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Etiological Profile of Interstitial Lung Disease Patients Attending Respiratory Medicine Department, Regional Institute of Medical Sciences, Imphal

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Abstract:
Background*: Interstitial Lung Disease (ILD) refers to a heterogenous collection of more than hundred distinct lung disorders that tend to be grouped together because they tend to share clinical, radiographic and pathologic features. The disorders are sometimes called diffuse parenchymal lung disease (DPLD). Diagnosis is based on comprehensive history, a careful physical examination, as well as review of laboratory data, physiologic studies, radiography and in some cases, pathologic tissue obtained from biopsy. The prominent feature in ILD is fibrosis in the interstitium, which produces derangement of alveolar architecture and loss of functional alveolar capillary units. The article by Gagiya Ashok K states that the most common etiological causes of ILD were occupational (46.2%), Rheumatoid arthritis (13.32%) and idiopathic pulmonary fibrosis (33.33%). Common symptoms are breathlessness on exertion, dry cough, anorexia and joint pain. Bilateral crepitations and clubbing are seen on examination. Chest X-ray shows reticulonodular pattern and restrictive pattern of PFT is observed in majority of patients.*
Materials and Methods*: This cross-sectional study was carried out from August 2018 to July 2020. A total of 94 patients were enrolled for the study who were more than 18 years with unexplained respiratory system and diffuse parenchymal abnormalities consistent with ILD on High Resolution Computed Tomography (HRCT). Spirometry was done for all selected patients according to ERS/ATS guidelines. They also underwent fiberoptic bronchoscopy and BAL. Patients suspected of connective tissue disorder-interstitial lung disease (CTD-ILD), underwent testing for serum biomarkers like ANA, Anti-dsDNA, RhF, Anti-Scl70, Anti-Jo1, p-ANCA and c-ANCA*
Results*: CTD-ILD was the most common etiology of ILD seen in this study; Scleroderma being the most common cause followed by Rheumatoid arthritis, Systemic lupus erythematosus and Polymyositis-Dermatomyositis. Idiopathic NSIP was the second most common cause and Idiopathic pulmonary fibrosis was the third most common cause. Other causes were Hypersensitivity pneumonitis, Smoking related ILD and pneumoconiosis respectively. The majority of the participants were form urban population (60.6%), followed by sub-urban (23.4%) and rural (16%).*
Conclusion: *ILD in India has likely been under reported, possibly because of lack of access to adequate tests, clinical expertise and facilities. Some studies in India have found IPF as the most common cause and others found CTD-ILD to be most common cause. However, there is lack of studies detailing its regional etiological profile. This study found CTD-ILD to be the most common cause of ILD among the population of Manipur attending RIMS, Imphal.*
Key Word*: Diffuse Parenchymal Lung Disease, Interstitial Lung Disease, Connective tissue disorder-Interstitial Lung Disease,*

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I. Introduction

Interstitial Lung Disease (ILD) refers to a heterogenous collection of more than hundred distinct lung disorders that tend to be grouped together because they tend to share clinical, radiographic and pathologic features. The disorders are sometimes called diffuse parenchymal disease (DPLD). Diagnosis is based on a comprehensive history, a careful physical examination, as well as review of laboratory data, physiologic studies, radiography and in some cases, pathologic tissue obtained from biopsy.Patients commonly present with dyspnea on exertion, diffuse bilateral infiltrates on chest imaging and restriction with diffuse impairment on physiologic testing.[1]The prominent feature in ILD is fibrosis in the interstitium, which produces derangement of alveolar architecture and loss of functional alveolar capillary units.[2] The article by Gagiya Ashok K[2] states that the most common etiological causes of ILD were occupational (46.62%), Rheumatoid Arthritis (13.32%) and idiopathic pulmonary fibrosis (33.33%).

II. Material And Methods

This cross-sectional study was carried out on patients of Department of Respiratory Medicine at Regional institute of medical sciences, Imphal, Manipur from August 2018 to July 2020. A total 94 adult subjects (both male and females) of aged ≥ 18, years were for in this study.

Study Design: Cross sectional study

Study Location: This was a tertiary care teaching hospital-based study done in Department of Respiratory Medicine, at Regional institute of medical sciences, Imphal, Manipur.

Study Duration: August 2018 to July 2020.

Sample size: 94 patients.

Sample size calculation: Prevalence is taken as 13.32% from the study by Gagiya AK et al[2], sample size is calculated by the formula$n = 4p(100 - p)/L^2$

Where, P = prevalence i.e., 13.32%, L=allowable error=7%.

The calculated sample size is equal to 94. Therefore, a minimum of 94 patients were taken up for the present study.

