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Original Article

Pulmonary Manifestations of Rheumatoid Arthritis in Patients Attending a Tertiary Care Hospital of North East India: A Cross-sectional Study

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Abstract

Background: Rheumatoid arthritis (RA) is a chronic inflammatory, systemic disease that produces its most prominent manifestations in the dirhrodial joints. The most common form of the disease is demonstrated by symmetrical, destructive, and deforming polyarthritis affecting small and large synovial joints with associated systemic disturbances, in addition to a variety of extraarticular features and the presence of circulating antiglobulin antibodies (rheumatoid factor). One of the most common extra-articular manifestations of RA is pulmonary involvement that can be seen in 30% of the cases. It is associated with a high titer of rheumatoid factor and is the second leading cause of death first being the infection.

Aims and Objectives: The aims of this study were to study the pattern of lung changes in patients with RA and to assess the change in lung function with respect to duration of disease and joint deformity.

Materials and Methods: Pulmonary function test was done in 80 RA patients aged between 30 and 60 years, attending the PMR department over a period of 3 months using Spirometry – model SPM –A. Spirometry parameters recorded were forced vital capacity (FVC), forced expiratory volume in 1 s (FEV_1), FEV_1/FVC, FEF_{25-75}, PEFR, and MVV. Data were entered in computer using Microsoft Excel. Descriptive statistics and other suitable statistical tests like χ^2 test were used as per applicability. A $P < 0.05$ will be considered as significant.

Results: Out of 80 RA patients, 54% showed changes in pulmonary function. About 44% of them had restrictive and 10% had obstructive type of lung changes. Among the spirometric parameters, most of them had normal FEV1/FVC and decreased FVC.

Conclusion: Different pattern of pulmonary function abnormalities could be manifested in RA patients and the restrictive pattern being the most common feature. Spirometry can be indicated as a baseline assessment and for follow-up of RA patient for the early detection and timely management of the pulmonary involvement.

Key words: FEF_{25-75}, Forced expiratory volume in 1 s, Forced vital capacity, MVV, PEFR, Pulmonary function test, Rheumatoid arthritis

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic inflammatory, systemic disease that produces its most prominent manifestations in the diarthrodial joints. The most common form of the disease is demonstrated by symmetrical, destructive, and deforming polyarthritis affecting small and large synovial joints with associated systemic disturbances, in addition to a variety of extra-articular features and the presence of circulating antiglobulin antibodies (rheumatoid factor). The disease has a global distribution and involves all ethnic groups. The prevalence varies from 0.3% to 1.5% worldwide; it is 2.5 times greater in females than in males.[1] Although it is more common in females, extra-articular manifestations of the disease are more common in males and are mostly is seen in the 25–55 year age group.[1] The measurements of disease activity include the duration of morning stiffness lasting at least 30 min that

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often improves gradually after physical activity, the patients assessment of pain (visual analog score), the patients global assessment of disease activity, the patients assessment of physical function (disability), and the acute phase reactant value, namely, erythrocyte sedimentations rate (ESR), C-reactive protein (CRP), and hemoglobin concentration (Hb%). Extra-articular manifestations of RA can emerge during the course of the disease and even before the onset of arthritis. Patients can experience alongside of joint deterioration and severe disability, decreased quality of life, and premature mortality.[2] The presence of comorbidities such as cardiovascular disease, cancer (specifically lymphoma and lymphoproliferative diseases, lung cancer, and melanomas), infections, depression, and gastrointestinal disease can deteriorate the disease condition.[3]

