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CLINICO RADIOLOGICAL MANIFESTATIONS IN ILD

Pulmonary Medicine

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ABSTRACT

Background: Interstitial lung disease is a term that mainly describes a diverse collection of more than 200 lung disorders. Interstitial lung diseases (ILD) are a heterogeneous group of disorders that were characterized by varying degrees of fibrosis and inflammation of lung parenchyma leading to restrictive pathology with a characteristic clinical, radiological, physiological, and pathological manifestations. The number of ILDs of unknown cause is also huge. The most common are Idiopathic Pulmonary Fibrosis (IPF), Nonspecific Interstitial Pneumonitis (NSIP), ILDs associated with connective tissue diseases (CTD-ILDs). So, establishing an accurate diagnosis of ILD can be challenging for clinicians. With diversities in the genetic profile, environmental factors, occupational exposures, farming practices, smoking habits and socio-cultural activities in developing countries, the spectrum of ILDs may be distinct from other regions of the world. The development of High Resolution Computed Tomography (HRCT) of the chest and availability of video-assisted thoracoscopic lung biopsy has added to our diagnostic strategies. A multi-disciplinary approach is necessary for the diagnosis of interstitial lung diseases. **Aim:** Our study was done to evaluate the clinical and radiological manifestations in interstitial lung diseases. **Material & Methods:** 100 patients of interstitial lung diseases were enrolled in this study after taking informed consent. All the patients were clinically examined and HRCT was done. Clinical and radiological manifestations in varies interstitial lung diseases were exhibited. **Results:** IPF is the most common ILD followed by NSIP. Results showed that collective approach of clinical and radiological manifestations are useful in diagnosing ILD. **Conclusion:** Many patients are mis-diagnosed as ILD as it is not possible to diagnose with clinical features, chest x-ray and spirometry findings. HRCT chest must be needed to confirm the diagnosis of ILD.

KEYWORDS

Interstitial Lung Disease (ILD), Idiopathic Pulmonary Fibrosis (IPF), Nonspecific Interstitial Pneumonitis (NSIP), High Resolution Computed Tomography (HRCT).

INTRODUCTION

Interstitial Lung Disease(ILD) is a term that mainly describes a diverse collection of more than 200 lung disorders. These diseases were classified together because they all affect the tissue and space around the alveoli, called the interstitium. The interstitium is a connective tissue within the lung that contains basement membrane of alveoli and capillaries and peri-vascular and peri-lymphatic tissues. It supports lung, helps in fluid balance, gas exchange and performs repair and re-modelling when damage occurs.

Interstitial lung diseases are a heterogeneous group of disorders that were characterized by varying degrees of fibrosis and inflammation of lung parenchyma leading to restrictive pathology with a characteristic clinical, radiological, physiological, and pathological manifestations[1]. The number of ILDs of unknown cause is also huge. The major types are Idiopathic Pulmonary Fibrosis(IPF), Sarcoidosis, Nonspecific Interstitial Pneumonitis(NSIP), Connective Tissue Diseases associated ILDs(CTD-ILDs).

The exact prevalence and incidence of ILDs are unknown. It was reported to be 81/100,000 for men compared with 67/100,000 for women in few studies and the incidence increases with age[1,2]. Among men and women who are 75 years or older the prevalence of idiopathic pulmonary fibrosis was 250/100,000, and the incidence was 160/100,000/year[1]. With diversities in the genetic profile, environmental factors, occupational exposures, farming practices, smoking habits and socio-cultural activities in developing countries, the spectrum of ILDs may be distinct from region to region[3,4]. It was challenging to differentiate alveolar filling pattern cases from ILD in the clinical picture, which results in a delay in diagnosis.

The development of High Resolution Computed Tomography(HRCT) of the chest and availability of video assisted thoracoscopic lung biopsy has added to our diagnostic strategies. A multidisciplinary approach is necessary for the diagnosis of interstitial lung diseases.