Inclusion criteria:

1. Male and Female patients age more than 18 years with unexplained respiratory symptoms and diffuse parenchymal abnormalities consistent with ILD on HRCT and willing to participate in the study were included.

Exclusion criteria:

1. Patients with clinical suspicion of active infection including tuberculosis or neoplasm.
2. Patients whose sputum are positive for AFB on direct smear or culture.
3. Among patients with radiographic findings particularly concerning for tuberculosis.
4. Patients who are very critically ill.

Procedure methodology

Patients who attended the Respiratory Medicine department, RIMS and fulfilled the inclusion and exclusion criteria with radiological features consistent with ILD were included in the study. Before the start of the study detailed history of the patients was recorded and every patient subjected through general, physical and clinical examinations. All the findings were recorded in the thesis proforma.

Routine investigations including Blood RE, Urine RE, Random Blood Sugar, LFT, KFT, ECG, Sputum for AFB, CBNAAT, GS, CS, X-ray chest PA view, Mantoux test.Spirometry was done for all selected patients according to the ERS/ATS guidelines. Reversibility testing was performed after using salbutamol nebulization and lung function was measured after 15mins.Bronchoscopy was done for the study population. The patients were advised to report nil per oral (atleast 6hours for solids and 4hours for liquids) on the day of procedure. All patients received 5ml of 4% lignocaine solution delivered through nebulization over 15mins immediately before bronchoscopy. After securing peripheral intravenous access, supplemental oxygen was administered via nasal cannula. Local anesthesia was obtained using topical spray with 10% lignocaine. BAL was taken and sent for analysis.

In patients suspected of CTD-ILD, serum Biomarkers-ANA, Anti-dsDNA, RhFactor, AntiScl70, Anti-Jo1, p-ANCA, c-ANCA were sent and reports were recorded in the thesis proforma. A proforma to suit the study was prepared and all the relevant findings were entered.

Statistical analysis

IBM SPSS software version 21 (IBM Corp., Armonk, NY, USA) was used for analyzing the data. Before analysis, data was checked for consistency and completeness. The data collected was analyzed using relevant descriptive and analytical statistical techniques. Descriptive statistics like percentage, mean and standard deviation were used.

III. Result

A total number of 94 patients were included in the study in the department of Respiratory Medicine, RIMS, Imphal during the study period of August 2018 to July 2020. Mean age of the participants was 60.2±8.7years. The oldest was 89years and youngest was 42years.Majority of participants belong to the age group of 51-60years. According to age wise distribution more than half of the participants were females (55.3%) and males were (44.7%). Among clinical symptoms at presentation, shortness of breath was the most common presenting symptom in 72 patients (76.5%). Dry cough was present in 31 patients (32.9%).And it shows that 43 (45.7%) of patients were smokers and 51 (54.3%) of patients were non- smokers.

Table1: Exposure history (N=13).

Exposure	N	%
Airconditioner	2	15.4
Birds	6	46.2
Hay	4	30.8
Molds	1	7.7

Table1 shows that exposure history was seen with 13 patients. Exposure to birds was seen in 6 patients (46.2%) followed by Hay in 4 patients (30.8%), air conditioner in 2patients (15.4%) and molds in 1 patient (7.7%).

Table 2: Co-morbidities associated with the patients (N=94).

Co-morbidities	N	%
Hypertension	15	16.0
Diabetes	10	10.6
Bronchial asthma	1	1.1
No co-morbidities	68	72.3

Table 2 shows that 15 (16%) patients had hypertension and 10 (10.6%) had diabetes.

Table 3: Physical examination findings among the patients (N=94).

Findings	N	%
Bilateral crepitations	48	51.0
Clubbing	9	9.5
Normal findings	39	41.5

Table 3 shows that most common physical examination finding was bilateral crepitations in 48 patients (51.0%), whereas clubbing was seen in 9 patients (9.5%).

Table 4: Extra pulmonary involvement among the patients (N=94).

Extra pulmonary findings	N	%
Joint pain	12	12.8
Raynaud's and skin lesions	6	6.4
Normal findings	76	80.9

Table 4 shows that joint pain was seen in 12 patients (12.8%) and Raynaud's phenomenon in 6 patients (6.4%).

Table 5: Chest X-ray findings of participants (N=94)

Characteristics	N	%
Reticulonodular opacities	48	51.1
Consolidation	8	8.5
Normal findings	38	40.4

Table 5 shows that Reticulo-nodular opacities (51.1%) was the most common finding in chest x-ray, normal finding in 40.4% and consolidation seen in 8.5% patients.

Table 6: HRCT pattern of patients (N=94).

