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A MULTIDISCIPLINARY APPROACH FOR THE CLINICAL, RADIOLOGICAL, HISTOPATHOLOGICAL & SEROLOGICAL PROFILE IN PATIENTS WITH INTERSTITIAL LUNG DISEASE

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ABSTRACT

Background: Interstitial Lung Disease (ILD) refers to a heterogeneous group of more than one hundred distinct lung disorders that are grouped together because they share similar clinical, radiographic, and pathologic features. Diagnosing ILDs in India has proven to be a challenge as it is confounded by environmental and cultural factors in the midst of infections, especially Tuberculosis. The country has a lack of resources, standardized health care and guidelines for approach to ILD. While approaching a patient suspected to have ILD one should use a combination of a detailed history, clinical examination, radiographic findings, pathological features and serological tests. **Method:** A descriptive study designed to evaluate 50 suspected ILD with multidisciplinary approach including clinical, radiological, serological and histopathological approaches. **Results:** We evaluated 50 patients (mean age 48.02 years; 54.0% females) of Interstitial Lung Diseases (ILD) with multidisciplinary approach. Connective tissue disease related ILD (26.0%) was the most common type of ILD, followed by Hypersensitivity pneumonitis (20.0%) and Idiopathic pulmonary fibrosis (18.0%). Sarcoidosis was diagnosed in a lesser proportion of patients (4.0%) as compared to other studies. **Conclusions:**. TBLB appears to be an important diagnostic tool for the diagnosis of DPLDs. The use of a pattern-based approach to TBLB adds to its diagnostic yield and can be helpful in cases where open lung biopsy is not available.

KEYWORDS: Trans-Brochial lung biopsy, serology, histopathology, radiography.

INTRODUCTION

Interstitial Lung Disease (ILD) refers to a heterogeneous group of more than one hundred distinct lung disorders that are grouped together because they share similar clinical, radiographic, and pathologic features. These disorders are sometimes called Diffuse Parenchymal Lung Disease (DPLD) to make the point that the interstitium is not the only compartment of the lung affected. Alveoli, alveolar epithelium, capillary endothelium, the spaces between these structures, and the perivascular and lymphatic tissues can be involved.

Commonly ILD presents with dry cough, progressive dyspnoea on exertion, diffuse bilateral infiltrates on chest imaging and restriction with diffusion impairment on physiologic testing. Abnormalities in any of them indicate a need for High Resolution Computed Tomography (HRCT) of chest. When tissue is obtained, the lung parenchyma may contain any combination of abnormalities, including inflammation, fibrosis, and granulomas. Once the diagnosis of ILD is clear, the sub-typing is needed. Other investigations such as Pulmonary Function Tests (PFT), bronchoscopy, serum collagen panel and serum ACE may be needed.

Diagnosing ILDs in India has proven to be a challenge as it is confounded by environmental and cultural factors in the midst of infections, especially Tuberculosis. The country has a lack of resources, standardized health care and guidelines for approach to ILD.[4] In addition, there is an apparent fear, reluctance, hesitancy, and uncertainty regarding surgical lung biopsy (SLB). All these factors contribute to the current conservative approach to the diagnosis of new onset of ILD in India. As a result, the diagnosis is an assumptive diagnosis relying on the individual clinician's judgment, and the treatment of ILDs is empirical in most patients.[4] While approaching a patient suspected to have ILD one should use a combination of a detailed history, clinical examination, radiographic findings, pathological features and biochemical tests. In fact, most guidelines recommend multidisciplinary discussions (MDD) conducted by a

team comprising of physicians, radiologists and pathologists.[5]

AIM AND OBJECTIVE

1. To evaluate different clinical pattern & presentation of ILD.
2. To define the role of chest x-ray & HRCT in patients with ILD.
3. To evaluate the histopathological pattern identification on TBLB and the clinical usefulness of TBLB in diagnosis of ILD.
4. To see association of various serological marker with different ILD.

