ORIGINAL RESEARCH PAPER

Pulmonary Medicine

# TO STUDY THE CLINICO-RADIOLOGICAL PROFILE AND PROGRESSION OF DISEASE IN PATIENTS OF INTERSTITIAL LUNG DISEASE IN TERTIARY CARE HOSPITAL

**KEY WORDS:**
6MWT – six minute walk test
CTD-ILD – connective tissue related interstitial lung disease
CHP- chronic hypersensitivity pneumonitis
PPFE- Pleuroparenchymal fibroelastosis

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**ABSTRACT**

**Background:** Interstitial lung disease is a group of lung disorders characterized by inflammation and scarring. 67% of ILD have unknown etiology and rest 33% is either caused by CTD or occupational exposure, or radiation. Dyspnea, dry cough, bilateral lower zone infiltrations on chest x-ray,restrictive lung function and impaired gas exchange are similar to all ILD.

**Objectives:** To study the clinic-radiological and functional parameters of patients with ILD,To assess the changes in spO2 and lung function through PFT and 6MWT,To study the morbidity in the course of the disease,To monitor the comorbid conditions in cases of ILD recruited in the study.

**Design:** crossectional

**Settings:** tertiary care centre kota Rajasthan

**Sample Size:** 33

**Materials And Methods:** All participantsof ILD were followed up for a period of 1 year and spiromertry, hrct , 6 mwt were performed and analysed.

**Results:** Out of total 33 patients 28% had IPF, 24% NSIP, 21% CTD-ILD, 12%, CHP, 6% PPFE, 6% undifferentiated ILD and 3% drug induced ILD .The average FVC at the time of recruitment was found to be 54% in IPF, 66% NSIP,55% CTD-ILD,50% PPFE, 43% undifferentiated ILD and 75% drug induced ILD .The most common morbidity was Type2DM 45% followed by PAH in 24 %, 21% systemic hypertension, 9%COPD and RA and 3% malignancy. All IPF had bilateral lower lobe involvement in form of honeycombing and reticulo-nodular shadows. 100% of the patients with PPFE, UNDIFFERENTIATED ILD and DRUG INDUCED ILD shows post exertional desaturation <85%. Functional deterioration in form of >10% fall in FVC was found. >5% spO2 drop and reduction in walk distance by >50meters was estimated.

**Conclusion:** In study percentage distribution of various ILD were comparable to other studies. Male gender with average age between 45 to 54 years is most common in various subtypes of ILD. Diabetes mellitus was most common comorbidity associated with ILD with dyspnea and dry coughing as the predominant symptoms. Bilateral lower zone involvement,honeycombing and reticulonodular shadows were found in CT thorax. The present study has better response to treatment in terms of spirometric and 6MWT worsening over 6 months .

## INTRODUCTION

Interstitial lung disease is a heterogenous group of parenchymal disease having different histopathologies but same clinical presentations which include dyspnea, dry coughing, bilateral lower zone consolidation, restrictive lung function and impaired gas exchange. It refers to a larger group of acute and chronic diseases characterized by damage to lung parenchyma with varying pattern of inflammation or fibrosis with pulmonary interstitium as the primary site of parenchymal damage.[1] It also involves air spaces, peripheral airways, vasculature and corresponding epithelial and endothelial surfaces.[2]

According to ATS (American thoracic society) and European respiratory society (ERS) ILD is classified into 4 main categories[3]

- Diffuse parenchymal lung diseases such as those associated with occupational or environmental exposures and/or collagen vascular disease.
- Granulomatous lung disorders such as sarcoidosis, Wegener's granulomatosis.
- several rare forms of DPLD with distinctive and well-defined clinicopathologic features such as lymphangioleiomyomatosis (LAM), pulmonary Langerhans' cell histiocytosis, and eosinophilic pneumonia
- *Idiopathic* indicates unknown cause and *interstitial pneumonia* refers to involvement of the lung parenchyma by varying combinations of fibrosis and inflammation, in contrast to airspace disease typically seen in bacterial pneumonia. The *idiopathic interstitial pneumonias* include the entities of idiopathic pulmonary fibrosis (IPF), nonspecific interstitial pneumonia (NSIP), cryptogenic organizing pneumonia (COP), acute interstitial pneumonia (AIP), respiratory bronchiolitis-associated interstitial lung disease (RB-ILD), desquamative interstitial pneumonia (DIP), and lymphocytic interstitial pneumonia (LIP).

