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Clinical Profile Of Connective Tissue Disease Related Interstitial Lung Disease At A Tertiary Care Centre In Western Maharashtra

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Abstract
Background and objectives*: Interstitial involvement is a common manifestation of connective tissue disorders, presenting with a number of different inflammatory responses within the lung. Connective tissue disorders-interstitial lung disease (CTD -ILD) represents a complex intersection of autoimmune disorders and pulmonary pathology significantly impacting patient morbidity and mortality. We aim to illustrate the clinical profile, diagnostic tests and outcome of CTD-ILD based on extensive review of the cases.*
Methods*: We evaluated patients diagnosed with ILD associated with connective tissue disorders who were selected based on predefined inclusion criteria which included clinical symptoms, radiological findings and serological markers.*
Results*: The study population predominantly had female preponderance with most patients aged 60 and above. Rheumatoid arthritis is the most common associated CTD and hypertension is the most common associated comorbid condition. HRCT revealed UIP as the most frequent pattern. Outcomes included a majority being discharged on oxygen therapy.*
Conclusion*: ILD can be a presenting condition in connective tissue disorders. If diagnosed early, it has a better outcome where extensive lung damage can be prevented. Given the high discharge on home oxygen therapy in our study, there is a critical need for targeted management strategies like regular monitoring, tailored rehabilitation programs, enhanced patient education on disease management and lifestyle modifications to reduce the morbidity.*
Keywords – *Interstitial lung Disease, Connective tissue disorders, Clinical profile, UIP*

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I. Introduction:

Interstitial lung diseases (ILDs) are a heterogeneous group of diffuse parenchymal lung disorders of known or unknown cause, with varying degrees of inflammation or fibrosis [(1)].The clinical spectrum ranges from mild, self-limiting disease to progressive irreversible pulmonary fibrosis. It can be seen due to various etiologies. Among Systemic diseases connective tissue diseases are one of the most common causes of ILD. In a minority of patients, ILD may be the presenting or the only manifestation of an underlying CTD. ILD may present even before the CTD diagnosis is made. Some patients who have ILD and do not meet clinical criteria for CTDs may have lung predominant form of a CTD.[(2)]Some evidence suggests that the incidence of ILD is increasing in CTD patients.[(3)]The prognosis of patients with connective tissue disease (CTD) has improved significantly in recent years, but interstitial lung disease (ILD) associated with connective tissue disease (CTD-ILD) remains a refractory condition, which is a leading cause of mortality. Because, the clinical course, treatment response, prognosis, degree of reversibility, and optimal therapy differ for each disease presentation, a thorough knowledge of the pulmonary clinical picture of each CTD-ILD is important. Hence, the present study was conducted to recognize clinico- radiological profile of pulmonary involvement associated with different forms of CTDs, which may impact survival of these patients.

II. Materials And Methods:

This prospective observational study was done in the department of respiratory medicine of a tertiary care centre, after obtaining ethical clearance. Analyzing the clinical profile of CTD-related ILD, particularly in a regional setting like Western Maharashtra, typically involve an evidence based approach.

About 15 cases of CTD-related ILDs were included in the study. Patients were followed over a time period of 18 months and clinical data was collected systematically. Data was collected using a multidisciplinary framework to ensure comprehensive evaluation of each patient.

Study population included OPD and IPD patients attending department of Respiratory medicine in a tertiary care centre.

Inclusion criteria- all patients clinically suspected, radiologically and serologically confirmed cases of CTD-ILD, and patients who were willing to participate in the study on their free consent.

Exclusion criteria- Patients age less than 12 years.

Patients were diagnosed with CTD-related ILD based on a multidisciplinary approach involving pulmonologist, rheumatologists and radiologists. Clinical diagnosis included a detailed history -taking for symptoms such as breathlessness, dry cough and fatigue, history of smoking or exposure to environmental toxins, past medical history, associated co morbidities, occupation of the patient and thorough physical examination for signs like clubbing, crackles on auscultation, and specific signs of underlying CTD like joint deformities, skin thickening or skin rash.