MATERIALS AND METHODS:

SOURCES:

The study was conducted on 100patients including both inpatients and outpatients of Respiratory Medicine department at NRI Medical College, General and Superspeciality Hospital, Chinakakani, Guntur from January 2021 to December 2022.

Inclusion Criteria:

1. All patients with interstitial lung diseases attending Respiratory Medicine department, NRI Medical College, General and Superspeciality Hospital.
2. Subjects of both sex and age more than 18years are included.

Exclusion Criteria:

1. Those patients who refuse to give consent.
2. Subjects below 18years of age.

METHODS:

After taking the consent, a detailed proforma was filled for each patient, covering various aspects like preliminary information like name, age, sex, occupation, presenting symptoms, past history, treatment history, family history and personal history. This was followed by a detailed physical examination of the patient, including general examination, respiratory system examination and other system examination. All patients were subjected to required investigations.

The Following Investigations Were Done

1. PULSE OXIMETRY both at rest and on exertion
2. 6 MINUTE WALK DISTANCE
3. CHEST X-RAY PA View
4. HRCT CHEST
5. ARTERIAL BLOOD GAS ANALYSIS
6. ELECTROCARDIOGRAM
7. ECHOCARDIOGRAPHY
8. BRONCHOSCOPY
9. SPIROMETRY
10. SERUM ANGIOTENSIN CONVERTASE ENZYME LEVELS
11. SERUM CALCIUM
12. ERYTHROCYTE SEDIMENTATION RATE
13. COMPLETE BLOOD PICTURE
14. CONNECTIVE TISSUE PROFILE

OBSERVATION AND RESULTS

A total of 100patients who met the inclusion and exclusion criteria are included in the study. Of them, 55 are males and 45 are females. About 62patients are below 60years with predominant cases in the age group of 50 to 59 & 60 to 69 consisting 56% of cases.

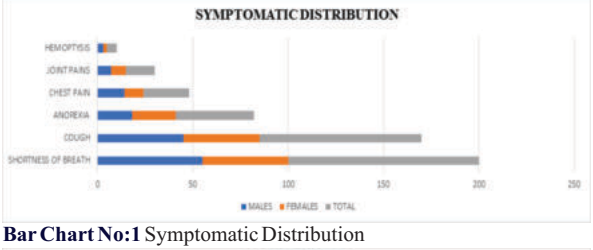
Table No:1 Age And Sex Distribution

AGE (Years)	MALES	FEMALES	TOTAL	PERCENTAGE (%)
20-29	02	02	04	04
30-39	05	01	06	06
40-49	10	10	20	20
50-59	18	14	32	32
60-69	12	12	24	24
70-79	06	06	12	12
>80	02	00	02	02
TOTAL	55	45	100	100

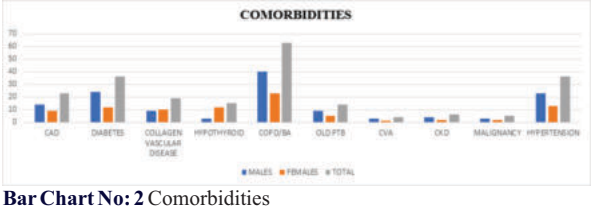
All the 100patients in the study has Velcro crepitations and 50patients with Clubbing.

