Comparison of Six-Minute Walk Test and Lung Function Test (Fev1%, Fvc%) in Patients with Interstitial Lung Disease and Connective Tissue Disorder

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ABSTRACT

Background:

Interstitial lung disease (ILD) associated with connective tissue disorders (CTD) represents a significant cause of morbidity and mortality due to progressive fibrosis and impaired gas exchange. While pulmonary function tests (PFTs) assess static lung mechanics, the six-minute walk test (6MWT) provides a practical measure of functional exercise capacity and exertional oxygen desaturation. An integrated evaluation of these parameters is essential for comprehensive assessment of CTD-ILD. This study aimed to evaluate and correlate the six-minute walk test (6MWT) with lung function parameters (FEV_1%, FVC%) in patients with ILD secondary to connective tissue disorders.

Materials and Methods:

This cross-sectional observational study was conducted in the Department of Respiratory Medicine at Sree BalajiMedical College and Hospital, Chennai, over a period of 18 months. A total of 30 patients aged 18–65 years with CTD-associated ILD (rheumatoid arthritis, systemic lupus erythematosus, systemic sclerosis, and Sjögren'ssyndrome) were included. All patients underwent clinical evaluation, autoantibody profiling, HRCT chest imaging, spirometry, and 6MWT as per standard guidelines. Data were analyzed using SPSS version 20, with $p < 0.05$ considered statistically significant.

Results:

The majority of patients were females (63.3%) and belonged to the 51–60 years age group. Rheumatoid arthritis was the most common underlying CTD (40%). Spirometry revealed a predominant restrictive pattern with mean FVC of 61.3 ± 12.8% and FEV_1 of 67.4 ± 13.2%. The mean six-minute walk distance (6MWD) was 362.8 ± 88.2 meters, with significant exertional desaturation (mean drop in SpO_2 of 4.7%). A statistically significant positive correlation was observed between 6MWD and FVC% ($r = +0.56$, $p = 0.001$) and FEV_1% ($r = +0.48$, $p = 0.006$). Increasing age and disease duration showed negative correlations with 6MWD. Multivariate analysis identified FVC% and post-test SpO_2 as significant positive predictors, while age and disease duration were negative predictors of functional capacity.

Conclusion:

The six-minute walk test is a valuable and practical tool for assessing functional impairment in CTD-associated ILD. It correlates significantly with lung function parameters, particularly FVC%, and provides additional insight into exercise limitation and gas exchange abnormalities. Combining spirometry with 6MWT enhances clinical evaluation and may aid in better disease monitoring and prognostication.

Keywords:
Connective tissue disease, interstitial lung disease, six-minute walk test, pulmonary function test, FVC, exercise capacity, oxygen desaturation

Introduction

Interstitial lung disease (ILD) represents a heterogeneous group of parenchymal lung disorders characterized by varying degrees of inflammation, fibrosis, and architectural distortion of the lung interstitium. These conditions encompass a wide spectrum of pathological entities, ranging from idiopathic forms such as idiopathic pulmonary fibrosis to secondary causes associated with systemic diseases, environmental exposures, and drug-induced injury. Among the secondary causes, connective tissue disease–associated interstitial lung disease (CTD-ILD) is one of the most clinically important categories, as autoimmune processes directly contribute to progressive pulmonary involvement [1–3]. The prevalence of CTD-ILD varies across different connective tissue diseases, with systemic sclerosis showing the highest frequency, followed by rheumatoid arthritis, Sjögren's syndrome, and systemic lupus erythematosus. The clinical significance of CTD-ILD lies in its substantial contribution to morbidity and mortality among patients with autoimmune diseases, often representing a major determinant of long-term outcomes and quality of life.

