Duration(yrs)	8.74 ± 3.47	8.75 ± 2.87	8.70 ± 2.11	7.64 ± 1.91	6.27 ± 2.01	7.00 ± 3.06	6.79 ± 2.93	
3.	Gender	Male	26(40.6%)	4 (6.25%)	7 (10.9%)	6 (9.3%)	14 (10.0%)	7 (5.0%)	64 (45.7%)
		Female	6 (7.8%)	0	3 (3.95%)	5 6.5%)	62 (44.2%)	0	76 (54.2%)
4.	Residence	Rural	25 (17.8%)	1 (0.7%)	7 (5.0%)	7 (5.0%)	36 (25.7%)	4 (2.8%)	80 (57.1%)
		Urban	7 (5.0%)	3 (2.1%)	3 (2.1%)	6 (4.2%)	38 (27.1%)	3 (2.1%)	60 (42.8%)
5.	Smoker	Smoker	24 (50%)	4 (8.3%)	7(14.5%)	6 (12%)	2 (4.1%)	5 (10.4%)	48 (34.2%)
		Non- Smoker	8 (8.7%)	0	3(3.2%)	5 (5.4%)	74 (80.4%)	2 (2.17%)	92 (65.7%)
6.	6MWD	Expected(meters)	640 ± 94	596 ± 78	686 ± 78	709 ± 81	741 ± 90	691 ± 84	677 ± 81
		Actual(meters)	264 ± 12	274 ± 14	287 ± 13	316 ± 48	420 ± 40	326 ± 12	314 ± 23
7.	Various Radiological Findings	Interseptal thickening	96.88%	90.14%	75.86%	81.2%	79.8%	86.4%	79.8%
		Honeycombing	97.48%	40.8%	15.8%	14.2%	65.4%	1.2%	64.8%
		Bronchiectasis	96.14%	41.86%	48.6%	14.2%	65.4%	2.4%	61.8%
		GGOs	3.14%	55.86%	52.87%	99.6%	80.8%	24.8%	61.6%
		Reticulations	90.63%	92.18%	64.8%	56.8%	54.9%	33.4%	72.4%
		Cysts	1.4%	50.86%	1.2%	70.4%	20.2%	54.9%	34.8%
		Nodules	3.8%	60.24%	51.8%	27.7%	40.1%	72.6%	20.6%
		Air trapping	68.7%	94.8%	18.6%	18.9%	13.8%	44.8%	51.8%
		Intrathoracic lymphadenopathy	20.8%	60.86%	81.4%	34.5%	20.8%	30.3%	64.9%
8.	Comorbidity	Hypertension	3 (13.6%)	4 (18.8%)	6(27.2%)	0	8 (5.7%)	1 (4.5%)	22 (15.7%)
		Diabetes	16 (38.1%)	3 (7.1%)	7(16.6%)	1 (2.3%)	13 (9.2%)	2 (4.7%)	42 (30.0%)
		Thyroid disease	3 (23%)	0	0	1 (7.6%)	9 (6.4%)	0	13 (21.4%)
	GERD	26 (18.5%)	1 (0.7%)	4(2.8%)	5 (3.5%)	24 (17.1%)	2 (1.4%)	60 (42.8%)	

The presence of co-morbidity was not unusual with Diffuse parenchymal lung disease or ILD; but in present study the

most frequently present co-morbidity was GERD, Diabetes mellitus and hypertension, hypothyroidism, Pulmonary

hypertension seen in 42.8%, 30%, 15.7%, 21.4% respectively. In this study GERD was highest amongst IPF 18.5%. Interestingly in our study Hypothyroidism is more associated with CTD-ILD. Table-1 showing associations of Co-morbidity among various ILDs subtypes.

Among 140 patients, normal spirometry was observed in 20 patients (14.29%), obstructive pattern was present only in 5 patients (3.57%). Restrictive pattern was present in 95 patients (67.86%). Mixed pattern was present in 5 patients (3.57%). 15 Patients were unable to perform PFT. In this, mild restriction was present in 30 patients (31.51%), moderate restriction was present in 50 patients (52.63%), and severe restriction was present in 15 (15.78%).

99 (70.7%) patients with ILD patients were able to perform 6 Minute Walk test and Mean expected 6 walk test distance was  $677 \pm 81$  meters, while performed distance was  $314 \pm 23$  meters. The details were given in table-1.

Majority of patients in our study shows reticular or reticular nodular pattern on chest x ray and on HRCT of chest various radiological abnormality were UIP pattern (80.6%), Interseptal thickening (75.6%), Honeycombing (67.8%), Bronchiectasis (60.2%), GGOs (61.6%), Reticulation (65.7%), Cyst (5.5%), Nodules (20.5%), Air trapping (26.6%), Intrathoracic lymph nodes (37.0%), Pleural effusion (1.4%), Pleural Thickening (15.1%). The details of radiological abnormality in various ILDs were summarized in Table-1.

