

# High Resolution Computed Tomography Scan Assessment of Different Interstitial Lung Diseases

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## ABSTRACT

### BACKGROUND

Interstitial Lung Disease (ILD) is a group of diffuse lung parenchymal diseases characterized by the involvement of pulmonary interstitium. High resolution computed tomography (HRCT) is the cross-sectional imaging modality of choice for the diagnosis and follow up of ILD as it is accurate as well as non-invasive. The present study was done to describe the basic HRCT patterns associated with Interstitial Lung Disease and to correlate the HRCT patterns with clinical data to obtain differential diagnosis of Interstitial Lung Disease (ILD).

### METHODS

100 patients (41 males and 59 females) with a mean age of 50 years were included in this study during the period from July 2017 to June 2018. These patients were primarily diagnosed as having interstitial lung disease solely on the basis of clinical findings and chest x-ray by the Chest Medicine Department of BMCH and then referred to Radiology Department BMCH for HRCT assessment.

### RESULTS

74 patients were diagnosed to have interstitial lung disease and 26 patients had airway disease as well. The common frequent findings in interstitial lung disease (ILD) were idiopathic pulmonary fibrosis (UIP) (30%), idiopathic NSIP (21%), connective tissue disease related ILD (15%), extrinsic allergic alveolitis (EAA) (9%), pulmonary lymphangitis carcinomatosis (PLC) (6%) and 4% for each respiratory bronchiolitis associated interstitial lung disease (RB-ILD), bronchiolitis obliterans organizing pneumonia (BOOP), and occupational lung disease. Breathlessness on exertion (93.3%) and dry cough (100%) were the most common presenting symptoms of UIP. The HRCT findings of UIP included reticular shadowing (100%), nodular shadowing (16%), associated ground-glass attenuation in 73.3% and peribronchovascular thickening in 53%. The signs of lung fibrosis were honeycombing in 83.3%, traction bronchiectasis (66%), septal thickening (66%), core pulmonale in 30% and associated lung cancer in 10%.

### CONCLUSIONS

UIP was the most common interstitial lung disease observed in our study. HRCT is the modality of choice in assessing diffuse parenchymal lung disease especially in the aspects of disease activity and earlier detection and characterization of disease.

### KEYWORDS

High Resolution Computed Tomography, Interstitial Lung Disease, Usual interstitial Pneumonia, NSIP, RBILD

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## BACKGROUND

Interstitial Lung Disease (ILD) is characterized by pathology in the pulmonary interstitium which comprises of connective tissue space between the alveolar epithelial cells and the adjacent capillary endothelial cells resulting in restrictive lung physiology, impaired gas exchange, pulmonary inflammation and fibrosis. In one third cases of ILD, various factors like cigarette smoking, aspiration, certain drugs, radiation therapy, cancer, systemic diseases, environmental and occupational factors had been reported to be associated with the ILD. However, in two-thirds cases of ILD no reportable association have been found.

Chest radiograph (CXR) may be normal during early in the course of ILD disease. Pulmonary function testing (PFT) too has little role in diagnosis of ILD and cannot diagnose a specific ILD or distinguish between restrictive physiology due to active lung inflammations versus lung fibrosis. High resolution computed tomography (HRCT) is the most accurate noninvasive, high spatial resolution cross sectional imaging modality available for evaluation of lung parenchyma. Compared to X-Ray, HRCT is far superior for detection, characterization and demonstration of the lung interstitium, air spaces and airways.<sup>1</sup>

It assesses the presence, type and extent of pulmonary disease in, the changes of active lung disease, changes in disease activity following treatment and characterization of interstitial lung disease (ILD) in appropriate clinical setting. HRCT also helps in localizing the appropriate site for lung biopsy.

HRCT is more sensitive than the plain radiograph in identifying ILD (sensitivity greater than 90%) and the image pattern of lung parenchymal abnormalities on HRCT is often suggestive of a particular set of diagnostic possibilities. Our present study aimed to study the basic HRCT patterns associated with Interstitial Lung Disease and correlation of HRCT patterns with clinical data to obtain a set of differential diagnosis of Interstitial Lung Disease. Also, as the facilities for open lung biopsies are not readily available in our setup, hence HRCT has special significance in this respect too.