Autoimmune injury is central to CTD-ILD pathogenesis, involving complex interactions between genetic susceptibility, environmental triggers, and dysregulated immune responses. The pathogenesis begins with loss of immune tolerance, leading to the production of autoantibodies that target self-antigens expressed in the lung parenchyma. Autoantibodies such as rheumatoid factor (RF) and anti-cyclic citrullinated peptide (anti-CCP) in rheumatoid arthritis, antinuclear antibodies (ANA) and anti-double-stranded DNA (anti-dsDNA) in systemic lupus erythematosus, anti–Scl-70 (topoisomerase I) and anticentromere antibodies (ACA) in systemic sclerosis, and anti-Ro/SSA and anti-La/SSB antibodies in Sjögren's syndrome contribute to chronic immune activation, endothelial injury, and fibroblast proliferation, culminating in interstitial fibrosis [4–6]. These autoantibodies not only serve as diagnostic markers but also reflect the underlying immunological activity driving pulmonary involvement. The presence of specific autoantibodies correlates with distinct patterns and severity of lung disease, highlighting the importance of comprehensive immunological profiling. Immunological profiling is therefore essential not only for diagnosing these diseases but also for understanding the extent and pattern of lung involvement, guiding prognostic assessment, and informing therapeutic decisions.

High-resolution computed tomography (HRCT) of the chest has emerged as the gold standard imaging modality for evaluating CTD-ILD, providing detailed visualization of lung parenchymal abnormalities with superior spatial resolution. HRCT patterns such as nonspecific interstitial pneumonia (NSIP), usual interstitial pneumonia (UIP), organizing pneumonia, and ground-glass opacities vary across different connective tissue diseases, reflecting the underlying pathological processes and their temporal evolution. NSIP is the predominant pattern in systemic sclerosis and Sjögren's syndrome, characterized by ground-glass opacities and reticular abnormalities with lower lobe predominance, whereas rheumatoid arthritis is more frequently associated with UIP, which carries a poorer prognosis due to its progressive fibrotic nature and higher mortality [7–9]. The distinction between these patterns is clinically significant, as UIP pattern is associated with worse outcomes and different therapeutic responses compared to NSIP. HRCT thus provides structural assessment, complements functional testing, and influences clinical decision-making, including the initiation and monitoring of immunosuppressive therapy and the assessment of disease progression.

Pulmonary function tests (PFTs), particularly forced vital capacity as percentage of predicted (FVC%) and forced expiratory volume in one second as percentage of predicted (FEV_1%), remain fundamental in assessing lung mechanics in ILD. These indices quantify the degree of restriction arising from fibrosis and reduced lung compliance, providing objective measures of disease severity and progression over time. Serial PFT monitoring is essential for tracking disease trajectory, evaluating treatment response, and predicting prognosis. However, spirometry alone may not adequately reflect exercise limitation or gas-exchange impairment, which are often more prominent than static volume reduction in CTD-ILD [10,11]. Resting pulmonary function tests may underestimate the functional impact of the disease on daily activities, as many patients experience significant exertional symptoms despite relatively preserved spirometric values. This discrepancy underscores the need for additional functional assessments that capture the dynamic aspects of respiratory impairment.

The six-minute walk test (6MWT) is a simple, standardized field test that evaluates submaximal exercise capacity and exertional desaturation. In CTD-ILD, 6MWT provides essential insights into functional limitation, diffusion impairment, and exertional hypoxemia — factors that correlate closely with patient symptoms and overall disease burden [12–14]. The test is practical, well-tolerated, and reproducible in clinical settings, making it an ideal tool for routine assessment of functional capacity. Many studies have shown that six-minute walk distance (6MWD) and desaturation during the test strongly correlate with fibrotic severity, HRCT extent, and spirometric decline, establishing the 6MWT as a valuable complementary assessment modality [15–17]. The magnitude of desaturation during exercise reflects the severity of gas-exchange impairment and provides prognostic information beyond that obtained from resting pulmonary function tests. Furthermore, the 6MWT can identify patients who may benefit from supplemental oxygen therapy or pulmonary rehabilitation, guiding comprehensive management strategies.

Given the complex interplay of autoimmunity, serological markers, radiological changes, and functional impairment in CTD-ILD, an integrated evaluation using antibody profile, HRCT, spirometry, and 6MWT is clinically valuable. Such a comprehensive approach enables accurate characterization of disease phenotype, assessment of disease activity and severity, prediction of prognosis, and individualized therapeutic planning. However, data specific to Indian populations, particularly involving rheumatoid arthritis, systemic lupus erythematosus, systemic sclerosis, and Sjögren's syndrome, remain limited. The prevalence, clinical features, and functional outcomes of CTD-ILD may differ across ethnic groups due to genetic, environmental, and healthcare-related factors. Furthermore, studies correlating 6MWT performance with lung function parameters in this specific CTD spectrum with adequate sample size are sparse, limiting the evidence base for clinical practice in Indian settings. This gap in knowledge underscores the need for comprehensive studies that evaluate the relationship between serological markers, radiological findings, and functional outcomes in Indian patients with CTD-ILD. The present study aims to address these gaps by systematically evaluating the clinical, immunological, radiological, and functional characteristics of CTD-ILD in a cohort of patients with rheumatoid arthritis, systemic lupus erythematosus, systemic sclerosis, and Sjögren's syndrome, with particular emphasis on correlating 6MWT performance with pulmonary function parameters and HRCT findings.

