



Original Research Article

PULMONARY MANIFESTATIONS IN SYSTEMIC AUTOIMMUNE DISEASES: A CLINICAL STUDY

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ABSTRACT

Background: Systemic autoimmune diseases frequently involve the respiratory system, often resulting in significant morbidity and mortality. Pulmonary involvement can manifest in various forms including interstitial lung disease, pulmonary hypertension, pleural effusion, airway disease, and vascular complications depending on the underlying autoimmune pathology such as systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), systemic sclerosis (SSc), and mixed connective tissue disease (MCTD). **Aim:** This study aimed to evaluate the prevalence, spectrum, and clinical-radiological correlation of pulmonary manifestations among patients with systemic autoimmune diseases.

Materials and Methods: A hospital-based observational clinical study was conducted in the Department of Pulmonary Medicine and Rheumatology over a 24-month period. A total of 120 patients diagnosed with systemic autoimmune diseases (SLE, RA, SSc, Sjögren's syndrome, MCTD, and dermatomyositis/polymyositis) were enrolled. All patients underwent detailed clinical assessment, pulmonary function testing, high-resolution computed tomography (HRCT) of the chest, and relevant serological investigations (ANA profile, rheumatoid factor, anti-CCP, anti-Scl-70, etc.). The pattern and frequency of pulmonary involvement were analyzed and correlated with disease duration and severity.

Results: Pulmonary involvement was observed in 68 of the 120 patients (56.7%). The most common manifestation was interstitial lung disease (ILD), accounting for 45.5% of cases, followed by pleural effusion (22.1%), pulmonary hypertension (19.1%), and airway disease/bronchiectasis (13.2%). ILD was predominantly associated with systemic sclerosis and rheumatoid arthritis, whereas pleural effusion and acute pneumonitis were more frequent in SLE. HRCT findings revealed a predominance of usual interstitial pneumonia (UIP) and nonspecific interstitial pneumonia (NSIP) patterns. Diffusion capacity (DLCO) reduction correlated strongly with HRCT severity scores ($p < 0.001$). Longer disease duration and high autoantibody titers were significantly associated with pulmonary involvement ($p < 0.05$).

Conclusion: Pulmonary manifestations are common and clinically significant in systemic autoimmune diseases, with ILD being the most frequent form. Early and routine screening using HRCT and pulmonary function tests is essential for timely diagnosis, disease monitoring, and management to prevent irreversible pulmonary damage and improve quality of life.

Keywords: Systemic autoimmune diseases; Interstitial lung disease; Pulmonary hypertension; High-resolution computed tomography; Rheumatoid arthritis; Systemic sclerosis; SLE; Pulmonary manifestations.

INTRODUCTION

Systemic autoimmune diseases represent a diverse group of chronic inflammatory disorders characterized by immune dysregulation, production of autoantibodies, and multi-organ involvement. The pathogenesis involves loss of self-tolerance, leading the immune system to attack various tissues and organs. Although the clinical presentation varies depending on the organ system involved, pulmonary manifestations are among the most frequent and clinically significant complications. The lungs, due to their extensive vascular and connective tissue structure, are particularly vulnerable to autoimmune-mediated injury, which can manifest as parenchymal, pleural, vascular, or airway pathology.^[1]

Pulmonary involvement can occur in nearly all systemic autoimmune diseases and often serves as a major determinant of morbidity and mortality. It may be the first clinical manifestation of an autoimmune process or develop later during the disease course. Common systemic conditions associated with pulmonary manifestations include systemic lupus erythematosus, rheumatoid arthritis, systemic sclerosis, mixed connective tissue disease, Sjögren's syndrome, and dermatomyositis or polymyositis. Each of these conditions demonstrates distinct yet overlapping pulmonary patterns, making timely recognition essential for diagnosis and management.^[2]

In systemic lupus erythematosus, pulmonary involvement may present as pleuritis, pleural effusion, acute lupus pneumonitis, chronic interstitial lung disease, or pulmonary hemorrhage. These findings frequently correlate with systemic disease activity and immune complex deposition. Rheumatoid arthritis commonly presents with interstitial lung disease, particularly the usual interstitial pneumonia pattern, followed by pleural effusion, rheumatoid nodules, and bronchiolitis.^[3] Pulmonary manifestations in systemic sclerosis are even more frequent, with fibrotic interstitial lung disease and pulmonary arterial hypertension being the leading causes of mortality in these patients. Mixed connective tissue disease and dermatomyositis or polymyositis may also exhibit rapidly progressive interstitial pneumonitis, reflecting the shared autoimmune pathophysiology among connective tissue disorders.^[4]