Table No:2 Clinical Findings

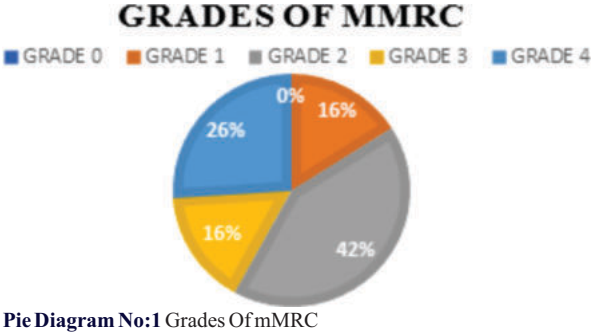
FINDINGS	MALES	FEMALES	TOTAL
CLUBBING	32	18	50
VELCRO CREPTATIONS	55	45	100



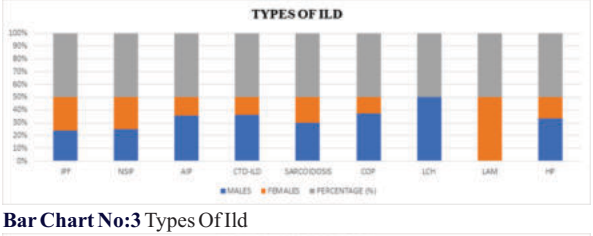
Bar Chart No:1 Symptomatic Distribution



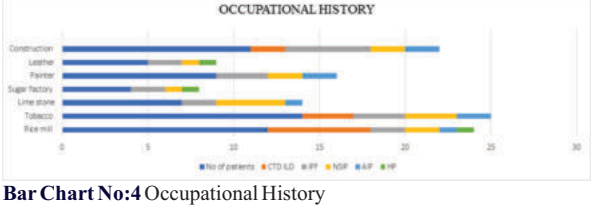
Bar Chart No: 2 Comorbidities



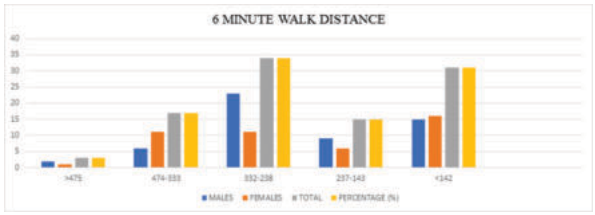
Pie Diagram No:1 Grades Of mMRC



Bar Chart No:3 Types Of Ild



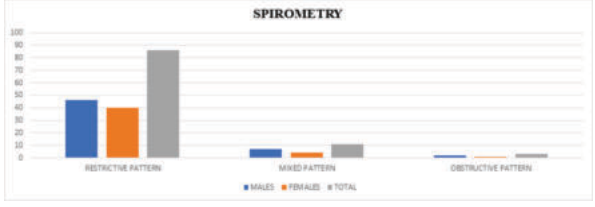
Bar Chart No:4 Occupational History



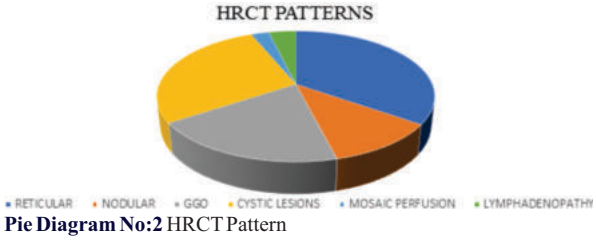
Bar Chart No:5 6 Minute Walk Distance

Table No:3 ABG Readings

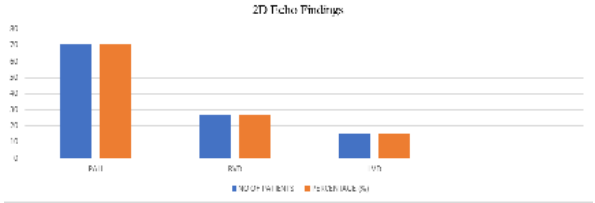
Pao2 in ABG (mm Hg)	MALES	FEMALES	TOTAL
79-70	14	13	27
69-60	19	13	32
59-50	11	9	20
<50	9	7	16



