Research Article

HRCT Chest Findings in Patients with Rheumatoid Arthritis Associated - Interstitial Lung Disease (RA-ILD)

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Abstract
Rheumatoid arthritis is a chronic inflammatory systemic disease with a number of extra-articular manifestations including lung disease. Our purpose of the study was to assess the HRCT findings in patients with rheumatoid arthritis associated lung diseases (RA-ILD).

Materials and Methods: A cross sectional study was conducted on a total of 36 patients of Rheumatoid arthritis associated interstitial lung disease (RA-ILD). Patients were evaluated by physiological (pulmonary function test) and radiological methods (chest X-ray, HRCT chest). Chi-square test was used for comparison of categorical variables. A p value of less than 0.05 was considered statistically significant

Results: UIP was the most common ILD seen in RA in our study. Chest X Ray showed reticulonodular pattern in 39.3% of patients, prominent vascular makings in 7.1% of patients and bilateral lower zone haziness in 32.1% of patients. PFT with restrictive pattern was seen in 50% of patients and obstructive pattern was seen in 7.1% of patients. On HRCT, reticulations were present in 35.7% of patients: honey combing was present in 53.6% of patients, ground glass opacities in 42.9%, pleural thickening in 10.7%, pleural effusion in 7.1%, pulmonary vascular prominence in 7.1%, rheumatoid nodules in 7.1% and bronchiectasis in 7.1%.

Conclusion: In the present study, UIP is the most common ILD. Honey combing and ground glass opacities most common finding on HRCT in these patients. As the duration of illness increases, need for screening for pulmonary involvement with Chest Xray, PFTs and HRCT is to be emphasized along with periodic chest examination.

Keywords: Pulmonary, Rheumatoid Arthritis, Interstitial lung diseases, RA-ILD.

Introduction
Rheumatoid arthritis affects ~1% of the population in developed countries. The incidence and prevalence of rheumatoid arthritis in developing countries is thought to be lower, but is difficult to quantify. (1,2) Although joint disease is the main presentation, there are a number of extra-articular manifestations including subcutaneous nodule formation, vasculitis, inflammatory eye disease and lung disease. (3,4) Of these manifestations, lung disease is a major contributor to morbidity and mortality.
ILD is the most common pulmonary manifestation of rheumatoid arthritis lung disease.\(^5\) Most of these patients have changes consistent with ILD on either chest radiograph, High-resolution computed tomography (HRCT), pulmonary function testing (PFT), bronchoalveolar lavage (BAL). Of these patients, 76% had clinically silent disease.\(^6\) It is currently estimated that ~30% of patients with rheumatoid arthritis have subclinical ILD noted on HRCT scans.\(^5\)

**Epidemiology/Risk Factors**

Although rheumatoid arthritis is more common in females, rheumatoid arthritis associated-ILD (RA-ILD) occurs more frequently in males, with a male to female ratio as high as 2:1 in some studies.\(^7,8\) Onset of lung disease typically occurs in the fifth to sixth decade of life.\(^9\) Age has consistently been shown to be a risk factor for the development of ILD.\(^10\) Another major risk factor is a history of smoking, with one study finding an odds ratio of 3.8 for those who smoked >25 pack-years.\(^11\) High levels of rheumatoid factor are a known risk factor involving formation of circulating immune complexes.\(^12\)

**Pathogenesis**

The mechanism of pulmonary fibrosis occurring in ILD is not well understood. Patients with rheumatoid arthritis typically have circulating autoantibodies, the most common being rheumatoid factor and anti-cyclic citrullinated peptide (CCP).\(^13\) Anti-CCP antibodies have also been associated with the development of airway disease.\(^14\)

Cigarette smoking may play a role in inducing antibody formation and has been linked to higher titres of rheumatoid factor.\(^11\) Smoking may promote citrullination of lung proteins, thus leading to the development of anti-CCP antibodies.

**Pulmonary Function Tests**

The majority of patients with RA-ILD will have a restrictive pattern on PFTs, with or without decreased diffusing capacity of the lung for carbon monoxide (DLCO) and hypoxemia.\(^7\) Airflow obstruction may coexist and be seen in patients manifesting airway involvement, i.e. bronchiolitis obliterans.

**Imaging**

In UIP, HRCT scans show subpleural, basal predominant, reticular abnormalities with honeycombing, and traction bronchiectasis but a relative absence of ground-glass opacities.\(^15\) NSIP is the second most common pattern, occurring in ~11–32% of patients. NSIP is characterised by basilar predominant ground-glass opacities and absence of honeycombing. Additional patterns less commonly seen in rheumatoid arthritis include other patterns of interstitial pneumonia, including organising pneumonia, diffuse alveolar damage (DAD), lymphocytic interstitial pneumonia (LIP) and desquamative interstitial pneumonia (DIP)-like patterns.\(^16\)

**Prognosis**

ILD is second only to cardiac disease as a cause of mortality in rheumatoid arthritis.\(^7,8\) The mean survival for RA-ILD overall has been estimated at 2.6 years from time of diagnosis compared to 9.9 years for rheumatoid arthritis patients without lung involvement; however, this probably reflects the predominance of the UIP pattern.\(^9\)

**Methodology**

A cross sectional study conducted in a tertiary centre after obtaining ethical clearance during a period of 1 year from Nov 2017 to Nov 2018. A total of 36 patients of Rheumatoid arthritis associated lung diseases of either sex having age >21 years who met the ACR EULAR (2010) criteria for RA were included.\(^1\) Patients with history of cardiopulmonary disorder, collagen vascular disease (SLE, scleroderma) , viral infection (hepatitis B & C, HIV), tuberculosis and inhalational exposure / occupational lung disease (asbestos, silica) were excluded.