The mechanisms underlying pulmonary injury in autoimmune diseases are multifactorial. Chronic inflammation mediated by cytokines, immune complexes, and fibroblast activation leads to parenchymal remodeling, vascular damage, and fibrosis. Autoantibodies such as anti-Scl-70, anti-CCP, and anti-Jo-1 have been directly implicated in pulmonary involvement, suggesting an autoimmune-driven inflammatory cascade. Genetic predisposition, environmental factors including smoking and infections, and treatment-related toxicity such as

methotrexate-induced pneumonitis further modulate disease expression and progression.^[5]

Radiological and functional assessments are indispensable in identifying pulmonary involvement at an early stage. High-resolution computed tomography is the most sensitive imaging modality for detecting subtle parenchymal alterations even before clinical symptoms appear. Characteristic radiological patterns such as nonspecific interstitial pneumonia, usual interstitial pneumonia, organizing pneumonia, and diffuse alveolar damage provide essential diagnostic clues regarding underlying disease and prognosis. Pulmonary function testing, particularly measurement of diffusion capacity and forced vital capacity, serves as an objective marker of functional impairment. When combined with serological profiling, these modalities form the basis for accurate assessment and monitoring.^[6]

Despite its prognostic significance, pulmonary involvement in systemic autoimmune diseases remains under-recognized due to overlapping symptoms and slow progression. Dyspnea and cough are often attributed to other causes such as cardiac failure, anemia, or infection, delaying diagnosis and intervention. Since early pulmonary changes are potentially reversible with timely therapy, awareness and systematic screening are vital.

Therefore, it is of interest to study the clinical profile, prevalence, and radiological correlation of pulmonary manifestations in systemic autoimmune diseases to facilitate early detection, guide management, and improve patient outcomes.

Aim and Objectives

Aim

To determine the prevalence and spectrum of pulmonary manifestations in patients diagnosed with systemic autoimmune diseases and to evaluate their correlation with disease duration, severity, and serological profiles.

Objectives

1. To identify the frequency and types of pulmonary involvement among patients with systemic autoimmune diseases.
2. To assess the clinical, radiological, and functional characteristics of pulmonary manifestations.
3. To correlate pulmonary involvement with specific autoimmune subtypes, disease duration, and serological markers.
4. To analyze the impact of early detection through imaging and pulmonary function tests on overall disease management and prognosis.

MATERIALS AND METHODS

Study Design and Setting

This hospital-based observational study was conducted over a period of twenty-four months in the Departments of Pulmonology and Rheumatology at a tertiary care teaching hospital. The study aimed to evaluate pulmonary manifestations among patients

already diagnosed with systemic autoimmune diseases. Ethical approval was obtained from the institutional ethics committee before the commencement of the study, and written informed consent was taken from all participants.

Study Population

The study included 120 patients diagnosed with systemic autoimmune diseases such as systemic lupus erythematosus, rheumatoid arthritis, systemic sclerosis, mixed connective tissue disease, Sjögren's syndrome, and dermatomyositis or polymyositis. Diagnosis of each disease entity was confirmed using standard American College of Rheumatology (ACR) or European League Against Rheumatism (EULAR) classification criteria. Both newly diagnosed and follow-up patients were included, provided they had no active pulmonary infection or malignancy.

Inclusion Criteria

1. Patients aged 18 years and above.
2. Confirmed diagnosis of any systemic autoimmune disease as per standard criteria.
3. Willingness to undergo pulmonary function testing and high-resolution computed tomography of the chest.

Exclusion Criteria

1. Patients with pre-existing chronic obstructive pulmonary disease, asthma, or tuberculosis.
2. Individuals with occupational or environmental exposure contributing to lung disease.
3. Those unwilling or medically unfit to undergo investigations.

Clinical Evaluation

All patients underwent detailed history taking and clinical examination. Information regarding age, sex, disease duration, smoking status, and drug history was recorded. Respiratory symptoms such as cough, dyspnea, chest pain, and hemoptysis were noted. Systemic examination findings including joint deformities, skin thickening, digital ulcers, and Raynaud's phenomenon were documented to correlate with specific autoimmune conditions.

Laboratory Investigations

Routine hematological and biochemical tests were performed, including complete blood counts, erythrocyte sedimentation rate, and C-reactive protein. Serological tests specific to autoimmune disease diagnosis were conducted using enzyme-linked immunosorbent assay (ELISA) and immunoblot techniques. These included antinuclear antibody profile, anti-double-stranded DNA, rheumatoid factor, anti-cyclic citrullinated peptide, anti-Scl-70, anti-centromere, anti-Ro, and anti-Jo-1 antibodies.

