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Original Research Article

Lung Function Impairment and Disease Activity in Rheumatoid Arthritis: A Cross-Sectional Study

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Conflict of interest: Nil

Abstract

Background: Rheumatoid arthritis (RA) is a systemic autoimmune disorder with substantial extra-articular involvement, of which pulmonary manifestations are an important cause of morbidity. Pulmonary abnormalities may occur in the absence of respiratory symptoms and can include interstitial, obstructive, restrictive, or mixed patterns. Pulmonary function tests, particularly spirometry and measurement of diffusing capacity for carbon monoxide (DLCO), may facilitate the detection of early pulmonary involvement.

Objective: To evaluate pulmonary manifestations in patients with rheumatoid arthritis and assess their association with spirometric parameters, DLCO, and disease activity.

Materials and Methods: A hospital-based cross-sectional study was conducted among 60 patients with clinically and/or serologically confirmed RA attending the Departments of Respiratory Medicine and Rheumatology at People's Hospital, Bhopal. Following informed consent, demographic characteristics, clinical history, respiratory symptoms, and examination findings were recorded. Participants underwent routine laboratory investigations, rheumatoid factor assessment, chest radiography, spirometry, and DLCO measurement. Disease activity was assessed using the Clinical Disease Activity Index (CDAI) and Simplified Disease Activity Index (SDAI). Pulmonary function abnormalities were analysed in relation to clinical characteristics and disease activity.

Results: The study included 60 patients with rheumatoid arthritis, of whom 46 (76.7%) were women. The largest proportion of participants belonged to the 41–50-year age group [24 (40.0%)]. More than half of the patients [31 (51.7%)] were asymptomatic, while dyspnoea was the most frequently reported respiratory symptom [16 (26.7%)]. Chest radiography was normal in 40 (66.7%) patients. Abnormal spirometric findings were observed in 29 (48.3%) patients, with a restrictive ventilatory pattern being the most common abnormality [18 (30.0%)]. Reduced DLCO was detected in 38 (63.3%) patients. Both spirometry and DLCO were abnormal in 24 (40.0%) patients, whereas isolated DLCO impairment was observed in 14 (23.3%). Pulmonary manifestations were identified in 32 (53.3%) patients, with interstitial lung disease being the most frequent [17 (28.3%)]. Pulmonary function abnormalities showed significant associations with disease activity assessed using CDAI and SDAI.

Conclusion: Pulmonary involvement was common among patients with RA, including those without respiratory symptoms. Reduced DLCO was more frequently observed than spirometric abnormalities, suggesting that DLCO may provide additional sensitivity for detecting early or subclinical pulmonary involvement. Incorporating DLCO along with spirometry into the pulmonary evaluation of patients with RA may facilitate earlier recognition of respiratory abnormalities and enable timely clinical assessment and management.

Keywords: Rheumatoid Arthritis, Pulmonary Manifestations, DLCO, Spirometry, Interstitial Lung Disease.

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Introduction

Rheumatoid arthritis (RA) is a chronic, immune-mediated inflammatory disease that predominantly affects the synovial joints but can also involve multiple extra-articular organs. Although joint pain, swelling, morning stiffness, and progressive deformity are its characteristic clinical features, RA is increasingly recognized as a systemic disorder in which persistent inflammation may affect the skin, eyes, cardiovascular system, nervous system, vasculature, and respiratory system. Extra-articular involvement contributes substantially to the overall disease burden and may influence functional capacity, quality of life, therapeutic decisions, and long-term outcomes. Among the various extra-articular manifestations, pulmonary involvement is of particular clinical significance because it may remain asymptomatic during the early stages and become apparent only after considerable functional impairment has developed. [1]

The respiratory system is commonly affected in RA, reflecting the complex interplay between systemic autoimmunity and pulmonary immune mechanisms. Pulmonary manifestations can involve virtually any thoracic compartment, including the lung parenchyma, pleura, airways, pulmonary vasculature, and respiratory muscles. Reported manifestations include interstitial lung disease (ILD), pleural effusion, pleural thickening, airway disease, bronchiectasis, bronchiolitis, pulmonary nodules, and drug-induced pulmonary toxicity. Clinical presentation is often variable, and symptoms such as exertional dyspnoea, persistent dry cough, chest discomfort, and reduced exercise tolerance may be mild, non-specific, or absent. Consequently, pulmonary involvement may remain undetected on the basis of clinical assessment alone, underscoring the importance of objective pulmonary evaluation, including in patients without overt respiratory symptoms. [2]

