# Scholars Journal of Applied Medical Sciences (SJAMS)

Sch. J. App. Med. Sci., 2016; 4(3F):1086-1105 ©Scholars Academic and Scientific Publisher (An International Publisher for Academic and Scientific Resources) www.saspublishers.com

# **Original Research Article**

# ISSN 2320-6691 (Online) ISSN 2347-954X (Print)

DOI: 10.36347/sjams.2016.v04i03.090

# Study of Clinico radiological Profile and Treatment Modalities in Interstitial Lung Disease

Dr Abhishek Tiwari<sup>1</sup>, Dr Kuldeep Kumar<sup>2</sup>, Dr. Bharat Bhushan<sup>2</sup>, Dr. Nirmal Chand Kajal<sup>2</sup>, Dr. Sandeep Gupta<sup>2</sup>, Dr. Daljit Singh<sup>2</sup>

<sup>1</sup>JR, pursuing MD degree in TB & Respiratory Diseases, Final Year, Baba Farid University of Health Sciences, Faridkot <sup>2</sup>Department of TB & Chest, Government Medical College Amritsar, near Radha swami satsang, Mall Avenue, Amritsar, Punjab-143001, India

# \*Corresponding author

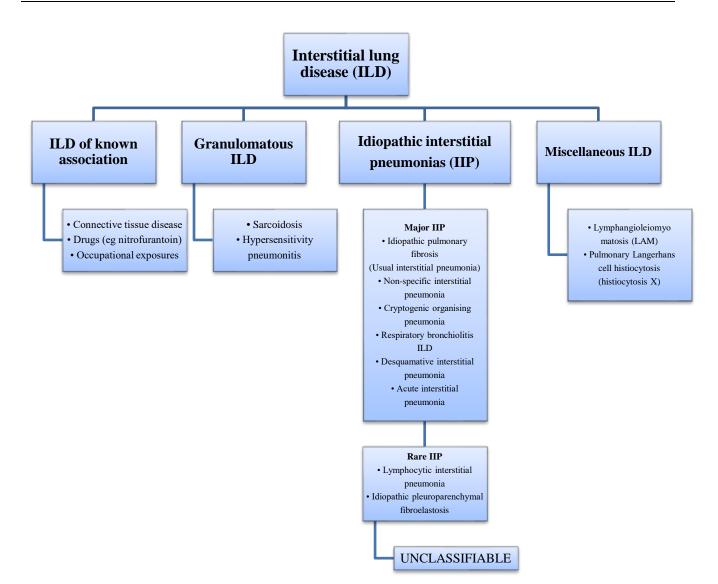
Dr. Abhishek Tiwari Email: <u>992876464zero@gmail.com</u>

**Abstract:** The main objective is to study the clinical and radiological presentation of interstitial lung disease and also various type of treatment modalities used in intestinal lung disease. The method in present study was conducted on 50 diagnosed patients of interstitial lung diseases attending OPD/Indoor of Tuberculosis & Chest Department, Govt. medical college, Amritsar. In results & conclusion of the study group of 50 patients with interstitial lung disease, Sarcoidosis is the most common cause of ILD consists of 18 patients forming 36% of the study group. Average duration of symptoms in ILD patients in this study is 2.5 years. On an average age at presentation in the study group came out to be 48.8 yrs. Age distribution of the cases in the study group shows age group 40-60 yrs form 80% of patients consisting of 40 patients. In the present study of 50 patients, 27 are females (54%) & 23 are males (46%). Cough & Dyspnoea are the most common feature at presentation on our study group present in 45 (90%) & 40 patients (80%) respectively. Most common Chest X ray feature in our study group is reticular/ reticulo nodular opacity which was present in 41 patients (82%), followed by hilar lymphadenopathy in 10 patients (20%) and honey combing in 3 patients (6%). **Keywords:** Interstitial lung disease, Sarcoidosis, Age, Symptom duration, Cough, Chest X-ray, CT scan etc

# **INTRODUCTION**

Interstitial lung disease (ILD) is a heterogeneous group of disorders that are characterized by varying degrees of fibrosis and inflammation of lung parenchyma leading to restrictive pathology and common clinical, radiological, physiological and pathological manifestations [1]. Establishing an accurate diagnosis of ILD can be challenging for clinicians as there are more than 200 different subtypes. Patients with ILD often report progressive shortness of breath, exercise intolerance and a pervasive dry cough. Fine crepitations may be appreciated on chest auscultation. Signs of pulmonary hypertension and right heart failure may also be present, particularly in advanced disease. Oxygen denaturation commonly occurs during exertion and is associated with poorer long-term survival [2, 3].

Determination of the disease subtype requires consideration of the patient's history of exposures, specific clinical features, serology, and radiological pattern and, in some cases, lung biopsy during multidisciplinary discussions. Surgical lung biopsy carries an inherent risk of morbidity and mortality and only a fraction of patients are deemed suitable [4]. Over the past decade, ILDs have been reclassified in comprehensive international consensus statements [6-9]. The major subgroups of ILD (Figure) are broadly defined as:



Establishing an accurate ILD diagnosis is critical, as different disease subtypes carry distinct prognoses and require tailored management strategies. Baseline and more detailed investigations are shown in Table. A 'clinical-radiological-pathological' diagnosis is most accurately established within multidisciplinary discussion, where ILD physicians, radiologists and pathologists collaborate dynamically. The multidisciplinary discussion is considered the gold standard for determining a diagnosis of ILD minimises observer bias and enhances diagnostic confidence [5, 6].

The idiopathic interstitial pneumonias (IIPs) are a heterogeneous group of non neoplastic disorders resulting from damage to the lung parenchyma by varying patterns of inflammation and fibrosis [10]. The interstitium includes the space between the epithelial and endothelial basement membranes and it is the primary site of injury in the IIPs. However, these

disorders frequently affect not only the interstitium, but also the airspaces, peripheral airways, and vessels along with their respective epithelial and endothelial linings[11]. 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.

Idiopathic Pulmonary Fibrosis (IPF) is the most common type of idiopathic interstitial pneumonia forming 50-60% of cases [12]. The prognosis is usually worse compared with other IIPs, with a median survival time of 2 to 3 years [7]. IPF is characterized by the radiological pattern of usual interstitial pneumonia (UIP). HRCT with features of definite UIP in patient with clinical evidences not suggestive of alternative diagnosis is sufficient for a confident diagnosis of IPF and carries an accuracy of 80% to 90% [7, 13]. Biopsy is usually reserved for atypical or uncertain cases [14, 15]. The chest radiograph is normal in most patients with early disease. In advanced disease, the chest radiograph shows decreased lung volumes and sub pleural reticular opacities that increase from the apex to the bases of the lungs [16]. This apico-basal gradient is even better seen on high-resolution CT images. Together with sub pleural reticular opacities and macrocystic honeycombing combined with traction bronchiectasis, the apicobasal gradient represents a trio of signs that is highly suggestive of UIP [17, 18]. Ground glass abnormality is minimal or absent, never being the predominant pattern. Many patients with IPF may show atypical pattern of UIP on HRCT, with

features of nonspecific overlapping interstitial pneumonia (NSIP), chronic HP, or sarcoidosis; in these patients open lung biopsy is usually necessary to establish a confident diagnosis [19]. The incidence of the disease increases with older age, with presentation typically occurring in the sixth and seventh decades [20, 21, 22]. IPF should be considered in all adult patients with unexplained chronic exertional dyspnea, and commonly presents with cough, bibasilar inspiratory crackles, and finger clubbing [23, 24, 25]. More men have been reported with IPF than women, and the majority of patients have a history of cigarette smoking [26], Exposure, medication, or systemic disease.