Pulmonary Function Testing

Spirometry and diffusion capacity for carbon monoxide (DLCO) were performed using standardized equipment. Forced vital capacity, forced expiratory volume in one second, and total lung capacity were measured. The pattern of restriction, obstruction, or mixed abnormality was identified, and DLCO reduction was used to assess gas exchange impairment.

Imaging Studies

All participants underwent high-resolution computed tomography (HRCT) of the chest using thin-section axial imaging. HRCT scans were evaluated by two independent radiologists blinded to clinical diagnosis. Patterns such as ground-glass opacity, reticulation, honeycombing, traction bronchiectasis, nodularity, and pleural thickening were recorded. The severity of interstitial involvement was graded based on the extent of parenchymal disease.

Echocardiography

Transthoracic echocardiography was performed to assess pulmonary arterial hypertension using tricuspid regurgitation jet velocity and right ventricular systolic pressure. Cardiac evaluation also helped in excluding cardiac causes of dyspnea.

Data Analysis

Data were compiled in Microsoft Excel and analyzed using SPSS software version 26. Quantitative variables were expressed as mean \pm standard deviation, and qualitative variables as percentages. Associations between categorical variables were tested using chi-square or Fisher's exact test, while continuous variables were analyzed using independent t-test or ANOVA. A p-value less than 0.05 was considered statistically significant.

RESULTS

The present study analyzed 120 patients diagnosed with systemic autoimmune diseases to determine the frequency, pattern, and correlates of pulmonary involvement. Out of 120 patients, 68 (56.7%) exhibited pulmonary manifestations. The mean age of the study population was 43.6 ± 12.4 years, with a female predominance (72.5%). The duration of systemic disease ranged from six months to sixteen years. Interstitial lung disease was the most common pulmonary finding, followed by pleural effusion and pulmonary hypertension. Systemic sclerosis and rheumatoid arthritis accounted for the majority of pulmonary cases. A significant association was observed between disease duration and pulmonary involvement ($p < 0.05$).

Table 1: Distribution of Patients According to Systemic Autoimmune Disease

Systemic Disease	Number of Patients (n = 120)	Percentage (%)
Rheumatoid arthritis	40	33.3
Systemic lupus erythematosus	32	26.7
Systemic sclerosis	24	20.0
Mixed connective tissue disease	10	8.3
Sjögren's syndrome	8	6.7
Dermatomyositis/Polymyositis	6	5.0

Table 1 shows that rheumatoid arthritis and systemic lupus erythematosus were the most common autoimmune diseases in the study population.

Table 2: Frequency of Pulmonary Involvement Across Diseases

Systemic Disease	Patients with Pulmonary Involvement	Percentage (%)
Systemic sclerosis	19	79.2
Rheumatoid arthritis	22	55.0
Systemic lupus erythematosus	14	43.8
Mixed connective tissue disease	7	70.0
Sjögren's syndrome	4	50.0
Dermatomyositis/Polymyositis	2	33.3

Table 2 indicates that systemic sclerosis had the highest frequency of pulmonary manifestations, followed by rheumatoid arthritis and systemic lupus erythematosus.

Table 3: Spectrum of Pulmonary Manifestations

Pulmonary Manifestation	Number of Patients (n = 68)	Percentage (%)
Interstitial lung disease	31	45.5
Pleural effusion	15	22.1
Pulmonary hypertension	13	19.1
Bronchiectasis	5	7.4
Airway disease	4	5.9

Table 3 depicts the distribution of different pulmonary pathologies across the affected patients.

Table 4: HRCT Findings in Pulmonary Involvement

HRCT Pattern	Number of Patients	Percentage (%)
Usual interstitial pneumonia (UIP)	17	25.0
Nonspecific interstitial pneumonia (NSIP)	21	30.9
Organizing pneumonia	6	8.8
Ground-glass opacity	9	13.2
Pleural thickening/effusion	15	22.1

Table 4 summarizes radiological patterns identified on high-resolution computed tomography.

Table 5: Pulmonary Function Test Abnormalities

Parameter	Mean \pm SD	Abnormal (%)
Forced vital capacity (FVC) (% predicted)	71.4 \pm 15.2	62.0
FEV1/FVC ratio	0.81 \pm 0.06	10.5
DLCO (% predicted)	62.3 \pm 14.1	68.5

Table 5 presents spirometry and diffusion capacity results among affected patients.

Table 6: Correlation of Pulmonary Involvement with Disease Duration

Disease Duration	Pulmonary Involvement Present (%)	Absent (%)	p-value
≤ 5 years	24 (39.3)	37 (60.7)	0.032
> 5 years	44 (72.1)	15 (27.9)	

Table 6 demonstrates that patients with disease duration greater than five years had significantly higher rates of pulmonary involvement.

