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An observational study of RA-ILD at tertiary care hospital in eastern India

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Abstract
Introductions: The spectrum of interstitial lung diseases (ILDs) have mainly been reported from the developed countries; data from developing countries is sparse and conflicting. The aim of this study is to describe the distribution of various RA-ILDs from a tertiary care hospital.
Methods: This is an analysis of prospectively collected clinical and demographic data of consecutive subjects with ILDs with special reference to RA-ILD from a single tertiary care medical center. The diagnosis of the specific subtype of ILD was made according to standard criteria for various ILDs.
Results: A total of 100 subjects with mean age and standard deviation 52.21 ± 14.41 and 37.0% male and 63.0% female were enrolled during the study period (March 2017 to December 2018). Cough was the most common symptoms 100.0% followed by 28.0%, shortness of breath (SOB) 98.0%, Wheezing 32.0%, Chest Pan (Pleuritic) 41.0% subjects had a restrictive defect on spirometry It was found that 61% subjects had pallor, 40% subjects had clubbing, 42% subjects had edema, 65% subjects had arthalgia (S/L), 37% subjects had skin manifestations and 14% subjects had mucosal involment. Total in16 no. of RA-ILD cases (9) male (7) female having UIP pattern n-11 & NSIP pattern in n-5 cases.
Conclusion: RA-ILD among the CTD-ILDs was the most common ILDs seen at a tertiary center in earthern India similar to the spectrum reported from developed countries. More studies are required from developing countries to ascertain the spectrum of ILDs in different geographic locales.

Keywords: RA-ILD, CTD-ILD

Introduction
Interstitial lung diseases (ILDs) or diffuse parenchymal lung diseases are a heterogeneous group of disorders characterized by varying degrees of inflammation and fibrosis in the lung parenchyma [1]. Lately, there has been an exponential increase in the understanding of various ILDs. It is essential to differentiate between these various disease entities, as there are significant differences amongst them in the risk factors, pathogenesis, treatment and outcomes [2]. Several studies from across the globe have reported on the incidence, prevalence and the relative frequency of ILDs [3-7]. The annual incidence of ILDs has variably been reported between 1 and 31.5 per 100,000 [3, 4, 6-11]. Unfortunately, a large number of these studies have not used the classification proposed by the 2002 American Thoracic Society (ATS)/European Respiratory Society (ERS) consensus statement on idiopathic interstitial pneumonias (IIPs), which is now considered a benchmark [3, 4, 6-10, 12-15]. Also, a majority of the studies have been performed in the developed countries (Europe and North America). With differences in the genetic profile, environmental factors, occupational exposures, smoking habits, socio-cultural and farming practices in developing countries, the spectrum of ILDs may be different from other regions of the world [16, 17]. There is an unmet need for studies on the epidemiology of ILDs from the developing world. Although, there are a few studies from developing countries that have reported the case-mix of ILDs from tertiary centers, majority of these studies were small and have not used the standard criteria for the diagnosis of various ILDs [15, 18-22]. Herein, we report the spectrum of ILDs from a tertiary care center in eastern India. We also analyze the similarities and differences of the profile of ILDs from other such studies reported from India and worldwide.

Materials and methods
This was an analysis of data prospectively collected between March 2017 and December 2018 in the IMS and SUM Hospital, Bhubaneswar. The Institute Ethics Committee approved the study protocol, and a written informed consent was obtained from all subjects.

Subjects and study procedures
All patients referred to the Chest Clinic with a diagnosis of ILD were included in the study. A detailed history was obtained with regards to the risk factors for various ILDs including

presence of a connective tissue disease (CTD), drug and environmental exposures. The following set of investigations was obtained on the basis of the suspected diagnosis: chest radiograph and high resolution computed tomography (HRCT) of the thorax. Subjects also underwent one or more of the following investigations to obtain a pathological diagnosis: bronchoalveolar lavage, transbronchial needle aspiration (conventional or endobronchial ultrasound-guided), endobronchial biopsy, transbronchial lung biopsy (TBLB) (performed using conventional forceps or with a cryoprobe [cryo-TBLB]), surgical lung biopsy, fine needle aspiration, biopsy of any other involved site such as skin, as required. For subjects who had undergone diagnostic evaluation before the start of the study period, all available data were recorded.

