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Original Article

PULMONARY FUNCTION IN RHEUMATOID ARTHRITS: A CROSS-SECTIONAL STUDY

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ABSTRACT

Objective: Rheumatoid arthritis (RA) is an autoimmune disease with many extraarticular manifestations. Pulmonary involvement is seen in 60-80% cases with and without symptoms. This research studies the pattern of PFT (Pulmonary Function Test) in RA and find the correlation between PFT and Disease activity. Secondary objectives were to evaluate the effect of use of Methotrexate (MTx) on disease activity and PFT.

Methods: An outpatient-based descriptive cross-sectional study was conducted in General Medicine department at a tertiary centre among 100 eligible patients. Disease activity score was recorded using DAS-28 (Disease Activity Score-28) and CDAI (Clinical Disease Activity Index). Patients underwent PFT by Spirometry thereafter.

Results: 45 % patients had restrictive pattern and 55% had normal PFT. None had an obstructive pattern. The mean FVC (Forced Vital Capacity), FEV1 (Forced Expiratory Volume in the first second), FEV1/FVC ratio, PEFR (Peak Expiratory Flow Rate) and FEF 25-75% (Forced mid expiratory flow) were 78.83±14.37, 79.24±16.96, 103.56±11.03, 71.73±22.39 and 76.56±23.72 respectively. Both FVC and FEV1 were found to be significantly associated with age, disease duration, CDAI score, MTx dose and duration ($P<0.05$). Age, ESR(erythrocyte sedimentation rate) and MTx dose were significantly associated with FEV1/FVC ratio ($P<0.05$). Age, duration of disease, ESR. MTx dose and duration were significantly associated with PEFR ($P<0.05$). Lastly age, CDAI score, MTx dose and duration were significantly associated with FEF 25-75% ($P<0.05$).

Conclusion: Restrictive pattern (45%) was the most common defect on PFT among RA patients. Severity of lung disease depends on age, MTx dose, disease activity (ESR, CDAI), duration of disease and MTx duration.

Keywords: Pulmonary function, Spirometry, Rheumatoid arthritis, Extraarticular manifestations, Disease activity, Methotrexate

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INTRODUCTION

Rheumatoid arthritis (RA) is a common systemic inflammatory autoimmune disease with a variety of extra-articular manifestations. Extra-articular manifestations of RA can emerge during the course of disease and even before the onset of arthritis. Extra-articular pulmonary manifestations range from 60–80% in RA patients, many of whom are asymptomatic. Pleuro-pulmonary involvement may occur in the form of interstitial lung diseases (ILD), pleural diseases, pulmonary nodule, airway obstruction and pulmonary vascular disease apart from drug-induced lung injury [1-3]. Rheumatoid lung is also a leading cause of mortality, accounting for approximately 10–20% of all RA-related deaths most of which are attributed to ILD [1-6].

Pulmonary function test (PFT) is widely used to provide objective measure of lung function for detecting and quantifying pulmonary impairment in patients with cardiopulmonary disease and monitoring response to therapy [7]. Spirometry is the most frequently used measure of lung function and is a measure of volume against time. It is a widely available, easy to perform and cost-effective technique [7, 8].

The early recognition of abnormal PFT may be used as early marker of pulmonary involvement secondary to RA and helps in limiting the morbidity and mortality related to rheumatoid lung [7].

Earlier studies have evaluated PFT in RA. Both restrictive and obstructive patterns are seen with RA [9]. However, the results of the relationship of disease activity scores and PFT findings are not consistent [10, 11]. With this background, the present study was planned to find the pattern of PFT and their relation with disease activity in RA.

MATERIALS AND METHODS

This is an outpatient-based descriptive cross-sectional study conducted at the General Medicine department of a Medical College in North India. Total 100 eligible patients with RA who attended the outpatient clinic of the department were enrolled into the study. All patients between ages of 18-60 y who were diagnosed with RA as per ACR-EULAR criteria and provided informed consent were included in the study. Patients with a history of smoking, presence of prior pulmonary disease, current respiratory complaints, known case of other collagen vascular diseases or history of pulmonary infection in the last 3 mo were excluded. Informed consent was obtained from each subject entering the study. The study was approved by the Institutional Ethics Committee.

Baseline clinical characteristics, including demographic, clinical and biochemical data were collected. For each enrolled subject, detailed history, including personal and family medical histories were obtained. All the subjects underwent clinical examination comprising of general physical examination, assessment of vital parameters and systemic examination. Patients were assessed for respiratory symptoms and activity score was recorded using DAS-28 (Disease Activity Score-28) and CDAI (Clinical Disease Activity Index) [9]. Blood samples were taken for measurement of ESR and other parameters. All parameters required for assessment of Disease activity score were taken into account. DAS28 and CDAI scores were computed accordingly.