Interstitial lung disea	se investigati	on	0		
	Invest	igation	Possible findings		
	• Ches	t X-ray	Non-specific infiltrates		
	• HRC	T scan	• Nodules		
			• Cysts		
			Ground glass change		
			Honeycomb change		
			Traction bronchiectasis		
Routine at			Intralobular septal thickening		
baseline and	Pulse	e oximetry/ arterial blood gas	• Low SpO2, Low PaO2		
follow up	• Com	nective tissue disease serology	• Positive auto antibodies (eg ANA, ENA, RF,		
			myositis antibodies, ANCA)		
	• Lun	g function tests (spirometry, lung	• Low FEV1, FVC		
	volum	es, DLCO)	<ul> <li>Normal or high FEV1/FVC ratio</li> </ul>		
			Reduced lung volumes		
			Reduced DLCO		
	• 6-mi	nute walk test	Reduced walk distance		
			Oxygen desaturation		
		<ul> <li>Bronchoscopy with lavage</li> </ul>	Variable, frequently normal		
			• May have elevated neutrophils, eosinophils		
			and/or lymphocytes		
• Surgica		<ul> <li>Surgical lung biopsy</li> </ul>	Variable and specific for diagnosis		
Occasional • ]		Echocardiogram	Pulmonary hypertension		
			Right ventricular dysfunction		
		• Right heart catheter	Confirmation of pulmonary hypertension		
		Overnight sleep study	Nocturnal hypoxia		
			Obstructive sleep apnoea		

Table 1: Interstitial lung disease investigations

NSIP is less common than UIP but is still one of the most common histologic findings in patients with IIPs [27] typical patient with NSIP is between 40 and 50 years old and is usually about a decade younger than the patient with IPF. Symptoms of NSIP are similar to those of IPF but usually milder. Although it is primarily defined as an idiopathic disease, the morphologic pattern of NSIP is encountered in association with frequent disorders, such as connective tissue diseases, hypersensitivity pneumonitis, or drug exposure [28, 29]. In patients with early NSIP, the chest radiograph is normal. In advanced disease, bilateral pulmonary infiltrates are the most salient abnormality. The lower lung lobes are more frequently involved, but an obvious apicobasal gradient, as seen in UIP, is usually missing. High-resolution CT typically reveals a sub pleural and rather symmetric distribution of lung abnormalities. The most common manifestation consists of patchy groundglass opacities combined with irregular linear or reticular opacities and scattered micro nodules [30-32]. In advanced disease, traction bronchiectasis and consolidation can be seen; Owing to the substantial overlap of high-resolution CT patterns, the major CT differential diagnosis for NSIP is UIP. The key CT features that favor the diagnosis of NSIP over UIP are homogeneous lung involvement without an obvious apicobasal gradient, extensive ground-glass abnormalities, a finer reticular pattern, and micro nodules [33-35].

Cryptogenic organizing pneumonia (COP), previously known as bronchiolitis obliterans organizing pneumonia is the idiopathic form of organizing pneumonia. On HRCT, the two most frequently seen features include bilateral, multifocal, patchy consolidation (present in upto 90% of cases) and ground glass abnormality [36]. The lung volumes are generally preserved, COP tends to preferentially involve the sub pleural and bronchovascular regions of the lung parenchyma [37].

Respiratory bronchiolitis (RB)-ILD is a part of the spectrum of smoking related lung diseases. The predominant finding on HRCT is ground-glass abnormality and preferentially involves the upper lobes. The ground glass abnormality of RB-ILD has been shown to represent areas of macrophage accumulation in the distal airspaces [38].

DIP (desquamative interstitial pneumonia) is a rare form of ILD. The usual age of presentation is 40-50 years, with men affected more than women (male/female >2:1). The disease predominantly affects smokers (90%) cases, but can also be seen secondary to lung infections, organic dust exposure, and marijuana smoke inhalation. HRCT typically shows a ground glass pattern, which is caused by diffuse macrophage infiltration of the alveoli along with interstitial septal thickening; this is generally present in all cases of DIP [42]. The ground glass pattern can either be patchy or diffuse, with a predilection for peripheral and basal lung zones [40].

Acute interstitial pneumonia (AIP) is notable for its acute presentation. On HRCT, the most common finding includes ground glass abnormalities, traction bronchiectasis, and architectural distortion. The ground glass pattern is patchy in most cases, with areas of lobular sparing; however some cases may show a more diffuse distribution [41].

ILDs can be associated with various occupational lung diseases (e.g. asbestosis, silicosis, coal worker pneumoconiosis, HP, berylliosis) [30, 31] and connective tissue disorders (e.g. rheumatoid arthritis, systemic sclerosis, systemic lupus erythematosus, mixed connective tissue disease).

Interstitial lung diseases of some specific type also show gender as well as age predilection in their prevalence. As women are more likely to have collagen vascular associated interstitial lung diseases due to increased risk of autoimmune diseases. Women are also almost exclusively affected by lymphangioleio myomatosis and tuberous sclerosis-associated lung diseases [33]. Particular ancestory also increases the likelihood of some interstitial lung diseases. Sarcoidosis occurs 10-to 12-fold more in blacks than in their white counterparts [42].

Patients with ILD frequently present with exertional dyspnoea which has been shown to be closely related to quality of life [34-36]. The mechanisms through which ILD produces dyspnoea include ventilation perfusion de-arrangements, diffusion impairment, neuro-mechanical dissociation, physiological restriction (due to reduced compliance and decreased elastic recoil), circulatory and cardiovascular limitation, anxiety and depression as well as skeletal and ventilatory muscle weakness [44].

The optimal therapy for interstitial lung diseases is an area of intense investigation. Current medical regimens have not shown to improve survival but nevertheless are routinely prescribed with hope of slowing of progression of disease. Immunosuppressive antiinflammatory agents are used to treat various forms of ILD [45, 46]. There is reasonably compelling evidence that the administration of agents such as corticosteroids is strongly associated with improvement or even clearing of lung pathology for many forms of ILD. This is particularly the case for disorders such as cryptogenic organizing pneumonia (COP), eosinophilic pneumonia, sarcoidosis, or cellular non-specific interstitial pneumonia (NSIP) [45]. Traditional therapies that were suggested to benefit patients with IPF included corticosteroids and cytotoxic drugs (e.g. azathioprine, cyclophosphamide) [47].

Regarding the role of anti fibrotic therapy in patients with interstitial lung disease, Following evaluation in Phase II and Phase III clinical trials in patients with IPF, [48-50] pirfenidone was approved by the European Commission in February 2011. Pirfenidone is indicated for the treatment of patients with mild-to-moderate IPF.

#### AIMS AND OBJECTIVES

- To study the clinical features of interstitial lung disease.
- To study the radiological presentation of interstitial lung disease.
- To study the treatment modalities in interstitial lung disease.

## MATERIALS AND METHODS

The present study was carried out on patients who were attending the outpatient department and/or admitted in Tuberculosis & Chest Department, Govt. Medical College, Amritsar, after taking approval from the ethical committee.

Study was conducted on 50 diagnosed patients of interstitial lung diseases attending OPD/Indoor of Tuberculosis & Chest Department, Govt. medical college, Amritsar after taking approval from ethical committee and informed consent from patient.

### **Inclusion criteria**

Diagnosed case of interstitial lung disease

## **Exclusion criteria**

- 1) Patient not willing to give consent
- 2) Age less than 12 years
- 3) Pregnant ladies
- Patients with obstructive lung disease such as COPD or asthma or active coronary disease or other co-morbid illness precluding performance of 6 min walk test.

Descriptive type of study of patients diagnosed as ILDs was done. Patient diagnosed as ILD based on clinical, radiological and PFT findings will be included in the study. Each patient was explained the purpose of the study and need for complete co-operation emphasized. Those who satisfied the inclusion and exclusion criteria were interviewed according to prepared pro forma. Interview was conducted in a well lit and ventilated examination room. Detailed clinical history, physical examination, routine investigations (Hemoglobin, total leucocyte count, differential leucocyte count, erythrocyte sedimentation rate, random blood sugar, renal function tests, liver function tests), sputum examinations (for acid fast bacilli, malignant cells), chest radiography, HRCT, PFT, ECG, investigations for connective tissue diseases according to patient's clinical profile, and 6 minute walk test was done on all the patients.

ECHO and related other cardiac investigations were done for selected patients, as and when required. Treatment details were also noted.

## **OBSERVATIONS & RESULTS**

Fifty patients diagnosed as ILD based on clinical, radiological and PFT findings attending OPD and/or admitted in Chest and TB hospital, Amritsar were included in the study. They were studied according to their demographic features, clinical characteristics, Radiological findings and treatment modalities and the following observations were made which have been depicted in tabular form.

#### Aetiology of Interstitial Lung Disease:

Table 1: Actiology Distribution of Patients with Interstitial Lung Disease											
		Total	Sarcoidosis	IPF	NSIP	HSP	RA-	SS-ILD	SLE	LIP	DIP
		(N)	(N)	(N)	(N)	(N)	ILD (N)	(N)	(N)	(N)	(N)
Number subjects	of	50	18	13	12	2	1	1	1	1	1

6 D - 4<sup>1</sup> - -- 4 - -- -- -- 4 - -- -- -- 4<sup>1</sup> - - - - - - - -

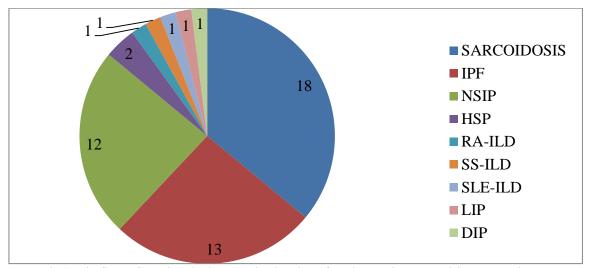


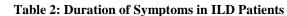
Fig 1: Pie Chart Showing Actiology Distribution of Patients with Interstitial Lung Disease

Of the study group of 50 patients with interstitial lung disease, Sarcoidosis is the most common cause of ILD consists of 18 patients forming 36% of the study group. IPF is the second most common cause with 13 patients (26%) followed by NSIP with 12 patients (24%).

