



A Cohort Study to Determine the Prevalence of Pulmonary Manifestations in Rheumatoid Arthritis

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: Rheumatoid arthritis is an ailment that has an effect on the lungs in cases of pleural inflammation; it affects the lower as well as upper lung airways. Other effects of the disease can be seen in interstitial lung problems (parenchyma) and pulmonary vasculature.

Aim: Evaluating the occurrence of pulmonary manifestations in RA patients was the objective of this study.

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Methods: An observatory method that was cross-section in nature was employed in this study which was held in the Rheumatology and Medicine department, Jinnah Medical and Dental College Karachi Pakistan for the one-year duration from June 2020 to June 2021. Eighty subjects were included in this study, and all of them underwent a general examination, their medical history was taken into account. Several lab tests were performed on the patients, ESR, BUN, CRP, HRCT, ALT, radiological investigations, and chest X-rays were included.

Results: In this study 42 percent of patients presented with pulmonary manifestations. About 45.70 percent of the patients presented with abnormalities in the spirometry test, 42.85 percent showed HRCT abnormalities. The HRCT scores vary with age, TJC (Tender Joint Count), ESR, and SJC. FEV₁, HRCT, and FVC showed a negative correlation among each other. However other variables did not show any statistically significant correlation.

Conclusion: RA showed the prevalence of pulmonary affection, and this can be observed in pulmonary and radiological functions. There was an association of age, pulmonary functions, and ESR.

Keywords: Rheumatoid arthritis; pulmonary manifestation; chest infection.

1. INTRODUCTION

Among the leading autoimmune diseases which cause inflammation, Rheumatoid arthritis is the most prevalent. The main affected areas are the joints but there are extra-articular effects of the disease which involve other systems such as the lungs which are most affected by the disease [1-2]. The vasculature, pleura, and airways of the lungs are affected by the disease and can cause lung parenchyma [3-4]. Evaluating the occurrence of pulmonary ailments in Pakistani patients presenting with RA was the main objective of this study.

2. METHODOLOGY

An observatory method that was cross-section in nature was employed in this study which was held in the Rheumatology and Medicine department, Jinnah Medical and Dental College Karachi Pakistan for the one-year duration from June 2020 to June 2021. The study was consistent with 80 patients and the criteria of the American College of Rheumatology / European League against Rheumatism (ACR/EULAR) 2010 classification was followed.

The following information was obtained from the patients:

- A detailed relevant data collection was performed including age, medical history, articular symptoms, smoking history, and a complete general examination.
- Lab tests were performed on patients, ESR, Complete Blood Count, ALT, CRP-titer, AST, Creatinine, and BUN.

- A thorough Musculoskeletal examination was performed on all patients.
- A latex agglutination test kit was used to find a Rheumatoid factor titer (RF).
- ELISA was used for Anti-CCP antibody titer

2.1 Radiographic Evaluation

1. An x-ray of the Chest (plain) for both the posterior and anterior view
2. Pulmonary high resolution computed tomography scan (HRCT): It was done using both techniques GE Light Speed Plus MSCT 4 channels set and Toshiba Aquilion MSCT 64 channels set. HRCT films were done in a supine position with full inspiration without contrast enhancement.

Spirometric pulmonary function test: Spirometry was performed according to American Thoracic Society guidelines (ATS) with an assessment of vital capacity, forced vital capacity (FVC), Forced expiratory volume in 1 second (FEV₁), FEV₁/FVC ratio.

SPSS version 22.0 was used to evaluate all statistical data. Standard deviation, range, mean was the qualitative variables, the number was described as (no) & (%) as a percentage, to compare all variables a qualitative Chi-square test was employed. We used a T-test to independently compare two quantitative variables. To rank the variable as negative or positive the Pearson correlation ranking test was performed. P-value > 0.05 was seen as significant.

3. RESULTS

Out of the 80 participants, 12 subjects were male and the remaining 68 were female 15 percent and 85 percent respectively. The range of age in patients included was 25-77 years in this study, with a mean age of 45 ± 11.17 -23 years. The duration of being illness was 0.8 to 24 years with the mean range of 7.4 ± 6.10 years. 9 patients were smokers that makes 11.25% of the patient number included in the study.

Arthralgia was found to be the most common element, 73.75%, active arthritis 77.5%. Deformed joints were found in 16.25%, dyspnea 31.25%, and cough in 41.25% of patients.

Methotrexate was the dominant steroid used in 83.75% of patients, hydroxychloroquine 71.25% and leflunomide in 46.25%, and sulfasalazine in 21.25% of patients. Abnormal spirometric results were found in 32(45.71%) patients. Severe

airflow restriction was observed in 11.90%, moderate in 23.81%, and mild in 19.05% of patients. 7.14% of patients showed a mild obstructive pattern, a mixed pattern was observed in 16.67% and early obstruction in 21.88% of patients.

