

## Original Research Article

# Spectrum of high-resolution computed tomography findings in interstitial lung diseases and their correlation with mediastinal lymphadenopathy

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## ABSTRACT

**Background:** Interstitial lung disease (ILD) represents a heterogeneous non-infectious group of acute and chronic diseases affecting the lung parenchyma. ILDs are usually associated with significant morbidity and mortality, particularly when fibrosis occurs. ILD is usually associated with mediastinal lymph node enlargement, the extent of lymph node enlargement may correlate to disease activity or progression of fibrosis. In the present study, authors have correlated the spectrum of high-resolution CT findings in ILDs with mediastinal lymph node enlargements.

**Methods:** One hundred and four cases of ILDs confirmed by HRCT findings and pulmonary function tests were included in this study. HRCT was performed using a GE 128 SLICE CT OPTIMA 660 scanner, USA with 1.5 mm collimation at full inspiration. The findings were classified into three groups-fibrotic, ground glassing and nodular pattern. Authors assessed the presence, number and sites of enlarged lymph nodes (short axis  $\geq 10$  mm in diameter).

**Results:** The largest subsets of patients were found in the 51-60 age groups. Fibrotic pattern was the most common pattern in this study (50%) followed by ground glassing (44%). Nodular pattern was the least predominant pattern (6%). Lymphadenopathy was seen in 84% of UIP and 63% cases of NSIP. P value was 0.049 which indicates a significant relation between lymphadenopathy and various ILDs. A strong relationship between lymphadenopathy and the predominant fibrotic pattern followed by ground glassing was observed.

**Conclusions:** A significant association was established between lymphadenopathy and the type of ILD where fibrotic pattern had the maximum association.

**Keywords:** Ground glass opacity, High resolution computed tomography, Honey combing, Interstitial lung diseases, Mediastinal lymphadenopathy

## INTRODUCTION

Interstitial lung disease (ILD) or diffuse parenchymal lung disease (DPLD) represents a heterogeneous non-infectious group of acute and chronic diseases affecting the lung parenchyma.<sup>1</sup> It uniformly affects the alveolar epithelium, pulmonary capillary endothelium, basement

membrane, perivascular and peri-lymphatic tissues. As a result, the tissues around the air sacs become scarred and thickened and makes it more difficult for oxygen to pass into the blood stream. ILDs are usually associated with significant morbidity and mortality, particularly when fibrosis occurs.<sup>2</sup> The ILDs consist of disorders of known causes viz., collagen vascular diseases, environmental or

drug related and of unknown causes. The latter include idiopathic interstitial pneumonias (IIPs), granulomatous lung disorders viz., sarcoidosis and other forms of interstitial lung disease (ILD) including lymph-angioleiomyomatosis (LAM), pulmonary Langerhan's cell histiocytosis (LCH), and eosinophilic pneumonia. occasionally, interstitial disease is associated with a familial cause or specific genetic disease.<sup>3</sup>

Mediastinal lymph node enlargement may be usually associated with interstitial lung disease and it is a frequent feature in certain forms of interstitial lung disease, the extent of lymph node enlargement may correlate to disease activity or progression of fibrosis. While many nodes may be larger than 10 mm it is uncommon to have nodes greater than 15 mm.<sup>4</sup> The high-resolution computed tomography (HRCT) is a well-established imaging technique for evaluation of interstitial lung disease, including idiopathic pulmonary fibrosis (IPF).<sup>5</sup>

The natural history of progression of IPF begins from isolated areas of ground glass opacity (GGO), which later advances to form honeycombing (HC). The ground glass attenuation is the result of interstitial thickening as well as airspace filling and is a non-specific finding and considered to be an important sign, which indicates the presence of active and potentially treatable disease.<sup>6</sup> In the present study, authors have evaluated the spectrum of HRCT findings in ILDs and try to correlate with mediastinal lymph node enlargements.

## METHODS

The present study was carried out in the Department of Radio-diagnosis, Amala Institute of Medical Sciences, Thrissur, Kerala in South India from December 2017 to October 2018. One hundred and four diagnosed cases of ILDs confirmed by HRCT findings and pulmonary function tests were included in this study. Known cases of infective etiology, chronic obstructive pulmonary disease, congestive cardiac failure, lung malignancy, hemodynamically unstable patients and polycythemia were excluded from this study.

