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Original Research Article

CLINICAL AND SPIROMETRIC PATTERN OF PULMONARY FUNCTION IN SUBJECTS WITH RHEUMATOID ARTHRITIS

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ABSTRACT

Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by a painful symmetrical peripheral polyarthritis. It affects multiple body organs in addition to joints and surrounding tissues and it is a leading cause of joints deformities and disabilities. **Objective:** To assess the clinical and spirometric pattern of pulmonary function in subjects with rheumatoid arthritis.

Material and Methods: The present study was carried out in the department of General medicine and Orthopedics, KC GENERAL HOSPITAL, Bangalore during the period from January 2019- March 2021. During the period of data collection,120 patients with rheumatoid arthritis were screened as per the inclusion and exclusion criteria.

Results: Majority of subjects were belonged to 4thand 5th decade with mean age of 47.2 years. female preponderance was seen in the present study with female: male ratio6.5:1, In this study slightly higher gender ratio was attributed to the exclusion of smokers. 70% of the study subjects had 20 or more joint involvement with symmetrical distal appendicular pattern. Although majority of patients in this study had short duration of illness, very few of the symptomatic patients had active signs of inflammation (15%). PFT revealed 16.7% abnormal patterns, with predominant restrictive pattern than obstructive pattern.

Conclusion: RA is a progressive symmetrical autoimmune disease characterized by erosive synovitis. Among the extra articular manifestations of RA, lung and pleura are the frequent sites of involvement. Majority of study population belonged to 4th and 5th decade with mean age 47.2

Pulmonary symptoms were seen in 26.6%. Major symptom was exertional dyspnea. Respiratory system examination was abnormal only in 6.6%, Chest X ray was abnormal in 3.3%. Whereas PFT revealed 16.7% abnormal patterns, with predominant restrictive pattern than obstructive pattern.

Keywords: Clinical and Spirometric Pattern, Pulmonary Function, Rheumatoid Arthritis.

INTRODUCTION

Rheumatoid arthritis can develop at any age with increased incidence between 35 and 55 years of age.[1] RA has a prevalence of 0.5 to 2% in general population.[2]

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.[3]

In patients of RA, extra-articular manifestations are common, approximately 50% and lung is affected in majority of cases. Extra articular manifestations including subcutaneous nodule formation, vasculitis, inflammatory eye disease and lung disease.[4] Lung involvement ranges between 67% to as low as 10% in different studies.[5,6] Mortality further increases in

cases of extra-articular affection in patients with RA, of which pulmonary involvement accounts for 10-20% mortality, mostly attributable to Interstitial Lung Disease (ILD).[7,8]

Patients with RA having high titers of rheumatoid factor, i.e., autoantibodies to the Fc component of immunoglobulin G are most likely to have extra-articular manifestations including rheumatoid nodules, rheumatoid vasculitis, and pleuropulmonary, neurologic, digestive, cardiovascular, cutaneous, hematologic and ocular complications.[9]

Respiratory symptoms in rheumatoid arthritis can be due to a variety of conditions that affect the parenchyma [Interstitial lung disease (i.e. usual interstitial pneumonia, nonspecific interstitial pneumonia, acute interstitial pneumonia/diffuse alveolar damage and organising pneumonia], pleural[pleural effusion, Pneumothorax, Bronchopleural fistula, Trapped lung syndrome], airways [Bronchiectasis, Follicular bronchiolitis, Obliterative (constrictive) bronchiolitis] Nodules [Rheumatoid nodules, Caplan syndrome] or vasculature [Rheumatoid vasculitis, pulmonary hypertension].[10]

The majority of respiratory manifestations occur within the first 5 years of disease.11Respiratory symptoms may precede onset of articular symptoms in 10–20% of cases.[12] Although HRCT of the chest is more sensitive than chest X-ray, 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 less common.[13]

Spirometry is an inexpensive, readily available tool for grading the severity of pulmonary impairment and can be used on a large scale. Studies employing spirometry have detected abnormalities, mainly obstructive and restrictive patterns, in approximately 30% of patients with RA.[14]

Patients with rheumatoid arthritis typically have circulating autoantibodies, the most common being rheumatoid factor and anti-cyclic citrullinated peptide (CCP).[15] Anti-CCP antibodies have also been associated with the development of airway disease.16 Cigarette smoking may play a role in inducing antibody formation and has been linked to higher titres of rheumatoid factor.[17] Smoking may promote citrullination of lung proteins, thus leading to the development of anti-CCP antibodies.

