

# Pulmonary Function Test among Asymptomatic Rheumatoid Lung Disease Patients

IZAZ-UR-RAHMAN<sup>1</sup>, HAMID JAVAID QURESHI<sup>2</sup>, BUSHRA GOHAR SHAH<sup>3</sup>

## ABSTRACT

**Background:** Among rheumatoid arthritis patients, extra-articular manifestations are common. Pulmonary disease is the second most common cause of death among rheumatoid arthritis patients after infections. There is a great lack of knowledge and awareness among rheumatoid arthritis patients regarding rheumatoid lung disease.

**Aim:** To compare the pulmonary function tests of asymptomatic rheumatoid lung disease patients with the pulmonary function test of healthy individuals.

**Design:** Cross-sectional analytical study.

**Place & duration of study:** Patients were recruited from Fatima Memorial Hospital, Lahore Rheumatology Outpatient Department, from January, 2010 to December, 2010. The research work was conducted at Department of Physiology and Cell Biology of University of Health Sciences, Lahore.

**Methods:** Pulmonary function test of 60 rheumatoid arthritis and 60 age, sex and BMI matched healthy individuals, having no pulmonary signs, symptoms or disease were compared. The data obtained was analyzed by using SPSS version 16.0.

**Results:** FEV<sub>1</sub>% in RA patients [84.50(77.0-92%)], was significantly less ( $p < 0.0001$ ) than in healthy individuals [96.0(96.0-97%)]. FVC% in RA patients [85.0(77.0-93.50%)], was significantly less ( $p < 0.0001$ ) than in healthy individuals [98.0(96.25-99%)]. There was a significant difference ( $p = 0.020$ ) of FEV<sub>1</sub>: FVC ratio [85.15(78.6-88.5)] in RA patients and healthy individuals [84.0(83.0-88.95)].

**Conclusion:** Spirometry (Pulmonary function test) is a cost effective test to detect early pulmonary function decline among asymptomatic rheumatoid lung disease patients.

**Keywords:** Rheumatoid arthritis, rheumatoid lung disease, pulmonary function test.

---

## INTRODUCTION

Rheumatoid arthritis (RA), is a systemic disease characterized by persistent inflammation of the diarthrodial joints with synovial hyperplasia that if continues, results in progressive joint destruction. The prevalence of RA in general population world over ranges from 0.5% to 2%<sup>1</sup>. Among rheumatoid arthritis patients, extra-articular manifestations are common. Pulmonary disease is the second most common cause of death among rheumatoid arthritis patients after infections. The first clinical report of pulmonary involvement in rheumatoid arthritis was published by Ellman and Ball (1948), describing three patients with polyarthritis and interstitial pneumonitis<sup>2</sup>. Caplan, described the classical observation of rheumatoid nodules in chest radiographs of coal miners suffering from rheumatoid arthritis<sup>3</sup>. The first case of rheumatoid lung disease was described by Cudkovic et al, they not only describing the clinical picture but also the spirometric and histological findings. Rheumatoid Arthritis is frequently

associated with pulmonary involvement, the most common manifestation being interstitial lung disease, rheumatoid nodules and pleural effusions, while less common include bronchiolitis obliterans and cricoarytenoid arthritis<sup>4</sup>. Interstitial fibrosis and airway diseases are detected in approximately 25% to 75% of patients with rheumatoid arthritis<sup>5,6</sup>. Rheumatoid arthritis associated interstitial lung disease (RA-ILD), has revealed itself as the true adverse clinical impact among the other pulmonary manifestations of rheumatoid arthritis<sup>7</sup>.

The main objectives of the study were to evaluate the outcome of pulmonary function test in asymptomatic rheumatoid lung disease patients and to compare the pulmonary functions of asymptomatic rheumatoid lung disease patients with the pulmonary functions of healthy subjects.