Diagnosis of ILDs

For the diagnosis of other IIPs, the ATS/ERS Multidisciplinary Consensus Classification of the IIPs was followed [1, 2]. A diagnosis of sarcoidosis was made on the basis of consistent clinical and radiological findings, and the presence of granulomatous inflammation in tissue specimens, in the absence of other known causes such as tuberculosis [24-26]. If granulomatous inflammation could not be demonstrated, the diagnosis of sarcoidosis was made after a follow up of six months. A diagnosis of HP was made based on a history of exposure to organic dusts, typical HRCT appearance (any combination of ground glass opacities, ground glass centrilobular nodules, septal thickening, mosaic attenuation and honeycombing), along with histological findings of HP on lung biopsy. A diagnosis of a CTD related ILD was made in the presence of a CTD (rheumatoid arthritis, systemic sclerosis, and others) and the presence of ILD on HRCT of the chest. The subjects were evaluated by a rheumatologist and a diagnosis of CTD was made based on standard criteria. A diagnosis of interstitial pneumonia with autoimmune features (IPAF) was made using the ATS/ERS research statement [27]. All clinical, radiologic, and histopathologic data were reviewed by a multidisciplinary team comprising of pulmonologists (with expertise in ILDs) along with a dedicated pulmonary radiologist and a pulmonary pathologist. In case, a biopsy not feasible, a best fit diagnosis was made on the basis of clinical details, HRCT findings and findings on ancillary investigations (such as ACE levels and autoantibodies). In case, all the available information did not suggest a particular type of ILD, a diagnosis of unclassifiable ILD was made. Subjects who were diagnosed during the study period were termed as incident cases. Subjects who were diagnosed before or during the study period were termed as prevalent cases.

Results

The study is an analysis of data prospectively studied on total 100 patients those are attended pulmonary medicine and rheumatology OPD and IPD of the hospital during study period. This study includes the patients diagnosed as Interstitial Lung Diseases (ILD) whose age ranging from 18 to 80 years old.

A total of 100 subjects with mean age and standard deviation 52.21 ± 14.41 and 37.0% male and 63.0% female were enrolled during the study period. The baseline characteristics of the study subjects are shown in Table 1. Cough was the most common symptoms 100.0% followed by 28.0% smoker, shortness of breath (SOB) 98.0%, Wheezing 32.0%, Chest Pan (Pleuritic) 41.0% subjects had a restrictive defect on spirometry (Table 1).

Table 1: Baseline characteristics of the study subjects (n = 100)

Characteristics		No. of Patients	Percentage (%)
Sex	Male	37	37.0%
	Female	63	63.0%
Clinical Features - Cough	Yes	100	100.0%
	No	0	0.0%
Clinical Features – Sputum	Scanty Expectoration	1	1.0%
	Copious Expectoration	21	21.0%
	No	78	78.0%
Clinical Features – SOB	Yes	98	98.0%
	No	2	2.0%
Wheezing	Yes	32	32.0%
	No	68	68.0%
Chest Pain (Pleuritic)	Yes	41	41.0%
	No	59	59.0%
Cough Duration	Below 6 month	22	22.0%
	6 – 12 month	14	14.0%
	1 – 2 Year	40	40.0%
	More Than 2 Year	24	24.0%
SOB Duration	Below 6 month	22	22.0%
	6 – 12 month	14	14.0%
	1 – 2 Year	37	37.0%
	More Than 2 Year	27	27.0%

From Table 1, it is observed that 78% subjects had dry sputum whereas 22% subjects had purulent and out of that 1% subjects had scanty expectoration and 21% had copious expectoration. Most of the 59% subjects had shortness of breath (SOB) MMRC grading 2 followed by 31% subjects had SOB MMRC grading 3. Overall 40.0% and 37.0% subjects were had past history of cough and shortness of breath (SOB) from last 1 – 2 Year respectively.