## Abhishek Tiwari et al., Sch. J. App. Med. Sci., March 2016; 4(3F):1086-1105

## **Duration of Symptoms:**

	Overall	Sarcoidosis	IPF	NSIP	HSP	RA- ILD	SS- ILD	SLE	LIP	DIP
Avg. Duration of symptoms (yrs)	2.5	2.2	2.2	2.5	2.8	4.5	3.5	3	4.2	3.5



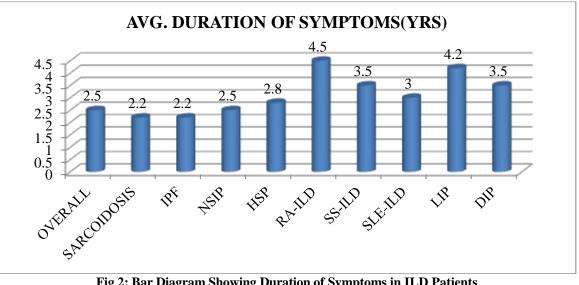


Fig 2: Bar Diagram Showing Duration of Symptoms in ILD Patients

Average duration of symptoms in ILD patients in this study is 2.5 years. Sarcoidosis and IPF both having average duration of symptoms 2.2 yrs which is minimum in the study group while RA-ILD patient have duration of symptoms for 4.5 yrs, maximum in the study group.

# AGE AT PRESENTATION:

	Table 3: Age at Presentation in ILD Patients									
	Overall (yrs)	Sarcoidosis (yrs)	IPF (yrs)	NSIP (yrs)	HP (yrs)	RA- ILD (yrs)	SS- ILD (yrs)	SLE (yrs)	LIP (yrs)	DIP (yrs)
Average Age at presentation	48.8	45.8	54.9	48.7	45	52	46	39	42	49.3

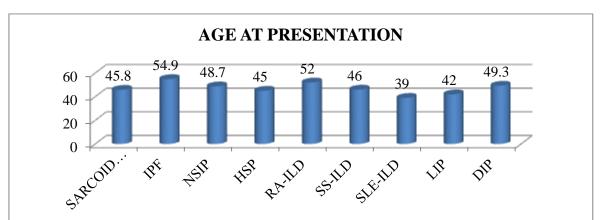


Fig 3: Bar Diagram Showing Age at Presentation in ILD Patients

## Abhishek Tiwari et al., Sch. J. App. Med. Sci., March 2016; 4(3F):1086-1105

On an average age at presentation in the study group came out to be 48.8 yrs. Average age at presentation in the sarcoidosis group is 45.8yrs, in IPF group it is 54.9yrs which is maximum in the study group, in NSIP group it is 48.7 yrs. Patient with SLE-ILD have age at presentation of 39 yrs.

## **Age Distribution**

Table 4: Age Distribution in ILD Patients									
	< 40 YRS	40-60 YRS	>60 YRS						
NO. OF CASES	6	40	4						
PERCENTAGE	12	80	8						

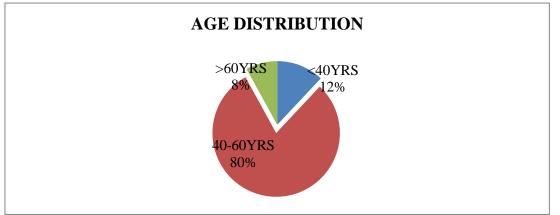


Fig 4: Pie Diagram Showing Age Distribution in ILD Patients

Age distribution of the cases in the study group shows age group 40-60 yrs form 80% of patients consisting of 40 patients. Age group of less than 40 yrs

have 6 patients (12%) while age group more than 60 yrs have 4 patients (8%).

## **Gender Distribution**

#### **Table 5: Gender Distribution in ILD Patients**

TOTAL SUBJECTS	MALE	FEMALE
50	23	27

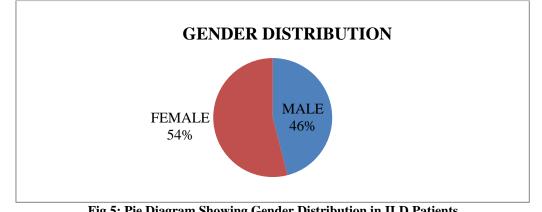


Fig 5: Pie Diagram Showing Gender Distribution in ILD Patients

Gender distribution of the cases in the study group shows increased disease prevalence in females. In the present study of 50 patients, 27 are females (54%) & 23 are males (46%).

## **Smoking Pattern:**

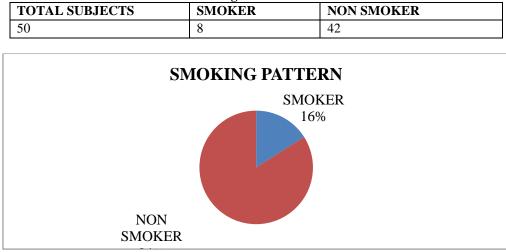


Table 6: Smoking Pattern in ILD Patients

Fig 6: Pie Diagram Showing Smoking Pattern in ILD Patients

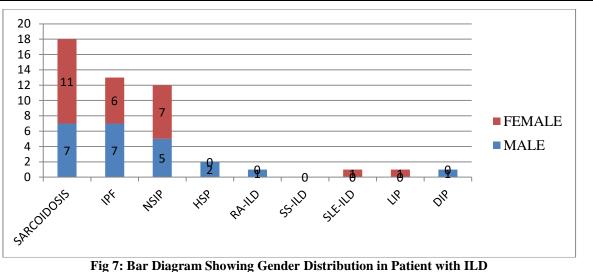
Smoking pattern in the study group shows that only 8 patients out of 50 patients are smoker (16%), While 42 patients are non smokers (84%).

## **Clinical Profile of ILD Patients**

	Total	Sarcoidosis	IPF	NSIP	HSP	RA-	SS-	SLE	LIP	DIP
	(N)	(N)	(N)	(N)	(N)	ILD	ILD(N)	(N)	(N)	(N)
						(N)				
Number of subjects	50	18	13	12	2	1	1	1	1	1
Mean age (yrs)	48.8	45.8	54.9	48.7	45	52	46	39	42	49.3
Male/Female	23/27	7/11	7/6	5/7	2/0	1/0	0/1	0/1	0/1	1/0
Smoking	8	2	3	2	-	-	-	-	-	1
<b>Duration of symptoms(yrs)</b>	2.5	2.2	2.2	2.5	2.8	4.5	3.5	3	4.2	3.5
Cough	45	16	11	11	2	1	1	1	1	1
Dyspnoea	40	15	10	10	1	1	1	0	1	1
Haemoptysis	2	1	-	1	-	-	-	-	-	-
Fever	8	2	2	1	-	1	-	1	1	-
Joint symptoms	6	2	1	1	-	1	-	1	-	-
ATT intake	9	4	2	1	1	1	-	-	-	-
Clubbing	6	1	4	1	-	-	-	-	-	-
<b>Desaturation on 6 MWT (SPo<sub>2</sub> &lt;</b>	17	5	4	6	1	1	-	-	-	-
88% or fall of 4% from										
baseline)										

	NO OF SUBJECTS	MALE	FEMALE
SARCOIDOSIS	18	7	11
IPF	13	7	6
NSIP	12	5	7
HSP	2	2	0
RA-ILD	1	1	0
SS-ILD	1	0	1
SLE-ILD	1	0	1
LIP	1	0	1
DIP	1	1	0





Gender distribution in the ILD cases with different etiology shows that, Out of 18 patients of sarcoidosis 11 were females (61%) & 7 were males

(39%). In IPF group of 13 patients, 6 were females (46%) & 7 were males (54%). In NSIP group out of 12 patients, 7 were female (58%) & 5 were males (42%).

