e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2026; 18(7); 552-558

Original Research Article

Assessment of Pulmonary Manifestations and Its Correlation with DLCO and Spirometry in Patients with Rheumatoid Arthritis

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Received: 01-04-2026 / Revised: 15-05-2026 / Accepted: 21-06-2026

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Conflict of interest: Nil

Abstract

Background: Rheumatoid arthritis is a chronic systemic autoimmune disease that primarily affects the joints but may also involve extra-articular organs, especially the lungs. Pulmonary involvement in rheumatoid arthritis may remain asymptomatic in the early stage and can present with restrictive, obstructive, or mixed ventilatory defects. Spirometry and diffusing capacity of the lung for carbon monoxide (DLCO) are important pulmonary function tests for detecting respiratory impairment and assessing subclinical lung involvement.

Aim: The aim of the study was to assess pulmonary manifestations and their correlation with DLCO and spirometry in patients with rheumatoid arthritis.

Material and Methods: This single-centre, hospital-based, cross-sectional study was conducted in the Outpatient Department of Respiratory Medicine and Rheumatology Department at People's Hospital, Bhopal. A total of 54 patients with clinically and/or serologically confirmed rheumatoid arthritis were included as per inclusion and exclusion criteria. After obtaining written informed consent, demographic details, clinical history, respiratory symptoms, and relevant examination findings were recorded. All participants underwent routine investigations, rheumatoid factor assessment, chest X-ray, spirometry, and DLCO testing. Disease activity was assessed using the Clinical Disease Activity Index and Simplified Disease Activity Index. Data were analysed to determine pulmonary manifestations and their correlation with spirometry and DLCO findings.

Results: Among 54 participants, the majority were in the 41–50 years age group, 22 (40.7%), and females predominated, 41 (75.9%). Respiratory symptoms were absent in 28 (51.85%) patients, while dyspnea was the most common symptom, seen in 14 (25.67%). Chest X-ray was normal in 36 (66.67%) patients. Spirometry was abnormal in 26 (48.15%) patients, with restrictive pattern being the most common abnormality, 16 (29.63%). DLCO was reduced in 34 (62.96%) patients. Both spirometry and DLCO were abnormal in 22 (40.74%) cases, while isolated DLCO abnormality was seen in 12 (22.22%). Significant correlation was observed between pulmonary function abnormalities and disease activity assessed by CDAI and SDAI.

Conclusion: Pulmonary involvement was common in rheumatoid arthritis patients, with interstitial lung disease being the most frequent manifestation. DLCO detected more abnormalities than spirometry and may help in early identification of subclinical pulmonary involvement.

Keywords: Rheumatoid arthritis, pulmonary manifestations, DLCO, Spirometry, Interstitial lung disease.

DOI: 10.25258/ijcpr.18.7.87

Introduction

Rheumatoid arthritis is a chronic, immune-mediated inflammatory disorder that primarily involves the synovial joints but may also affect several extra-articular organs. Although joint pain, swelling, morning stiffness, and deformity are the most recognized features, rheumatoid arthritis is now understood as a systemic disease in which persistent inflammation can involve the skin, eyes, cardiovascular system, nervous system, blood vessels, and lungs. The extra-articular burden of the disease is clinically important because it may influence functional status, quality of life, treatment

selection, and long-term prognosis. Among the extra-articular manifestations, pulmonary involvement has special importance because it may remain silent in the early stage and may become clinically evident only after significant functional impairment has developed. [1] The lungs are frequently affected in rheumatoid arthritis because of the shared immunological relationship between the respiratory system and systemic autoimmunity. Pulmonary manifestations may involve almost every part of the thorax, including the lung parenchyma, pleura, airways, pulmonary vasculature, and respiratory muscles. Common pulmonary manifestations include interstitial lung disease, pleural effusion, pleural thickening, airway disease, bronchiectasis, bronchiolitis, pulmonary nodules, and drug-related lung toxicity.

