



Original Research Article

A cross-sectional study on the correlation of pulmonary function with duration of Rheumatoid arthritis

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ABSTRACT

Introduction: Rheumatoid arthritis (R.A.) is characterized by chronic inflammatory symmetrical peripheral polyarthritis associated with systemic involvement. Pulmonary involvement is one of them. Therefore, early assessment of pulmonary function may help identify the type of respiratory involvement and hence can contribute to properly managing pulmonary complications.

Aims: The study aims to evaluate the type and extent of pulmonary function abnormality in relation to the duration of Rheumatoid Arthritis. Settings and Design: tertiary care treating hospital- a cross-sectional observational study

Methods and Material: A cross-sectional study was conducted at Department of General Medicine in forty R.A. cases in whom spirometry was performed and values of spirometry results were statistically compared with the duration of R.A. using S.P.S.S. software.

Results: Cases were grouped into three categories based on the duration of the disease. Category A –less than 5 yrs, category B– 5 to 9 yrs and category C – more than 9 yrs duration. In category A, abnormal pulmonary function test (PFT) was observed in 43.5% of cases in the form of obstructive 17.4%, restrictive 17.4% and mixed pattern in 8.7% of cases. In category B, the restrictive pattern was found in 63.6% and a mixed pattern in 9.1% of cases. However, abnormal pulmonary function test (PFT) was observed in all cases in category C, with obstructive pattern in 16.7%, restrictive 66.7% and mixed 16.7% cases.

Conclusions: From the study, it was found that early pulmonary involvement occurs in R.A. With an increase in the duration of R.A., pulmonary involvement becomes a more severe and restrictive pattern. Most cases with a duration of more than 9yrs had significant pulmonary involvement either in the form of restrictive or obstructive pattern. Hence PFT should be done at the earliest as a routine and repeated periodically in R.A. cases.

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1. Introduction

Rheumatoid arthritis (R.A.) is a multisystem chronic inflammatory and autoimmune disorder. The characteristic feature of R.A. is persistent inflammatory synovitis, usually involving small and large peripheral joints in a symmetrical distribution. The synovial inflammation has the potential

to cause cartilage destruction and bony erosion with subsequent surrounding soft tissue damage leading to deformities.¹

Rheumatoid arthritis affects approximately 0.5-1 % of the adult population worldwide. Like other autoimmune disorders, R.A. also has a female preponderance affecting them approximately three times more often than men. The disease onset is often during the fourth and fifth decades but can also affect children as early as two years of age. In India,

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the prevalence of R.A. is similar to global indices, with a prevalence rate of 0.75%. If it is to be projected for the entire Indian population, it will give a total of seven million R.A. cases in India.²

R.A. is most often associated with multisystemic disturbances. The clinical course is usually a lifelong affliction with intermittent remissions and exacerbations. Despite the destructive potential, the course can be variable. Some cases have a mild disease involving oligo articular illness of brief duration with minimal joint damage, whereas others have a relentlessly progressive polyarthritis with marked functional impairment. It is currently not possible to predict prognosis at presentation accurately. However, irreversible joint damage occurs early in R.A.³

Extra-articular manifestations are common in cases with a higher titre of rheumatoid factor contributing to morbidity requiring separate management. Various extra-articular manifestations encountered in R.A. are known to involve one or more than one organ system in the body, and their clinical features also show lots of variations, mostly involving cutaneous system with features like rheumatoid nodules, Raynaud's phenomenon, palmar erythema, leukocytoclastic vasculitis; visual system causing keratoconjunctivitis sicca; cardiovascular manifestation like atherosclerosis, MI, pericarditis, valvular heart disease, arrhythmia; neurological systems like entrapment neuropathy, mononeuritis complex; musculoskeletal system like osteoporosis, tendon and ligament rupture; renal system like glomerulonephritis, amyloidosis; haematological systems like Felty's syndrome, anaemia, thrombocytosis; vascular system and pulmonary system involvement.⁴