Among pulmonary complications of RA, interstitial lung disease represents one of the most clinically important manifestations. Chronic inflammatory processes can result in injury and subsequent fibrotic remodeling of the pulmonary interstitium, leading to impaired gas exchange and progressive reduction in pulmonary reserve. RA-associated ILD may be characterized by restrictive ventilatory abnormalities, impaired pulmonary diffusion capacity, and radiological evidence of interstitial involvement. The onset and progression of ILD may be insidious, and its recognition can be delayed when respiratory symptoms are absent or are attributed to other conditions such as ageing, anaemia, physical deconditioning, cardiovascular disease, or pre-existing respiratory disorders. Early identification of RA-associated ILD is therefore important, given its potential impact on morbidity, mortality, prognosis, and therapeutic decision-making. [3] Airway disease constitutes another important component of pulmonary involvement in RA. Both large and small airways may be affected, resulting in obstructive airway disease, bronchiectasis, bronchiolitis, or mixed ventilatory abnormalities. Unlike parenchymal disease, airway involvement may not produce a restrictive ventilatory pattern and can remain undetected when assessment is based solely on respiratory symptoms or conventional chest radiography. Pleural involvement may manifest as pleural effusion, pleural thickening, or pleuritic chest pain, while pulmonary nodules may occur in some patients and may require differentiation from infectious, malignant, or granulomatous conditions. The diverse spectrum of pulmonary manifestations highlights the heterogeneous nature of RA-associated respiratory disease and the need for systematic assessment. [4]

Pulmonary function testing (PFT) has an important role in the detection and characterization of respiratory involvement in patients with RA. Spirometry is a simple, non-invasive, reproducible, and widely accessible investigation that provides an assessment of airflow and ventilatory function. Parameters including forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), and the FEV_1/FVC ratio aid in identifying obstructive, restrictive, and mixed ventilatory patterns. In RA, spirometry can detect restrictive abnormalities associated with interstitial lung involvement as well as obstructive changes related to airway disease. However, spirometric measurements may remain within normal limits during the early stages of pulmonary involvement, particularly when parenchymal disease is mild or when impairment predominantly affects gas exchange rather than lung volumes. [5]

Material and Methods

After obtaining written informed consent, baseline demographic characteristics, clinical history, and relevant examination findings were recorded for all participants. The cross-sectional study included clinically and serologically confirmed patients with rheumatoid arthritis (RA) attending the Rheumatology Clinic or Department of Respiratory Medicine who fulfilled the predefined inclusion and exclusion criteria.

All participants underwent routine laboratory investigations, including complete blood count, liver function tests, kidney function tests, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP), along with rheumatoid factor (RF) estimation, chest radiography, and pulmonary function testing comprising spirometry and

measurement of diffusing capacity of the lung for carbon monoxide (DLCO). RA was defined as a systemic autoimmune inflammatory disease characterized predominantly by inflammatory polyarthritis with potential extra-articular involvement and was classified according to the 2010 American College of Rheumatology/European Alliance of Associations for Rheumatology (ACR/EULAR) classification criteria. The classification score was based on the number and site of involved joints, serological findings including RF and anti-citrullinated protein antibody (ACPA), duration of symptoms, and acute-phase reactants including ESR and CRP; a total score of ≥6/10 was considered consistent with definite RA.

Disease activity was assessed using the Clinical Disease Activity Index (CDAI) and Simplified Disease Activity Index (SDAI). CDAI was calculated from the tender joint count, swollen joint count, patient global assessment, and evaluator global assessment of disease activity. CDAI scores were categorized as remission (≤2.8), low disease activity (>2.8 to ≤10), moderate disease activity (>10 to ≤22), and high disease activity (>22). SDAI was calculated using the tender joint count, swollen joint count, patient global assessment, evaluator global assessment, and CRP level (mg/dL), with disease activity categorized as remission (≤3.3), low disease activity (>3.3 to ≤11), moderate disease activity (>11 to ≤26), and high disease activity (>26). Spirometric parameters were assessed to identify obstructive and restrictive ventilatory patterns. An obstructive pattern was characterized by a reduced FEV_1 and FEV_1/FVC ratio <0.70, whereas a restrictive pattern was suggested by reduced FEV_1 and FVC with a preserved or increased FEV_1/FVC ratio (>0.70). DLCO was categorized according to the percentage of predicted value, with values >75% considered normal, 60–75% indicating mild reduction, 40–59% indicating moderate reduction, and <40% indicating severe reduction.