Most patients with pulmonary fibrosis have lung findings characterized by fine inspiratory, basilar Velcro crackles and most of the patients have digital clubbing. In contrast to patient with non fibrotic lung have clear lung fields on auscultation. Many other system involvements help in differential diagnosis such as dermatologic and musculoskeletal signs of connective tissue diseases including

skin rashes, sclerodactyly, digital ulceration, mechanic hands, synovitis, Raynaud's phenomenon. Gastrointestinal symptoms such as acid reflux indicate esophageal motility problems related to connective tissue disease such as systemic sclerosis and polymyosits. Musculoskeletal symptoms such as arthralgia, morning stiffness, swelling, and erythema may be evidence of Rheumatoid arthritis, mixed connective tissue disorder or Sjogren syndrome. Digital ulceration and rarely digital gangrene strongly suggests scleroderma, mixed connective tissue disorder.

Chest X-ray and High Resolution Computed Tomography (HRCT) are the radiological modalities help in differential diagnosis. Hrct chest is more sensitive than chest x-ray for ILD. The characteristic radiographic features of IPF are collectively known as UIP pattern. In more than 50% of cases suspected to be IPF/UIP, the presence of typical clinical and HRCT features of UIP, when identified by expert clinicians and radiologists, is sufficiently characteristic to allow a confident diagnosis and eliminate the need for surgical lung biopsy. Therefore, the primary role of HRCT is to separate patients with UIP from those with non-UIP lesions or those with less specific findings associated with other idiopathic interstitial pneumonias (NSIP, RB-ILD, ,AIP)as shown in figure 1.

Laboratory testing such as raised calcium level and liverv enzymes in sarcoidosis, abnormal renal function test in pulmonary renal syndromes and mixed connective disorder. Most advanced include serologic testing for CTDs.

Pulmonary function test are main stay in the evaluation and management of ILD. They help in assessing the severity and prognosis in many forms of the disease[4,5]. They are relatively noninvasive method to evaluate disease progression and measure response to therapy.It includes spirometry, measurement of lung volumes and diffusing capacity. Exercise testing such as 6MWT is particularly important in patients of ILD.Typically spirometry in most form of ILD demonstrates a restrictive ventilatory defects due to decreased compliance and increased recoil of lung parenchyma.[4]

Bronchoscopy and surgical lung biopsy are other methods which help in distinguishing non UIP pattern.[5-6]

There are several treatment modalities such as removal from the exposure such as immediate withdrawal of the drug or eliminating environmental exposure. Immunosuppressive therapy such as corticosteroids and other agents such as azathioprine are used help in improving PFT, 6MWT. Antifibrotic drugs such as pirfenidone help in stabilizing lung function through its anti-inflammatory, anti- fibrotic and antioxidant properties.[7] Tyrosine kinase inhibitor NINTEDANIB has statistically demonstrated significant reduction in the rate of decline of lung function.[8] Treatment of comorbidities such as diabetes mellitus most common associated with ILD others include pulmonary hypertension, GERD, and palliative care in form of pulmonary rehabilitation is encouraged to improve dyspnea in all symptomatic patients.[9-10] Lung transplantation is an important life extending alternative in progressive fibrotic lung disease patient particular in IPF patients.

mGAP score is used for survival prediction of ILD patients as shown in figure 5 .

Progressive fibrosis is associated with worsening respiratory symptoms, lung function decline, limited response to immunomodulatory therapies, decreased quality of life and, potentially, early death. Idiopathic pulmonary fibrosis may be regarded as a model for other progressive-fibrosing ILD

## AIMS AND OBJECTIVES

- To study the clinic-radiological and functional parameters of patients with ILD
- To assess the changes in $spO_2$ and lung function through PFT and 6MWT
- To study the morbidity in the course of the disease.
- To monitor the comorbid conditions in cases of ILD recruited in the study.

