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PROFILE OF INTERISTIAL LUNG DISEASES AT TERTIARY CARE CENTRE OF NORTHERN INDIA

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ABSTRACT

Background: Interstitial lung disease (ILD) is a heterogeneous group of lung diseases which are challenging to the clinicians. There is limited data on the presentation and diagnosis of these patients from India. The present study was planned to analyse the spectrum of ILD encountered at a tertiary referral centre in India to determine the clinical profile of the disease. **Material and Methods:** This study includes 116 patients diagnosed to have ILDs during the years 20013–2015 at tertiary care centre of north India. The diagnosis of ILD was based on clinical, radiological parameters, laboratory parameters, spirometric parameters and histopathology wherever available. Classification of ILD was done as per The American Thoracic Society/European Respiratory Society International Multidisciplinary Consensus Classification of Idiopathic Interstitial Pneumonias 2001 guidelines were used in the diagnosis. **Result:** The overall mean age at presentation was 45.24 years, 54.83 years in IPF, 44.60 years in HSP, 43.60 years in NSIP and 41.56 years in Sarcoidosis. Of the 116 ILD cases there were 70 male (60.34%) and 46 (39.66%) females. The overall mean duration of symptoms at diagnosis was 2.47 years, 1.5 years in IPF, 1.2 years in HSP, 1.5 years in NSIP and 3 years in Sarcoidosis. The most frequent presenting symptom in the ILD was cough present in 98 (84.45%), followed by exertional dyspnoea in 86 (74.13%). **Conclusion:** Interistial pulmonary fibrosis is the most common and Hypersensitivity Pneumonitis is the second common Interistial Lung Disease in our study. Being progressive disease most of the patients presented to us in advance stage of disease and in most of the cases anti tubercular treatment was started by the treating physician without being extensive evaluation because of lack of awareness among physicians.

KEYWORDS: Interistial Lung Disease, Idiopathic Pulmonary Fibrosis, Diffuse Parechymal Lung Disease.

INTRODUCTION

Interstitial lung disease is a heterogeneous group of lung diseases which are challenging to the clinicians. Interstitial lung diseases are also referred to as diffuse parenchymal lung diseases. [1] Interstitial lung disease (ILD) represents a group of about 200 distinct disorders involving lung parenchyma. ILD is also termed as Diffuse parenchymal lung disease (DPLD) and classified broadly into idiopathic interstitial pneumonia (IIP) and other than IIP. [2]

In 2002, the American Thoracic Society/European Respiratory Society (ATS/ERS) guidelines classified idiopathic interstitial pneumonias (IIPs) into seven specific entities and offered standardized terminology and diagnostic criteria. In the revision of the IIP classification by ATS/ERS in 2013 major IIPs are distinguished from rare IIPs and unclassifiable IIPs. [2] The need for histological diagnosis was changed to a multidisciplinary approach. Patients with ILD must undergo complete evaluation to establish specific form of ILD. An accurate diagnosis of ILD needs a thorough history elicitation including the past medical, social, family and occupational histories.

The prominent feature in interstitial lung diseases is fibrosis in the interstitium, which produces derangement of alveolar architecture and loss of functional alveolar capillary units. The process of achieving a diagnosis in a patient with ILD requires close communication between clinician, radiologist and pathologist. There is limited data on the presentation and diagnosis of these patients from India. The present study was, therefore, planned to analyse the spectrum of ILD encountered in a tertiary referral centre in India to determine the clinical profile of the disease. The available data on the frequency of occurrence of ILDs is sparse.[3] The incidence of ILDs is variable around the world. Literature shows the incidence of ILDs varying from 3.62 per 100,000 person-years in southern Spain [4] to 31.5 per 100,000 person-years in males and 26.1 per 100,000 person -years in females in New Mexico, USA, [5] a huge eightfold deviation in incidence across the globe. In a developing country like India, with a high prevalence of tuberculosis (TB), ILDs are often initially misdiagnosed as TB. Data on ILDs has been limited to just a few dispersed studies.[6–9] The largest ILD series published from India comprised just 274 patients reports from western literature show an increase in the prevalence and incidence of ILD in recent decades. [10,11]

The demographic profile and clinical, radiological and pathological characteristics along with physiological parameters of these ILD patients were retrospectively analysed.

