

## Pulmonary Function Test Disorders in Rheumatoid Arthritis Patients – A Hospital Based Study

Iqra Jan<sup>1</sup>, Parvaiz A Koul<sup>2</sup>, Mohd I dar<sup>3\*</sup>, Fayaz A Sofi<sup>4</sup><sup>1</sup>PhD, Immunology and Molecular Medicine Skims, Soura<sup>2</sup>HOD, Department of Medicine Skims, Soura<sup>3</sup>Senior Resident, Cardiology Skims, Soura<sup>4</sup>Head Division of Rheumatology Skims, SouraDOI: [10.36347/sjams.2020.v08i01.046](https://doi.org/10.36347/sjams.2020.v08i01.046)

| Received: 16.01.2020 | Accepted: 23.01.2020 | Published: 29.01.2020

\*Corresponding author: Mohd Iqbal Dar

### Abstract

### Original Research Article

In a hospital based case control study, in which 50 patients of RA and 50 healthy controls were studied with respect to their demography, disease activity, disease duration and PFT. Mean age of Rheumatoid arthritis (RA) patients and controls was  $46.86 \pm 10.51$  and  $46.68 \pm 10.65$  years respectively. Patients and controls were in the age group of 40-49 and 50-59. RA group constituted 16(32%) and control group constituted 6(12%) of smokers ( $p=0.0016$ ). Mean BMI in the RA patients was significantly lower compared to controls ( $p=0.027$ ). RA patients had significantly lower mean FVC% compared to controls ( $p<0.001$ ). Mean FEV1% was also significantly lower in RA patients compared to the controls ( $p<0.001$ ). Mean FEV1/FVC in RA patients was significantly reduced than in controls ( $p=0.012$ ). However mean disease duration  $5.98 \pm 4.3$  years showed no significance with PFT abnormality. Also mean DAS28 showed no relation with PFT abnormality. Obstructive and Restrictive pulmonary dysfunction was found in 14(28%) and 19(38%) in RA patients respectively compared to that of 0% and 2(4%) in healthy controls respectively ( $p<0.001$ ). However use of drugs like Methotrexate, Leflunomide and others in RA patients showed less significance with lung function abnormality. Also spirometric indices like FVC, FEV1, and FEV1/FVC were found to be reduced in smoking RA patients compared to RA patients independent of smoking. From the above observations it can be concluded that pulmonary dysfunction in RA patients diagnosed by Pulmonary Function Test may pick up the abnormality early and confer a chance of early intervention.

**Keywords:** Rheumatoid arthritis, pulmonary function tests, FVC.

**Copyright @ 2020:** This is an open-access article distributed under the terms of the Creative Commons Attribution license which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use (NonCommercial, or CC-BY-NC) provided the original author and source are credited.

## INTRODUCTION

Rheumatoid arthritis is a chronic, systemic and inflammatory disorder primarily affecting joints. It may result in painful and deformed joints which can lead to loss of function. Signs and symptoms may prevail in other organs also. RA affects about 0.5% to 1% of adults in the developed world with 5 to 50 per 100,000 people newly developing the condition each year [1]. Onset is uncommon under the age of 15 and from then on the incidence rises with age until the age of 80. Women are affected 3 to 5 times as often as men [2]. Women usually develop the disease between 40 and 50 years of age and for men somewhat later [3]. RA primarily affects joints but other organs are also affected in more than 15-20% of individuals. Various other commonly affected systems are skin, lungs, kidneys, heart, blood vessels, eyes, liver, blood, brain, bones. Constitutional symptoms of the disease include fatigue, low grade fever, morning stiffness, loss of

appetite, loss of weight are common manifestations seen in people with active RA [4]. RA is often associated with Pleural disease (20-40%), interstitial pneumonitis (5-10%), Nodules (1%), interstitial fibrosis, Bronchiolitis obliterans, Organizing pneumonia, Pulmonary vasculitis [5]. Interstitial lung disease is not only the most common but also the most serious form of the lung involvement in RA and its incidence in different individuals varies from 1-58% [6-10]. ILD is clinically detected in less than 5% of the RA patients [11], although studies have shown much high prevalence of ILD by aid of HRCT [12], which closely co-relates with the results of the open lung biopsy in other connective tissue disorder [13], although less well with PFTs [14]. Limited evidence is available to suggest that relatively small number of patients die from respiratory failure in Rheumatoid Arthritis patients [15,16]. Tools to monitor remission in RA are: DAS28, ACR-EULAR criteria, Provisional Definition of