Characteristics of HRCT pattern	ILD diagnosis	N	%
Subpleural and basilar predominant ground-glass opacities, reticular abnormality, honeycombing (UIP)	IPF	22	23.4
Basilar –predominant ground-glass opacities with or without subpleural sparing, reticular abnormality and no honeycombing (NSIP)	CTD- ILD	27	28.7
	iNSIP	24	25.5
Upper lobe predominant ground-glass opacities, poorly defined centrilobular nodules, mosaic attenuation, air trapping	HP	13	13.8
Diffuse bronchial thickening with micronodules	RB-ILD	5	5.3
Diffuse bronchial thickening with micronodules	DIP	1	1.1

Upper predominant dense micronodules with current or past work occupation	Pneumoconiosis	2	2.1

Table 7: Spirometry pattern (N=58).

Characteristics	N	%
Restrictive	40	68.9
Obstructive	8	13.7
Normal	10	17.2

Table 7 shows that spirometry pattern in most of the patients was restrictive (68.9%), normal in 13.7% and 17.2% obstructive pattern. Restrictive pattern was most commonly with IPF patients (77.3%). Mean FVC was 75.47%±11.9. 19.1% of patients had FVC >/=80% and 42.6% had FVC 50%-79%.

Table 8: Broncho-alveolar lavage (BAL) (N=94).

Characteristics	N	%
Lymphocytes	6	6.4
Neutrophils	4	4.3
Multicellular	5	5.3
Macrophages	3	3.2
Uninterpretable	76	80.9

Table 8 shows that among the patients undergone for bronchoscopy and BAL, lymphocytes was seen in 6.4%, neutrophils in 4.3%, multicellular in 5.3% and macrophages in 3.2%.

Table 9: Serum markers (N=27)

Serum markers	Type of CTD	N	%
Anti-scl70	Scleroderma	16	59.3
Rh F	Rheumatoid arthritis	7	25.9
Anti-dsDNA	Systemic lupus erythematotosis	3	11.1
Anti-JO1	Polymyositis/dermatomyositis	1	3.7

Table 9 shows anti-scl 70 in 16patients, RhF in 7 patients, anti-dsDNA in 3 patients, anti-JO1 in 1 patient.

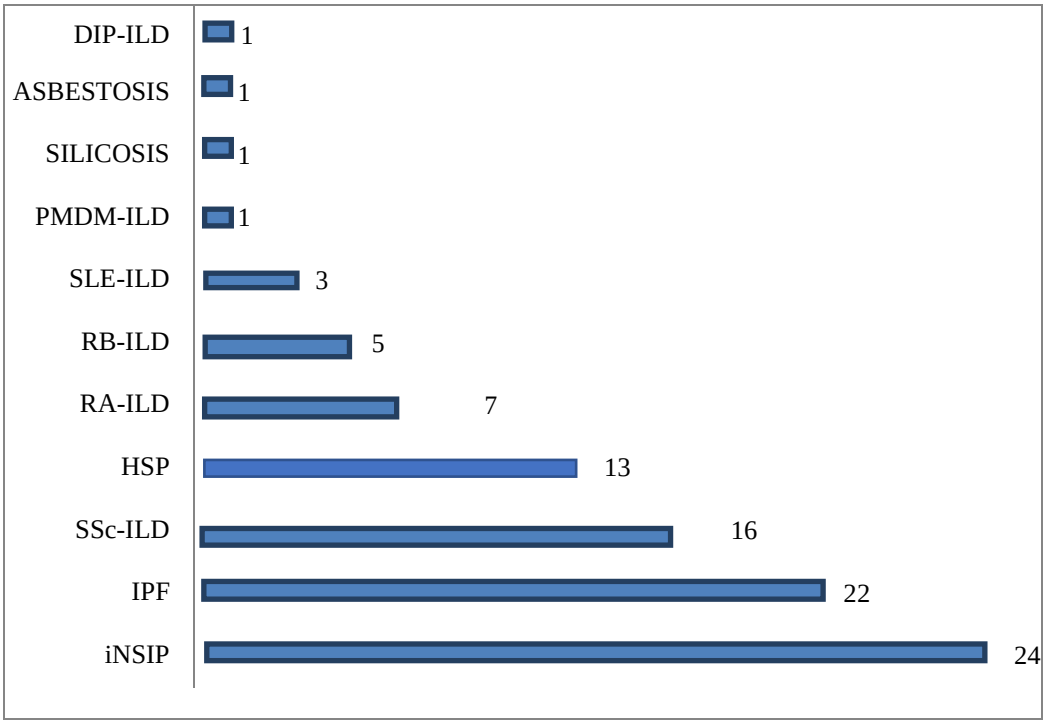

Table 10: Etiologicaldiagnosis of ILDpatients.