## MATERIALS AND METHODS

This is an observational study conducted in outpatient and inpatient section between September 2020 to November 2021 in . A total of 33 subjects were recruited in the study. Pregnant females, adolescents and children, an active respiratory tract infection (TB or COVID-19) are excluded from the study. Complete history including smoking status, occupational history, comorbidities, symptoms, drug history, and family history was taken. Complete routine investigations including CBC, liver function test, renal function test, 2D echo, sputum for AFB, serological investigation like RA factor, serum ANA titre (if possible), chest x-ray and HRCT chest at the time of admission and lyr of recruitment. Post exertional desaturation, spirometry, 6MWT at the time of admission, 6 months and 1 year was evaluated. Treatment molecules used were corticosteroids, immunomodulatory such as azathioprine , cyclophosphamide and antifibrotic agent pirfenidone.

The data entry was done, analytical tables were prepared and statistical significance was done using SSPV.

## RESULTS:

### Distribution of ILD:

Out of total 33 patients 28% had IPF, 24% had NSIP, 21% had CTD-ILD, 12% had CHP, and 6% had PP: FE, 6% had undifferentiated ILD and 3 % had drug induced ILD as shown in figure 2.

### Gender Distribution:

MALE GENDER is overall dominant with 54% in this study as depicted in figure 3.

### Age Distribution:

Mean age at the time of diagnosis is 45 to 54 years as shown in table 1

### Fall In Functional Vital Capacity:

Fall of >10% is seen more in IPF patients 66.6% and 2 patients succumb to death before 1year of complete treatment and thus not included. Undifferentiated ILD and drug induced ILD have good results with maintenance treatment as no patient had >10% fall inFVC % after 1year of treatment as compared to IPF AND CT-ILD as depicted in table 2 .

### Comorbidities In Ild Patient:

Most common comorbidity associated with ILD id diabetes mellitus followed by pulmonary hypertension as shown in table 5.

Most common symptoms with dry cough which was present in 100% of the patient with IPF followed by dyspnea and bilateral fine crepts. Clubbing was seen in all types of ILD. Weight loss and anorexia was seen in 66% of IPF.

### Post Exertional Desaturation (<85%) In ILD Patients:

Above table suggests that almost 100% of the patients with PPFE, UNDIFFERENTIATED ILD and DRUG INDUCED ILD shows post exertional desaturation <85%. Shown in table 3.

### HRCT FEATURES:

All 9 (100%) IPF cases show involvement in lower lobes, honey combing, reticulonodulars and 2 (22.2%) cases have upper and middle lobe involvement.

All 8(100%) NSIP cases show involvement in upper, middle and lower lobes with ground glass opacities, 2% cases have

mosaic attenuation.

All 7(100%) CT-ILD cases have lower lobe involvement and reticulonodular shadows whereas 4(57.1%) cases also have upper and middle lobe involvement , 6(85.7%) shows honeycombing and 3(42.8) cases show mosaic attenuation.

All 4(100%) CHP cases have upper and middle lobe involvement, reticulonodular shadows and mosaic attenuation, 3(75%) also have lower lobe involvement and ground glass opacities whereas only 1 (25%) has honeycombing.

All 2(100%) cases have upper, middle and lower lobe involvement, honeycombing and reticulonodular shadows.

All UNDIFFERENTIATED ILD AND DRUG INDUCED ILD cases show 100% involvement of upper, middle and lower lobe involvement with reticulonodular shadows and ground glass opacities.

**6MWT DESATURATION:**

In this study the worsening in 6MWT results after 1 year of optimum treatment have been interpreted on the basis of fall in spO2 desaturation >5% or reduction in walk distance by>50 meters. The results are as shown in above table. All 100% cases of IPF, PPFE and undifferentiated ILD showed significant worsening as depicted in table 4.