One of the most common extra-articular manifestations of RA is pulmonary involvement that can be seen in 30% of the cases.[4,5] It is associated with a high titer of rheumatoid factor and smoking. It is the second leading cause of death first being the infection. This may present as interstitial pneumonitis, fibrosis, pleural involvement, pulmonary nodule, bronchiolitis obliterans organizing pneumonia, arthritis associated with pulmonary hypertension, and involvements of small and large airways.[4,5] The majority of lung disease occurs within the first 5 years after the initial diagnosis and may be a presenting manifestation in 10–20% of patients. Pleural disease is common but, usually, asymptomatic; autopsy studies have reported pleural involvement in 50% of cases, with only 10% clinically detected.[4,5] Interstitial lung disease (ILD) in patients with RA usually has a poor prognosis. Early studies identified a high postmortem incidence of RA-ILD, and this was subsequently supported by high-resolution computed tomography (HRCT) which confirmed that up to 25% of RA patients had ILD.[3] Spirometry is an inexpensive, readily available tool for assessing the lung function and can be applied on a large scale. Studies employing spirometry have detected abnormalities, mainly obstructive and restrictive patterns, in approximately 30% of patients with RA. It is a simple test to measure static lung volumes at rest – slow (inspiratory or expiratory) vital capacity (SVC), forced vital capacity (FVC) – and dynamic volumes forced expiratory volume in 1 s (FEV1), and flow-volume loops. Understanding the pattern of pulmonary abnormalities and its early detection can improve the quality of life and reduce mortality rate in patients with RA. Hence, the study was taken up to assess the pattern of lung changes in patients with RA and to assess the change in lung function with respect to duration of disease and joint deformity.

Primary Objective

The primary objectives of this study were as follows:

- To estimate the pattern of lung changes in patients of RA.

Secondary Objective

The secondary objectives of this study were as follows:

1. To assess the change in lung function with respect to duration of disease
2. To ascertain any association with joint deformity and lung changes.

MATERIALS AND METHODS

A hospital-based cross-sectional study was done in 80 adult patients with RA attending the PMR department, AGMC and GBPH, Agartala. Ethical clearance was obtained from the Institutional Ethical Committee of AGMC and GBPH. The study subjects were evaluated by general history, clinical examination, blood reports, and chest X-rays. Study was conducted from November 2022 to January 2023.

Inclusion Criteria for Cases

The following criteria were included in the study:

1. Based on the 2010 ACR classification criteria for RA (A Score of ≥6 out of 10 is needed to define RA)[14]

A. Joint involvement	Score
1 large joint	0
2–10 large joint	1
1–3 small joint (with or without involvement of large joints)	2
4–10 small joint (with or without involvement of large joints)	3
>10 joints (at least 1 small joints)	5
B.Serology (at least 1 test is needed for classification)	
Negative RF and Negative ACPA	0
Low positive RF or low positive ACPA	2
High positive RF or high positive ACPA	3
C.Acute phase reactants (at least 1 test is needed for classification)	
Normal CRP and normal ESR	0
Abnormal CRP and abnormal ESR	1
D.Duration of symptoms	
<6 weeks	0
≥6 weeks	1

ESR: Erythrocyte sedimentations rate, CRP: C-reactive protein

2. Age group of 30–60 years of both sexes
3. All the patients were consuming at least one disease-modifying antirheumatic drugs
4. Patients having no cardiovascular and respiratory complaints
5. Co-operative and willing to participate in the study.

Exclusion Criteria

The following criteria were excluded from the study:

1. History of any pulmonary disease
2. Clinical or radiological evidence of lung disease
3. Clinical or ECG evidence of cardiac disease
4. History of smoking, alcoholism or pregnancy
5. Treatment with corticosteroids
6. Those who are not willing to participate in the study
7. Patients with mixed connective tissue disease.

Study Tools

1. Electronic Spirometer – Model SPM – A
2. HRCT
3. Sphygmomanometer
4. Stethoscope
5. Case study format.

Recording of Spirometry

The participants were made to relax and wear comfortable loose clothing. The participant sat comfortably and nose clip was applied on the nose. The spirette was kept in the mouth with the lips sealing around it and was instructed to breathe calmly and care was taken not to block or bite the spirette. They were asked to do tidal breathing and fill the lungs completely and then asked to exhale as hard and fast as possible until the lungs were completely empty and inhale as hard and fast as possible until the end of the test. All the tests were conducted according to the American Thoracic Society/European Respiratory Society guidelines in a quiet room in sitting position by the Spirometer SPM-A for 3 times at every 15 min interval and best of 3 was taken into account.