In these cases of CTD-ILD, the clinical history, examination, ABG, hematological, biochemical laboratory investigations, CTD profile, spirometry, and HRCT thorax findings were noted. Specific autoimmune markers including anti-nuclear antibodies(ANA) Blot, rheumatoid factor and anti-cyclic citrullinated peptide (anti-CCP) antibodies were tested to confirm underlying connective tissue disorders. Two-dimensional echocardiography was done to rule out pulmonary hypertension. Data was analyzed and presented as percentages and mean.

III. Results:

Clinical profile of 15 cases of CTD-related ILDs was noted. Of these, 4 (27%) were male patients, while 11 (73%) were females with M: F of 1:2.75 as shown below in figure 1. Most of the patients fell in the age group 60-69 years of age, comprising 7 patients (46%) as shown in figure 2. The most common occupation noted was housewife and the most common presenting symptom that was cough and dyspnea on exertion as shown in figure 3. The most common comorbid condition associated with CTD-ILD was hypertension. Other comorbid conditions associated were diabetes (1 patient) and ischemic heart disease (2 patient).

Post-exercise desaturation and bibasilar fine end inspiratory rales were seen in all patients.

The most common type of CTD-ILD was RA-related ILD, seen in 5 patients (33%), next being Sjogren's syndrome-related ILD, and the mixed CTD-related(MCTD) ILD seen in 3 patients each (20%), followed by SLE-related ILD and ILD related to dermatomyositis seen in 2 patients each (13%).On HRCT thorax, usual interstitial pneumonia (UIP) was the most common pattern seen in 10 patients (67%), NSIP was seen in 4 patients (27%), and cystic bronchiectasis was seen in one patient.5 out 15 patients had mild Pulmonary artery hypertension (PAH) with dilated right atrium and right ventricle and good ejection fraction.1 patient had concentric Left ventricular hypertrophy with grade 1 diastolic dysfunction. Other patients had no PAH with good ejection fraction.

Majority of patients (8 out of 15) were discharged on home oxygen therapy. Outcome also included 1 death and remaining patients (6) were discharged off oxygen.