Materials and Methods

Study Design and Setting

This cross-sectional observational study was conducted in the Department of Respiratory Medicine at Sree Balaji Medical College and Hospital, Chennai, India. The hospital serves as a tertiary care referral center, providing comprehensive diagnostic and therapeutic services for patients with complex respiratory and systemic diseases. The study was carried out over a period of 18 months, allowing for adequate patient recruitment and comprehensive evaluation of the study parameters. A cross-sectional design was chosen to evaluate the clinical, immunological, radiological, and functional characteristics of patients with connective tissue disease-associated interstitial lung disease at a single point in time, facilitating the assessment of associations between various disease parameters without the need for

longitudinal follow-up. This design is particularly appropriate for describing the burden and patterns of CTD-ILD in the Indian population and for generating hypotheses regarding the relationships between serological markers, radiological findings, and functional outcomes.

Study Population

The study population comprised adult patients aged 18 to 65 years diagnosed with interstitial lung disease secondary to one of four connective tissue diseases: rheumatoid arthritis, systemic lupus erythematosus, systemic sclerosis, or Sjögren's syndrome. Patients were recruited from the outpatient and inpatient services of the Department of Respiratory Medicine, as well as through referrals from the Department of Rheumatology and other clinical specialties. Only patients who were clinically stable at the time of evaluation and capable of performing spirometry and the six-minute walk test were included in the study. All participants were required to provide written informed consent, ensuring voluntary participation and adherence to ethical research principles.

Sample Size Calculation

The sample size was calculated based on the prevalence of CTD-ILD as reported in previous studies. Murudkar et al. reported a prevalence of approximately 20% in their study population, and this estimate was used as the basis for sample size calculation [18]. Using the standard formula for estimating prevalence in cross-sectional studies, with a 95% confidence level and 5% allowable error, the calculated sample size was approximately 28 patients. Considering the feasibility of patient recruitment, the availability of eligible cases meeting the inclusion criteria, and the need for adequate statistical power for subgroup analyses, the sample size was rounded off to 30 patients, which were included in the present study.

Inclusion and Exclusion Criteria

A comprehensive set of inclusion and exclusion criteria was established to ensure the enrollment of an appropriate and homogeneous study population. The inclusion criteria were designed to capture patients with well-characterized CTD-ILD while excluding those with confounding conditions. Adults aged 18 to 65 years with ILD secondary to rheumatoid arthritis, systemic lupus erythematosus, systemic sclerosis, or Sjögren's syndrome were eligible for inclusion. Patients were required to be clinically stable and able to perform spirometry and the 6MWT, ensuring that functional assessments could be completed safely and reliably. Patients providing written informed consent were included after a thorough explanation of the study procedures, risks, and benefits.

Several exclusion criteria were established to minimize confounding and ensure patient safety. Patients with co-existing chronic respiratory diseases such as chronic obstructive pulmonary disease, bronchial asthma, or bronchiectasis were excluded, as these conditions independently affect lung function and exercise capacity, potentially confounding the assessment of CTD-ILD. Patients with recent acute cardiovascular events, including myocardial infarction or unstable angina, were excluded due to safety concerns during exercise testing. Severe musculoskeletal, neurological, or systemic limitations that prevent walking constituted an exclusion criterion, as such limitations would preclude valid completion of the 6MWT. Patients on long-term oxygen therapy were also excluded, as supplemental oxygen would affect exercise performance and desaturation assessment during the 6MWT.