**Treatment Molecules Used In Various Types Of Ild:**

In this study steroids were used in 77% cases of IPF, 100% cases of NSIP, CT-ILD, PPFE, CHP, and UNDIFFERENTIATED ILD AND DRUG INDUCED ILD.

Immunomodulatory such as azathioprine , cyclophosphamide were used in 87.5% cases of NSIP , 100% cases of CT-ILD and UNDIFFERENTIATED ILD , 75% cases of CHP and 50% cases of PPFE.

Ant fibrotic agents were used in 100% cases of IPF and PPFE, 25% cases of NSIP 14.3% cases of CT-ILD and 50% cases of UNDIFFERENTIARED ILD as shown in figure 4.

**DISCUSSION:**

In the present study 28% had IPF, 24% had NSIP, 21% had CTD-ILD, 12% had CHP, 6% had PPFE, 6% had undifferentiated ILD and 3 % had drug induced ILD. The results are comparable to study conducted by Dhooria et al in 803 patients which 22% cases of IPF, 7.8 % cases of NSIP, 12.7%cases of CT-ILD.

Male gender is predominant in this study 54% as compared to hyldgaard in which 55 % male were involved.

The present study shows lower average age of presentation in ILD as compared to all other studies which is due to inclusion of PPFE subtype of ILD which has a younger age of onset .Mean age of presentation for IPF , NSIP , CT-ILD and CHP are comparable to the study conducted by hyldgaard which is approximately 55to 65years. The average FVC at the time of recruitment was found to be 54% in IPF, 66% in NSIP, 55% in CTD-ILD, 50% in PPFE, 43% in undifferentiated ILD and 75% in drug induced ILD.

The most common morbidity was Type 2 diabetes mellitus 45% followed by PAH in 24 %, 21 % had systemic hypertension, 9 % COPD and RA each and 3 % had malignancy. All IPF had bilateral lower lobe involvement in form of honeycombing and reticulo- nodular shadows. Functional deterioration in form of >10 % fall in FVC was found. >5% $spO_2$ drop and reduction in walk distance by >50meters was estimated. This was comparable to study conducted by kundu ET l in which 100% patients of IPF and 69.9% patients of CT-ILD could walk <300meters after 6 months of treatment.

There are certain limitations to the study first of all sample size is small , sampling method used was convenience sampling which is non-random and may lead to selection bias.

**CONCLUSION:**

In the present study percentage distribution of various ILD were comparable to other international studies. Male gender with average age between 45 to 54 years is most common in various subtypes of ILD except PPFE which has younger age of onset. Diabetes mellitus was most common comorbidity associated with ILD with dyspnea and dry coughing as the predominant symptoms and clubbing was the most common physical findings associated with bilateral crepitations. In the present study bilateral lower zone involvement, honeycombing and reticulonodular shadows were found in CT scan of thorax. The present study has better response to treatment in terms of spirometric worsening and 6MWT worsening over 6 months as compared to other studies and post ecertional desaturation <85% were seen in allm patients of PPFE , UNDIFFERENTIATED ILD and DRUG INDUCED ILD.

**TABLES AND FIGURES:**

***Table 1: Mean (SD) Age At The Presentation Of Different Types Of Ild***

| SUBTYPE OF ILD | MEAN(SD) AGE AT PRESENTATION(YEARS) |
|---|---|
| IPF ( n =9) | 65(9) |
| NSIP ( n=8) | 54(8) |
| CT-ILD ( n=7) | 45(10) |
| CHP ( n=4) | 53(8) |
| PPFE ( n=2) | 19(1) |
| UNDIFFERENTIATED ILD (n=2) | 36(23) |
| DRUG INDUCED ILD (n=1) | 60(0) |
| TOTAL | 47(8) |