The pleuropulmonary involvement in R.A. is one manifestation contributing to significant morbidity and mortality. The pleuropulmonary manifestation associated with rheumatoid arthritis includes pulmonary parenchymal disease causing interstitial lung disease (I.L.D.), fibrosing alveolitis, cryptogenic organizing pneumonia, bronchiolitis obliterans, bronchiectasis; airway disease including obstructive airway disease, cricoarytenoid arthritis; pleural disease including pneumothorax, pleural effusion, pleurisy and others including vascular disease like pulmonary H.T.N., vasculitis, shrinking lung, pulmonary amyloidosis, and eosinophilic pneumonia.⁵

Lung involvement in R.A. carries a worse prognosis. Clinical symptoms of pulmonary insufficiency occur less frequently than the histological changes because R.A. imposes limitations that make physical exertion difficult. Thus respiratory involvement may be asymptomatic. Early assessment of pulmonary function with spirometry may help identify the type of respiratory involvement and can contribute to proper management at an early stage.

1.1. Why spirometry?

Spirometry is a simple, non-invasive, cheap method of assessing pulmonary function.

Radiological investigations like an x-ray chest cannot detect obstructive or restrictive patterns at an early stage of pulmonary involvement. Similarly, other radiological investigations like H.R.C.T. chest, besides being expensive and prone to radiation exposure, are mainly concerned with structural defects of the lungs rather than a functional abnormality. Though there have been many studies on pulmonary morbidities in R.A. cases worldwide, studies about identifying the correlation between the duration of R.A. and the PFT pattern are still scarce. Additionally, the various studies in past literature on this topic show a lot of variabilities, which necessitates further studies.⁶⁻⁹ Therefore, the study aims to evaluate the type and extent of pulmonary function abnormality and to correlate it with the duration of R.A.

2. Materials and methods

2.1. Study design and setting

A cross-sectional, observational study was conducted in the Department of General Medicine in a tertiary care teaching hospital (M.K.C.G. Medical College, Brahmapur, Odisha, India) for two years (November 20th, 2019 to November 20th, 2021). The ethical approval has been taken from the institutional ethical committee (IEC-958/IEC) of M.K.C.G. medical college, Brahmapur, Odisha, India.

2.2. Sample selection and methodology

Out of 280 cases of Rheumatoid Arthritis admitted to the hospital, 40 were included in this study after considering the required sample size (32 or more measurements/surveys are needed to have a confidence level of 95% and that the real value is within $\pm 3\%$ of the measured/surveyed value considering the population proportion to be 0.75%). Eligible Cases who satisfied the European League Against Rheumatism/ American College of Rheumatology 2010 Criteria in the age group ranging from 15yr to 65yr, irrespective of their respiratory symptoms, were included in the study.¹⁰ While the patients who were less than 15 years and more than 65 years of age, had a smoking habit or had systemic conditions like pregnancy, bronchial asthma, chronic obstructive airway diseases known as current or past pulmonary tuberculosis (T.B.), cases with occupations prone to develop occupational lung disease and cases with conditions interfering with the performance of PFT were excluded from the study.

Informed written consent was obtained from each of the cases and attendants before taking any interviews, after describing the study's purpose and methods, the confidentiality of the interviews, risks, and benefits of

participating in the study. All information was collected confidentially with complete respect to the patient without force or pressure. The selected cases were evaluated for detailed history regarding the duration of articular and extra-articular symptoms, followed by a detailed clinical assessment of swollen, tender and deforming joints along with rheumatoid nodules. A detailed respiratory system examination was done. For every patient, routine laboratory investigations like Hb, E.S.R., and C.R.P. and serological markers including R.F. and anti-CCP were done.