The study was approved by ethical committee of the institution. After obtaining informed consent from patients, demographic data was collected, and findings of HRCT were recorded on a structured format.

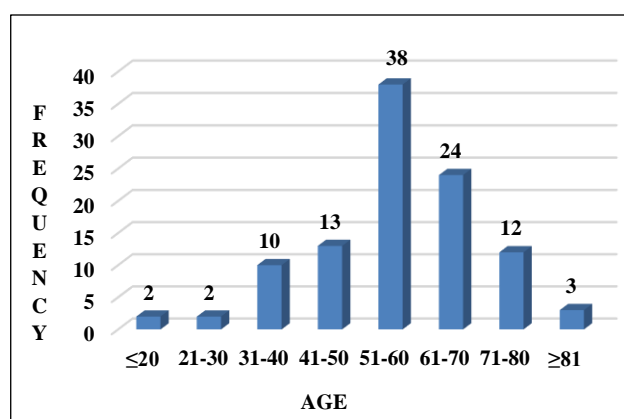
HRCT was performed using a GE 128 SLICE CT OPTIMA 660 scanner, USA with 1.5 mm collimation at full inspiration. Scans were obtained at 5 mm slice thickness in the supine position. The images were reconstructed using a high spatial frequency algorithm to 0.6 mm with appropriate window settings for viewing the lung parenchyma (window width 1500 HU and window level-600 HU). From the raw data, images were reconstructed in axial, coronal and sagittal planes for multiplanar image viewing on a work station (AW

Volume Share 5, GE). The patient's HRCT findings were analyzed and reported by two different radiologists to eliminate intra observer variability. The HRCT findings were classified into three groups viz., group I-fibrotic pattern including reticular pattern/honeycombing/tractional bronchiectasis or bronchiolectasis, group II-ground glass pattern and group III- nodular pattern.<sup>7</sup>

The lymph nodes were assessed using only the mediastinal windows (level 35 HU, width 450 HU). Author assessed the presence, number and sites of enlarged lymph nodes (short axis  $\geq 10$  mm in diameter). The sites of enlarged lymph nodes were assessed in reference to American Thoracic society mediastinal map.<sup>8</sup> Mediastinal lymph node enlargement was considered significant if the short axis diameter was more than 10 mm. The results obtained were analyzed using SPSS 23 software.

## RESULTS

Present study population included subjects whose age ranged from 19 years to 87 years with mean age being  $56.2 \pm 13.33$ . Largest subsets of patients were found in the 51-60 age groups (Figure 1).



**Figure 1: Age distribution in ILD shows the patients with age ranged from 19 years to 87 years and the largest subsets of patients in the 51-60 age groups.**

**Table 1: Statistical significance of age in various ILDs and the mean age of different ILDs.**

HRCT diagnosis	Age		P value (Anova)
	Mean	SD	
UIP	62.227	11.2040	0.002
COP	55.750	16.2147	
HSP	48.250	22.9837	
NSIP	51.878	12.2927	
Sarcoidosis	51.500	19.0919	

Age of silicosis case-46.0.

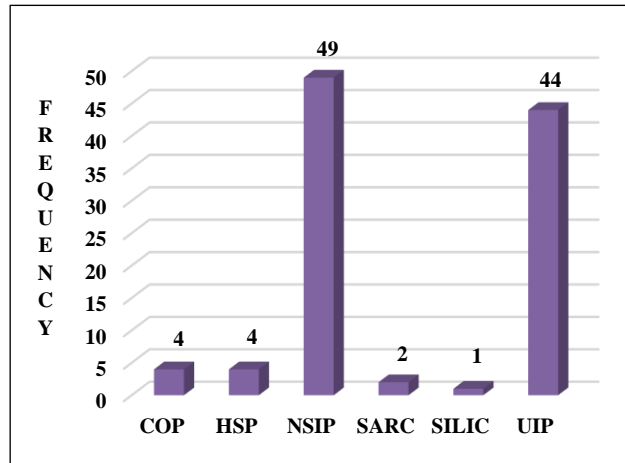
The following table shows the mean age for various ILDs. The mean age for UIP patients were  $62.23 \pm 11.20$  which was definitely higher compared to the mean age

for NSIP patients being  $51.88 \pm 12.29$ . The mean age for COP (cryptogenic organizing pneumonia) patients and HSP (hypersensitivity pneumonitis) patients was  $55.75 \pm 16.21$  and  $48.25 \pm 22.98$  respectively. The mean age for sarcoidosis was  $51.50 \pm 19.09$  and for the single case of silicosis the age was 46 years (Table 1).