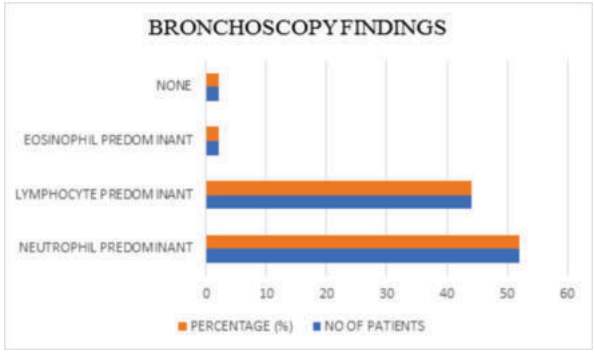
Bar Chart No:6 Spirometry



Pie Diagram No:2 HRCT Pattern



Bar Chart No:7 ECHO Findings



Bar Chart No:8 Bronchoscopy Findings

DISCUSSION

The burden of ILD was unknown in India due to under-recognition, lack of awareness, scarcity of diagnostic facilities as well as to the vast spectrum of differential diagnosis. Data on clinical presentation and diagnosis of the spectrum of ILDs from India was minimal. The current study is on clinical and radiological presentations in ILD patients attending NRI General and Super Speciality Hospital, Guntur.

Sex Ratio:

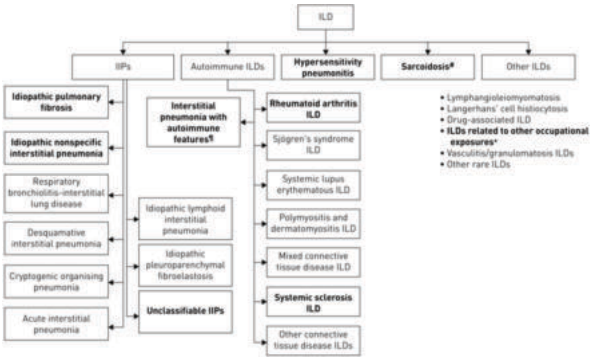
In the present study of 100patients, male patients are 55(55%), and female patients are 45(45%). Male sex predilection is seen in our study.

Mean Age:

In the current study, the average age of the study population is 55years,

with a standard deviation of 12.46years.

Out of the total 100patients, 62patients were found to be below 60years of age, and the other 38patients were above 60years of age. The peak incidence is found in between 50-69years. Majority of the patients about 32% were between 50-59years age group.



Symptomatology in ILDs:

In present study, the most common symptom at the time of presentation was breathlessness seen in all 100cases (100%), cough in 85(85%)patients followed by loss of appetite in 41patients(41%), chest pain in 24(24%)patients and joint pains in 15(15%)patients, hemoptysis was seen only in 05patients(05%).

Dyspnea in interstitial lung diseases is believed to be due to altered mechanics of breathing involving increased work of ventilation. The cough may be due to the cough receptors in the lung that are sensitive not only to mucosal and pleural stimuli but also to the changes in the mechanism of lung expansion. It may be due to chronic hypoxia and its effect on metabolism.

In Abhishek et al. study[5], cough and dyspnea are the most common features present in 45(90%) & 40patients (80%). This feature was similar to our study. Other features at presentation include fever, hemoptysis, and joint symptoms in a few patients.

Similar findings observed in a study by Varun das et al[6], where cough and progressive breathlessness were the most common symptoms observed in 97.1% and 98.5% while other symptoms like fever and chest pain were rare.

In the present study, the most common clinical findings observed were end inspiratory crepitations in all 100 patients(100%), and clubbing observed in 50patients(50%). Crepitations might be produced by fluid accumulation in the tiny air passages, where drainage was hampered by peri-bronchial and interstitial fibrosis. Clubbing may be due to associated anorexia that leads to nutritional deficiency.

In Abhishek et al. study[5], Clubbing(12%) was seen.

In Varun das, et al. study[6], End inspiratory velcro crackles or crepitations were the most common examination finding in 138(98.57%) followed by clubbing in 78(55.7%).

In present study patients shows shortness of breath with mMRC grade1 in 16(16%), mMRC grade2 in 42(42%), mMRC grade3 in 16(16%) and mMRC grade4 in 26(26%) cases.

