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# Assessment of pulmonary function (PFT) among patients of rheumatoid arthritis (RA)

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**Abstract**
**Aim:** To assess pulmonary function (PFT) among patients of rheumatoid arthritis (RA).
**Material and Method:** The present observational study was conducted in the department of Medicine at Chattrapati Shivaji Subharti Hospital from February 2019 to January 2021 among 50 patients with active rheumatoid disease (RA). Selected patients underwent simple spirometry as per the standard protocol described below i.e. on day of procedure; the patient was instructed to have a light breakfast. The spirometric parameters derived by the FVC maneuver were computed. Obstructive ventilatory defect and Restrictive ventilatory defect along with Small airway defect were recorded.
**Results:** Cough, shortness of breath, wheezing and crepitations was reported among 26%, 16%, 12% and 18% of the subjects respectively. Obstructive, restrictive and mixed type was found among 24%, 18% and 2% of the subjects respectively. Mean duration of disease (in years) was comparatively more among subjects with abnormal PFT (4.48) as compared to subjects with normal PFT (3.19 years) with statistically significant difference as $p<0.05$. Abnormal PFTs was found among 55.56% and 14.29% of subjects with and without symptoms & signs.
**Conclusion:** We observed a high prevalence of pulmonary function abnormalities as measured by spirometry in this RA population. The commonest ventilator defect pattern was obstructive followed by restrictive.

**Keywords:** PFT, RA, spirometry

## Introduction

Rheumatoid arthritis (RA) is a multisystem disease of unknown cause. It is a common inflammatory arthritis and an important cause of potentially preventable disability. The characteristic feature of RA is persistent inflammatory synovitis usually involving peripheral joints both small and large in a symmetric distribution. The synovial inflammation has the potential to cause cartilage destruction and bony erosions. Subsequent changes in joint integrity lead to deformities [1]. Rheumatoid arthritis (RA) affects about 0.92% of adult population in India. Rheumatoid arthritis can develop at any age with increased incidence between 35 and 55 years of age [2]. The prevalence of RA is approximately 0.5-1% worldwide with some variability among different populations [3]. Rheumatoid arthritis more commonly occurs in females than in males with age related differences. Younger onset RA female to male ratio is 4.4:1 while in elderly onset RA, the ratio is 1.6:1[4].

Pulmonary involvement is a frequent and among the most severe extra-articular manifestation of RA. It is a leading cause of excess death in patients with RA and the second cause of death in this patient population [5]. Pulmonary complications are directly responsible for 10 to 20% of all mortality [6, 7]. When compared with control populations, patients with RA and with a respiratory disease have an estimated standardized mortality ratio that ranges from 2.5 to 5.06. The majority of lung disease occurs within the first 5 years after the initial diagnosis, and may be a presenting manifestation in 9 to 20% of patients. The onset of respiratory manifestation may even precede the onset of symptoms of arthritis [8].

Chest x-ray has the low sensitivity of identifying interstitial lung disease (ILD). High-resolution computerized tomography is a more sensitive means of detecting ILD [9]. The spirometric analysis shows a restrictive or obstructive pattern in rheumatoid lung disease. The restrictive pattern is characterized by reduced total lung capacity and reduced vital capacity. The obstructive pattern is characterized by decreased FEV1/FVC ratio. Reduced mid-expiratory flow rate (FEF 25%-75%) detects early small airway involvement. Till date, there is paucity of study on pulmonary manifestations of RA from Northern India. The present study has intended to bridge this gap by evaluating the spectrum of pulmonary affection in RA patients in a tertiary care hospital of Uttar Pradesh, by clinical, spirometric, thoracic C.T scan and echocardiographic assessment. This will enhance the understanding of clinical course of the pulmonary manifestations of RA and will facilitate early detection and appropriate management for better outcome.

## Material and Method

The present observational study was conducted in the department of Medicine at Chattrapati Shivaji Subharti Hospital from February 2019 to January 2021 among 50 patients with active rheumatoid disease (RA). Patients with active rheumatoid disease (RA), cooperative RA patients able to perform PFT (pulmonary function tests) and patients having age>18 years were included in the study. RA patients with pre-existing pulmonary diseases like pulmonary TB (even history of old PTB), COPD, Bronchiectasis, ILD (interstitial lung disease) due to other

causes, musculoskeletal disorders etc, patient not able to open mouth due to sub-mandibular joint involvement and patient not able to perform PFT and smokers were excluded from the study.
The patients were interviewed that requests for the demographic, socioeconomic status, medical history and previous history of taking any medications and supplements.