This study is a descriptive study time period from October 2018 - July 2020. conducted at tertiary care centre, Department of Tuberculosis and Respiratory Diseases, Sir Sunderlal Hospital, Institute of Medical Sciences, Banaras Hindu University, Varanasi. After inclusion and exclusion criteria only 50 patients were enrolled for this study.

Inclusion Criteria

Patient presenting with the following

1. Respiratory symptoms such as shortness of breath and cough.
2. Bilateral abnormalities in X ray/ HRCT thorax suggestive of ILD.

Exclusion Criteria

1. Any infectious or malignant diseases.
2. Patient not giving consent.
3. Unstable patient.
4. Pregnant females.

MATERIALS AND METHOD

- Pulse oximeter, Stop-watch, Dispovan 1 ml (pre-heparinised) and 5 ml syringe, ABG analyzer machine, Spiroexcel PFT machine,Auto analyzer of Complete blood count, Renal function test, Liver function test, random blood sugar.Kits for serum markers of connective tissue diseases and vasculitides (RA factor, anti CCP, ANA, anti dsDNA, anti Sm, anti RNP, anti Scl 70, anti SSA, anti SSB, anti Jo-1, ANCA), ACE.Multi-detector row 128 slice CT scanner (Light speed, General Electric Medical Systems, Milwaukee, WI).
- Seimens Sonoline G20 ultrasound equipment, Olympus flexible bronchoscope with transbronchial needle aspiration (TBNA) needle and transbronchial lung biopsy (TBLB) forceps (when patients gave consent).

OBSERVATION AND RESULTS

A total of 50 patients with ILD met the inclusion and exclusion criteria and were recruited. 6 Minute Walk Test, arterial blood gas analysis, relevant routine laboratory investigations, serology for connective tissue diseases, High Resolution Computed Tomography (HRCT) thorax and transthoracic ultrasound were performed for all the 50 patients. Histopathological examination by means of bronchoscopy guided procedures (like bronchoalveolar lavage cytology, transbronchial needle aspiration and transbronchial lung biopsy).

Table No 1: Types of ILD among patients in current study.

Type of ILD	No. of patients (%)
Connective tissue disease related ILD (CTD-ILD)	13 (26.0)
Hypersensitivity Pneumonitis (HP)	10 (20.0)
Idiopathic pulmonary fibrosis (IPF)	9 (18.0)
Pneumoconiosis	3 (6.0)
Eosinophilic pneumonia	3 (6.0)
Idiopathic Non-specific interstitial pneumonia (iNSIP)	2 (4.0)
Sarcoidosis	2 (4.0)
Diffuse alveolar hemorrhage (DAH)	2 (4.0)
Pulmonary alveolar proteinosis (PAP)	1 (2.0)
Desquamative interstitial pneumonia (DIP)	1 (2.0)
Lymphocytic interstitial pneumonia (LIP)	1 (2.0)
Langerhans cell histiocytosis (LCH)	1 (2.0)
Lymphangioleiomyomatosis (LAM)	1 (2.0)
Pleuroparenchymal Fibroelastosis (PPFE)	1 (2.0)
Total	**50 (100.0%)**

Table No 2: Different Reactive Auto Antibody In Ctd-Ild.

	ANA	SSA	SSB	SCL70	DSDNA	RA FACTOR	ANTI CCP	ANTI Sm	ANTI RNP
RA (n=5)						5	5		
SCL (n=3)	3			3					2
SJOGREN (n=2)	2	2	2			1			
MCTD (n=2)	2								2
SLE (n=1)	1		1		1			1	

Table No 3: HRCT Patterns.

