

# A Cross Sectional Study on Pleuropulmonary Manifestations of Rheumatoid Arthritis

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## ABSTRACT

**Background:** Rheumatoid arthritis is a systemic, inflammatory, autoimmune disorder. Pleuropulmonary (PP) involvement in rheumatoid arthritis (RA) is associated with high morbidity and mortality. The objectives of the current study were to determine the prevalence and pattern of pleura pulmonary manifestations and to assess the spirometric and radiological changes of lung disease in RA, in patients attending rheumatology clinic of Govt Medical College Thrissur January 2009 to October 2009. **Methods:** This was a cross sectional involving 75 patients diagnosed at a tertiary center from January 2009 to October 2009. The frequency of pulmonary manifestations was recorded based on combined results from chest X-rays, pulmonary function tests, and high-resolution computed tomography scan of the chest. **Results:** The RA patients from our population proved to have 18.7% of pulmonary involvement. The predominant pulmonary manifestation was ILD (11/14). Among patients with pulmonary involvement spirometry showed mild restriction in 3 moderate restriction in 6 and severe restriction in 4. Breathlessness was the most common symptom seen in 7 patients (50%) followed by cough and wheeze. 40% of patients with lung involvement were asymptomatic. Physical findings in the form of crepitations were found in 5 patients (35.7%). CXR was normal in 9 patients (66.3%) and abnormal in 5 patients (35.7%). The most common abnormality in CXR was interstitial opacity. **Conclusion:** Pleuro pulmonary involvement is common in patients with rheumatoid arthritis. ILD is the most common manifestation. The risk of pulmonary involvement increases with duration of disease. There was also no significant increase in mean duration of DMARD in the two groups. This suggests that DMARDs are not playing a major role in development of ILD. Spirometry can be used as a reliable and cost effective screening method for pulmonary involvement in patients with rheumatoid arthritis.

**Keywords:** High resolution computed tomography, lung disease, pleuropulmonary manifestations, rheumatoid arthritis.

## INTRODUCTION

Rheumatoid arthritis is a systemic, inflammatory, autoimmune disorder.<sup>[1]</sup> Although rheumatoid arthritis (RA) develops its central pathology within the synovium of joints, many non articular organs become involved, particularly in patients with severe joint disease. The predominant extra-articular manifestations include subcutaneous nodules, pleuro-pulmonary, cardiac and neurological involvement, vasculitis and Felty's syndrome.<sup>[2]</sup> Pleuro-pulmonary involvement is an important cause of morbidity and mortality in the patients of RA.<sup>[3]</sup> Following its first description by Ellmann and Ball in 1948 in 3 patients with RA, ILD quickly appeared as the predominant pulmonary manifestation of Rheumatoid Arthritis (RA).<sup>[4]</sup> Pulmonary involvement is frequent in the course of rheumatological diseases, and may be due to various causes including infection, drug toxicity and specific

manifestations of the immune process.<sup>[5]</sup>

The involvement of lung is important in that though RA is common in females pulmonary manifestations is more common in males. Various studies have reported a prevalence of ILD of 5-40%.<sup>[6]</sup> Although cardiovascular disease is responsible for the majority of RA-related deaths, pulmonary complications are common and directly responsible for 10 to 20% of all mortality. The majority of lung disease occurs within the first 5 years after the initial diagnosis, and may be a presenting manifestation in 10 to 20% of patients. Many of the intra thoracic manifestations have the potential to cause critical illness and respiratory distress. Early recognition and treatment immensely help to decrease morbidity and mortality due to these extra articular manifestations.<sup>[7-10]</sup>

The present study Cross sectional descriptive study was carried out to find out the prevalence and pattern of pleura pulmonary manifestations and to assess the spirometric and radiological changes of lung disease in RA, in patients attending rheumatology clinic of Govt Medical College Thrissur from January 2009 to October 2009.

