Original Article

Clinical Profile of Interstitial Lung Disease at a Tertiary Care Centre in India

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Abstract

Background. The prevalence and spectrum of interstitial lung diseases (ILDs) varies from region to region depending upon genetic and environmental factors.

Methods. This was a descriptive observational study of 262 consecutive ILD patients diagnosed in the Pulmonary Medicine Department over a period of four years.

Results. The mean age of the patient was 52.7±14.9 years; there were 120 males. All types of ILDs were more common in women except idiopathic pulmonary fibrosis (IPF) which was found predominantly (90.6%) in male patients. High resolution computed tomography (HRCT) showed definite usual interstitial pneumonia (UIP), possible UIP and inconsistent with UIP patterns in 50.4%, 9.5% and 40.1%, respectively. IPF was the most commonly found ILD (24.1%) followed by connective tissue disease related ILD (CTD-ILD) (22.1%), non-specific interstitial pneumonia (NSIP) (17.2%), hypersensitivity pneumonitis (HSP) (15.6%), sarcoidosis (7.6%), combined pulmonary fibrosis and emphysema (CPFE) (4.6%), cryptogenic organising pneumonia (4.2%), and occupational lung disease (2.7%), respectively.

Bronchoscopic procedures were performed in 66 (25.2%) of patients which were diagnostic in 27 (44.9%); overall pathological diagnosis was possible in 10.2%. Univariate analysis showed smoking and hypothyroidism as statistically significant risk factors associated with IPF.

Conclusions. Idiopathic pulmonary fibrosis was found as most common ILD; UIP pattern was seen in IPF, CTD-ILDs, chronic HSP and fibrotic NSIP. **[Indian J Chest Dis Allied Sci 2021;63:23-28]**

Key words: Interstitial lung disease, Risk factors, Usual interstitial pneumonia, Idiopathic pulmonary fibrosis, Hypothyroidism.

Introduction

Interstitial lung diseases (ILDs), a heterogeneous group of more than hundred disorders, that are grouped together because these have common clinical, radiographic and pathological features.[1] It has been classified in to ILD of known cause, idiopathic interstitial pneumonia, sarcoidosis and other rare ILDs, such as lymphangiomyomatosis (LAM).[2] Diagnosis required a multi-disciplinary approach based upon detailed history, physical examination, laboratory results, pulmonary function testing, imaging and in selected cases lung biopsy to reach a final diagnosis.

The actual incidence of ILDs remain unknown, as very limited data are available from our country about the ILD prevalence, risk factor, diagnosis, and prognostic evaluation. The available studies showed wide variations in the incidence and prevalence of the various ILDs among countries.[3-7] The spectrum of ILDs varies from country to country, within a country; and depends upon genetic factor, environmental factors, occupational exposures, smoking habits, socio-cultural and farming practices.[8-9] Recently, a multi-centre study[10] in India showed hypersensitivity as most common ILD in contrary to other studies[5,11-12] which showed sarcoidosis and connective tissue disease related ILD (CTD-ILD) as the most common ILD. The present study was performed to describe the clinical and radiological profile of patients with ILD, registered at a tertiary care hospital in Bihar; and to study the risk factors associated with IPF.

Material and Methods

This was a cross-sectional, observational study done from January 2015 to December 2018. Newly diagnosed consecutive patients with ILD were included in the study. Patients aged less than 15 years were excluded from the study. A detailed history including different risk factors as obtained from each patient followed by general and systemic examinations and were

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documented in a proforma used in Indian ILD Registry.[11] All patients underwent laboratory tests including complete blood count (CBC), thyroid profile, rheumatoid factor, anti-nuclear antibodies (ANAs), anticyclic citrullinated protein antibodies (anti-CCP). Other ANAs were done depending upon the type of CTD. High resolution computed tomography (HRCT), pulmonary function assessment using spirometry, six-minute walk test (6MWT) and carbon monoxide diffusion capacity of lung (DLCO) were done. Patients were also subjected for bronchoscopy in selected cases and bronchoalveolar lavage, transbronchial needle aspiration (conventional), endobronchial biopsy, transbronchial lung biopsy (TBLB) were done depending upon the indication.