In a study done by Spyros A. Papiris et al[7]. 26 patients were studied; all patients claimed some degree of dyspnea. There were 7(26.9%) patients with mMRC grade1, patients with grade2 are 11(42.3%), 6(23.07%) patients are with mMRC grade3 dyspnea and 2(7.6%) patients with mMRC grade4 dyspnea.

In Ramakrishna R et al. study[8], among 52 cases, 12(23%) were of grade1 mMRC, 24(46%) were of grade2, mMRC, 11(21%) were of grade3 mMRC, 5(9%) were of grade4 mMRC.

Co-morbidities and ILDs:

In the present study, the most common co-morbidities noted are obstructive airway diseases seen in 63(63%), followed by diabetes mellitus and hypertension in 36(36%) cases each, coronary artery disease in 23(23%), collagen vascular disease in 19(19%), hypothyroid in 15(15%), past history of tuberculosis in 14(14%), chronic kidney disease in 06 (06%), cerebrovascular accident in 04(04%) and malignancy in 05(05%) cases.

In Varun das, et al. study[6], common co-morbidities are gastroesophageal reflux disease, sleep disordered breathing, coronary artery disease, psychiatric manifestations like depression and anxiety, chronic obstructive lung disease, venous thromboembolism and lung cancer. In their study, the most common co-morbidity was gastroesophageal reflux disease seen in 76.42%.

In Kumar A et al. study[9], the presence of co-morbidities was not unusual with diffuse parenchymal lung disease but in their study most frequently associated co-morbidity was hypertension and diabetes seen in 16.4% and 12.3% cases. In this study, gastroesophageal reflux was seen in 17.8% cases, commonly observed among IPF(24%) cases.

Types of ILDs:

Most common etiology seen in the present study is Idiopathic pulmonary fibrosis(IPF). It is found in 46 cases (46%). Next common etiologies are Non specific interstitial pneumonia(NSIP) in 20(20%) cases followed by Connective tissue disease related interstitial lung disease in 11(11%), Acute interstitial pneumonia in 07(07%), Sarcoidosis in 05(05%) cases, Cryptogenic organising pneumonia(COP) 04(04%), Hypersensitivity pneumonitis 03(03%), Langerhans cell histiocytosis(LCH) 02(02%), Lymph angio-leio myomatosis(LAM) 02(02%) cases.

HRCT PATTERN	PRESENT STUDY SEN AT AL	MUHAMMED ET AL BADARKHE PATIL ET AL
IPF	46%	39%
	43%	36%
NSIP	20%	24%
	18%	14%
CTD-ILD	11%	24%
	18%	30%
AIP	07%	00%
	01%	14%
SARCOIDOSIS	05%	13%
	22%	02%
COP	04%	04%
	02%	10%
HP	03%	17%
	06%	02%

As compared to literature, more patients of COP (Cryptogenic organising pneumonia) and AIP (Acute interstitial pneumonia) were noted in our study and which might be due to the difference in the selection criteria.

In Sanjeev Kumar et al. study[10], etiological distribution was IPF 28(34.14%), desquamative interstitial pneumonia 14(17.07%), cryptogenic organizing pneumonia 08(09.75%), nonspecific interstitial pneumonia 17(32.92%), and RB-ILD - 15(18.29%) types of ILDs. Most of the differentiation was based on the HRCT pattern.

In Ramakrishna R et al. study[8], a total of 52 patients were diagnosed to have interstitial lung diseases. Among these cases, Idiopathic pulmonary fibrosis accounted for 46%. Non-IPF interstitial lung diseases accounted for 54%, Among 28 cases of Non-IPF constituting of 54% of ILD patients, in those NSIP constituted 21%, NSIP with CTD(12%), Hypersensitivity pneumonitis(13%), Rare ILDs - LAM and LCH for (4%) and drug-induced ILD (4%).