RA ILD (n=16)		No. of Patients	Percentage (%)
Sex	Male	9	56.0%
	Female	7	44.0%

A complete physical examination was done for the study subjects are shown in Table 2. It was found that 61% subjects had pallor, 40% subjects had clubbing, 42% subjects had edema, 65% subjects had arthalgia (S/L), 37% subjects had skin manifestations and 14% subjects had mucosal involment. Also it was found that, no any subjects had icterus, cyanosis, lymphadenopathy.

Table 2: HRCT findings of the study subjects (n = 100)

HRCT		No. of Patients	Percentage (%)
UIP	Yes	70	70.0%
	No	30	30.0%
NSIP	Yes	20	20.0%
	No	80	80.0%
Honey Combing	Yes	69	69.0%
	No	31	31.0%
Sub Pleural Reticulations	Yes	58	58.0%
	No	42	42.0%

All 100 subjects underwent an HRCT scan. In 70% subjects HRCT showed a definite UIP pattern, 20% subjects with NSIP, 69% subjects with honey combing, in 58% subjects had presence of sub pleural reticulations. In our study among RA-ILD UIP pattern 11 cases and NSIP pattern in 5 cases. (Table 2).

Table 3: Different Diagnoses of ILDs of the study subjects (n = 100)

Radiological Findings	Yes (%)	No (%)
IPF	28 (28.0%)	72 (72.0%)
Dermatomyosistis -ILD	5 (5.0%)	95 (95.0%)
Polymysositis	4 (4.0%)	96 (96.0%)
Systemic Sclerosis/Scleroderma	9 (9.0%)	91 (91.0%)
Rheumatoid Arthritis	16 (16.0%)	84 (84.0%)
COP	6 (6.0%)	94 (94.0%)
Sjogrens	4 (4.0%)	96 (96.0%)
MCTD	7 (7.0%)	93(93.0%)
SLE	8 (8.0%)	92 (92.0%)
HP	5 (5.0%)	95 (95.0%)
Sarcoidosis	5 (5.0%)	95 (95.0%)
Occupational ILD	1 (1.0%)	99 (99.0%)
Drug Induced-Amiodarone	2 (2.0%)	98 (98.0%)

The results of this study suggest that IPF (28%) and Rheumatoid Arthritis (16%) are the most common ILDs in patients presenting to a tertiary health care center followed by Systemic Sclerosis/Scleroderma (9%), SLE (8%), MCTD (7%), COP (6%), Sarcoidosis (5%), Dermatomyosistis (5%), Hp (5%), Sjogrens (4%) are found ILDs in patients (Table 3).

ECHO finding in RA ILD (n=16)		
PAH	8	50%
NO PAH	8	50%

A total of 100 patients (100%) were diagnosed with Interstitial Lung Diseases (ILD). IPF was the most common diagnosis was found in 28% patients (n=28/100, 28%) followed by Rheumatoid Arthritis was found in 16% patients (n=16/100, 16%). In patients with IPF, most of the 21 patients were male and 7 patients were female. Mean age of IPF patients was 62.36 with S.D. 6.76 and mean age of Rheumatoid Arthritis patients was 50.19 with S.D.11.03. There is significance difference in the mean age of patients with IPF and Rheumatoid Arthritis. In patients with IPF, out of 28 patients, 17 patients had smoking habits, 22 patients had Diabetes, 17 patients had hypertension, 2 patients had hypothyroid, 28 patients had UIP and 6 patients had PAH.