For the diagnosis of IPF and other idiopathic interstitial pneumonia (IIPs), the American Thoracic Society/European Respiratory Society (ATS/ERS) guidelines were followed.[1,2,13] HRCT of patients classified in to either usual interstitial pneumonia (UIP) pattern, possible UIP pattern, or inconsistent with UIP pattern based on classification used by ATS guidelines.[13]

The diagnosis of sarcoidosis[10] was made on the basis of typical clinical and radiological findings, and the presence of granulomatous inflammation in tissue specimens, in the absence of tuberculosis. If pathological sample was not obtained or granulomatous inflammation could not be demonstrated in the sample, the diagnosis was made on basis of serum angiotensin converting enzyme level, tuberculin skin test (Mantoux test) and on clinical response to steroids.

Diagnosis of hypersensitivity pneumonitis (HP) was made based on history of exposure to organic dusts, typical HRCT appearance (any combination of ground-glass opacities, ground-glass centrilobular nodules, septal thickening, mosaic attenuation and honey-combing), along with histological findings of HP on lung biopsy. A diagnosis of a CTD related ILD was made in the presence of a CTD (rheumatoid arthritis, systemic sclerosis, and others) and the presence of ILD on HRCT of the chest. Patients diagnosed as non-specific interstitial pneumonia (NSIP), if HRCT and/or biopsy suggestive of NSIP pattern with unidentifiable etiology. If patients had NSIP pattern due to identifiable factors, like CTD or HP, then the patient was labeled as under CTD-ILD or HP. The diagnosis of combined pulmonary fibrosis and emphysema have been made in the presence upper-lobe emphysema, lower-lobe fibrosis.[14]

All the patients suspected as ILD, discussed in clinico-radiological meet with Radiologist and/or Pathologist and final diagnosis was made as consensus opinion. In case, all the available information did not suggest a particular type of ILD, patients were classified into other or unclassified group of ILDs.

Statistical Analysis

Quantitative data are expressed as mean ± standard deviation (SD). Categorical data are expressed as median (interquartile range), or as number (percentage). Categorical data were compared using the Chi-square test. A P-value of <0.05 was considered as statistically significant. Data were analysed using the Statistical Package for the Social Sciences (SPSS, version 20, for Windows; IBMSPSS Inc., Chicago, IL).

Results

A total of 282 new patients were diagnosed with ILD during our study period. Thirty patients were excluded because of incomplete data, and so a total 262 patient data were analysed. The baseline characteristics of the study subjects are shown in table 1. Out of 262 enrolled patients, 120 were males. All types of ILDs were more common in females except IPF which was found predominantly 90.6% of the male patients (Table 2). The mean age of the patients was 52.7±14.9 years. The most common affected age group was 51-70 years. Most common symptoms were dyspnoea (95.8%) followed by cough (86.3%), joint pain (22.9%), chest pain (15.3%), fever (14.5%), anorexia (13.7), weight loss (12.2%) and haemoptysis (4.6%) (Table 3).

One-third (34.4%) of the study patients had past history of anti-tuberculosis treatment. Clubbing and basal crepitations were observed in 48.1% and 83.2%, respectively. Mean forced vital capacity (% predicted) was 56.62%± 18.63. We were able to perform DLCO in 88 patients only with a value of 47.75±24.02 of the % predicted. HRCT showed definite UIP pattern, possible UIP pattern and inconsistent with UIP pattern in 50.4%, 9.5% and 40.1%, respectively (Table 3). Most common cause for UIP pattern was IPF (47.7%) followed by CTD-ILD (10.7%), HP (10.6%) and fibrotic NSIP (12.1%) (Table 4).

Bronchoscopic procedure including bronchoalveolar lavage, transbronchial needle aspiration from lymph node, endobrochial biopsy or transbronchial biopsy was performed in 62 (25.2%) patients. But pathological diagnosis was confirmed only in 27 patients (12 sarcoidosis, 3 HP, 10 supportive of NSIP, 2 organising pneumonia).

Idiopathic pulmonary fibrosis was found to be the most common ILD (24.4%) followed by CTD-ILD (22.1%), NSIP (idiopathic) (17.2%), HP (15.6), sarcoidosis (7.6%), combined pulmonary fibrosis and emphysema (CPFE) (4.6%), cryptogenic organising pneumonia (4.2%), occupational lung disease (2.7%), respectively (Table 1).