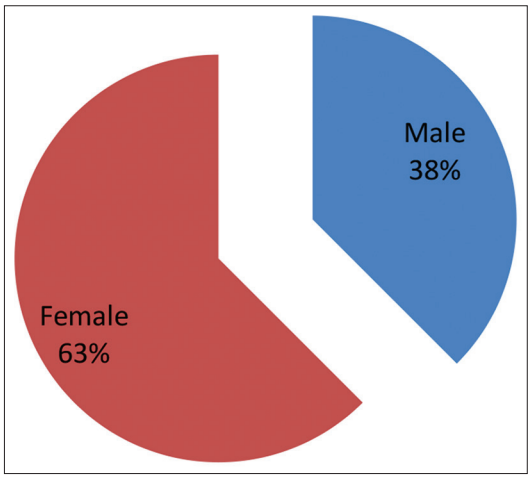

Figure 1: Gender-wise distribution of study participants

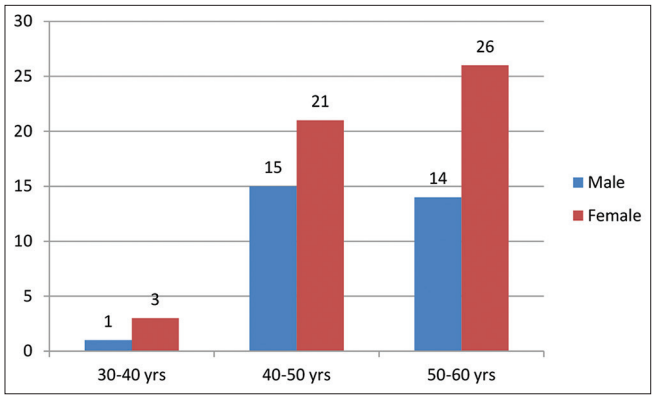

Figure 2: Age-wise distribution of patients

RESULTS

Data were entered in computer using Microsoft Excel. A $p < 0.05$ were considered as significant. A total of 80 RA patients had participated in this study. Among them, 62.5% were female and 37.5% were male, as shown in Figure 1. Mean age group was 43.24 ± 4.43 years. Age-wise distribution of study participants is shown in Figure 2. Mean duration of the disease was 7 ± 3.34 years. Disease duration of the study participants are shown in Figure 3. The lung function parameters interpreted were FVC, FEV_1, FEV_1/FVC, FEF_{25-75}, PEFR, and MVV which are shown in Figure 4 and Table 1. Changes in FVC ($P = 0.002$), FEV_1 ($P = 0.01$), and FEV_1/FVC ($P = 0.042$) were statistically significant. A significant negative correlation (r value = −0.239, $P = 0.053$) was found between FVC and duration of disease, as shown in Figures 5 and 6 which show the type of ventilatory defect in the study population. Figure 7 shows the frequency of presenting symptoms in RA patients. Figure 8 shows the result of rheumatoid factor tests in study group. Spirometric changes and its association with RA factor are shown in Figures 9 and 10 which show the laboratory investigation reports of CRP, ESR, and Hb% among the participants. The interpretation of X-rays among the study participants is shown in Figure 11.

