Original Article

Retrospective Study of Interstitial Lung Disease in a Tertiary Care Centre in India

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ABSTRACT

Background. There has been a recent surge in the recognition of interstitial lung disease (ILD) in India.

Methods. We conducted a retrospective study based on the available medical records of 274 patients with biopsy proven ILD seen during the period 1994-2001 at our tertiary care referral hospital.

Results. Idiopathic pulmonary fibrosis (43%), sarcoidosis (22%), ILDs secondary to collagen vascular disease (19%) and extrinsic allergic alveolitis, among others, were the most common aetiological causes of ILD. The diagnostic yield from transbronchial lung biopsy (TBLB) was high (96%).

Conclusions. Interstitial lung diseases (ILDs) appear to be under-reported from India. Lack of recognition and inadequate availability of diagnostic facilities, like high resolution computed tomography (HRCT) of the chest may be some of the reasons for this. The diagnostic yield from TBLB in our study was high at 96 percent. The TBLB may be used as the initial, cost-effective and safe tool for confirmation of aetiological diagnosis in most patients with diffuse parenchymal lung diseases.
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Key words: Interstitial lung disease, Spectrum, Diagnosis.

INTRODUCTION

Interstitial lung diseases (ILDs) are a group of diseases, also described as diffuse parenchymal lung diseases. The ILDs include diseases of unknown aetiology, such as, those secondary to drugs, collagen vascular disease, granulomatous conditions like sarcoidosis and other forms of ILDs like lymphangioleiomyomatosis or histiocytosis X. Most published series on ILDs are from the West. There is a paucity of data on ILD in India, where these diseases are under-estimated and remain under-diagnosed and under-reported for various reasons. This is probably due to lack of awareness among physicians, and lack of availability of diagnostic modalities like computed tomography (CT), bronchoscopy and video-assisted thoracoscopic surgery (VATS) and the high cost involved in getting these investigations done. Tuberculosis (TB) mimics some of the ILDs, like sarcoidosis, leading to diagnostic errors and delays. Thus, the incidence of ILDs in the developing countries has been considerably under-estimated.

There are no large series of ILDs from India. However, in the last few decades scattered case reports have emerged including various aetiological factors responsible for ILDs from India.[1-5]

The present study was, therefore, planned to analyse the spectrum of ILD encountered in a tertiary referral centre in India to determine the clinical profile of the disease.

MATERIAL AND METHODS

This was a retrospective, observational, epidemiological study. The medical records of patients with either TBLB or open lung biopsy (OLB) proven ILD, presenting at our tertiary care referral centre over a period of seven years from 1994 to 2001 were analysed. Two hundred and seventy-four patients met the inclusion criterion of histopathological confirmation of ILD and formed the study group.

Patients initially suspected to have ILD, who subsequently were proven to have an alternative diagnosis on histpathology (n=26), like TB or bronchoalveolar cell carcinoma, etc, were excluded from the study. Of these, 20 patients had TB with a microbiological confirmation of the presence of acid-

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fast bacilli, either in the sputum or in the broncho-alveolar lavage (BAL) fluid. After a detailed history, a contact source was identified in 15 of them. All the 20 patients had fever, loss of appetite, loss of weight, along with cough, sputum production and dyspnoea. Erythrocyte sedimentation rate (ESR) was raised more than 100mm at the end of first hour, in all the patients. Imaging studies like chest radiograph and CT of the chest either showed a cavity (n=5) or pulmonary infiltrate (n=7), pleural effusions (n=4), consolidation (n=3) or a miliary pattern (n=1).

The other six patients had bronchoalveolar carcinoma. Clinically they presented with breathlessness and cough. All the six patients had bronchorhea. Four out of the six patients had haemoptysis. Sputum for malignant cells were positive in two patients. The BAL for malignant cells was positive in five patients. The diagnosis was confirmed by a TBLB in four cases and by a CT-guided biopsy in two patients.