## SUBJECTS AND METHODS

This was a comparative cross-sectional study, conducted at Physiology Department, University of Health Sciences, Lahore from January, 2010 to December, 2010. Sixty known Rheumatoid arthritis patients fulfilling the American College of Rheumatology criteria for RA<sup>8</sup>, aged 20-60 years,

---

<sup>1</sup>Assistant Professor of Physiology, Saidu Medical College, Swat

<sup>2</sup>Professor of Physiology, Akhter Saeed Medical College, Lahore

<sup>3</sup>Assistant Professor of Physiology, Avicenna Medical College

Correspondence to Dr. Izazur Rahman, Assistant Professor Email: rahmanizaz@yahoo.com Cell: 0345-7272244

having no pulmonary symptoms were taken from Rheumatology Outdoor Patient Department of Fatima Memorial Hospital, Lahore. Purposive non-probability sampling technique was used to recruit volunteers for the study. Control group comprised sixty (60) healthy subjects with matched age, sex and BMI who were attendants of the patients and from the residential areas near University of Health Sciences, Lahore. **Exclusion criteria:** Subjects with following conditions were excluded: Systemic pulmonary disorders, smokers and ex-smokers, chest wall and spinal column abnormalities, obesity, patients having BMI >30Kg/m<sup>2</sup>, failure to produce acceptable and reproducible spirometry, other rheumatological conditions and any cardiac disease.

Written informed consent was taken from each study participant. Complete demographic information, history, physical and systemic examination were taken. Height, weight were recorded and BMI was calculated and the data was recorded on pre-designed data form. Blood samples were taken by aseptic technique.

**Spirometry (Pulmonary Function Test):** Pulmonary function was assessed by Spirometry. Spirogram was obtained from all participants according to the American Thoracic Society (ATS) criteria<sup>9</sup>. A flow measuring type spirometer (Spirolab II, bidirectional digital turbine type; MIR srl, Rome, Italy) that meets the ATS accuracy criteria was used in this study.

**Spirometric data:** The measurements used in data analysis are (1) FVC% (2) FEV<sub>1</sub>% and (3) FEV<sub>1</sub>: FVC ratio. The FVC and FEV<sub>1</sub> are reported as both the measured volume in litres and as a percentage of the predicted or reference value for individual of that age, height, gender and ethnicity. FEV<sub>1</sub>: FVC ratio was calculated from the measured volume in liters and then percentage was taken.

The data was entered and analyzed by SPSS 17.0. The data was expressed as mean±SD for normally distributed quantitative variables and median (IQR) for non-normally distributed quantitative variables. Frequencies, percentages or graphs were given for categorical variables. The data was non-normally distributed for the quantitative variables, so non-parametric statistics i.e., Mann-Whitney U test was applied. A *p*-value of < 0.05 was considered statistically significant for all purposes.

## RESULTS

One hundred and twenty (120) subjects were recruited for this study, out of which 60 were rheumatoid arthritis patients and 60 were age and sex matched healthy individuals. In the RA group, there were 51 females and 9 males and in healthy

individuals group, 51 were females and 9 were males. Mean±SD age of the RA group was 41.45±10.58 years while the mean±SD age of the healthy individuals group was 43.38±7.36 years.

Median disease duration of the RA patients was 5.50(4-8) years. 32(53.33%) patients were RA factor positive, while 28(46.66%) patients were RA factor negative. 10(16.66%) patients were having positive family history for RA, while 50(83.33%) had no family history of RA. 17(28.33%) had knowledge about RA, while only 03(5%) patients had knowledge about extra articular manifestations of RA. Median FEV<sub>1</sub>% was 84.50(77.0-92.0%), median FVC% was 85(77.0-93.50%), median FEV<sub>1</sub>: FVC was 85(78.67-88.51) (Table 1).

Among healthy group, 3 individuals were RA factor positive, while 57 were RA factor negative. 2 individuals had positive family history for RA, while 58 had no family history for RA. Median FEV<sub>1</sub>% was 96.0(96.0-97.0%), median FVC% was 98(96.25-99%), median FEV<sub>1</sub>: FVC was 84(81.0-87.7).

