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RESEARCH ARTICLE

Role of spirometry in the evaluation of lung involvement in non-smoker rheumatoid arthritis patients

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ABSTRACT

Background: Interstitial lung disease (ILD) is a common and serious complication of rheumatoid arthritis (RA). Risk of obstructive lung disease is also higher in adult RA. **Aim and Objective:** This study aimed at evaluating the frequency of obstructive and restrictive pattern of pulmonary impairment in non-smoking Indian RA patients. **Materials and Methods:** A cross-sectional study involving adult RA patients was carried out for 1½ years. The study parameters included tender joint counts, swollen joint counts, erythrocyte sedimentation rate, C-reactive protein, disease activity score 28, clinical disease activity index, forced vital capacity (FVC), forced expiratory volume in 1 s (FEV1), FEV1/FVC, forced expiratory flow between 25 and 75% of vital capacity, and peak expiratory flow rate (PEFR). Fisher's exact test was used to compare the data. **Results:** Out of 203 patients included in the study, 177 were female. Spirometry was normal in 63% of female and 42% of male. Overall frequency of restrictive, obstructive, and mixed pattern of spirometry was 33.3%, 0.6%, and 2.8% in females, respectively, in contrast to 42.3%, 11.5%, and 3.8% in males. Moderate to very severe degree of restrictive pattern of impairment was noted in 9.6% of female and 15.4% of male patients. Decreased FEV1/FVC was more frequent in male patients compared to female (15.4% vs. 3.4%). PEFR was within normal limit in about 86% of patients. **Conclusion:** One-third of female and about two-fifth of male patients had restrictive pattern of spirometry with most being mild in nature. Obstructive disease was uncommon in female in contrast to male.

KEY WORDS: Rheumatoid Arthritis; Interstitial Lung Disease; Non-Smokers

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease affecting about 0.5–2% of the population worldwide. Although persistent joint inflammation and damage dominate the clinical picture, extra-articular manifestations are common and can occur in up to 40% of patients during the course of disease.[1] Pulmonary involvement is a common extra-articular manifestation and may affect parenchyma, pleura, airway, and vasculature.[2] In 10–20% of patients, respiratory symptoms may occur before the articular inflammation.[3] Interstitial lung disease (ILD) is the most common form of lung involvement and associated with high morbidity and mortality.[4] It has been described in 58% of recently diagnosed RA patients in one study of which three-fourth were clinically silent.[5] Obstructive lung disease has also been found to be more common in RA.[6] Smoking is an important risk factor for both ILD and obstructive lung disease.

Ethnic variation in the extra-articular manifestations of RA has been described earlier.[7] Literatures on pulmonary

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function in non-smoker RA in India are scarce to the best of authors' knowledge.[8,9] Spirometer, an inexpensive and easily available screening tool, can be utilized not only in diagnosing obstructive disease but also in excluding restrictive disease. This study was carried out to determine the frequency of obstructive and restrictive pattern of spirometry in non-smoker adult RA in Indian population.

MATERIALS AND METHODS

This was a cross-sectional study that lasted for 1½ years and involved adult RA patients attending in a tertiary care center in East India. Permission from the Institutional Ethics Committee was sought at the outset and the study commenced only after due approval. Patients were provided information brochure in their vernacular to clarify their disease- and study-related queries. Informed consent was obtained from all those who agreed to participate in the study. A pre-printed case record format was used for all subjects to fill up the required data.

Previously diagnosed (based on revised 1987 ACR classification criteria) adult RA patients of 18 years or more attending outpatients department of rheumatology with no history of smoking in the past 5 years were randomly selected for the study. Severely ill and incapacitated patients, those with heart failure or renal failure or pre-existing lung disease or with history of surgery on head and neck, were excluded from the study. Blood samples were analyzed for complete blood counts, rheumatoid factor, antibodies to cyclic citrullinated peptides, C-reactive protein, and erythrocyte sedimentation rate. Disease activity was measured by DAS 28 (disease activity score) and CDAI (clinical disease activity index).[10,11]