# Signs & Symptoms at Presentation

Table 8: Signs &	& Symp	otoms Of Patients	With ILD	At Presentation
------------------	--------	-------------------	----------	-----------------

Symptom	Number of cases	Percentage
Cough	45	90.0
Dyspnoea	40	80.0
Haemoptysis	2	4.0
Fever	8	16.0
Joint symptoms	6	12.0
Clubbing	6	12.0
Desaturation at 6 MWT	17	34.0

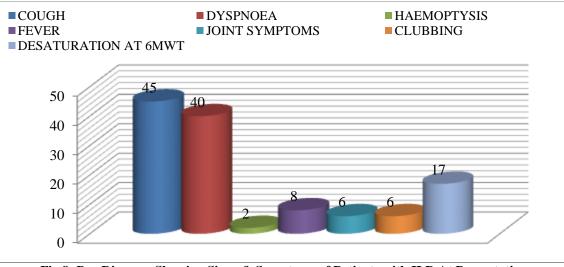


Fig 8: Bar Diagram Showing Signs & Symptoms of Patients with ILD At Presentation

Cough & Dyspnoea are the most common feature at presentation on our study group present in 45 (90%) & 40 patients (80%) respectively. Other features at presentation include fever, haemoptysis, joint symptoms, clubbing etc.

# Frequency of Cough & Dyspnoea

CAUSE OF ILD	NO OF CASES	PRESENCE	OF		OF
		COUGH		DYSPNOEA	
SARCOIDOSIS	18	16		15	
IPF	13	11		10	
NSIP	12	11		10	
HSP	2	2		1	
RA-ILD	1	1		1	
SS-ILD	1	1		1	
SLE-ILD	1	1		0	
LIP	1	1		1	
DIP	1	1		1	

Table 9: Frequency of Cough & Dyspnoea in ILD Patients

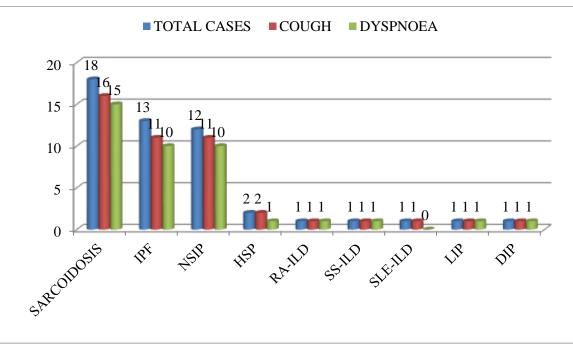


Fig 9: Bar Diagram Showing Frequency of Cough & Dyspnoea in ILD Patients

# **History of ATT Intake:**

# Table 10: History of ATT Intake in ILD Patients

	NO OF CASES	POSITIVE HISTORY OF ATT INTAKE
OVERALL	50	9
SARCOIDOSIS	18	4
IPF	13	2
NSIP	12	1
HSP	2	1
RA-ILD	1	1
SS-ILD	1	0
SLE-ILD	1	0
LIP	1	0
DIP	1	0

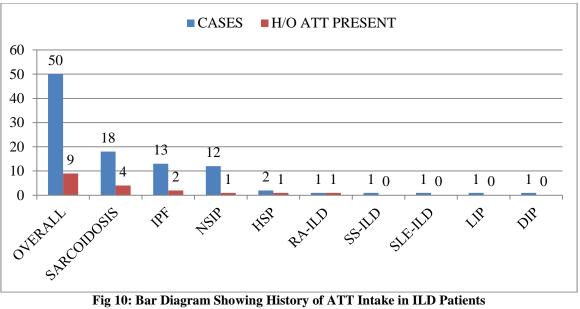


Fig 10: Bar Diagram Showing History of ATT Intake in ILD Patients

As the radiological presentation of ILD some time simulate TB, there is significant number of patients have history of ATT intake. 9 (18%) of total 50

patients have history of ATT intake, most significant in sarcoidosis group in which 4 (22%) out of 18 patients have history of ATT intake.

0	Total	Sarcoidosis	IPF	NSIP	HSP(N)	RA-	SS-	SLE	LIP	DIP
	(N)	(N)	(N)	(N)		ILD (N)	ILD (N)	(N)	(N)	(N)
CHEST X-RAY FINDIN	CHEST X-RAY FINDINGS								.1	
Reticular/Reticulo- nodular	41	13	11	11	1	1	1	1	1	1
Hilar lymph- adenopathy	10	7	-	2	-	1	-	-	-	-
Honey combing	3	1	2	-	-	-	-	-	-	-
HRCT FINDINGS										
Fibrosis	26	3	13	7	-	1	1	1	-	-
Honey combing	17	1	13	2	-	-	-	-	-	1
Ground glass opacity	19	7	1	7	1	-	1	-	1	1
Interstitial infiltrate	20	6	-	8	2	1	-	1	1	1
Sub pleural opacity	18	2	13	3	-	-	-	-	-	-
Traction Bronchiectasis	9	-	6	2	-	-	1	-	-	-
Lymphadenopathy	10	8	-	2	-	-	-	-	-	-
Pleural opacity	3	2	-	-	-	1	-	-	-	-
Nodules	3	2	-	-	1	-	-	-	-	-
Cysts	-	-	-	-	-	-	-	-	-	-

**Radiological Profile of ILD Patients** 

**Chest X-ray Features:** 

#### Table 10: Chest X Ray Features of ILD Patients

PATTERN	NO OF CASES	PERCENTAGE OF CASES
RETICULAR/RETICULONODULAR	41	82.0
HILAR LYMPHADENOPATHY	10	20.0
HONEY COMBING	3	6.0

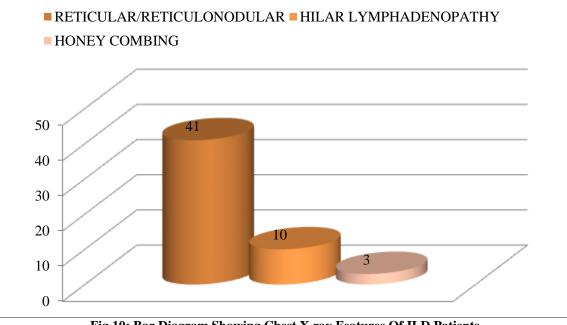


Fig 10: Bar Diagram Showing Chest X ray Features Of ILD Patients

Most common Chest X ray feature in our study group is reticular/ reticulo nodular opacity which was present in 41 patients (82%), followed by hilar lymphadenopathy in 10 patients (20%) and honey combing in 3 patients (6%).

## **HRCT Features of ILD Patients**

Table 11: Table Showing HRCT Pattern in ILD Patients						
HRCT PATTERN	NO OF CASES	PERCENTAGE OF				
		CASES				
FIBROSIS	26	52.0				
HONEYCOMBING	17	34.0				
GROUND GLASS OPACITY	19	38.0				
INTERSTITIAL INFILTRATES	20	40.0				
SUBPLEURAL OPACITY	18	36.0				
TRACTION BRONCHIECTASIS	9	18.0				
LYMPHADENOPATHY	10	20.0				
PLEURAL OPACITY	3	6.0				
NODULES	3	6.0				

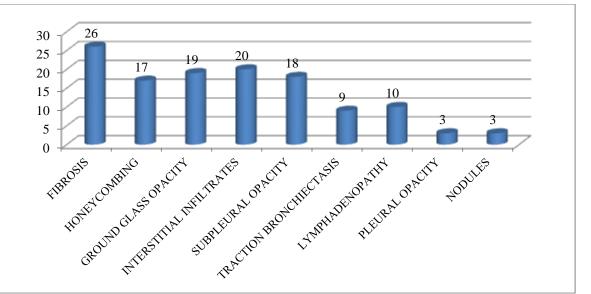


Fig 11: Bar Diagram Showing HRCT Pattern in ILD Patients

Fibrosis (52%) is the most common HRCT feature in our study group followed by interstitial infiltrate (40%), ground glass opacity (38%), sub

pleural opacity (36%), honey combing (34%), lymphadenopathy (20%), traction bronchiectasis (18%), pleural opacity (6%), and nodules (6%).