After assessing baseline clinical and laboratory parameters, all cases were subjected to spirometric evaluation using a computerized spirometer following ethical principles and instructions. Spirometry was done thrice in all cases, and the best of the three readings was included in the study. The variables of PFT taken in the study were forced vital capacity (F.V.C.), forced expiratory volume in the first second (FEV1), Peak expiratory flow rate (P.E.F.R.), F.V.C. predicted %, FEV1 %, F.E.F. 25-75%, FEV1/FVC.

2.3. Statistical analysis

Data was collected in a Case Investigating Proforma that has been pre-designed and documented methodically. The data collected above were compiled and tabulated in Microsoft. Excel and statistically analyzed using IBM SPSS 17.0 for Windows. Qualitative Variables were calculated using Fischer Exact Test (or) Chi-Square Test. Quantitative Variables were calculated using Mann-Whitney U-test (or) Wilcoxon Rank Test. Descriptive statistical values like specificity, sensitivity, Positive Predictive Value and Negative Predictive value were calculated using cross-tabulation statistics. Mean and Standard Deviation was calculated for continuous variables. An unpaired t-test was used to compare the mean value between the two groups. The ANOVA test was used to compare the mean values among more than two groups. Pearson and Spearman's Tests were used for correlation between two continuous variables. $P < 0.05$ Considered Statistically Significant.

2.3.1. Elimination of bias

Selection Bias, which was ruled out by including all the cases satisfying the Inclusion and Exclusion criteria and Information bias was ruled out by accurately measuring and cross-checking all the critical study variables at least three times before classifying them in the study.

3. Result

The average age of the study participants, as determined by their demographic information, was 39.92 years. The majority of them, 31 (77.5%), were female. The averages of height, weight, and B.M.I. were 158.08 cm, 64.79 kg, and 26.01 kg/m², respectively. Rheumatoid arthritis had a mean

duration of 5.38 years [Table 1, Figure 1].

According to the study, 27(67.5%) cases of the population had a cough, compared to 13 (32.5 %) cases who did not. Similarly, 17 (42.5%) cases had dyspnoea, and 9 (22.5%) cases reported chest discomfort during the presentation [Table 2, Figure 2].

After evaluating the rheumatoid features of the cases, it was found that all of them had morning stiffness. 16 (40%) instances had both small and large joint engagement, compared to 20 (50%) cases that had only small joint involvement and 4 (10%) cases that had large joint involvement. Twenty (50%) of the subjects had subcutaneous nodules. In 12 cases (30%), there was joint deformity [Table 3, Figure 3].

Table 1: Demographic details.

| Demographic Details | | |
|-----------------------------|--------|-------------|
| Age in completed years | | 39.92±10.89 |
| Gender | Male | 9 (22.5%) |
| | Female | 31 (77.5%) |
| Height (in cm) | | 158.08±9.53 |
| Weight (in Kg) | | 64.79±11.37 |
| B.M.I. | | 26.01±3.71 |
| Duration of R.A. (in years) | | 5.38±3.43 |

Table 2: Pulmonary manifestations

| Pulmonary manifestations | | |
|--------------------------|---------------|------------|
| Cough | No Cough | 13 (32.5%) |
| | Dry cough | 18 (45.0%) |
| | Expectoration | 9 (22.5%) |
| Dyspnoea | Yes | 17 (42.5%) |
| | No | 23 (57.5%) |
| Chest pain | Yes | 9 (22.5%) |
| | No | 31 (77.5%) |

Table 3: Rheumatoid manifestations

| Rheumatoid manifestations | | |
|---------------------------|-------------|-------------|
| Morning Stiffness | Yes | 40 (100.0%) |
| | Large joint | 4 (10.0%) |
| Joint involvement | Small joint | 20 (50.0%) |
| | Both | 16 (40.0%) |
| Subcutaneous nodules | Yes | 20 (50.0%) |
| Deformity | Yes | 12 (30.0%) |

