

A COMPARATIVE STUDY OF PULMONARY INVOLVEMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS

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ABSTRACT

BACKGROUND

Rheumatoid arthritis (RA) is a chronic systemic inflammatory disorder that affects many organs but principally affects joints. Pulmonary manifestations in RA are varied as the pleura, lung, parenchyma, airways and pulmonary vasculature can be involved. Aims- To measure the alterations of lung function parameters with the help of spirometry in patients of RA in a semi-urban population of a developing country.

MATERIALS AND METHODS

A total of fifty patients of RA were recruited into the study. Different parameters studied were forced vital capacity (FVC), FVC%, forced expiratory volume in 1s (FEV1), FEV1%, FEV1/FVC, forced expiratory flow (FEF25-75), FEF25-75%, peak expiratory flow rate (PEFR), PEFR%.

Settings and Design- A prospective hospital based study was conducted for one year period.

Statistical Analysis-The group data was introduced with the mean and standard deviation. Quantitative and qualitative data were analysed using student's t-test and Chi-square tests respectively. P values less than 0.05 were considered as statistically significant.

RESULTS

Out of 50 cases, majority (70%) of cases were females and belonged to the age group of 31 to 40 years (44%). Among respiratory symptoms, dyspnoea was the most common (20%) followed by cough (14%), chest pain and wheezes (10% each). The Rheumatoid factor and anti CCP positivity was seen in 76% and 82% of patients with significant association with PFT abnormalities ($p=0.04$ and $p=0.01$) respectively. The high disease activity were observed to have PFT abnormalities ($p<0.05$). Chest X-rays findings were hyperinflation (36%), interstitial pattern (28%) and volume loss (08%). In 86% of patients, HRCT showed the most common findings were bronchiectasis (34%), rheumatoid nodules (26%) and air trapping (20%). Among RA patients, 28 (56%) were normal, 08 (16%) had obstructive and 14 (28%) had restrictive lung diseases.

CONCLUSION

Pulmonary abnormalities were found significantly higher in female patients with 31-40 years of age group, rheumatoid factor and anti CCP positivity, high disease activity score patients. It is recommended that in the above circumstances, patients with RA should be follow up on a regular basis and PFT should be done for the early diagnosis of pulmonary involvement.

KEYWORDS

Dyspnoea, Lung Diseases, Peak Expiratory Flow Rate, Rheumatoid Factor, Spirometry.

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BACKGROUND

Rheumatoid arthritis (RA) is a systemic autoimmune disease characterized by persistent joint inflammation resulting in joint damage and loss of function. Rheumatoid arthritis is widely prevalent throughout the world and affects 1% of adult population worldwide.¹

Pulmonary involvement in Rheumatoid arthritis is seen in 30% of the cases. The majority of lung disease occurs within the first 5 years after the initial diagnosis, and may be a

presenting manifestation in 10 to 20% of patients.² Within the lung, manifestations of RA may include airways, parenchymal, vascular, and/or pleural disease.³

Although HRCT of the chest is more sensitive than chest X-ray, the former detecting 50% of abnormalities, it is not recommended as a screening tool for pulmonary involvement in patients with RA, because the disease is highly prevalent and lung abnormalities in RA patients are often minimal.^{4,5,6} Spirometry is an inexpensive, readily available tool for grading the severity of pulmonary impairment 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.⁷ Although low DLCO is a reliable early marker of pulmonary impairment, the diagnostic tool required in order to determine DLCO is not widely available.⁸

A proper knowledge in respect to this early screening of pulmonary function abnormalities in these patients may decrease the social burden of the disease by reducing morbidity and mortality. The present study was conducted to

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measure the alterations of lung function parameters with the help of spirometry in patients of RA in a semi-urban population of a developing country.

MATERIALS AND METHODS

This is a prospective hospital based study conducted in a time span of 1 year in Silchar Medical College and hospital after taking Institutional Ethical Clearance and informed consent of the subjects. A total of fifty patients of Rheumatoid Arthritis were recruited into the study. The 2010 American College of Rheumatology criteria was used to diagnose the patients. In the present study, pulmonary manifestations are studied in these patients who are having rheumatoid arthritis.

Inclusion Criteria

All patients of Rheumatoid Arthritis (according to the 2010 American College of Rheumatology criteria) who are more than 16 years of age and who have been screened for pulmonary manifestations in both symptomatic and asymptomatic patients. All the patients were consuming at least one Disease Modifying Anti Rheumatic Drugs (DMARDs).