The subjects were told to come after a light breakfast in the morning. A digital spirometer "Spirowin" (Genesis Medical Systems Pvt. Ltd.) was used for spirometry. The study parameters included forced vital capacity (FVC), forced expiratory volume in 1 s (FEV1), FEV1/FVC ratio, forced expiratory flow between 25 and 75% of vital capacity ($FEF_{25–75\%}$), and peak expiratory flow rate (PEFR). Acceptability and repeatability criteria of spirometry as suggested by American Thoracic Society (ATS) were stringently followed.[12] Patients with inadequate effort had to undergo repeat spirometry in next visit few weeks later. Spirometric parameters were considered to be decreased if they were below lower limit of normal (LLN) as per ATS criteria.[13] Restrictive pattern was defined as FVC below LLN with FEV1/FVC equal to or above LLN. FEV1/FVC below LLN with FVC equal to or above LLN defined the obstructive pattern. Both FVC and FEV1/FVC below LLN were defined as mixed pattern.[14] Abnormal spirometry was graded on the basis of FEV1 percentage of predicted. FEV1 percentage of predicted ≥70, 60–69, 50–59, 35–49, and <35 was graded as mild, moderate, moderately severe, severe, and very severe impairment.[13]

Statistical analysis was performed using software, GraphPad Prism (Version 5, 2007). Data were compared by Fisher's exact test. $P < 0.05$ was considered statistically significant.

RESULTS

Initially, 226 RA patients were enrolled in the study, out of which 23 patients had to be excluded as per exclusion criteria. Of these 23 patients, 2 were severely ill, 2 had heart failure, 2 patients were suffering from chronic renal failure, 2 patients were diagnosed later as Sjogren's syndrome, and the rest were excluded from the study because their spirometry did not meet acceptability and repeatability criteria. The data of remaining 203 patients were taken for analysis.

The baseline, disease activity, and pulmonary parameters of 203 RA patients, 177 of which were female, are shown in Table 1. Mean age was 44.6 years and mean disease duration was 7.1 years. Fifty-six patients were overweight and 16 were obese. None of the patients had any respiratory distress at rest.

The frequency and severity of restrictive, obstructive, and mixed pattern of spirometry are presented in Table 2. Overall, restrictive, obstructive, and mixed pattern was noted in 59 (33.3%), 1 (0.6%), and 5 (2.8%) female patients, respectively, in contrast to 11 (42.3%), 3 (11.5%), and 1 (3.8%) male. Severity of restrictive pattern was mild to moderate in 53 out of 59 females and 9 out of 11 male subjects. Obstructive pattern was mild to moderate and mixed pattern was moderate to severe in all of those affected. Figures 1 and 2 depict frequency of respiratory parameters in terms of percent predicted value in female and male RA, respectively. FVC was more than >80% of predicted value in 103 (58.2%) female and 12 (46.2%) male patients. PEFR was >80% of predicted in 153 (86.4%) female and 22 (84.6%) male patients.

Table 3 compares frequency of decreased pulmonary parameters of female and male patients. They did not differ significantly in frequency of decreased FVC, FEV1, $FEF_{25–75\%}$, and PEFR. However, number of decreased FEV1/FVC significantly differed between them.

DISCUSSION

Overall 63% of female and 42% of male had normal spirometry. Restrictive pattern was found in one-third of female and 42% of male subjects. About 9.6% of female and 15.4% of male patients exhibited moderate to very severe degree of restrictive impairment. A higher frequency of decreased FEV1/FVC was noted in male patients compared to female (15.4% vs. 3.4%). PEFR was within normal limit in around 86% of patients.