***Table 2: Mean FVC At The Time Of Recruitment And After 1year***

| ILD SUBTYPE | MEAN FVC % AT THE TIME OF RECRUITMENT | AVERAGE FALL >10% AFTER 1 YEAR TREATMENT (%) |
|---|---|---|
| IPF (n =9) | 53(9) | 66.6 |
| NSIP (n=8) | 66(7) | 37.5 |
| CT-ILD (n=7) | 56(10) | 42.8 |
| CHP (n=4) | 53(8) | 25 |
| PPFE (n=2) | 50(8) | 50 |
| UNDIFFERENTIATED ILD (n=2 ) | 43(3) | 0 |
| DRUG INDUCED ILD (n=1) | 75(0) | 0 |
| TOTAL | 56(6) | |

***Table 3: Post Exertional Desaturation (<85%>)In ILD Patients***

| ILD SUBTYPE | POST EXERTEIONAL DESATURATION (%) |
|---|---|
| IPF (n =9) | 77 |
| NSIP (n=8) | 25 |
| CT-ILD (n=7) | 57 |
| CHP (n=4) | 50 |
| PPFE (n=2) | 100 |
| UNDIFFERENTIATED ILD (n=2) | 100 |
| DRUG INDUCED ILD (n=1) | 100 |

***Table 4 :Worsening In 6 Minute Walk Test***

| ILD SUBTYPE | WORSENING IN 6MWT(>5% FALL , FALL TOTAL DISTANCE>50m) | PERCENTAGE (%) |
|---|---|---|
| IPF (n =9) | 9 | 100 |
| NSIP (n=8) | 3 | 37.5 |
| CT-ILD (n=7) | 3 | 42.8 |

| | | |
|---|---|---|
| CHP (n=4) | 2 | 50 |
| PPFE (n=2) | 2 | 100 |
| UNDIFFERENTIATED ILD(n=2) | 2 | 100 |
| DRUG INDUCED ILD(n=1) | 0 | 0 |

***Table 5: Comorbidities In ILD***

| DISEASE(COMORBIDITIES) | PERCENTAGE |
|---|---|
| DIABETES MELLITUS | 45 |
| SYSTEMIC HYPERTENSION | 21 |
| PULMONARY ARTERIAL HYPERTENSION | 24 |
| HYPOTHYROIDISM | 1 |
| COPD | 9 |
| RHEUMATOID ARTHRITIS | 9 |
| MALIGNANCY | 3 |

| IIP Group and Clinical-Radiologic-Pathologic Diagnosis | CT Pattern | Typical CT Distribution | Typical CT Findings | CT Differential Diagnosis |
|---|---|---|---|---|
| Chronic fibrosing IIPs | | | | |
| IPF | Usual interstitial pneumonia (UIP) | Peripheral, subpleural, basal | Reticular opacities, honeycombing, traction bronchiectasis or bronchiolectasis, architectural distortion, focal ground-glass attenuation | Collagen vascular disease, hypersensitivity pneumonitis, asbestosis, sarcoidosis |
| Idiopathic NSIP | NSIP | Peripheral, basal, symmetric | Ground-glass attenuation, irregular lines, traction bronchiectasis, consolidation | UIP, desquamative interstitial pneumonia, cryptogenic organizing pneumonia, hypersensitivity pneumonitis |
| Smoking-related IIPs | | | | |
| Desquamative interstitial pneumonia | Desquamative interstitial pneumonia | Lower zone, peripheral predominance in most cases | Ground-glass attenuation, reticular lines, cysts | RB-ILD, NSIP, hypersensitivity pneumonitis |
| RB-ILD | Respiratory bronchiolitis | Often upper lung predominant, centrilobular | Bronchial wall thickening, centrilobular nodules, patchy ground-glass opacity | Desquamative interstitial pneumonia, NSIP, hypersensitivity pneumonitis |
| Acute or subacute IIPs | | | | |
| Cryptogenic organizing pneumonia | Organizing pneumonia | Subpleural or peribronchial | Patchy consolidation or nodules, perilobular pattern, reverse halo sign | Infection, aspiration, eosinophilic pneumonia, NSIP, vasculitis, sarcoidosis, mucinous adenocarcinoma, lymphoma |
| Acute interstitial pneumonia | Diffuse alveolar damage | Diffuse or patchy | Consolidation and ground-glass opacity, often with lobular sparing; traction bronchiectasis later | Hydrostatic edema, pneumonia, pulmonary hemorrhage, acute eosinophilic pneumonia |
| Rare IIPs | | | | |
| Lymphoid interstitial pneumonia | Lymphoid interstitial pneumonia | More commonly, lower lung predominant | Centrilobular nodules, ground-glass attenuation, septal and bronchovascular thickening, thin-walled cysts | NSIP, sarcoidosis, Langerhans cell histiocytosis and other cystic lung diseases |
| Idiopathic pleuroparenchymal fibroelastosis | Idiopathic pleuroparenchymal fibroelastosis | Peripheral, upper lung predominant | Pleural thickening and subpleural fibrotic changes | Sarcoidosis, pneumoconiosis, familial pulmonary fibrosis, connective tissue disease, hypersensitivity pneumonitis |