Remission of Rheumatoid Arthritis, Simplified Disease Activity Index (SDAI) and Clinical Disease Activity Index (CDAI) [17].

Pulmonary involvement is common in RA and the most severe extra articular involvement ranking second cause of mortality in this population. RA can affect lung parenchyma airways and pleura which is responsible for 10-20% of all mortality in these patients. Spirometry being widely available can be utilized to screen and monitor RA patients to detect PFT abnormality early as most of these patients are asymptomatic for long time and hence will help in early intervention.

Since RA is the widely encountered disease in medical and pulmonary clinics there is paucity of literature about the prevalence of spirometric abnormalities in these patients so as to understand if early spirometric abnormalities could point to an underlying disorder and a serious inquiry into the causation of such abnormalities. The current study was designed against this backdrop to study the presence of spirometric abnormalities in patients with RA and try to co-relate the presence of these abnormalities with other indicators of disease severity. The study is aimed to implement the positive results of the study for following our RA patient population and manage their disease in better fashion.

### MATERIALS AND METHODS

This study which was carried out in the department of General Medicine and Division of Rheumatology at SKIMS Soura from Dec 2013-Dec 2014. Written informed consent was taken from the participants of study. The case group include diagnosed patients of RA which had age above 20 yrs. from both genders. Individuals having any collagen vascular/autoimmune disease, exposure to dust such as asbestos/silica, having any lung disease, undergone any recent surgery, having unstable cardiovascular status and were in last trimester of pregnancy were excluded from the study. The evaluation for all studied individual included Haemogram with ESR, C reactive protein, Rheumatoid Factor, Chest X-Ray, Electrocardiogram and Spirometry according to standards of ATS/ERS criteria.

The various parameters measured by spirometry, on the basis of which different lung function abnormalities could be detected were Forced Vital Capacity (FVC), Forced Expiratory Volume in First second (FEV1), Forced Expiratory Flow (FEF), Peak Expiratory Flow (PEF), Total Lung Capacity (TLC), and Residual Volume (RV). Five step approach of spirometric interpretation was applied for diagnosis of different lung function. Before doing Spirometry all base line parameters like height, weight, blood pressure, respiratory rate, SpO2, and pulse were measured and spirometric procedure was repeated 15-20 minutes after the inhalation of the bronchodilator (mainly Salbutamol). Individuals having DAS28 score of 3.2 or more were taken for having active disease.

### RESULTS AND OBSERVATIONS

In this study which included 50 cases of RA patients and 50 controls. Mean age of cases was 46.86±10.51 as compared to 46.68±10.65 in controls (p=0.932) the difference being non-significant. Among both case control group the no of females was 36(72%). The number of smokers among Rheumatoid Arthritis patients was 32% compared to 12% among control group. The difference being significant (p=0.016). Control group in this study had higher mean BMI compared to case group (p=0.027 significant). On comparing different spirometric parameters mean percentage of predicted FVC was significantly lower in cases compared to that of controls (p<0.001). Mean percentage of predicted FEV1 also was significantly lower in Rheumatoid Arthritis patients compared to that of controls (p<0.001) Figure1.