# **Spirometry Pattern**

Table 12: Spirometric Parameters in ILD Patients										
SPIROMETRY										
	Total (N)	Sarcoidosis (N)	IPF (N)	NSIP (N)	HSP (N)	RA- ILD (N)	SS- ILD (N)	SLE (N)	LIP (N)	DIP (N)
FEV <sub>1</sub> % (mean % predicted)	60	65	55	60	75	58	53	43	53	68
FVC%(mean % predicted)	66	71	58	68	79	68	59	52	58	76
FEV <sub>1</sub> /FVC (mean)	87	86	91	87	90	80	95	71	87	95

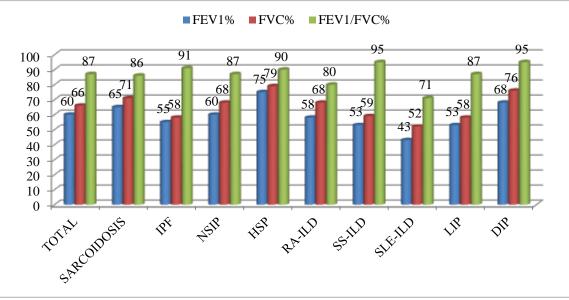


Fig 12: Bar Diagram Showing Spirometric Parameters in ILD Patients

#### Abhishek Tiwari et al., Sch. J. App. Med. Sci., March 2016; 4(3F):1086-1105

In our study group of 50 patients average  $FEV_1\%$  came around 60%, FVC around 66%, and

FEV<sub>1</sub>/FVC around 87%. Group wise spirometric parameters are as described above.

#### **Treatment Modalities:**

Table 13: Treatment Modalities in ILD Patients						
TREATMENT MODALITY	NO OF CASES TAKING	PERCENTAGE				
CORTICOSTEROIDS	50	100				
ANTI FIBROTICS	13	26				
OTHERS	17	34				

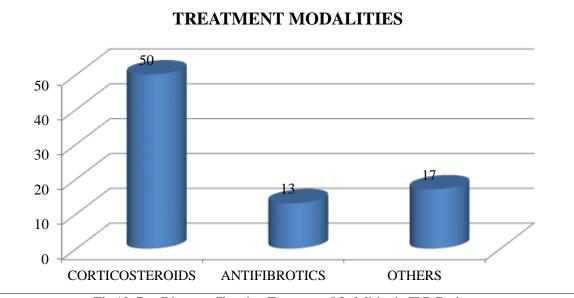


Fig 13: Bar Diagram Showing Treatment Modalities in ILD Patients

Corticosteroids group is the most commonly prescribed group of medication in our study group & was prescribed to almost all patients. Antifibrotic medication was prescribed to around 26% of patients while other medications like mucolytics, cyclophosphamide, azathioprine etc were prescribed to around 34% of patients.

## DISCUSSION

The true burden of ILD in India is not clearly known due to under recognition, attributed to lack of awareness, paucity of diagnostic facilities as well as to the huge spectrum that this entity encompasses. Reports from western literature show an increase in the prevalence and incidence of ILD in recent decades [79]. However, data on clinical presentation and diagnosis of the spectrum of ILDs from India is limited. The present study is the study of clinical features, radiological presentation, treatment modalities in ILD patients attending Chest & TB hospital, Amritsar.

In our study, the mean age at presentation is greater than 40 years. This finding is similar to previous studies from India [81-89] as well as western literature [90, 91]. The present study observed increased prevalence in females (54%) as compared to male patients (46%). Similar observations have been reported in other Indian studies [82, 84, 87, 88] and also in a study from Greece. However, an increased prevalence in males has been documented in other studies [85, 87]. This can be explained by the fact that the majority of our subject population consisted of patients with sarcoidosis and nonspecific interstitial pneumonia (NSIP), which are female preponderant diseases. In the pool of ILDs analysed, sarcoidosis (36%) was found to be the most common subgroup, followed by IPF (26%) and NSIP (24%). The results were similar to another Indian study [95] and studies from western literature [92, 93]. However, in a study on the occurrence of ILD in Poland based on patients hospitalised in the Regional Pulmonary Unit in Radom, IPF (27.5%) was the most common, followed by sarcoidosis (25%). The incidence of ILDs calculated for the adult population of this region was 5/100,000 [94]. Similarly, studies by Subhash et al.; [87] and Udwadia et al.; [88] from India, reported a higher prevalence of IPF in the study population.

Another important observation is that almost 18% of cases of ILDs had a history of anti-tubercular treatment, and in the sarcoidosis subgroup this figure was 22%. 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 current study included 18 (36%) cases of pulmonary sarcoidosis, 11 (61.1%) being females. The higher prevalence in females is coherent with findings in western literature [93]. The mean age at presentation was 48.8 years with the average duration of symptoms being 2.5 years; the majority were non-smokers (84%). This data is similar to other Indian studies [95, 96]. In contradiction with the literature [93] clubbing (12%) was an uncommon finding in our study. 6MWT showed significant desaturation (SPo<sub>2</sub>< 88% or 4 % fall from the baseline) in 17 (34%) cases. The plausible explanation of this could be the advanced stage of the disease at presentation.

Idiopathic pulmonary fibrosis is a specific type of ILD, with characteristic radiological features and histopathology. In the present study we had 13 (26%) cases of IPF, and it was the second most common subgroup in the pool of ILDs. In contrast, IPF was observed as the most common ILD in other Indian [86-88] and western studies [97]. In the current study, mean age at presentation was 54.9 years, male to female ratio was 7:6 and 23.07% of cases were smokers. The current study agrees with data from western literature in terms of age at presentation with disease typically occurring in 6th-7th decade of life. The literature [92] shows more men being diagnosed with IPF than women and the majority being smokers. However, our study reported around equal prevalence in male and female subjects and a more prevalence of smoking. In another Indian study by Subhash et al.; [87] out of 33 cases of IPF, 16 were females and smoking was present in only 18% of all IPF cases. Another point that merits mention is that diagnostic criteria vary across studies, leading to differences in epidemiological parameters of IPF. In our study, on 6MWT, 34% of cases showed significant desaturation (SPo<sub>2</sub>< 88% or 4 % fall from the baseline) at presentation. This finding has clinical implications as studies have advocated that desaturation (i.e. a decline in oxygen saturation to below 88%) during 6MWT is a marker for increased risk of mortality[100].

In the present study, we had 12 (24%) cases with a diagnosis of NSIP based on clinical, radiological and pathological features, but we were unable to elucidate the cause. The mean age at presentation was 48.7 years, 7 were females and only 16.6% were smokers. The review of literature shows NSIP has a mean age of 52 years and is more common in females and never smokers [101].

Of 3 cases diagnosed as CTD -associated interstitial lung disease (CTD-ILD), lung involvement at presentation was observed in 1 case each of rheumatoid arthritis (RA), scleroderma & SLE. The prevalence of RA-ILD varies from 5–58% [102] and ILD in systemic sclerosis is observed in 40–80% of cases [103]. The prevalence of CTD–ILD in India has been reported as ranging from 5.6% to 50.8% in various studies [87, 91].

Hypersensitivity pneumonitis (HP) was diagnosed in 2 (4%) cases; all were associated with pigeon exposure, with duration of exposure ranging from 3-6 years. In a previous study from India, Udwadia *et al.;* [94] reported HP in 15 (6%) from a total of 273 cases. Other ILDs diagnosed as per clinicoradio-pathological criteria in the current study were desquamative interstitial pneumonia (DIP) 1 case, lymphocytic interstitial pneumonia (LIP) 1 case.

Regarding treatment modalities patients using in our study group, Corticosteroids is the most commonly used group, with all 50 patients (100%) taking this medication, followed by anti fibrotic medication in 13 patients (26%), other less commonly used medications like mucolytics, cyclophosphamide, azathioprine etc in 17 patients (34%)

#### SUMMARY AND CONCLUSION

In present study, fifty patients diagnosed as ILD based on clinical, radiological and PFT findings attending OPD and/or admitted in Chest and TB hospital, Amritsar are included in the study. They were studied according to their demographic features, clinical characteristics, Radiological findings and treatment modalities.

- 1. There were 23 males and 27 females yielding a male: female ratio of 23:27.
- 2. 40 patients (83.3%) were between 40-60 years of age. The mean overall age of patients was 48.8 years.
- 8 patients (16%) were smokers and 42 patients (84%) non smokers, yielding a smoker: nonsmoker ratio of 4:21. All smokers are of male gender.
- Sarcoidosis came out as most common cause of ILD with 18 patients (36%) followed by IPF (26%) & NSIP (24%) respectively.
- 5. Mean duration of symptoms of illness at presentation overall came out around 2.5 years.
- The common symptoms at presentation included cough (90%), breathlessness (80%) followed by fever (16%), joint symptoms (12%), hemoptysis (4%).
- 7. There is history of ATT intake in 9 patients (18%), more frequently in sarcoidosis group (22%).
- 8. Of the total 50 patients 17 (34%) were showing significant desaturation on 6 minute walk test, that is  $SPo_2$  less than 88% or more than 4% fall in baseline  $SPo_2$ .

