

A CLINICAL AND RADIOLOGICAL PROFILE OF PATIENTS OF INTERSTITIAL LUNG DISEASES, ATTENDING THE CHEST HOSPITAL OF MEDICAL COLLEGE FROM NORTH INDIA

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ABSTRACT

OBJECTIVE

To know the clinical and radiological profile of patients of Interstitial Lung Diseases attending the Chest Hospital of Medical College from North India from February 2014 to December 2015.

MATERIAL AND METHODS

The study was conducted in Department of Tuberculosis and Respiratory Diseases, G.S.V.M. Medical College, Kanpur (India). The patients were subjected to complete clinical history (Including work environment and occupational history), physical examination, various haematological investigations, spirometry and high resolution computerized tomography thorax.

RESULTS

In present study a total of 80 patients with interstitial lung disease were analysed. There were 36 males and 44 females (mean age was 54.4±1.8 years). Of 80 patients of interstitial lung diseases examined, Idiopathic Pulmonary Fibrosis (IPF) pattern was present in maximum number (38.8%) followed by sarcoidosis (17.5%), Hypersensitivity pneumonitis (15%) Non-specific interstitial pneumonias (10%), Connective Tissue Disorder (C.T.D.) associated ILD (7.5%) and Cryptogenic Organizing Pneumonias (C.O.P.) in 5% of cases.

CONCLUSION

IPF was the most common subgroup among ILDs.

KEYWORDS

Interstitial Lung Diseases, Idiopathic Pulmonary Fibrosis, Sarcoidosis.

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INTRODUCTION

The term Diffuse Parenchymal Lung Disease (DPLD) often used synonymously with Interstitial Lung Disease (ILD), refers to diseases that cause inflammation of the pulmonary interstitium. About 200 disorders have been implicated in the causation of DPLD.¹ The ILDs include diseases of unknown aetiology such as those secondary to drugs, collagen vascular disease, granulomatous conditions like sarcoidosis and other forms of ILDs like lymphangioleiomyomatosis or histiocytosis X. Diagnosis can be made by the combination of clinical and roentgenographic features and pulmonary function tests. Histopathological confirmation of the diagnosis is not required in most of the cases. There has been a resurgence of interest in the study of these disorders chiefly on account of the availability of less invasive methods.

Development of high resolution computed tomography and availability of video-assisted thoracoscopic lung biopsy has added to our diagnostic strategies.²

The present study was, therefore, planned to analyse the spectrum of ILD encountered in a tertiary referral centre and determine the clinical profile of the disease.

MATERIAL AND METHODS

The study was conducted in Department of Tuberculosis and Respiratory Diseases (Dr. M L Chest Hospital), G.S.V.M. Medical College, Kanpur (India) from February 2014 to December 2015. The patients were subjected to complete clinical history (Including work environment and occupational history) and complete physical examination.

Complete blood count, liver function test, kidney function test, serum electrolyte, fasting and post prandial blood sugar, urinalysis, sputum, chest X-ray - PA view, spirometry, diffusion study (If required), 2D Echo, High Resolution Computerized Tomography Thorax, 6 minute walk test. Other tests as per requirement would be done. Oxygen saturation and baseline Arterial Blood Gas analysis was done.

Inclusion Criteria

Patients Presenting with Following

- Respiratory symptoms such as shortness of breath and cough.

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- Bilateral abnormality in Chest X-ray/High Resolution Computerized Tomography scan thorax.

Exclusion Criteria

- Any infectious or malignant disease.

RESULT

In present study, a total of 80 patients with interstitial lung disease were analysed. There were 36 males and 44 females (Mean age was 54.4±1.8 years). The female patients presented at an earlier age (54.4±1.8 years) as compared to male patients (58.3±1.5 years); 37 patients were from rural background (46.3%) and 43 were from urban area (53.8%). Mean B.M.I. of ILD patients was 21.58±5.0 kg/m². Of 80 patients of interstitial lung diseases examined, Idiopathic Pulmonary Fibrosis (IPF) pattern was present in maximum number (38.8%) followed by sarcoidosis (17.5%), hypersensitivity pneumonitis (15%), non-specific interstitial pneumonias (10%), Connective Tissue Disorder (C.T.D.), associated ILD (7.5%) and Cryptogenic Organizing Pneumonias (C.O.P) in 5% of cases (Table 1).

In ILD patients 95.9% presented with cough, among which 39.7% had expectoration, while 56.2% patients had dry cough and 4.1% of patients did not have cough as a presenting symptom (p=0.0624). Breathlessness was most consistent symptom present in all patients. Chest pain was present in 38.8% of ILD patients, most commonly associated with NSIP (75%) and sarcoidosis (42.9%).

