

Study of interstitial lung diseases at a tertiary care center

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Abstract

Introduction: Interstitial Lung Diseases are frequent causes of morbidity and mortality and are frequently diagnosed because of the usage of High Resolution Computerised Tomography (HRCT). Interstitial Lung Diseases (ILDs) result from known and unknown causes and result in variable amount of interstitial and pulmonary parenchymal inflammation and fibrosis.

Material and Methods: A total of 104 patients diagnosed on the basis of clinical and radiological criteria as interstitial Lung disease attending Katuri Medical College Hospital, Guntur from June 2015 to June 2018 above 18 years of age were taken in to the study.

Results: Predominant interstitial lung disease was idiopathic interstitial fibrosis (IPF) (46%). Non-IPF interstitial lung diseases constituted 56%. Females outnumbered males in our study with a ratio of 1.7:1. Mean age of the ILD patients was 50.19. Cough and breathlessness were universal in our ILD patients. There are equal number of smokers and nonsmokers. > 75% of patients presented with Grade II MMRC or more. 75% of our patients of ILD desaturated on 6 minute walk testing. PFT revealed restrictive pattern in 69%, mixed pattern in 26.92% and obstructive pattern in 4%. 50% of patients had DLCO of more than 60%. Smoking history correlated with decrease in DLCO. BAL fluid analysis suggested neutrophilic preponderance in 42% and lymphocytic preponderance in 58%. Basing on the clinical and radiological criteria IPF was diagnosed in 46%, NSIP in 21%, NSIP CTD in 12% and Hypersensitivity Pneumonitis in 14%. 62.5% had associated pulmonary arterial hypertension. Smoking history correlated with presence of PAH.

Conclusions: ILDs are common in clinical practice. Diagnosed predominantly after the frequent usage of HRCT in symptomatic patients. History analysis, clinical examination, chest X-ray, bronchoscopy, bronchoalveolar lavage (BAL), pulmonary Function Testing, six minute walk test, echocardiography, carbon dioxide diffusion capacity (DLCO) testing help in the diagnosis.

Keywords: Desaturation; Sarcoidosis; Hypersensitivity pneumonitis; Pulmonary arterial hypertension.

Introduction:

The interstitial lung diseases are a clinically challenging and diverse group of disorders characterized by varying degrees of fibrosis and inflammation of the lung parenchyma or interstitium. The interstitial lung diseases have similar symptoms, similar radiological presentation. More than 150 interstitial lung diseases with known or unknown etiology have been identified. Occupational lung diseases, drug induced lung diseases, hypersensitivity pneumonitis, granulomatous lung disease, lung diseases associated with exposure to organic and inorganic dusts and idiopathic interstitial pneumonias share the common signs and symptoms of interstitial lung diseases associated with variable amount of interstitial and pulmonary fibrosis. For each ILD there may be an acute phase followed by a phase of chronicity with acute exacerbation. Among ILDs of known cause, the largest group includes diseases due to inhalation of inorganic dusts, organic dusts and various irritant and noxious gases. The number of ILDs of unknown cause is also very large. The major ones are Idiopathic Pulmonary Fibrosis (IPF), Sarcoidosis, Nonspecific Interstitial Pneumonitis (NSIP), ILD associated with collagen vascular diseases (CTD-ILDs). Time of diagnosis differs between the ILD diseases, ranging from the fourth decade for sarcoidosis to the sixth decade for IPF. Some interstitial lung diseases like

hypersensitivity pneumonitis and connective tissue disease associated ILD are diagnosed in patients less than 50 years of age [1]. A multi disciplinary approach is necessary in the diagnosis of interstitial lung diseases. In view of the comorbidities it is not always possible to do a biopsy [2].

Among the ILDs idiopathic pulmonary fibrosis is the most lethal entity and shows high heterogeneity in clinical behavior [3]. IPF is the commonest idiopathic ILD and IPF represents nearly 30% of the incident case. The disease process extends into alveolar spaces, acini, bronchiolar lumen and bronchioles [2,4].

Aims and Objectives:

To study the clinical profile, the radiological profile (chest X-ray and HRCT Scan), spirometry profile, BAL fluid analysis, results of 6 minute walk test values, DLCO, echocardiography findings in patients of ILD and analyze the results and compare with the severity of ILDs.

Material and Methods:

The present study comprises of 104 patients who are admitted in the Department of Pulmonary Medicine, Katuri Medical College, Guntur, from November 2015 to June 2018.