**Table 2: Statistical significance of age in predominant HRCT patterns with the highest age group in the fibrotic pattern followed by ground glassing and nodular patterns.**

Predominant pattern	Age		P value (Anova)
	Mean	SD	
Fibrotic	61.135	11.5691	0.001
Ground glassing	51.522	12.4360	
Nodular	49.333	19.8158	

The mean age for fibrotic pattern was  $61.13 \pm 11.57$  which was again higher than mean age for ground glassing being  $51.52 \pm 12.44$ . The mean age for nodular pattern was  $49.33 \pm 19.82$  (Table 2). There was a statistically significant relation between the age of patients with different ILDs and the 3 patterns of ILDs. Out of the total 104 cases, NSIP with 49 cases (47.1%) constituted the most common ILD followed by UIP with 44 cases (42.3%). 3.8% of the cases were constituted by COP and HSP each in this study followed by 2 cases (2.0%) of sarcoidosis and 1 case (1%) of silicosis (Figure 2).



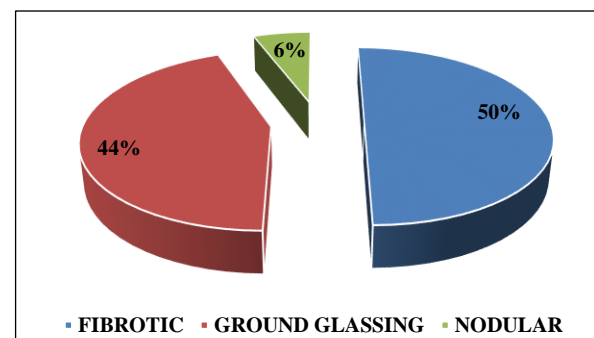
**Figure 2: HRCT type and distribution with NSIP in 47.1% cases followed by UIP in 42.3% cases among the common ILDs.**

Fibrotic pattern was the most common pattern in this study with 52 cases (50%) followed by ground glassing with 46 cases (44%). Nodular pattern was the least predominant pattern with 6 cases (6%) (Figure 3 and 4). Lymphadenopathy was seen in 37 cases (84%) of UIP and 31 (63%) cases of NSIP. Three out of four cases of COP and 1 out of 4 cases of HSP had lymphadenopathy. Remaining 2 cases of sarcoidosis and 1 case of silicosis had lymphadenopathy (Figure 5, 6, 7, 8, 9, 10, 11, 12 and

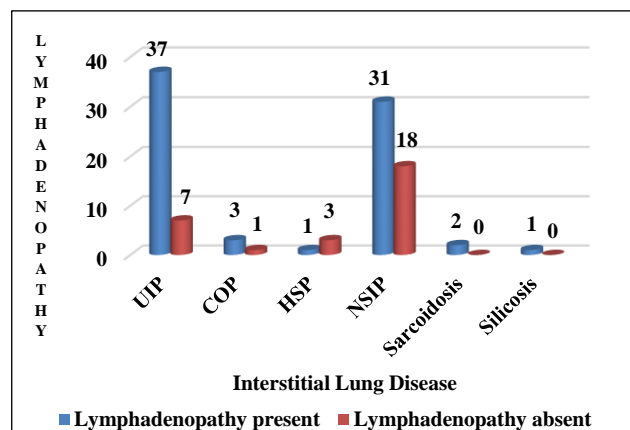
13). Fisher's exact test p value=0.049. P value indicates a significant relation between lymphadenopathy and various ILDs.