In many patients, respiratory complaints such as exertional dyspnea, dry cough, chest discomfort, and reduced exercise tolerance may be mild or non-specific, making clinical detection difficult. Therefore, objective pulmonary assessment is necessary even in patients who do not have obvious respiratory symptoms. [3] Interstitial lung disease is one of the most clinically significant pulmonary complications of rheumatoid arthritis. It occurs due to chronic inflammation and fibrotic remodeling of the pulmonary interstitium, leading to impaired gas exchange and progressive reduction in respiratory reserve. Rheumatoid arthritis-associated interstitial lung disease may present with restrictive ventilatory impairment, reduced diffusion capacity, and radiological evidence of interstitial involvement. The disease may develop gradually and may be under-recognized when symptoms are absent or attributed to age, anemia, deconditioning, cardiac disease, or other respiratory disorders. Early detection is therefore essential because pulmonary involvement may affect morbidity, mortality, and therapeutic decisions.[3] Airway involvement is another important pulmonary manifestation of rheumatoid arthritis. It may affect both large and small airways and can present as obstructive airway disease, bronchiectasis, bronchiolitis, or mixed ventilatory defects. Unlike interstitial lung disease, airway involvement may not always produce classical restrictive patterns and may be missed if only symptoms or chest radiography are considered.

In addition, pleural disease may present as pleural effusion, pleural thickening, or pleuritic chest pain. Pulmonary nodules may also occur and may require differentiation from infection, malignancy, and other granulomatous disorders. Thus, rheumatoid arthritis-related lung disease is heterogeneous and requires systematic evaluation. [4] Pulmonary function testing plays a central role in detecting respiratory involvement in rheumatoid arthritis. Spirometry is a simple, non-invasive, reproducible, and widely available test used to assess airflow limitation and ventilatory patterns. It helps identify obstructive, restrictive, and mixed abnormalities by measuring parameters such as forced vital capacity, forced expiratory volume in one second, and the FEV1/FVC ratio. In rheumatoid arthritis, spirometry is useful for detecting restrictive impairment due to interstitial lung disease as well as obstructive changes due to airway involvement. However, spirometry may remain normal in early pulmonary disease, especially when parenchymal involvement is mild or predominantly affects gas exchange rather than lung volume. [5] Diffusing capacity of the lung for carbon monoxide is an important functional marker of alveolar-capillary gas transfer. DLCO may become abnormal before obvious spirometric impairment develops, particularly in early interstitial lung disease, pulmonary vascular involvement, or subclinical parenchymal disease. A reduced DLCO reflects impaired diffusion across the alveolar-capillary membrane and may indicate early pulmonary involvement even when chest X-ray and spirometry are normal. For this reason, DLCO provides complementary information to spirometry and is considered valuable in screening and monitoring patients with systemic autoimmune rheumatic diseases who are at risk of interstitial lung disease. [6]

Material and Methods

A single centre, hospital-based, cross-sectional study was designed to assess the pulmonary manifestations and its correlation with DLCO and spirometry in patients with rheumatoid arthritis. The study was conducted in the Outpatient Department (OPD) of Respiratory Medicine and Rheumatology Department at People's Hospital, Bhopal. The total duration of the study was 18 months, from April 2024 to October 2025. The study population included all patients attending the Department of Respiratory Medicine and Rheumatology during the study period and fulfilling the inclusion criteria.

The research protocol, data collection form, and informed consent form underwent thorough review and scrutiny by the Institute's Ethical Committee to ensure that the study adhered to ethical guidelines. The study complied with the principles outlined in the Declaration of Helsinki, ensuring that all participants' rights, safety, and well-being were protected. Written informed consent was obtained from all participants before enrolment in the study.

Patients with known rheumatoid arthritis aged above 18 years, who were seropositive for rheumatoid factor and/or clinically diagnosed rheumatoid arthritis with lung involvement, and who were willing to give written informed consent were included in the study. Patients aged more than

60 years, smokers, alcoholic patients, patients with baseline lung disease due to other aetiologies such as COPD, bronchiectasis, post-tuberculosis lung disease, COAD, post-infective fibrosis, patients with cardiac dysfunction, severe anaemia, overlap of myositis or scleroderma, pregnant females, neoplasms, and patients not willing to participate in the study were excluded.