Results

A total of 60 patients with rheumatoid arthritis were included in the study. The majority were females (46, 76.7%), while 14 (23.3%) were males. The most commonly represented age group was 41–50 years, comprising 24 (40.0%) participants (Table 1). Regarding respiratory symptoms, 31 (51.7%) patients were asymptomatic, whereas dyspnoea was the most frequently reported symptom (16, 26.7%), followed by cough (10, 16.7%) and chest pain (3, 5.0%). Chest radiography was normal in 40 (66.7%) patients, while interstitial infiltrates, pleural effusion, reticulonodular opacities, and bronchiectatic changes were observed in 8 (13.3%), 7 (11.7%), 3 (5.0%), and 2 (3.3%) patients, respectively (Table 2).

Spirometry was normal in 31 (51.7%) participants, whereas 29 (48.3%) demonstrated ventilatory abnormalities. A restrictive pattern was the most frequent abnormality (18, 30.0%), followed by obstructive (7, 11.7%) and mixed patterns (4, 6.7%). DLCO was normal in 22 (36.7%) participants, while 38 (63.3%) had reduced DLCO, including mild, moderate, and severe reductions in 20 (33.3%), 14 (23.3%), and 4 (6.7%) patients, respectively. Both spirometry and DLCO were abnormal in 24 (40.0%) patients, whereas isolated DLCO abnormality and isolated spirometric abnormality were observed in 14 (23.3%) and 4 (6.7%) patients, respectively (Table 3).

The distribution of disease activity and its association with pulmonary function parameters is presented in Tables 4 and 5. Increasing disease activity was associated with a greater proportion of spirometric and DLCO abnormalities. CDAI demonstrated a statistically significant association with spirometric abnormalities (p=0.02) and DLCO impairment (p=0.005). Similarly, SDAI was significantly associated with spirometric abnormalities (p=0.02) (Tables 4 and 5).

Overall, pulmonary manifestations were identified in 32 (53.3%) participants. Interstitial lung disease was the most frequent pulmonary manifestation (17, 28.3%), followed by pleural effusion (7, 11.6%), airway disease (5, 8.3 %), and pulmonary nodules (3, 5.0%) (Table 6). Notably, pulmonary abnormalities were observed even among patients without overt respiratory symptoms, highlighting the potential value of objective pulmonary function assessment in patients with RA.

Table 1: Demographic Distribution of Participants (n=60)

Variable	Category	n	%
Age of participant (years)	<30	6	10
	31–40	13	21.7
	41–50	24	40.0
	51–60	11	18.3
	>60	6	10.0
Gender	Female	46	76.7
	Male	14	23.3

Table 2: Clinical Presentation and Chest X-Ray Findings in RA Participants (n=60)

Variable	Findings	n	%
Symptoms	Asymptomatic	31	51.7
	Dyspnea	16	26.7
	Cough	10	16.7
	Chest Pain	3	5.0
CXR Findings	Normal	40	66.7
	Interstitial infiltrates	8	13.3
	Pleural Effusion	7	11.7
	Reticulonodular opacities	3	5.0
	Bronchiectasis	2	3.3

Table 3: Spirometry, DLCO and Spirometry vs DLCO Findings in RA Participants (n=60)

Variable	Pattern / Pulmonary Status	Number	%
Spirometry Findings	Normal	31	51.7
	Restrictive	18	30.0
	Obstructive	7	11.7
	Mixed	4	6.7
DLCO Findings	Normal	22	36.7
	Mild Reduction	20	33.3
	Moderate Reduction	14	23.3
	Severe Reduction	4	6.7
Spirometry and DLCO Comparison Findings	Both Normal	18	30.0
	Isolated DLCO abnormality	14	23.3
	Isolated spirometry abnormality	4	6.7
	Both Abnormal	24	40.0
p value	0.02		<0.05 Significant

Table 4: Correlation of CDAI with Spirometry and DLCO in Study Participants (n= 60)

CDAI	Spirometry Normal	Spirometry Abnormal	Total	DLCO Normal	DLCO Abnormal	Total
Remission	8	1	9	7	2	9
Low	10	6	16	7	9	16
Moderate	9	13	22	6	16	22
High	4	9	13	2	11	13
Total	31	29	60	22	38	60
p value		0.02	Significant		0.005	Significant