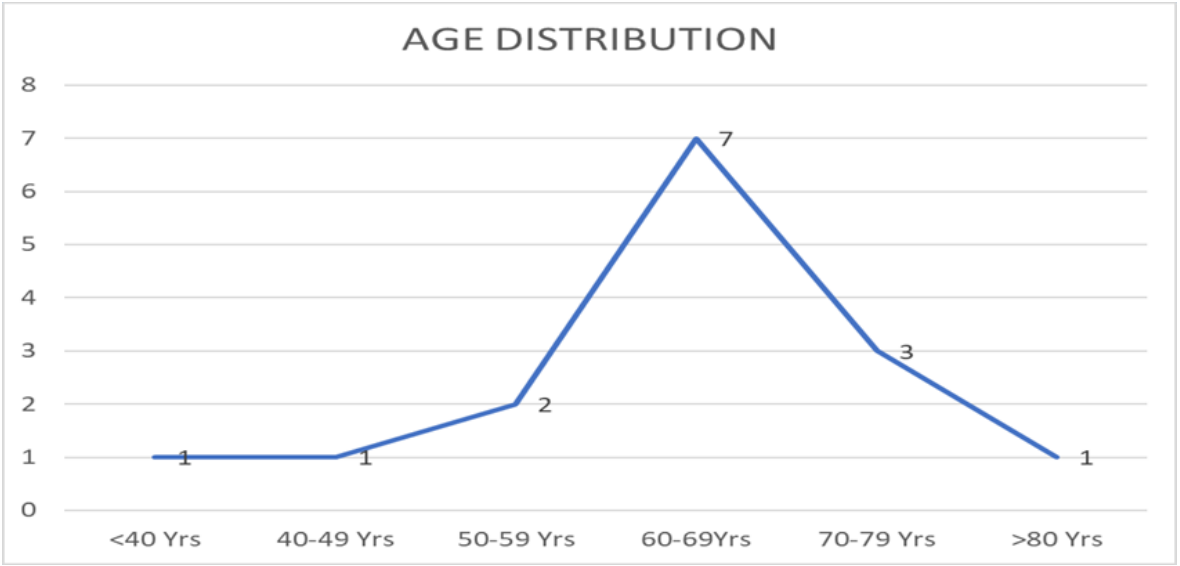


Figure 2: age distribution of study population

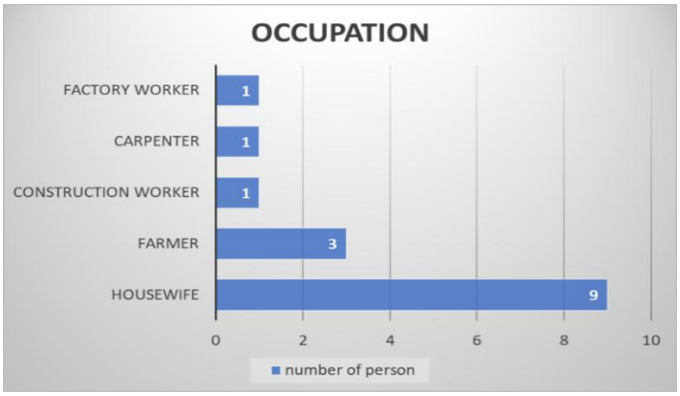


Figure 3: occupation distribution of study population

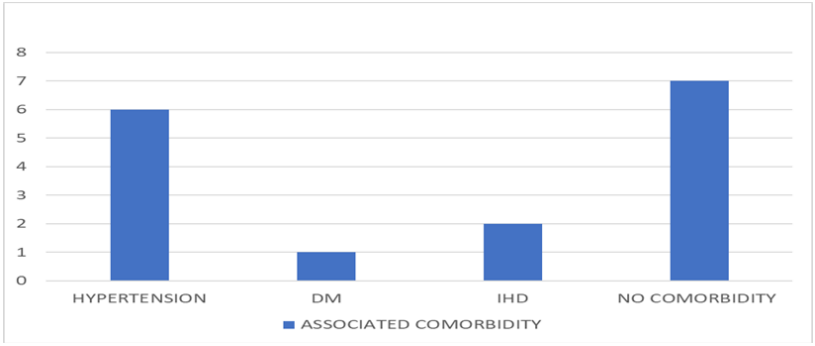


Figure 4: Distribution of associated comorbidity

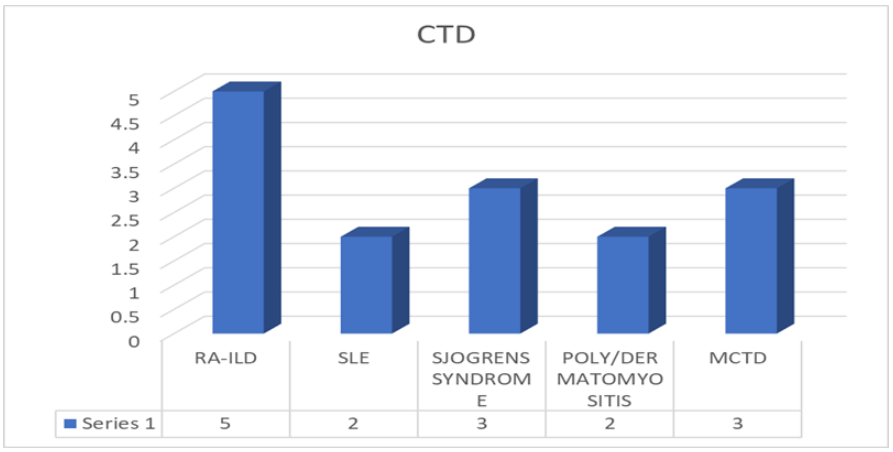


Figure 5: Distribution of CTD related to ILD.