Weight loss, difficulty in swallowing, skin changes and pedal oedema were found in 36.3%, 5%, 6.3% and 16.3% patients respectively. Bibasilar crepitation was the most consistent sign (95.5%), clubbing and pallor were present in 61.1% and 58.9% of ILD patients. Joint pain was another symptom and was present in 27.8% cases in our study.

In this study, the percentage of non-smoker, ex-smoker and current smoker were 71.3%, 17.5% and 11.3% respectively. The disease wise details are given in Table No. 2.

In present study, the details of exposure to various noxious substance and environmental factors in relation to various ILDs are given in Table 2.

The presence of co-morbidity was not unusual with DPLD; but in present study, most frequently present co-morbidity was hypertension and diabetes seen in 16.4% and 12.3% cases. In this study, gastroesophageal reflux as a symptom was seen in 17.8% cases; highest amongst IPF (24.1%). In present

study 31.5% cases of ILD, misdiagnosed as pulmonary tuberculosis and 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. (The description of other medical histories are summarized in Table 3).

59 (80.8%) patients with ILD were able to perform 6 minute walk test (6 MWT) and Mean expected 6 minute walk test distance was 658±94 meters, while performed distance was 278±131 meters (43.5%). (The details are summarized in Table No. 2).

Spirometry was performed by 55 patients only and in Spirometry most common abnormality among ILD patients was restrictive pattern in 78.2%, was normal in 10.9% cases.

Majority of patients shows reticular or reticulonodular patterns on chest X-ray and on HRCT of chest various radiological abnormality were Interseptal Thickening (72.6%), Honeycombing (54.8%), 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%) and Consolidation (8.21%). (The details are summarized in Table No. 2).

Disease	No. of Patients	Percentage
Idiopathic pulmonary fibrosis (I.P.F.)	31	38.8%
Sarcoidosis	14	17.5%
Hypersensitivity pneumonitis (H.P.)	12	15%
Non-Specific Interstitial pneumonias (N.S.I.P.)	08	10%
Cryptogenic Organizing Pneumonias (C.O.P.)	04	5%
Connective Tissue Disorder (C.T.D.) Associated ILD	06	7.5%
Others	05	6.3%
Total	80	100%

Table 1: Various Diagnoses Found among Patients of Interstitial Lung Diseases

Sl. No.	Parameter	IPF (n=31)	Sarcoidosis (n=14)	HP (n=12)	NSIP (n=8)	COP (n=4)	CTD-ILD (n=6)	Others (n=5)	Total (n=80)	
1	Mean age	Male	62.8 ± 1.7	54.0 ± 4.2	45.0	70.0	52.5	37.0	45.2 ± 22.2	58.3 ± 1.5
		Female	61.7 ± 1.7	41.9 ± 4.2	63.1 ± 8.0	47.5 ± 1.7	53.0 ± 31.8	39.7 ± 11.8	54.0	54.4 ± 1.8
2	Age Distribution (Years)	>30	0	4 (28.6)	0	3 (37.5)	0	1 (16.7)	1 (20)	9 (11.3)
		30-39	2 (6.5)	1 (7.1)	0	0	2 (50)	2 (33.3)	0	7 (8.8)
		40-49	5 (16.1)	4 (28.6)	3 (25)	0	0	2 (33.3)	2 (40)	16 (20)
		50-59	6 (19.4)	4 (28.6)	1 (8.3)	2 (25)	1 (25)	1 (16.7)	1 (20)	16 (20)
		60-69	5 (16.1)	1 (7.1)	6 (50)	2 (25)	0	0	0	14 (22.5)