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**MATERIALS AND METHODS**

We studied 75 consecutive RA patients satisfying the 1987 ARA classification criteria 11, who reported to the rheumatology OPD of Govt Medical College Thrissur during the period January 2009 to October 2009. Patients who satisfied the revised ARA criteria, irrespective of whether respiratory signs or symptoms were present or not were included in study. Patients having pulmonary TB, Bronchial asthma, Occupational lung diseases were excluded from study group. The presence of pulmonary manifestations and predictors was sought in this group. A standard form was used to record the data from all the patients. All relevant parameters in the history and clinical examination were noted. These included early morning stiffness (EMS), tender joint count (TJC), swollen joint count (SJC) and deformities. The laboratory investigations done were hemoglobin, total and differential leukocyte counts, platelet count, ESR, RF (latex agglutination), liver and renal function tests. Chest, cervical spine and bilateral hand X-rays were obtained from all patients.

Pulmonary function tests (PFT) were done in all patients, and a chest CT was done in those with an abnormal PFT or clinical/x-ray suspicion of ILD. An active search for coexisting infections was done. There was a provision for further analysis by a cardiologist with echocardiography for patients who had symptoms and signs suggestive of pulmonary hypertension. The ethics committee of the Govt Medical College Thrissur cleared the study design. Informed consent was obtained from all the patients. Qualitative data were analyzed using the Pearson’s Chi-square test (c2) and Fischer exact test. All quantitative data were subjected to the 2-tailed Mann-Whitney U test. The statistical analysis was done using Epi info 3.5.1

**RESULTS**

Out of 77 RA patients who attended the rheumatology OPD, two patients had past tuberculosis and were excluded from the study. No other patient had any confounding conditions. The study group (75 patients) consisted of 58 females (77.3%) and 17males (22.7%).

The mean age of onset of RA was 42.6 yrs, and the average duration of disease at diagnosis was 5.9 yrs. The mean age of onset in males was 47 yrs, and that in females 41.3yrs. Morning stiffness was present in 94.7%. History of weight loss was given by 49.3% of patients and fever in 25%. Respiratory symptoms were present in 42.7%. Breathlessness was the most common respiratory symptom. 88% of patients were on DMARD and 54% on steroids. The mean duration of DMARD was 1.8 yrs. The mean TJC was 6 and mean SJC was 3.6. Deformities were present in 29 patients (38.7%). Rheumatoid nodule

was present in 21.3%. RF was positive in 57 patients (76 %).CRP was positive in 65.6%. Spirometry was normal in 62.7%. Mild restriction was seen in 20%.Moderate restriction seen in12% and severe restriction seen in 5.3%. Pulmonary manifestations were present in 14 patients (18.7%).

**Table 1: Demographic profile of study group**

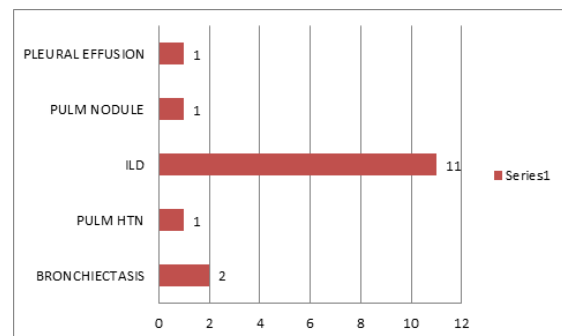
Age of onset	42.6 yrs
Duration of disease	5.9 yrs
Females	77.3%
Morning stiffness	94.7%
Weight loss	49.3%
TJC	6
SJC	3.6
Deformity	38.7%
Rheumatoid nodule	21.3%
Rheumatoid factor	76%
Pulmonary involvement	18.7%
DMARD	88%
Duration of DMARD	1.8 yrs
Steroids	54%

**Table 2: Treatment profile of study group**

Treatment	Frequency	Percent	95% Conf Limits		
No treatment	10	13.3%	0	6.6%	23.2%
Single DMARD	1	1.3%	1	0.0%	7.2%
Combo DMARD	24	32.0%	2	21.7%	43.8%
Single+steroids	9	12.0%	3	5.6%	21.6%
Combo+steroids	31	41.3%	4	30.1%	53.3%

**Table 3: Spirometry in rheumatoid patients**

Spirometry	Frequency	Percent	95% Conf Limits	
normal	47	62.7%	50.7%	73.6%
Mild restriction	15	20.0%	11.6%	30.8%
Moderate restriction	9	12.0%	5.6%	21.6%
Severe restriction	4	5.3%	1.5%	13.1%