According to the distribution of pulmonary function patterns in the study, R.A. cases were divided into three categories based on the length of the disease (category A – less than 5 yrs, category B – between 5 to 9 yr, and category C – more than nine years). In cat-(A) cases, aberrant PFT was seen in 43.5 per cent of cases as obstructive (17.4 per cent), restrictive (17.4 per cent), and mixed (8.7 per cent) instances [Figure 4], whereas in cat-(B) cases, normal PFT was found in 27.3 per cent of cases, the restrictive pattern

Table 4: PFT findings

| Duration of RA | CAT A (< 5) years CAT B (5 – 9) years C.A.T. C (> 9) years | PFT Findings | | | | p-value |
|----------------|--|--------------|-------------|-------------|-----------|---------|
| | | Normal | Obstructive | Restrictive | Mixed | |
| | CAT A (< 5) years | 13 (56.5%) | 4 (17.4%) | 4 (17.4%) | 2 (8.7%) | 0.016 |
| | CAT B (5 – 9) years | 3 (27.3%) | 0 (0.0%) | 7 (63.6%) | 1 (9.1%) | |
| | C.A.T. C (> 9) years | 0 (0.0%) | 1 (16.7%) | 4 (66.7%) | 1 (16.7%) | |

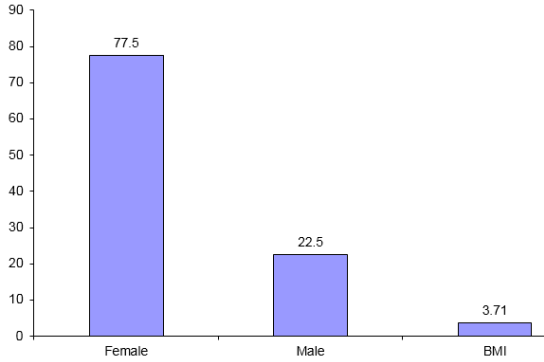


Figure 1: Demography

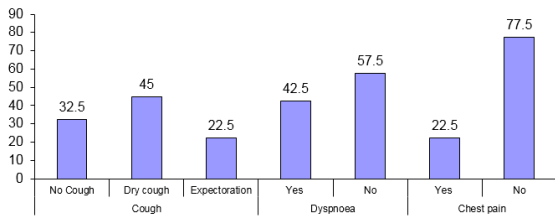


Figure 2: Pulmonary manifestations

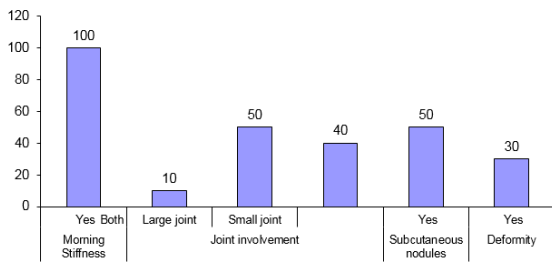


Figure 3: Rheumatoid manifestation

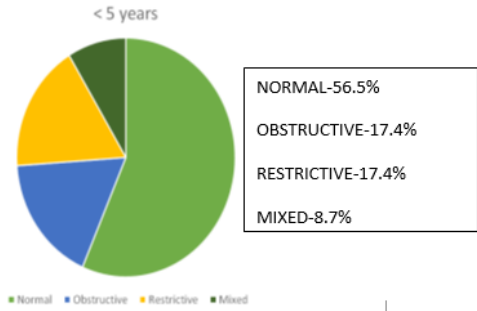


Figure 4: PFT findings in less than five year old

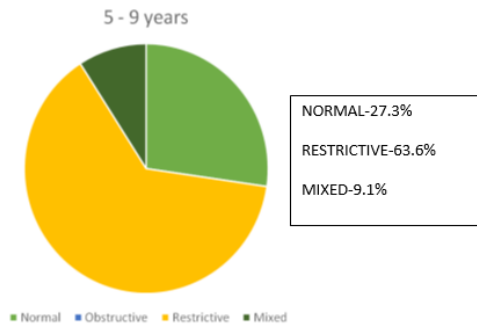


Figure 5: PFT findings in 5-9 years age

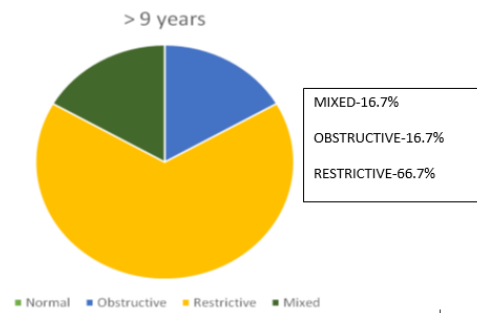


Figure 6: PFT findings in more than 9 years age

was found in 63.6 per cent of cases, and the mixed pattern was found in 9.1 per cent of cases [Figure 5]. Similar to cat-(C) cases, aberrant PFT was seen in every instance, with obstructive pattern occurring in 16.7% of cases, restrictive pattern in 66.7 per cent of cases, and mixed pattern in 16.7% of cases. The study’s p-value is determined to be 0.016 [Table 4, Figure 7].

4. Discussion

Rheumatoid arthritis (R.A.) is a chronic multi-system disease of autoimmune aetiology. It is a systemic inflammatory disease and affects 0.5 -1% of the general population. A variety of pulmonary manifestations are associated with R.A., and lung disease is the second most common cause of death (18%) after infection (27%) in cases