Data Collection Procedure

Clinical Evaluation

A comprehensive clinical evaluation was performed for every patient enrolled in the study. Detailed history was obtained using a structured proforma designed specifically for this study. The history included demographic information, duration of connective tissue disorder, and characterization of respiratory symptoms including dyspnea grade using standardized scales, cough, fatigue, and chest symptoms. Smoking history and occupational exposure to potentially fibrogenic agents were documented to assess their potential contribution to lung disease. A complete clinical examination was performed, including assessment of vital signs, respiratory examination with auscultation for crackles and other abnormal breath sounds, and evaluation for extrapulmonary manifestations of connective tissue diseases such as skin changes, joint involvement, and systemic features.

Autoantibody Testing

As part of the diagnostic workup for connective tissue diseases and to characterize the immunological profile of each patient, comprehensive autoantibody testing was performed for all patients. The testing included antibodies specific to each connective tissue disease: rheumatoid factor and anti-cyclic citrullinated peptide antibodies for rheumatoid arthritis, antinuclear antibodies and anti-double-stranded DNA antibodies for systemic lupus erythematosus, anti-Scl-70 (topoisomerase I) and anticentromere antibodies for systemic sclerosis, and anti-Ro/SSA and anti-La/SSB antibodies for Sjögren's syndrome. Testing was performed using standardized serological methods in the hospital's accredited laboratory, ensuring accuracy and reproducibility of results.

HRCT Chest Evaluation

High-resolution computed tomography of the chest was performed for all patients to evaluate the pattern and extent of interstitial lung disease. HRCT scans were acquired using standardized protocols with thin-section imaging (1-2 mm slice thickness) to provide detailed visualization of lung parenchymal abnormalities. The following radiological patterns were documented based on established criteria: nonspecific interstitial pneumonia pattern, usual interstitial pneumonia pattern, ground-glass opacities, reticular opacities and honeycombing, and consolidation or organizing pneumonia pattern. The distribution and extent of involvement were assessed, and predominant patterns were identified for each patient. HRCT interpretation was performed by experienced radiologists with expertise in interstitial lung disease, ensuring reliable characterization of imaging findings.

Six-Minute Walk Test

The six-minute walk test was conducted according to the American Thoracic Society guidelines, following standardized procedures to ensure reliability and reproducibility of results. The test was performed on a 30-meter corridor, with the walking course clearly marked and standardized for all patients. Patients were instructed to walk as far as possible for six minutes, with standardized encouragement provided at regular intervals. The distance walked was recorded in meters as the primary outcome measure. Oxygen saturation was monitored continuously using pulse oximetry, and the presence and degree of desaturation during exercise were documented. The test was stopped if patients developed severe dyspnea, chest pain, dizziness, fatigue, or any other concerning symptoms, ensuring patient safety throughout the procedure.

Spirometry

Spirometry was performed according to American Thoracic Society and European Respiratory Society standards using a calibrated spirometer. Testing was conducted in a comfortable environment with patients in a seated position. Each patient performed at least three forced expiratory maneuvers to ensure reproducibility, with the best values recorded for analysis. The primary parameters measured included forced vital capacity as percentage of predicted (FVC%), forced expiratory volume in one second as percentage of predicted (FEV_1%), and the FEV_1/FVC ratio. Predicted values were calculated using population-specific reference equations. Spirometry was performed before the 6MWT to avoid the effects of exercise-induced fatigue on lung function measurements.

Statistical Analysis

Data were entered into Microsoft Excel for organization and preliminary verification. Statistical analysis was performed using SPSS software version 20. Descriptive statistics were used to summarize the demographic and clinical characteristics of the study population. Continuous variables such as age, disease duration, FVC%, FEV_1%, and six-minute walk distance were expressed as mean with standard deviation or median with interquartile range based on the distribution of data. Categorical variables including disease type, radiological patterns, and autoantibody positivity were presented as frequencies and percentages. Comparisons between groups were performed using appropriate statistical tests: the Student's t-test or Mann-Whitney U test for continuous variables and the chi-square test or Fisher's exact test for categorical variables. Correlation analyses were performed to evaluate relationships between six-minute walk test performance and pulmonary function parameters, autoantibody profiles, and HRCT findings. A p-value of less than 0.05 was considered statistically significant for all analyses.