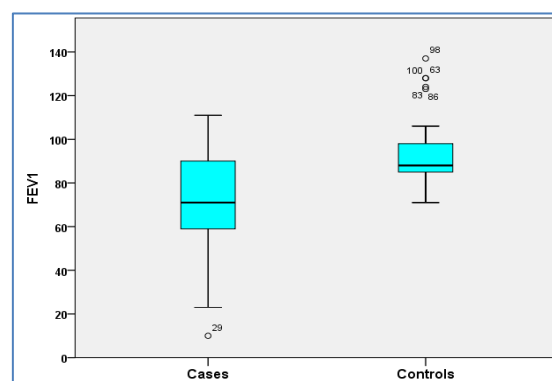


Fig-1: Error bar showing FEV1 in study subjects: cases versus controls

Table-1: Disease activity versus PFT

Disease	N	PFT			
		Normal	Abnormal		Total
			Obstructive	Restrictive	
Inactive	12	3(25.0%)	5(41.7%)	4(33.3%)	9(75.0 %)
Active	38	14(36.8%)	9(23.7%)	15(39.5%)	24(63.2%)

Mean FEV1/FVC also was significantly lower in RA patients compared to that of controls (p<0.012). In our study it was found that mean duration of RA

disease of patients was 5.98±4.3 years. Mean Disease Activity Score of 28 joints (DAS28) in RA patients was found to be 3.9±1.1, which implied that overall

Rheumatoid Arthritis was active. On the basis of DAS28 score of individual RA pts it was found that active RA was found in 76% of cases. On comparing DAS28 values with spirometric parameters, it was found that 63% of patients with active disease had abnormal PFT among which 23.7% had obstructive type and 39.5% had restrictive type pulmonary dysfunction (table1).

The commonest symptom manifested by RA patients was cough followed by reflux syndrome and breathlessness. On comparing PFT abnormality among cases and controls, it was found that obstructive abnormality was found in 14(28%) of patients in RA group compared to 0% in control group, and restrictive abnormality was found in 19(38%) of RA pts compared to that of 2(4%) in controls, the difference being statistically highly significant ( $p < 0.001$ ). However drug intake like Methotrexate and Leflunomide showed no significance with relative lung function abnormalities. Also lung function abnormalities showed no significance with relation to duration of RA among case group. This study proved good evidence that the spirometric indices like FVC, FEV1, and FEV1/FVC had positive co-relation with RA independent of smoking.

## DISCUSSION

Our study which was primarily based to evaluate out the lung function abnormality in Rheumatoid Arthritis (RA) patients. Many parameters were evaluated and our observation found link with other studies. Mean age of the RA pts was consistent with the literature [18]. Risk factor of smoking which was found in 32% of RA group and 12% of control group, which was statistically significant ( $P = 0.016$ ), similar results were found in literatures [19, 20]. RA pts which were having significantly lesser BMI than control group, is understandably due to debilitating nature of RA. Well characterized pulmonary disorder found in RA pts include pleural effusion, Rheumatoid nodules, pulmonary fibrosis and caplans syndrome [21, 22], the existence of the specific airway obstruction is a subject of debate as we found obstructive abnormality in 14(28%) and restrictive abnormality in 19(38%) of RA pts compared to that of 0% and 2(4%) in control group respectively ( $p < 0.001$ ), however Novet et al. found obstructive disorders in 50% of their RA cases. Like other studies we also found significant decrease in different spirometric parameters like FEV, FVC and FEV1/FVC in RA pts compared to that of controls, and also significant reduction was also found in same parameters when case group was adjusted for smoking. Respiratory disorder in RA can be due to various factors which include underlying bronchial hyperreactivity [23], abnormalities in distal bronchioles [24], and association with the deficit in  $\alpha$ -1 antitrypsin [25], recurrent respiratory infection [26] or treatment with pencillinamine [27]. Although the relationship between the two needs to be established in future

epidemiological studies. No significant relation was observed between RA disease duration and any pulmonary function abnormality in our study which in harmony with literature with Avnon et al. [28] but different from that found out by Vergnenegre et al. [29]. Also no relation was found out between RA disease activity and spirometric indices which are same as that of literature [29], but different from observation found by Tariq Al Assadi [30], as their sample size was quiet small. Although Methotrexate and Leflunomide effect lungs in RA patients [31, 32], but our observation did not find any significant relation between the two, which is same as that of literature [33]. Significant Restrictive and Obstructive spirometric defects in RA group co-relate with disease activity.