FEV<sub>1</sub>% in RA patients [84.50(77.0-92%)], was significantly less (*p*=0.001) than in healthy individuals [96.0(96.0-97%)]. FVC% in RA patients [85.0(77.0-93.50%)], was significantly less (*p*=0.001) than in healthy individuals [98.0(96.25-99%)].

There was a significant difference (*p*=0.020) of FEV<sub>1</sub>: FVC ratio [85.15(78.6-88.5)] in RA patients and healthy individuals [84.0(83.0-88.95)] (Table 2).

Table 1: Data of the rheumatoid arthritis group.

Variables	Median (IQR)
FEV <sub>1</sub> %	84.50(77-92%)
FVC%	85(77-93.50%)
FEV <sub>1</sub> : FVC	85.15(78.6-88.5%)
RA factor positive	32(53.33%)
Disease duration (years)	7.33±12.0
Positive family history	10(16.66%)
Knowledge about RA	17(28.33%)
Knowledge about extra articular manifestations of RA	3(5%)

Table 2: Comparison of pulmonary functions in study groups.

	Rheumatoid arthritis	Healthy individuals	<i>p</i> -value
FEV <sub>1</sub> %	84.50(77.0-92.0)	96.0(96.0-97.0)	0.001*
FVC%	85.00(77-93.5)	98(96.25-99)	0.001*
FEV <sub>1</sub> : FVC ratio	85.15(78.6-88.5)	84.0(83.0-88.95)	0.020*

Data presented as Median (IQR)

\*Significant at *p* < 0.05 level

## DISCUSSION

It is very important to timely recognize the pulmonary involvement in RA, because respiratory involvement is the second leading cause of mortality in patients with RA. Pulmonary involvement or decline in its

function may not be routinely sought by physicians and rheumatologists in the absence of cost-effective and time-efficient means of screening.

In the present study, it has been demonstrated that PFTs, could screen-out pulmonary function decline in patients with RA and could identify patients, who were to be further worked up. A significant decline in FEV<sub>1</sub>% and FVC% among RA patients as compared to healthy subjects was observed. These results were present in those RA patients, who had no pulmonary signs and symptoms. So, it demonstrated early pulmonary decline in asymptomatic rheumatoid lung disease patients.

A lot of work has been done on the pre-clinical rheumatoid lung disease internationally, but most of the work is on detection of rheumatoid lung disease on HRCT, not on its detection by spirometry. Gochuicoet al<sup>10</sup> and Karazincir et al<sup>11</sup> reported the pre-clinical decline in pulmonary functions in rheumatoid disease patients. Same results comparable to our results were observed by them, i.e., decline in FEV<sub>1</sub>% and FVC%. Similar results were also observed by other researchers among RA patients but they had selected all patients having RA, irrespective of pulmonary signs and symptoms. Banks et al<sup>12</sup> reported a significant decline in FEV<sub>1</sub>% and FVC% in RA patients with normal FEV<sub>1</sub>: FVC ratio. Mohd Noor et al<sup>13</sup> reported FEV<sub>1</sub>% (85.8%), FVC% (83.4%). Sheianovet al<sup>14</sup> observed a decline in both FEV<sub>1</sub> (83%) and FVC% (78.7%). Pappas et al<sup>15</sup> found FEV<sub>1</sub>% (85%), FVC% (71%) among RA patients.

In a retrospective study done by Bongartz et al<sup>16</sup>, a decrease in both FEV<sub>1</sub>% and FVC% in patients with RA, with a more decline in FVC% was shown. Bilgiciet al<sup>17</sup> and Habibet al<sup>18</sup> have reported obstructive, restrictive and mixed pattern of pulmonary involvement in patients with RA.

In a prospective study done by Linstowet al<sup>19</sup>, a progressive decline in pulmonary functions over eight years was reported. Cortet et al<sup>20</sup> observed a significant decline in FEV<sub>1</sub>% as compared to FVC% in their study. Zrouet al<sup>21</sup> showed decline in both FEV<sub>1</sub>% and FVC% among RA patients. In a 5 years prospective study done by Avon et al<sup>22</sup>, a significant decline in pulmonary functions was observed and they noted small airways obstruction as well as restrictive pattern among RA patients.