Patients underwent PFT by Spirometry thereafter. FVC, FEV1, FEV1/FVC, PEFR and FEF 25-75% were collected and recorded for each patient. Obstructive pattern was defined as FEV1/FVC<70 and restrictive pattern was defined as FEV1/FVC>70 and FVC%<80%.

Sample size

A sample size of 100 RA patients was calculated as previous studies show 52.2% of patients with RA shows altered PFT for 80% power, 0.05 α error and 10% absolute error [10].

Statistical analysis

Data were analysed and statistically evaluated using Statistical Package for Social sciences (SPSS)-PC-20 software (version 20, SPSS,

Inc, Chicago, IL, USA). Data were presented as mean and standard deviation (SD) for continuous variables and as frequencies for categorical variables. Comparisons were made for means of two sample using Student's t-test for continuous variables and by chi-square analysis for categorical variables. Multiple linear regression analyses were performed to find the relation of PFT with disease activity scores and other parameters depicting RA. All statistical analyses were performed, taking level of significance at p-value<0.05.

RESULTS

Mean age of the subjects was 43.6 y and the majority of them belonged to age of 41-50 y and were females (79%). Mean disease duration was 71.8±62.5 mo. Mean MTx dose was 16.4±5.5 mg/week and mean duration of MTx use was 58.4±28.7 mo. The disease activity scores i. eESR, DAS-28 and CDAI were 46.6±18.5 mm in 1st h, 5.17±0.82 and 22.8±7.3, respectively (table 1).

Table 1: Baseline characteristics of the study population

Variable	mean±SD or n (%)
Age (years)	43.6±9.4
Female	79 (79%)
Disease Duration (months)	71.8±62.5
Methotrexate Dose (mg/week)	16.4±5.5
Methotrexate use Duration (months)	58.4±28.7
ESR (mm in 1sthour)	46.6±18.5
Disease Activity-DAS-28	5.17±0.82
Disease Activity-CDAI	22.8±7.3

ESR (Erythrocyte Sedimentation Rate), DAS-28(Disease Activity Score-28) and CDAI (Clinical Disease Activity Index), On PFT none of the patients showed obstructive pattern (FEV1/FVC<70%), 45 % had restrictive pattern while other 55% were normal. The mean FVC, FEV1, FEV1/FVC ratio, PEFR and FEF 25-75% were 78.83±14.37, 79.24±16.96, 103.56±11.03, 71.73±22.39 and 76.56±23.72 respectively (table 2).

Table 2: Pulmonary function test of the study population

Normal Pulmonary Function (>80%)	55 (55% of study population)
Mild Restriction (70-80%)	13 (13% of study population)
Moderate Restriction (50-70%)	26 (26% of study population)
Severe Restriction (<50%)	6 (6% of study population)
FVC %	78.83±14.37
FEV1%	79.24±16.96
FEV1/FVC ratio	103.56±11.03
PEFR%	71.73±22.39
FEF 25-75%	76.56±23.72

FVC (Forced Vital Capacity), FEV1(Forced Expiratory Volume in the first second), PEFR (Peak Expiratory Flow Rate and FEF 25-75%(Forced mid expiratory flow), Both FVC and FEV1 was found to be significantly associated with age, disease duration, CDAI score, MTx dose and duration (P<0.05). Age, ESR and MTx dose were significantly associated with FEV1/FVC ratio (P<0.05). Age, duration of disease, ESR, MTx dose and MTx duration were significantly associated with PEFR (P<0.05). Lastly age, CDAI score, MTx dose and MTx duration were significantly associated with FEF 25-75% (P<0.05) (table 3).

Table 3: Relation of pulmonary function test parameters with studies variables

Duration	FVC	FEV1	FEV1/FVC	PEFR	FEF 25-75%
Age	-0.75 (-1.03,-0.47)	-1.11 (-1.41,-0.81)	-0.64 (-0.85,-0.43)	-1.14 (-1.58,-0.70)	-1.31 (-1.77,-0.86)
	<0.05	<0.05	<0.05	<0.05	<0.05
Duration of disease	-0.14 (-0.18,-0.11)	-0.15 (-0.20,-0.11)	-0.02 (-0.06, 0.01)	-0.14 (-0.21,-0.08)	-1.82 (-13.43, 9.79)
	<0.05	<0.05	>0.05	<0.05	>0.05
ESR	-0.09 (-2.44,-0.06)	-0.17 (-0.35, 0.01)	-0.12 (-0.24,-0.01)	-0.25 (-0.49,-0.01)	-0.25 (-0.50, 0.01)
	>0.05	>0.05	<0.05	<0.05	>0.05
DAS-28	-2.88 (-6.33, 0.58)	-3.27 (-7.36, 0.81)	-1.82 (-4.49, 0.84)	-5.20 (-10.56, 0.15)	-4.92 (-10.63, 0.78)
	>0.05	>0.05	>0.05	>0.05	>0.05
CDAI	-0.48 (-0.86,-0.09)	-0.57 (-1.02,-0.12)	-0.28 (-0.58, 0.01)	-0.56 (-1.16, 0.05)	-0.65 (-1.29,-0.01)
	<0.05	<0.05	>0.05	>0.05	<0.05
Methotrexate dose	-1.73 (-2.12,-1.34)	-1.85 (-2.35,-1.36)	-0.42 (-0.82,-0.03)	-1.22 (-1.99,-0.44)	-1.61 (-2.42,-0.81)
	<0.05	<0.05	0.05	<0.05	<0.05
Methotrexate duration	-0.15 (-0.19,-0.11)	-0.15 (-0.20,-0.10)	-0.01 (-0.05, 0.02)	-0.15 (-0.22,-0.08)	-0.15 (-0.23,-0.08)
	<0.05	<0.05	>0.05	<0.05	<0.05