Exclusion Criteria

1. Subjects with respiratory illness.
2. Subjects with coronary artery disease.
3. Subjects with thoracic and vertebral abnormality.
4. Cases of juvenile Rheumatoid Arthritis.
5. Patients with mixed connective tissue disease.

The control group was selected among the patients' fellows or individuals without RA. The patients in the control group were assessed and rule out RA.

A total of 50 diagnosed cases of RA was taken as cases, and 50 normal individuals were selected as a control.

A detailed history and clinical examination was performed with special emphasis on the respiratory system. Routine investigations included are complete blood count, urine microscopy, serum creatinine, serum electrolytes, liver function tests, serum total proteins and serum calcium were done. Rheumatoid arthritis factor, C-reactive protein, ASO titres, sputum microscopy were done. Pulmonary function tests, chest x-ray, and HRCT chest were performed.

Disease severity was assessed using DAS (disease activity score) 28 scoring system which includes number of tender joints, number of swollen joints, ESR and global assessment of health using visual analogue scale of 0-100.

$$\text{DAS28 (ESR)} = 0.56 \sqrt{\text{TJC}} + 0.28 \sqrt{\text{SJC}} + 0.014 \text{GH} + 0.70 \ln(\text{ESR})$$

TJC=tender joint count

SJC=swollen joint count.

GH= patient assessment of disease activity using a 100 mm visual analogue scale (VAS) with 0=best, 100=worst. Twenty-eight tender and swollen joint scores include the same joints: shoulders (2), elbows (2), wrists (2), metacarpophalangeal joints (10), proximal interphalangeal joints (10) and the knees (2).

This score may range from 0 to 9.3, where a DAS28 score ≤ 3.2 is considered to reflect low disease activity, moderate (>3.2 to <5.1) and >5.1 high disease activity.

The evaluated indices in pulmonary function test included forced expiratory flow (FEF 25%-75%), FEF 75, FEF 50, FEF 25, forced vital capacity (FVC), forced expiratory volume (FEV1), FEV1/FVC and peak expiratory flow (PEF). Based on the ATS criteria, those who had an FEV1/FVC of less than 70%, were identified as having obstructive disease; its severity was determined according to FEV1 decline. The patients with normal FEV1/FVC and decreased FVC ($< 80\%$) were diagnosed as having restrictive disease; its severity was determined by the decrease in FVC.

Statistical Analysis

The Collected data was compiled, tabulated and analysed in terms of descriptive statistics using SPSS version 22.0 software. Continuous variables were presented as mean \pm SD and categorical variables were expressed as frequencies and percentages. Nominal categorical data between the groups were compared using Chi-squared test or Fisher's exact test as appropriate. $P < 0.05$ was considered statistically significant.

RESULTS

Fifty cases of RA were selected for the study. Out of 50 cases, majority (70%) of cases were females (35) with a female to male ratio 2.33:1.

Most of the patients from both sexes belonged to the age group of 31 to 40 years (44%). The mean (\pm SD) age of the studied patients in the case group was 46 (± 10.5) years. (Table 1).

Most of the patients (36%) had their duration of illness between 5 to 10 years. Mean disease duration was 6.13 years. (Table 2)

Morning stiffness, joint pain and swelling were present in all the cases. Among respiratory symptoms, dyspnoea was the most common presenting symptom (20%) followed by cough (14%), chest pain and wheezes (10% each) (Table 3)

Rheumatoid factor was positive in 38 (76%) and negative in 12 (24%) patients. 20 out of the 22 patients with PFT abnormalities had positive rheumatoid factors ($p = 0.0447$). Anti CCP was positive in 41 (82%) and negative in 09 (18%) patients. All patients with PFT abnormalities had Anti CCP positivity ($p = 0.0136$).

Disease severity was assessed using DAS (disease activity score) 28 scoring system. The disease activity was low in 3 (06%) cases, moderate in 27 (54%) cases and high in 20 (40%) cases. 12 out of the 20 patients with high disease activity were observed to have PFT abnormalities compared to one who had mild and seven had moderate disease activity ($p = 0.0037$).

Chest X-rays were normal in 20 (40%) of the patients; hyperinflation was present in 18 (36%); the interstitial pattern was observed in 14 (28%); volume loss was observed in 04 (08%).