**Procedure**

a. Enrolled patients of RA were investigated after fulfilling the criteria of inclusion and exclusion. It included haemogram, X-ray of involved joints, chest X-ray PA view, and RA factor.
b. After excluding other pulmonary pathologies, patients underwent pulmonary function testing in respiratory laboratory.
c. Selected patients underwnet simple spirometry as per the standard protocol described below i.e. on day of procedure, the patient was instructed to have a light breakfast. The test was conducted in the morning. During testing, patient was asked to sit in front of the spirometer (Schiller, Spirovit SP1) on a stool. Then mouthpiece is to be fitted in each subject snugly so that all the air breath goes into the spirometer. In addition, a nose clip was clamped on nose so that the patient cannot exhale any air through nose.
d. The steps of procedure were explained to the patient by technician. Initially patient is asked to breathe normal tidally. Once patient stabilizes, he/she was told to inhale and exhale as deeply and rapidly while connected with spirometer.

**Procedure generation of FVC (Forced vital capacity) manoeuvre and FV loop**

A flow-volume loop is generated by having the patient inhale deeply to total lung capacity (TLC), and forcefully exhale until the lungs have been emptied to residual volume (RV), and that then inhale rapidly to reach TLC. Flow is plotted on the Y axis and the volume on the X axis of a typical FV loop. The upper portion of the curve above the X-axis shall reflect the expiratory portion; and lower portion of curve below X-axis represents inspiratory portion of FV Loop. In presence of one or all three faults of slow start, coughing and premature termination of FVC maneuver; graph of FV Loop was accepted for recording. A minimum of three acceptable FVC maneuvers were performed. Only the best test was accepted. The spirometric parameters derived by the FVC maneuver was computed as below:

- Forced vital capacity (FVC)
- Forced expiratory flow in the first second (FEV1)
- FEV1/FVC ratio
- Forced expiratory flow FEF (25%-75%).

Following interpretations were derived from these parameters and Flow-Volume Lop (FV Loop)

**Obstructive ventilatory defect**

A disproptionate reduction of maximal airflow from the lung of the maximal volume displaced from the lung and expressed as:
FEV/FVC ratio of less than 70%. The severity of the obstructive ventilation defect was determined by the reduction in FEV1 predicted. The airway obstruction was further categorised as mild, moderate and severe when the observed FEV1 is 60-80%, 40-60% and less than 40% respectively.
F/V loop showed concave upper curve.

**Restrictive ventilatory defect**

- Present when FVC is reduced <79% of predicted. The restrictive ventilatory disease was further categorised as mild, moderate and severe when the observed FVC is 60-79%, 40-60% and less than 40% respectively.
- With a normal FEV1/FVC when a restrictive ventilatory defect is associated with low FVC and TLC.
- Since the airways are normal, the flow volume loop have a normal shape: the expiratory curve descended in a straight line from the PEF to the X-axis. The size of the FV Loop must be small.

**Small airway defect**

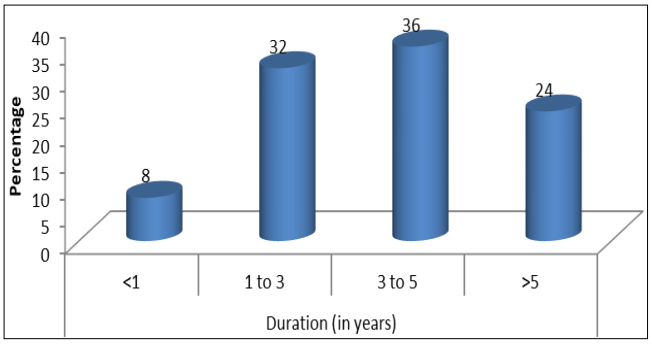
A reduction in the mid expiratory flow without reduction expressed as reduced FEF (25-75%) of predicted.

**Statistical analysis**

Data so collected was tabulated in an excel sheet, under the guidance of statistician. The means and standard deviations of the measurements per group were used for statistical analysis (SPSS 22.00 for windows; SPSS inc, Chicago, USA). Difference between two groups was determined using student t-test as well as chi square test and the level of significance was set at $p < 0.05$.