		>70	13 (41.9)	0	2 (16.7)	1 (12.5)	1 (25)	0	1 (20)	18 (24.6)
3	Gender	Male	22 (71)	2 (14.3)	2 (16.7)	2 (25)	2 (50)	2 (33.3)	4 (80)	36 (45)
		Female	9 (29)	12 (85.7)	10 (83.3)	6 (75)	2 (50)	4 (66.7)	1 (20)	44 (55)
4	Residence	Rural	18 (58.1)	4 (28.6)	7 (58.3)	4 (50)	1 (25)	2 (50)	1 (20)	37 (46.3)
		Urban	13 (41.9)	10 (71.4)	5 (41.7)	4 (50)	3 (75)	4 (50)	4(80)	43(53.8)
5	Exposure to various noxious & toxic substance	Cooking on fire wood/ cow dung	26 (83.9)	6 (42.9)	9 (75)	6 (75)	2 (50)	2 (33.3)	2 (40)	53 (66.3)
		Kerosene	12 (38.7)	2 (14.3)	4 (33.3)	3 (37.5)	2 (50)	2 (33.3)	1 (20)	26 (32.5)
		Coal	6 (19.4)	1 (7.1)	2 (16.7)	0	0	0	0	09 (11.3)
		LPG	17 (54.8)	12 (85.7)	8 (66.7)	4 (50)	3 (75)	3 (50)	4 (80)	51 (63.8)
6	Exposure to various environmental factors	Dust	13 (41.9)	6 (42.9)	2 (16.7)	1 (12.5)	2 (50)	1 (16.7)	2 (40)	27 (33.8)
		Mold	4 (12.9)	2 (14.9)	2 (16.7)	0	0	2 (50)	1 (20)	11 (13.8)
		AC	3 (9.7)	5 (35.7)	3 (25)	2 (25)	0	0	2 (40)	15 (18.8)
		Cooler	17 (54.8)	13 (92.9)	11 (91.7)	5 (62.5)	3 (75)	0	4 (80)	53 (66.3)
		Birds/pets	2 (6.5)	1 (7.1)	3 (25)	0	0	1 (16.7)	0	7 (8.8)
7	Tobacco smoker	Non-smoker	18 (58.1%)	11 (78.6%)	10 (83.3%)	7 (87.5%)	3 (75%)	5 (83.3%)	3 (60%)	57 (71.3)
		Ex-smoker	7 (22.6%)	2 (14.3%)	2 (16.7%)	1 (12.5%)	1 (25%)	0	1 (20%)	14 (17.5)
		Current smoker	6 (19.4%)	1 (7.1%)	0	0	0	1 (16.7%)	1 (20%)	9 (11.3)
8	6 MWD	Expected walk distance	640 ±94	686 ±78	596 ±78	709 ±82	751 ±152	741 ±90	691 ±84	658 ±94
		Actual walk distance	269 ±125	287 ±131	272 ±146	315 ±180	420 ±42	326 ±126	182 ±17	278 ±131
9	Pulmonary hypertension		06.8%	7.7%	27.2%	14.2%	00	20%	00	12.3%
10	Various radiological findings	Interseptal thickening	100%	30.7%	63.6%	85.7%	33.3%	80%	60%	72.6%
		Honey combing	86.2%	15.4%	54.5%	14.2%	66.6%	60%	20%	54.8%
		Bronchiectasis	86.2%	30.7%	54.5%	28.4%	66.6%	60%	40%	60.2%
		GGOs	51.2%	53.8%	63.3%	100%	66.6%	80%	60%	61.6%
		Reticulations	96.5%	23.1%	63.3%	56.8%	33.3%	80%	20%	65.7%
		Cyst	3.4%	00	27.2%	00	00	00	00	5.5%
		Nodules	17.2%	30.8%	36.3%	00	00	20%	20%	20.5%
		Air Trapping	17.2%	15.4%	27.2%	14.2%	00	40%	40%	26.6%
		Intrathoracic LN	24.1%	92.3%	18.2%	14.2%	33.3%	20%	60%	37.0%
		Pleural effusion	00	00	00	00	00	00	20%	01.4%
		Pleural thickening	13.8%	7.7%	18.2%	28.4%	00	20%	20%	15.1%
		Consolidation	00	7.7%	0	14.2%	66.6%	20%	00	8.21%
UIP Pattern	93.2%	7.7%	36.3%	00	00	60%	20%	49.3%		

Table 2: Showing Various Clinical Parameter

Sl. No.	Past Medical H/O	Variety of ILD							Total (n=80)
		IPF (n=31)	Sarcoidosis (n=14)	HP (n=12)	NSIP (n=8)	COP (n=4)	CTD-ILD (n=6)	Others (n=5)	
1	H/o ATT	31.1%	53.8%	18.9%	28.4%	33.3%	0	40%	31.5%
2	Hypertension	6.9%	23.1%	27.2%	42.8%	33.3%	0	0	16.4%
3	Diabetes	3.4%	15.3%	36.3%	28.4%	0	0	0	12.3%
4	Thyroid disease	3.4%	15.3%	18.8%	0	0	0	0	6.8%
5	Kidney disease	3.4%	7.7%	0	0	0	0	0	2.9%
6	Pleural effusion	3.4%	7.7%	9.1%	0	0	20%	40%	8.21%
7	G.E.R.D.	24.1%	15.4%	9.1%	14.1%	0	20%	20%	17.8%

Table 3: Showing Associations of Other Comorbidity among ILDS Patients

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.

