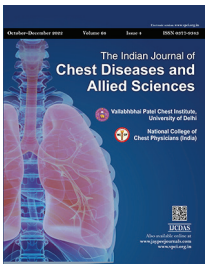
SHORT COMMUNICATION

Clinical Profile of Connective Tissue Disease-related Interstitial Lung Diseases at a Tertiary Care Center in Western India



Dharani M[1], Ketaki Utpat[2], Unnati Desai[3], Jyotsna Joshi[4], Ramesh N Bharmal[5]

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Abstract

Connective tissue disorders (CTDs) are one of the common causes of interstitial lung diseases (ILDs). This prospective observational study included around 51 patients of CTD-ILDs, and their demographic, clinical, radiological, and laboratory profiles were studied. The most common type of CTD-ILD in our study is rheumatoid arthritis-related ILD. On high-resolution computed tomography (HRCT) thorax, nonspecific interstitial pneumonia (NSIP) was the most common pattern seen in 30 patients (59%), followed by usual interstitial pneumonia (UIP) seen in 20 patients (39%). Even though CTD-ILDs are similar to other idiopathic ILDs in clinical and radiological presentation, patients with CTDs have to be evaluated clinically and radiologically for early diagnosis. Early treatment initiation and pulmonary rehabilitation help in delaying the progression of disease. Among all ILDs, CTD-ILDs are associated with better prognosis and survival.

Keywords: Connective tissue disease, Interstitial lung disease, Nonspecific interstitial pneumonia.

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Abbreviations used in this Article

CTDs = Connective tissue disorders; ILD = Interstitial lung disease; NSIP = Nonspecific interstitial pneumonia; UIP = Usual interstitial pneumonia; HRCT = High-resolution computed tomography; SLE = Systemic lupus erythematosus; RA = Rheumatoid arthritis; PSS = Progressive systemic sclerosis; DM = Dermatomyositis; PM = Polymyositis, AS = Ankylosing spondylitis, SS = Sjogren syndrome; MCTD = Mixed connective tissue disease; OP = Organizing pneumonia; DAD = Diffuse alveolar damage; LIP = Lymphocytic interstitial pneumonia; GERD = Gastroesophageal reflux disease.

Introduction

Connective tissue diseases are a heterogeneous group of autoimmune disorders characterized by the presence of autoantibodies. They include systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), progressive systemic sclerosis (PSS), dermatomyositis (DM)/polymyositis (PM), ankylosing spondylitis (AS), Sjogren syndrome (SS), and mixed connective tissue disease (MCTD).[1] Many experts include the ANCA-related vasculitides and Goodpasture syndrome in this group because of the presence of autoantibodies.[2] Connective tissue disorders can affect different components of the respiratory system. Interstitium is the most common component to get affected causing ILD.[3] Underlying CTD is seen in approximately 15% of patients with an ILD.[4] Associated ILD has been reported in various autoimmune conditions. Interstitial lung disease may present even before the CTD diagnosis is made, as the initial manifestation of a CLD.[5] Some patients who have ILD and do not meet clinical criteria for CTDs may have a lung-predominant form of a CTD.[6] It is usually present with dry cough and shortness of breath. It may lead to pulmonary hypertension, cor pulmonale, and right heart failure as the disease progresses, which may contribute to significant mortality and morbidity if it is not diagnosed on time. Clubbing may be present, associated with end-inspiratory crackles and post-exercise desaturation. In HRCT thorax, except for RA, in which UIP pattern is more common, NSIP is the most common pattern of lung injury seen among CTD-ILD.[7,8] Nonspecific interstitial pneumonia is the most common histopathological pattern seen on lung biopsy in CTD-ILD. Various other patterns include UIP, organizing pneumonia (OP), diffuse alveolar damage (DAD), and lymphocytic interstitial pneumonia (LIP).[9] A LIP is most often seen in the context of SS, can be found in RA, but is rarely seen in the other CTDs. A DAD pattern is most frequently seen in the context of RA, PM/DM, SLE, or of an undifferentiated CTD,[10] while it is exceedingly rare in SSc.[11,12] Some evidence suggests that the incidence of ILD is increasing in CTD patients.[13,14] Because the prognosis, degree of reversibility, and optimal therapy differ for each disease presentation, a thorough knowledge of the pulmonary clinical picture of each CTD is important.