	HP (n=10)	CTD-ILD (n=13)	IPF (n=9)	Pneumo-coniosis (n=3)	Sarcoidosis (n=2)	Insip (n=2)	DAH (n=2)	PAP (n=1)	Eosinophilic pneumonia (n=3)	DIP (n=1)	LIP (n=1)	LCH (n=1)	LAM (n=1)	PPFE (n=1)	Total (n=50)
UIP	0	7	9	0	0	0	0	0	0	0	0	0	0	0	**16**
	0.00%	53.85%	100.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	**32.00%**
Possible UIP	0	3	0	0	0	0	0	0	0	0	0	0	0	0	**3**
	0.00%	23.08%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	**6.00%**
NSIP	2	2	0	0	0	2	0	0	0	0	0	0	0	0	**6**
	20.00%	15.38%	0.00%	0.00%	0.00%	100.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	**12.00%**
Reticular Pattern	2	0	0	0	1	0	0	0	0	1	0	0	0	0	**4**
	20.00%	0.00%	0.00%	0.00%	50.00%	0.00%	0.00%	0.00%	0.00%	100.00%	0.00%	0.00%	0.00%	0.00%	**8.00%**
Reticulonodular pattern	4	0	0	1	1	0	0	0	0	0	0	0	0	0	**6**
	40.00%	0.00%	0.00%	33.33%	50.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	**12.00%**
Nodular pattern	0	0	0	2	0	0	0	0	1	0	0	0	0	0	**3**
	0.00%	0.00%	0.00%	66.67%	0.00%	0.00%	0.00%	0.00%	33.33%	0.00%	0.00%	0.00%	0.00%	0.00%	**6.00%**
Predominant Ground glass	2	1	0	0	0	0	2	0	2	0	0	0	0	0	**7**
	20.00%	7.69%	0.00%	0.00%	0.00%	0.00%	100.00%	0.00%	66.67%	0.00%	0.00%	0.00%	0.00%	0.00%	**14.00%**
Cystic ILD	0	0	0	0	0	0	0	0	0	0	1	1	1	0	**3**
	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	100.00%	100.00%	100.00%	0.00%	**6.00%**
Crazy pavement	0	0	0	0	0	0	0	1	0	0	0	0	0	0	**1**
	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	100.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	**2.00%**
Fibrocystic and fibroparenchymal	0	0	0	0	0	0	0	0	0	0	0	0	0	1	**1**
	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	100.00%	**2.00%**

Table No 4: Histology Pattern of Different Ild.

	HP (n=4)	CTD-ILD (n=5)	IPF (n=4)	Sarcoidosis (n=2)	iNSIP (n=1)	DAH (n=2)	PAP (n=1)	DIP (n=1)	LIP (n=1)	LCH (n=1)	PPFE (n=1)	Total (n=23)
UIP Pattern	0	2	4	0	0	0	0	0	0	0	1	**7**
	0.00%	40.00%	100.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	100.00%	**30.43%**
NSIP Pattern	0	1	0	0	1	0	0	0	0	0	0	**2**
	0.00%	20.00%	0.00%	0.00%	100.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	**8.70%**
Non-Cessesating Epihaloid Granuloma	0	0	0	2	0	0	0	0	0	0	0	**2**
	0.00%	0.00%	0.00%	100.00%	100.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	**8.70%**
Lymphocytic Intestitial Pattern	0	0	0	0	0	0	0	0	1	0	0	**1**
	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	100.00%	0.00%	0.00%	**4.35%**
Loosly Formed Granuloma	3	0	0	0	0	0	0	0	0	0	0	**3**
	75.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	**13.04%**
Langerhan's Cell Pattern	0	0	0	0	0	0	0	0	0	1	0	**1**
	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	100.00%	0.00%	**4.35%**

Diffused alveolar hemorrhage pattern	0	1	0	0	0	2	0	0	0	0	0	**3**
	0.00%	20.00%	0.00%	0.00%	0.00%	100.00%	0.00%	0.00%	0.00%	0.00%	0.00%	**12.50%**
Advanced UIP Pattern (Honeycomb Lung)	0	1	0	0	0	0	0	0	0	0	0	**1**
	0.00%	20.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	**4.35%**
Abundant Alveolar Macrophage	0	0	0	0	0	0	0	0	0	0	0	**0**
	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	**0.00%**
Diffused Intestitial Inflammation Pattern	1	0	0	0	0	0	0	1	0	0	0	**2**
	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	100.00%	0.00%	0.00%	0.00%	**8.70%**
Dead Macrophases + Acellular Eosinphilic Material	0	0	0	0	0	0	1	0	0	0	0	**1**
	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	100.00%	0.00%	0.00%	0.00%	0.00%	**4.35%**