3.1 The HRCT Findings are Given in Table-3

More active arthritis $p=0.004$ and older patients $p=0.005$ showed pulmonary affection, swollen joint count ($p= 0.002$), dyspnea($P<0.001$), cough ($P= 0.001$), crepitations ($P=0.002$), chest pain ($P=0.027$) and wheezing ($P= 0.022$). RA patients with pulmonary affection by HRCT showed more affection regarding FVC ($P= 0.0045$ and FEV1 ($P= 0.022$), but there was no significant difference regarding FEV1/FVC ratio ($P= 0.641$.) (Table 3).

Table 1. Shows the demographic data of the patients

Males	12	15%
Females	68	85%
Age Range	25-77 Years	
Mean Age	45 ± 11.1 years	
Mean Duration of Illness	0.8 to 24 years	

Table 2. Abnormal spirometry (n=42) and its percentage

Parameter	Pts with abnormal spirometry (n=42)	Percent
Abnormal spirometric patterns	32	45.70%
Mild restrictive	8	19.05%
Moderate restrictive	10	23.81%
Severe restrictive	5	11.90%
Mild obstructive	3	7.14%
Small airway (early obstructive)	9	21.43%
Mixed	7	16.67%

Table 3. HRCT findings

HRCT finding	No. of pts (80)	Percent
Abnormal HRCT findings	30	42.85
Ground glass appearance	15	18.75%
Pleural irregularities	13	16.25%
Reticulation	21	26.25%
Honey combing	9	11.25%
Subpleural cyst	4	5.00%
Airspace consolidation	3	3.75%
Nodules	5	6.25%
Emphysema	8	10.00%
Bulla	5	6.25%
Bronchiectasis	15	18.75%
Mosaic perfusion	6	7.50%
Pleural effusion	6	7.50%
Air trapping	7	8.75%

A positive statistical difference between age and score was found in total HRCT score and disease parameters ($r=0.380$, $P=0.002$), TJC showed ($r=0.459$, $P < 0.001$), SJC difference was ($r=0.370$, $P = 0.001$) while ESR showed ($r=0.252$, $P= 0.033$) as a positive correlation. However, HRCT and AST showed negative difference ($r=-0.242$ $P= 0.041$). FVC and FEV1 showed noteworthy negative correlation ($r=- 0.521$, $P < 0.001$), ($r=-0.438$, $P < 0.001$) respectively. Table 3 shows other parameter results where no significant effect was observed.

4. DISCUSSION

The etiology of Rheumatoid arthritis (RA) is unknown, and this disease is responsible for inflammation of numerous organs and tissues [5-6]. This disease is known to target synovial joints primarily by causing symmetric affection in peripheral joints. An extra-articular effect of the disease is on the lungs in RA patients. RA affects the respiratory system holistically including vasculature, parenchyma, pleura, and airways. RA lung manifests in a progressive disease of the parenchyma of the lungs ILD (Interstitial lung disease), clinically 10 percent of RA subjects suffer from this condition and 30 percent never go to clinics. Even if the articular disease is not present ILD can occur [7-8].

We included 80 patients in our study out of which 12 were male and 68 were female subjects 15 percent and 85 percent, respectively. These patients showed mean age \pm SD 45 ± 11.1 years and the age was between 25-77 years, spanning between 0.8-24yr of progressive disease, mean \pm SD 7.4 ± 6.10 yr. Zurouret *al* had involved 12 males and 63 females 16 and 84 percent, respectively. The age of the subjects ranged between 20 and 84 years and 48 years was the mean age of these patients, duration of the disease ranging between 60 days to 27 years. 11.25% percent patients were smokers in our study compared to Zurouret *al* who had 11 smokers included in his study making up 14.6 percent of the study population [9-10]. Smoking patient percentage is low due to a small number of male subjects as compared to females due to cultural trends.

37 (46.25%) patients of our study showed symptoms of respiration dyspnea being present in 25(31.25%), cough 41.25%, 9(12.8) wheezing, and 11 chest pain patients making up 15.7%. When compared to Zurouret *al* 32% showed respiratory ailments where wheezing was least

common and dyspnea was the most occurring symptom, 13.3% cough patients, chest discomfort in 10.7 %, wheezing in 6.7 % and 25.3% Dyspnea [11-12].