Univariate analysis of the risk factors for IPF showed smoking andhypothyroidism to be statistically significant risk factors associated with IPF (Table 5).[16]

Table 1. Baseline characteristics of the study patients

Variables	No. (%)
Age (Years)	
<30	21 (8.0)
31-50	85 (32.4)
51-70	127 (48.4)
>70	29 (11.1)
Gender	
Male	120 (45.8)
Female	142 (54.2)
Total duration of illness (years)	**2.8±2.7**
Smoking	
Smoker	40 (15.3)
Non-smoker	222 (84.7)
Tobacco chewer	32 (12.2)
Past history of anti-tuberculosis treatment	
Yes	90 (34.4)
No	172 (65.6)
Co-morbidities	
Hypothyroidism	42 (16.0)
GERD	98 (37.4)
Diabetes	38 (14.5)
Hypertension	42 (16.0)
Coronary artery disease	16 (6.1)
Pathological diagnosis	27 (10.2)
ILD type in cohort	
IPF	64 (24.4)
Idiopathic NSIP	45 (17.2)
HP	41 (15.6)
Sarcoidosis	20 (7.6)
CTD-ILD	58 (22.1)
COP	11 (4.2)
OLD	07 (2.7)
CPFE	12 (4.6)
Other	04 (1.5)

Definition of abbreviations: GERD=Gastro-esophageal reflux disease, ILD=Interstitial lung disease, IPF=Idiopathic pulmonary fibrosis, NSIP=Non-specific interstitial pneumonia, HP=Hypersensitivity pneumonitis, CTD-ILD=Connective tissue disorder-interstitial lung diseases, COP=Cryptogenic organising pneumonia, OLD=Occupational lung disease, CPFE=Combined pulmonary fibrosis and emphysema.

Table 2. Comparison of different features among ILD

	IPF (n=64)	NSIP (n=45)	HP (n=41)	CTD-ILD (n=58)	Sarcoidosis (n=20)
Age	64.4±8.4	55.6±11.1	53±12.3	43.1±12.5	35±14.9
Male/ Female	58/6	18/27	15/26	10/50	13/7
TDI (Years)	2.6±3.1	2.53±2.1	2.39±2.3	3.04±2.5	2.47±2.2
Dyspnoea (mMRC>1) No (%)	22 (34.4)	16 (35.6)	18 (43.9)	26 (44.8)	4 (20.0)
Clubbing No (%)	48 (75.0)	22 (48.9)	16 (39.0)	21 (36.2)	4 (20.0)
Crepitation No (%)	61 (95.3)	40 (88.9)	34 (82.9)	51 (87.9)	5 (25.0)
Oxygen saturation	93.6±3.5	94.6±3.2	93.11±4.6	95.42±3.2	96.45±5.7
FVC (%Pred)	61.6±17.3	58.84±13.31	67±23.09	50.95±14.16	72.42±24.18
6MWD (meter)	234.1±186.6	304.7±152.4	201±60.72	282±68.2	322±79.3

Definition of abbreviations: ILD=Interstitial lung disease, IPF=Idiopathic pulmonary fibrosis, NSIP=Non-specific interstitial pneumonia, HP=Hypersensitivity pneumonitis, CTD-ILD=Connective tissue disorder-interstitial lung disease, TDI=Total duration of illness, mMRC=modified Medical Research Council, FVC=Forced vital capacity, 6MWD=Six-minute walk distance.

A comparison of the present study results with the previous studies is shown in table 6.[3-6,12,15,22]

Discussion

This was a prospective, observational study conducted to find out the clinical profile of ILD patients and risk factors associated with IPF coming to tertiary care centre of Bihar region, India. Two hundred sixty-four patients diagnosed as ILD after multi-disciplinary discussion were included in the study. The most common affected age group affected was 51-70 years with a mean age of 52.7±14.9 years. This was similar to other studies.[6,14,16] But different from the observations of another study[5] which reported a mean age of 40–43 years.