[1–5]Department of Pulmonary Medicine, Topiwala National Medical College and B.Y.L. Nair Charitable Hospital, Mumbai, India

Corresponding Author: Unnati Desai, Department of Pulmonary Medicine, Topiwala National Medical College and B.Y.L. Nair Charitable Hospital, Mumbai, India, Phone: +91 2223027643, e-mail: unnati_desai82@yahoo.co.in

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Materials and Methods

This prospective observational study was done in the pulmonary unit of a tertiary care center after Ethics committee approval. About 51 cases of CTD-related ILDs were included in the study. Inclusion criteria were all patients aged above 18 years with confirmed diagnosis of CTD-related ILD over a 2-year period, and patients who were not willing to give consent were excluded.

In cases of CTD-ILD, the clinical history, examination, ABG, hematological, biochemical laboratory investigations, CTD profile, spirometry, and HRCT thorax findings were noted. Two-dimensional echocardiography was done to rule out pulmonary hypertension. Comorbidities and addictions were noted. Data were analyzed and presented as percentages and mean.

Results

Clinical profile of 51 cases of CTD-related ILDs was noted (Table 1). Of these, 9 (18%) were male patients, while 42 (82%) were females with M:F of 1:4.7. Mean age of the study group was 47.8 years. Most of the patients fell in the age group 40–49 years of age, comprising 17 patients (33%). The most common presenting symptom that was seen was cough and dyspnea seen in 46 patients constituting 90%. Almost 47 patients (92%) had 1–5 years of symptoms before the diagnosis of ILD was made with average duration of 32 months (SD – 18.37). The most common type of CTD-ILD is RA-related ILD, seen in 23 patients (45%), next being scleroderma-related ILD, then comes the mixed CTD-related ILD seen in 10 patients (20%), SLE-related ILD seen in 2 patients, and DM-related ILD in 1 patient (2%). Clubbing was seen in 37 patients (73%). Post-exercise desaturation and bibasilar Velcro crackles were seen in all patients (100%). Type I respiratory failure is noted in 4 patients (8%), and increased A–a gradient was seen in 38 patients (74%). The average Six-minute walk distance (6MWD) noted was 299 m. Spirometry was suggestive of restrictive abnormality in 50 patients with average FVC of 52%. Majority of the patients demonstrated mild PH seen in 45 patients (88%). The most commonly seen comorbid condition among CTD-ILD patients in this study was gastroesophageal reflux disease (GERD), seen in 30 patients (59%). Other comorbidities like hypertension, seen in 13 patients (25%), diabetes mellitus in 8 patients (15%), osteoporosis in 11 patients (21%), hypothyroidism in 6 patients (12%), and conditions like ischemic heart disease, chronic liver disease, sleep apnea, etc. seen in 7 (14%) patients. On HRCT thorax, NSIP was the most common pattern seen in 30 patients (59%), usual interstitial pneumonia was seen in 20 patients (39%), and lymphocytic interstitial pneumonia was seen in one patient (2%). Among 23 patients of RA, 13 patients (57%) had UIP patterns and 10 (43%) patients had NSIP. Among 15 patients of scleroderma, 4 (27%) patients had UIP and 11 (73%) patients had NSIP. Among 10 patients of MCTD, 6 (60%) patients had NSIP, 3 (30%) patients had UIP, and 1 (10%) patient had LIP pattern. Nonspecific interstitial pneumonia pattern was seen in 1 DM patient and 2 patients of SLE.

Table 1: Characteristics of CTD-ILD patients

Characteristics	*Number of patients*
Sex	
Male	9 (18%)
Female	42 (82%)
Age group	
20–29 years	4 (8%)
30–39 years	8 (15%)
40–49 years	17 (33%)
50–59 years	12 (24%)
60–69 years	7 (14%)
70–79 years	3 (6%)
Symptoms	
Cough	46 (90%)
Dyspnea	46 (96%)
Type of CTD-ILD	
Rheumatoid arthritis	23 (45%)
Scleroderma	15 (29%)
MCTD	10 (20%)
SLE	2 (4%)
Dermatomyositis	1 (2%)
ILD pattern	
NSIP	30 (59%)
UIP	20 (39%)
LIP	1 (2%)

Discussion

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 complications of the CTDs are ILDs. Approximately 15% of patients with an ILD have an underlying CTD.