80 patients of ILD were included in the study and in this study there were 64 (80%) patients >40 years of age, which is comparable to a study done in Kuwait.³ A study from India found that peak incidence was between 40-49 years' age group and then 30-39 years' age group.⁴ Jindal et al showed that peak incidence was between 30 to 59 years.⁵ In another study done revealed the peak incidence was in 20-29 and 40-49 years' age group.⁶

Mean age in present study was 54.4±1.8 years (58.3±1.5 in males and 51.9±1.6 years in females). The mean age of patients in various other studies varied from 43.5 to 52.4 years.^{4,7-10}

In present study, ILD was seen more in females 44/80 (55%) than males 36/80 (45%). Various authors reported variable findings on either sex predominance. Contrary to our study, Gagiya et al showed male preponderance (66.5%).⁴ Another study from India reported that females were twice compared to male.⁷ In another study, male and female incidence was 42.4% and 57.4% respectively.⁵ A study from Lucknow, India, reported that the prevalence of DPLD among male and female were 66.5% and 33.5% respectively.⁶ Another study from India revealed the prevalence of diffuse fibrosing alveolitis among male and female were 53% and 47% respectively.¹¹ A study from Trivandrum, India, found 48.6% males and 51.4% females among ILDs patients.⁹ D B Coultas et al, studied to describe the prevalence and incidence of ILDs a population-based registry in Bernalillo County, New Mexico. In October 1988, the prevalence of ILDs was 20% higher in males (80.9 per 100,000) than in females (67.2 per 100,000). Similarly, the overall incidence of ILDs was slightly more common in males (31.5 per 100,000/year) than females (26.1 per 100,000/year).¹²

The interstitial lung diseases are diverse group of over 150 disorders.¹³ In our study, among the 80 cases Idiopathic Pulmonary Fibrosis (IPF) was present in maximum number of patients (38.8%), followed by Sarcoidosis (17.5%), Hypersensitivity pneumonitis (15%), Non-specific interstitial pneumonias (10%) and Connective tissue disorder associated with ILDs in 7.5% cases.

A study from Mexico also found that the most common disease diagnosed among both sexes were idiopathic pulmonary fibrosis accounting for 46.2% of all ILD diagnoses in males and 44.2% in females.¹² Another study from Lucknow (India) reported IPF, Cryptogenic Organising Pneumonia

(COP), Non-Specific Interstitial Pneumonia (NSIP) and Sarcoidosis in 48.7%, 20.5%, 17.9% and 7%, respectively.⁶

Tiyas Sen et al, observed idiopathic pulmonary fibrosis, sarcoidosis and ILDs secondary to connective tissue disorder in 43%, 22% and 19% respectively.⁷ S Kundu et al concluded that Idiopathic Pulmonary Fibrosis (IPF) was the most common variety in 38.04% followed by CTD in 31.5%, hypersensitivity pneumonitis (10.9%), sarcoidosis (5.4%) and silicosis (5.4%) being the common causes of ILDs.¹⁴ Rajkumar et al reported that sarcoidosis (37.3%) was found to be the most common subgroup followed by IPF (27.6%) and NSIP (25.6%) among study group with various ILDs.¹⁰ Another study from Trivandrum (India) found Idiopathic pulmonary fibrosis (39%), CTD associated ILD (24%), Hypersensitivity Pneumonitis 17% and Sarcoidosis 13% in study group.⁹ Gagiya et al, found Idiopathic Pulmonary Fibrosis and Rheumatoid Arthritis in 33.3% and 13.2% respectively in various patients of ILDs.⁴ A study from Saudi Arabia reported that the most frequent disease among newly diagnosed ILDs were Connective Tissue Disease (CTD)-associated ILD (34.8%) followed by Idiopathic Pulmonary Fibrosis (IPF) (23.3%), Sarcoidosis (20%), and Hypersensitivity Pneumonitis (6.3%).³

In our study, IPF was more common in males (71%) than females (29%). Similar observations were made in the study conducted by Turner et al, where out of 220 IPF cases 66.8% were males and 32.2% were females.¹⁵ In the study done by Maheshwari et al, they found that there were 35 males and 41 females.⁸ In a study done by Subhash et al, amongst 33 patients who had IPF 17 were males.¹⁶ Our finding was also supported by Raghu et al, where more men were reported with IPF than women.¹⁷

In present study, two-thirds of the IPF cases present in patients over the age of 60 years with a mean age of 66 years at the time of diagnosis and mean age of presentation in IPF was 61.9±1.3 years. In the study conducted by Turner et al, the mean age at presentation was 54 years ±12SD years.¹⁵ In Maheshwari et al study, the mean age was 50.6±11.9SD years.⁸ In our study, there was no significant difference between the mean age of males (62.8±1.7 years) and females (61.7±1.7 years) amongst IPF cases.