The aims and objectives of this study was to study the profile of ILD at tertiary care centre in northern India.

MATERIAL AND METHODS

This study includes 116 patients diagnosed to have ILDs during the years 20011–2015 at tertiary care centre of north India. The diagnosis of ILD was based on clinical, radiological parameters, spirometric parameters and histopathology wherever available. Classification of ILD was done as per The American Thoracic Society/European Respiratory Society International Multidisciplinary Consensus Classification of Idiopathic Interstitial Pneumonias 2001 guidelines were used in the diagnosis.

A detailed history and examination done at the time of initial presentation. Laboratory investigations such as haemogram, chest radiograph, electrocardiogram and sputum smear examination for acid-fast bacilli (AFB), Mantoux test and pulmonary function test (PFT) were recorded. All serological investigations such as serum anti-nuclear antibody (ANA), serum calcium, serum angiotensin converting enzyme (ACE) levels, cytoplasmic antineutrophil cytoplasmic antibodies (c-ANCA), perinuclear anti-neutrophil cytoplasmic antibodies (p-ANCA), anti topoisomerase I antibody (Scl-70), rheumatoid factor (RA), anti-cyclic citrullinated peptide antibodies (anti-CCP), anti double-stranded DNA (anti-dsDNA), along with other relevant investigations such as 24-hour urinary calcium records, were obtained.

Chest radiograph and high-resolution computed tomography (HRCT) findings were analysed.

Fibre optic bronchoscopy (FOB), trans-bronchial lung biopsy (TBLB), endobronchial biopsy (EBB) and trans-bronchial needle aspiration (TBNA) had been performed in stable patients willing to undergo the procedure , patients who were either not fit to undergo FOB or refused, the diagnosis was made on the basis of clinical, laboratory and radiological features.

RESULT

The overall mean age at presentation was 45.24 years, 54.83 years in IPF, 44.60 years in Hypersensitivity Pneumonitis (HSP), 43.60 years in Nonspecefic Interistial Pneumonitis (NSIP) and 41.56 years in Sarcoidosis. Of the 116 ILD cases there were 70 male (60.34%) and 46 (39.66%) females. The overall mean duration of symptoms at diagnosis was 2.47 years, 1.5 years in IPF, 1.2 years in HSP, 1.5 years in NSIP and 3 years in Sarcoidosis. The most frequent presenting symptom in the ILDs was cough present in 98 (84.45%), followed by exertional dyspnoea in 86 (74.13%), fever in 36 (31.10%), joint symptoms in 17 (14.65%), and (3.8%). Haemoptysis was present in 12 (10.34%) patients. Out of 116 Patients, 60 (51.7%) were smoker and 56 (48.3%) were nonsmoker. Among smokers 50 were male and 10 were female. Biomass fuel smoke exposer present in 30 (25.86%) cases of ILD. Out of 30 patients who have biomass fuel smoke exposer, 21 were female and 9 were male. Biomass fuel smoke exposer and smoking both present in 23 cases. Smoking present in 37(78.7%) cases of IPF and Biomass fuel smoke present in 15 (31.90%) cases.

On examination, digital clubbing was noted in a total of 48 (41.13%) patients, with 42 (89.36%) in cases of Idiopathic Pulmonary Fibrosis (IPF), 3(11.11%) in HSP and 2 (11.11%) NSIP. Chest crepitations were present in 112 (96.55%) of all patients. Prior history of anti-tuberculosis treatment due to misdiagnosis as tuberculosis was present in 24 (20.68%) cases of ILD, with it being most common in Sarcoidosis 6 (50%). All patients were sputum smear-negative for acid fast bacilli. Significant desaturation on 6 Minute Walk Test (MWT) was observed in 73 (62.93%) cases of ILD at presentation, with a frequency of 84.10% in IPF and 32.12% in Sarcoidosis. Chest roentgenogram revealed reticular/ reticulo- nodular pattern in 96 (82.75%) and hilar-adenopathy in 23 (19.82%) patients of ILD. The overall patterns documented on HRCT (n = 116) were interstitial fibrosis 63 (54.31%), honeycombing 41 (35.34%), ground glass opacities 71 (61.20%), intrathoracic lymphadenopathy (20.76%), traction bronchiectasis 48 (41.37%) and pleural fibrosis (4.31%).