Duration Of Illness:

The mean average duration of illness in the present study is 6.44months. In IPF the mean average duration of illness is 7.43months, in NSIP 5.21months, in AIP 3months, in CTD-ILD 7months, in Sarcoidosis 6.66months, in COP 6months, in LCH 9months, in LAM 5months and HP is 8months respectively.

In Gagiya Ashok et al. study[11], patients present with 1-3 years duration of illness (33.33%) but many patients also present below one year (23.31%) or above three year duration (20%).

Mahasur et al[12] had found that duration of illness was up to 1 year in 30%, 1-2 year in 18%, 3-5 year in 24% and beyond five years in 28%.

In the present study, female sex preponderance observed in IPF

patients. A total of 46cases seen in which 24cases are females, and 22cases are males. Non-IPF cases reported in 54cases in which predominant are NSIP.

Virendra Singh study[13] showed female preponderance in ILD patients. In Ramakrishna, R et al[8] study had female preponderance, and IPF constituted 46% of total ILD patients.

Smoking and ILDs:
In the current study, most of them are non-smokers. Out of 42 smokers, 40 are males, only 2 females, In these 25 cases are below 20 pack years, and 17cases are above 20 pack years.

In Abhishek et al. study[5], Smoking pattern in their study group shows that only eight patients out of 50patients are a smoker (16%), While 42 patients are non-smokers (84%).

In Ramakrishna R et al. study[8], the majority of their patients are non-smokers. Among 48 patients of IPF 18 of the twenty male patients were smokers. Two male patients were non-smokers. Among twenty-eight female IPF patients, twenty-seven were non-smokers. One patient gave a history of limited cigar smoking.

Occupational History:
In our study, 12rice mill workers are associated with ILDs like CTD-ILD in 6cases and NSIP and IPF in 2 cases each, Tobacco workers and construction works are the next major occupations of patients with painters and lime stone workers to follow.

In Kathy B Baumgartner study[14], Occupational and Environmental Risk Factors for Idiopathic Pulmonary Fibrosis: A Multicenter Case-Control Study; Although not statistically significant regarding 248 cases observed for occupational exposures, at least a 50 percent increase in risk for IPF was associated with farming, hairdressing, painting, printing, textile work, welding, and wood dust for all subjects combined.

In Kaushik Saha et al[15] study showed at-risk occupations include miners (pneumoconiosis); sandblasters and granite workers (silicosis); welders, shipyard workers, pipefitters, electricians, automobile mechanics (asbestosis); farm workers, poultry workers, bird fanciers, bird breeders (HP); and workers in aerospace, nuclear, computer and electronic industries (berylliosis). History of existing, persistent environmental "fibrogenic" factors at home; in the workplace; in automobiles; infrequently visited facilities/homes; associated with hobbies, like exposure to birds, molds, woodworking; or the use of saunas and hot tubs usually were ignored but are equally important and they may provide useful clues.

6MWD:
In the present study, six-minute walk distance (6MWD) is divided into four groups with their distance covered. Reasonable distance achieved is seen in 3cases(3%), mild restriction (474m-333m) is seen in 17cases(17%), moderate restriction (332m-238m) is seen in 34cases(34%), severe restriction (237m-143m) is seen in 15cases (15%) and very severe restriction (<142m) is seen in 31cases(31%). The mean distance covered is 191.2m. This finding has clinical implications as studies have advocated that desaturation during 6MWD is a marker for increased risk of mortality.

In Abhishek et al. study[5], on 6MWT, 34% of cases showed significant desaturation (SPo2< 88% or 4 % fall from the baseline) at presentation. In Ramakrishna R et al. study[8], six-minute walk test revealed 75% of ILD patients desaturated to >4% of their resting SpO2 on exercise.

