European Journal of Molecular & Clinical Medicine

ISSN 2515-8260 Volume 09, Issue 04, 2022

Original Research Article

To study the role of HRCT & flexible fiberoptic bronchoscopy in diagnosis of interstitial lung disease

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Abstract

Background: High-resolution computed tomography (HRCT) is more sensitive than plain chest radiograph in distinction of ILD (affectability more conspicuous than 90%) and the image illustration of parenchymal peculiarities on HRCT consistently propose a particular course of action of scientific abnormalities.
Aim: To assess the usefulness of HRCT chest and flexible optic bronchoscopy concerning Bronchoalveolar lavage cellular analysis in the diagnosis of interstitial lung disease.
Materials and Methods: A prospective observational study was conducted at tertiary hospital in south India. 50 patients who are suspected to have interstitial lung infection by clinical assessment and history with manifestations and signs are assessed with HRCT chest and HRCT affirmed patients are exposed to fiber optic bronchoscopy and bronchoalveolar lavage is performed and their cytological profiles are investigated.
Results: The mean age of the patients was 50.18 years (SD ±14.3), with an age range from 18 to 70years and most of the study subjects were males. Dyspnoea was the most common presenting symptom (90% of patients), followed by cough (84%) and least is dysphagia (6%). In one young female, a cystic pattern was seen on HRCT with multiple diffuse thin-walled cysts which made us to make a diagnosis of LAM.
Conclusion: Thus, HRCT and BAL when combined, help us in making a confident diagnosis of ILD, obviating the need of a lung biopsy which is not feasible in routine practice due to lack of expertise, facilities and patient reluctance in undergoing a biopsy procedure.

Keywords: Bronchoalveolar lavage, bronchoscopy, interstitial lung diseases, hypersensitivity pneumonitis, idiopathic pulmonary fibrosis

Introduction

Diffuse parenchyma lung illness (DPLD) incorporates a heterogeneous group of disorders, described by a range of inflammatory and fibrotic changes influencing alveolar walls and air spaces [1]. They involve more than 200 elements which incorporate a wide range of infections, numerous extraordinary and large numbers of obscure etiology [2, 3]. High-resolution computed tomography (HRCT) is more touchy than plain chest radiograph in distinguishing

ISSN 2515-8260 Volume 09, Issue 04, 2022

ILD (affectability more prominent than 90%) and the picture example of parenchymal anomalies on HRCT regularly propose a specific arrangement of analytic irregularities. Fiber-optic bronchoscopy with bronchoalveolar lavage (BAL) may prove explicit determination in certain patients and BAL might be sufficient to analyze explicit infections [1]. The group of interstitial lung diseases (ILDs) comprises of an extraordinary assortment of elements, and multidisciplinary sheets are viewed as the most fitting way to deal with unhesitatingly accomplish a final diagnosis [4]. However IPF (Idiopathic Pulmonary Fibrosis) has been analyzed in people from young into their late eighties, it is normally seen between the ages of 40 and 70. In IPF, there is a gender inclination towards males. IPF is discovered similarly in rural and urban conditions. Interstitial lung disease is dominatingly a sickness of adults, in spite of the fact that it likewise happens in kids. Certain interstitial infections like sarcoidosis, pneumonic Langerhans cell histiocytosis, and immune system related lung sicknesses, will in general create in youthful grown-ups, though idiopathic aspiratory fibrosis frequently happens between the ages of 40 and 70. Both occurrence and mortality of interstitial illness increment with age [5]. Cigarette smoking is a perceived danger factor for the development of interstitial lung disease [6]. Four interstitial lung diseases (ILDs) have been identified with cigarette smoking: respiratory bronchiolitis (RB) - related ILD (RB-ILD), desquamative interstitial pneumonia (DIP), Idiopathic aspiratory fibrosis (IPF), and aspiratory Langerhans cell histiocytosis (PLCH) [7, 8]. Several types of drugs such as chemotherapeutic agents, antibiotics, antiarrhythmic drugs, and immunosuppressive agents can cause drug-induced interstitial lung disease (DILD) [9]. High-resolution computed tomography (HRCT) is the radiological imaging technique best suited to revealing changes in lung structure. Various HRCT findings, taken together, can represent typical patterns. These patterns, in conjunction with the anatomical distribution of findings and with clinical data, can narrow the differential diagnosis of diffuse interstitial lung disease and, in many cases, indicate the correct diagnosis with a high degree of accuracy [10]. The present study was to assess the usefulness of HRCT chest and flexible optic bronchoscopy concerning Bronchoalveolar lavage cellular analysis in the diagnosis of interstitial lung disease.