RESULTS

The mean age of the patients was 48 years. The male:female ratio was 1:2. The clinical presentation of all the 274 patients (100%) was dry cough and progressive dyspnoea. These symptoms were present for a varied duration of time, from two months to five years. Constitutional symptoms, like loss of appetite and loss of weight, were noted in 28 (10%) patients. Purulent sputum was present in 192 (70%) patients, when they got admitted with a super added lower respiratory tract infection or a consolidation. Chest pain was present in 19 (7%) patients, who developed pneumothorax (n=14) and pulmonary embolism (n=5). Haemoptysis was present in five (2%) patients, who had pulmonary hypertension. Seventy-one (26%) patients presented with bilateral swelling of lower limbs, ascites and raised jugular venous pressure, suggestive of a cor-pulmonale. One hundred and seventeen (43%) patients manifested classical "velcro-crepts". The blood counts showed a predominance of either neutrophils (n=230 patients; mean±SD=2) or lymphocytes. The ESR was raised (>100 mm at the end of first hour) in all the patients. Antinuclear antibody was detected in patients with ILD secondary to collagen vascular disease. Anti-topo-isomerase (SCL-70) was positive in patients with systemic sclerosis and ILD, anti-double stranded deoxyribonucleic acid was positive in 4% patients with systemic lupus erythromatosus (SLE) and ILD. The chest radiograph of the patients showed ground-glass appearance at the bases (Figure 1) in 82% of the patients. The high resolution CT (HRCT) also showed ground-glass appearance (Figure 2) in 90% of the patients in our study.

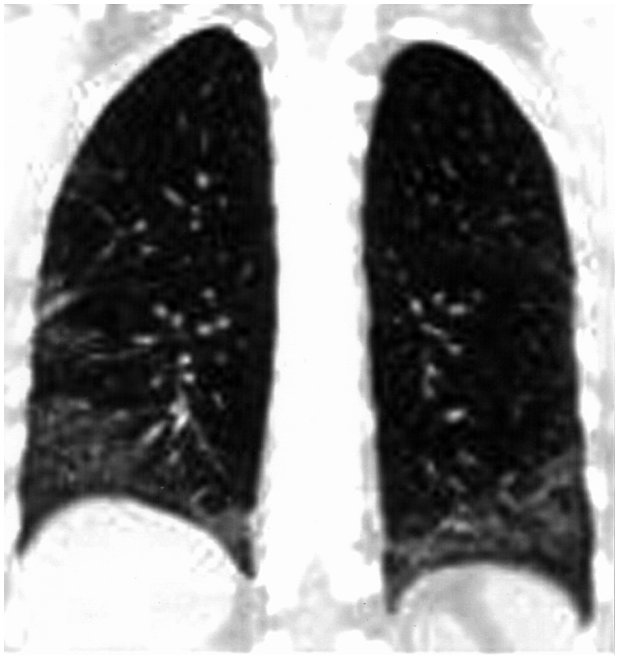

Figure 1. Chest topogram showing ground-glass appearance with ill-defined haziness in the bilateral lower lung zones.

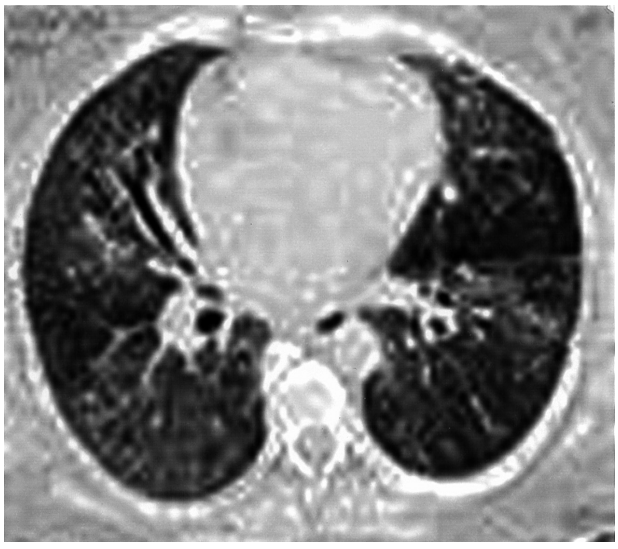

Figure 2. HRCT chest showing ground-glass appearance with haziness of the lung parenchyma and prominence of the underlying vessels.

Honey-combing on HRCT (Figure 3) was observed in 43% of the patients. The lung function tests of these patients revealed restrictive pattern with a decrease in diffusion capacity and six-minute walk distance test (6MWDT) pointing at functional disability.