Study design: It is a prospective study consisting of 104 patients examining the clinical, radiological and pulmonary function test profile

Inclusion criteria: Patients having symptoms suggestive of interstitial lung disease by clinical, radiological and extrapulmonary symptoms above 18 years of age are included in the study. Patients with known connective tissue disease with respiratory symptoms referred to the department of Pulmonary medicine of Katuri Medical College, Guntur are taken in to the study.

Exclusion criteria: ILD like infections eg. miliary tuberculosis and pneumocystis jirovecii pneumonia (PJP). 2. ILD like malignancies eg. lymphangitis carcinomatosa 3. pulmonary kochs co-existing with ILD. 4. Patients of age less than 18 yrs. 5. Patients having serious interstitial disease with resting hypoxia requiring ICU admission and moribund patients are excluded from the study

Study protocol

Prior to the investigation hospital ethical committee approval was taken and consent from the individual patients were taken.

Among a total of 104 patients of interstitial lung disease a detailed history of symptoms, age, sex, occupation and habits like smoking were taken. Clinical symptoms like cough, haemoptysis, breathlessness, loss of appetite, loss of weight, and clinical signs were evaluated in all patients. Baseline Chest X-ray both PA (Postero-anterior view, Base line blood investigations like Haemoglobin, TLC, DLC, ESR, peripheral smear, blood urea, serum creatinine, random blood Sugar, serum bilirubin, BT,CT were done. Mantoux, sputum for AFB, sputum for malignant cytology, sputum for gram stain and Culture & Sensitivity were done. Patients were screened for HIV and HBsAg. HRCT Chest and FOB were done. BAL fluid analyses for total leukocyte count (TLC), Differential leukocyte count (DLC) were sent. Pulmonary function tests like Spirometry, 6 minute walk test and DLCO were done. Radiological assessment was done in all patients. The diagnosis of interstitial lung disease was established by HRCT or Chest X Ray PA view correlating with history and clinical examination.

Results were analyzed with minitab 17 software and results verified. DLCO and PAH results were correlated with smoking history and Chi-square values and p-values were calculated for statistical significance.

Observations and Results:

Among 104 patients of interstitial lung disease, 48 patients (46%) are diagnosed as IPF and 56 patients (54%) are diagnosed as non IPF.

Sex distribution

In the present study total number of patients are 104 and among them 38 (36.5%) were males and 66(63.5%) were females. Male: female ratio is 1:1.7.

Age distribution

The mean age of patients in this study was 50.19 years. Most of the patients were in 56-65 years age group.

Table 1: Age and sex distribution of patients

Age (years)	Male	Female	Percentage
16-25	0	4	1.92%
26-35	6	4	9.6%
36-45	6	26	30.76%
46-55	8	12	19.2%
56-65	16	22	36.53%
66-75	0	0	0%
76-85	0	0	0%
86-95	2	0	1.92%

Table 2: Symptomatic analysis of patients of Interstitial Lung disease

Symptoms	Percentage
Cough	100%
Breathlessness	100%
Loss of weight	15.38%
Loss of appetite	15.38%
Haemoptysis	3.84

Table 3: Shortness of breathlessness --- Grade of MMRC

Grade of MMRC	No. of patients	Percentage
I	24	23%
II	48	46.15%
III	22	21.15%
IV	10	9.6%

Smoking

In the present study of total 104 patients 52 patients were smokers and 52 Patients were non smokers.

Table 4: Smoking in males and females

Sex	Males	Females
Smokers	36	16
Nonsmokers	2	50

Pulmonary function tests

Observation of six minute walk test performance among patients of interstitial lung disease. Among 104 patients 78 patients (75%) were desaturated with a decrease in SPO₂ of 4% or more on six minute walk testing and 26 patients (25%) were not desaturated spirometry.

Table 5: Result of spirometry among patients of ILD

Pattern of spirometry	Number of patients	Smokers	Non Smokers	Percentage of patients
Restrictive	72	28	44	69%
Obstructive	4	4	0	4%
Mixed pattern	28	20	08	26.92%

Though there are equal number of smokers and nonsmokers in our study of ILDs spirometric observation of mixed pattern and obstructive pattern are more among smokers and restrictive pattern is more among nonsmokers and chi-square statistic is 12.6984 and p value is 0.001748 and the result is statistically significant at a p-value of <0.05.