Materials and Methods

A prospective observational study was conducted at tertiary hospital in south India. The study group included 50 patients who are suspected to have interstitial lung disease by clinical examination and history with symptoms and signs are evaluated with HRCT chest and HRCT confirmed patients are subjected to fibre optic bronchoscopy and bronchoalveolar lavage is performed and their cytological profiles are analysed. After institutional ethics committee approval was obtained, consent is taken from all study subjects before the study. All ILD patients diagnosed based on clinical and HRCT findings and age 18 years and above, both male and female were included in the study. Patients with active pulmonary tuberculosis, Immunocompromised states, unfit for bronchoscopy, lung malignancy, pregnant women, corticosteroid therapy for more than one month were excluded. Statistical Analysis – Nonparametric analysis was performed on the prospective data after finding the median values of different cell counts obtained from the fluid analysis and cell counts between different ILD's when compared to healthy non-smoker individuals and has been presented in the form of tables was assessed using the SPSS version.18 (statistical package for social sciences, Chicago, IL) and $p< 0.05$ were considered significant.

Results

The study included 50 patients with interstitial lung disease as shown in HRCT and fiber optic bronchoscopy. The mean age of the patients was 50.18 years (SD ±14.3), with an age

ISSN 2515-8260 Volume 09, Issue 04, 2022

range from 18 to 70years and most of the study subjects were males. 32(64%) of the subjects had a habit of smoking and the majority of the participants was in the 46 to 55 age group. The baseline characteristics of the study population are shown in Table 1.

In the current study, the characteristic radiographic appearances observed are honeycombing (54%), reticulation (40%), and traction bronchiectasis, ground-glass opacities 38%, the least HRCT pattern that was reported in this study are cysts with pneumothorax and pleural thickening (1%) which is shown in Table 2.

Among 50 cases, 45 cases were able to perform spirometry as per ATS guidelines. In the remaining five cases, in some cases where the general condition of the patient is poor and those in acute exacerbations, spirometry was not done. The most common X-ray findings are Reticulo-Nodular Infiltrates followed by reduced lung volumes.

Table 3 depicts the most common pattern is of UIP type with 46% of cases having a UIP pattern. This finding of UIP being the most common HRCT pattern followed by NSIP which reveals UIP as the most common finding in interstitial lung diseases. Septal thickening, reticular opacities, honeycombing, and traction bronchiectasis are the commonest findings observed in almost all cases of UIP seen predominantly in basal and subpleural regions.

Graph 1 shows Dyspnoea was the most common presenting symptom (90% of patients), followed by cough (84%) and least is dysphagia (6%). Eight cases (16%) that were serologically positive for rheumatoid arthritis were reported in our study. The most common pattern found with rheumatoid arthritis was reticular opacity associated with UIP (6 out of 8).

Table 4 shows the alveolar macrophages in lung secretions were significantly high in PAM, PAP, pneumoconiosis, and lymphocytes were seen high in hypersensitivity pneumonitis than compared to other subgroups of ILD. In eosinophilic lung disease patients, 47% showed alveolar macrophages 30% eosinophils were recorded.

Table 5 depicts sixteen patients who were diagnosed with IPF based on clinical evaluation, pulmonary function test (restrictive pattern), and HRCT findings (subpleural/basal reticulation and honeycomb appearance). In one young female, a cystic pattern was seen on HRCT with multiple diffuse thin-walled cysts which made us to make a diagnosis of LAM.