Fibrosis present in 46 (97.8 %) patients of IPF, 7 (25.9%) patients of HSP and 4 (33.34%) patients of Sarcoidosis. Honeycombing was present in 33 (70.21%) cases of IPF 7(25.9%) patients of HSP . Ground glass opacity present in 43 (91.45%) cases of IPF, in 12 (44.45%) cases of HSP, and in 9 (50%) cases of NSIP. Traction bronchiectasis present in 36 (76.60%) cases of IPF and 4 (33.34%) patients of Sarcoidosis. Pleural involvement was seen in 16.66% of Sarcoidosis subjects and in 3(42.85%) cases of rheumatoid arthritis-associated ILD and in 1 subject of Systemic Lupus Erythematous (SLE).

Serological evaluation in cases of Sarcoidosis found that the mean level of serum ACE was 82.84 IU/L, serum calcium was 8.9 mg/dL and 24-hour urinary calcium levels were 302.26 mg/day. In cases of rheumatoid disease-associated ILDs, rheumatoid factor was positive in all patients. SLE was diagnosed in one patient with positive anti ds-DNA antibody. Skin biopsy showing granulomatous lesions consistent with Sarcoidosis was reported in 1 patient.

Spirometry was done in 98 cases, as 18 patients could not perform spirometry. Spirometry followed by static lung volume and diffusion capacity wherever possible. The mean TLC was 58.3% of predicted and diffusion capacity (DLCO) was 45.56% of predicted. FOB was performed in all 79 (68.10%) patients, and biopsy reports (TBLB) were suggestive of interistial lung disease 46 cases.

Another important observation is that almost 24 (2068%) cases of ILDs had a history of anti-tubercular treatment with it being most common in Sarcoidosis 6 (50%). This might be due to radiological similarities between ILD and pulmonary tuberculosis and a lack of awareness and paucity of diagnostic facilities in remote areas.

Table.1 CLINICAL PROFILE OF INTERSTITIAL LUNG DISEASE PATIENTS

S/N	IPF	HSP	NSIP	SARCOIDOSIS	RA- ILD	SLE	LCH	AIP	COP
TOTAL N=116 NUMBER OF PATIENTS	47 (40.51%)	27 (23.27%)	18 (15.51%)	12 (10.34%)	7 (6.03%)	2 (1.7%)	1 (0.8%)	1 (0.8%)	1 (0.8%)
AGE (in years)	54.83	44.60	43.60	41.56	59.78	37	27	25	33
MALE / FEMALE	36/11	17/ 10	10/08	8/4	5/ 2	0/ 2	1/0	0/1	0/1
DURATION OF SYMPTOMS (in years)	1.5	1.2	2.5	3	2.5	3	4	15 Days	1.5
COUGH	39 (82.97 %)	24 (88.8%)	15 (83.3%)	10 (83.3%)	5 (71.14%)	2	1	1	1
DYSPNEA	36 (76.59 %)	19 (70.3%)	14 (77.7%)	8 (66.66%)	4 (57.14%)	2	1	1	1
HAEMOPTYSIS	2	2	4	0	2	0	0	1	1
FEVER	9 (19.1%)	9 (33.3%)	5 (27.7%)	4 (33.3%)	4 (57.14%)	2	1	1	1
JOINT SYMPTOMS	0	5 (18.5%)	2 (11.11%)	2 (16.66%)	5 (71.14%)	2	0	0	1
ATT INTAKE	7 (14.89%)	5 (18.5%)	2 (11.11%)	6 (50%)	2 (28.57%)	0	0	1	1
CLUBBING	42 (89.36%)	3 (11.11%	2 (11.11%)	1 (8.3%)	0	0	0	0	0
SMOKING	37 (78.7%)	7 (25.9%)	10 (55.5%)	2 (16.6%)	3 (42.85%)	0	1	0	0
BIOMASS FUEL EXPOSER	15 (31.91%)	6 (22.2 %)	5 (27.7%)	1 (8.3%)	1 (14.28%)	2	0	0	0