Results:

Table 1. Baseline demographic and clinical characteristics of patients with CTD-associated ILD (n = 30)

Variable	n (%)
Age group (years)	
21–30	2 (6.7)
31–40	5 (16.7)
41–50	7 (23.3)
51–60	10 (33.3)
61–70	6 (20.0)
Sex	
Male	11 (36.7)
Female	19 (63.3)
Connective tissue disorder	
Rheumatoid arthritis	12 (40.0)
Systemic sclerosis	9 (30.0)
Systemic lupus erythematosus	5 (16.7)
Sjögren syndrome	4 (13.3)

Among the 30 patients, the largest proportion belonged to the 51–60-year age group (10, 33.3%), followed by 41–50 years (7, 23.3%) and 61–70 years (6, 20.0%). Females predominated (19, 63.3%) compared with males (11, 36.7%). Rheumatoid arthritis was the most common underlying connective tissue disorder (12, 40.0%), followed by systemic sclerosis (9, 30.0%), systemic lupus erythematosus (5, 16.7%), and Sjögren syndrome (4, 13.3%).

Table 2. Radiological and pulmonary function characteristics (n = 30)

Variable	Value
HRCT pattern	n (%)
NSIP	14 (46.7)
UIP	7 (23.3)
Ground-glass opacity	5 (16.7)
Reticulation/Honeycombing	3 (10.0)
Organizing pneumonia	1 (3.3)
Spirometry	Mean ± SD
FVC (L)	1.68 ± 0.47
FVC (% predicted)	61.3 ± 12.8
FEV_1 (L)	1.43 ± 0.41
FEV_1 (% predicted)	67.4 ± 13.2
FEV_1/FVC (%)	86.9 ± 6.5

NSIP was the predominant HRCT pattern, observed in 14 patients (46.7%), followed by UIP in 7 (23.3%). Ground-glass opacities were present in 5 (16.7%), reticulation/honeycombing in 3 (10.0%), and organizing pneumonia in 1 (3.3%). Spirometry demonstrated a restrictive ventilatory defect with a mean FVC of 61.3 ± 12.8% predicted, mean FEV_1 of 67.4 ± 13.2% predicted, and preserved mean FEV_1/FVC ratio of 86.9 ± 6.5%.

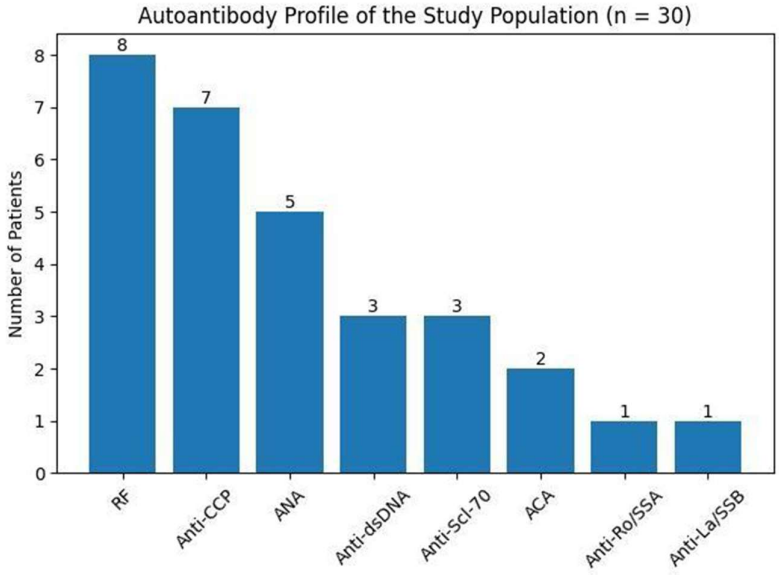

Fig 1: Autoantibody Profile

Rheumatoid factor (RF) was present in 8 patients (26.7%), followed closely by anti–cyclic citrullinated peptide (anti-CCP) antibodies in 7 patients (23.3%), reflecting the predominance of rheumatoid arthritis–associated cases in the study population. Antinuclear antibodies (ANA) were observed in 5 patients (16.7%), while anti–double stranded DNA (anti-dsDNA) antibodies were detected in 3 patients (10.0%), corresponding to patients with systemic lupus erythematosus.