Cortet et al<sup>20</sup> showed an obstructive pattern in a cohort of RA patients, FEV<sub>1</sub>: FVC ratio was 78.9%. Perez et al<sup>23</sup> and Collins et al<sup>24</sup> had also reported a decreased FEV<sub>1</sub>: FVC ratio among RA patients, showing obstructive pattern of lung involvement. These results were contradictory to our results in which we observed a higher value of FEV<sub>1</sub>: FVC ratio

than healthy subjects, which shows a restrictive pattern among our RA patients. Similar results were observed by Pappas et al<sup>25</sup>, i.e., 85%. Similarly in a prospective study done by Hyland et al<sup>26</sup> a restrictive pattern in 155 RA patients as compared to 95 control subjects was observed. It becomes evident from our study that it is not the duration of the primary disease (RA) which affects the pulmonary functions of patients with RA; it is the aggressiveness of the rheumatoid arthritis disease, which affects the pulmonary function in rheumatoid arthritis patients.

It has been observed that only 17(28.33%) RA patients were having sound knowledge about their disease (diagnosis, management and prognosis). It clearly shows lack of awareness among our RA patients about their long life disease. Similarly, when we inquired from them about extra-articular manifestations of RA, only 03(05%) RA patients had satisfactory knowledge. This again shows unawareness of our RA patients about the extra-articular manifestations including pulmonary involvement, which can affect them in their future life and can have a high morbidity and mortality.

## CONCLUSION

Pulmonary functions decrease early in rheumatoid arthritis patients, even when they have no pulmonary signs and symptoms. Detection of early rheumatoid lung disease can be done by spirometry, which is a cost effective test and can be done in routine clinical practice.

## REFERENCES

1. Anthony SF, Eugene B, Dervis LK, Stephen LH, Dan LL, Jameson JL and Joseph L. (eds) (2008). *Harrison's Principles of Internal Medicine*. 17<sup>th</sup>ed. New York: USA. 2083-2092.
2. Ellman P and Ball RE. Rheumatoid disease with joint and pulmonary manifestations. *Br Med J*. 1948; 2: 816-20.
3. Caplan A. Certain unusual radiological appearances in the chest of coal miners suffering from rheumatoid arthritis. *Thorax*. 1953; 8: 29-37.
4. Cudkowicz I, Madof IM and Abelmann WH. Rheumatoid lung disease. *Br J Dis Chest*. 1961; 55: 35-9.
5. Akira M, Sakatani M and Hara H. Thin-section CT findings in rheumatoid arthritis associated lung disease: CT-patterns and their courses. *J Comput Assist Tomogr*. 1999; 23: 941-8.
6. Demir R, Bodur H, Tokoglu F, Olcay I, Ucan H and Borman P. High resolution computed tomography of the lungs in patients with rheumatoid arthritis. *Rheumatol Int*. 1999; 19: 19-22.
7. Brown KK. Rheumatoid Lung Disease. *Proc Am Thorac Soc*. 2007; 4: 443-8.