In present study, gastroesophageal reflux as a symptom was seen in 17.8% cases; highest amongst IPF (24.1%). A study conducted by Shafeeq M et al reported the incidence of GERD to be in 20% of ILD cases.⁹ Another study done by Savarino E et al finds IPF patients had significantly higher ($p<0.01$) 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.¹⁸

Schwartz DA et al done a study in 73 confirmed cases of IPF and of them 62% were men and 70% were either former or current cigarette smokers.

They concluded that among patients with IPF, current cigarette smokers will tend to trap air (Higher RV and FRC) and that cigarette smoking appears to adversely alter gas exchange.¹⁹

In this study, 28.8% patients were smokers (Both current and ex-smokers) and majority of them were in IPF. A study done by Shafeeq MK et al reported smoking in 37% patients in idiopathic pulmonary fibrosis.⁹

In our study, sarcoidosis was more commonly seen in females (85.7%) and which is supported by most studies, which suggest a slightly higher disease rate for women.¹⁸ Benjamin et al studied and found that the female preponderance of sarcoidosis appears to be consistent across ethnic groups.²⁰ Mean age of presentation of sarcoidosis in our study 43.7±3.6SD years. Similar observation was also made by Benjamin et al.²¹

Most common pattern in spirometry in ILD is restrictive.²² In our study, it was seen in 87.3% cases. While in other various studies, restrictive pattern ranged from 84.4% to 98%.^{4,6,9}

In present study, Pulmonary Hypertension by 2D Echocardiography was seen in 12.3% cases. While in other studies, it was ranged from 17-30%.^{9-10,14} A study from India reported pulmonary hypertension in 38% patients with DPLD on the basis of clinical, radiological and electrocardiogram findings.⁵ A study from Denmark reported pulmonary hypertension in 14% with mixed types of ILD and who were screened for PH by echocardiography and concluded that 8% of them had mild PH (Mean PAP >25 mmHg, but <35 mmHg) and 6% of them had severe PH (Mean PAP >35 mmHg).²³⁻²⁴ Hamada et al observed that the prevalence of PH in this patient population was as low as 8.1%.²⁵

Abeles AM et al reported that C-Reactive Protein was raised in 45.2% cases and was the most consistent finding followed by serum ANA positivity in 17.8% cases (Maximum in IPF: 27.6%) and also found that Serum DsDNA was positive in 6.9% cases with IPF and 20% in CTD associated ILDs.²⁶ Weinberg et al found ANA were positive in 10 of 34 of the patients screened and 2 patients with sarcoidosis had antibodies to dsDNA.²⁷ Fischer et al reported that ANA and RF are poor screening tests because they have low specificity, particularly when present at low titer and can be seen in healthy individuals.²⁸

In our study, interstitial septal thickening was most consistent radiological finding seen in 72.6% cases; other findings were reticulation (65.7%), ground glass opacity (61.6%), tractional bronchiectasis (60.2%), honeycombing (54.8%) mediastinal lymph node (37.0%) and air trapping (26.6%) cases. Other infrequent radiological finding was nodules (20%), pleural thickening (8.21%) and cyst in 5.5% cases, which is most frequent in hypersensitivity pneumonitis. A study from India, studied HRCT Thorax of 70 DPLDs cases and they found Ground glass opacity 46%, Septal thickening 69%, Honeycombing 43%, Nodules 16% Mediastinal nodes 11.4% cases.⁹ Another one from India studied and found the overall patterns documented on HRCT (n=289) were Interstitial fibrosis (49.9%), Honeycombing (37.71%), Ground glass opacities (34.25%), Intrathoracic lymphadenopathy (20.76%), Traction bronchiectasis (17.64%) and Pleural fibrosis (5.8%). Honeycombing was present in 4.62% cases of

sarcoidosis, 31.08% cases of NSIP and in all IPF cases.¹⁰ Maheshwari et al studied HRCT thorax of 69 IPF cases and found all patients had features suggestive of diffuse interstitial fibrosis. Other abnormalities noted on HRCT chest included Honeycombing (88.4%), Ground glass haziness (23.2%), Parenchymal nodules (7.2%) and Mediastinal lymphadenopathy (5.7%). Mild air trapping was observed in three patients.⁸ UIP pattern in HRCT thorax was observed in 49.3% cases of DPLD and 93.2% in IPF in present study. While it was observed in 42% in other study.⁹ Ganguly et al observed all cases of IPF (n = 35, 100%) showed a classical UIP pattern on the HRCT thorax.

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