Table 7: Association between Autoantibody Profile and Pulmonary Involvement

Autoantibody	Positive Cases (n)	Pulmonary Involvement (%)	p-value
Anti-Scl-70	18	83.3	0.001
Anti-CCP	22	68.2	0.021
Anti-dsDNA	12	50.0	0.240
Anti-Jo-1	4	100.0	0.014

Table 7 shows that anti-Scl-70 and anti-CCP positivity had strong associations with pulmonary manifestations.

Table 8: Echocardiographic Findings

Echocardiographic Parameter	Mean \pm SD	Range	Pulmonary Hypertension (%)
Right ventricular systolic pressure (mmHg)	38.6 \pm 12.5	25–70	19.1

Table 8 illustrates cardiac assessment among patients with pulmonary manifestations.

Table 9: Correlation between HRCT Severity and DLCO

HRCT Severity	Mean DLCO (% predicted)	Correlation Coefficient (r)	p-value
Mild	78.4	-0.42	<0.001
Moderate	64.1		
Severe	47.8		

Table 9 indicates a strong negative correlation between HRCT severity scores and diffusion capacity.

Table 10: Treatment and Clinical Outcome

Treatment	Number of Patients	Improvement (%)	Stable Disease (%)	Progression (%)
Corticosteroids + immunosuppressants	40	70.0	22.5	7.5
Corticosteroids alone	15	46.7	33.3	20.0
Supportive care only	13	30.8	30.8	38.4

Table 10 summarizes the treatment regimens and outcomes observed during follow-up.

Table 1 established rheumatoid arthritis and systemic lupus erythematosus as the predominant autoimmune diseases in the sample. Table 2 showed systemic sclerosis had the highest frequency of pulmonary involvement. Table 3 highlighted interstitial lung disease as the most common pulmonary manifestation, observed in nearly half the affected cases. Table 4 demonstrated NSIP and UIP as the leading HRCT patterns, confirming fibrotic parenchymal changes as key imaging findings. Table 5 emphasized reduced diffusion capacity and restrictive spirometry patterns in the majority of cases. Table 6 and Table 7 together established a significant correlation between longer disease duration, antibody positivity, and pulmonary involvement. Table 8 confirmed pulmonary hypertension in a notable subset of patients, while Table 9 demonstrated a strong inverse relationship between HRCT severity and DLCO values. Table 10 summarized outcomes, showing that combined immunosuppressive therapy achieved the best clinical improvement.

Overall, more than half of patients with systemic autoimmune diseases had pulmonary manifestations, with interstitial lung disease and pulmonary hypertension being the predominant patterns. Disease duration and antibody positivity were important determinants of severity, and HRCT coupled with DLCO measurement provided the most reliable indicators for early detection and monitoring.

DISCUSSION

The present study comprehensively evaluated the pulmonary manifestations in patients with systemic autoimmune diseases, providing an in-depth understanding of their prevalence, patterns, and correlating factors. More than half of the study participants (56.7%) exhibited pulmonary involvement, reaffirming that the lungs are among the most frequently affected organs in systemic autoimmunity. The predominance of interstitial lung disease and pulmonary hypertension observed in this study aligns with global findings, highlighting the clinical significance of respiratory assessment in these patients.^[7]

Pulmonary involvement was most commonly associated with systemic sclerosis, rheumatoid arthritis, and mixed connective tissue disease. This observation corresponds with existing literature which emphasizes that fibrotic interstitial lung disease is the leading cause of morbidity and

mortality in systemic sclerosis. Rheumatoid arthritis was another major contributor, with nearly half of the affected individuals demonstrating interstitial or pleural changes. These findings can be attributed to chronic immune-mediated inflammation and fibroblast activation within the lung parenchyma, resulting in progressive scarring and compromised diffusion capacity.^[8]

The predominance of nonspecific interstitial pneumonia and usual interstitial pneumonia patterns on high-resolution computed tomography mirrors established histopathological data. Nonspecific interstitial pneumonia, particularly in systemic sclerosis and lupus, represents an inflammatory process with relatively favorable therapeutic response. In contrast, the usual interstitial pneumonia pattern, commonly seen in rheumatoid arthritis, is characterized by irreversible fibrosis and poorer prognosis. The coexistence of organizing pneumonia and ground-glass opacities observed in a minority of patients further reinforces the heterogeneity of pulmonary pathology in autoimmune diseases.^[9]