Discussion

Interstitial lung diseases are a group of heterogeneous disorders which differ significantly in their presentation, treatment, and prognosis. These issues can show up exclusively in the lung, or as either the underlying indication or a critical part of a multisystem disorder. Also, a significant number of these diseases are an outcome of explicit openings that the patient experiences either at the work environment, at home, or from medications or dietary supplements. Interstitial lung diseases are difficult to characterize, diagnose, and treat, thus they can pose a challenge to the practicing pulmonologist. Bronchoalveolar lavage (BAL) has been used to evaluate patients with suspected interstitial lung disease (ILD) to recognize the specific type. HRCT helps in identifying specific radiological patterns which are associated with certain forms of ILD. These imaging patterns have greatly helped the clinician in narrowing down the differential diagnosis. After the clinical examination and radiological evaluation are completed, BAL cellular analysis may be a useful adjunct in the diagnostic evaluation of individuals to confirm the HRCT findings and also to refine their clinical diagnosis for better management of ILD patients, thus avoiding the need for a lung biopsy.

As HRCT imaging patterns were consistent with express types of ILD like IPF or sarcoidosis, the likelihood of making a finding was high. In spite of the acknowledgment of getting HRCT check during the underlying phases of patients with ILD, many patients with new-onset ILD may not have the characteristic patterns that allow diagnosis to be made with a significant degree of certainty by HRCT imaging alone. Notwithstanding, when clinical data and HRCT findings were combined with BAL fluid analysis, certain determination might arise that

forestall the requirement for careful lung biopsy. HRCT findings limited the type of ILD as well as improved the findings for better management procedure.

The most common ILD in our study is Idiopathic pulmonary fibrosis which occurred in 16 (32%) cases followed by CTD – ILD occurring in 12 (24%) cases and hypersensitivity pneumonitis which occurred in 12 (24%) cases, which is in similar to the study conducted by T. Sen *et al*. [11] and Muhammad Shafeeq k *et al*. [12]. However, recently published results of Indian ILD registry [13] revealed that Hypersensitivity pneumonitis is the most common cause of ILD in the registry. This discrepancy in results could be attributed to the multi-disciplinary approach used in the evaluation of ILD patients in the registry, whereas in our settings many cases of hypersensitivity pneumonitis are being treated as community-acquired pneumonia based on a radiological pattern of consolidation and lack of proper exposure history.

In our study, the mean age of diagnosis of interstitial lung disease is 50.18 years to be more specific, which correlated nearly with the ILD India registry. There is a male preponderance in our study which had 68% of male and 32% female subjects, this male predominance raises may be due to findings with the possibility of more smoking history and more exposure to air pollution as etiological factor to ILD. Which is in accordance with the study done by M. Turner *et al*. [14].

In this current study dyspnoea was the most common presenting symptom (90% of patients), followed by cough (84%) which is similar to the study conducted by Sheetu Singh *et al*.[13] and M. Turner *et al*.[14].

In this study group of 50 cases, 32 (64%) were smokers and 18 (36%) were nonsmokers. In 16 patients with IPF, 10 (62.5%) were associated with smoking and IPF is the most common ILD among smokers in our study. Thus, our study supports the evidence that smoking is a risk factor for IPF as indicated by other studies [15, 16]. Among 50 cases, 45 cases were able to perform spirometry as per ATS guidelines. In the remaining five cases, patient was unable to perform spirometry because of poor effort. The restrictive pattern is the most common spirometry defect in our study with 28 (56%) cases revealing a restrictive abnormality. This finding is similar to other studies by Boros PW *et al*. [17], Ashok K Gagiya *et al*. [18] which showed that restriction is the most common spirometry abnormality in interstitial lung diseases. The mixed defect is seen in 7 (14%) cases which could be due to the smoking history of patients with underlying chronic obstructive pulmonary disease.

Although the chest X-ray can be helpful in suggesting the diagnosis of UIP, HRCT is both more sensitive and more specific in making this diagnosis of interstitial lung diseases [19, 20].