Methodology

After obtaining written informed consent, baseline demographic and clinical data were collected from all participants. Detailed clinical evaluation and relevant history were recorded. This cross-sectional study was carried out among clinically and serologically confirmed rheumatoid arthritis patients, as per the inclusion and exclusion criteria, attending the Rheumatology clinic or the Department of Respiratory Medicine.

All patients underwent routine investigations including complete blood count, liver function tests, kidney function tests, ESR, and CRP. Pulmonary function tests including spirometry and DLCO, rheumatoid factor estimation, and chest X-ray were also performed.

Rheumatoid arthritis was defined as a systemic autoimmune disease characterized by inflammatory arthritis and extra-articular manifestations. Rheumatoid arthritis was diagnosed using the 2010 American College of Rheumatology and European League against Rheumatism classification criteria. The scoring system included joint involvement, serology including RF and ACPA, symptom duration, and acute phase reactants including CRP and ESR. A total score of ≥6 was considered diagnostic of definite rheumatoid arthritis.

Assessment of Disease Activity and Pulmonary Function: Disease activity was assessed using the Clinical Disease Activity Index and Simplified Disease Activity Index. CDAI was calculated using swollen joint count, tender joint count, patient global assessment of disease activity, and evaluator global assessment of disease activity. CDAI interpretation was done as follows: ≤2.8 was considered remission, >2.8 and ≤10 was considered low disease activity, >10 and ≤22 was considered moderate disease activity, and >22 was considered high disease activity. SDAI was calculated using swollen joint count, tender joint count, and patient global assessment of disease activity, evaluator global assessment of disease activity, and CRP in mg/dL. Remission was defined as SDAI <3.3, low disease activity as ≤11, moderate disease activity as ≤26, and high disease activity as >26.

Pulmonary function test criteria were used to assess lung disease activity. Typical spirometry findings in obstructive lung disease included reduced FEV1 of <80% of the predicted normal, reduced FVC to a lesser extent than FEV1, and reduced FEV1/FVC ratio of <0.7. Typical spirometry findings in restrictive lung disease included reduced FEV1 of <80% of the predicted normal, reduced FVC of <80% of the predicted normal, and normal FEV1/FVC ratio of >0.7. DLCO was interpreted as normal when DLCO was >75% to 140%, mild when DLCO was 60% to the lower limit of normal, moderate when DLCO was 40% to 60% of the lower limit of normal, and severe when DLCO was <40% of the lower limit of normal.

Results

Table 1 presents the demographic distribution of the 54 study participants diagnosed with rheumatoid arthritis. The majority of the participants belonged to the 41–50 years age group, accounting for 22 (40.7%) patients, indicating that rheumatoid arthritis with pulmonary evaluation was most commonly observed in middle-aged adults. This was followed by the 31–40 years age group with 12 (22.2%) participants and the 51–60 years age group with 10 (18.5%) participants. The youngest age group (<30 years) and participants aged >60 years each comprised 5 (9.26%) individuals. Gender distribution demonstrated a marked female predominance, with 41 (75.9%) females compared to 13 (24.1%) males.

Table 2 summarizes the clinical presentation and chest radiographic findings among the study participants. More than half of the patients, 28 (51.85%), were asymptomatic with respect to respiratory symptoms, suggesting that pulmonary involvement may remain clinically silent in a substantial proportion of rheumatoid arthritis patients.

Among symptomatic individuals, dyspnea was the most common presenting complaint, observed in 14 (25.67%) participants, followed by cough in 9 (16.67%) patients and chest pain in 3 (5.56%) patients. Chest X-ray examination revealed normal findings in 36 (66.67%) participants, whereas 18 (33.33%) patients demonstrated radiological abnormalities. Among these abnormalities, interstitial infiltrates were the most frequent finding, present in 7 (12.96%) participants, followed by pleural effusion in 6 (11.11%), reticulonodular opacities in 3 (5.56%), and bronchiectasis in 2 (3.70%) patients.