IPF — Idiopathic Pulmonary Fibrosis, **HSP** — Hypersensitivity Pneumonitis, **NSIP** — Non-Specific Interstitial Pneumonitis, **RA-ILD** — Rheumatoid Arthritis Associated Interstitial Lung Disease, **SLE** — Systemic Lupus Erythematosus, **LCH** — Langerhan`S Cell Histiocytosis, **AIP** — Acute Interstitial Pneumonitis, **COP-** Cryptogenic Interistial Pneumonia ; **ATT** — Anti Tubercular Therapy.

Table.2 RADIOLOGICAL FINDINGS OF ILD

CHEST - X RAY FINDINGS	**TOATAL NUMBER =116**
RETICULAR/RETICULO- NODULAR	96 (82.75%)
HILAR-ADENOPATHY	19 (16.37%)
HRCT FINDINGS	
FIBROSIS	63 (54.31%)
HONEYCOMBING	41 (35.34%)
GROUND GLASS OPACITY	74 (63.80%)
PATCHY CONSOLIDATION	5 (4.31%)
TRACTION BRONCHIECTASIS	48 (41.37%)
LYMPHDENOPATHY (HILAR/MEDIASTINAL)	23 (19.82%)
PLEURAL INVOLVEMENT	6 (5.17%)

Table.3 RADIOLOGICAL FINDINGS OF ILD

CHEST - X RAY FINDINGS	**IPF (47)**	**HSP (27)**	**NSIP (18)**	**SARCOIDOSIS (12)**	**RA- ILD (7)**	**SLE (2)**	**COP (1)**	**LCH (1)**	**AIP (1)**
RETICULAR/ RETICULO- NODULAR	46	23	12	8	6	0	0	1	0
HILAR-ADENOPATHY	3	2	3	7	4	0	0	0	0
HRCT FINDINGS									
FIBROSIS	46	7	3	4	2	0	0	1	0
HONEYCOMBING	33	7	1	0	0	0	0	0	0
GROUND GLASS OPACITY	43	12	9	5	2	1	1	0	1
PATCHY CONSOLIDATION	0	1	0	2	0	0	1	0	1
TRACTION BRONCHIECTASIS	36	6	0	4	2	0	0	0	0
NODULES	5	17	8	6	0	0	1	0	0
LYMPHDENOPATHY (HILAR/ MEDIASTINAL)	7	2	3	7	4	0	0	0	0
PLEURAL INVOLVEMENT	0	0	0	2	3	1	0	0	0

IPF — Idiopathic Pulmonary Fibrosis, **HSP** — Hypersensitivity Pneumonitis, **NSIP** — Non-Specific Interstitial Pneumonitis, **RA-ILD** — Rheumatoid Arthritis Associated Interstitial Lung Disease, **SLE** — Systemic Lupus Erythematosus, **LCH** — Langerhan`S Cell Histiocytosis, **AIP** — Acute Interstitial Pneumonitis, **COP-** Cryptogenic Interistial Pneumonia

DISCUSSION

The process of achieving a diagnosis in a patient with ILD requires close communication between clinician, radiologist and pathologist. There is limited data on the presentation and diagnosis of these patients from India. The two main issues that are important for diagnosis of pulmonary fibrosis in this part of the world are differentiation from other illnesses with similar presentation and establishing the aetiology of pulmonary fibrosis.

The common conditions causing progressive breathlessness which can mimic the clinical presentation of an ILD would include pulmonary oedema and left heart failure, Tropical Pulmonary Eosinophilia, Hypersensitivity Pneumonitis, and Bronchiectasis . Due to the very high burden of pulmonary Tuberculois in this part of the world, most patients with pulmonary symptoms and diffuse radiological opacities are labelled as suffering from TB, unless another diagnosis is proven.

normal chest radiograph can occur in around 10% to 15% of the patients with ILD, and thus, a normal looking chest radiograph does not rule out pulmonary fibrosis.

