

**A Study of Pleuro-Pulmonary Manifestations of Rheumatoid Arthritis**

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**Abstract**

**Introduction:** Rheumatoid arthritis (RA) is a chronic inflammatory disease of unknown etiology marked by a symmetric, peripheral polyarthritis. Because it is a systemic disease, RA may result in a variety of extraarticular manifestations, including fatigue, subcutaneous nodules, lung involvement, pericarditis, peripheral neuropathy, vasculitis, and hematologic abnormalities. Aim of our study was to evaluate RA patients in terms of history, clinical examination, chest X-ray (CXR), PFT, and HRCT to ascertain pulmonary involvement in RA.

**Materials & Method:** This was an observational, cross sectional, uncontrolled, open label, single centre study in Indian patients. In this study, 100 consecutive patients, diagnosed with RA were enrolled. All subjects were evaluated with chest X-ray (CXR), pulmonary function test (PFT), and High resolution computerised tomography (HRCT) of lungs. Analysis was performed by *t*-test, Chi-square, and Fisher's exact tests. All statistical analyses were done by SPSS software 20.0. *P* < 0.05 was considered significant.

**Results:** One hundred patients were included in this study, 20 (20%) males and 80 (80%) females, all were 21–73 years old and their mean age was 39 ± 12.8 years. Dyspnea and crackles were most common symptom and

sign respectively in RA with pulmonary involvement. Lung fibrosis was seen in 22% of cases. PFT was normal in 25% cases.

**Conclusion:** The results of our study support that HRCT, regardless of respiratory symptoms or clinical examination as independent parameters can have positive findings and in the evaluation of asymptomatic patients, using of HRCT is more rational than PFT.

**Key words:** RA, PFT, HRCT

**Introduction**

Rheumatoid arthritis (RA) is a chronic inflammatory disease of unknown etiology marked by a symmetric and peripheral polyarthritis. It is the most common form of chronic inflammatory arthritis and often results in joint damage and physical disability. The prevalence is lowest in black Africans and Chinese, and highest in Pima Indians. In Caucasians, it is 1.0–1.5%, with a female to male ratio of 3:1. The clinical course is prolonged, with intermittent exacerbations and remissions. Patients with RA have an increased mortality when compared with age-matched controls, primarily due to cardiovascular disease. This is most marked in those with severe disease, with a reduction in expected lifespan by 8–15 years. Around 40% of RA patients are registered disabled within 3 years; around 80% are moderately to severely disabled within 20 years; and 25% will require a large joint replacement.

Functional capacity decreases most rapidly at the beginning of disease and the functional status of patients within their first year of RA is often predictive of long-term outcome. Factors that associate with a poorer prognosis are disability at presentation, female gender, involvement of metatarsophalangeal joints, smoking and a positive rheumatoid factor (RF) and anti-CCP. It is hoped that the prognosis of RA will improve as more aggressive early treatment is used but this has yet to be demonstrated. Both genetic and environmental factors appear to be involved in the pathogenesis of RA. The concordance rate of RA is higher in monozygotic (12–15%) than in dizygotic twins (3%), and there is an increased frequency of disease in first-degree relatives of patients. Up to 50% of the genetic susceptibility is due to genes in the HLA region. HLA-DR4 is the major susceptibility haplotype in most ethnic groups, occurring in 50–75% of Caucasian patients with RA compared to 20–25% of the normal population. However, DR1 is more important in Indians and Israelis, and DW15 in Japanese. Severity is also under genetic influence, with DR4 positivity being more common in those with severe erosive disease. Although it is thought that RA may be triggered by an infectious agent in a genetically susceptible host, a specific pathogen has not been identified. Susceptibility is increased post-partum and by breastfeeding. Cigarette smoking is a strong risk factor for developing RA and also associates with greater severity. Whatever the initiating stimulus, RA is characterised by infiltration of the synovial membrane with lymphocytes, plasma cells and macrophages. CD4+ T cells play a central role by interacting with other cells in the synovium. Activated T cells stimulate B cells to produce immunoglobulins including RF, and macrophages to produce pro-inflammatory cytokines. These act on endothelium, synovial fibroblasts, bone cells and chondrocytes to promote swelling and congestion of

the synovial membrane and destruction of bone, cartilage and soft tissues. Because it is a systemic disease, RA may result in a variety of extraarticular manifestations, including fatigue, subcutaneous nodules, lung involvement, pericarditis, peripheral neuropathy, vasculitis, and hematologic abnormalities. Extraarticular manifestations may occur in about 40 percent of patients with RA over a lifetime of disease.<sup>[1,2]</sup> Among these manifestations, lung involvement in RA reviewed here. Aim of our study was to evaluate RA patients in terms of history, clinical examination, chest X-ray (CXR), pulmonary function test (PFT), and High resolution computerised tomography (HRCT) to ascertain pulmonary involvement in RA.

## **Materials & Methods**

### **Study Design**

An observational, cross sectional, uncontrolled, open label, single centre study in Indian patients.

### **Place and Duration of Study**

Patients were enrolled from outpatient medicine department of a tertiary care hospital from January 2016 to January 2018.

### **Methodology**

In this study, 100 consecutive patients, diagnosed with RA according to American College of Rheumatology-European League Against Rheumatism classification criteria for RA 2010,<sup>[3]</sup> were enrolled. Patients with a history of smoking, known pulmonary diseases, mixed connective tissue disorder and the long term use of drug known to cause lung disease were excluded from the study.