In this study reticulonodular pattern is the most common chest x-ray abnormality which occurred in 44% of the patients followed by reduced lung volumes which occurred in 40% of the patients which is in accordance with the results shown by Ashok K Gagiya *et al*. [18] where the reticulonodular pattern is the most common chest x-ray abnormality in 30 ILD patients.

In the present study incidence of Reticular & Reticulo nodular patterns is 66% which is, in contrast, to the study done by Johnston *et al*. [21]. Which is high in the present study may be because, selection of patient is done mainly on typical X-ray chest findings, while in Johnston *et al*. study patients with normal and ill-defined opacities on chest X-ray are also included.

Pneumothorax is seen in chest x-ray in one case of LAM which could be because of rupture of peripheral cysts into the pleural space. This finding is similar to x-ray findings described by Gerald.F. Abbott in their study of 32 patients out of which 13 had pneumothorax.[22]

When evaluating HRCT, honeycombing is the predominant finding in our study which occurred in 27 (54%) cases which are followed by reticular opacities in 20 (40%) cases, traction bronchiectasis, and ground-glass opacities in 19 (38%) cases. Air trapping is seen in 14 (28%) cases reflecting HRCT pattern of hypersensitivity pneumonitis and it may also occur because of coexistent obstructive lung disease.

Calcified nodules occurred in 3 (6%) cases of which two were diagnosed as cases of pneumoconiosis and a diagnosis of pulmonary alveolar microlithiasis was made in another

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case. Cystic pattern with diffuse thin-walled cysts with pneumothorax is seen in one case of lymphangioleiomyomatosis as classically described in the radiological pattern of LAM which is similar to the study conducted by Gerald F. Abbott. *et al*. [22].

In this study, the common radiographic abnormalities were honeycombing, Reticular opacities, traction bronchiectasis, and GGOs which is different from the study by Glazer. C *et al*. [23] described the most common radiographic characters of ILD as ground-glass opacities, consolidation, cysts, honeycombing, pulmonary nodules, and interstitial thickening.

Diffuse involvement was noted on HRCT in Hypersensitivity Pneumonitis which includes tiny centrilobular nodules with ground-glass haziness. These findings were similar to a study done by Martin Schwaiblmair *et al*. [9].

Eight cases (16%) cases which were serologically positive for rheumatoid arthritis were reported in our study. The most common pattern found with rheumatoid arthritis was reticular opacity associated with UIP (6 out of 8) in our study. These findings correlated with J K Dawson *et al*. [24]and Kinoshita F *et al*. [25].

BAL fluid analysis in IPF revealed a mean lymphocyte count of 20% and a mean neutrophil count of 32%. Neutrophils had a range of 14 to 56%.About lymphocytes, neutrophils, and eosinophils. Neutrophils are the predominant cell type in IPF patients in our study. However, a significant increase in the number of neutrophils is observed in all samples which could be because of added secondary infections and smoking history. This increased finding of neutrophils correlates with the studies of A. Pesci *et al*. [26] and Keith C. Meyer [27]. As described by Keith C. Meyer [27] and Wim.A.Wuyts[28] BAL fluid analysis alone is not useful in making a confident diagnosis of IPF. But when combined with clinical features and consistent UIP pattern of HRCT, BAL can be a useful adjunct, thus avoiding the use of lung biopsy.

BAL fluid in two cases of NSIP revealed lymphocytosis of nearly 25%. Findings of lymphocytosis observed in our study are similar to observations made by Micaela Romagnoli *et al*. [29], A.U. Wells *et al*. [30], Meyer KC *et al*. [31].

Limitations

- Due to the small sample size of the study, observations cannot be related to the general population.
- Due to lack of expertise and reluctance of patients in undergoing an invasive procedure for diagnosis. A surgical lung biopsy was not done for histopathological confirmation of diagnosis. Thus, ILD diagnoses made on clinical grounds may not be 100% correct in some patients.
- Lymphocyte subsets were not analysed in our study which could have refined the diagnosis to a more specific level.