FVC: Forced Vital Capacity; FEV1: Forced Expiratory Volume in the first second; PEFR: Peak Expiratory Flow Rate; FEF 25-75%: Forced mid expiratory flow

(Regression coefficients with 95% confidence intervals and P value)

DISCUSSION

In this study, we found that restrictive lung disease is the most common ventilatory abnormality seen in RA patients. We also found that only age and MTx dose were significantly associated with all ventilatory parameters (FEV1, FVC, FEV1/FVC, PEFR and FEF 25-75%). Similarly, duration of disease and MTx duration was associated with FVC, FEV1 and PEFR. MTx duration was further associated with FEF 25-75% too. ESR was associated with FVC, FEV1/FVC and PEFR while CDAI score was associated with FVC, FEV1 and FEF 25-75%.

In our study, 45% of the patients had abnormal PFT. Prior studies have investigated the relationship between RA and PFT parameters and have reported a prevalence of 28-63% of abnormal PFT among

RA patients [11-13]. In our study, we found only restrictive pattern and no obstructive pattern. A study among subjects from the UK Biobank found that RA patients were more likely to have abnormal spirometry as compared to controls [9]. While the study found both restrictive and obstructive pattern in RA patients, they reported restrictive pattern to be more likely in RA patients [9]. Similarly, other studies found the predominance of restrictive ventilatory defect in RA patients [12, 13]. However, a study has also reported predominant obstructive pattern in RA patients [11]. The most common form of RA-associated lung disease is ILD followed by pleural disease [3, 14]. Both interstitial and pleural diseases are associated with restrictive patterns on spirometry [15]. Hence, it explains the predominant restrictive pattern seen in RA. As we excluded smokers in our studies, it may be one of the reasons for absence of obstructive pattern seen in our study.

Advanced age was found to be consistently associated with poor lung function parameters. Longer duration of disease was also associated with poor FVC, FEV1 and PEFR.

A retrospective cohort study of 923 patients investigated the factors affecting ILD development and progression [16]. They reported that advanced age and shorter duration of disease were significantly associated with RA-ILD [16]. However, a nested case-control study of 84 RA-ILD cases and 233 controls reported no significant association of age and disease duration with RA-ILD [17].

Disease activity was measured by ESR, DAS-28 score and CDAI scores. While DAS-28 score did not show any significant association, both ESR and CDAI score showed variable inverse association with different parameters. ESR and CDAI were both associated with FVC while only ESR was associated with FEV1/FVC and PEFR. CDAI was associated with FEV1 and FEF25-75%. Earlier studies in RA patients have shown that higher disease activity is associated with increased risk of developing lung disease [12, 16-19]. A cross-sectional study of 40 RA patients found inverse relationship of FEV1 and FEV1/FVC with ESR and articular index [12]. Similarly, another study which measured disease activity using CDAI found a positive correlation of RA disease activity and ground-glass appearance in RA-ILD patients [19].

MTx dose was also inversely associated with all parameters of PFT while MTx duration was inversely associated with all, except FEV1/FVC. A meta-analysis of 22 randomized controlled trials concluded that MTx use in RA patients is associated with small but significant increase in the risk of lung disease [20]. However, another recent research which was a case-control study found inverse relationship between MTx use and RA-ILD risk. They found that RA patients using MTx developed ILD later as compared to who never used [21].

LIMITATION

The current study was a cross-sectional single-centre study. A multicentric study with larger sample size is required for results to be widely generalised.

CONCLUSION

Restrictive pattern (45%) was the most common defect on PFT in RA patients. The severity of lung disease is dependent on many RA-related factors, the most consistent being age and MTx dose. Other factors such as disease activity (ESR, CDAI), duration of disease and MTx duration are variably associated with different parameters of lung function.

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AUTHORS CONTRIBUTIONS

All authors have contributed equally

CONFLICT OF INTERESTS

No conflict of interests to disclose

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