In HRCT of thorax was done in all case of RA. In 86% of patients, HRCT showed the most common findings were bronchiectasis in 34%, rheumatoid nodules in 26% and air trapping in 20% of patients. (Table 4).

FVC, FEV1, FEV1/FVC, FEF25-75, PEF, and PEF% were significantly decreased ($P < 0.05$) in cases (Table 5). Among RA patients, 28 (56%) were normal, 08 (16%) had obstructive and 14 (28%) had restrictive lung diseases (RLDs).

Age (Years)	Male	Female	Total	Percentage
21-30	0	0	0	0%
31-40	06	16	22	44%
41-50	05	12	17	34%
51-60	04	05	09	18%
> 60	0	02	02	04%
Total	15	35	50	100%

Table 1. Age distribution of rheumatoid arthritis patients

Duration	No. of Cases	Percentage
< 5 years	13	26%
5 to 10 years	18	36%
10 to 15 years	11	22%
>15 years	08	16%

Table 2. Duration of illness of rheumatoid arthritis patients

Presenting Symptoms	Number of Cases	Percentage
Morning stiffness	50	100%
Joint pain	50	100%
Joint swelling	50	100%
Deformity	19	39%
Dyspnoea	10	20%
Cough	07	14%
Chest pain	05	10%
Wheezes	05	10%

Table 3. Frequency of presenting symptoms in rheumatoid arthritis patients

HRCT Findings	Number of Cases	Percentage
Abnormal pattern	43	86%
Bronchiectasis	17	34%
Nodules	13	26%
Air trapping	10	20%
Ground glass attenuation	07	14%
Honeycombing	06	12%
Pleural effusion	05	10%

Table 4. HRCT findings in rheumatoid arthritis patients

Spirometric Parameters	Case Group (Mean ± SD)	Control Group (Mean ± SD)	P value
FVC	98.9±20.90	105.50±3.23	0.0297
FEV1	93.1±23.90	99.99±3.10	0.0488
FEV1/FVC	82.31±14.93	95.43±1.98	0.0001
FEF 25%	66.00±20.67	75.24±17.71	0.0183
FEF 50%	61.76±20.86	76.45±18.81	0.0004
FEF 75%	67.75±27.53	78.69±17.81	0.0243
FEF 25-75%	72.9±35.4	79.74±5.68	0.1804
PEFR%	67.85±17.70	79.16±3.93	0.0001

Table 5. Spirometric parameters in rheumatoid arthritis patients

DISCUSSION

In present study, fifty cases of RA were selected for the study. Out of 50 cases, majority (70%) of cases were females (35) and 30% were males (15) with a female to male ratio 2.33:1. In the study by Karvounaris et al,⁹ 73.5% of patients were female, and 26.5% were male. In another study, Doran, Michele F et al,¹⁰ female patients constituted 73.1% of total patients which was close to our study.¹⁰

In present study, most of the patients belonged to the age group of 31 to 40 years (44%) with mean (±SD) age in the case group was 46 (±10.5) years. So, 78% of patients were belong to the age group of 40-60 years. Sahebari et al¹¹

reported similar age distribution of RA in their patients with mean age of RA patients was 45.5±13 yrs which was very close to our study. Dao et al¹² in their prospective study found maximum number of RA patients (48.57%) was seen in the 40-59 age group which was similar to our study.

Most of the patients (36%) had their duration of illness between 5 to 10 years with mean disease duration was 6.13 years. Similar findings were reported by Doran, Michele F et al¹⁰ and Hadda et al¹³ that median duration of disease was 7 yrs (4.1-12.8) and 5.5 yrs. respectively.

Morning stiffness, joint pain and swelling were present in all the cases of present study. Among respiratory symptoms, dyspnoea was the most common presenting symptom (20%) followed by cough (14%), chest pain and wheezes (10% each). Zayeni, et al¹⁴ found that dyspnoea (22.7%) and chest pain (22.3%) were the most common complaints of patients with RA.¹⁵ Nazish Fatima et al¹⁵ revealed most pulmonary symptoms in RA were exertional dyspnoea in 21%, cough with expectoration in 17.7%, fine respiratory rales in 11.3%.

In present study, rheumatoid factor was positive in 38 (76%) and negative in 12 (24%) patients. Similar reports were found by Hadda et al¹³ and Doran, Michele F et al¹⁰ studies were 77.1% and 69% RA factor positivity respectively.