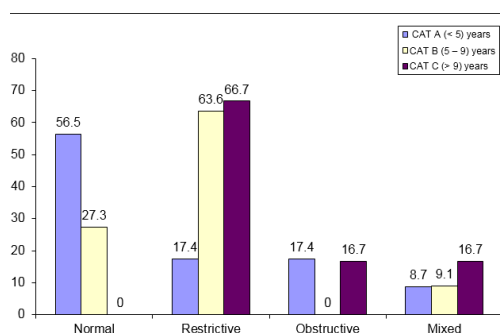


Figure 7: PFT findings

with R.A.^{11,12}

In this study, 40 cases were selected after satisfying inclusion and exclusion criteria. After detailed history taking and clinical assessment of articular and respiratory symptoms, baseline investigations and serological markers were done for every patient, followed by spirometry and radiological investigations. The gender distribution in this study was predominately female, with a female-to-male ratio of 3.4:1 (22.5% men and 77.5% women). According to Ankoor Shah et al.,⁴ females were affected three times more than males. Males made up 26.9% of the population, while females made up 73.1%, according to a study by Doran MF, Ponal et al.¹³ In a study conducted by Raniga S, Sharma P et al.¹⁴ in 2006, the female-to-male ratio was 3.193:1 (23.3% males and 76.7% females)

The mean age in this study was 39.92 years. In a study by Raniga et al.,¹⁴ the patient's average age was 47.1 years, almost identical to the present study. The mean age of the study group in a study by R Prasad et al.¹⁵ was 52.6 years (18–66 years). This study's age distribution is nearly comparable to theirs.

According to this study, the mean height, weight, and B.M.I. of the cases were 158.08 cm, 64.79 kg, and 26.01, respectively, matches the study by Premsundar et al.,¹⁶ where the average weight and height were 61.46 kg and 156.7 cm, respectively.

In this study, it was observed that rheumatoid arthritis had an average duration of 5.38 years. For most cases (57.5%), it was between 5 and 9 years. The average disease duration in a study by Tanaka et al.¹⁷ on rheumatoid arthritis-related pulmonary disorders was 7.6–9.2 years. The average disease duration in a study by Stephen C. Morrison et al.¹⁸ was 12.4 years

In this study, it was observed that the most common respiratory symptom was a dry cough, which was present in 18 out of 40 cases (45%) and was followed by dyspnea in 17 out of 40 cases (42.5%). In a study conducted by G S Gaude et al.,¹² dyspnea was the most prevalent symptom in 57% of cases (68 out of 119), followed by dry cough (59 out of 119)