Among patients with systemic sclerosis, anti–Scl-70 antibodies were present in 3 patients (10.0%) and anticentromere antibodies (ACA) in 2 patients (6.7%). Antibodies associated with Sjögren's syndrome were relatively uncommon. Anti-Ro/SSA antibodies were detected in 1 patient (3.3%), while anti-La/SSB antibodies were identified in 1 patient (3.3%).

Table 3. Six-minute walk test findings (n = 30)

Variable	Mean ± SD
Six-minute walk distance (m)	362.8 ± 88.2
Resting SpO_2 (%)	96.3 ± 1.5
Post-test SpO_2 (%)	91.6 ± 3.4
Mean oxygen desaturation (%)	4.7 ± 2.3
Resting heart rate (beats/min)	84.2 ± 8.6
Post-test heart rate (beats/min)	108.5 ± 12.3

The mean six-minute walk distance was 362.8 ± 88.2 m. Mean resting oxygen saturation was 96.3 ± 1.5%, decreasing to 91.6 ± 3.4% after exercise, corresponding to a mean oxygen desaturation of 4.7 ± 2.3%. Heart rate increased appropriately from 84.2 ± 8.6 beats/min at baseline to 108.5 ± 12.3 beats/min following exercise, indicating significant physiological response during the six-minute walk test.

Table 4. Correlation between six-minute walk distance and pulmonary function parameters (n = 30)

Variable	Correlation coefficient (r)	p value
FVC (% predicted)	+0.56	0.001
FEV_1 (% predicted)	+0.48	0.006
FEV_1/FVC ratio	+0.10	0.570

Six-minute walk distance showed a moderate positive correlation with FVC (r = 0.56, p = 0.001) and FEV_1 (r = 0.48, p = 0.006), indicating that better pulmonary function was associated with greater

functional exercise capacity. No statistically significant association was observed between six-minute walk distance and the FEV_1/FVC ratio (r = 0.10, p = 0.570).

Table 5. Correlation matrix among key physiological variables (n = 30)

Variable	6MWD	FVC (%)	FEV_1 (%)	Post-test SpO_2
6MWD	—	0.56	0.48	0.41
FVC (%)	0.56	—	0.71	0.44
FEV_1 (%)	0.48	0.71	—	0.39
Post-test SpO_2	0.41	0.44	0.39	—

A positive correlation was observed between six-minute walk distance and FVC (r = 0.56), FEV_1 (r = 0.48), and post-exercise oxygen saturation (r = 0.41). FVC and FEV_1 demonstrated a strong inter-correlation (r = 0.71), reflecting their close physiological relationship in restrictive lung disease. Post-exercise oxygen saturation also correlated positively with both spirometric indices.

Table 6: Multivariate Linear Regression Analysis — Independent Predictors of Six-Minute Walk Distance (6MWD) (n = 30)

Independent Variable	Regression Coefficient (β)	Standard Error (SE)	p-value	Interpretation
Age (years)	–2.45	1.02	0.02	Significant Negative Predictor
Sex	+10.62	12.14	0.38	Not Significant
Disease Duration (years)	–5.10	2.41	0.04	Significant Negative Predictor
FVC (%)	+3.48	1.20	0.006	Significant Positive Predictor
FEV_1 (%)	+1.62	1.03	0.12	Not Significant
Post-Test SpO_2 (%)	+6.94	2.70	0.01	Significant Positive Predictor

- Dependent Variable: Six-Minute Walk Distance (6MWD, meters)
- $R^2 = 0.57$, Adjusted $R^2 = 0.52$
- Overall Model $p < 0.001$ (statistically significant)

On multivariate analysis, age (β = –2.45, p = 0.02) and disease duration (β = –5.10, p = 0.04) were significant negative predictors of six-minute walk distance. FVC% showed a statistically significant positive association (β = +3.48, p = 0.006), indicating that better-preserved lung volumes contributed to higher functional capacity. Post-test SpO_2 also emerged as a significant positive predictor (β = +6.94, p = 0.01). Sex and FEV_1% did not show statistically meaningful contributions to the model. The overall regression model was significant, explaining 52% of the variability in 6MWD.