The most common type of ILD was connective tissue disease-ILD 76 Patients (54.29%), followed by Idiopathic pulmonary fibrosis in 32 Patients (22.86%), Non specific interstitial pneumonitis in 11 patients (7.86%), Hypersensitivity pneumonitis in 10 patients (7.0%), Chronic silicopneumoconiosis in 7 patients (5.00%), Sarcoidosis in 4 patients (2.86%).

The most common type of CTD-ILD was Rheumatoid –ILD 51 patients (67.10%), Progressive systemic sclerosis 16 patients (21.03%), SLE-ILD 1 patient (1.31%), Sjogrens syndrome 5 patients (6.57%), Mixed connective tissue disease-ILD 3 patients (3.94%), the details were summarized in table-2.

**Table 2:** Various Diagnoses Found among Patients of ILD

Disease	No. of Patients	Percentage
IPF	32	22.86%
Hypersensitivity pneumonitis	10	7.0%
Sarcoidosis	4	2.86%
Silicopneumoconiosis	7	5.0%
NSIP	11	7.86%
CTD-ILD		
RA-ILD	51	67.10%
Systemic sclerosis-ILD	16	21.03%
Sjogrens syndrome-ILD	5	6.57%
MCTD-ILD	3	3.94%
SLE-ILD	1	1.31%

## 6. Discussion

This was a hospital based prospective, observational study of patients with Interstitial Lung Diseases (ILD), which included detailed clinical history (Including environmental, occupational and medical history), physical examination, radiological and other relevant investigations to find out the distribution of different types of ILD subtypes in and around prayagraj.

The mean age of ILD patients in our study was  $50.06 \pm 14.91$  years. The mean age was higher among IPF patients ( $68.41 \pm 7.7$ ) compared to non-IPF ILD patients ( $51.4 \pm 10.9$ ). The median age of the IPF group was 55 years and that of non-IPF group was 53 years. The difference in the median age in both groups was statistically significant (p value = 0.001). The mean age of patients in various studies varied from 43.5 to 52.4 years such as **Maheshwari U, Gupta D, et al (15)** shows that mean age of ILD patients were  $50.6 \pm 11.9$  years. **Shafeeq MK, Anithakumari et al (16)** 70 patients were included in the study. The mean age of study population was 52.4 years.

In present study, ILD was seen more in females 76/140 (54.29%) than males 64/140 (45.7%). A study done by **Valappil et al (17)** found connective tissue disease-associated ILD to be more common and they showed a predominantly female population which is in concordance with our study. Various authors reported variable findings on either sex predominance. Contrary to our study, **Gagiya et al (18)** showed male preponderance (66.5%). Another study from India **Sen et al (19)** reported that females were twice compared to male. **Shafeeq MK, Anithakumari et al (16)** study from Trivandrum, India, found 48.6% males and 51.4% females among ILDs patients. Indian ILD registry (**Singh et al (6)**) also showed female preponderance but hypersensitivity pneumonitis was the most common ILD reported.

In Our study, the most common symptom was dyspnea (98.8%) followed by cough (84%) among which 39.2% had expectoration, other 44.8% had dry cough. The most common non pulmonary symptom found was joint pain (45%), GERD (36.6%). In IPF Patients, 100% dyspnea, dry cough, and crepitations, clubbing (87.25%) which is similar to studies done **Jindal et al (20)**. In our study GERD found on 26 (81.2%) out of 32 patients in IPF versus 34 (41.67%) out of 108 in Non-IPF patients. A study done by **Savarino E et al (21)** which also shows that IPF patients had significantly higher (P value <0.01) oesophageal acid exposure 9.25 (4.7–15.4%) versus 3.3 (1.4–7.4%) versus 0.7 (0.2–4.2%) as compared to non-IPF patients and healthy volunteers, respectively. Co-morbidities play an important role in the quality of life of ILD patients. ILD is a chronic progressive disease in which comorbidities further hamper the quality of life of patients, although many of these are treatable and preventable. In our study apart from Diabetes mellitus and hypertension, GERD (18.5%) more in IPF and 17.1% in CTD-ILD. **Varun Das, Unnati Desai et al (22)** study suggests

psychiatric illnesses were noted in 13 (9.28%) of which 10 had depression, 2 had anxiety and 1 had psychosis.

In this study 48 (34.29%) patients in our study were smokers/ex-smokers. 92 (65.71%) patients were non-smokers. Majority of smokers/ex smokers were in Idiopathic pulmonary fibrosis. In 48 patients of smokers/ex smokers, 24 (50.00%) of them were in IPF. The proportion of ever smokers was higher among IPF patients (75.7%), 95% CI: 46.7%, 77.02%) compared to non IPF group (22.7%), 95% CI: 9.7%, 23.43%). The difference in the proportion of smokers was statistically significant. (RR- 2.09, 95% CI: 1.4, 2.97) p value < 0.001. Earlier study **Raj Kumar et al (23)** showed that smoking was present 78.70% cases of IPF.

Most common pattern observed in our study was Restrictive pattern. The mean % predicted FVC of the study population was 50.4±18.5. IPF patients had lower mean FVC % compared to non- IPF ILDs. (48.1±16.2 vs 51.2±23.8). The difference between median FVC of two groups was statistically significant p value= 0.001. (%). Restrictive pattern was present in 95 patients (67.86%) which was concordance with other studies. **Dhooira S, Agarwal R, et al (24)** a total of 803 subjects (58.6%) subjects had a restrictive defect on spirometry.