Table 1: Descriptive statistics of baseline, disease activity, and pulmonary parameters of patients with rheumatoid arthritis (***n***=203)

Parameter	Minimum	25th percentile	Median	75th percentile	Maximum	Mean	Standard deviation (SD)
Age (years)	21	37	45	52	78	44.6	9.983
Height (cm)	140	148	152	157	176	153.2	6.781
Weight (kg)	33.9	48	55	62.2	88	55.85	10.48
Duration (years)	0.5	2.5	5	10	40	7.145	6.407
TJC	0	2	4	8	28	5.419	5.549
SJC	0	0	1	2	25	1.970	3.198
VAS (0–10)	0	3	5	7.5	10	5.180	2.701
ESR (mm)	6	20	31.5	45	100	36.45	22.12
CRP(mg/L)	0.03	0.6	2.99	10.13	97.8	9.980	17.33
CDAI	0.5	8	14	21	71	16.42	11.48
DAS28	1.934	3.080	3.801	4.471	7.639	3.820	1.039
FVC (L)	0.817	1.752	2.068	2.357	3.780	2.086	0.504
FEV1 (L)	0.619	1.449	1.765	2.043	3.292	1.768	0.455
FEV1/FVC (%)	63.46	81.00	85.31	89.62	98.61	84.74	7.629
FEF25–75% (L/s)	0.319	1.451	1.964	2.454	4.480	2.006	0.771
PEFR (L/s)	0.966	2.897	3.687	4.478	7.638	3.774	1.260

TJC: Tender joint count, SJC: Swollen joint count, VAS: Visual analog scale, ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein, CDAI: Clinical disease activity index, DAS: Disease activity score, FVC: Forced vital capacity, FEV1: Forced expiratory volume in 1 s, $FEF_{25–75\%}$: Forced expiratory flow between 25 and 75% of vital capacity, PEFR: Peak expiratory flow rate

Table 2: Gradation of severity abnormal spirometry (on the basis of FEV1 percentage predicted) in patients with RA

Spirometric pattern	Gender	Mild (≥70%)	Moderate (60–69%)	Moderately severe (50–59%)	Severe (35–49%)	Very severe (<35%)	Total
Restrictive	Female	42 (23.7)	11 (6.2)	4 (2.3)	2 (1.1)	0 (0)	59 (33.3)
	Male	7 (26.9)	2 (7.7)	0 (0)	1 (3.8)	1 (3.8)	11 (42.3)
Obstructive	Female	0 (0)	1 (0.6)	0 (0)	0 (0)	0 (0)	1 (0.6)
	Male	3 (11.5)	0 (0)	0 (0)	0 (0)	0 (0)	3 (11.5)
Mixed	Female	0 (0)	2 (1.1)	2 (1.1)	1 (0.6)	0 (0)	5 (2.8)
	Male	0 (0)	0 (0)	1 (3.8)	0 (0)	0 (0)	1 (3.8)

Values are frequency (%). FEV1: Forced expiratory volume in 1 s

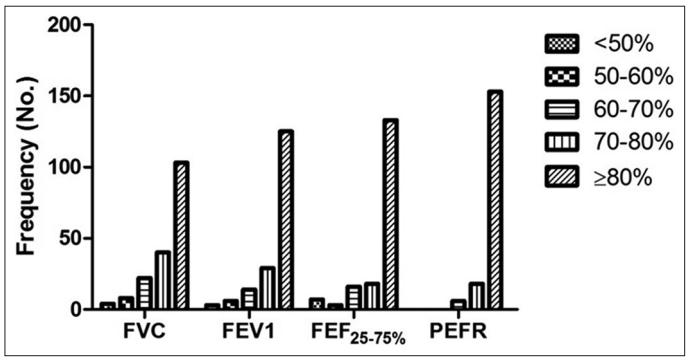

Figure 1: Frequency of spirometric parameters in terms of percent predicted value in female rheumatoid arthritis

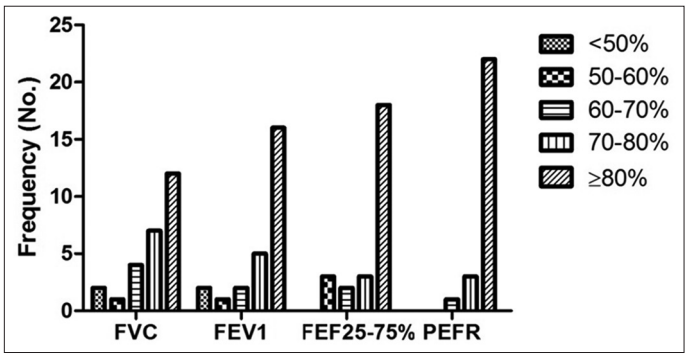

Figure 2: Frequency of spirometric parameters in terms of percent predicted value in male rheumatoid arthritis