Discussion:

The present cross-sectional study evaluated the demographic, clinical, immunological, radiological, and functional characteristics of patients with connective tissue disease-associated interstitial lung disease (CTD-ILD) in a tertiary care setting. The findings demonstrate that CTD-ILD predominantly affects middle-aged and older adults, with a female predominance, restrictive pulmonary dysfunction, impaired exercise capacity, and nonspecific interstitial pneumonia (NSIP) as the most frequent radiological pattern. Furthermore, forced vital capacity (FVC) and post-exercise oxygen saturation emerged as significant determinants of functional exercise capacity, emphasizing their importance in the clinical assessment of CTD-ILD.

Most patients were between 51 and 60 years of age, with females accounting for nearly two-thirds of the study population. This demographic profile is consistent with the epidemiology of connective tissue

diseases, which predominantly affect women during middle age [1,5]. Previous studies have similarly reported that CTD-ILD usually develops after several years of underlying autoimmune disease, explaining its higher prevalence in older individuals [4,8]. Indian studies have also demonstrated comparable age and sex distributions, supporting the generalizability of the present findings within the regional context [19,20].

Rheumatoid arthritis (RA) was the most common connective tissue disease associated with ILD, followed by systemic sclerosis, systemic lupus erythematosus (SLE), and Sjögren's syndrome. This distribution parallels previous reports in which RA represents the leading cause of CTD-ILD because of its high prevalence and chronic inflammatory burden [2,8]. Systemic sclerosis remains the connective tissue disease with the highest propensity for pulmonary involvement, although its lower overall prevalence explains its smaller proportion in mixed CTD cohorts [5]. Similarly, pulmonary manifestations of SLE and Sjögren's syndrome are less common but remain clinically important because delayed diagnosis may contribute to disease progression [21,22].

Dyspnea was the predominant presenting symptom, affecting all patients, while dry cough and fatigue were also frequently encountered. These observations agree with previous studies identifying exertional breathlessness as the earliest and most consistent manifestation of CTD-ILD, reflecting progressive restriction of lung volumes and impaired gas exchange [1,11]. Dry cough has similarly been recognized as a characteristic symptom, particularly in fibrotic RA-associated ILD [8]. The predominance of moderate-to-severe dyspnea in the present study may indicate delayed referral to specialized centers, a finding reported previously in Indian studies [18,19].

The autoantibody profile largely reflected the distribution of underlying connective tissue diseases. Rheumatoid factor and anti-cyclic citrullinated peptide antibodies were the most frequently detected autoantibodies, corresponding to the predominance of RA [2]. Antinuclear and anti-double-stranded DNA antibodies were observed primarily among patients with SLE [21], whereas anti-Scl-70 antibodies were predominantly associated with systemic sclerosis, consistent with their established association with fibrotic lung involvement [5]. Sjögren's syndrome-associated antibodies (anti-Ro/SSA and anti-La/SSB) were infrequently detected, reflecting the relatively smaller proportion of patients with this disorder [22]. Overall, the immunological profile was concordant with previously published international and Indian studies.

High-resolution computed tomography demonstrated NSIP as the predominant imaging pattern, followed by usual interstitial pneumonia (UIP). NSIP has consistently been reported as the most common radiological pattern in CTD-ILD, particularly in systemic sclerosis, and is generally associated with a more favorable prognosis than UIP [11,23]. Conversely, UIP is encountered more frequently in RA-associated ILD and is associated with greater fibrosis, accelerated disease progression, and poorer survival [4,8]. The presence of ground-glass opacities and organizing pneumonia in a smaller proportion of patients suggests potentially reversible inflammatory disease in selected cases, emphasizing the value of HRCT in differentiating fibrotic and inflammatory phenotypes [24]. Similar HRCT distributions have been reported in Indian CTD-ILD cohorts [25,26].

Pulmonary function testing demonstrated a characteristic restrictive ventilatory defect, with reduced FVC and preserved FEV_1/FVC ratio. These findings are consistent with the pathophysiology of ILD, in which progressive fibrosis reduces lung compliance while maintaining relatively preserved airflow [10,11]. The mean FVC observed in the present study is comparable with previous reports in RA-ILD and systemic sclerosis-associated ILD, where moderate restriction represents the predominant physiological abnormality [8,18]. These findings further reinforce the importance of spirometry as an objective measure of disease severity and longitudinal progression.