- 9. Common Chest X ray findings were reticular/reticulo nodular pattern (82%), hilar lymphadenopathy (10%), honeycombing (6%) etc.
- Common HRCT findings were fibrosis (52%), interstitial infiltrates (40%), ground glass opacity (38%), sub pleural opacity (36%), honeycombing (34%), lymphadenopathy (20%), traction bronchiectasis (18%), pleural opacity (6%), nodules (6%) etc.
- 11. Average FEV<sub>1</sub>, FVC, FEV<sub>1</sub>/FVC came around 60, 66, and 87 respectively. SLE-ILD group has worst pulmonary function test.
- 12. All 50 patients were taking corticosteroids (100%), 13 patients were on anti fibrotic & anti inflammatory drugs (26%), 17 patients were on other medications (34%).

This study describes the spectrum of ILDs prevalent in patients presenting to outdoor & indoor department of Chest & TB hospital, Govt. Medical College, Amritsar (Punjab). Diagnosis of ILDs at an early stage is paramount to prevent/delay progression to irreversible damage to the lungs, especially in treatment-responsive ILDs like sarcoidosis. Hence, in a developing country like India, with high prevalence of pulmonary tuberculosis, education and awareness of general practitioners and physicians about ILDs deserves special attention.

#### REFERENCES

- American Thoracic Society, European Respiratory Society. American Thoracic Society/European Respiratory Society International Multidisciplinary Consensus Classification of the Idiopathic Interstitial Pneumonias. Am J Respir Crit Care Med 2002; 165:277–304.
- 2. Flaherty KR, Andrei AC, Murray S, Fraley C, Colby T.V, Travis WD *et al.*; Idiopathic pulmonary fibrosis: prognostic value of changes in physiology and six-minute-walk test. Am J Respir Critic Care Med 2006; 174(7):803–09.
- Lama VN, Flaherty KR, Toews GB, Colby, T.V, Travis W.D, Long Q *et al.*; Prognostic value of desaturation during a 6-minute walk test in idiopathic interstitial pneumonia. Am J Respir Critic Care Med 2003; 168(9):1084–90.
- Park JH, Kim DK, Kim DS, Koh Y, Lee S.D, Kim W.S *et al.*; Mortality and risk factors for surgical lung biopsy in patients with idiopathic interstitial pneumonia. Eur J Cardio thorac Surg 2007; 31(6):1115–19.
- Flaherty KR, King TE Jr, Raghu G, Lynch III J.P, Colby T.V, Travis W.D *et al.*; Idiopathic interstitial pneumonia: What is the effect of a multidisciplinary approach to diagnosis? Am J Respir Critic Care Med 2004; 170(8):904–10.
- 6. Travis WD, Costabel U, Hansell DM, King Jr T.E, Lynch D.A, Nicholson A.G *et al.*; An official

American Thoracic Society/ European Respiratory Society statement: Update of the international multidisciplinary classification of the idiopathic interstitial pneumonias. Am J Respir Critic Care Med 2013; 188(6):733–48.

- Raghu G, Collard HR, Egan JJ, Martinez F.J, Behr J, Brown K.K *et al.*; An official ATS/ERS/JRS/ ALAT statement: Idiopathic pulmonary fibrosis: evidence-based guidelines for diagnosis and management. Am J Respir Critic Care Med 2011; 183(6):788–824.
- Bradley B, Branley HM, Egan JJ; Interstitial lung disease guideline: The British Thoracic Society in collaboration with the Thoracic Society of Australia and New Zealand and the Irish Thoracic Society. Thorax 2008; 63 Suppl 5:v1-58.
- 9. American Thoracic Society, European Respiratory Society. American Thoracic Society/European Respiratory Society International Multidisciplinary Consensus Classification of the Idiopathic Interstitial Pneumonias. This joint statement of the American Thoracic Society (ATS), and the European Respiratory Society (ERS) was adopted by the ATS board of directors, June 2001 and by the ERS Executive Committee, June 2001. Am J Respir Critic Care Med 2002; 165:277–304.
- 10. American Thoracic Society; European Respiratory Society. Idiopathic pulmonary fibrosis: diagnosis and treatment: international consensus statement. Am J Respir Crit Care Med 2000; 161:646–664.
- 11. Cushley MJ, Davison AG, du Bois RM, Egan J, Flower CD, Gibson GJ, *et al.*; The diagnosis, assessment and treatment of diffuse parenchymal lung disease in adults. Thorax 1999; 54:S1–S30.
- 12. Travis WD, King TE Jr, Bateman ED, Lynch D.A, Capron F, Center D *et al.;* American Thoracic Society/European Respiratory Society international multidisciplinary consensus classification of the idiopathic interstitial pneumonias. Am J Respir Crit Care Med 2002; 165(2):277.
- Tsubamato M, Muller NL, Johkoh T, Ichikado K, Taniguchi H, Kondoh Y *et al.;* Pathologic subgroups of nonspecific interstitial pneumonia: differential diagnosis from other idiopathic interstitial pneumonias on high resolution computed tomography. J Comput Assist Tomogr 2005; 29(6):793.
- Hunninghake GW, Zimmerman MB, Schwartz DA, KING JR T.E, Lynch J, Hegele R *et al.*; Utility of a lung biopsy for the diagnosis of idiopathic pulmonary fibrosis. Am J Respir Crit Care Med 2001; 164(2):193-196.
- Raghu G, Mageto YN, Lockhart D, Schmidt R.A, Wood D.E, Godwin J.D; The accuracy of the clinical diagnosis of new-onset idiopathic pulmonary fibrosis and other interstitial lung disease: a prospective study. Chest 1999; 116(5):1168-74.

- Chandler PW, Shin MS, Friedman SE, Myers JL, Katzenstein AL; Radiographic manifestations of bronchiolitis obliterans with organizing pneumonia vs usual interstitial pneumonia. AJR Am J Roentgenol 1986; 147:899–906.
- 17. Hunninghake GW, Lynch DA, Galvin JR, Gross B.H, Muller N, Schwartz D.A *et al.*; Radiologic findings are strongly associated with a pathologic diagnosis of usual interstitial pneumonia. Chest 2003; 124(4):1215–1223.
- Johkoh T, Muller NL, Cartier Y, Kavanagh P.V, Hartman T.E, Akira M *et al.*; Idiopathic interstitial pneumonias: diagnostic accuracy of thin-section CT in 129 patients. Radiology 1999; 211(12):555– 560.
- Sverzellati N, Wells AU, Tomassetti S, Desai S.R, Copley S.J, Aziz Z.A *et al.*; Biopsy-proved idiopathic pulmonary fibrosis: spectrum of nondiagnostic thin section CT diagnoses. Radiology 2010; 254(3):957.
- Scott J, Johnston I, Britton J; What causes cryptogenic fibrosing alveolitis? A case-control study of environmental exposure to dust. BMJ 1990; 301:1015–1017.
- Mannino DM, Etzel RA, Parrish RG; Pulmonary fibrosis deaths in the United States, 1979–1991: an analysis of multiple-cause mortality data. Am J Respir Crit Care Med 1996; 153:1548–1552.
- 22. Raghu G, Freudenberger TD, Yang S, Curtis JR, Spada C, Hayes J, *et al.*; High prevalence of abnormal acid gastro-oesophageal reflux in idiopathic pulmonary fibrosis. Eur Respir J 2006; 27:136–142.
- Douglas WW, Ryu JH, Schroeder DR; Idiopathic pulmonary fibrosis: Impact of oxygen and colchicine, prednisone, or no therapy on survival. Am J Respir Crit Care Med 2000; 161:1172–1178.
- 24. King TE Jr, Tooze JA, Schwarz MI, Brown KR, Cherniack RM; Predicting survival in idiopathic pulmonary fibrosis: scoring system and survival model. Am J Respir Crit Care Med 2001; 164:1171–1181.
- 25. Gribbin J, Hubbard RB, Le Jeune I, Smith CJ, West J, Tata LJ; Incidence and mortality of idiopathic pulmonary fibrosis and sarcoidosis in the UK. Thorax 2006; 61:980–985.
- Iwai K, Mori T, Yamada N, Yamaguchi M, Hosoda Y; Idiopathic pulmonary fibrosis: epidemiologic approaches to occupational exposure. Am J Respir Crit Care Med 1994; 150:670–675.
- 27. Travis WD, Matsui K, Moss J, Ferrans VJ; Idiopathic nonspecific interstitial pneumonia: prognostic significance of cellular and fibrosing patterns— survival comparison with usual interstitial pneumonia and desquamative interstitial pneumonia. Am J Surg Pathol 2000; 24:19–33.
- 28. Kim EA, Lee KS, Johkoh T, Kim T.S, Suh G.Y, Kwon O.J *et al.;* Interstitial lung diseases

associated with collagen vascular diseases: radiologic and histopathologic findings. Radio Graphics 2002; 22(1):S151–S165.