**Figure 3: Axial HRCT section of a 60-year-old male patient with UIP showing extensive honeycombing with macrocysts, tractional bronchiectasis and reticulation in bilateral lung parenchyma.**

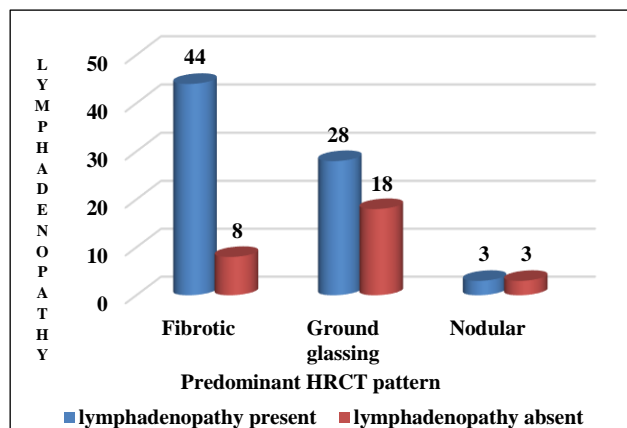


**Figure 4: Predominant HRCT pattern and distribution with the fibrotic pattern being the most common followed by ground glassing and nodular patterns.**



**Figure 5: Frequency of lymphadenopathy in various ILDs with the highest frequency of lymphadenopathy in UIP followed by NSIP and rest by others.**

The following chart shows the frequency of lymphadenopathy in the predominant HRCT pattern (Figure 6).



**Figure 6: Frequency of lymphadenopathy in the predominant morphological HRCT pattern with fibrotic being the commonest followed by ground glassing and nodular patterns.**



**Figure 7: Axial HRCT section of a 50 year old female patient with fibrotic NSIP (lung window) shows) diffuse areas of ground glassing, tractional bronchiectasis and peripheral reticulation with subpleural sparing.**



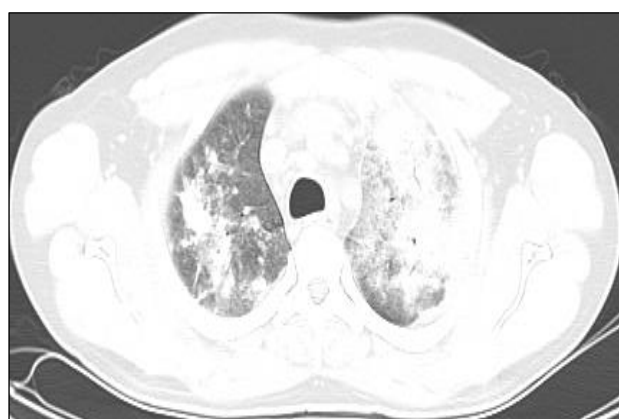
**Figure 8: Axial HRCT section of the same patient in the mediastinal window enlarged mediastinal lymph nodes, largest in the right paratracheal region (black arrow).**



**Figure 9: Axial HRCT section of a 58-year-old female patient with UIP in the lung window shows extensive honeycombing with tractional bronchiectasis involving the basal sections of the bilateral lung parenchyma.**



**Figure 10: Axial HRCT section of the same patient in the mediastinal window shows enlarged mediastinal lymph nodes largest in the precarinal location (arrow).**

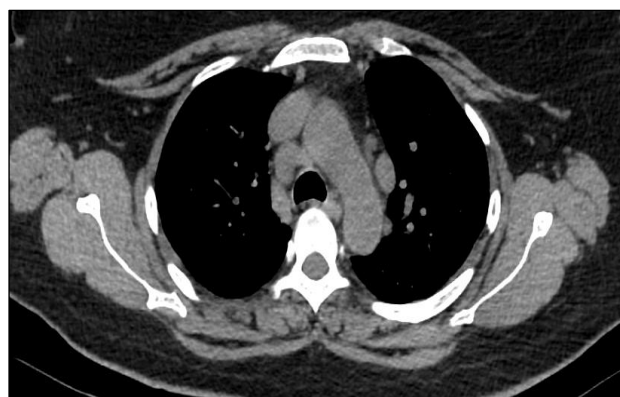


**Figure 11: Axial HRCT section of a 46 year old male patient with silicosis in the lung window shows conglomerate fibrotic masses in the bilateral upper lobes.**