8. Arnett FC, Edworthy SM, Bloch DA, MacShane DJ, Fries, JF and Cooper NS. The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. *Arthritis Rheum.* 1988; 31: 315-24.
9. Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R and Coates A. Standardization of spirometry. *EurRespir J.* 2005; 26: 319-38.
10. Gochuico BR, Avila NA, Chow CK, Novero LJ, Wu HP, Ren P, et al. Progressive preclinical interstitial lung disease in rheumatoid arthritis. *Arch Intern Med.* 2008; 168: 159-66.
11. Karazincir S, Akoglu S, Guler H, Balci A, Babayigit C and Egilmez E. The evaluation of early pulmonary involvement with high resolution computerized tomography in asymptomatic and non- smoker patients with Rheumatoid Arthritis. *TuberkToraks.* 2009; 57: 14-21.
12. Banks J, Banks C, Cheong B, Umachandran V, Smith AP, Jessop JD, et al. An epidemiological and clinical investigation of pulmonary function and respiratory symptoms in patients with Rheumatoid arthritis. *QJ Med.* 1992; 85: 795-806.
13. Mohd Noor N, MohdShahrir MS, Shahid MS, Abdul Manap R, ShahizonAzura AM and Azhar Shah S. Clinical and resolution tomography characteristics of patients with Rheumatoid Arthritis Lung Disease. *Int J Rheum Dis.* 2009; 12: 136-44.
14. Sihvonen S, Korpela M, Laippala P, Mustonen J and Pasternack A. Death rates and causes of death in rheumatoid arthritis: a population based study. *Scand J Rheumatol.* 2004; 33: 221-7.
15. Pappas DA, Giles JT, Connors G, Lechtzin N, Bathon JM and Danoff SK. Respiratory symptoms and disease characteristics as predictors of pulmonary function abnormalities in patients with Rheumatoid arthritis: an observation cohort study. *Athritis Res Ther.* 2010; 12: 104-9.
16. Bongartz T, Nanninic C, Medina-Velasquez YF, Achenbach SJ, Crowson CS, Ryu JH, et al. Incidence and mortality of interstitial lung disease in rheumatoid arthritis: a population based study. *ArthritisRheum.* 2010; 62: 1583-91.
17. Bilgici A, Ulusoy H, Kuru O, Celen KC, Unsal M and Danaci M. Pulmonary involvement in rheumatoid arthritis. *Rheumatol Int.* 2005; 25: 429-35.
18. Habib HM, Eisa AA, Arafat WR. and Marie MA. Pulmonary involvement in early rheumatoid arthritis patients. *Clinical Rheumatol.* 2011; 30: 217-21.
19. Linstow M, Ulrik CS, Kriegbaum NJ, Backer V and Oxholm P. An 8-year follow-up study of pulmonary function in patients with rheumatoid arthritis. *Rheumatol Int.* 1994; 14: 115-8.
20. Cortet B, Flipo R, Remy-Jardin M, Coquerelle P, Duquesnoy B, Remy J, et al. Use of high resolution computed tomography of lungs in patients with Rheumatoid Arthritis. *Annals of the Rheumatic Diseases.* 1995; 54: 815-9.
21. Zrour SH, Touzi M, Beji I, Golli M, Rouatbi N, Younes M, et al. Correlations between high-resolution computed tomography of the chest and clinical function in patients with rheumatoid arthritis: prospective study in 75 pateints. *Joint Bone Spine.* 2005; 72: 41-7.
22. Avon LS, Manzur F, Bolotin A, Heimer D, Flusser D, Buskila D, et al. Pulmonary function testing in patients with rheumatoid arthritis. *Isr Med Assoc J.* 2009; 11: 83-7.
23. Perez T, Remy-Jardin M. and Cortet B. Airways involvement in rheumatoid arthritis: clinical functional and HRCT findings. *Am J RespirCrit Care Med.* 1998; 157: 1658-65.
24. Collins RL, Turner RA, Myron JA, Whitley NO and McLean, RL. Obstructive pulmonary disease in rheumatoid arthritis. *Arthritis & Rheumatism.* 2005; 19: 623-8.
25. Pappas DA, Giles JT, Connors G, Lechtzin N, Bathon JM. andDanoff, SK. Respiratory symptoms and disease characteristics as predictors of pulmonary function abnormalities in patients with Rheumatoid arthritis: an observation cohort study. *Athritis Res Ther.* 2010; 12: 104-9.
26. Hyland RH, Gordon DA, Broder I, Davies GM, Russell ML, Hutcheon MA, Reid GD, et al. A systemic controlled study of pulmonary abnormalities in rheumatoid arthritis. *J Rheumatol.* 1983;10: 395-405.