In this study, all the cases had morning stiffness. Only small joints were involved in 20 no. of the cases (50%), only large joints were involved in 4 cases (10%), and both small and large joints were involved in 16 cases (40%). Subcutaneous nodules were found in 20 cases (50%). The joint deformity was seen in 12 cases (30%). According to a study by Vedula Murugan et al.,¹⁹ 12 out of 13 cases (92%) who had rheumatoid nodules were R.F. positive. Similar to this study, Tarik al assadi et al.²⁰ all study participants had morning stiffness that lasted longer than an hour.

In this study, it was found that 24 out of 40 cases (60%) had abnormal PFT patterns, including restrictive patterns in 15 (37.5%), obstructive patterns in 5 (12.5%) and mixed patterns in 4 (10.0%) cases. As far as the relationship between the duration of disease and a pattern of PFT is concerned, 43.5% of cases (10 out of 23) had PFT changes with a duration of fewer than five years., 72.7% of cases (8 out of 11) with a duration between 5 to 9 years showed abnormal PFT pattern. Those having a duration of more than nine years had an aberrant PFT pattern in all cases. PFT pattern was abnormal, which was equally distributed between obstructive and restrictive patterns (17.4% cases each) among cases with less than the five-year duration of R.A. However, the cases with more than five years disease duration had PFT pattern that was most of the restrictive pattern. A p-value of the study was found to be 0.016, suggesting a significant relation of PFT changes with the duration of disease in this study. In a study by Madhavan et al.⁶ on 30 R.A. cases, 11 (36.6%) had abnormal lung function tests. Six cases (20%) had a mild airway blockage, three (10%) had a restrictive lung disease, and two (6.6%) had a considerable airway illness. In a study by R Prasad et al.,¹⁵ spirometry revealed restrictive patterns in 52.9% of cases (Mean FEV1/FVC 86.9% and Mean FVC 1.16 Liter), obstructive patterns in 11.8% of cases, and mixed patterns in 35.3% of cases. This study is comparable to Prasad et al.¹⁵ no relationship between the number of cases, disease duration, or severity of the restricted PFT anomaly was found in a study by Cervantes-Perez et al.⁷ Though according to a study by Müller-Leisse C et al.,⁸ R.A. with H.R.C.T. results was linked to greater levels of R.F., they could not find any relation between pulmonary structural alterations and the length of the disease. However, like this study, a study by Vedula Murugan et al.,¹⁹ the length of R.A. and variations in PFT are positively correlated, and a study by Lauren Prismo, Matthew et al.⁹ also found R.A. is linked to an increased risk of both restrictive and obstructive patterns.

4.1. Strength and limitations

Though this study was done in a single centre during covid-19 pandemic restrictions, it still shows significant PFT abnormalities during the duration of the disease.

5. Conclusion

Rheumatoid arthritis is an autoimmune disease characterized by chronic inflammatory symmetrical polyarthritis associated with multi-systemic involvement. Pulmonary involvement frequently co-exists with rheumatoid arthritis. Assessment of pulmonary function gives insight into various types of pulmonary function abnormalities. It was found that early pulmonary involvement in the form of PFT abnormalities was observed in rheumatoid arthritis. With the increased duration of rheumatoid arthritis, pulmonary involvement becomes more severe. Cases with longer duration of rheumatoid activity had significant pulmonary involvement either in restrictive and/or obstructive patterns. It was also observed that pulmonary involvement becomes a more restrictive pattern with a prolonged duration of rheumatoid arthritis. With the increased duration of rheumatoid arthritis, radiological abnormalities, either in chest X-Ray or H.R.C.T. chest, were present in most cases. However, the PFT abnormalities were observed earlier than the radiological findings. Hence PFT should be done at the earliest as a routine and repeated periodically in rheumatoid arthritis cases.

6. Source of Funding

None.

7. Conflict of Interest

None.

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