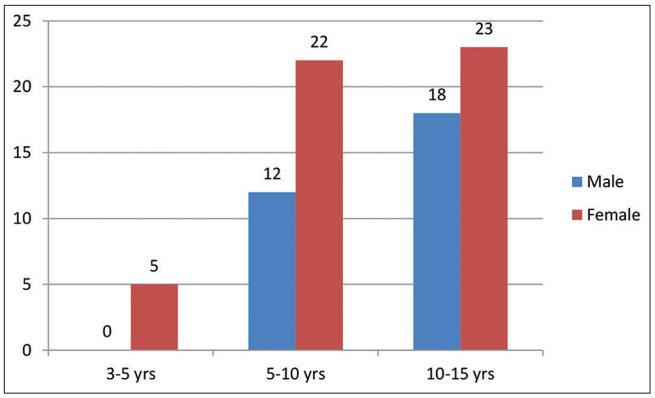

Figure 3: Disease duration of the study participants

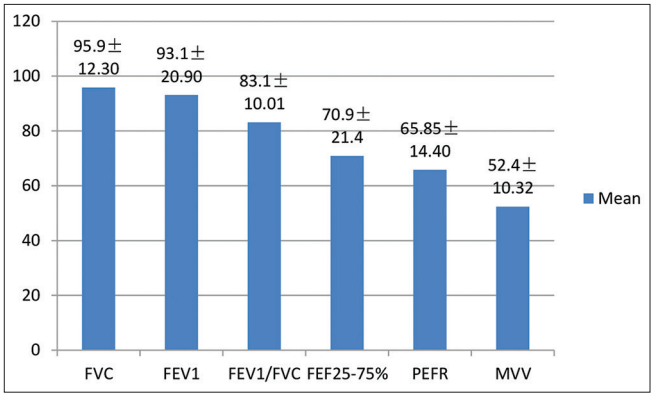

Figure 4: Mean ± Standard deviation of the spirometric parameters

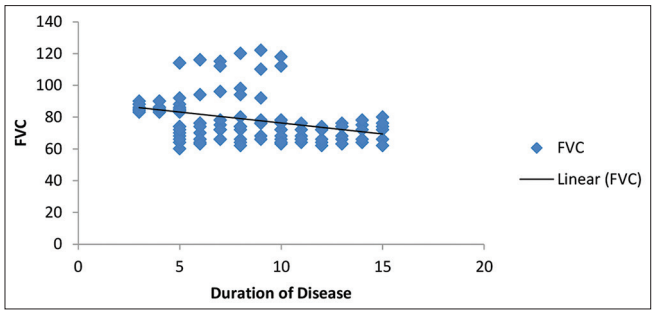

Figure 5: Correlation of forced vital capacity with duration of disease

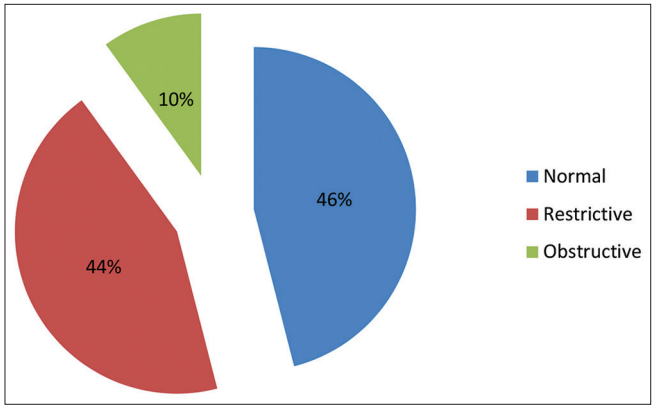

Figure 6: Ventilatory defect among the study subjects

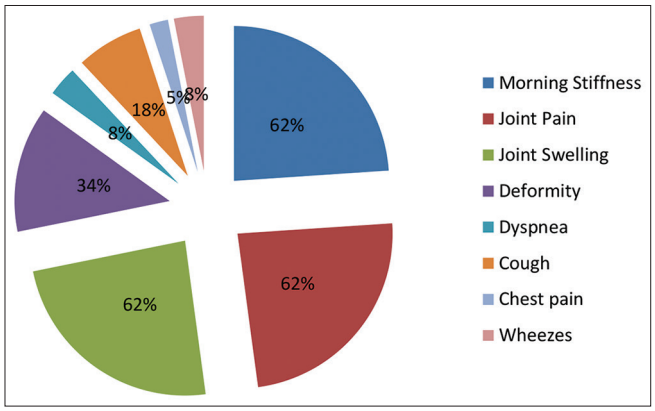

Figure 7: Frequency of presenting symptoms in rheumatoid arthritis patients

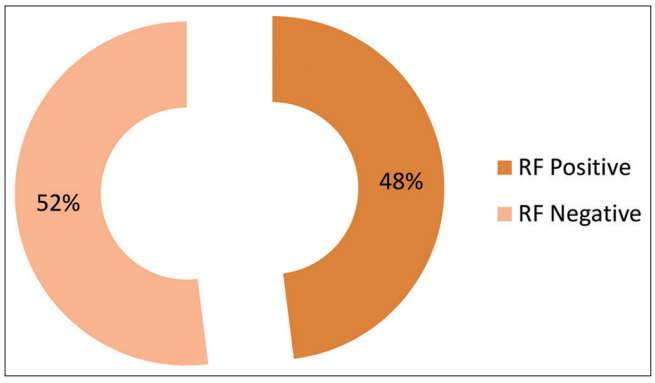

Figure 8: Rheumatoid factor test in the study participants

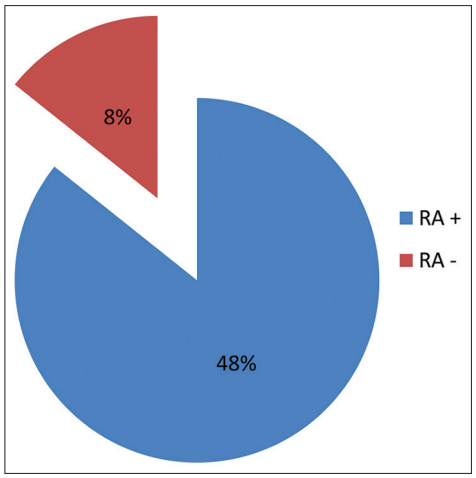