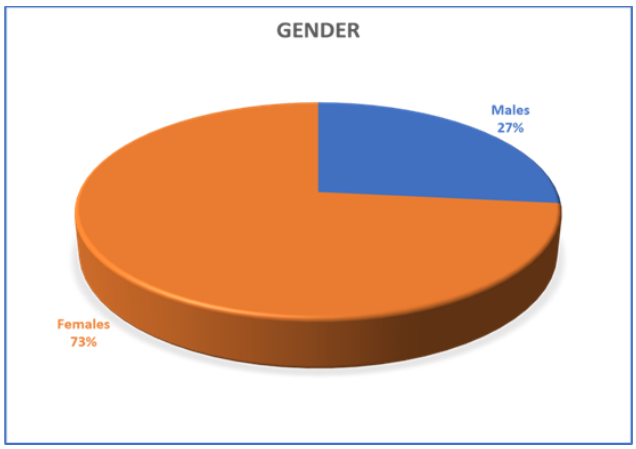


Fig 1: Gender distribution of the study population

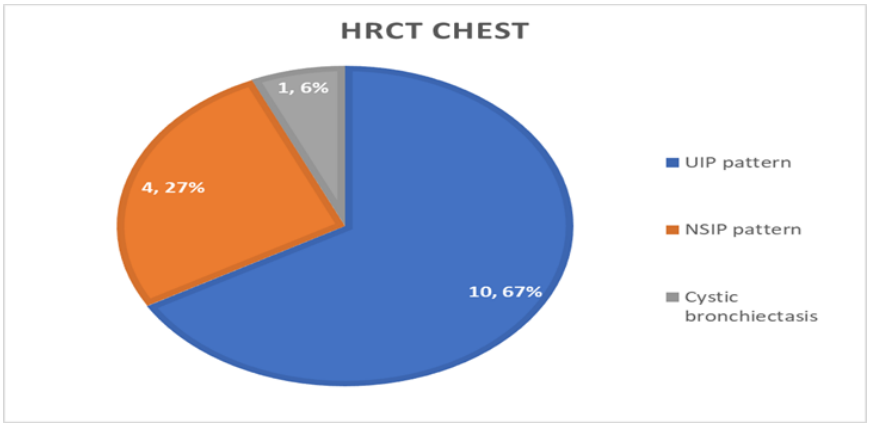


Figure 6: HRCT thorax findings

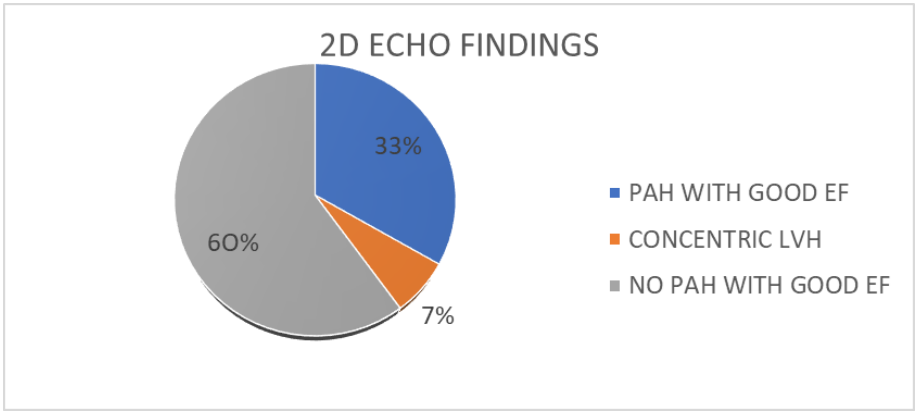
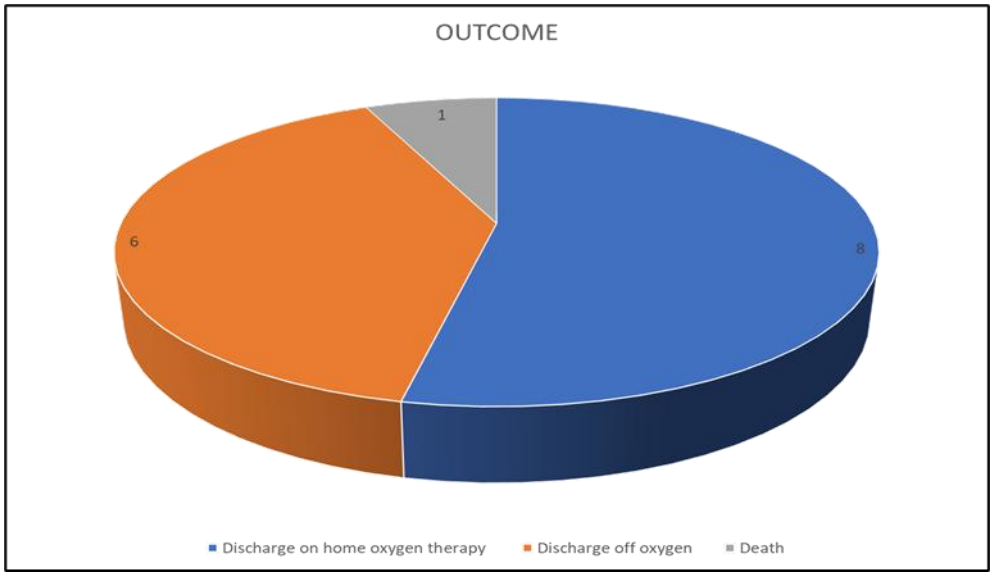


Figure 7:2D-ECHO Findings



IV. Discussion:

Our study was aimed to study the clinical and radiological profile of interstitial lung disease patients. Connective tissue diseases are a heterogeneous group of autoimmune disorders that can involve the lungs either directly or as a complication of treatment of the CTD. The most common pulmonary manifestation of CTDs are ILDs. Approximately 15% of patients with an ILD have an underlying CTD. Therefore, a high index of suspicion is to be kept for diagnosing this condition. Very few studies have been undertaken to study this disease, especially in India. Hence we undertook this study.

Fifteen consecutive patients of CTD related ILD, diagnosed with multi-disciplinary discussion were included in the study. Patients having respiratory symptoms suggestive of ILD, who were either diagnosed cases of CTD or had clinical manifestations of underlying CTD, were included in the study.

Our study showed a female preponderance with male: female ratio of 1:2.75. This is in concordance with other studies where CTD-ILD is more common in females[4,5]

We observed a peak incidence in the age group 60-69 years. It is consistent with other Indian and western studies[6] previously conducted, where most CTDs were common between the fourth and sixth decade except SLE, which is commonly seen in younger age.