Table 3 illustrates the pulmonary function assessment using spirometry and DLCO, along with their combined comparison. Spirometry findings were normal in 28 (51.85%) participants, while 26 (48.15%) patients exhibited abnormal pulmonary function. Among abnormal spirometry patterns, the restrictive pattern was the most common, affecting 16 (29.63%) participants, followed by the obstructive pattern in 6 (11.11%)

and the mixed pattern in 4 (7.4%) patients. DLCO assessment demonstrated normal diffusion capacity in only 20 (37.04%) participants, whereas 34 (62.96%) patients had impaired gas diffusion. Mild reduction in DLCO was the most frequent abnormality, occurring in 18 (33.33%) patients, followed by moderate reduction in 12 (22.22%) and severe reduction in 4 (7.41%) patients.

Comparison of spirometry and DLCO findings revealed that 22 (40.74%) participants had abnormalities in both investigations, while 16 (29.63%) had both tests within normal limits. Importantly, 12 (22.22%) participants demonstrated isolated DLCO abnormalities despite normal spirometry, whereas only 4 (7.41%) had isolated spirometric abnormalities.

The association between spirometry and DLCO findings was statistically significant ($p = 0.02$), indicating that DLCO detected pulmonary impairment in several patients who still had preserved spirometric values, highlighting its usefulness for identifying early pulmonary involvement in rheumatoid arthritis. Table 4 demonstrates the correlation between Clinical Disease Activity Index (CDAI) and pulmonary function abnormalities assessed by spirometry and DLCO.

Spirometry abnormalities increased progressively with increasing disease activity. Among patients in remission, only 1 of 8 patients had abnormal spirometry, whereas abnormalities were observed in 5 of 14 patients with low disease activity, 12 of 20 patients with moderate disease activity, and 8 of 12 patients with high disease activity. This association was statistically significant ($p = 0.02$). A similar but stronger trend was observed with DLCO. Abnormal DLCO findings were present in 2 of 8 patients in remission, 7 of 14 patients with low disease activity, 15 of 20 patients with moderate disease activity, and 10 of 12 patients with high disease activity.

The correlation between CDAI and DLCO abnormalities was highly statistically significant ($p = 0.005$). Table 5 presents the correlation between the Simplified Disease Activity Index (SDAI) and spirometric findings. Among patients in SDAI remission, only 1 of 6 participants demonstrated abnormal spirometry.

The frequency of abnormal spirometry gradually increased with disease activity, affecting 4 of 14 patients with low disease activity, 13 of 22 patients with moderate disease activity, and 8 of 12 patients with high disease activity. This progressive increase in pulmonary function abnormalities with worsening SDAI scores was statistically significant ($p = 0.02$).

Table 6 describes the overall pattern of pulmonary manifestations observed among the rheumatoid arthritis patients. Twenty-five (46.3%) participants had no evidence of pulmonary involvement, whereas 29 (53.7%) demonstrated one or more pulmonary manifestations. Interstitial lung disease (ILD) was the most common pulmonary complication, affecting 15 (27.7%) participants. Pleural effusion was observed in 7 (13.0%) patients, followed by airway disease in 4 (7.4%) participants and pulmonary nodules in 3 (5.6%) patients.

Table 1: Demographic Distribution of Participants (n=54)

Variable	Category	n	%
Age of participant (years)	<30	5	9.26
	31–40	12	22.2
	41–50	22	40.7
	51–60	10	18.5
	>60	5	9.26
Gender	Female	41	75.9
	Male	13	24.1

Table 2: Clinical Presentation and Chest X-Ray Findings in RA Participants (n=54)

Variable	Findings	n	%
Symptoms	Asymptomatic	28	51.85
	Dyspnea	14	25.67
	Cough	9	16.67
	Chest Pain	3	5.56
CXR Findings	Normal	36	66.67
	Interstitial infiltrates	7	12.96
	Pleural Effusion	6	11.11
	Reticulonodular opacities	3	5.56
	Bronchiectasis	2	3.70

Table 3: Spirometry, DLCO and Spirometry vs DLCO Findings in RA Participants (n=54)