**Figure 12: Axial HRCT of the same patient in the mediastinal window shows consolidation with calcific areas in the left lung parenchyma. Mediastinal lymphadenopathy with calcification is noted with the image showing calcified nodes in the right hilar and subcarinal region (black arrows).**



**Figure 13: Axial HRCT section of a 50 year old female patient with sarcoidosis shows mediastinal lymphadenopathy with enlarged lymph nodes in the para-aortic and pretracheal region (black arrows).**

**Table 3: Various percentage distribution of lymphadenopathy in various predominant morphologic patterns with fibrotic accounting for 84% cases followed by ground glassing in 61% cases and nodular in 50% cases.**

Predominant pattern	Lymphadenopathy present (%)	Lymphadenopathy absent (%)	Total
Fibrotic	44 (84)	8 (16)	52
Ground glassing	28 (61)	18 (39)	46
Nodular	3 (50)	3 (50)	6
Total	75	29	104

The following table shows the frequency and percentage of lymphadenopathy in the final ILD pattern (Table 3).

Fisher's exact test p value=0.014. P value indicates a strong relation between lymphadenopathy and the predominant pattern. Fibrotic pattern is the most frequent pattern associated with lymphadenopathy with 84% cases followed by ground glassing in 61% cases.

## DISCUSSION

In this study, NSIP (47.1%) was the most common ILD followed by UIP (42.3%). A total of 3.8% of the cases were constituted by COP and HSP, followed by sarcoidosis (2%) and 1 case (1%) of silicosis. Recent study conducted by Dhooria S et al, showed that sarcoidosis, IPF and connective tissue disease-ILDs were the most common ILDs at a tertiary care centre in North India, which is more or less similar to these findings.<sup>9</sup>

The fibrotic pattern (50%) was the most common morphologic pattern in this study followed by ground glassing (44%). The nodular pattern (6%) was the least predominant. The results are similar to the study conducted by Hussain K et al.<sup>10</sup>

In this study, the mediastinal lymphadenopathy was seen in 84% cases of UIP, 75% cases of COP, 63% cases of NSIP and 25% cases of HSP. It was also seen in all cases of sarcoidosis and silicosis. Calcifications of enlarged lymph nodes were also noted in silicosis.

Fibrotic pattern (84%) was the most frequent predominant morphologic pattern associated with lymphadenopathy followed by ground glassing (61%) and nodular pattern (50%). Present study showed a significant association between lymphadenopathy and the fibrotic pattern of ILD (p value <0.05).

The mediastinal lymph node enlargement on HRCT is common in patients with ILDs and it occurs without any significant superimposed infection or coexistent malignant condition. The hilar lymphadenopathy may occur as a part of chronic inflammatory process and the presence of lymph node enlargement in chronic ILDs does not always imply lung carcinoma.<sup>4</sup>

The lymph node enlargement in chronic ILDs may be due to an evoked inflammatory response. The cytokines, viz., interleukin-1 released by activated alveolar macrophages facilitate expansion of the lymphocyte population into

nearby lymphoid tissue, resulting in lymphoid hyperplasia.<sup>11</sup>

Sin S et al, hypothesized that lymphadenopathy in IPF could be related to disease severity and could be a predicting factor in disease prognosis.<sup>12</sup> Attili AK et al, concluded that intrathoracic lymphadenopathy is common in UIP and NSIP with an increase in lymphadenopathy over time which is associated with the progression of fibrosis.<sup>13</sup>

Recent studies have attempted to establish a correlation between disease severity and the enlarged lymph node diameter. They concluded that the total score as well as ground glass score were found to correlate well with the increased short axis diameter of the enlarged lymph node.

However, fibrosis scores did not correlate with short axis diameter of lymph node. The ground glass opacity, the predominant group had larger short axis diameter of enlarged node than the fibrosis-predominant group.<sup>14,15</sup> In the present study, authors have found that enlarged mediastinal lymph nodes were more commonly seen in fibrotic than ground glassing pattern.

## CONCLUSION

The study found that the mean age of ILD was  $56.2 \pm 13.33$  where UIP cases and fibrotic cases had a higher age group compared to NSIP cases and ground glassing pattern. A statistical association between age and type of ILD was noted. A significant association was also established between lymphadenopathy and the type of ILD where fibrotic pattern had the maximum association. This was also proved statistically.

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