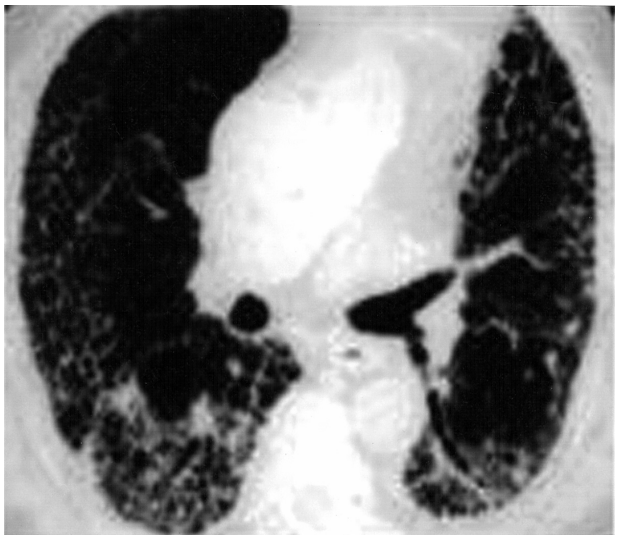

Figure 3. HRCT showing honey-combing with multiple cysts in the sub-pleural region.

The TBLB provided adequate tissue to allow an accurate diagnosis of the histopathological type of ILD in 96% patients. An OLB was needed to make a definitive diagnosis in only 10 patients. The most common ILD was idiopathic pulmonary fibrosis (IPF) seen in 43% of our patients (Table). There was presence of fibroblastic foci on histopathology in these patients. Sarcoidosis was the next common histopathological subtype, occurring in 22% of the patients.

Table. Clinical spectrum of ILD in 274 patients

Type of ILD	Number of Patients
Idiopathic pulmonary fibrosis	117(43%)
Sarcoidosis	61(22%)
ILD secondary to collagen vascular disease	51(18%)
Extrinsic allergic alveolitis	15(6%)
Cryptogenic organising pneumonia	6
Drug-induced ILD	3
Eosinophilic pneumonia	3
Pneumoconiosis	2
Histiocytosis X	1
LIP	5
Lymphangitis carcinomatosa	3
Amyloidosis	2
Pulmonary alveolar proteinosis	2
Churg-Strauss disease	1
Lymphomatoid granulomatosus	1

ILD=Interstitial lung disease; LIP=Lymphocytic interstitial pneumonia

In 18% of our patients, ILD was secondary to collagen vascular diseases, like systemic sclerosis, rheumatoid arthritis, or SLE. Hypersensitivity pneumonitis occurred in 15 patients and six patients had cryptogenic organising pneumonia (COP). We also encountered other rare clinical entities, like lymphangitis carcinomatosa, pulmonary alveolar proteinosis, hisiocytosis X; the diagnosis of which was confirmed only after an OLB.

DISCUSSION

The process of achieving a diagnosis in a patient with ILD requires close communication between clinician, radiologist and pathologist. There is limited data on the presentation and diagnosis of these patients from India. The two main issues that are important for diagnosis of pulmonary fibrosis in this part of the world are differentiation from other illnesses with similar presentation and establishing the aetiology of pulmonary fibrosis.

The common conditions causing progressive breathlessness which can mimic the clinical presentation of an ILD would include pulmonary oedema and left heart failure, tropical pulmonary eosinophilia, hypersensitivity pneumonitis, bronchiectasis and TB. Due to the very high burden of pulmonary TB in this part of the world, most patients with pulmonary symptoms and diffuse radiological opacities are labelled as suffering from TB, unless another diagnosis is proven.

Similar to the Western data, the commonest presenting symptoms were dry cough and breathlessness in the present study. Most of the patients required admission due to an infective exacerbation. Chest pain developed when the patient with an underlying ILD developed a pneumothorax (n=14) or a pulmonary embolism (n=5) and both these complications resulted in acute worsening of the disease. There remains a diagnostic delay in India due to varied reasons. In our resource-limited country, chest radiographs are over relied for the diagnosis or exclusion of any respiratory condition. In pulmonary fibrosis, standard chest radiographs characteristically shows the presence of diffuse or focal reticular, nodular or reticulonodular opacities, usually more predominant in the lower lobes. Both alveolar and interstitial shadows may be present. The presence of multiple layers of cysts or honey-combing mainly involving bilateral basal lung fields in an asymmetric pattern indicates end-stage fibrosis. However, there is no distinct correlation between the extent of fibrosis and the severity of the disease with radiographic findings. Abnormal chest radiograph can occur in around 10% to 15% of the patients with ILD, and thus, a normal looking chest radiograph does not rule out pulmonary fibrosis.