- Rossi SE, Erasmus JJ, McAdams HP, Sporn TA, Goodman PC; Pulmonary drug toxicity: radiologic and pathologic manifestations. RadioGraphics 2000; 20:1245–1259.
- Johkoh T, Muller NL, Colby TV, Ichikado K, Taniguchi H, Kondoh Y *et al.;* Nonspecific interstitial pneumonia: correlation between thinsection CT findings and pathologic subgroups in 55 patients. Radiology 2002; 225(1):199–204.
- Akira M, Inoue G, Yamamoto S, Sakatani M; Nonspecific interstitial pneumonia: findings on sequential CT scans of nine patients. Thorax 2000; 55:854–859.
- Kim EY, Lee KS, Chung MP, Kwon OJ, Kim TS, Hwang JH; Nonspecific interstitial pneumonia with fibrosis: serial high-resolution CT findings with functional correlation. AJR Am J Roentgenol 1999; 173: 949–953.
- 33. MacDonald SL, Rubens MB, Hansell DM, Copley SJ, Desai S.R, du Bois R.M *et al.;* Nonspecific interstitial pneumonia and usual interstitial pneumonia: comparative appearances at and diagnostic accuracy of thin-section CT. Radiology 2001;221(3):600–605.
- Flaherty KR, Thwaite EL, Kazerooni EA, Gross B.H, Toews G.B, Colby T.V *et al.*; Radiological versus histological diagnosis in UIP and NSIP: survival implications. Thorax 2003; 58(2): 143– 148.
- Do KH, Lee JS, Colby TV, Kitaichi M, Kim DS; Nonspecific interstitial pneumonia versus usual interstitial pneumonia: differences in the density histogram of high-resolution CT. J Comput Assist Tomogr 2005;29:544–548.
- Jara-palomares L, Gomez-Izquierdo L, Gonzalez-Vergara D, Rodriguez-Becerra E, Marquez-Martin E, Barrot-Cortés E, *et al.*; Utility of high-resolution computed tomography and BAL in cryptogenic organizing pneumonia. Respir Med 2010; 104(11):1706-1711.
- Lee KS, Kullnig P, Hartman TE, Müller N.L; Cryptogenic organizing pneumonia: CT findings in 43 patients. AJR Am J Roentgenol 1994; 162: 543-546.
- 38. Remy-Jardin M, Remy J, Boulenguez C, *et al.*; Morphologic effects of cigarette smoking on airways and pulmonary parenchyma in healthy adult volunteers: CT evaluation and correlation with pulmonary function tests. Radiology 1993; 186:107.
- Johkoh T, Muller NL, Cartier Y, Kavanagh P.V, Hartman T.E, Akira M *et al.*; Idiopathic interstitial pneumonias: diagnostic accuracy of thin section CT in 129 patients. Radiology 1999; 211(2):555.

- Hartman TE, Primack SL, Swensen SJ, Hansell D, McGuinness G, Müller N.L; Desquamative interstitial pneumonia: thin section CT findings in 22 patients. Radiology 1993; 187(3):787-790.
- Primack SL, Hartman TE, Ikezoe J, Akira M, Sakatani M, Müller N.L; Acute interstitial pneumonia: radiographic and CT findings in nine patients. Radiology 1993; 188(3):817.
- 42. Michael A. Nead, David G Morris, *et al.*; Interstitial Lung Disease: A Clinical Overview and General Approach. In. Fisherman's Pulmonary Diseases and Disorders. 2008; 4: 1105-7.
- Hansen JE, Wasserman K; Pathophysiology of activity limitation in patients with interstitial lung disease. Chest 1996; 109:1566–76.
- 44. Schwarz M, King TE Jr.; Physiology of interstitial lung disease. In: Schwarz M, King TE Jr. Interstitial lung disease. 2003; 4:54–74.
- 45. Kim R, Meyer KC; Therapies of interstitial lung disease—past, present, and future. Therapeutic Advances Respir Dis 2008, 2:319–338.
- Meyer KC, Bierach J; Immunosuppressive therapy for autoimmune lung diseases. Immunol Allergy Clin North Am 2012, 32:633–639.
- American Thoracic Society: Idiopathic pulmonary fibrosis: diagnosis and treatment. International consensus statement. American Thoracic Society (ATS) and the European Respiratory Society (ERS). Am J Respir Crit Care Med 2000, 161:646– 664.
- 48. Azuma A, Nukiwa T, Tsuboi E, Suga M, Abe S, Nakata K *et al.;* Double-blind, placebo-controlled trial of pirfenidone in patients with idiopathic pulmonary fibrosis. Am J Respir Crit Care Med 2005, 171(9):1040-1047.
- Taniguchi H, Ebina M, Kondoh Y, Ogura T, Azuma A, Suga M *et al.*; Pirfenidone in idiopathic pulmonary fibrosis. Eur Respir J 2010; 35(4):821-829.
- Noble PW, Albera C, Bradford WZ, Costabel U, Glassberg M.K, Kardatzke D *et al.*; Pirfenidone in patients with idiopathic pulmonary fibrosis (CAPACITY): two randomised trials. Lancet 2011, 377(9779):1760-1769.
- Coultas DB, Zumwalt RE, Black WC, Sobonya RE; The epidemiology of interstitial lung diseases. Am J Respiratory Critical Care Medicine 1994; 150:967-72.
- 52. A U Wells, N Hirani; Interstitial lung disease guideline: the British thoracic society in collaboration with the Thoracic society of Australia and New Zealand and the Irish thoracic society. Thorax 2008; 63:1-9.
- 53. Travis WD, Costabel U, Hansell DM, King Jr T.E, Lynch D.A, Nicholson A.G *et al.*; An official American Thoracic Society/European Respiratory Society statement: update of the international multidisciplinary classification of the idiopathic

interstitial pneumonias. Am J Respir Crit Care Med 2013; 188(6): 733–748.

- 54. Thomeer M, Demedts M, Behr J, Buhl R, Costabel U, Flower C.D.R *et al.*; Multidisciplinary interobserver agreement in the diagnosis of idiopathic pulmonary fibrosis. Eur Respir J 2008; 31(3): 585–591.
- 55. Meyer KC, Raghu G; Patient evaluation. In Interstitial Lung Disease: A Practical Approach. Secondth edition. Edited by Baughman RP, Du Bois RM. New York: Springer; 2011:3–16.
- Meyer KC; Interstitial lung disease in the elderly: pathogenesis, diagnosis and management. Sarcoidosis Vasc Diffuse Lung Dis 2011; 28:3–17.
- Raghu G, Weycker D, Edelsberg J, Bradford W.Z, Oster G; Incidence and prevalence of idiopathic pulmonary fibrosis. Am J Respir Crit Care Med. 2006, 174(7): 810-816.
- Raghu G, Mageto YN, Lockhart D, Schmidt R.A, Wood D.E, Godwin J.D; The accuracy of the clinical diagnosis of new-onset idiopathic pulmonary fibrosis and other interstitial lung disease: A prospective study. Chest. 1999, 116(5): 1168-1174.
- Hunninghake GW, Zimmerman MB, Schwartz DA, KING JR T.E, Lynch J, Hegele R *et al.*; Utility of a lung biopsy for the diagnosis of idiopathic pulmonary fibrosis. Am J Respir Crit Care Med. 2001; 164(2): 193-196.
- Martinez FJ, Safrin S, Weycker D, Starko K.M, Bradford W.Z, King T.E *et al.*; The clinical course of patients with idiopathic pulmonary fibrosis. Ann Intern Med. 2005, 142(12\_part\_1): 963-967.
- Collard HR, King TE Jr, Bartelson BB, Vourlekis J.S, Schwarz M.I, Brown KK; Changes in clinical and physiologic variables predict survival in idiopathic pulmonary fibrosis. Am J Respir Crit Care Med. 2003, 168(5): 538-542.
- Richeldi L, Davies HR, Ferrara G, Franco F; Corticosteroids for idiopathic pulmonary fibrosis. Cochrane Database Syst Rev 2003; (3): CD002880.
- Davies HR, Richeldi L, Walters EH; Immunomodulatory agents for idiopathic pulmonary fibrosis. Cochrane Database Syst Rev 2003 ;( 3): CD003134.
- 64. Collard HR, Ryu JH, Douglas WW, Schwarz M.I, Curran-Everett D, King T.E *et al.;* Combined corticosteroid and cyclophosphamide therapy does not alter survival in idiopathic pulmonary fibrosis. Chest. 2004, 125(6): 2169-2174.
- Martinez FJ; Idiopathic interstitial pneumonias: Usual interstitial pneumonia versus nonspecific interstitial pneumonia. Proc Am Thorac Soc. 2006, 3: 81-95.
- Cha SI, Fessler MB, Cool CD, Schwarz M.I, Brown K.K; Lymphoid interstitial pneumonia: Clinical features, associations and prognosis. Eur Respir J. 2006, 28(2): 364-369.