A female predominance (54.2%) was seen in our study which is in agreement with the other studies.[5,7,17] However, male predominance was also observed in a study.[14] Female predominance can be explained by the female preponderance for CTD-ILDs, like scleroderma, systemic lupus erythematosus, and rheumatoid arthritis, which were the second commonest ILDs observed in this study. Idiopathic pulmonary fibrosis was found as most common ILD (24.1%) followed by CTD-ILD (22.1%), NSIP (idiopathic) (17.2%), HP (15.6%), sarcoidosis (7.6%), cryptogenic organising pneumonia (4.2%), occupational lung disease (2.7%) respectively,

Table 3. Clinico-radiological presentation of ILD

Variable	No. (%)
Symptoms	
Cough	226 (86.3)
Dry	182 (69.5)
Productive	56 (21.4)
Dyspnoea (mMRC grade)	251 (95.8)
0	12 (5.3)
1	129 (52.7)
2	67 (26.7)
3	31 ((12.2)
4	12 (5.3)
Fever	38 (14.5)
Chest pain	40 (15.3)
Haemoptysis	12 (4.6)
Anorexia	36 (13.7)
Weight loss	32 (12.2)
Joint pain	60 (22.9)
clubbing	126 (48.1)
Basal crepitation	218 (83.2)
Wheeze	46 (17.6)
HRCT pattern	
UIP	132 (50.4)
Possible UIP	26 (9.9)
Inconsistent with UIP	106 (40.5)
Pulmonary function	
FVC (% Predicted)**	56.62±18.63
DLCO (% Predicted)*	47.75±24.02
Oxygen saturation at rest	93.9± 3.86
6MWD	245.81±122.14

*DLCO performed only in 88 patients,
**Spirometry performed in 212 patients

Definition of abbreviations: mMRC=modified Medical Research Council, HRCT=High-resolution computed tomography, UIP=Usual interstitial pneumonia, FVC=Forced vital capacity, DLCO=Diffusion capacity of the lung for carbon monoxide, 6MWD=Six-minute walk distance.

similar to other studies.[6,14,18] On the contrary, another multi-centre study[11] showed HP as the most common ILD, while in two other studies,[5,10] sarcoidosis was the most common ILD. The low incidence of sarcoidosis in the present study could be due to low index of suspicion, less number of pulmonologist in that area and most of the patients has been put on empirical anti-tuberculosis treatment. Hypersensitivity pneumonitis incidence varies from region to region depending upon the type of exposure and actual figure is difficult to estimate unless the patient have classical HRCT pattern, exposure

Table 4. Relation between HRCT pattern and ILD diagnosis

ILD type (n=264) (100%)	UIP Pattern (n=132) No. (%)	Possible UIP Pattern (n=25) No. (%)	Inconsistent with UIP Pattern (n=105) No. (%)
IPF (n=64)	63 (47.7)	1 (3.8)	0
NSIP(n=45)	16 (12.1)	9 (3.5)	20 (18.9)
HP (n=41)	14 (10.6)	3 (1.2)	24 (22.6)
Sarcoidosis (n=20)	2 (1.5)	0	18 (17.0)
CTD-ILD (n=58)	28 (10.7)	12 (4.6)	18 (17.0)
COP (n=11)	2 (1.5)	0	9 (8.5)
CPFE (n=12)	6 (4.5)	0	6 (5.7)
OLD (n=07)	01 (0.1)	–	06 (5.7)
Others (n=04)	–	–	04 (3.8)

Definition of abbreviations: HRCT=High-resolution computed tomography, ILD=Interstitial lung disease, UIP=Usual interstitial pneumonia, IPF=Idiopathic pulmonary fibrosis, NSIP=Non-specific interstitial pneumonia, HP=Hypersensitivity pneumonitis, CTD-ILD=Connective tissue disorder-interstitial lung disease, COP=Cryptogenic organising pneumonia, CPFE=Combined pulmonary fibrosis and emphysema.

Table 5. Association between risk factors and ILD

Risk Factors	IPF (n=64)	Non IPF (n=198)	Crude Odds Ratio (95% CI)	P value
Smoking				
Yes	19 (29.7)	21 (10.6)	3.6 (1.6–7.6)	**0.0005**
No	45 (70.3)	177 (89.4)		
GERD				
Yes	24 (37.5)	74 (37.4)	1.0 (0.5–1.9)	0.5493
No	40 (62.5)	124 (62.6)		
Hypothyroidism				
Yes	16 (25.0)	26 (13.1)	2.2 (1.0–4.7)	**0.0228**
No	48 (70.3)	172 (86.9)		
Past history of ATT				
Yes	24 (37.5)	66 (33.3)	1.21 (0.6–2.2)	0.3210
No	40 (62.5)	132 (66.7)		

Definition of abbreviations: ILD=Interstitial lung disease, IPF=Idiopathic pulmonary fibrosis, CI=Confidence interval, GERD=Gastro-esophageal reflux disease, ATT=Anti-tuberculosis treatment.