Patients were examined clinically for respiratory signs and symptoms. Patients were further evaluated for pulmonary manifestations by physiological (pulmonary function test) and radiological methods (chest X-ray, HRCT chest).
In patients with clinical suspicion of tuberculosis sputum for AFB was done for exclusion of pulmonary tuberculosis. Patients with evidence of pulmonary fibrosis on HRCT chest were further investigated for HBsAg, anti-HCV, HIV to rule out pulmonary fibrosis secondary to viral infections. Majority of our patients were on DMARDs and were not excluded from our study.

Statistical Analysis
Continuous variables were expressed as Mean±SD and categorical variables were summarized as percentages. Chi-square test was used for comparison of categorical variables. Graphically the data was presented by bar and pie diagrams. A p value of less than 0.05 was considered statistically significant.

Results
Age distribution of RA-ILD patients shows that 7.1% of patients were in 31-40 years of age group, 25% of patients were in 41-50 years of age group, 39.3% of patients were in 51-60 years of age group and 28.6% of patients were in > 60 years of age. (Figure 1)

Chest X Ray was normal in 28.6% of patients, reticulonodular pattern in 39.3% of patients, prominent vascular markings in 7.1% of patients and bilateral lower zone haziness in 32.1% of patients. (Table 1)
PFT was normal in 28.6% of patients, restrictive pattern was seen in 50% of patients, obstructive pattern was seen in 7.1% of patients and 14.3% of patients were not cooperative for PFT. (Figure 2)

As per HRCT Pattern. Reticulations were present in 35.7% of patients: honey combing was present in 53.6% of patients, ground glass opacities in 42.9%, pleural thickening in 10.7%, pleural effusion in 7.1%, pulmonary vascular prominence in 7.1%, rheumatoid nodules in 7.1% and bronchiectasis in 7.1%.(Figure 3)

Among the patients with RA-ILD, 72.73% of males had UIP while 47.06% of females had UIP and 27.27% of males had NSIP while 52.94% of females had NSIP. (Figure 4)

Figure 1 Age Distribution of RA-ILD Patients

| Chest X-Ray Findings            | No. of patients | Percentage |
|---------------------------------|----------------|------------|
| Normal                          | 8              | 28.6%      |
| Reticulonodular Pattern         | 11             | 39.3%      |
| Prominent Vascular Markings     | 2              | 7.1%       |
| Bilateral Lower zone Haziness   | 9              | 32.1%      |

Table 1: Distribution of RA-ILD patients as per chest X-Ray findings
Figure 2: Distribution of RA-ILD patients as per PFT findings

![PFT * RA-ILD](image)

Figure 3: Distribution of RA-ILD patients as per HRCT findings

![HRCT pattern](image)

Figure 4: Distribution of RA-ILD patients according to gender and pattern of involvement

![Showing RA-ILD patients as per gender](image)
Discussion

Rheumatoid arthritis (RA) is an autoimmune disease affecting 0.5-1% of the world population. Being a multisystem disorder, RA virtually affects every organ system of the body and one of the major causes of mortality in patients of RA is lung involvement, cardiovascular involvement being most important cause.

The percentage of patients with lung involvement in age group > 60 years dropped to 28.6% as compared to 39.3% in age of 51-60 years. The lesser proportion of patients in age more than 60 years can be attributed to higher mortality of RA in this age group, but further studies are needed to validate our assumption. The results in our study were in comparison with the study conducted by Kelly et al. (2014) who demonstrated that median age at diagnosis of RA was 56 years (range 23-76). Similarly Assayag D et al. (2014), studies mean age ranged 55 to 69 years in RA-ILD. Our findings were also consistent with study done by Bilgici A et al. (2005).

Chest X ray being the primary imaging modality for screening of lung pathology revealed abnormality in about three quarters of patients with reticulonodular pattern and lower lobe haziness in 39.3% and 32.1% of patients respectively. Similar findings were demonstrated by N. Fatima et al. (2013) who found that the predominant finding on chest X-ray was reticulonodular pattern.

Sixteen (57.1%) patients had UIP with reticulation with or without honeycombing on HRCT and 12 (42.9%) patients had NSIP with predominant ground glass opacities on HRCT. UIP was the most common ILD seen in RA in our study. In the study done by DeLauretis et al (2011), NSIP was the most common pattern in all CTDs, except for RA which is characterized by a higher frequency of UIP. Similarly, Kelly et al (2014) also studied that UIP was the most common subtype on HRCT. UIP was predominantly seen in 65% followed by NSIP in 24%. In our study, second most common pattern was NSIP; Similar results were seen by Lee HK et al. (2005). UIP was more common in males compared to NSIP as reported by similar studies.

Pulmonary function test was abnormal in 16 (57.1%) patients with predominant restrictive pattern in 14 (50%) patients. In the study done by N. Fatima et al. (2013), 27 patients (43%) had abnormal PFT with restrictive pattern in 18 (29%) and obstructive pattern in 5 (8%) of patients. In similar studies, restrictive pattern was seen in 52.9% and obstructive pattern in 11.8% of patients.

Stressing upon the fact, that, early recognition and treatment of RA-ILD can halt or modify lung involvement in RA. These findings on the imaging modalities and physiological testing can be used for the early diagnosis of the entity.

Conclusion

In the present study, UIP is the most common ILD. Honey combing and ground glass opacities most common finding on HRCT in these patients. As the duration of illness increases, need for screening for pulmonary involvement with Chest X ray, PFTs and HRCT is to be emphasized along with periodic chest examination.

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