Figure 9: Spirometric changes and its association with rheumatoid arthritis factor

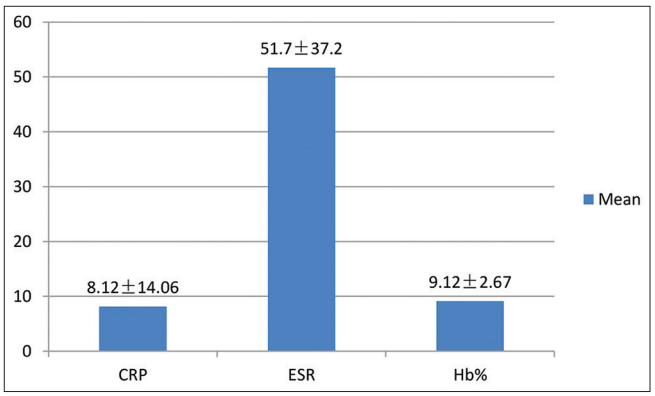

Figure 10: Other laboratory tests in study groups (C-reactive protein, erythrocyte sedimentations rate, and Hb%)

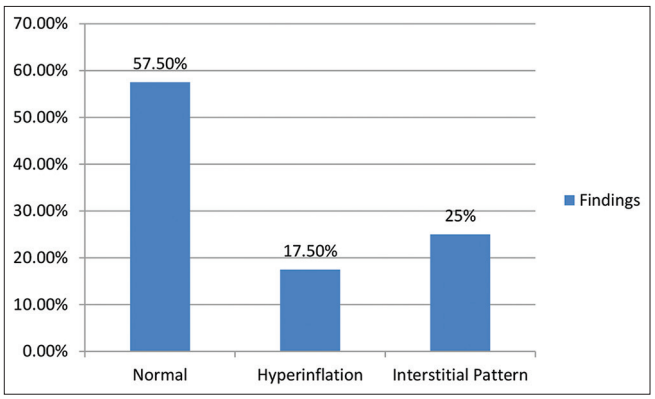

Figure 11: Interpretation of chest X-rays

DISCUSSION

RA is a chronic inflammatory, systemic disease involving mainly dirhrodial joints. One of the most common extra-articular manifestations of RA is pulmonary involvement. In our study, we assessed the pulmonary manifestations of RA using spirometry. Among the study population, 39% were male and 63% female. Mean age