***Figure 1 :** HRCT Features Of ILD*

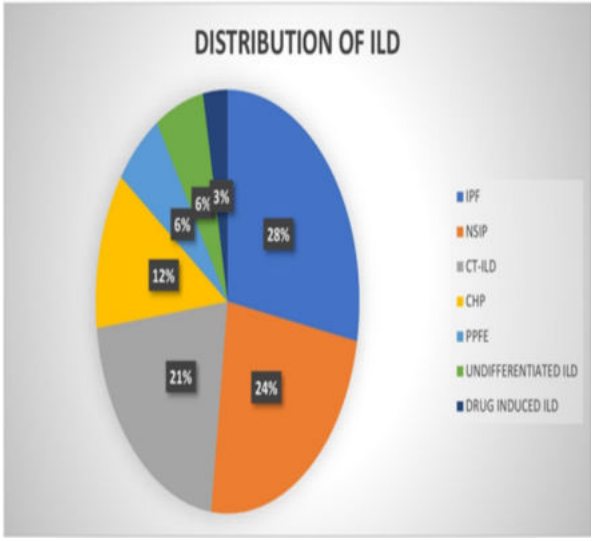


***Figure :2** Distribution Of ILD*

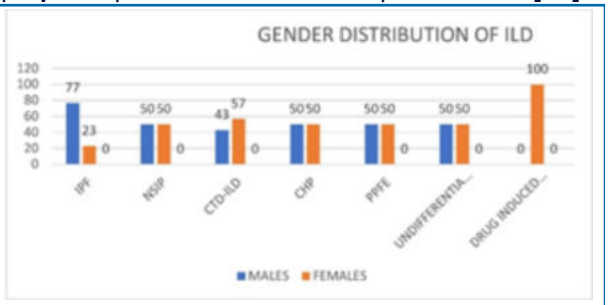


***Figure 3:** Gender Distribution Of ILD*

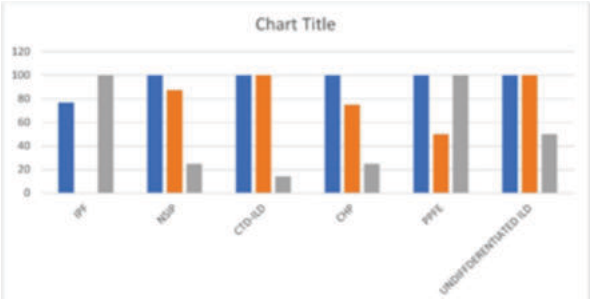


***Figure 4:** Treatment Distribution In ILD*

| | | |
|---|---|---|
| G | Gender | |
| | Female | 0 |
| | Male | 1 |
| A | Age, years | |
| | ≤60 y | 0 |
| | 61-65 y | 1 |
| | >65 y | 2 |
| P | Physiology, FVC % predicted | |
| | >75% | 0 |
| | 50-75% | 1 |
| | <50% | 2 |

| m-GAP score | |
|---|---|
| Stage 1 | Score 0-3 |
| Stage 2 | Score 4-5 |

***Figure 5:** m GAP Score In ILD*

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