**Figure 1: Types of pulmonary involvement**

**Table 4: Demographic profile of RA patients with pulmonary manifestations**

Age of onset	49.2yrs
Duration of disease	9.14yrs
Females	64.3%
Morning stiffness	92.9%
Weight loss	71.4%
TJC	4.7

SJC	3.7
Deformity	50%
Rheumatoid factor	100%
Duration of DMARD	2.1yrs
Steroids	42.9%

The predominant pulmonary manifestation was ILD (11/14). There were 2 cases of bronchiectasis and 1 case of pleural effusion, pulmonary nodule and pulmonary hypertension each.

Breathlessness was the most common symptom seen in 7 patients (50%) followed by cough and wheeze.40% of patients with lung involvement were asymptomatic. Physical findings in the form of crepitations were found in 5 patients (35.7%).CXR was normal in 9 patients (66.3%) and abnormal in 5 patients (35.7%). The most common abnormality in CXR was interstitial opacity. Among patients with pulmonary involvement spirometry showed mild restriction in 3 moderate restriction in 6 and severe restriction in 4.

**Table 5: CRP in patients with pleuro pulmonary manifestation**

CRP	Frequency	Percent	95% Conf Limits	
Positive	10	71.4%	41.9%	91.6%
Negative	4	28.6%	8.4%	58.1%

**Table 6: Deformity in patients with pleuro pulmonary manifestation**

Deformity	Frequency	Percent	95% Conf Limits	
Present	7	50.0%	23.0%	77.0%
Absent	7	50.0%	23.0%	77.0%

## DISCUSSION

**Table 7: Comparison of Demography profile study group with QUEST RA trial**

Profile	Present study	QUEST RA study
Age of onset	42.6 yrs	44 yrs
Duration of disease	5.9 yrs	11.2
Females	77.3%	79.2
SJC	3.6	2
Rheumatoid factor	76%	73.6%
ESR	60.52	22
Steroids	54%	49.2%

The main aim of the study was to identify extend and type of pleuro pulmonary involvement in patients with rheumatoid arthritis. At the same time an attempt was made to compare the demographic profiles of rheumatoid arthritis patients with and without pulmonary involvement.

The RA patients from our population proved to have 18.7% of pulmonary involvement. A retrospective study of medical records of patients with RA in Olmsted County, Minnesota, USA, diagnosed during the period 1955–1995<sup>12</sup> and a Swedish study of RA patients revealed a cumulative incidence of ILD of 9.4% during 30 years of follow-up and 6.8%, respectively. In our study 14.6% of the patients had ILD, compared to only 5.8% of the patients in the Turesson study<sup>16</sup>, and 3.7% in a Spanish study by

Carmona et al<sup>13</sup>. This is a relatively high figure compared to western statistics. The prevalence of ILD has varied widely in various studies done worldwide probably due to the various method of investigation used and because of the absence of standardized diagnostic criteria in retrospective data. A study done in Calicut by Koshy et al<sup>14</sup> using similar tools as in this study showed pleuropulmonary involvement in 32.7%. Among the patients with ILD most common pattern was UIP in 7 patients.

**Table 8: Comparison of patients with and without pulmonary involvement**

Charecteristic	With Pulmonary	Without Pulmonary	P value
Age of onset	49.2 yrs	41.2 yrs	0.027 (U test)
Duration of disease	9.14 yrs	5.2 yrs	0.035 (U test)
Females	64.3%	80.3%	0.196 (chi square)
Smoking	42.9%	37%	0.721 (chi square)
Parity in females	2.4	2.2	0.740 (U test)
TJC	4.7	6.3	0.257 (U test)
SJC	3.7	3.5	0.790 (U test)
Deformity	50%	36%	0.330 (chi square)
Rheumatoid nodule	43.8%	11%	0.003 (chi square)
Rheumatoid factor	100%	70.5%	0.013 (fisher exact)
CRP	71.4%	65.6%	0.467 (fisher exact)
Dur of DMARD	2.1	1.73	0.881 (U test)
Steroids	42.9%	55.7%	0.383 (chi square)
Hb	10.9	10.7	0.617 (U test)
TC	7900	8800	0.145 (U test)
ESR	67	59	0.078 (U test)