Mathieson and his colleagues first highlighted the potential clinical impact of HRCT in ILD by comparing chest radiograph with HRCT. This nearly doubled the confidence of radiologist in diagnosing ILDs such as idiopathic pulmonary fibrosis (UIP), sarcoidosis, lymphangitis carcinomatosa and when the experienced radiologist was confident about the diagnosis, they were almost always correct.<sup>2</sup>

Comparative studies in patients with disease proved by biopsy have shown that HRCT has sensitivity of about 94% for the detection of chronic infiltrative lung disease, compared with 80% for chest radiography.

## Objectives

1. To describe the HRCT findings in different diffuse ILD.
2. To define local distribution of different diffuse interstitial lung disease among patients attending outdoor and

indoor at Chest Medicine Department of Burdwan Medical College & Hospital.

## METHODS

A retrospective and prospective study was done in patients who had provisional diagnosis of diffuse lung disease and referred to Radiology Department of Burdwan Medical College and Hospital, Burdwan for High Resolution CT chest evaluation from the Chest Medicine Department were included in this study in the period from June 2017 to July 2018.

## Study Population

The study population consisted of 100 patients, aged between 20 and 80 years old (59 females and 41 males), primarily diagnosed with interstitial lung diseases at Chest Medicine Out and Inpatient Department, BMCH.

## Study Tools

- 1) Semi structured socio-demographic proforma.
- 2) Hitachi Model Scenaria 128 Slice CT Scanner.

## Inclusion Criteria

- a) Patients presenting with collagen vascular diseases like SLE, rheumatoid disease, systemic sclerosis.
- b) Patients of systemic vasculitis like Wegener's granulomatosis.
- c) Industrial exposure related diseases like asbestosis, silicosis, coal worker's pneumoconiosis, etc.
- d) Medication, drugs and radiation exposure related cases
- e) Cases of idiopathic interstitial pneumonias and hypersensitivity pneumonias
- f) Cases of allergic bronchopulmonary aspergillosis, invasive aspergillosis and lymphangitic spread of tumours.

## Exclusion Criteria

- a) Patients presenting with like asthma, COPD etc.
- b) Patients presenting with infectious lung parenchymal disease like pneumonia, Tuberculosis and HIV.
- c) Patients age less than 20 years.
- d) Patients of CCF, lung malignancy or haemodynamically unstable patients.

## Methodology

After inclusion of the patient in the study, detailed proforma was filled. The proforma included the patient's name, age, address, medical record number, complaints, risk factors, past history, laboratory investigation, and chest radiograph findings. Thereafter HRCT chest was done on 128 slice CT scanner in supine position using standard HRCT protocol.

Prone and expiratory scanning was done wherever needed. Parenchymal abnormalities were categorized into different basic patterns of HRCT with their distribution and predominant involvement. Final possible diagnosis was made as per HRCT findings and clinical information. All patients had chest X-ray and HRCT chest done.

Every patient underwent CT scanning with spiral CT (Hitachi scenario 128 slice CT scanner) 1.5 mm as thin section at 1 cm interval were obtained from the lung apex to base. The images were visualized in both lung window (at - 800 HU window level and width of 1500 HU), and mediastinal window (at window level of 0 - 40 HU and window width 250 HU)

The clinical information and CT findings were introduced into a questionnaire. The data gathered was analysed by computer using SPSS and the results were put in tables and figures.

RESULTS

One hundred patients participated in the study, aged 20 years to 80 years with female predominance (male 41%, female 59%). The predominant age group that was found to be associated with ILD were 41-55 years (45%) and 56-70 years (31%).The least common age group were 15-25 years (3%) and 71+ years (3%). The youngest age group was associated with PLCH, Alveolar Microlithiasis and oldest age group was associated with UIP (Table 1, Figure 1).