ABG and ILDs:
In the present study, arterial blood gas analysis values are divided into four groups based on pao2 levels. In this study mild hypoxemia (79-70mmhg) is seen in 27cases(27%), moderate hypoxemia (69-60mmhg) is seen in 32 cases(32%), severe hypoxemia (59-50mmhg) is seen in 20cases(20%), very severe hypoxemia (<50mmhg) is seen in 16cases(16%) and normal pao2 levels seen in 5 cases. The average Pao2 value is 60mmHg.

In Varun das et al. study[6], on ABG, the average PaO2 was 73.22 (12.16) mmHg, PaCO2 was 37.445 (SD) mmHg, and A-a gradient was 29.25 (13.16).

Spirometry and ILDs:
In the present study, Spirometry is done in all patients, shows the restrictive pattern in most commonly in 86cases (86%), the mixed pattern is seen in 11cases(11%), and the obstructive pattern is seen in 3cases(3%).

In Ramakrishna R et al. study[8], Spirometry revealed 69% of the ILD patients have the restrictive defect, 4% of ILD patients have obstructive defect and 26.92% have a combined obstructive and restrictive defect.

In Varun das, et al. study[6], the most characteristic spirometry abnormality in ILD is a restrictive abnormality with decreased DLCO. Due to easy availability, Spirometry can be a beneficial aid in the diagnosis, prognostication and assessing response to therapy.

In our study, all the patients showed restrictive abnormality. The average FVC was 1.58(53%)litres.

In Sanjeev Kumar et al. study[10], PFTs were done in 71 of the total 82 patients, and the results were the mild restriction in 12 (16.90%), moderate in 36 (50.70%), and severe in 23 (32.39%) of them.

HRCT Patterns:
In the present study, the most common HRCT chest pattern observed is the reticular pattern in 83cases, followed by cystic lesions in second place with 67cases, ground-glass opacities seen in 47cases, nodular opacities seen in 27 cases, mosaic perfusion seen in 6cases and Hilar lymphadenopathy is seen in 9cases.

In Varun das, et al. study[6], the most important HRCT findings were interlobular and intralobular septal thickening in 111cases(79.8%), Honeycombing in 56cases(40%), centrilobular nodules in 24cases(17.14%), ground-glass opacities in 21cases(15%), mediastinal lymphadenopathy and emphysema.

A study done by Venkata Ramana et al[16] showed septal thickening in 42%, honeycombing in 38% and ground-glass opacities in 20%.

2D-ECHO Findings:
In present study, most common presentation seen in echocardiography (2D ECHO) is pulmonary arterial hypertension (RVSP > 25mmhg), which is seen in 71cases(71%), followed by right ventricular dysfunction and corpulmonale changes in 27cases(27%) and isolated left ventricular dysfunction and ischemic heart disease is seen in 15cases(15%).

In Kumar A et al. study[9], Pulmonary Hypertension by Echocardiography was seen in 12.3% cases. While in other studies, it was seen from 17-30%.

In Ramakrishna R et al. study[8] among 52 patients, 45(86%) patients have pulmonary hypertension. Among them mild PHTN was present in 11patients(21.15%), moderate PAH was present in 23patients(44.23%), severe PAH was present in 11patients(21.15%), PAH was absent in 7patients(13.4%).

Bronchoscopic Findings:
In the present study, the most common cells present in bronchial washings are Neutrophils with 52cases(52%), followed by Lymphocyte predominant in 44cases(44%), eosinophil predominant in 02cases(2%) and no specific pattern of cells seen in 02cases(2%).

In Ramakrishna R et al. study[8] out of 52 patients, 22(42.3%) patients of IPF had predominant neutrophil cytology in BAL fluid, and 2(3.8%) patients with IPF had lymphocyte-predominant cytology. All of the 28patients (53.8%) with non-IPF showed lymphocyte-predominant cytology.

In a study done by Boubacar Efared1 et al[17], out of 141 patients, 22% had Sarcoidosis, 15.6% had idiopathic pulmonary fibrosis(IPF), 14.18% had other idiopathic interstitial pneumonia(IIP), and 9.9% had connective tissue disease, IPF had higher neutrophils count (87%).