The major population with RA-ILD will have a restrictive pattern on PFTs, with or without decreased diffusing capacity of the lung for carbon monoxide (DLCO) and hypoxaemia. Abnormalities of both forced vital capacity (FVC) and DLCO is associated with poorer prognosis.[18]

MATERIAL AND METHODS

This Prospective Observational study was conducted among male and female patients with rheumatoid arthritis who visited the outpatient and inpatient Department of General Medicine and Orthopedics KC General Hospital, Bangalore Karnataka during study period from January 2019 – March 2021

Sample size

N = (Z for alpha)2 * p *q/d2 =61

Q =100-P

P= 20% of RA patients having dyspnea

d= absolute precision = 10%

Z= z score for 95% confidence interval =1.96

All the 60 eligible subjects with rheumatoid arthritis who full filled the inclusion and exclusion criteria underwent detailed examination and series of investigations including PFT.

Inclusion Criteria

- Subjects above 18 years of age with rheumatoid arthritis
- Subjects who signed in written informed consent to get involved in the study were included

Exclusion Criteria

- Patients with known respiratory disease-infective or non-infective
- Patients with known cardiovascular disease
- Patients with other connective tissue disorders
- Patients with congenital skeletal deformities

Methodology

During the period of data collection 60 subjects of rheumatoid arthritis who presented to department of general medicine and department of orthopaedics, KC General hospital were selected as per the 2010 ACR/EULAR criteria. 2 subjects were newly diagnosed whereas 58 of them were already diagnosed. All subjects were explained about the study, advantages and disadvantages. Written informed consent was taken in their own understandable language. All of them were screened with above mentioned inclusion and exclusion criteria.

A detailed history and examination was done as per the proforma. They underwent haematological tests (including CBC, ESR, RF, Anti CCP), imaging studies (chest x ray) and spirometry. PFT was done using innotechrespiscan spirometer. subjects were instructed

- To avoid heavy exercise 30min before the test
- To avoid tight clothing that makes it difficult to breath deeply
- To avoid large meal within 2 hours before test.

In the beginning of the procedure subjects were instructed to sit straight, with head erect and holding the mouthpiece tightly between the lips. Initially, they were instructed to breathe in and out at the tidal volume (VT: normal quiet breathing). Then, when the subjects were ready, we instructed him/her to inhale maximally to TLC and then exhale as fast and as completely as possible to record the FVC. Subjects were instructed to continue expirationatleast 6 seconds and atleast 3 readings were obtained without cough, air leak and false start.

FEV1, FVC, FEV1/FVC were analysed. Post bronchodilator studies were done in patients who had abnormal PFT, those with improvement more than 15% were considered as obstructive lung disease.

Statistical Analysis

Data was entered into Microsoft Excel (Windows 7; Version 2007) and analyses were done using the Statistical Package for Social Sciences (SPSS) for Windows software (version 22.0; SPSS Inc, Chicago). Descriptive statistics such as mean and standard deviation (SD) for continuous variables, frequencies and percentages were calculated for categorical Variables were determined. Bar charts and Pie charts were used for visual representation of the analyzed data.

RESULTS

A total of 60 subjects were included in the final analysis.

A total of 60 individuals of both sex were selected in this study. Majority of the population belongs to 4th and 5th decade. Mean age was 47.22 years, ranged between 23 to 70 years.

Major population of the study were females (86.7%) with a ratio of 6.5:1, as age advances (>50 years) female: male = 2.5:1. [Table 1]

More than 2/3rd (76%) patients had duration of RA < 5 years. 26% of them were older subjects (>50 years). 18.3% of study population had duration of RA from 5-10 years. Only 5% of study population had duration of illness more than 10 years. [Table 2]

More than ½ of the patients had symmetrical distal appendicular skeleton involvement, upper limb > lower limb. Majority (70%) had >20 joint involvement. Out of 8 males everyone had upper limb involvement, 3 of them had lower limb involvement, one subject had axial skeleton involvement in the form of low backache. All 52 female subjects had upper limb involvement, 12 of them had lower limb involvement and 3 of them had axial skeleton involvement as 2 cervical spine and luumbar spine involvement. One male and 3 females reported ankle joint involvement.

15% of study population showed signs of active inflammation in the form of swelling and redness, however many of them had pain, tenderness , joint stiffness and restricted mobility. [Table 3]

Majority of subjects (86.7%) had morning stiffness lasting for ~ 1 hour. 13.3% had fever history. Weight loss was reported by 8.3% subjects. 28.3% participants had pulmonary symptoms and 8.3% presented with chronic deformities. The deformities reported were loss of hand grip by 2 subjects(3%) , Flexion at PIP and MCP joints by 1 subject (1.6%) , flexion of MCP joint alone by 1 subject (1.6%) , ulnar deviation of bilateral hands reported by 1 participant. [Table 4]

Majority of population under study were asymptomatic (71.7%). Easy fatigability and Dyspnoea on exertion was reported by 10% of subjects. Dry cough were reported in 8.3% of participants. [Table 5]

Investigations of study population revealed majority with normal haemoglobin (55%). Mild and moderate anaemia were recorded 21.6% and 23.4 % respectively. None of the participants had severe anaemia. [As majority of population were females, haemoglobin was taken as normal above 12gm %]. Normocytic normochromic anaemia typical of chronic inflammatory state of mild to moderate severity was seen in this study. The mechanism involves inflammatory cytokines that increase the level of hepcidin, which restricts availability of stored iron to be incorporated in RBC production.