Most of the patient (75%) presented with long duration of symptoms, more than 6 months. The common presenting symptoms include cough (99%), shortness of breath (86%), chest pain (24%), fever (38%), haemoptysis (8%) and loss of weight (27%). Clubbing (30%) and cyanosis (5%) were two important signs of ILD. Clubbing was predominantly associated with UIP (46%), CTD-ILD (40), HP (33%). Cyanosis was mainly associated with UIP, CTD-ILD and HP. In CTD-ILD clubbing was found mainly due to association with Systemic Sclerosis. Cough and dyspnea was found in almost all the patients of our study. Fever was predominantly associated with CTD-ILD (67%) and COP (100%). Incidence of fever in CTD-ILD was high due to association with rheumatoid arthritis and systemic sclerosis. Weight loss was significantly associated with PLC (100%), UIP (33%), and CTD-ILD (33%).

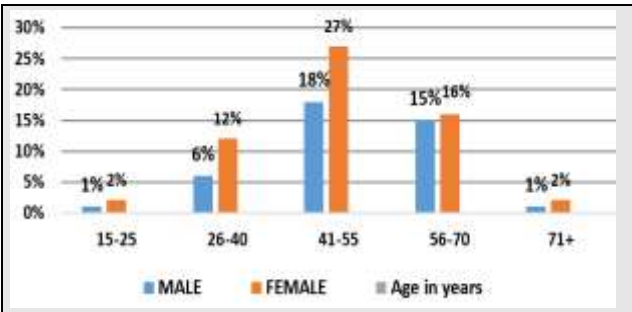


Figure 1. Age and Sex Distribution among 100 Patients Referred to BMCH for HRCT Chest with the Provisional Diagnosis of ILD

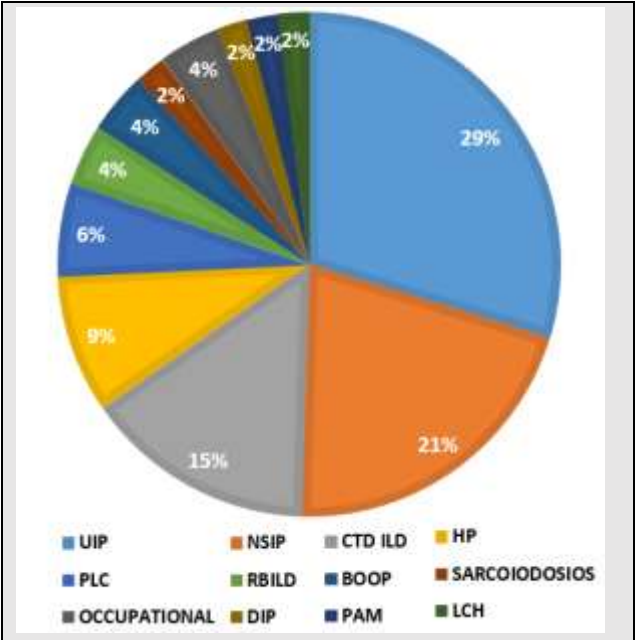


Figure 2. HRCT Diagnoses among 100 Patients Referred to BMCH for HRCT Chest with the Provisional Diagnosis of ILD

Disease	Age Group					Total
	15 -25	26 - 40	41-55	56- 70	71+	
UIP	0	0	9	18	3	30
Idiopathic NSIP	0	4	12	5	0	21
CTD-ILD	0	5	8	2	0	15
EAA(HP)	0	1	6	2	0	9
RB-ILD	0	1	2	1	0	4
COP	0	2	0	2	0	4
Occupational ILD	0	1	2	1	0	4
Sarcoid	0	0	2	0	0	2
Micro alveolar	1	0	0	0	0	1
Lithiasis						
DIP	0	1	1	0	0	2
PLCH	2	0	0	0	0	2
Total	3	18	45	31	3	100

Table 1. Age Distribution According to ILD (N=100)