The demographic profile of study group is shown in [Table 1]. The results were compared to that in QUEST RA<sup>15</sup> trial, a large multinational cross-sectional cohort of patients with RA called Quantitative Standard Monitoring of Patients with RA (QUEST RA) done in over 6000 patients across 25 countries. The mean age of onset was 42.6 yrs in present study while 44 yrs in QUEST trial. Sex distribution was also similar 77.3% and 79.2% respectively. Mean duration of disease was much more in QUEST trial, 11.2yrs compared to 5.9yrs in present study. Rheumatoid factor positivity was similar in the two studies around 75%. The use of steroids was also similar in the two studies around 50%. SJC was much more in present study, 3.6 compared to 2 in QUEST trial. This suggests greater

disease activity and possibly be the reason for a much higher ESR (60.52) in present study compared to that in QUEST trial.

Mean age of onset of RA in the pulmonary group (49.2yrs) was significantly greater than patients without pulmonary manifestation (41.2 yrs). Their duration of illness (9.14yrs) was also significantly greater.

The proportion of males was greater in pulmonary group compared to non pulmonary group but it was not statistically significant. Study by Weyand et al,<sup>[16]</sup> had shown increased incidence of pulmonary involvement in males

Studies by Albano et al,<sup>[17]</sup> had identified increased incidence of pulmonary involvement with smoking. In the present study though the incidence of smoking was more in pulmonary group it was not statistically significant.

The mean TJC was 4.7 and mean SJC 3.7 in pulmonary group which was not significantly greater than non pulmonary group. Deformity was more in pulmonary group (50%) but was not statistically significant.

The incidence of rheumatoid nodule was significantly more in patients with pulmonary manifestation. Similar results were shown by studies done by Gabbay et al.<sup>[18]</sup>

Japanese study by Sakaida et al,<sup>[19]</sup> had identified increased rheumatoid factor positivity in patients with pulmonary manifestations. The present study also shows a significant increase in rheumatoid factor positivity in patients with pulmonary manifestation.

There was no statistically significant difference in hemoglobin, TC and DC in the two groups

A very interesting finding in the study has been the absence of significant increase in mean duration of DMARD in patients with pulmonary manifestation. This suggests that DMARD does not play an important role in the development of ILD.

Steroid use was less in the pulmonary group but it was not statistically significant.

Among patients with pulmonary involvement respiratory symptoms were present in 60%. Breathlessness was the most common symptom. Physical findings and positive CXR was present in only 35.7%. In study done by Raniga and Sharma.<sup>[20]</sup> In Baroda physical finding could be obtained in only 20% and CXR in 13%. These data suggest that physical examination and CXR has a very poor sensitivity in detecting ILD.

3 of the 15 patients with mild restriction in spirometry showed pulmonary symptoms while 6 out of 9 with moderate restriction and 4 out of 4 with severe restriction had pulmonary involvement. These data suggest that spirometry is highly sensitive in detecting ILD in rheumatoid arthritis. It can detect the disease much before physical signs appear and CXR becomes abnormal. CT chest remains the gold

standard in the diagnosis of ILD in RA patients. Spirometry is a good cost effective screening method for ILD in RA patients. Specificity of the test is increased if moderate to severe restriction is taken up for further evaluation.

## CONCLUSION

Pleuro pulmonary involvement is common in patients with rheumatoid arthritis. ILD is the most common manifestation. The risk of pulmonary involvement increases with duration of disease. Rheumatoid factor positivity and rheumatoid nodules are significantly higher in patients with lung involvement. There is no significant difference in sex distribution, smoking, disease activity and deformity between the two groups. There was also no significant increase in mean duration of DMARD in the two groups. This suggests that DMARDs are not playing a major role in development of ILD. Spirometry can detect lung involvement early even before physical signs appear and CXR becomes abnormal. Spirometry can be used as a reliable and cost effective screening method for pulmonary involvement in patients with rheumatoid arthritis.

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