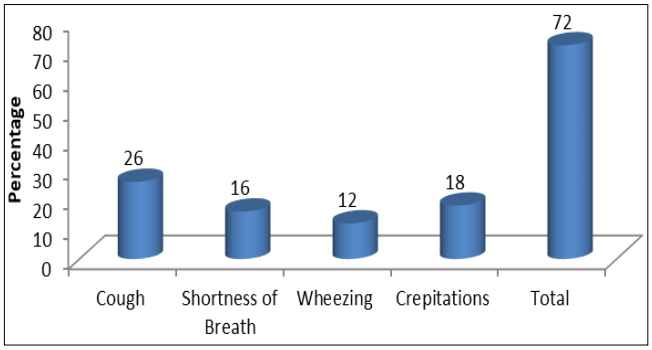
**Results**

Out of 50 subjects, 37 (74%) were female and 13 (26%) were males (table 1). 6%, 22%, 42% and 30% of the subjects were having age between 18-30, 30-45, 45-60 and >60 years respectively. Duration of RA *viz.* <1, 1 to 3, 3 to 5 and >5 years was reported among 8%, 32%, 36% and 24% of the subjects respectively (graph 1).




**Graph 1:** Duration of disease (in years) among the study subjects

Cough, shortness of breath, wheezing and crepitations was reported among 26%, 16%, 12% and 18% of the subjects respectively (graph 2).




**Graph 2:** Symptoms and signs among the study subjects

Mean±SD FVC, FEV 1, FEV1/FVC, FEF 50% and FEF 25-75% was 87.8±8.07, 83.92±8.12, 97.08±12.18, 77.58±9.04 and 80.11±15.43 respectively. Normal and abnormal PFT was revealed among 28 (56%) and 22 (44%) subject's respectively. Abnormal PFT were further divided into obstructive, restrictive and mixed type. Obstructive, restrictive and mixed type was found among 24%, 18% and 2% of the subjects respectively (table 1).

**Table 1:** Prevalence of PFTs abnormalities among the study subjects

| PFTs | N | % |
|---|---|---|
| Normal | 28 | 56 |
| Abnormal | 22 | 44 |
| Obstructive | 12 | 24 |
| Restrictive | 9 | 18 |
| Mixed | 1 | 2 |

Abnormal PFTs was found among 40.54% and 53.85% of the female and male respectively. Mean age was comparatively more among subjects with abnormal PFT (53.98 years) as compared to subjects with normal PFT (47.19 years) with statistically significant difference as p<0.05 (table 2).

**Table 2:** Association of PFTs abnormalities among the study subjects W.R.T. gender

| PFTs | Female | | Male | | Chi Square | P value |
|---|---|---|---|---|---|---|
| | N | % | N | % | | |
| Normal | 22 | 59.46 | 6 | 46.15 | 3.41 | 0.12 |
| Abnormal | 15 | 40.54 | 7 | 53.85 | | |
| Obstructive | 9 | 24.32 | 3 | 23.08 | | |
| Restrictive | 5 | 13.51 | 4 | 30.77 | | |
| Mixed | 1 | 2.71 | 0 | 0 | | |
| PFTs | Age (in years) | | | | t test | P value |
| | Mean | | SD | | | |
| Normal | 47.19 | | 10.81 | | 3.89 | 0.021* |
| Abnormal | 53.98 | | 12.63 | | | |

***:** statistically significant

Mean duration of disease (in years) was comparatively more among subjects with abnormal PFT (4.48) as compared to subjects with normal PFT (3.19 years) with statistically significant difference as p<0.05. Abnormal PFTs was found among 55.56% and 14.29% of subjects with and without symptoms & signs. When PFTs was compared statistically according to symptoms and signs, it was found to be statistically significant as p<0.05 (table 3).

**Table 3:** Association of PFTs abnormalities among the study subjects w.r.t. duration of disease (in years)

| PFTs | Duration of disease (in years) | | | | t test | P value |
|---|---|---|---|---|---|---|
| | Mean | | SD | | | |
| Normal | 3.19 | | 1.73 | | 3.32 | 0.037* |
| Abnormal | 4.48 | | 1.56 | | | |
| PFTs | Symptoms and Signs | | | | Chi Square | P value |
| | Yes (N=36) | | No (N=14) | | | |
| | N | % | N | % | | |
| Normal | 16 | 44.44 | 12 | 85.71 | 13.82 | 0.004* |
| Abnormal | 20 | 55.56 | 2 | 14.29 | | |

***:** statistically significant

## Discussion

Lung disease in RA occurs as: an extra-articular manifestation of the disease; related to the drug therapy for RA; or due to co morbid conditions. Pulmonary parenchyma, airways, pleura and vasculature all can be involved in RA; either in the forms of infection or inflammation [10]. However, there are only few studies on this issue in Indian subcontinent especially from the western India. Hence the present observational study was conducted in the department of Medicine at Chattrapati Shivaji Subharti Hospital from February 2019 to January 2021 among 50 subjects having active rheumatoid disease (RA).