Disease	Male	Female	Total
UIP	13 (43.3%)	17 (56.7%)	30
Idiopathic NSIP	5 (16.6%)	16 (83.3%)	21
CTD RELATED ILD	6 (40%)	9 (60%)	15
Extrinsic Allergic Alveolitis (HSP)	3 (33.3%)	6 (66.7%)	9
Lymphangitis Carcinomatosis	2 (33.3%)	4 (66.7%)	6
Respiratory Bronchiolitis ILD	4 (100%)	0 (0%)	4
BOOP	1 (25%)	3 (75%)	4
Occupational ILD	3 (75%)	1 (25%)	4
Sarcoidosis	0	2 (100%)	2
Microalveolar lithiasis	0 (0%)	1 (100%)	1
DIP	2 (100%)	0	2
PLCH	2 (100%)	0 (0%)	2
Total	41	59	100

Table 2. Sex Distribution According to the Type of Disease Among the Study Group (n= 100)

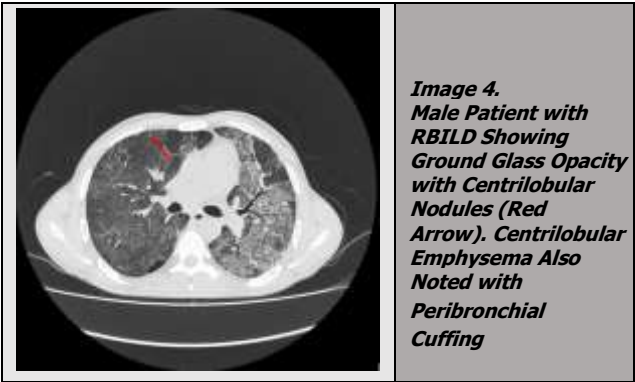
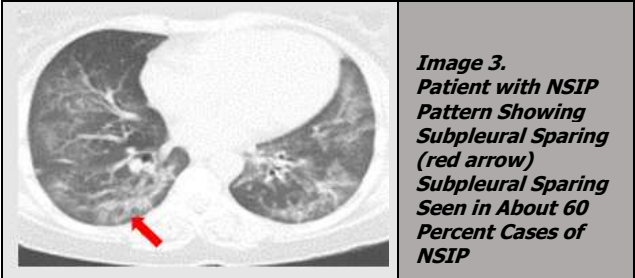
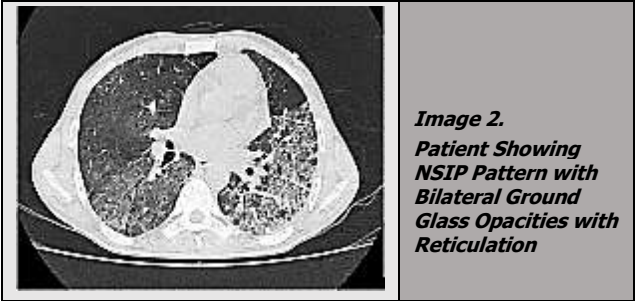
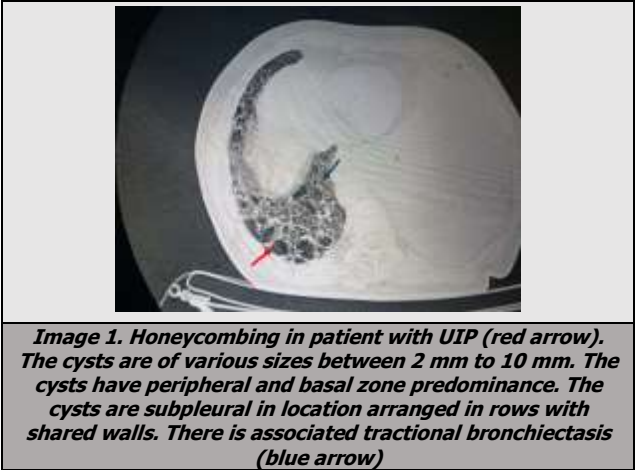
CT Appearance	Male	Female	Total
UIP	13(43.3%)	17(56.7%)	30 (56.6%)
NSIP	5(16%)	16(84%)	21(39.6%)
DIP	2(100%)	0	2 (3.7%)

Table 3. The HRCT Radiopathological Distribution in Idiopathic Interstitial Pneumonias (n = 53)

Male predominant diseases were RBILD, DIP, LCH AND occupational lung disease. Female dominant diseases were UIP, NSIP, CTD RELATED ILD and HP (Table 2). The most common HRCT patterns were reticular opacity (75%), ground glass opacity and consolidation (70%), nodular opacity (29%) and honeycombing (34%).

