

Clinical and radiological correlation of pulmonary manifestations in rheumatoid arthritis



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ABSTRACT

Background: Rheumatoid arthritis (RA) is a chronic inflammatory arthritis with various extra-articular manifestations, pulmonary being the most involved. **Aims and Objectives:** This study aims to identify the radiological patterns in the lungs among patients with RA. **Materials and Methods:** A total of 39 patients with RA were chosen randomly. They were examined and imaged by chest X-ray and high-resolution computed tomography (HRCT) thorax, and findings were analyzed. **Results:** The mean age of patients was 53.9 and had a female preponderance of 74.4%. Among the 39 patients studied, 30 had no respiratory symptoms. The most common HRCT thorax findings were bronchiectasis and ground-glass opacities. **Conclusion:** Radiological pulmonary manifestations of RA identified in HRCT imaging are wide and occur in the majority of clinically asymptomatic patients.

Key words: Rheumatoid arthritis; Chest X-ray; High-resolution computed tomography thorax; Bronchiectasis; Ground-glass opacities; Asymptomatic

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INTRODUCTION

Rheumatoid arthritis (RA) is a chronic inflammatory disease of synovial joints of unknown etiology. It is typically characterized by symmetrical, destructive, and deforming polyarthritis of small and large joints with various extra-articular manifestations.¹⁻³ RA is an autoimmune disorder with a female preponderance and a worldwide prevalence of 1–2%.⁴ The extra-articular manifestations of RA could be respiratory, cardiac, neurological, renal, ocular, or hematological. Pulmonary involvement is the most common among these manifestations.¹ The pulmonary manifestations of RA could be due to the disease or the drugs used in its treatment. It is unclear if radiological features in the lung precede symptoms and if early institution of disease-modifying anti-rheumatic drugs (DMARDs) can delay the

occurrence of pulmonary manifestations in RA. Evidence suggests disability to occur very early in RA, which is amenable to treatment at an early stage.⁵

Extra-articular manifestations of RA involve the skin, heart, lungs, eyes and nervous, renal, or hematological systems. It results in higher morbidity and mortality in patients younger than 50 years.⁶ The most common extra-articular manifestation of RA is pleuropulmonary, with a male predominance.^{1,6}

The prevalence of lung manifestations is as high as 35% in RA.⁷ The lung involvement in RA is associated with high morbidity and mortality. Although advances in the diagnostics and therapeutics of RA have improved its outcome, they have little effect on pulmonary morbidities.

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The lung involvement in RA is multiple (Table 1),⁶ causing varying respiratory symptoms and signs.

The pulmonary manifestations and their radiological features are well documented in the literature. The data on the clinical and radiological correlation of RA are sparse in Indian literature. We intended to correlate the clinical presentation and radiological features of pulmonary manifestations of RA.

Aims and objectives

The aim of the study is to know the radiological changes in lungs among patients with rheumatoid arthritis.

MATERIALS AND METHODS

This descriptive cross-sectional study was initiated after obtaining approval from the Institutional Ethics

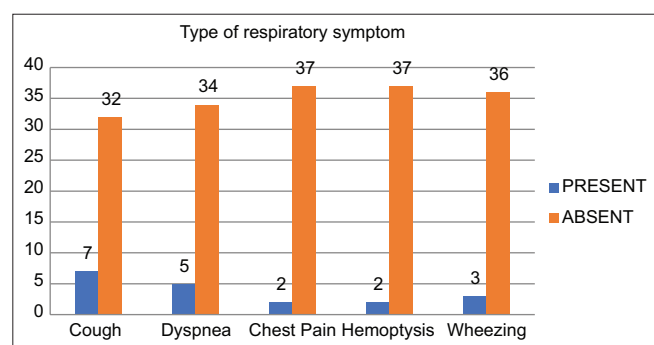


Figure 1: Distribution of respiratory symptoms in patients with Rheumatoid arthritis.

Table 1: Pleuropulmonary manifestations of rheumatoid arthritis

Parenchyma and airways
Rheumatoid nodules
Necrobiotic nodules
Caplan's syndrome
Rheumatoid nodulosis
Bronchiectasis
Bronchiolitis obliterans with organizing pneumonia
Bronchiolitis obliterans
Vessels
Pulmonary vascular disease
Vasculitis
Primary or Secondary pulmonary hypertension
Pleura
Pleuritis
Pleural effusion
Pneumothorax
Bronchopleural fistula
Empyema
Interstitialium
Interstitial lung disease
Miscellaneous
Drug-related lung disease
Infection
Fibro-bullous disease
Amyloidosis
Cricoarytenoid arthritis

Committee. The patients diagnosed with RA (American Rheumatism Association criteria) attending the out-patient and in-patient services of Father Muller Medical College Hospital; newly detected or those on follow-up were chosen at random.