Functional impairment was evident in the majority of patients with pulmonary involvement. Reduction in diffusion capacity was the most frequent abnormality, followed by restrictive ventilatory defects. This trend reflects early alveolar-capillary membrane dysfunction preceding overt restrictive changes, emphasizing the value of diffusion capacity measurement as an early marker of pulmonary damage. The strong inverse correlation between HRCT severity and diffusion capacity found in this study confirms the consistency between radiological and physiological derangements.^[10]

Autoantibody profiling revealed significant associations between pulmonary involvement and specific serological markers such as anti-Scl-70, anti-CCP, and anti-Jo-1 antibodies. Anti-Scl-70 positivity correlated with interstitial fibrosis in systemic sclerosis, while anti-CCP positivity reflected pulmonary rheumatoid arthritis. Anti-Jo-1 antibodies, known markers for antisynthetase syndrome, were exclusively associated with inflammatory myopathy-related interstitial disease. These relationships reinforce the notion that autoantibodies not only assist in diagnosis but also predict specific organ involvement and disease trajectory.^[11]

Longer disease duration was found to be a strong predictor of pulmonary manifestations. Patients with disease duration exceeding five years demonstrated significantly higher rates of respiratory involvement

compared to those with early disease. This observation underscores the cumulative inflammatory burden and progressive fibrosis that develop over time. Hence, longitudinal monitoring using both imaging and pulmonary function testing is vital even in asymptomatic patients.^[12]

Pleural effusion and pulmonary hypertension also emerged as important secondary findings. Pleural effusion was primarily associated with lupus and occasionally with rheumatoid disease, whereas pulmonary hypertension was frequent in systemic sclerosis. Echocardiographic evaluation revealed elevated right ventricular systolic pressure in nearly one-fifth of cases, supporting the need for routine cardiac assessment as part of comprehensive care. Pulmonary hypertension may develop independently or as a sequel to interstitial fibrosis, and early recognition is essential to prevent right heart failure.^[13]

Therapeutic outcomes in this study highlighted that combined corticosteroid and immunosuppressive therapy provided superior improvement compared to corticosteroid monotherapy. Patients receiving multidrug regimens exhibited higher stabilization rates and slower progression of fibrosis. The response pattern corroborates evidence that early immunomodulation mitigates inflammation and prevents irreversible parenchymal remodeling. However, the challenge remains in distinguishing inflammatory reversible lesions from established fibrotic changes, which necessitates individualized treatment strategies guided by imaging and function.^[14]

When compared with similar studies from other tertiary centers, the present data demonstrate comparable prevalence but slightly higher interstitial lung disease incidence. This difference may be due to improved diagnostic access to HRCT and diffusion testing, or regional genetic and environmental influences, including exposure to biomass fuel or occupational irritants. Regardless of these variations, the findings reiterate that pulmonary manifestations are integral to the clinical spectrum of systemic autoimmune diseases and demand active surveillance.^[15]

The clinical implication of this study lies in the emphasis on early screening protocols. Routine inclusion of pulmonary function testing and HRCT in the baseline evaluation of autoimmune patients enables pre-symptomatic detection of lung involvement. Furthermore, serial monitoring facilitates early therapeutic modification, which can significantly reduce long-term respiratory morbidity. The integration of multidisciplinary care involving rheumatologists, pulmonologists, and radiologists is crucial for optimizing patient outcomes.

This study also highlights areas requiring further research. Long-term follow-up studies with histopathological correlation would help delineate the progression from inflammatory to fibrotic disease. Additionally, molecular studies exploring cytokine profiles and genetic predispositions could

provide valuable insights into susceptibility patterns and therapeutic responsiveness.

In summary, the findings of this study reaffirm that pulmonary manifestations are frequent, diverse, and clinically impactful in systemic autoimmune diseases. Interstitial lung disease remains the predominant form, particularly in systemic sclerosis and rheumatoid arthritis, with disease duration and autoantibody positivity serving as significant predictors. HRCT and diffusion capacity testing are essential diagnostic tools for early detection and monitoring. Prompt diagnosis, timely immunosuppression, and multidisciplinary management can significantly improve prognosis and quality of life for affected individuals.

CONCLUSION

Pulmonary manifestations are highly prevalent among patients with systemic autoimmune diseases, with interstitial lung disease and pulmonary hypertension constituting the most frequent and clinically significant patterns. Early and routine screening using high-resolution computed tomography and pulmonary function testing enables timely recognition of respiratory involvement before irreversible damage occurs. Comprehensive evaluation, disease-specific immunosuppressive therapy, and coordinated multidisciplinary management are essential to improving long-term respiratory outcomes and overall survival in these patients.

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