Demographic and clinical data such as sex, age, occupation, comorbidities, drug history and history of systemic and respiratory symptoms were collected. A complete physical examination of the joints was performed in all subjects. The activity of RA was

evaluated in all patients by Disease Activity Score 28 (DAS28). All subjects were evaluated with CXR, PFT, and HRCT of lungs. Statistical analysis was performed by *t*-test, Chi-square, and Fisher's exact tests. All statistical analyses were done by SPSS software 20.0. *P* < 0.05 was considered significant.

**Results**

One hundred patients were included in this study, 20 (20%) males and 80 (80%) females, all were in between 21–73 years old and their mean age was 39 ± 12.8 years. Respiratory symptoms and signs of RA patients are described in Table 1.

**Table 1:** Respiratory symptoms and signs of RA patients

| Respiratory Symptoms     | n=100(%) |
|--------------------------|----------|
| Dyspnea                  | 19 (19%) |
| Dry Cough                | 18 (18%) |
| Productive Cough         | 9 (9%)   |
| Chest pain               | 8 (8%)   |
| Hemoptysis               | 2 (2%)   |
| <b>Respiratory Signs</b> |          |
| Crackles                 | 17 (17%) |
| Wheezing                 | 9 (9%)   |
| Decreased Air Entry      | 2 (2%)   |
| Pleural friction rub     | 1 (1%)   |

HRCT chest findings are mentioned in Table 2.

**Table 2:** HRCT chest findings of RA patients

| HRCT Findings              | n=100 (%) |
|----------------------------|-----------|
| Fibrosis                   | 22 (22%)  |
| Nodules                    | 8 (8%)    |
| Localised bronchiectasis   | 8 (8%)    |
| Generalised bronchiectasis | 6 (6%)    |
| Cyst                       | 2 (2%)    |
| Pleural effusion           | 2 (2%)    |
| Bronchiolitis obliterans   | 1 (1%)    |

|                      |  |
|----------------------|--|
| organizing pneumonia |  |
|----------------------|--|

PFT findings are mentioned in Table 3.

**Table 3:** PFT findings of RA patients

| PFT findings                 | n=100 (%) |
|------------------------------|-----------|
| Normal                       | 25 (25%)  |
| Air Trapping                 | 19 (19%)  |
| Mild Obstructive pattern     | 2 (2%)    |
| Moderate Obstructive pattern | 2 (2%)    |
| Mild Restrictive pattern     | 2 (2%)    |
| Moderate Restrictive pattern | 2 (2%)    |

**Discussion**

RA affects approximately 0.5–1% of the adult population worldwide. The incidence of RA increases between 25 and 55 years of age, after which it plateaus until the age of 75 and then decreases. The presenting symptoms of RA typically result from inflammation of the joints, tendons, and bursae. Patients often complain of early morning joint stiffness lasting more than 1 hour and easing with physical activity. The earliest involved joints are typically the small joints of the hands and feet. The initial pattern of joint involvement may be monoarticular, oligoarticular (4 joints), or polyarticular (>5 joints), usually in a symmetric distribution. Some patients with an inflammatory arthritis will present with too few affected joints and other characteristic features to be classified as having RA so-called undifferentiated inflammatory arthritis. Those with an undifferentiated arthritis, who are most likely to be diagnosed later with RA, have a higher number of tender and swollen joints, test positive for serum RF or anti-CCP antibodies, and have higher scores for physical disability. As RA-ILD is often asymptomatic, the reported frequency depends upon the investigation used and the severity of RA in the population studied. In one study, the prevalence of ILD on HRCT chest, regardless of pulmonary

symptoms, abnormal lung function, or the duration of the rheumatoid disease, was nearly 20 percent among RA patients.<sup>[4]</sup>

The most common finding in abnormal HRCTs, in the present study, was fibrosis (with the prevalence of 22%) while Perez and Cortet studies showed bronchiectasis as most common finding (30% and 30.5%, respectively).<sup>[5,6]</sup>

### **Conclusion**

The results of our study support that HRCT, regardless of respiratory symptoms or clinical examination as independent parameters can have positive findings and in the evaluation of asymptomatic patients, using of HRCT is more rational than PFT.

### **References**

1. Turesson C, O'Fallon WM, Crowson CS, et al. Extra-articular disease manifestations in rheumatoid arthritis: incidence trends and risk factors over 46 years. *Ann Rheum Dis* 2003; 62:722.
2. Myasoedova E, Crowson CS, Turesson C, et al. Incidence of extraarticular rheumatoid arthritis in Olmsted County, Minnesota, in 1995-2007 versus 1985-1994: a population-based study. *J Rheumatol* 2011; 38:983.
3. Aletaha D, Neogi T, Silman AJ, Funovits J, Felson DT, Bingham CO 3<sup>rd</sup>, et al. 2010 rheumatoid arthritis classification criteria: An American College of Rheumatology/European League Against Rheumatism collaborative initiative. *Ann Rheum Dis* 2010;69:1580-8.
4. Dawson JK, Fewins HE, Desmond J, Lynch MP, Graham DR, Fibrosing alveolitis in patients with rheumatoid arthritis as assessed by high resolution computed tomography, chest radiography, and pulmonary function tests. *Thorax*. 2001;56(8):622.

5. Cortet B, Perez T, Roux N, Flipo RM, Duquesnoy B, Delcambre B, et al. Pulmonary function tests and high resolution computed tomography of the lungs in patients with rheumatoid arthritis. *Ann Rheum Dis* 1997;56:596-600.
6. Perez T, Remy-Jardin M, Cortet B. Airways involvement in rheumatoid arthritis: Clinical, functional, and HRCT findings. *Am J Respir Crit Care Med* 1998;157:1658-65.