Anti CCP was positive in 41 (82%) and negative in 09 (18%) patients. Rostom et al¹⁶ and Tom et al¹⁷ found 85% and 67.6% anti-CCP positivity in their total patients respectively.

The disease activity score was low in 3 (06%) cases, moderate in 27 (54%) cases and high in 20 (40%) cases. In a study by Dao et al,¹² the proportion of patients with low, moderate and high disease activity were 36.2%, 52.5%, and 11.3%, respectively. Sahebari et al¹¹ in their study found that 36.66% of RA patients were moderate and 38.33% of patients with high disease activity score.

20 out of the 22 patients with PFT abnormalities had positive rheumatoid factors (p=0.0447). Anti CCP was positive in 41 (82%) and negative in 09 (18%) patients. All patients with PFT abnormalities had Anti CCP positivity (p=0.0136). 12 out of the 20 patients with high disease activity were observed to have PFT abnormalities compared to two who had mild and eight had moderate disease activity (p=0.0037). Biomdo et al¹⁸ observed that 47 out of the 64 patients with PFT abnormalities had positive rheumatoid factors (p = 0.03). Fifty six patients with DAS 28 score of 3.2 to 7.6, depicting moderate to high disease activity, were observed to have abnormalities compared to 25 who had mild disease activity (p=0.001). Pappas et al¹⁹ observed that seropositivity to rheumatoid factor (P=0.011), presence of high titres of anti CCP antibodies (P=0.003) and ongoing steroid therapy (P=0.018) were associated with abnormalities in pulmonary functions.

Chest X-rays were normal in 20 (40%) of the patients; hyperinflation was present in 18 (36%); the interstitial pattern was observed in 14 (28%); volume loss was observed in 04 (08%). Alexandre Melo Kawassaki et al²⁰ observed the chest X-rays were normal (55.3%) of the patients; hyperinflation was present in (24.8%); the interstitial pattern was observed in (14.6%); volume loss was observed in

(2.4%) and miscellaneous abnormalities were observed in the remaining (2.8%).

In HRCT of thorax was done in all case of RA. In 86% of patients, HRCT showed the most common findings were bronchiectasis in 34%, rheumatoid nodules in 26% and air trapping in 20% of patients. The rare findings in HRCT were Ground glass attenuation seen in 14%, Honeycombing in 12% and Pleural effusion in 10% of patients. Bernard Cortet et al⁷ noticed the most frequent HRCT findings were: bronchiectasis (30.5%), pulmonary nodules (28%), and air trapping (25%). Thierry Perez et al²¹ reported HRCT demonstrated bronchial and/or lung abnormalities in 35 cases (70%), consisting of air trapping (32%), cylindrical bronchiectasis (30%), mild heterogeneity in lung attenuation (20%), and/or centrilobular areas of high attenuation (6%).

Among RA patients, 56% were normal, 16% had obstructive and 28% had restrictive lung diseases (RLDs). In the USA, a study done in John Hopkins University by Pappas et al¹⁹ on 159 RA patients, found a 28% prevalence of pulmonary function abnormalities on spirometry. The most common ventilatory defect was obstructive at 11.3%, restrictive pattern was observed in 7.6% and an isolated impaired diffusing capacity of carbon monoxide in 9.6%.

In Africa, Amir et al²² studied 36 RA Egyptian patients and 64% of them demonstrated abnormalities in their pulmonary function tests, Mixed restrictive and obstructive pattern was commonest and reported in 11 (30.6%), restrictive pattern at 8 (22.2%) and obstructive pattern in 4 (11.1%).

Limitation

As this study comprised of limited numbers of patients, a larger multi-centric study including more number of population for longer duration is required for detailed assessment and definite conclusion.

CONCLUSION

The incidence of rheumatoid arthritis was more common in female and more in age group of 31-40 years. Among respiratory symptoms, dyspnoea was the most common followed by cough, chest pain and wheezes. Pulmonary abnormalities were more common in the patients with rheumatoid factor and anti CCP positivity, high disease activity score. The most common HRCT findings were bronchiectasis, rheumatoid nodules and air trapping. Pulmonary functions were reported that restrictive lung diseases were more common than obstructive lung disease. So, our study recommended that patients with RA should be visited on a regular basis and PFT be done for them for the early diagnosis of pulmonary involvement.

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