Table 6: DLCO Test results among patients of ILD

DLCO%	Males	Females	Total n=104
30-40%	6	4	10
41-50%	12	12	24
51-60%	2	18	20
61-70%	14	22	36
71-80%	2	10	12
81-90%	2	0	2

Table 7: DLCO Test results among smokers and nonsmokers

DLCO%	Smokers N=52	Non-smokers N=52	Total
30-40%	08	02	10
40-50%	18	06	24
50-60%	08	12	20
60-70%	08	28	36
>70%	10	04	14

Smokers in our study have a lower DLCO compared to the non smokers and the Chi-square statistic is 24.0825 and p-value is 0.000077 and the value is statistically significant at a p- value of <0.05.

Table 8: Diagnosis based on Clinical and radiological examination

	Number of patients n=104	Percentage
IPF	48	46%
NSIP	22	21%
NSIP with CTD	12	12%
Hypersensitivity pneumonitis	14	13%
Rare forms (LAM,LCH)	4	4%
Drug induced	4	4%

Table 9: Bronchoscopy and BAL fluid analysis

BAL fluid Analysis	Number of patients	Percentage
Neutrophil predominant	44	42.30%
Lymphocyte predominant	60	57.70%

Table 10: Pulmonary arterial Hypertension among Patients of ILD

Total No. of ILD	No. having PAH by Echo	No PAH
104	65(62.5%)	39(37.5%)
Mild PAH	11 (16.92%)	
Moderate PAH	23 (35.38%)	
Severe PAH	31(47.69%)	

Table 11: Correlation of PAH among smokers and Non smokers

No. Patients 104	PAH – Smoker 48	PAH Nonsmoker 17	No PAH - Smoker 04	NO PAH Nonsmoker 35
Type of PAH	48	17	04	35
Mild	08	03		
Moderate	16	07		
Severe	24	07		

Severity of Pulmonary artery Hypertension is correlated with the smoking status by Chi-square test. The Chi-square statistic is 0.4303. p-value is 0.806417 and the value is not statistically significant at a p-value of <0.05

Table 12: Smoking status correlated with presence of PAH

PAH N=65 No PAH N=39	Smokers	Nonsmokers
PAH =65	48	17
No PAH =39	04	35

When presence or absence of PAH was correlated with the smoking status by Chi-square test the Chi-square statistic is 39.4256 and the p-value is <.00001. The value is statistically significant for a p-value of <0.05.

Pulmonary arterial hypertension is more among smoker ILD patients and the value is statistically significant. Severity of PAH did not correlate with the smoking status.

Summary of results:

The mean age of patients of ILD in this study is 50.19 years. 36.53% of the patients are in 56-65 years age group. Among males no ILD case was reported below 25 years in our study. 86% of ILD patients are present in 36-65 years age group. No ILDs were reported among female patients in extreme age group. Cough and breathlessness were the predominant symptoms among ILD patients and were present in all the patients. Majority of patients presented in Grade II and Grade III MMRC scale of breathlessness. There were equal number of smokers and nonsmokers among ILD patients. Among smokers 69% were male 31% female (When active smoking and significant passive smoking were taken in to consideration). 75% of the patients desaturated on 6 minute walk test with more than 4% decrease in SPO2 suggesting that the disease is advanced among the patients studied. Spirometry revealed 69% of the patients had restrictive disease and 14% both obstructive and restrictive disease. More than two thirds presented with a DLCO of more than 60%.

Predominant ILD detected among 104 patients was IPF amounting to 46%. NSIP was seen in 33% and half of them had associated connective tissue disease. Hypersensitivity pneumonitis both acute and chronic was frequent occurring in 13%. BAL fluid revealed lymphocytic predominance in 58% and neutrophilic predominance in 42%. Two thirds of the patients of ILD had pulmonary arterial hypertension and nearly half of them had severe PAH

Discussion:

Interstitial lung diseases are frequently diagnosed in clinical practice particularly after HRCT chest has been popularized. Idiopathic pulmonary fibrosis is the commonest ILD in our study followed by NSIP and NSIP associated with CTD. European studies and some Indian studies showed sarcoidosis is the commonest cause of ILD followed by IPF and Hypersensitivity Pneumonitis [5,6]. There is an increased risk of ILD among the patients with Rheumatoid arthritis prognosis of ILD associated with Rheumatoid arthritis is worse compared to RA patients without ILD. [3] ILDs with unknown cause always outnumber ILDs with known cause.

Indian registry of ILDs revealed sarcoidosis as the commonest cause of interstitial lung disease (ILD), followed by idiopathic pulmonary fibrosis (IPF), connective tissue disease (CTD) related ILD and Hypersensitivity pneumonitis (HP). Histopathological confirmation could be obtained from 40% of cases [7]. In the Pakistani registry of ILD, interstitial pulmonary fibrosis (IPF) was the commonest cause accounting for 33% [8]. Singh S, Collins BF study had hypersensitivity pneumonitis (HP) as the commonest ILD amounting to 45% , CTD-ILD in 13.9%, and idiopathic pulmonary fibrosis in 13.7% [9] Srikala study from Kerala study showed IPF in 26% and non IPF in 74%. HRCT was diagnostic in all patients of IPF. PAH was more common among IPF patients [10].