SUMMARY:
In the present study, 100patients diagnosed as ILD based on Clinical, Radiological and PFT findings, attending OPD or admitted in NRI General and Superspeciality Hospital, Chinakakani were included. They were observed according to their demographic features, clinical

characteristics and radiological findings. The Clinical, Radiological and Spirometry findings were included in a specific proforma designed for the study.

- There were 55males and 45females, with slight male sex predilection seen in the study.
- Sixty-two patients were between 50-69 years of age. The mean overall age of patients was 55years.
- The common symptoms at presentation included breathlessness(100%), cough(85%) followed by anorexia (41%), chest pain(24%), joint symptoms(15%) and hemoptysis(5%).
- The most common clinical finding noted was end-inspiratory crepitations(100%), and clubbing(50%).
- The common co-morbid conditions associated were obstructive airway diseases(63%), hypertension(36%), diabetes mellitus(36%), coronary artery disease(23%), collagen vascular disease(19%), hypothyroid(15%), past history of tuberculosis(14%), chronic kidney disease(06%), cerebrovascular accident(04%) and malignancy(05%).
- IPF came out as the most common cause of ILD with 46patients(46%) followed by NSIP(20%) and others with low percentages.
- The Mean duration of illness at presentation was 6.44 months.
- Among IPF cases, female sex predilection was seen, out of 46cases, 24 are females, and 22 are males.
- Twelve rice mill workers were associated with 6cases of CTD-ILD(6%) and a 2cases each with both IPF and NSIP. Fourteen tobacco factory workers were associated with 3cases each of IPF, NSIP, and CTD-ILD. 11construction workers with 5cases of IPF, and 2cases each of CTD-ILD, NSIP and AIP. Some cases in lime stone workers, painters, leather workers are also seen.
- The average Pao2 value is 60mmHg. Most of the patients 52 were in between 50-69 mmHg.
- Spirometry showed a restrictive pattern in most of the cases(86%), mixed pattern(11%), and obstructive pattern in 3cases (3%).
- Most common HRCT chest pattern noted was the reticular pattern(84%), followed by cystic lesions(62%), ground-glass opacities(48%), nodular opacities(26%), mosaic perfusion(6%) and Hilar lymphadenopathy (6%).
- Most common presentation seen in 2D echocardiography was pulmonary arterial hypertension(70%), followed by right ventricular dysfunction and cor-pulmonale changes(26%) and isolated left ventricular dysfunction and ischemic heart disease(14%).
- Most common cells present in bronchial washings are Neutrophils with 52cases(52%), followed by Lymphocyte predominant in 44cases(44%), eosinophil predominant in 02cases(2%) and no specific pattern of cells seen in 2cases(2%).

CONCLUSION:

Interstitial lung diseases are a diverse group of acute and chronic bilateral lung diseases of known and unknown etiologies that pose a diagnostic and therapeutic challenge to the clinician. Both the clinicians and patients confronted with ILD are understandably frustrated as there is no cause or cure for most of ILDs. To add to the concern, studies on the spectrum of interstitial lung diseases in developing countries are sparse and conflicting. ILDs are now frequently diagnosed. Many patients are misdiagnosed ILD as it is not possible to diagnose with clinical features, chest x-ray and spirometry findings. HRCT chest must be needed to confirm the diagnosis of ILD. With the advent of HRCT chest in ILD cases, the clinician may avoid lung biopsy to conclude the disease. It is essential to differentiate ILD of known etiology from unknown etiology, because of poor prognosis noted in unknown etiology. It is essential to diagnose ILD early in the course of the disease to prevent progression of the disease into fibrosis state and improve the outcome. More extensive clinical studies need to establish the true incidence and spectrum of interstitial lung diseases. Increased awareness in patients provides early diagnosis, and this may control the high mortality rate on the disease.

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