Conclusion

A combination of BAL along with clinical findings and HRCT findings also improves diagnostic accuracy by establishing the acute or chronic nature of the disease and the cause for acute exacerbation, which helps in the better management of ILDs. In cases like IPF, CTD – ILD, Silicosis, Pulmonary Alveolar Microlithiasis, and LAM diagnosis is made mainly by clinical features and HRCT patterns. BAL has a limited role in diagnosis. A multidisciplinary approach is required in the management of a case of ILD.

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Table 1: Distribution of study participants according to Age & Gender

Age Group	Males	Females	Total(n=50)
15-25	0	2	2
26-35	2	0	2
36-45	4	2	6
46-55	16	8	24
56-65	11	3	14
66-75	1	1	2

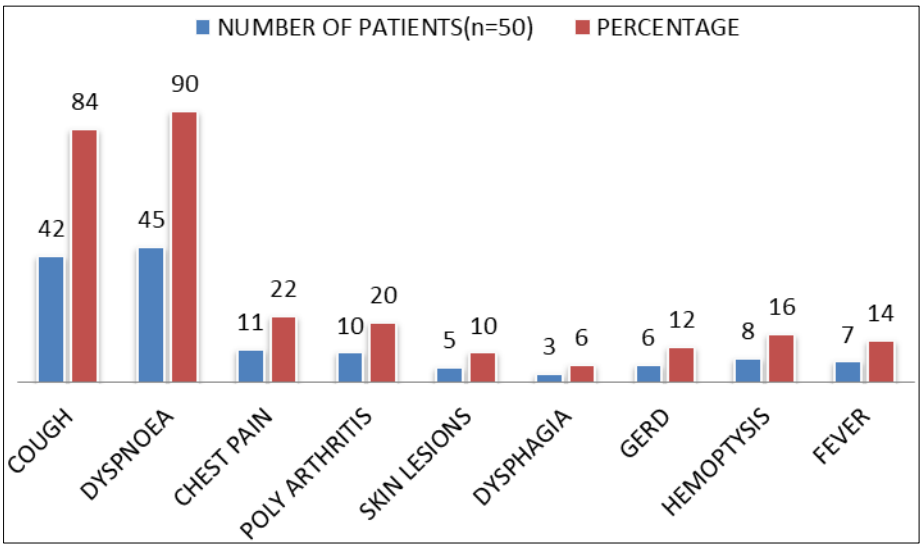

Fig 1: Clinical presentations among the study participants

Table 2: HRCT Chest predominant Patterns among the study participants

HRCT Abnormality	Number of patients	Percentage
Reticular opacities	20	40
Nodules	13	26
Reticulo nodular	7	14
Honeycombing	27	54
Traction bronchiectasis	19	38
Ground glass opacities	19	38
Septal thickening	18	36
Consolidation	7	14
Air trapping	14	28
Calcified nodules	3	6
Mediastinal adenopathy	3	6
Cysts with pneumothorax	1	2
Pleural effusion	3	6
Pleural thickening	1	2
Oesophageal dilatation	3	6

Table 3: HRCT Pattern among the study participants

HRCT Pattern	Number	Percentage
UIP	23	46
NSIP	7	14
Consolidation	7	14
CYSTS	1	2
Calcified nodules	3	6
Others	9	18

Table 4: Bronchoalveolar Lavage Fluid White Blood Cell profile in ILD

Etiology	AM	LYM	NEU	EOS
IPF	47	20	32	0
Hypersensitivity Pneumonitis	47	34	17	0
CTD - ILD	54	22	23	0
NSIP	46	24	21	0
Eosinophilic lung diseases	47	16	8	30
Pneumoconiosis	72	16	12	0
COP	51	27	20	0
LAM	65	12	22	0
PAP	66	20	12	0
PAM	77	16	6	0

Table 5: Etiology wise profile in the study group

Etiology	Number(n=50)	Percentage
IPF	16	32
CTD-ILD	12	24
Hypersensitivity pneumonitis	12	24
Pneumoconiosis	2	4
Eosinophilic lung diseases	2	4
NSIP	2	4
LAM	1	2
PAP	1	2
PAM	1	2
COP	1	2

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