Cough and dyspnea on exertion were the cardinal symptoms, which is in concordance with various studies on ILD[7-9]. The most common clinical signs that were seen in ILDs were clubbing, desaturation on exertion, and bilateral Velcro crackles. Among the CTD-related ILDs, Rheumatoid arthritis (RA) formed the most common CTD followed by Mixed connective tissue disorder (MCTD) and Sjogren's syndrome. This is in concordance with other studies on CTD – ILD, where RA is the most common CTD to be associated with ILD[10]. In one cross sectional study done in AIIMS Jodhpur, India between March 2017 to February 2018 comprising of 100 patients 27% of patients belonged to the age group of 41-50 years and 78% were females, chief respiratory complaint were cough and dyspnea and the common CTD associated was rheumatoid arthritis followed by systemic sclerosis and MCTD[11]. Another prospective observational study including 51 patients of CTD-ILD was conducted in Topiwala National medical college, Mumbai, India also showed female preponderance, cough and dyspnea in 90% of the cases, clubbing and Velcro crepts was observed in 73% of patients and RA formed the most common CTD to be associated with ILD[12].Another study conducted in CMC Vellore between November 2018 and January 2020 also showed mean age to be 50.37yr and among them 71% were female with 90% of them having cough and breathlessness as their chief complaint. Most common CTD associated was Undifferentiated (U)CTD followed by RA[13].