- 67. Strange C, Highland KB; Interstitial lung disease in the patient who has connective tissue disease. Clin Chest Med. 2004, 25: 549-559.
- Tanaka N, Newell JD, Brown KK, Cool C.D, Lynch D.A; Collagen vascular disease-related lung disease: High-resolution computed tomography findings based on the pathologic classification. J Comput Assist Tomogr. 2004, 28(3): 351-360.
- Tashkin DP, Elashoff R, Clements PJ, Goldin J, Roth M.D, Furst D.E *et al.;* Cyclophosphamide versus placebo in scleroderma lung disease. N Engl J Med. 2006, 354(25): 2655-2666.
- Swigris JJ, Olson AL, Fischer A, Lynch D.A, Cosgrove G.P, Frankel SK *et al.*; Mycophenolate mofetil is safe, well tolerated, and preserves lung function in patients with connective tissue diseaserelated interstitial lung disease. Chest. 2006, 130(1): 30-36.
- Baughman RP; Pulmonary sarcoidosis. Clin Chest Med. 2004, 25: 521-530.
- Shorr AF, Torrington KG, Hnatiuk OW; Endobronchial involvement and airway hyper reactivity in patients with sarcoidosis. Chest. 2001, 120: 881-886.
- Paramothayan NS, Lasserson TJ, Jones PW; Corticosteroids for pulmonary sarcoidosis. Cochrane Database Syst Rev 2005; (2): CD001114.
- Selman M; Hypersensitivity pneumonitis: A multifaceted deceiving disorder. Clin Chest Med. 2004, 25: 531-547.
- 75. Monkare S; Influence of corticosteroid treatment on the course of farmer's lung. Eur J Respir Dis. 1983, 64: 283-293.
- Camus P, Bonniaud P, Fanton A, Camus C, Baudaun N, Foucher P; Drug-induced and iatrogenic infiltrative lung disease. Clin Chest Med. 2004, 25(3): 479-519.
- American Thoracic Society. Diagnosis and initial management of non-malignant diseases related to asbestos. Am J Respir Crit Care Med. 2004, 170: 691-715.
- Schwartz DA, Davis CS, Merchant JA, Bunn W.B, Galvin J.R, Van Fossen D.S *et al.*; Longitudinal changes in lung function among asbestos-exposed workers. Am J Respir Crit Care Med. 1994, 150(5): 1243-1249.
- 79. Kornum J.B., Christensen S., Grijota M, Pedersen L, Wogelius P, Beiderbeck A *et al.*; The incidence of interstitial lung disease 1995–2005: a Danish nationwide population-based study. BMC Pulm. Med. 2008; 8(1): 1.
- American Thoracic Society, European Respiratory Society, World Association of sarcoidosis and Other Granulomatous Disorders. Statement on sarcoidosis. Am. J. Respir. Crit. Care Med. 1999; 160: 736-55.

- Shah J.R; Diffuse interstitial pulmonary fibrosis: course and prognosis. Indian J. Chest Dis. Allied Sci. 1974; 21: 174–179.
- Jindal S.K., Malik S.K., Deodhar S.D., Sharma B.K; Fibrosing alveolitis: a report of 61 cases seen over the past five years. Indian J. Chest Dis. Allied Sci. 1979; 21: 174–179.
- Mahasur A.A., Dave K.M., Kinare S.G., Kamat S.R., Shetye V.M., Kolhatkar V.P; Diffuse fibrosing alveolitis-an Indian experience. Lung India 1983; 5: 171–179.
- Sharma S.K., Pande J.N., Guleria J.S; Diffuse interstitial pulmonary fibrosis. Indian J. Chest Dis. Allied Sci. 1984; 26: 214–219.
- Sharma S.K., Pande J.N., Verma K., Guleria J.S; Bronchoalveolar lavage fluid (BALF) analysis in interstitial lung diseases. Indian J. Chest Dis. Allied Sci. 1989; 31: 187–196.
- Kalra S., D'Souza G., Bhusnuramth B., Jindal S.K; Transbronchial lung biopsy in diffuse lung disease. Indian J. Chest Dis. Allied Sci. 1989; 31: 265–270.
- Subhash H.S., Ashwin I., Solomon S.K., David T., Cherian A.M., Thomas K; A comparative study on idiopathic pulmonary fibrosis and secondary diffuse parenchymal lung disease. Indian Journal of Medical Science 2004; 58: 185–190.
- Sen T., Udwadi Z.F; Retrospective Study of Interstitial Lung Disease in a Tertiary Care Centre in India. Indian J. Chest Dis. Allied Sci. 2010; 52: 207–211.
- Gagiya A.K., Suthar H.N., Bhagat G.R; Clinical profile of interstitial lung diseases cases. Natl. J. Med. Res. 2012; 2: 2–4.
- Raghu G., Nyberg F., Morgan G; The epidemiology of interstitial lung disease and its association with lung cancer. Br. J. Cancer. 2004; 91: S3–10.
- 91. Kornum J.B., Christensen S., Grijota M, Pedersen L, Wogelius P, Beiderbeck A *et al.*; The incidence of interstitial lung disease 1995–2005: a Danish nationwide population-based study. BMC Pulm. Med. 2008; 8(1): 1.
- Karakatsani A., Papakosta D., Rapti A, Antoniou K.M, Dimadi M, Markopoulou A *et al.;* Hellenic Interstitial Lung Diseases Group. Epidemiology of interstitial lung diseases in Greece. Respir. Med. 2009; 103(8): 1122–1129.
- 93. Schweisfurth H., Kieslich C., Satake N, Loddenkemper R, Schönfeld N, Mäder I *et al.*; How are interstitial lung diseases diagnosed in Germany? Results of the scientific registry for the exploration of interstitial lung diseases ("Fibrosis registry") of the WATL. Pneumologie 2003; 57(7): 373–382.
- 94. Szafrański W; Interstitial lung diseases among patients hospitalized in the Department of Respiratory Medicine in Radom District Hospital

during the years 2000–2009. Pneumonol. Alergol. Pol. 2012; 80: 523–532.

- 95. Sharma S.K, Mohan A; Sarcoidosis in India: not so rare! J. Indian Acad. Clin. Med. 2004; 5: 12–21.
- 96. Sharma S.K, Mohan A, Guleria J.S; Clinical characteristics, pulmonary function abnormalities and outcome of prednisolone treatment in 106 patients with sarcoidosis. J. Assoc. Physicians India 2001; 49: 697–704.
- Xaubet A., Ancochea J., Morell F, Rodriguez-Arias J.M, Villena V, Blanquer R *et al.*; Report on the incidence of interstitial lung diseases in Spain. Sarcoidosis Vasc. Diffuse Lung Dis.2004; 21(1): 64–70.
- Scott J, Johnston I, Britton J; What causes cryptogenic fibrosing alveolitis? A case-control study of environmental exposure to dust. BMJ 1990; 301: 1015–1017.
- Mannino D.M, Etzel R.A, Parrish R.G; Pulmonary fibrosis deaths in the United States, 1979–1991: an analysis of multiple- cause mortality data. Am. J. Respir. Crit. Care Med. 1996; 153: 1548–1552.
- 100.Lama V.N., Flaherty K.R., Toews G.B, Colby T.V, Travis W.D, Long Q *et al.*; Prognostic value of desaturation during a 6-minute walk test in idiopathic interstitial pneumonia. Am. J. Respir. Crit. Care Med. 2003; 168(9): 1084–1090.
- 101. Travis W.D, Hunninghake G, King T.E. Jr, Lynch D.A, Colby T.V, Galvin JR, *et al.*; Idiopathic nonspecific interstitial pneumonia: report of an American Thoracic Society project. Am. J. Respir. Crit. Care Med. 2008; 177(12): 1338–1347.
- 102.Fischer A, West S.G, Swigris J.J, Brown K.K, du Bois R.M; Connective tissue disease-associated interstitial lung disease: a call for clarification. Chest. 2010; 138: 251–256.
- 103.Gabbay E., Tarala R., Will R, Carroll G, Adler B, Cameron D *et al.*; Interstitial lung disease in recent onset rheumatoid arthritis. Am. J. Respir. Crit. Care Med. 1997; 156(2): 528–535.