HRCT Findings	UIP	HP	PLC	RBILD	Sarcoidosis	Idiopathic NSIP	CTD ILD	BOOP	Occupational ILD	DIP	PLCH	Alveolar Microlithiasis
	30	9	6	4	2	21	15	4	4	2	2	1
Nodular Opacity	5 (16%)	6	2	2	2	3 (14%)	3 (20%)	1	2	1	1	1
Reticular opacity	30 (100%)	2	5	1	1	18 (85%)	11 (73%)	1	3	1	1	1
Ggo/consolidation	22 (73%)	7	0	2	1	17 (80%)	14 (93%)	4	1	2	0	0
Honey combing	25 (83%)	1	0	0	1	1 (4%)	5 (33%)	0	1	0	0	0
Peribronchovascular Thickening	16 (53%)	1	5	1	2	11 (52%)	7 (46%)	1	2	1	0	1
Traction Bronchiectasis	20 (66%)	1	0	0	1	11 (52%)	5 (33%)	1	2	0	0	0
Septal thickening	20 (66%)	2	5	0	2	12 (57%)	9 (60%)	1	2	1	0	1
Pleural thickening	2(7%)	0	2	0	1	7 (33%)	6 (40%)	0	2	0	0	0
Cor pulmonale	9 (30%)	3	0	0	1	2 (9.5%)	5 (33%)	0	1	0	0	0
Air trapping/cysts	6 (20%)	5	0	2	1	4 (19%)	5 (33%)	1	2	1	2	0
Lymphadenopathy	20 (67%)	0	4	0	2	16 (76%)	9 (60%)	1	2	0	0	0
Pleural effusion	0	0	4	0	1	2 (9.5%)	6 (40)	1	3	0	0	0
Subpleural sparing	0	0	0	0	0	11 (52%)	5 (33%)					
Oesophageal dilatation							5 (33%)					

**Table 4. HRCT Findings in the Common ILDs in the Study Group**



The most prevalent interstitial lung disease was UIP (30%) followed by idiopathic NSIP (21%), CTD related ILD (15%), HP (9%), PLC (6%), RBILD (4%), COP/BOOP (4%), occupational ILD (4%), DIP (2%), LCH (2%), sarcoidosis (2%), alveolar microlithiasis (1%) (Figure 3). Half of the patients (50%) were housewives followed by employee (17%), farmers (11%), factory workers (9%). HP was most commonly found in farmers and smokers and occupational lung diseases were most commonly found in factory workers.

**DISCUSSION**

UIP is commonly seen in the middle-aged patients usually between 40 to 70 years of age and the incidence advances with increasing age. Approximately two third of patients are over 60 years of age at the time diagnosis. In present study more than 64% of patients with UIP were above 60 years old (19 patients) with average 60 years, and with slight female predominance was 17 (57%). In similar study conducted by Maheshwari, et al<sup>3</sup> in India, reported more female predominance 54% (41 female, 35 male). Primack et al. reviewed the HRCT scans of 61 consecutive patients who had end-stage lung disease (defined by the presence of honeycombing, extensive cystic changes, or conglomerate fibrosis). A correct first-choice diagnosis of UIP was made in 23 of the 26 cases (88%); when the observers were confident in their first-choice diagnosis of UIP (based on the presence of predominantly subpleural and lower lung zone honeycombing), they were correct in 100% of cases.<sup>4</sup>