In our study, ABG showed type I respiratory and increased A–a gradient. This is consistent with other studies where hypoxemic (type I) respiratory failure was more common in ILD patients[14,15,16].

Multidisciplinary diagnosis involving clinical and radiological correlation is needed to diagnose and classify most of the ILDs. Radiology is an important tool for diagnosis. Newer advances in imaging modalities have obviated the need for surgical lung biopsy. Radiologically, high resolution computed topography (HRCT) scans can be effectively used to diagnose and identify disease and assess disease improvement or progression. CTD-ILD may manifest as a focal or a diffuse pulmonary abnormality, especially at the periphery of the lung, such as reticulation, ground-glass opacities (GGOs) and nodules. We note that NSIP is the most common histopathologic type in CTD-ILDs (with the exception of RA).In our study since the most common CTD associated was RA, the most common pattern on HRCT thorax was UIP followed by NSIP pattern. Other similar studies[11,12,13,17]showed the most common pattern on HRCT to be NSIP followed by UIP.

In addition, we also note that the frequency and severity of fibroblastic lesions in CTD-ILDs is lower than IPF-UIP and the coexistence of UIP and NSIP patterns is one of the most significant features that distinguishes CTD-UIP from IPF-UIP.

ILD itself being a chronic progressive disease, co morbidities further hamper the quality of life of such patients. In our study the common co morbid condition associated was hypertension. Pulmonary artery hypertension is associated with reduced exercise capacity and worse survival. It is most likely due to destruction of the pulmonary vasculature from lung fibrosis and honeycomb change.2DECHO is a good diagnostic tool to detect pulmonary hypertension in ILD patients. In our study, Pulmonary hypertension with dilated right atrium and right ventricle with good ejection fraction was seen in33% of cases compared to 40% in the study at AIIMS Jodhpur[13].In our study we also noted that majority of patients were discharged on home oxygen therapy.

V. Conclusion:

CTD-ILD is underdiagnosed. Apart from systemic sclerosis, lung disease is absent from the diagnostic criteria for CTD,and yet lung disease may be the only manifestation. Currently there is lack of awareness about the various ILD, their profile and management in India. Being a chronic respiratory disease, it requires a thorough counselling by explaining the natural course, the available treatment options, their adverse effects and optimal management of associated treatable comorbidities. A structured approach to CTD-ILD is necessary since treatment may vary considerably depending on the diagnosis.

Diagnosis is based upon 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 lung biopsy. Multidisciplinary review is an important part of the process and can have significant impact on diagnostic and management decisions. For each patient, decision regarding diagnostic approach and therapy must be individualized based upon the patient's respiratory status, comorbid medical conditions and personal approach to medical care.

In general, prognosis of CTD-ILD is more favorable than the IPF, the most common of ILDs. Prognosis is influenced by factors such as ILD subtype, age and type of connective tissue disease associated. In our study we observed that the prevalence and presentation of CTD-ILD, is very significantly influenced by demographic factors. Early diagnosis is essential for improved patient outcomes underscoring the importance of multidisciplinary approach including pulmonologists, rheumatologists, radiologists and physiotherapists. The study findings also point the need for standardized diagnostic criteria and treatment protocols tailored to the unique clinical characteristics seen in our patient population.

Our insights pave the way to future studies aimed at enhancing diagnostic accuracy, treatment effectiveness and overall patient care in CTD-ILD. By refining our approach, we hope to reduce morbidity and improve the quality of life for patients with this complex condition.

Acknowledgement:

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CONFLICT OF INTEREST: None

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