The six-minute walk test (6MWT) demonstrated marked functional limitation, with reduced walking distance, significant exertional oxygen desaturation, and increased Borg dyspnea scores. Similar observations have been reported in ILD cohorts, where impaired exercise performance reflects the combined effects of restrictive lung mechanics, diffusion limitation, and reduced cardiopulmonary reserve [13,15]. Exercise-induced oxygen desaturation was particularly common in the present study, despite relatively preserved resting oxygen saturation, highlighting the sensitivity of the 6MWT in

detecting early physiological impairment [13,27]. These findings support current international recommendations advocating incorporation of the 6MWT into routine assessment of patients with ILD.
A significant positive correlation was observed between six-minute walk distance and FVC, whereas no meaningful correlation was found with the FEV_1/FVC ratio. This finding is physiologically expected because FVC reflects the degree of pulmonary restriction and available ventilatory reserve, whereas the FEV_1/FVC ratio generally remains preserved in restrictive lung diseases [10,11]. Similar correlations between functional exercise capacity and lung volumes have been reported previously in CTD-ILD and idiopathic pulmonary fibrosis, supporting the utility of FVC as a surrogate marker of disease severity [15,28]. These observations also suggest that combining spirometry with functional exercise assessment provides a more comprehensive evaluation than either modality alone.
Multivariable regression analysis further demonstrated that FVC and post-exercise oxygen saturation were independent predictors of six-minute walk distance, whereas increasing age and longer disease duration were associated with poorer exercise performance. These findings are consistent with previous studies demonstrating that preserved lung volumes and adequate oxygenation are the principal determinants of functional capacity in ILD [11,15,29]. The influence of age likely reflects declining cardiopulmonary reserve and cumulative disease burden, while longer disease duration probably represents progressive pulmonary fibrosis and irreversible structural damage [11,15,30]. Together, these findings emphasize that spirometric assessment and exercise oxygenation should be routinely monitored during follow-up to identify patients at increased risk of functional decline.
The present study has several limitations. The cross-sectional design precludes assessment of disease progression or causal relationships, while the relatively small sample size and single-center setting may limit generalizability. Diffusing capacity for carbon monoxide (DLCO), an important physiological marker of ILD severity, was not evaluated. In addition, disease activity indices, treatment regimens, inflammatory biomarkers, and longitudinal outcomes were not systematically assessed. Future multicenter prospective studies incorporating serial pulmonary function testing, HRCT, DLCO, biomarkers, and long-term follow-up are required to validate these findings and better characterize disease progression.
This study demonstrates that CTD-ILD predominantly affects middle-aged women, with rheumatoid arthritis representing the most common underlying connective tissue disease and NSIP being the predominant HRCT pattern. Restrictive pulmonary impairment and reduced exercise capacity were common, with FVC and post-exercise oxygen saturation emerging as important determinants of functional performance. These findings support the routine use of spirometry, HRCT, and the six-minute walk test for comprehensive assessment and monitoring of CTD-ILD and highlight the importance of multidisciplinary management for optimizing patient outcomes.

Conclusion

The present cross-sectional study evaluated the clinical, immunological, radiological, and functional characteristics of CTD-ILD in 30 patients from a tertiary care center. The findings demonstrate that CTD-ILD predominantly affects middle-aged and older adults, with a marked female predominance reflecting the underlying epidemiology of autoimmune connective tissue diseases. Rheumatoid arthritis was the most common underlying CTD, followed by systemic sclerosis, while SLE and Sjögren's syndrome constituted smaller subsets. Dyspnea and dry cough were the most frequent clinical presentations, and NSIP was the predominant HRCT pattern, with UIP being more common in RA-associated cases. Spirometry revealed a restrictive ventilatory defect with preserved FEV_1/FVC ratios, confirming the characteristic pattern of interstitial lung disease. The six-minute walk test demonstrated significantly reduced exercise capacity, with exertional desaturation being a prominent feature. 6MWD showed a significant positive correlation with FVC% and post-test SpO_2, and multivariate analysis identified age, disease duration, FVC%, and post-test SpO_2 as independent predictors of functional exercise capacity. These findings reinforce the importance of comprehensive assessment combining clinical evaluation, HRCT, spirometry, and the six-minute walk test in the management of CTD-ILD.

The study highlights the substantial functional impairment associated with CTD-ILD and underscores the need for early diagnosis, integrated multidisciplinary care, and targeted therapeutic interventions to optimize patient outcomes.

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