Forty-two patients had HRCT that makes up 52.5% and 30(42.85%) patients had abnormalities, ILD was in 24(30%) patients. 13 (16.25%) subjects showed pleural irregularities, 4 (5%) subjects had subpleural cysts, ground glass in (15)18.75% patients, septal lines in 23% and honeycomb appearance in 11.25 %, 9 patients. The less observed airway issues included 8.75% air trapping subjects, mosaic perfusion 7.50%, bulla 6.25% patients, emphysema 10%, 2 patients showed airway consolidation, and 18.75% patients showed bronchiectasis. Pulmonary nodule and pleural effusion were found in 6.25% and 7.50% patients respectively.

Our results are consistent with the study done by Youssef *et al* where RA patients 47% showed ILD as most occurring in 38.9%. Reticular opacities were found in 8 patients 22.2%, while 4 (11.1%) showed ground-glass opacity while 2 (5.6%) patients presented with honeycombing [13-14]. 13 patients presented with a bronchial abnormality that is 36.1%, 2 patients with emphysema 5.6%, pleural effusion patients were 5.6% 2, and 4 patients with rheumatoid pulmonary nodules 11.1%.

Cortet *et al* found in his study that abnormal HRCT was present in 80.9% patients out of a total of 68 patients, most common being bronchitis which was present in 30.5%, nodules in patients 28%, ground glass 17.1%, air trapping in 25% and honeycombing in 2.9 percent, only 1.5% pleural effusion was found in this cohort [15-16]. The variable results indicate differences in the definition of the disease or the characteristics, another reason could be differences in methodology. PFTs in 52.5% of the study population were found to be abnormal in our study, they showed an obstructive pattern in the small airway and restrictive pattern. This result was consistent with the results of a study undertaken by Farrage *et al* where he found that 37% of patients showed Abnormal PFT's. The obstructive pattern was detected to be 31.4 percent while obstructive was present in 12.8 percent [17].

In another study conducted by Joshi *et al*, 31.4% of patients showed the obstructive PFT outline, and 12.8% of patients showed an obstructive pattern. Conflicting results were found in a study

undertaken by Biomdo et al where the total abnormality percentage of PFT was 38.5% however, the obstructive pattern was found dominant, which stood at 20.4% compared to 16.9% restrictive pattern, the authors of that study found environmental and climate reasons to be responsible for unusual results [18].

In our study a significant association between HRVT score (P-value <0.0001) and FVC and FEV1 was found which is consistent with Zurour et al. However, this result was inconsistent with Bilgici et al; the substantial correlation was not present. The severity score of HRCT and age were correlated in our study. Zhang et al found that age is correlated with RA-ILD. That makes it important to screen elder patients [19]. No correlation was found by Sakre et al regarding the age of the patients.

Consistent with Yilmazer et al and Bilgici et al; No association between disease duration and disease severity was found in our study. Hence, suggesting that the severity of the disease is not dependent on the duration [20]. In this regard another study conducted by Joshi et al found ILD to be more probable in extended disease periods. It is safe to say that duration of disease in his cohort may have been longer.

We could not establish a connection between disease and smoking history. Other studies also found the same results and couldn't establish the relationship between smoking and pulmonary issue, Sakre et al and Bilgici et al in RA [21]. However, Zhang *et al* found conflicting results and established smoking as a significant risk factor of ILD.

No significant relation between medication and HRCT can be established in our study, Sakre et al agree with our results in their findings where no association of medication could be established.

Methotrexate, however, was found to be a small risk factor which was attributed to an increase in pulmonary abnormality in RA patients in a study conclusion of Conway *et al*. Rheumatoid had no association with severity of the disease and there was no significant difference found in groups for anti-CCP. Two studies, however, found its correlation with RF but they could not establish it with anti-CCP by Zhang et al and Joshi et al, no connotation was found. Skare et al, Zrour et al, however, found it with RF but no evaluation of anti-CCP was undertaken in this study [22].

A study conducted by Doyle however, demonstrated that titers of RF and anti-CCP antibodies were advanced in RA-ILD subjects. RF and anti-CCP are found to be noteworthy ILD predictors; anti-citrullinated peptide antibody-positives suggests the presence of ILD, and more severe ILD is associated with advanced titers of ACPA. The variance however is thought to be linked with lesser male participants, duration, and fewer smokers.

5. CONCLUSION

RA-affected subjects showed more occurrence than expected and can be a dominant risk of more age, ESR, PFT irregularities. It can be suggested that respiratory symptoms and PFT abnormalities can be used as predictors of lung disease. To provide optimal treatment, physicians must always consider the possibility of associated pulmonary manifestations when patients with RA are evaluated. It is concluded that early identification and timely therapeutic intervention may alter the prognosis of pulmonary fibrosis in patients with Rheumatoid arthritis.

CONSENT

As per international standard or university standard, patient's written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

The study was conducted after obtaining ethical approval from the Ethical committee.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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