Discussion

This study collected data 100 patients those are attended pulmonary medicine and rheumatology OPD and IPD in Tertiary Health Care Centre during study period. This study includes the patients diagnosed as Interstitial Lung Diseases (ILD) whose age ranging from 18 to 80 years old. Coultas *et al*. (1994) attempted to record existing incidence and prevalence rates of interstitial lung diseases in a population-based study in Bernalillo Country, New Mexico from oct 1988 till sept 1990. The prevalence rates of various interstitial diseases for 105 populations were put as Total interstitial lung disease – 80.9% (male) and 67.2% (female). In present study 37.0% male and 63.0% female were enrolled during the study period with ILDs.

According to Sahajal Dhooria *et al*. Cough was the most common symptom (86.1%) followed by breathlessness (76.1%), weight loss (30.9%), anorexia (24.2%), joint pains (23.9%), and fatigue (17.9%). Most (58.6%) subjects had a restrictive defect on spirometry. In present study Cough was the most common symptoms 100.0% followed by 28.0% smoker, shortness of breath (SOB) 98.0%, Wheezing 32.0%, Chest Pan (Pleuritic) 41.0% subjects had a restrictive defect on spirometry. According to Sahajal Dhooria *et al*. total of 803 subjects (mean age, 50.6 years; 50.2% women) were enrolled between March 2015 to February 2017 of which 566 (70.5%) were diagnosed during the study period. In present study total of 100 subjects with mean (SD) age, 52.21 (14.41) years, whose mean Body mass index 22.87 (1.51) were enrolled during the study period. According to Joh Koh *et al*. 1999 included 129patiermtsd with histologically proven idiopathic interstitial pneumonia (UIP – 35, COP – 24, DIP – 23, AIP – 20, NSIP – 27) in their study. Two observers made correct diagnosis with HRCT in 57% of cases overall, *viz* 25 cases of UIP (71%), 19 cases of COP (79%), 14.5 cases of DIP (63%), 13 cases of AIP (65%), 2.5 cases of NSIP (9%). According to Charlotte Hyldgaard, All 121 patients underwent an HRCT scan. In 60 cases (50%), HRCT showed a definite UIP pattern according to 2011 criteria: presence of subpleural, basal predominance, reticular abnormality, honeycombing with or without traction bronchiectasis, and no inconsistent findings. Of the 61 patients with possible UIP on HRCT, 38 had a biopsy: 30 had a definite UIP pattern on histopathology, 7 had probable UIP and 1 patient had a possible UIP pattern.

According to G.S. Gaude, V. Mahishale and A. Srivastva in 2006 studied Pulmonary Manifestations in HRCT in Connective Tissue Disorders between January 2002 and December 2006, 195 patients with various CTDs having respiratory symptoms were evaluated for respiratory system involvement. Interstitial lung disease (ILD) was the commonest (38.5%) presentation of CTDs. It was observed in nearly three fourth of the cases with scleroderma followed by rheumatoid arthritis (RA) cases (44.5%). In the present study All 100 subjects underwent an HRCT scan. In 70% subjects HRCT showed a definite UIP pattern, 20% subjects with NSIP, 69% subjects with honey combing, in 58% subjects had presence of sub pleural reticulations. In present study it was found that in RA- ILDs patients 8 no out of 16 had PAH in ECHO study.

Conclusion

IPF and Rheumatoid Arthritis were the most common ILDs seen at a Tertiary Health Care Centre in India similar to the spectrum reported from developed countries. In our study significant no of 16 male (9) female (6) with UIP pattern most common presentation with the presenting symptoms of dry cough and breathlessness. In our study out of 16 RA-ILD cases we found PAH in 8 cases. More studies are required from developing countries to ascertain the spectrum of ILDs in different geographic locales.

Among CTD we found RA-ILD was the most frequent diagnosis, and the demographic characteristics were typical. The re-evaluation of CTD-ILD clinical and physical examination, past history of pateints and HRCT finding plays an important role in diagnosis of Rheumatoid Arthritis of ILDs patients. A simple HRCT algorithm with a multicentric approach with Rheumatologist, Pulmonologists and Radiologist experienced in ILD, will be useful in the prediction of outcome in CTD-ILD.

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