Almost all the patients presented with UIP had dry cough and shortness of breath on exertion, 46% of patients presented with clubbing of fingers and cyanosis in 6.6%, weight loss in 33.3% On HRCT, 100% of patients with UIP showed reticular shadowing, 16% with nodular shadowing, associated with ground glass opacification in 73%, honeycombing was seen in 83%, 66% showed traction bronchiectasis and peribronchovascular thickening were seen in 53%. Only 2 cases showed pleural thickening and septal thickening in 30% of patients. Cor-pulmonale and pulmonary hypertension as a result of long-standing fibrotic process encountered in 9 cases (30%). Air trapping and mediastinal lymphadenopathy was found on 20% and 67%

patients (table 4). Three patients (10%) of UIP presented with associated bronchial carcinoma as a complication, all were males. Wells, et al found that the presence of ground-glass opacity and its extent, relative to the findings of fibrosis (honeycomb, traction bronchiectasis) was related to prognosis and likelihood of response to treatment.<sup>5</sup> Staples et al. compared CT with clinical, functional, and radiologic findings in 23 patients who had UIP. The CT scans provided a better estimate of the pattern, distribution, and extent of pulmonary fibrosis and showed more extensive honeycombing than did radiographs. In this study, there was also good correlation between the extent of fibrosis on CT, and the severity of dyspnoea ( $r = 0.64$ ,  $p < 0.001$ ). In our study nearly 100% patients presented with dyspnoea and this is due to evidence established fibrosis in all the 30 patients almost.<sup>6</sup>

So, HRCT play a decisive role in the early diagnosis and assessment of disease activity in patients with UIP prior to biopsy and treatment as biopsy is the gold standard for diagnosis and not readily amenable at least now in our country so HRCT play an important role in this respect.

Regarding Idiopathic NSIP, 21 patients had classical HRCT findings of NSIP with the female preponderance (83.3%) (Table 3) and the most predominant age group involved was 41-55 years (57%) (Table 1). 17 (80%) patients out of 21 were diagnosed as fibrotic NSIP, only 4 were diagnosed as cellular NSIP. Dry cough and dyspnoea were the most common symptoms. (Table 2) The common HRCT patterns were reticular opacity 85%, ground glass opacity 80%, nodular opacity 14%, honeycombing 4%, peribronchovascular thickening 52%, traction bronchiectasis 52%, septal thickening 57%, pleural thickening 33%, air trapping 19%, lymphadenopathy 76%. Silva et al. demonstrated that a characteristic feature of NSIP is relative sparing of the immediate subpleural lung in the dorsal regions of the lower lobes. This relative subpleural sparing can be helpful in distinguishing fibrotic NSIP from UIP because UIP is typically most severe in the subpleural regions. The prevalence of relative subpleural sparing in NSIP in various studies has ranged from 20% to 64% of patients. In our study, we found that immediate subpleural sparing was noted in 52% patients which was significant in differentiating NSIP from UIP.<sup>7</sup> In one study of 206 patients, mediastinal lymphadenopathy was seen in 90 of 136 (66%) patients with IPF, 38 of 47 (81%) with NSIP, in our study we found mediastinal lymphadenopathy in 76% patients of NSIP.

Tanaka et al reviewed the HRCT findings in 63 patients with RA seen at an ILD clinic. The most common abnormalities evident on HRCT were reticulation (98% patients) and ground-glass opacities (90% patients). The authors identified four major CT patterns: UIP (41%), NSIP (30%), bronchiolitis (17%), and OP (8%).<sup>8</sup> In our study, we found that out of 5 RA related ILD 60% had UIP and 40% had NSIP. 40% had follicular bronchiolitis resulting in air trapping. In our study, 5 (100%) patients had reticular opacity and 4 (80%) patients had Ground glass opacities

among total 5 patients of RA related ILD. These findings are very similar to Tanaka et al study.

Goldin et al reviewed the HRCT scans in 162 patients with symptomatic PSS-related ILD. The main findings consisted of ground-glass opacities (90%) including areas of ground-glass attenuation without evidence of fibrosis (49%), evidence of fibrosis (93%), and honeycombing (37%). All findings involved mainly the lower lung zones. The authors concluded that in the majority of cases the findings were consistent with NSIP but that the presence of honeycombing in 37% of HRCT scans suggests that some patients may have a mixture or overlap of NSIP and UIP patterns.<sup>9</sup> In our study, 100% patients had ground glass opacities, 80% had associated with NSIP out of total 10 PSS related ILD. Honeycombing was seen in 30% patients of PSS related ILD. These findings were very similar to Goldin et al.