Variable	Pattern / Pulmonary Status	Number	%
Spirometry Findings	Normal	28	51.85
	Restrictive	16	29.63
	Obstructive	6	11.11
	Mixed	4	7.4
DLCO Findings	Normal	20	37.04
	Mild Reduction	18	33.33
	Moderate Reduction	12	22.22
	Severe Reduction	4	7.41
Spirometry and DLCO Comparison Findings	Both Normal	16	29.63
	Isolated DLCO abnormality	12	22.22
	Isolated spirometry abnormality	4	7.41
	Both Abnormal	22	40.74
p value	0.02		<0.05 Significant

Table 4: Correlation of CDAI with Spirometry and DLCO in Study Participants (n=54)

CDAI	Spirometry Normal	Spirometry Abnormal	Total	DLCO Normal	DLCO Abnormal	Total
Remission	7	1	8	6	2	8
Low	9	5	14	7	7	14
Moderate	8	12	20	5	15	20
High	4	8	12	2	10	12
p value		0.02	Significant		0.005	Significant

Table 5: Correlation of SDAI with Spirometry in Study Participants (n=54)

SDAI	Normal	Abnormal	Total
Remission	5	1	6
Low	10	4	14
Moderate	9	13	22
High	4	8	12
p value		0.02	Significant

Table 6: Percentage of Pulmonary Manifestation in RA Study Participants (n=54)

Pulmonary Manifestation	Number (n=54)	Percentage
No pulmonary involvement (Normal)	25	46.3%
Interstitial Lung Disease (ILD)	15	27.7%
Pleural effusion	7	13.0%
Airway disease	4	7.4%
Pulmonary nodules	3	5.6%

Discussion

In the present study, most participants were in the 41–50 years age group [22 (40.7%)], followed by 31–40 years [12 (22.2%)], showing that pulmonary assessment in rheumatoid arthritis was mainly required in middle-aged patients. Female predominance was also marked, with 41 (75.9%) females and 13 (24.1%) males. This finding was comparable with Robles-Pérez et al. (2020), who studied early rheumatoid arthritis patients and reported 40 patients, of whom 30 (75%) were women, with a mean age of 47.1 years, which closely matches the female predominance and middle-age distribution observed in the present study. [7] In this study, 28 (51.85%) patients were asymptomatic, while dyspnea was present in 14 (25.67%), cough in 9 (16.67%), and chest pain in 3 (5.56%) patients. Chest X-ray was normal in 36 (66.67%) patients and abnormal in 18 (33.33%). These findings indicate that respiratory involvement may remain silent in a considerable number of RA patients. Kawassaki et al. (2015) also observed that pulmonary abnormalities could be detected even in patients without respiratory complaints; in their study of 246 RA patients, spirometry was abnormal in 30%, chest X-ray in 45%, and only 41% had normal chest X-ray, spirometry, and SpO_2 simultaneously.

Thus, compared with their study, the present study showed a slightly lower frequency of chest X-ray abnormalities but similarly supports screening even in asymptomatic RA patients. [8] Among chest X-ray abnormalities in the present study, interstitial infiltrates were seen in 7 (12.96%), pleural effusion

in 6 (11.11%), reticulonodular opacities in 3 (5.56%), and bronchiectasis in 2 (3.70%) patients. These radiological findings reflect parenchymal, pleural, and airway involvement in RA. Wilsher et al. (2012) reported pulmonary abnormalities in newly diagnosed RA patients, where respiratory symptoms were present in about 30%, airflow obstruction in 20%, reduced gas transfer in 40%, and HRCT findings included bronchiectasis in 35%, bronchial wall thickening in 50%, ground-glass opacification in 18%, and reticular changes in 12%. Compared with their HRCT-based study, the present study showed lower bronchiectasis detection, probably because chest X-ray is less sensitive than HRCT, while the frequency of reticular/interstitial changes was broadly comparable. [9]

Spirometry in the present study showed normal findings in 28 (51.85%) participants, whereas abnormal spirometry was observed in 26 (48.15%). The most common abnormality was a restrictive pattern in 16 (29.63%), followed by obstructive pattern in 6 (11.11%) and mixed pattern in 4 (7.4%) patients. Mehrabi et al. (2022) reported a prospective cross-sectional study of 57 RA patients, in which 50% had normal spirometric pattern, 45% had restrictive pattern, and 5% had obstructive pattern. Compared with their study, the present study showed a similar proportion of normal spirometry but a lower restrictive pattern and slightly higher obstructive pattern, confirming that restrictive abnormality remains the predominant spirometric defect in RA. [10] DLCO evaluation in the present study revealed normal diffusion capacity in only 20 (37.04%) patients, while 34 (62.96%) had reduced DLCO. Mild reduction was seen in 18 (33.33%), moderate reduction in 12 (22.22%), and severe reduction in 4 (7.41%) patients.