Our study showed female preponderance where as other studies from India and abroad showed male predominance. A multi disciplinary approach is needed in the diagnosis of ILDs. Prevalence of ILD increased with age and smoking, history of Pneumonia, COPD, male sex are associated with increased risk of ILD as according to an east Asian study [11].

More than 80% of cases in our study were diagnosed in patients between 36 and 65 years of age. Mean age in our study was 50.9 years. A Turkish study and several other studies also showed a mean age of 51.8 years. This study showed sarcoidosis as the

commonest ILD followed by IPF [12]. Rajkumar study showed a mean age of 44.24 in their study of 289 cases with a female preponderance in nearly 55% of cases [13].

Thus various studies in India and abroad showed variable preponderance of ILD among male and female population. Our study showed a female: male ratio of 1.73:1 among ILD patients

Spirometry is important in the diagnosis of restrictive lung disease. Decreased total lung capacity (TLC) is an earlier parameter in ILDs [14]. In our study of ILD Patients spirometric observation of mixed pattern and obstructive pattern are more among smokers and restrictive pattern is more among nonsmokers and the values are statistically significant.

Evaluation of diffusing capacity of the lung for carbon monoxide normalized per liter alveolar volume as a parameter for assessment of interstitial lung diseases is very useful. Decreased FVC and exertional desaturation to < 88% are important criteria in the assessment of ILDs [15].

Smokers in our study have lower DLCO values compared to nonsmokers and the values are statistically significant. Najeeb Hassan Mohammed study from Iraq showed lower values of DLCO among smokers which correlates with our study [14]. Tobacco smoke exposure increases the incidence of Pulmonary arterial Hypertension especially among male smokers [16].

Nermine M. Riad stated that evaluation DLCO and DLCO/VA (Alveolar volume) should be interpreted coherently with each other especially in restrictive lung diseases. (Alveolar Volume)VA and TLC-SB (Single breath) give a good guide for lung volume in interstitial lung disease evaluation [17]. According to Hoda, Aliae AR Mohamed-Hussein study evaluation of FVC/DLCO ratio is a predictor for pulmonary hypertension in patients with interstitial lung diseases [18]. In Siribaddana *et al.*, study HRCT findings do not correlate with spirometry and six minute walk performance [19]. In our study radiologically diagnosed cases of ILD presented in severe stage and three fourths of them showed desaturation on 6 minute walk test. In our study there is a statistically significant increase in the incidence of Pulmonary Arterial Hypertension among smokers compared to non-smokers. But the severity of PAH did not correlate with the smoking status.

Katerina D. Samara study showed smoking as a pathogenetic factor and causes increased pulmonary fibrosis among patients of Interstitial Lung Disease [20]. Hussein, *et al.* study among a total of 44 ILD patients showed mean age was 45.7 years. Male preponderance was seen. Frequent HRCT parameter was fibrotic with reticular and honey combing pattern in 45%. TLC and DLCO correlated with severity of disease [21].

In Boubacar Efares study, the mean age was 52.78 years; 74.83% were women 22% had sarcoïdosis,

15.6% had idiopathic pulmonary fibrosis (IPF), 14.18% had other idiopathic interstitial pneumonia (IIP) and 9.9% had connective tissue disease (CTD). They observed that in the diagnosis of ILD BAL cytological analysis has a limited value and should be accompanied by other investigation [22]. Jesudason *et al.*, study (2015) showed Symptoms, PFT and exercise testing had good correlation with HRCT. DLCO corrected % of predicted correlated best with HRCT [24].

Pulmonary arterial Hypertension in Interstitial Lung disease is associated with increased symptoms, reduced exercise capacity and poor prognosis [24]. Sometimes pulmonary hypertension can be high out of proportion to the hypoxia and amount of parenchymal damage. Our study also showed two thirds of the patients had pulmonary arterial hypertension and nearly half of them had severe hypertension by echocardiography [18].

Conclusions:

Interstitial Lung diseases are now frequently diagnosed because of HRCT. They cause considerable morbidity and mortality. Identification etiology and early diagnosis and treatment can prevent long term complications. Smoking correlates with low DLCO and presence of pulmonary arterial hypertension.

Conflicts of interests: The authors have no conflicts of interests with any one.

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