Majority (81.7%) had ESR >20 mm/hr and 18.3% had ESR <20mm/hr. ESR value of above 20 is suggestive, and more than 40 is diagnostic of RA.

Majority of the study population (96.7) had normal chest x ray pattern. 3.3% of subjects had chest x ray suggestive of ILD, in the form of bilateral lower zone diffuse shadow and prominent pulmonary vasculature. [Table 6]

Majority of the population (83.4%) had normal PFT. Restrictive pattern was observed in 10% of study population, in which 2 subjects were asymptomatic, 3 of them had dyspnoea on exertion and 1 of them had dry cough. 1 of the 6 restrictive pattern was in male and other 5 subjects were females. Chest x ray was suggestive of ILD in 1 patient with restrictive pattern of spirometry.

Mixed pattern was observed in 5% of population under study. 1subject had dyspnoea on exertion, 1 subject had dry cough and 1 participant had easy fatigability. Chest x ray was suggestive of ILD in one subject with mixed pattern spirometry. All the subjects with mixed pattern spirometry were females. [Table 7]

Obstructive pattern of spirometry was seen in 1.7% of population under study. Subject was male and asymptomatic and x ray was normal.

Table 1: Table showing age distribution (N = 60)

Age (in Years)	No.	Percent
≤ 30	5	8.3
31-40	16	26.7
41-50	18	30.0
51-60	12	20.0
61-70	9	15.0
Mean (SD)	47.22 (11.38)	
Range	23-70	

Table 2: Table showing duration of RA (N = 60)

Duration (in Years)	No.	Percent
0-5	46	76.7
6-10	11	18.3
>10	3	5.0
Mean (SD)	4.38 (3.43)	
Range	1-15	

Table 3: Tables showing number of Joints Involved (N = 60)

Number of Joints	No.	Percent
≤ 20	18	30
>20	42	70
Mean (SD)	22.07 (3.63)	
Range	Oct-32	

Table 4: Table showing clinical features (N=60)

Symptoms	No.	Percent
Fever	8	13.3
Morning Stiffness/Pain	52	86.7
Weight Loss	5	8.3
Pulmonary Symptoms	17	28.3
Chronic deformity	5	8.3

Table 5: Table showing symptoms suggestive of respiratory involvement (N=60)

Pulmonary Symptoms	No.	Percent
Asymptomatic	43	71.7
Fatigue	6	10
Cough	5	8.3
Dyspnoea on Exertion	6	10

Table 6: Table showing investigation results (N = 60)

	Interpretation	No	Percent
Haemoglobin (gm/dl)	>12 (normal)	33	55
	<12 (mild)	13	21.6
	Moderate (>10)	14	23.4
ESR (mm/hr)	<20	11	18.3
	>20	49	81.7
Chest x ray	s/o ILD	2	3.3
	Normal	58	96.7

Table 7: Table showing pattern of PFT (spirometry) (N=60)

PFT Interpretation	No.	Percent
Mixed	3	5.0
Normal	50	83.4
Obstructive	1	1.7
Restrictive	6	10.0

DISCUSSION

Rheumatoid arthritis (RA) is a generally progressive autoimmune disease characterised by chronic symmetrical erosive synovitis with a prevalence of 0.5- 2% in general population, slightly higher in developed countries compared to developing nations. Among the extra articular manifestations of this disease lung and pleura are frequent sites of involvement contributing 10-12% of mortality and morbidity

Active disease, symptomatic articular manifestations, and chronic deformities – all limit the physical activity of patients with RA. Hence, early involvement of lung – mainly restrictive which usually manifest as exertional dyspnoea, goes unnoticed and they remain asymptomatic.

Awareness of these facts are likely to help the treating physician to prognosticate and formulate management to alter the course of pulmonary disease in RA.

Although RA is known to be a disease of all ages, in our study most of the patients were in 4th and 5th decade. Age range varied from 23-70 years. This observation corroborates with the study done by J Ravikumar et al,[19]

Like most autoimmune diseases with female preponderance, RA is also a disease commonly affecting female gender. This affinity of female gender wane as age advances with narrowing of ratio between female and male.