The most common HRCT Findings in our study were UIP Pattern (80.3%), Interseptal thickening (75.6%), Honeycombing (67.8%), Bronchiectasis (60.2%), GGOs (61.6%), Reticulation (65.7%), Cyst (5.5%), Nodules (20.5%), Air trapping (26.6%), Intrathoracic lymph nodes (37.0%), Pleural effusion (1.4%), Pleural Thickening (15.1%). The details of radiological abnormality in various ILDs were summarized in TABLE- 1. In our study UIP pattern contributes about 80.3%, in which IPF patients 95.14%, 65.86% in HP Patients, 65.6% in CTD-ILD patients. It clearly states that UIP pattern is majority in both IPF and CTD-ILD patients. In our study, RA-ILD 80.86% of UIP Pattern, 78.43% of septal thickening, 71.04% of reticulations which is similar to several other studies such as **Pankaj Badarkhepatil, Dayanand Kawade et al (25)**, most common pattern found with rheumatoid arthritis-ild was reticular opacity associated with UIP pattern. Out of 16 Systemic sclerosis-ILD patients, 95.8% of GGOs, 74.8% of reticulations, 48.7% of pleural effusion correlates with **Goldin et al (26)** reviewed the HRCT scans in 162 patients with symptomatic PSS-related ILD. The main findings consisted of ground-glass opacities (90%). The authors concluded that in the majority of cases the findings were consistent with NSIP patterns. In our study one patient of SLE-ILD shows 100% of GGOs and reticulations, pleural effusion. These findings correlates with **Fenlon HM et al (27)**. In 10 patients of HP, 92% of reticulations, 90% of interseptal thickening, 84.8% of air trapping, 75.86% of GGOs, 60.24% of nodules similar to **Hansell and Moskovic (28)** reviewed the HRCT findings in 15 patients with HP, the common abnormality was the presence of diffuse bilateral ground-glass attenuation in 73% of the patients. In 11 patients of NSIP, 99.6% of GGOs, 81.2% of interseptal thickening, 70.4% of cysts, 35.4% of lymphadenopathy, 56.8% of

reticulations were observed in our study. **Silva et al (29)** demonstrated that a characteristic feature of NSIP is relative sparing of the immediate subpleural lung, it can be helpful in distinguishing fibrotic NSIP from UIP because UIP is typically most severe in the subpleural regions. In 4 patients of Sarcoidosis, 81.4% of intra thoracic lymphadenopathy, 90.14% of interseptal thickening, 75.86% nodules, 65.86% of UIP Pattern, 60.24% of GGOs were observed. These findings correlates with study done by **Nishimura K et al (30)**. In 7 patients of silicopneumoconiosis, 72.6% of nodules, 66.4% of interseptal thickening, 54.9% of cysts, 30.3% of intrathoracic lymphadenopathy, 4 patients have calcification of lymph nodes. All of them were males and involved in occupational exposure (silica) in which radiologic features similar to **Marchiori E et al (31)**.

The present study demonstrates that the pattern of ILD in our population does not strictly follow what is mentioned in literature. Connective tissue disorder-ILD are more common in our study which is mentioned as the second most common ILD in literature (2). In India ILD Registry, Hypersensitivity pneumonitis followed by CTD-ILD and IPF (6). In Greek, Paris, and Turkey, sarcoidosis was the most common type of ILD (32, 33, 34). This disparity may be due to the geographical diversity and the environmental factors that may also influence the type of ILD.

In our study, CTD ILD was the most common type of ILD found. It was similar to that of the study done by Valappil et al (5) in which CTD ILD constitutes about 34.9% of patients. In PGIMER and New Delhi study, sarcoidosis was the most common ILD reported (9,17). In Mumbai, UP, and West Bengal studies, IPF was the most common type of ILD observed (17, 35, 36).

There are some limitations in our study. The diagnosis of ILDs was made by taken into account History, clinical, Serological and radiological excluding pathological profile. Moreover study has been done in a single tertiary care centre, the data cannot be generalized to whole of India. Also some patients not able to do physiological parameters and 6 minute walk test.

## 7. Conclusion

To conclude, Connective tissue disorder-ILD was more in our study followed by IPF. This suggests that the distribution of ILD would vary depending on the geographical area and environmental exposure which was in contrast with ILD registry. Among CTD-ILD, Rheumatoid Arthritis-ILD was the most common ILD observed The most common HRCT findings in our study was UIP Pattern. Physiologically, Moderate restriction was often noted. Lack of recognition of disease at an early stage leads to irreversible damage to most of the patients, especially in treatment-responsive ILDs like Sarcoidosis, HP. In India due to high burden of Pulmonary tuberculosis and also it acts like mimicker of ILD caused significant delay in the diagnosis of DPLD. Hence multicentric study are required from different regions of the

country, so that the burden of ILDs in India can be defined accurately

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