Table 5: Correlation of SDAI with Spirometry in Study Participants (n=60)

SDAI	Normal	Abnormal	Total
Remission	6	1	7
Low	11	4	15
Moderate	10	14	24
High	4	10	14
Total	31	29	60
p value		0.02	Significant

Table 6: Percentage of Pulmonary Manifestation in RA Study Participants (n=60)

Pulmonary Manifestation	Number (n=60)	Percentage
No pulmonary involvement (Normal)	28	46.7
Interstitial Lung Disease (ILD)	17	28.3
Pleural effusion	7	11.6
Airway disease	5	8.3
Pulmonary nodules	3	5
Total	60	100

Discussion

Rheumatoid arthritis (RA) is a systemic autoimmune disease with substantial extra-articular involvement, of which pulmonary manifestations are an important cause of morbidity. Pulmonary disease may remain clinically silent and can involve the lung parenchyma, airways, pleura, and pulmonary vasculature. [1-4] In the present study, 60 patients with RA were evaluated for pulmonary involvement using clinical assessment, chest radiography, spirometry, and DLCO. Females predominated [46 (76.7%)] and the largest proportion belonged to the 41–50-year age group [24 (40.0%)] (Table 1). This pattern was comparable with Robles-Pérez et al., who reported 75% female participants with a mean age of 47.1 years in a cohort of early RA patients. [7]

More than half of the participants [31 (51.7%)] were asymptomatic, while dyspnoea was the most common respiratory symptom [16 (26.7%)], followed by cough [10 (16.7%)] and chest pain [3 (5.0%)] (Table 2).

Chest radiography was normal in 40 (66.7%) patients, whereas interstitial infiltrates, pleural effusion, reticulonodular opacities, and bronchiectatic changes were observed in 8 (13.3%), 7 (11.7%), 3 (5.0%), and 2 (3.3%), respectively.

Kawassaki et al. similarly demonstrated that pulmonary abnormalities may occur in RA patients without respiratory complaints. [8] Wilsher et al. reported a higher frequency of airway and parenchymal abnormalities using HRCT, including bronchiectasis and interstitial changes. [9] The lower radiographic abnormality rate in the present study may reflect the lower sensitivity of conventional chest radiography compared with HRCT.

Spirometry was abnormal in 29 (48.3%) patients, with restrictive impairment being the predominant pattern [18 (30.0%)], followed by obstructive [7 (11.7%)] and mixed abnormalities [4 (6.7%)] (Table 3). Mehrabi et al. reported normal spirometry in 50% and restrictive impairment in 45% of RA patients, showing a similar predominance of restrictive dysfunction. [10]

DLCO was reduced in 38 (63.3%) participants, exceeding the frequency of spirometric abnormalities. Al-Assadi et al. also reported impaired pulmonary function and demonstrated a relationship between lung function and RA disease activity. [11] Importantly, 14 (23.3%) patients had isolated DLCO impairment, supporting the complementary role of diffusion assessment. Bessa et al. similarly demonstrated significant associations between pulmonary functional abnormalities and DLCO in RA patients. [12]

Disease activity showed significant associations with pulmonary dysfunction. CDAI was associated with abnormal spirometry (p=0.02) and DLCO impairment (p=0.005), while SDAI was associated with spirometric abnormalities (p=0.02) (Tables 4 and 5). Sparks et al. reported that increasing RA disease activity was associated with a higher risk of incident RA-associated ILD.[13] Overall, pulmonary manifestations were present in 32 (53.3%) patients, with ILD being the most frequent [17 (28.3%)] (Table 6). Bilgici et al. reported pulmonary abnormalities in 67.3% of RA patients using HRCT and pulmonary function testing. [14] The present findings reinforce the importance of combining spirometry and DLCO for early detection of pulmonary involvement, particularly in asymptomatic patients and those with higher disease activity.

Conclusion

Pulmonary involvement was common among patients with rheumatoid arthritis, with interstitial lung disease being the predominant manifestation. DLCO detected pulmonary abnormalities more frequently than spirometry, highlighting its potential value for early identification of subclinical pulmonary involvement. Combined assessment with spirometry and DLCO may facilitate timely detection and management of respiratory complications in RA.

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