Hypersensitivity pneumonitis is one of the few potentially curable forms of ILD by keeping this diagnosis in mind when confronted with unexplained ILD. Nine patients presented with HRCT signs of hypersensitivity pneumonitis; it was common in farmers. Clubbing was seen in 33% patients. There was nodular shadowing in 67% of patients mainly involving the centrilobular regions, ground glass opacity was seen in 77% patients. 11% of patients showed honeycombing and traction bronchiectasis in 11% of patients, in 55% there was associated with lobular air trapping. All these findings were due to predominance of acute and subacute stage of HP (Table 4).

Hansell and Moskovic reviewed the HRCT findings in 15 patients with subacute HP, the common abnormality was the presence of diffuse bilateral ground-glass attenuation in 73% of the patients, which was mostly marked at middle and lower zone. The most 2nd findings in 40% was the presence of poorly defined nodules measuring approximately 4 mm. the findings were similar to our study.<sup>10</sup>

Regarding RBILD, 4 patients had classical CT features of RBILD with male predominant (100%). Predominant age group was 41-55 years (50%). Predominant HRCT features were nodular opacity (50%), ground glass opacities (50%) upper lobe emphysema (50%). Heyneman et al. reviewed the HRCT findings in eight patients who had RB-ILD. Of the eight patients, four (50%) had ground-glass opacities and three (38%) had centrilobular nodules. Only two (25%) showed evidence of fibrosis, as determined by the presence of intralobular linear opacities and honeycombing in the lower lobes. Emphysema was evident on HRCT in 50% of cases similar to our study.<sup>11</sup>

2 patients in our study had classical HRCT features of DIP, with male preponderance. Common HRCT findings were patchy ground glass opacities (100%), nodular opacity (50%). Sumikawa et al reviewed the HRCT scans of 92 patients with various IIPs, including 26 with DIP or RBILD. The main findings in patients with DIP and RB-ILD were bilateral ground-glass opacities (average extent 27% of the lung parenchyma), poorly defined centrilobular nodules (average extent 9%), and mild reticulation (average extent 7%).<sup>12</sup>

4 patients had the classical features of BOOP with female predominance (75%). Most common age group involved were 26-40 years (50%) and 41-55 years (50%). The common HRCT patterns were peripheral and peribronchial consolidation (100%), ground glass opacity (75%).

Regarding Occupation lung diseases, 4 patients had classical features of ild with history of factory work. 2 patients had findings of asbestosis and 2 patients had findings of silicosis & Cwp. Males (75%) were mainly involved. Common HRCT findings were reticular opacity (75%), nodular opacity (50%), honeycombing (25%), peribronchovascular thickening (50%), traction bronchiectasis (50%), septal thickening (50%) lymphadenopathy (50%), pleural thickening (50%) and effusion (75%).

Regarding Pulmonary Langerhans cell histiocytosis (PLCH), 2 patients had classical HRCT features of PLCH with male preponderance (100%) The predominant age group involved was younger 15-25 years (100%). Common HRCT patterns were lung cysts (100%), nodular opacity (50%).

### CONCLUSIONS

HRCT accurately demonstrates the pattern, distribution and extent of diffuse infiltrative lung disease. The nature of pulmonary fibrosis including reticulation, ground-glass attenuation and honeycombing can all be characterized. As open lung biopsy and pulmonary histopathology are not at least now amenable, so spiral CT with HRCT technique is reliable and effective method in diagnosing and characterizing interstitial lung disease. HRCT is of great value in patients with normal or questionable chest radiograph and with symptoms in detecting subtle alveolitis.

The most frequent diffuse parenchymal lung diseases were UIP, bronchiectasis, hypersensitivity pneumonitis and lymphangitis carcinomatosa.

All radiological departments in the major teaching hospitals and states hospitals should be equipped with faster scanner (spiral or multi-slice), CT for prompt, quick examination and early detection of diffuse parenchymal lung disease. Finally, effective collaboration between expert radiologist, pulmonologist and technician well-trained in HRCT helps in an early detection of interstitial lung disease.

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