Our study is limited by a small sample size and the possibility of an already existing disorder that could be the confounder of the final analysis. Radiological evaluation, bronchoscopy or other invasive diagnostic tests like lung biopsies, that were not the part of the current study, could be added to the evaluation scheme so as to better understand the profile of lung diseases in RA patients in Kashmiri population.

## CONCLUSION

Combination of smoking and progressive rheumatoid arthritis in this study population lead to abnormal pulmonary functions. Progressive RA is also a responsible factor for lowering of BMI in affected individuals. Early diagnosis of RA with the aid of better diagnostic evaluation is necessary, in order to save the patients from debilitating effects of this noxious disease.

## REFERENCE

1. Scott DL, Wolfe F, Huizinga TW. "Rheumatoid arthritis". *Lancet*. 2010; 376 (9746): 1094–108.
2. Shah, Ankur. *Harrison's Principle of Internal Medicine* (18th Ed.). United States: McGraw Hill, 2738.
3. Alamanos Y, Voulgari PV, Drosos AA; Voulgari; Drosos. "Incidence and prevalence of rheumatoid arthritis based on the 1987 American College of Rheumatology criteria: a systematic review". *Semin. Arthritis Rheum*. 2006; 36 (3): 182–8.
4. Epler GR. Bronchiolitis obliterans organizing pneumonia, 25 years: a variety of causes, but what are the treatment options? *Expert Rev Respir Med*. 2011; 5(3):353-61.
5. Kim DS. Interstitial lung disease in rheumatoid arthritis: Recent advances. *Curr Opin Pulm Med*. 2006; 12(5):346-53.
6. Gabbay E, Tarala R, Will R, Carroll G, Adler B, Cameron D, et al. Interstitial lung disease in recent onset rheumatoid arthritis. *Am J Respir Crit Care Med*. 1997; 156(2 Pt 1):528-35.
7. Nannini C, Medina Y, Achenbach SJ, Crowson CS, Ryu JH, Gabriel SE, et al. Does the incidence and