RA is 3 times more common in female.[15] A large number of male patients were smokers and did not fulfill the inclusion criteria resulting in high female-to-male ratio (7:1) in this study. RA, a systemic inflammatory disease, is characterized by several extra-articular manifestations including rheumatoid nodules, vasculitis, and pleura pulmonary, neurologic, digestive, cardiovascular, cutaneous, hematologic, and ocular complications.[16] ILD is a common pulmonary manifestation having significant prognostic implication. The reported prevalence of RA-ILD varies with population studied and

Table 3: Frequency of decreased (below lower limit of normal) spirometric parameters in patients with RA

Parameters	Female (*n*=177)	Male (*n*=26)	Total (*n*=203)	*p* value
Decreased FVC	64 (36.2)	12 (46.2)	76 (37.4)	0.3867
Decreased FEV1	36 (20.3)	8 (30.8)	44 (21.7)	0.3058
Decreased FEV1/FVC	6 (3.4)	4 (15.4)	10 (4.9)	0.0262
Decreased $FEF_{25–75\%}$	10 (5.6)	3 (11.5)	13 (6.4)	0.2225
Decreased PEFR	25 (14.1)	4 (15.4)	29 (14.3)	0.7712

Values are frequency (%); *P* values obtained by Fisher's exact test for individual parameters, FVC: Forced vital capacity, FEV1: Forced expiratory volume in 1 s, $FEF_{25–75\%}$,: Forced expiratory flow between 25 and 75% of vital capacity, PEFR: Peak expiratory flow rate

investigative methods used for diagnosis.[17-19] Abnormal high-resolution computed tomography (HRCT) has been found in up to one-third of asymptomatic patients in some studies.[20,21] Restrictive type of spirometry was found in 29–33% of patients in earlier studies.[8,9] This is in agreement with our findings where overall 34% had restrictive pattern. Another study, in contrast, revealed restrictive pattern in 64% of patients.[22] A higher risk of obstructive lung disease has also been noted in RA in a recent population-based longitudinal study.[6,23] About 8–12% of patients have been reported to have obstructive pattern in spirometry.[8,9,22] This is in conformity with our result on frequency of obstructive disease in male. However, this contrasts with the finding on female where obstructive disease was uncommon. Higher frequency of obstructive disease in male in this study may be due to their history of smoking. Since smoking is an important risk factor for both RA and chronic obstructive pulmonary disease, it may have a confounding effect on the observed association between RA and obstructive lung disease.[24]

There are only few studies on pulmonary involvement in RA in India and almost all of them lack sufficient sample size.[8,9] Moreover, studies on non-smoker RA are scarce. Strength of our study lies in focused evaluation of pulmonary function in a larger group of non-smoker RA. However, small number of non-smoking males is a limitation. It would have been better if spirometric findings were corroborated with diffusing capacity of the lung for CO (DLCO) and HRCT which could not be afforded by all due to financial reasons. Restrictive pattern of spirometry warrants further investigation to confirm the diagnosis of ILD. In developing countries like India, periodic HRCT is not practicable, especially for poor patients. Spirometry, if performed serially, can play a key role not only in early prediction of restrictive disease but also in evaluating the disease course in those with ILD. Even though spirometry is not sufficient for diagnosis, it can be used for excluding restrictive lung disease.

CONCLUSION

One-third of female and about two-fifth of male patients had restrictive pattern of spirometry. Obstructive disease was infrequent in female in contrast to male. Periodic evaluation through spirometry is suggested for all patients in view of above findings. A decline in the lung volumes in serial spirometry should alert the clinician about suspected ILD that requires to be confirmed by HRCT and DLCO. The progression of ILD can also be easily monitored by spirometry and direct the physician for appropriate actions to halt the progress of disease.

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