Table 6. Comparison of present study with previous studies

Study	IPF	Idiopathic NSIP No (%)	HP No. (%)	CTD –ILD No (%)	Sarcoidosis No (%)	CPFE No (%)	Occupational lung disease, No (%)	COP No (%)
Kumar *et al*[5]	80 (27.7)	74 (25.6)	7 (2.4)	13 (4.4)	108 (37.4)	–	–	–
Sen and Udwadia[6]	117 (43.0)	–	15 (6.0)	51 (18.0)	61 (22.0)	–	–	–
Shafeeq *et al*[15]	27 (39.0)	–	12 (17.0)	17 (24.0)	9 (13.0)	–	–	–
Kundu *et al*[22]	35 (38.0)	–	10 (10.9)	29 (31.5)	5 (5.4)	–	5 (5.4)	–
Subhash *et al*[23]	34 (53.9)	–	–	6 (9.5)	2 (3.1)	–	–	–
Valappil *et al*[12]	30 (23.3)	10 (7.8)	7 (5.4)	45 (34.9)	22 (17.1)	–	–	8 (6.2)
Singh *et al*[11]	148 (13.7)	92 (8.5)	513 (47.3)	151 (13.9)	85 (7.8)	–	33 (3.0)	34 (3.1)
Dhooria *et al*[10]	170 (21.2)	63 (7.8)	86 (10.7)	102 (12.7)	339 (42.2)	–	7 (0.9)	4 (0.5)
Present study	64 (24.4)	45 (17.2)	41 (15.6)	58 (22.1)	20 (7.6)	12 (4.6)	7 (2.7)	11 (4.2)

Definition of abbreviations: IPF=Idiopathic pulmonary fibrosis, NSIP=Non-specific interstitial pneumonia, CTD-ILD=Connective tissue disease related-interstitial lung disease, CPFE=Combined pulmonary fibrosis and emphysema.

history and pathological diagnosis. UIP pattern was found most commonly with IPF followed by NSIP, HP. NSIP generally do not associated with UIP pattern and even opinion varied in our multi-disciplinary team but most of them were in favour of UIP pattern.

In 2005, Cottin *et al*[19] first time coined the term combined pulmonary fibrosis and emphysema (CPFE) which is defined radiographically by the presence of classic features of centrilobular and/or paraseptal emphysemas in the upper lobes and pulmonary fibrosis (mainly IPF/UIP) in the lower lobes. We have used this criteria and observed an incidence of CPFE as 4.6% in ILD cohort. Interstitial lung disease is mainly characterised by gradually progressive dyspnoea and dry cough. We observed every fifth patients having productive cough, could be due to associated respiratory tract infection or traction bronchiectasis associated with fibrotic ILD. The most characteristic examination findings in ILD are clubbing and fine end inspiratory Velcro crepitations. Studies[20-21] have shown that clubbing may be seen in 25% to 50% patients and 'velcro' crackles seen in more than 80% patients. This study had similar results with clubbing and crackles reported in 48.1% and 83.2%, respectively.

We are able to perform bronchoscopic procedure in 66 (25.2%) of the study patients, which was diagnostic in 27 (44.9%) patients and overall pathological diagnosis possible in 10.2% patients. Other patients either deny for the test or unfit for the test. We achieved pathological diagnosis in 12 patients of sarcoidosis, 3 HP, 10 supportive of NSIP, 2 organising pneumonia. None of the patients underwent open lung biopsy or cryo biopsy as our centre did not have facility for that.

Interstitial lung diseases is a chronic progressive lung disease associated with many co-morbidities which impair the quality-of-life of the patients. We found gastro-esophageal reflux disease (GERD) as most common co-morbidity followed by hypothyroidism and hypertension.

We are able to achieved pathological diagnosis in only in 10.2% patients, rest of the patients were diagnosed based on clinical and radiological findings. This is one of the major limitation of our study. We have seen how the diagnosis change in Indian ILD Registry from site investigator to experts present in or out of the country.[11]

Conclusions

The idiopathic pulmonary fibrosis was found as most common ILD, in contrast to many other studies. UIP pattern is not only due to IPF but also due to CTD-ILDs, chronic HP and fibrotic NSIP. Smoking and hypothyroidism were found statistically significant risk factors associated with IPF.

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