Table 1: Spirometric parameters of the study participants

S. No.	Spirometric parameters	Mean±SD	*P*-value
1.	FVC	95.9±12.30	0.01*
2.	FEV1	93.1±20.90	0.002*
3.	FEV1/FVC	83.1±10.01	0.045*
4.	FEF 25–75%	70.9±21.4	1.26
5.	PEFR	65.85±14.40	0.45
6.	MVV	52.4±10.32	0.23

FEV1: Forced expiratory volume in 1 s, FVC: Forced vital capacity

group was 43.24 ± 4.43 years and the mean duration of the disease was 7 ± 2.23 years. The spirometry showed significant changes in FVC, FEV1, and FEV1/FVC and significant negative correlation of FVC with duration of the disease. The ventilatory defect pointed more toward the restrictive pattern. Interpretation of chest X-rays shows 57.5% normal, 17.5% hyperinflated, and 25% interstitial pattern.

The findings of our study are in association with the study of Ravikumar *et al.*[1] who concluded FVC, FEV1, FEV1/FVC, FEF 25–75%, and PEFR which were significantly decreased in patients with RA and 16% had obstructive and 28% had restrictive lung diseases. It is also in association with studies by Kalyani *et al.*[6] where they found restrictive ventilatory defect in 64% of rheumatoid patients with FEV1/FVC >70% and reduced vital capacity and total lung capacity. Obstructive ventilatory defect was seen in 10% of rheumatoid patients since FEV1/FVC <80% with increased residual volume and total lung capacity ratio. Remaining 26% of participants were normal. Lung parameters such as FVC, FEV1, FEV1/FVC, FEF 25–75%, and PEF were significantly lower in RA patients.

Fuld *et al.*[7] found that the prevalence of pulmonary function abnormalities was higher in asymptomatic rheumatoid patients when compared with the reference population. Avnon *et al.*[8] noted restrictive pulmonary abnormalities in 25.6% small airway disease in 14.6% and obstructive in 27%. Cortet *et al.*[9] and Radoux *et al.*[10] found that small airway obstruction is seen in 50% of cases with decrease in FEF 25–75%. Bilgici *et al.*[11] and Vergnenegre *et al.*[12] noted obstructive type of lung disease and reported a significant reduction in FEF 25–75%, FEV1/FVC. Devouassoux *et al.*[13] found that there is airflow obstruction with decreased FEV1/FVC and hyperinflation with increased residual volume and total lung capacity ratio. Findings of all these studies are in affirmation with findings of our study.

In our study, there was also significant negative correlation between FEV_1/FVC and duration of disease. Vergnenegre *et al.*[12] reported a significant negative relationship between FEF 25 and 75% and duration of articular disease in their study, whereas Cortet *et al.*,[9] Gabby *et al.*,[14] and Jamsshidi *et al.*,[15] found no relationship between disease duration and activity with PFT abnormalities in patients with RA.

In RA, restrictive ventilatory defect may be due to the activation of immune complexes in the alveolar walls. It results in the release of myeloperoxidase, collagenase, and elastase. There is destruction of lung tissue by phagocytosis and protease – anti-protease imbalance preventing the lung expansion and obstructive ventilator defect may be due to airway inflammation. Plasma immunoglobulin E level increases. Neuropeptides and chemokines are released from eosinophils, and mast cell damages the airway epithelium and causes hyper-responsiveness. This may result in partially reversible airway obstruction due to bronchial narrowing.

CONCLUSION

Lung is a potential target organ of the RA inflammatory disease process that can be manifested as different pattern of pulmonary function abnormalities. A restrictive pattern represents the most common feature. Spirometry can be indicated as a baseline assessment and for follow-up of RA patient for the early detection and timely management of the pulmonary involvement.

Limitations of the Present Study

The sample size in the present study is relatively small. Furthermore, unknown and subclinical complications, which are unaccounted for, may contribute to changes in lung function.

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