Given these limitations of the chest radiograph, HRCT of the chest has become an integral part of the evaluation of patients with ILD. The primary aim of HRCT is to separate patients with typical findings of IPF, from those with the less specific findings associated with other ILDs. Currently, it is estimated that India has an installed CT scanner base of 3000 machines which works out to three CT scanners per one million population. This penetrance is still considered very low compared to other countries in the region; China 5.5 per million, Korea 31.3 per million and Japan 92.6 per million. A rough estimate would be that no more than 600 to 700 CT scan machines (*i.e.*, <1 machine per million population) would be capable of performing good quality HRCT and no more than 50 to 100 radiologists in the country would have an interest in chest imaging and be using the correct end-expiratory breath holding techniques to provide good quality images. (*Dr Bhavin Jhankaria, personal communication*). The cost of a CT scanner is also undoubtedly a factor which is responsible for their limited penetrance. Moreover, most of the machines are concentrated around the bigger metropolitan cities, so large populations in rural areas do not get access to CT scan machines. This further adds to the delay in the diagnosis of ILDs in India.

The lung function tests in ILDs usually show a restrictive pattern. The most sensitive parameter of the pulmonary function is the diffusion capacity of carbon monoxide (DLCO). The exercise capacity and its objective evidence of impairment, is reflected by the 6MWDT. In India only a limited number of pulmonary function labs have the facility and expertise to conduct tests of diffusion capacity and the 6MWDT. This further causes a delay in diagnosing the functional disability in patients with ILDs in India.

Invasive diagnostic procedures, like TBLB, have a role in specific conditions like sarcoidosis with a diagnostic yield of around 85% and in excluding infectious conditions like TB and *Pneumocystis jiroveci* pneumonia or malignancies. In India, the availability of TBLB and the degree of expertise required in performing a TBLB procedure is limited. The role of TBLB in diagnosing IPF still remains an issue needing clarification. Whilst most experts would feel an OLB is needed to diagnose IPF, the current American Thoracic Society criteria[7] which include a combination of clinical, CT, pulmonary function test along with a TBLB to exclude other causes were followed in each of the patients given the label of IPF in our series.

In the present study, TBLB had a diagnostic yield of 80.7% and only 10 patients required an OLB. Another study from our tertiary care centre[8] on the clinical profile of 34 biopsy proven cases of COP revealed that the diagnosis of COP was confirmed by TBLB (fluoroscopically directed) in all the patients. As compared to other large series, none of our patients needed VATS or OLB to establish the diagnosis. Thus, both these series document that though OLB remains the gold standard, TBLB can be the first diagnostic step and has a high yield in certain forms of ILDs, especially sarcoidosis and COP.

The IPF and the other idiopathic interstitial pneumonias were the commonest cause of ILDs in the present study. Although a highly probable diagnosis of IPF and of the other forms of interstitial pneumonias can usually be established only with the aid of a surgical lung biopsy. In the Indian context, the main benefits of obtaining a surgical lung biopsy would be to avoid diagnostic uncertainty, and thus, minimise the risks and side effects of the current treatments, to establish a definite diagnosis and allow the patient and clinician to make more informed decisions about therapy and prognosis. Surgical lung biopsies can be either via open thoracotomy or with the help of VATS. Open thoracotomy gives a high diagnostic yield[9-12] but is associated with perioperative mortality, morbidity and significant hospital expenses. Video-assisted thoracoscopy is available in only a few specialised centres in India since the 1990s and there are only a handful of thoracic surgeons, with enough experience to perform this procedure. This again leads to a delay in obtaining a tissue diagnosis of ILD .

Finally, the classification of ILDs is based on biopsy, for example, fibroblastic foci and temporal heterogeneity is the characteristic feature of IPF. Unfortunately in India, few experts can be relied on to provide accurate pathological identification of the lung biopsy material. A detailed report on histopathology may not be obtained even after subjecting the patient to an OLB, and thus, add on to the diagnostic delay. There is need for capacity building in this area.

CONCLUSIONS

Our study suggests that ILDs are not uncommon in India. Lack of recognition and inadequate diagnostic facilities, like HRCT, bronchoscopy services, may explain why there are so few Indian series on this subject. Idiopathic pulmonary fibrosis constitutes the single largest disease group accounting for 43% of all our patients presenting with ILD. Sarcoidosis, which was in earlier decades considered rare in India, was second in frequency accounting for 22% of the study population. Larger prospective epidemiological studies will also be needed to establish the true incidence and spectrum of these diseases. Increased awareness would serve to provide early diagnosis. This would impact favourably on the high mortality traditionally associated with this group of disease.

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