DISCUSSION

In our study 50 patients met the inclusion criteria and we found that connective tissue ILD (CTD-ILD) was the most common ILD (26.0%), followed by Hypersenstive pneumonitis (20.0%), Idiopathic pulmonary fibrosis (IPF) (18.0%), Pneumoconiosis (6.0%), Sarcoidosis (4.0%), Idiopathic non-specific interstitial pneumonia (iNSIP) (4.0%), Diffuse alveolar haemorrhage (DAH) (4.0%) and Eosinophilic pneumonia in 6.0%. We also encountered rare ILDs like Pulmonary alveolar proteinosis (PAP) in 2.0%, Desquamative interstitial pneumonia (DIP) in 2.0%, Lymphocytic interstitial pneumonia (LIP) in 2.0%, Langerhans cell histiocytosis (LCH) in 2.0% and Lymphangioleiomyomatosis (LAM) and Pleuroparenchymal elastosis in 2.0% of our patients. The recent multi-centre ILD India Registry (Singh et al.) including 1084 patients also reported HP as the most common ILD (47.3%) followed by CTD-ILD (13.9%), IPF (13.7%), iNSIP (8.5%), Sarcoidosis (7.8%), Pneumoconiosis (3.0%) and other ILDs (5.7%).[2]

Mean age of the patients in our study was 48.02 (SD, 14.22) years and 46.0% were male. Average duration of symptoms before diagnosis was 3.62 (SD, 4.99) years. 30.0% patients were smokers and 22.0% had a history of tuberculosis at the time of diagnosis. Singh et al. described mean age of 55.3 (SD, 18.7) years, 46.2% males and a duration of 4.1 (SD, 4.01) years of symptoms before diagnosis.[2] Dhooria et al described mean age of 50.6 (SD, 13.8) years, 49.8% males and an average duration of 6 years of symptoms before diagnosis.

Cough was the most common (94.0%) symptom at presentation in the current study, followed by breathlessness (92.0%). This was in keeping with numerous other studies, which have also described cough and breathlessness as the most common symptoms.[2,3,5,7,1]

Females marginally outnumbered males in our study. 40.0% of our patients were housewives. 10.0% were involved in animal husbandry, 8.0% were farmers, 4.0% were stone blasters and 2% were student, Remaining patients were blacksmith, coal mine worker, carpet maker and flourmill worker, clerk, teacher, shopkeeper. Dhooria et al. reported 40.3% of their patients to be housewives, however this was followed by 17.4% patients with office job, 13.1% farmers, 7.5% private enterprise owners, 5.0% teachers and 3.1% medical or paramedical workers.3 This difference may be present because of predominant patients from urban areas in their study.

All the HRCTs were diagnosed as per the ATS/ ERS guidelines by multidisciplinary discussions in our study. 32.0% (n=16) patients had Usual interstitial pneumonia (UIP) pattern and 12.0% (n=6) had Non-specific interstitial pneumonia (NSIP) pattern. The ILD India Registry reported UIP pattern in 24.4% and NSIP pattern 14.8% patients respectively.[2]

We had performed biopsy on 48.0% of our patients.If we compare this with other studies. we can see that our biopsy rate was higher than that in two large studies from India and Saudi Arabia, but lower than that reported from developed countries like Germany, Italy, Spain, Turkey and Greece.

SUMMARY AND CONCLUSION

TBLB appears to be an important diagnostic tool for the diagnosis of DPLDs. The use of a pattern-based approach to TBLB adds to its diagnostic yield and can be helpful in cases where open lung biopsy is not available.

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