IV. Discussion

Epidemiologic information regarding ILDs has varied, likely in part because of differences in patient selection and study design. Differences are also caused by variable reporting of invalidated diagnoses and geographic differences in diagnostic criteria caused by differences in data collection, diagnostic criteria, and strategies.ILD in India has likely been under reported, possibly because of lack of access to adequate diagnostic tests, clinical expertise, and facilities. Some studies in India have found IPF as the most common cause and others CTD-ILD.In our current study, Connective tissue disease-ILD is the most common with Scleroderma as most cases followed by Rheumatoid arthritis, Systemic lupus erythematosus, followed by idiopathic NSIP and IPF. Hypersensitivity pneumonitis is 4rd common cause followed by Smoking related ILD and then Pneumoconiosis. In Kheliouen A[17] study sarcoidosis is the most common disease, followed by ILD associated with connective tissue diseases. In Singh S et al[24] study the most common diagnosis was HP (47.3%) followed by CTD-ILD (13.9%) and IPF (13.7%). Retrospective Study of Interstitial Lung Disease by Sen T and Udwadia ZF[35] showed that Idiopathic pulmonary fibrosis (43%), sarcoidosis (22%), ILDs secondary to collagen vascular disease (19%) as the cause of ILD. The study by Lopez-Campos JLet al[31] reported that most frequent diseases were: idiopathic interstitial pneumonias (38.58%), ILD associated with systemic diseases (20.97%) and sarcoidosis (11.69%).

In the present study most of the patients were found between 51-60 years age group and then 61-70 years age group. Kheliouen A[17] study also correlate with peak incidence between 50 to 59 years. Mean age of patients in thepresent study was 60.18± 8.7. In study by Singh Set al[24], the mean age is 55.3 years. There were 44.7% male and 55.3% female patients which is comparable to 53.8% of females in Singh S et al[24] study. Female predominance is because of more collagen vascular disease group in our study.In the current study 45.7% of patients are smokers and 54.3% of patients are nonsmokers.In the present study exposure history was seen in 20.2% of the patients, where exposure to birds was seen in 7 patients (7.4%), hay exposure in 5 patients (5.3%), air conditioner exposure in 2 patients (2.1) and molds in 1 patient (1.1%). Occupational exposure to silica and asbestosis was seen in 4 patients (4.3%). Recticulo-nodular opacities (51.1%) was the most common finding radiologically (HRCT Thorax) in our study while 76.65% in Gagiya AK et al[2] study. HRCT of the chest is a major help in the diagnosis of ILD and IPF All patients had HRCT chest. It is now well recognized that IPF can be diagnosed based on clinical features and HRCT pattern and may well restricts the indication for surgical lung biopsy.

Although full pulmonary function tests (spirometry, lung volumes, diffusing capacity of carbon monoxide [DLCO] measurements) were not required for inclusion, spirometry was attempted in all patients. A total of 36 patients were unable to perform spirometry in accordance with American Thoracic Society/European Respiratory Society standards, largely because of coughing spells. Among 58 patients who had acceptable and reproducible spirometry, 40 patients had restrictive pattern most commonly seen with IPF and chronic HP, 8 patients had obstructive pattern, and 10 patients had normal spirometry findings. Mean FVC was 75.47%±11.9 in our study. Mean FVC was 75±18 in Kheliouen A[17] study. In Du Bois RM et al[14] study, mean FVC was 77% predicted, with 24% of patients presenting with FVC >90% predicted and 63% with FVC 50-90% predicted.

Serum markers for anti-scl 70 was positive in 16 patients, Rh Factor in 7 patients, anti-dsDNA in 3 patients, anti-JO1 in 1 patient which gives diagnosis for CTD-ILD. HP diagnosis in particular strongly relies on a high index of clinical suspicion and a thorough history to elicit environmental exposures known to be associated with HP andconsistent HRCT imaging patterns. Diagnosis by histopathology would be ideal, but all patients were not be able to be subjected to lung biopsy.BAL findings showed that among the patients undergone for bronchoscopy and BAL, lymphocytes were seen in 6.4% most common in iNSIP patients. Neutrophils was seen in 4.3% mostly in IPF patients, multicellular in 5.3% and macrophages in 3.2% seen common with smoking related ILD.

Limitations of the study was histopathology by surgical lung biopsy (SLB) was not done as it was not feasible to perform SLB in RIMS. Thus, ILD diagnoses made on clinical grounds may not be precise in a proportion of patients.

V. Conclusion

Finding etiology of ILD is must as it will guide in the early diagnosis and management of the disease.Clinical prognosis and response to immunosuppressive therapies are more likely to be determined by the etiology of ILD than any particular radiologic or histopathologic pattern.

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