Out of 60 subjects of our study population, 86.7% were females and 13.3% were males, with a female to male ratio 6.5:1. But as age advances (>50 years) female: male =2.5:1. In the study done by N fathima20 et al female: male =3:1.

Our gender ratio is slightly higher than what has been reported in other populations because most of the RA male subjects were excluded from the study due to tobacco smoking, however gender ratio in older subjects is consistent with similar studies.

Since this study was conducted in a referral hospital, symptomatic patients sought medical help from physicians and orthopedicians because of active disease. Chronic patients who had stabilized on medications and those with chronic deformities with minimal symptoms are few in number.

In the current study 76% of the population had duration of RA less than 5 years which was consistent other similar study done by S. Madhavan et al,[21] and Sandipanbanik et al,[22]

RA by definition is a symmetrical polyarticular disease involving small joints of hands and feet. 70% of our study population had more than 20 joint involvement with upper limb more affected than lower limb. 6% of study population had axial sketelon involvement.

Although majority of patients in this study had short duration of disease, very few of the symptomatic patients had active signs of inflammation.

In our study majority (86.7%) of the study population had morning stiffness and pain which last for ~1 hour. Other symptoms include fever (13.3%), weight loss (8.3%), pulmonary symptoms (28.3%), chronic disability (8.3%). Similar studies done both inside the country (Ravi kumar et al,[19]) and outside the country (Haji Abbasi A et al23) had similar clinical features. In the study by Haji Abbasi et al23 pulmonary manifestations were 81% which is more than two and a half times the present study. This difference can be attributed to inclusion of smokers who are excluded from the present study.

In our study majority of study population (71%) were asymptomatic for respiratory pathology. 28.3% of the study population who were symptomatic presented with cough (8.3%), easy fatigability (10%), dyspnoea on exertion (10%). Similar findings were seen in other studies done by Sandipanbanik et al,[22] Ravikumar et al.[19]

In our study 45% of study population had anaemia. 21.6% had mild anemia whereas moderate anemia was found in 23.4%. None of the subjects had severe anemia. Patients with rheumatoid arthritis can have mild normocytic normochromic anemia with inappropriately low reticulocyte count which is typical of anemia of chronic inflammation.

Although HRCT thorax is a better radiological diagnostic tool in identifying early lung parenchymal disease, for logistic reasons, only chest x ray – a cheaper alternative radiological modality was used in the present study.

In our study, 96.7% of study population had normal chest x ray. Another study done by Ravikumar et al19 with a larger male population have described hyperinflation in 36% of their study population. Sanjoysen et al24 described pleural effusion in 10% and ILD in 24 % of their study population and his study had longer duration of disease, 51% of their population had duration of RA more than 11 years. Both these study groups had all patients on at least one disease modifying drugs in their treatment.

DLCO and HRCT thorax are better diagnostic tools for early asymptomatic parenchymal lung disease. However, both these are not easily accessible, expensive, hence cannot be used as screening modality in RA patients who were asymptomatic for early detection of lung involvement. Spirometry being non-invasive and low risk diagnostic tool can be a good diagnostic modality which can be repeated for better correlation of PFT for screening such patients. Analysis of PFT in the present study showed the following pattern. Normal spirometry in 83.4%, restrictive pattern in10%, mixed pattern in 5% and obstructive pattern in 1.5%(confirmed by post bronchodilator improvement) of study population.

Study done by Ravikumaret al,[19] showed similar pattern with majority of them having normal pattern, followed by restrictive pattern > obstructive pattern. Although the percentage of abnormal pattern were higher than present study.

CONCLUSION

Rheumatoid arthritis (RA) is a generally progressive autoimmune disease with a prevalence of 0.5- 2% in general population. Lung and pleura are frequent sites of involvement contributing 10-12% of mortality and morbidity. It is noteworthy to look for axial skeleton involvement as it is not unlikely in RA. Patients with rheumatoid arthritis can have mild normocytic normochromic anaemia with inappropriately low reticulocyte count which is typical of anaemia of chronic inflammation. Although severe anaemia was not seen in study population, 45% had anaemia in which mild cases were 21.6 and moderate cases were 23.4% respectively. Pulmonary symptoms were seen in 26.6%. Active disease, symptomatic articular manifestations and chronic deformities limit the physical activity of patients with RA, hence, early involvement of lung disease, mainly restrictive goes unnoticed. Major respiratory symptom was exertional dyspnoea. Although pulmonary symptoms were reported by 26.6%, espiratory system examination was abnormal only in 6.6%, chest x ray was abnormal in 3.3%. Whereas PFT revealed 16.7% abnormal patterns, with predominant restrictive pattern than obstructive pattern PFT is a low risk, non-invasive, economical and reproducible better diagnostic tool. Hence, it can be used for screening of early asymptomatic and symptomatic RA and for follow up evaluation.

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