In this study, out of 50 subjects, 37 (74%) were female and 13 (26%) were males. Similar female dominancy was reported by Sandipan Banik *et al* [11] and Biomdo I *et al* [12]. Maximum subjects were from the age group of 45-60 years (42%) followed by >60 years (30%) in our study. Sandipan Banik *et al*[11] in their study found that mean age was 45.22 years (median 46.13 years) with age range between 25-66 years. In a study by Biomdo I *et al* [12], ages ranged from 14 to 65 years with a mean of 47±13years.

Cough, shortness of breath, wheezing and crepitations was reported among 26%, 16%, 12% and 18% of the subjects respectively in the present study. The prevalence of symptoms was lesser than the findings of another similar study carried out by Wilsher M *et al* [13], from New Zealand revealing that 30% patients with RA reported respiratory symptoms: cough (11%), dyspnoea (11%) and wheeze (8%). However, a Malaysian study by Mohd. Nur *et al* [14], revealed 48% patients of RA with pulmonary symptoms, among them 20% having cough, 18% having dyspnoea and about 11% wheezing. These findings are in agreement with ours.

Normal and abnormal PFT was revealed among 28 (56%) and 22 (44%) subject's respectively. Abnormal PFT were further divided into obstructive, restrictive and mixed type. Obstructive, restrictive and mixed type was found among 24%, 18% and 2% of the subjects respectively. Similarly Biomdo I *et al* [12] in their study revealed that the overall six month prevalence of pulmonary function abnormalities was 38.5% as measured by spirometry. The predominant ventilatory defect was obstructive pattern at 20.4%, followed by restrictive pattern at 16.8% and least common being a mixed picture at 1.2%. When evaluation of severity was done majority of these patients had mild defects (83.3% in the obstructive pattern and 60.7% in the restrictive). In France, Thierry *et al* [15] found an obstructive pattern of lung changes in 18% of RA patients using spirometry. Abnormal PFTs was found among 40.54% and 53.85% of the female and male respectively. When PFTs was compared statistically among male and female, it was found to be statistically insignificant as p>0.05. Mean age was comparatively more among subjects with abnormal PFT (53.98 years) as compared to subjects with normal PFT (47.19 years) with statistically significant difference as p<0.05. Mean duration of disease (in years) was comparatively more among subjects with abnormal PFT (4.48) as compared to subjects with normal PFT (3.19 years) with statistically significant difference as p<0.05. These findings are comparable to Amir *et al*[16], who observed that pulmonary abnormalities by PFT or HRCT were associated with older age and the RA clinical features that proved to associate with pulmonary involvement were joint tenderness index, duration of morning stiffness, and clinical disease severity. In France, Thierry *et al* [15] found no significant difference in the proportion of airflow obstruction among smokers and non smokers suggesting a minor role of tobacco smoke in such manifestations. Respiratory symptoms were statistically more significant in patients with

abnormal PFTs.

In Sandipan Banik *et al* [11] study, there is an association between disease duration with spirometric changes (p=0.001) and obstructive spirometric changes with smoking (p=0.048). Development of pulmonary interstitial change had a correlation with age (p=0.006) and duration of disease. A North American study carried out by Fischer A *et al*[17], found a significant correlation with advanced age and duration of disease to the development of ILD, thus corroborating our finding. Assayag D *et al*[18], has pointed out the importance of age and smoking habit as the risk factors for developing RA-ILD. The compounding effect of smoking for RA-ILD is also suggested by Klareskeg L *et al* [19].

**Limitations**

The study had the following limitations;

1. PFTs are not the gold standard for detecting respiratory disease. We chose to use PFTs as our marker of lung disease in this analysis as they provide a common and low-risk diagnostic modality that often precedes radiographic evaluation in clinical practice.
2. Recruitment of patients from a university hospital rheumatology department could introduce some bias through selection of patients with somewhat more severe articular involvement than that in the overall RA population.

Pulmonary involvement is an important part of the systemic affection of RA. The role of surveillance for lung disease in patients with RA is clear and necessary. Rheumatologists and internists should routinely screen patients for early detection and intervention. Respiratory symptoms, older age and ongoing disease activity can identify patients in greatest need of further pulmonary workup.

**Conclusion**

We observed a high prevalence of pulmonary function abnormalities as measured by spirometry in this RA population. The commonest ventilator defect pattern was obstructive followed by restrictive. There was an increased frequency of reported respiratory symptoms in RA patients with abnormal tests. Rheumatoid disease activity, older age and respiratory symptoms were identified as predictors of lung impairment as determined by spirometry.

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