Table 2: Frequency distribution of age, gender, duration of rheumatoid arthritis, respiratory symptoms, skeletal changes, seropositivity, and HRCT findings

Parameters	Count (N)	n %
Age distribution		
50 and below	17	43.6
51–60	13	33.3
Above 60	9	23.1
Gender distribution		
Female	29	74.4
Male	10	25.6
Duration of RA		
<2 years	3	7.7
2–10	30	76.9
Above 10	6	15.4
Respiratory symptoms		
Absent	30	76.9
Present	9	23.1
Skeletal changes		
Absent	16	41.0
Present	23	59.0
Seropositivity - RA factor		
Negative	7	17.9
Positive	32	82.1
HRCT findings		
Absent	17	43.6
Present	22	56.4

HRCT: High-resolution computed tomography

Table 3: Frequency of respiratory symptoms in patients with rheumatoid arthritis

Type of respiratory symptom	Present (%)	Absent (%)
Cough	7 (17.9)	32 (82.1)
Dyspnea	5 (12.8)	34 (87.2)
Chest pain	2 (5.1)	37 (94.9)
Hemoptysis	2 (5.1)	37 (94.9)
Wheezing	3 (7.7)	36 (92.3)

Table 4: Frequency distribution of the various HRCT findings

Type of HRCT finding	Present	Absent
Bronchiectasis	10 (25.6)	29 (74.4)
Ground glassing opacities	8 (20.5)	31 (79.5)
Parenchymal reticulations	4 (10.3)	35 (89.7)
Non-homogenous opacities	2 (5.1)	37 (94.9)
Nodules	1 (2.6)	38 (97.4)
Honeycombing	1 (2.6)	38 (97.4)
Hyperinflation	1 (2.6)	38 (97.4)
Mosaic pattern	1 (2.6)	38 (97.4)
Subpleural reticulation	1 (2.6)	38 (97.4)
PAH	1 (2.6)	38 (97.4)

HRCT: High-resolution computed tomography

Table 5: Association of HRCT findings with age, gender, duration of rheumatoid arthritis, respiratory symptoms, skeletal changes, and seropositivity

Parameters	HRCT Findings		Total	P-value (Chi-square/fishers exact test)
	Absent	Present		
Age distribution				
50 and below	8	9	17	0.478 (NS)
51–60	4	9	13	
Above 60	5	4	9	
Gender distribution				
Female	13	16	29	0.791 (NS)
Male	4	6	10	
Duration of RA				
<2 years	0	3	3	0.042 (SIGNIFICANT)
2–10	12	18	30	
Above 10	5	1	6	
Respiratory symptoms				
Absent	13	17	30	0.478 (NS)
Present	4	5	9	
Type of respiratory symptom				
Cough				
Absent	13	19	32	0.425 (NS)
Present	4	3	7	
Dyspnea				
Absent	16	18	34	0.255 (NS)
Present	1	4	5	
Chest pain				
Absent	16	21	37	0.851 (NS)
Present	1	1	2	
Hemoptysis				
Absent	16	21	37	0.851 (NS)
Present	1	1	2	
Wheezing				
Absent	15	21	36	0.401 (NS)
Present	2	1	3	
Skeletal changes				
Absent	8	8	16	0.501 (NS)
Present	9	14	23	
Seropositivity- RA factor				
Negative	5	2	7	0.101 (NS)
Positive	12	20	32	

HRCT: High-resolution computed tomography

Table 6: Association of each of the HRCT findings with various parameters

Type of HRCT finding	Age distribution	Gender	Duration of RA	Respiratory symptoms	Skeletal changes	Seropositivity RA factor
Non homogenous opacities	0.030 (sig)	0.394	0.066	0.354	0.082	0.497
Ground glassing opacities	0.926	0.963	0.614	0.426	0.563	0.652
Parenchymal reticulations	0.118	0.975	0.512	0.923	0.078	0.323
Nodules	0.358	0.552	0.002 (HS)	0.064	0.398	0.636
Honeycombing	0.515	0.552	0.857	0.579	0.225	0.030 (sig)
Hyperinflation	0.515	0.084	0.857	0.579	0.398	0.636
Bronchiectasis	0.521	0.636	0.292	0.789	0.939	0.448
Mosaic perfusion	0.515	0.552	0.857	0.579	0.225	0.636
Subpleural reticulation	0.181	0.552	0.857	0.579	0.398	0.636
PAH	0.358	0.552	0.857	0.064	0.398	0.636

HRCT: High-resolution computed tomography

Patients below 15 years of age, those with past pleural diseases, thoracic surgeries, tuberculosis, chronic obstructive pulmonary disease, heart failure, valvular heart disease, and chronic kidney disease were excluded from the study.