- mortality of obstructive lung disease differ between subjects with and those without rheumatoid arthritis? A population-based study. *Arthritis Rheum.* 2010; 62(6): 1583-1591.
8. Kelly CA. Rheumatoid arthritis, classical lung disease. *Bailliere's Clin Rheumatol.* 1993; 7:1-16.
  9. Fewins HE, McGowan I, Whitehouse GH, Williams J, Mallya R. High definition computed tomography in rheumatoid arthritis associated pulmonary disease. *Br J Rheumatol.* 1991; 30:214-6.
  10. McDonagh J, Greaves M, Wright AR, Heycock C, Owen JP, Kelly CA. High resolution computed tomography of the lungs in patients with rheumatoid arthritis and interstitial lung disease. *Br J Rheumatol.* 1994; 33:118-22.
  11. Wells AU, Hansell DM, Corrin B, Harrison NK, Goldstraw P, Black CM, Du Bois RM. High resolution computed tomography as a predictor of lung histology in systemic sclerosis. *Thorax.* 1992 Jul 1; 47(7):508-12.
  12. Cruikshank B. Interstitial pneumonia and its consequences in rheumatoid disease. *Br J Dis Chest.* 1959; 53:226-35.
  13. Kelly, Janis. DAS28 not always a reliable indicator of treatment effect in RA, *Medscape Medical News.* 2005, 538134.
  14. Doctor L, Snider GL. Diffuse interstitial pulmonary fibrosis associated with arthritis. *Am Rev Respir Dis.* 1962; 85:413-22.
  15. Prevoo ML, Van't Hof M, Kuper HH, Van Leeuwen MA, Van De Putte LB, Van Riel PL. Modified disease activity scores that include twenty-eight-joint counts development and validation in a prospective longitudinal study of patients with rheumatoid arthritis. *Arthritis & Rheumatism: Official Journal of the American College of Rheumatology.* 1995 Jan; 38(1):44-8.
  16. Yazici, Yusuf. "Tools for monitoring remission in rheumatoid arthritis: any will do, let's just pick one and start measuring". *Arthritis Research & Therapy.* 2013; 15: 104.
  17. Atzeni F, Turiel M, Caporali R, Cavagna L, Tomasoni L, Sitia S, Sarzi-Puttini P. The effect of pharmacological therapy on the cardiovascular system of patients with systemic rheumatic diseases. *Autoimmunity reviews.* 2010 Oct 1; 9(12):835-9.
  18. Franck ST, Weg JG, Harkleroad LE, Fitch RF. Pulmonary dysfunction in rheumatoid disease. *Chest.* 1973; 63:27-34.
  19. Sassoon CSH, Mcalpine SW, Tashkin DP, Baydur A, Quismorio FP, Mongan ES. Small airways function in nonsmokers with rheumatoid arthritis. *Arthritis Rheum.* 1984; 27: 1218-1226.
  20. Banks J, Banks C, Cheong B, Umachandran V, Smith AP, Jessop JD, Pritchard MH. An epidemiological and clinical investigation of pulmonary function and respiratory symptoms in patients with rheumatoid arthritis. *QJM: An International Journal of Medicine.* 1992 Nov 1; 85(2-3):795-806.
  21. Nouvet G, Decoux L, Lerebours Pigeonnière C, Thiberville L, Tardif C, Le Loet X. L'exploration fonctionnelle respiratoire au cours de la polyarthrite rhumatoïde: aspect évolutif chez 50 patients (Abstract). *Rev Mal Respir.* 1988; 5: S139.
  22. Shadick NA, Fanta CH, Weinblatt ME, O'Donnell W, Coblyn JS. Bronchiectasis: a late feature of severe rheumatoid arthritis. *Medicine.* 1994; 73: 161-170.
  23. Hassan WU, Keaney NP, Holland CD, Kelly CA. Bronchial hyperreactivity and airflow obstruction in rheumatoid arthritis. *Ann Rheum Dis.* 1994; 53: 511-514.
  24. Le Coz A. Polyarthrite rhumatoïde et dilatation des bronches. Medical thesis, Université de Rennes, France. *Eur Respir J.* 1990; 10: 1072-1078.
  25. Mountz JD, Turner RA, Collins RL, Gallys KR, Semble EL. Rheumatoid arthritis and small airway function. *Arthritis Rheum.* 1984; 27: 728-736.
  26. Geddes DM, Webley M, Emerson PA. Airways obstruction in rheumatoid disease. *Ann Rheum Dis.* 1979; 38:222-225.
  27. Radoux V, Menard HA, Begin R, Decary F, Koopman WJ. Airways disease in rheumatoid arthritis patients. *Arthritis Rheum.* 1987; 30: 249-256.
  28. Avnon LS, Manzur F, Bolotin A, Heimer D, Flusser D, Buskila D, Sukenik S, Abu-Shakra M. Pulmonary Functions Testing in Patients with Rheumatoid Arthritis. 2009; 11:83-87.
  29. AVernenegre, N Pugnere, M T Antonini, M Arnaud, B Milloni, R Treves, F Bonnaud. *Eur Respir J.* 1997; 10: 1072-1078.
  30. Tarik Al Assadi. *Oman Med J.* 2009; 24(2): 84-88.
  31. Gupta A and Fomberstein B. "Evaluating cardiovascular risk in rheumatoid arthritis". *Journal of Musculoskeletal Medicine.* 2009; 26 (8): 481-94.
  32. Saravanan V. Committee on Safety of Medicines. Methotrexate and pneumonitis: new recommendations on monitoring for pulmonary symptoms. *Curr Probl Pharmacovigilance.* 2003; 29:5.
  33. Beyeler C, Jordi B, Gerber NJ, V. Hof IM. Pulmonary function test in Rheumatoid Arthritis treated with low dose Methotrexate: A Longitudinal Study *British Journal of Rheumatology.* 1996; 35:446-452.