The mean age of the study group was 47.8 years. The most common age group affected in our study was 40–49 years, comprising 17 patients (33%). It is consistent with other studies, where most CTDs were common between the fourth and sixth decade except SLE, which was commonly seen in younger age.[15] Our study showed a female preponderance with male:female ratio of 1:4.7. This is in concordance with other studies where CTD-ILD is more common in females.[16,17] Cough and dyspnea on exertion were the cardinal symptoms in 46 patients accounting for 90% of cases, which is in concordance with various studies on ILD.[18–20] The most common clinical signs that were seen in ILDs were clubbing, post-exercise desaturation, and bilateral Velcro crackles. In our study, clubbing was observed in 73% of cases, and post-exercise desaturation and crackles were seen in all patients. This is in concordance with other studies where crackles and clubbing are the most common physical finding in ILD patients.[20]

Among the CTD-related ILD studied, RA formed the most common CTD to be associated with ILD. And the DM was the least common among the CTDs. This is in concordance with other studies on CTD-ILD, where RA is the most common CTD to be associated with ILD.[21] Total duration of symptoms before the diagnosis of ILD in 51 patients was noted. Almost 47 patients (92%) had 12–60 months of symptoms before the diagnosis of ILD was made. Only 2 patients (4%) presented with less than 12 months of symptoms and more than 60 months of symptoms each, with average duration of 32 months (SD – 18.37). This is almost in concordance with other studies where the disease duration at presentation ranges from 0.3 to 5.3 years.[22] In our study, ABG showed type I respiratory failure in 8% of patients and 74% of patients had

increased A–a gradient. This is consistent with other studies where hypoxemic (type I) respiratory failure was more common in ILD patients.[23] Six-minute walk distance (6MWD) of 50 out of 51 patients was noted. Average 6MWD of 50 patients was 299 m. This is similar to various studies on ILD where average 6MWD was 249 m.[24,25] Spirometry was suggestive of restrictive abnormality in all 50 patients with average FVC of 52% and standard deviation of 17.06. This is similar to various studies on ILD.[25,26] Nonspecific interstitial pneumonia was the most common pattern seen in 59% of CTD-related ILDs. Similar results are reported in various studies such as Gutsche et al.[8] Other patterns seen in our study being UIP and LIP. Among 23 patients of RA, 13 patients (57%) had UIP patterns and 10 (43%) patients had NSIP. Among 15 patients of scleroderma, 4 (27%) patients had UIP and 11 (73%) patients had NSIP. It is similar to various studies, where UIP is the most common pattern associated with RA-ILD and NSIP is the most common to be associated with scleroderma-ILD.[18,27] Among 10 patients of MCTD, 6 (60%) patients had NSIP, 3 (30%) patients had UIP, and 1 (10%) patient had LIP pattern. Nonspecific interstitial pneumonia pattern was seen in 1 DM patient and 2 patients of SLE. Comorbidities commonly seen in our study include GERD, diabetes mellitus, hypertension, osteoporosis, hypothyroidism, and others like sleep apnea and ischemic heart disease. This is in concordance with various studies on comorbidities associated with ILD.[28] Here, in our study, GERD was the most common among all comorbidities.

Interstitial lung involvement is common and potentially life-threatening in CTDs. Early detection of pulmonary involvement is very important for the initiation of a targeted therapy, because the damage to the lung parenchyma may be already irreversible at the time of the onset of respiratory symptoms. Early diagnosis and management help in prevention of development of sequelae and thus help in reducing frequent hospitalizations and thereby, reduce morbidity and mortality, and decrease the burden on healthcare services. Multidisciplinary approaches involving pulmonologists, rheumatologists, radiologists, and pathologists in treatment decisions are necessary for optimal outcomes.

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