The sample size was calculated using a 95% confidence interval. A total of 39 patients were studied after obtaining their written informed consent. A clinical history and examination with an emphasis on the respiratory system

along with details of medications and articular and extra-articular involvement in RA were captured on a preformatted data sheet. A chest X-ray and high-resolution computed tomography (HRCT) thorax were done on these patients which was reported by an expert radiologist. This data were later analyzed using mean frequencies and Chi-square tests.

RESULTS

In the present study of a total of 39 patients, the age of the patients ranged from 39 to 87 years with a mean of 53.9 years. Most of the patients, that is, 43.6% of the patients, were below 50 years of age. Out of these patients, 74.4% were females and 25.6% were males. About 15.4% of the total number of patients were suffering from RA for more than 10 years (Table 2).

On examination, skeletal changes such as joint deformities and joint line tenderness were present in 59% of the patients, and two patients had rheumatoid nodules on their arms.

Out of these 39 patients, 30 patients did not have any respiratory complaints such as cough, breathlessness, or wheezing. Among others, 7 patients had complaints of coughing with expectoration. Dyspnea on exertion was present in about 5 patients. Three of the patients had wheezing as a complaint, and two patients each had chest pain and hemoptysis. Figure 1 and Table 3 show the distribution of respiratory symptoms in our study.

Out of these 39 patients, 22, that is, 56.4% had abnormalities on imaging the lung with HRCT. The most common manifestation was bronchiectatic changes, that is, dilated bronchi with mild wall thickening, irregular bronchial dilatation, and tram track appearance which were observed in 25.6% of the patients. The changes were bilateral, and the lower zone was predominant. This was followed by ground-glass opacities in 20.5% of the patients. 10.3% of the patients had reticulations in the parenchyma as a finding. Non-homogenous opacities were present in two patients. One patient each had nodules, honeycombing, hyperinflation, mosaic perfusion, subpleural reticulation, and pulmonary artery hypertension (Table 4).

We analyzed if there was any association between HRCT thorax imaging findings and the duration of illness or seropositivity. There was no significant association between CT image findings and age, gender, symptomology, or seropositivity (Table 5). However, there was a significant association between lesser duration of RA which could possibly be due to the lesser number of patients in that group. Furthermore, we analyzed to check for associations between each of the HRCT findings with various

parameters. There was a significant association between non-homogenous opacities and age distribution, nodules, duration of RA, honeycombing, and seropositivity (Table 6). This could be due to the lesser number of patients in each group.

DISCUSSION

The aim of our study was to know the different pulmonary manifestations in HRCT thorax among patients with RA. RA has a plethora of extra-articular manifestations that contribute to the substantial morbidity and mortality observed with this disease.⁸ Pulmonary disease is a major contributor, accounting for approximately 10–20% of the mortality. Pulmonary complications can occur in 60–80% of RA patients, many of whom are asymptomatic.^{9–12} The reduced mobility and exertion due to the joint pains of RA could be a likely reason for fewer respiratory symptoms.

In the present study, 23.1% of the patients had respiratory symptoms such as cough, dyspnea, and wheezing, whereas radiological features were present in 56.4% of the patients. The most common finding was bronchiectatic changes and ground-glass opacities suggestive of interstitial lung disease, followed by parenchymal reticulations and non-homogenous opacities. The other radiological features noticed were nodules, hyperinflation, pulmonary artery hypertension, honeycombing, a mosaic pattern, and subpleural reticulation.

In a similar study among forty-three non-smoking patients with early RA, HRCT revealed bronchiectasis in 58% of the patients.¹³ In a meta-analysis that included 23 studies, the pooled prevalence of bronchiectasis in RA was 21.1%.¹⁴ Patients with RA-associated bronchiectasis have a poorer prognosis than those with either RA or bronchiectasis alone and require regular follow-up under the joint care of a rheumatologist and a pulmonologist.¹⁵ Our study revealed bronchiectatic changes in about 25.6% of the patients.