This shows that DLCO was more frequently abnormal than spirometry. Al-Assadi et al. (2009) also reported reduced DLCO in 23 (51.5%) RA patients, restrictive ventilatory defect in 15 (37.5%), and obstructive defect in 10 (25%) patients. Compared with their study, the present study demonstrated a higher frequency of DLCO abnormality, supporting that DLCO is a sensitive marker for early pulmonary involvement in RA, even when spirometry is normal. [11] The present study showed a statistically significant association between spirometry and DLCO findings ($p = 0.02$). Both spirometry and DLCO were abnormal in 22 (40.74%) patients, while 12 (22.22%) had isolated DLCO abnormality and only 4 (7.41%) had isolated spirometric abnormality. This indicates that DLCO detected additional pulmonary impairment not identified by spirometry alone. Bessa et al. (2023) evaluated 60 RA patients and found that 39 (65%) had abnormal ventilation distribution, with significant correlations between ventilation abnormality and FVC ($r = -0.67$, $p<0.0001$) and DLCO ($r = -0.45$, $p = 0.0003$). The present study similarly supports the role of diffusion testing as an important tool for detecting pulmonary dysfunction beyond routine spirometry. [12]

Disease activity showed a significant relationship with pulmonary dysfunction in the present study. CDAI correlated significantly with spirometry abnormality ($p = 0.02$) and DLCO abnormality ($p = 0.005$). Abnormal DLCO increased from 2 of 8 patients in remission to 10 of 12 patients with high disease activity, showing a clear trend of worsening pulmonary involvement with increasing RA activity. Similarly, SDAI showed a significant association with spirometry abnormality ($p = 0.02$), increasing from 1 of 6 patients in remission to 8 of 12 patients with high disease activity. Sparks et al. (2019) also demonstrated that RA disease activity predicted incident RA-associated interstitial lung disease, with each unit increase in DAS28 associated with a 35% increased risk of RA-ILD, and moderate/high disease activity associated with an approximately two-fold higher risk. These findings strongly support the association between higher systemic inflammatory activity and lung involvement. [13] Overall pulmonary manifestations were present in 29 (53.7%) patients in the present study, while 25 (46.3%) had no pulmonary involvement. Interstitial lung disease was the commonest manifestation [15 (27.7%)], followed by pleural effusion [7 (13.0%)], airway disease [4 (7.4%)], and pulmonary nodules [3 (5.6%)]. Bilgici et al. (2005) evaluated 52 RA patients using HRCT and pulmonary function tests and reported pulmonary abnormalities in up to 67.3% of patients.

Compared with their study, the present study showed a slightly lower overall frequency of pulmonary involvement, but both studies confirm that lung involvement is common in RA, with interstitial lung disease being one of the major pulmonary manifestations. [14]

Conclusion

The present study demonstrated that pulmonary involvement is a frequent extra-articular manifestation in patients with rheumatoid arthritis, with interstitial lung disease being the most common abnormality. Diffusing capacity of the lung for carbon monoxide (DLCO) detected pulmonary impairment more frequently than spirometry, highlighting its value in identifying early subclinical lung involvement. Pulmonary function abnormalities showed a significant association with increasing rheumatoid arthritis disease activity as assessed by CDAI and SDAI. Routine assessment using both spirometry and

DLCO may facilitate early diagnosis, timely intervention, and improved respiratory outcomes in patients with rheumatoid arthritis.

Acknowledgement

The authors sincerely thank the Department of Respiratory Medicine, People's College of Medical Sciences & Research Centre, Bhopal, for their guidance and support throughout the study. We are also grateful to all the patients who participated in this research.

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