In the present study most of the patients were above 45.24 years of age which was observed in other studies as well. [3] However patients of Acute Interstitial Pneumonitis *(*AIP) and Langerhan`S Cell Histiocytosis (LCH) patients belong to younger age. This finding is similar to previous studies from India as well as western literature. [6-9,10] In 116 ILD cases there were 70 male (60.34%) and 46 (39.66%) females. Similar observations have been reported in other studies. [8, 11,12] Howevever prevalence of ILD was found more in female in other Indian studies. [7, 9,] This can be explained by the fact that the majority of our subject population consisted of patients with IPF which is a male preponderant disease. The commonest presenting symptoms were dry cough (84.45%) and breathlessness (74.13%) in the present study and the same has been observed in other Indian studies. [13] HRCT is considered as a standard investigation during the initial evaluation of all patients

with ILD.[14] It is a useful diagnostic tool for IPF without performing invasive biopsy.[15]

Idiopathic pulmonary fibrosis was the most common diagnosis with 47 patients (male 36, female 11) and the same has been reported in other studies.[8] Smoking were present in 37 (78.70%) cases of IPF.

The literature shows more men being diagnosed with IPF than women and the majority being smokers. [16-18] In another Indian study by Subhash et al. out of 33 cases of IPF, 16 were females and smoking was present in only 18% of all IPF cases. [19]

In HRCT Fibrosis was present in 63 (54.31%) cases and Honeycombing was present in 41 (35.34%) patients . Honeycombing was observed in 43% of the patients by Sen &Udwadia.[13]

Hypersensitivity Pneumonitis (HSP) was diagnosed in 27 (23.27%) Cases. Out of 27 , 8 were associated with birds exposure, with duration of exposure ranging from 2–12 years. 13 cases had histopathological confirmation of features consistent with diagnosis of HSP. In a previous study from India, Udwadia et al. [13] reported HSP in 15 (6%) from a total of 273 cases.

NSIP was found in 18(15.51%) cases. Mean age of presentation was 43 years and 10 were male and 8 were female. Smoking was found in 10 patients and biomassfuel smoke exposer present in 7 cases. The review of literature shows NSIP has a mean age of 52 years and is more common in females and never smokers. [20]

9 (7.73%) cases diagnosed as Connective tissue disorder (CTD)-associated interstitial lung disease (CTD-ILD), The prevalence of CTD–ILD in India has been reported as ranging from 5.6% to 50.8% in various studies. [7, 9] There were 7 cases of RA-ILD and 2 cases of SLE were diagnosed. Lung involvement at presentation was observed in 5 cases of rheumatoid arthritis (RA). Prevalence of RA-ILD varies from 5–58%. [21]

In the current study there was one case of pulmonary Langerhans cell histiocytosis (LCH), Acute Interistial Pneumonia (AIP) and Crytogenic Organising Pneumonia (COP) each found.

Another important observation is that almost 24 (20.68%) cases of ILDs had a history of anti-tubercular treatment. This might be due to radiological similarities between ILD and pulmonary tuberculosis and a lack of awareness and paucity of diagnostic facilities in remote areas.

CONCLUSION

Interistial pulmonary fibrosis is the most common and Hypersensitivity Pneumonitis is the second common Interistial Lung Disease in our study. Being progressive disease most of the patients presented to us in advance stage of disease and in most of the cases anti tubercular treatment was started by the treating physician without being extensive evaluation. Interstitial lung disease is under-diagnosed because of lack of awareness among physicians. Lack of recognition at an early stage lead to delayed diagnosis in most of the patients.This stresses on the importance of taking detailed history and clinical evaluation with appropriate imaging modalities with multidisciplinary approach involving radiologist and pathologist to make an early specific type of diagnosis of ILD, More and more research in this field so that we better stand the pattern of ILD in India.

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