Interstitial involvement is common in RA and most remain asymptomatic or present with progressive dyspnea on exertion or a dry cough. In a study conducted by Bilgici et al., among 52 patients with RA, HRCT was abnormal in 35 patients (67.3%); the most frequent abnormalities were reticulonodular patterns, which were found in 22 patients (62.9%), ground-glass attenuation in 20%, and bronchiectasis in 17% of the patients.¹⁰ An Australian cohort study among RA patients with a disease duration of <2 years showed 58% of patients to have ILD. Among them, 76% had no clinical symptoms.¹⁶ A similar Egyptian study found 27% to have interstitial disease on HRCT, but only 10% had clinically significant disease.¹⁷ Interstitial lung

disease is a leading cause of death in patients with RA and is associated with significant morbidity and mortality.¹⁸

Pleural involvement is a common pulmonary manifestation of RA. Small pleural effusions are noted in up to 70% of the patients.^{19,20} However, only about 3–5% of patients were symptomatic. Pleural disease is more common in men over 35 years of age and those with pulmonary nodules. Fever and chest pain are the usual symptoms, and most effusions are unilateral.²⁰ Blunt costophrenic angles, pneumothorax, hydropneumothorax, or bronchopleural fistulas are the common pleural manifestations.

Large airways are involved in long-standing and severe disease forms. Nodules on the vocal cords, vocal cord paralysis due to vasculitis of the recurrent laryngeal/vagal nerve, arthritis of the cricoarytenoid joint due to synovial thickening, and subluxation of the joint are the usual features identified by HRCT of the neck. These features are often present before the development of clinical symptoms.²¹ Patients may have symptoms of stridor, dysphagia, throat pain or fullness, or dyspnea, but most remain asymptomatic until significant obstruction occurs.²¹ Lower airway involvement includes bronchial hyperresponsiveness, bronchiolitis, or bronchiectasis.

Rheumatoid nodules can occur in patients with longstanding disease and subcutaneous nodules. Nodules remain asymptomatic until they cavitate or rupture. They are typically located along the interlobular septa or in subpleural regions. Nodules may be single or multiple, ranging in size from a few millimeters to several centimeters.²² Complications occur when a lesion cavitates, becomes infected, or ruptures into the pleural space.²³

Pulmonary hypertension can occur in RA; Udayakumar et al., found a higher rate of asymptomatic pulmonary hypertension among RA.²⁴ A similar study among 40 Turkish patients with RA found that 11 (27.5%) had pulmonary artery systolic pressure ≥ 30 mmHg on echocardiography.²⁵ In a larger study involving 146 patients with RA, 21% of patients were found to have mild-to-moderate pulmonary hypertension on echocardiography in the absence of clinically significant heart or lung disease.²⁶ In each of these studies, none of the patients who had pulmonary hypertension were symptomatic. It is possible that these patients were less active due to their arthritis and perhaps did not notice dyspnea. One of our patients had pulmonary artery hypertension who was asymptomatic clinically.

The drugs used in the treatment of RA could result in lung toxicity. DMARDs used in RA causing lung damage include non-steroidal anti-inflammatory drugs such as methotrexate, leflunomide, penicillamine, gold, or cytotoxic drugs.

HRCT is the most practical imaging tool to screen for pulmonary manifestations of RA. It is superior to a chest X-ray in demonstrating abnormalities. For multiple reasons, the lung manifestations of RA are not diagnosed as early as other extra-articular manifestations. As rheumatological symptoms make the patient restrict physical activities, most of the respiratory symptoms are masked, resulting in a delayed diagnosis. Although it is believed that radiological manifestation precedes clinical features, screening for lung involvement in RA has remained low. Screening by imaging may identify a few of these manifestations early in the disease.

The spectrum of pulmonary manifestations of RA varies. The disease's therapy alters the immune system, and patients are more susceptible to infections during the disease. It is often difficult to identify such infections in the background of rheumatoid lung involvement. Screening for radiological features of rheumatoid lung disease is important and can differentiate new-onset insults. It may also aid in assessing the therapeutic response and predicting the prognosis in RA.

Limitations of the study

As the study was a descriptive cross-sectional study, patients could not be followed up for the development of symptoms in those with radiological abnormalities.

CONCLUSION

According to our study, we conclude that patients with RA can have radiological manifestations in the lungs though they might be asymptomatic with respect to respiratory symptoms. However, these manifestations did not have any relation to age, gender, or seropositivity.

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SMP- Definition of intellectual content, literature survey, prepared first draft of manuscript, implementation of study protocol, data collection, data analysis, manuscript preparation and submission of article, concept, design, clinical protocol, manuscript preparation, editing, and manuscript revision, design of study, statistical analysis and interpretation; **RSB-** Review manuscript, coordination and manuscript revision, radiological interpretation and analysis.

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