Original Article

Pulmonary involvement for patients with Rheumatoid Arthritis: Spirometric study

Ahmed S. Hameed Al-Tayyar* **MBChB.**
Najeeb H. Mohammed* **MBChB , PhD.**
Nizar A. Jasim** **MBChB , FICMS(int.Med) , FICMS(Rheu.&med.Rehab).**

Summary:

Background: Pulmonary involvement in patients with Rheumatoid Arthritis (RA) is a serious extra articular manifestation.

Objective: The aim of the study is to detect pulmonary involvement, classify the type of involvement (whether obstructive, restrictive or mixed), and to find out whether pulmonary system was involved in the early stage of the disease and is asymptomatic and to determine the associated possible risk factors.

Patients and Methods: 82 patients with RA and 40 control subjects were included in this prospective study. They were submitted to medical history, physical measurements (height, weight and BMI) and spirometric evaluation for FVC, FEV1, FEV1%, PEFR and FMF (FEF25-75%).

Results: 42 patients with RA (51%) show abnormal spirometric results, mostly in the form of respiratory restriction in 33 patients (40%), obstructive results in 7 patients (9%); while mixed abnormality in 2 patients (2%). Various risk factors are correlated with reduced spirometric results.Asymptomatic patients with abnormal spirometry found in 9 (11%) and 6 patients (7%) had abnormal results within two years of their articular disease.

Conclusion: Pulmonary involvement is common in Iraqi patients with RA, mostly in the form of respiratory restriction. Pulmonary involvement is believed to be asymptomatic in some patients and even occurs early in the disease process. Various risk factors are found to be correlated with the abnormal spirometry.

Keywords: RA(Rheumatoid Arthritis), Pulmonary Involvement.

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Introduction:

Rheumatoid arthritis (RA) is a systemic autoimmune disorder characterized by inflammatory joint disease as well as extra-articular manifestations. The disease is common; it affects about 1% of adult population (1). The lungs are commonly involved in RA patients in which any of the anatomic compartments can be affected: airways (bronchiectasis, bronchiolitis), vasculature (pulmonary hypertension, vasculitis), pleura (pleuritis, effusions) or parenchyma (rheumatoid nodules, interstitial lung disease [ILD] which can be primary or directly affected by RA. Patients are also at risk for secondary pulmonary complications, with drug toxicities during treatment and opportunistic infections from immunosuppressive therapy being a major concern(2).Multiple risk factors for its development have been identified such as disease duration, smoking, advanced age, disease activity, positive Rheumatoid factor (RF) (3,4).

The prevalence of asymptomatic (preclinical) ILD among individuals with RA is unknown (5). Asymptomatic ILD may be prevalent and progressive among patients having RA (3). Earlypulmonary involvement in patients with RA has been identified and multiple risk factors may increase the incidence of its development (6).

However, No study evaluated pulmonary involvement for Iraqi patients with RA which is the aim of this study.

Patients and Methods:

Eighty two (24 males and 58 females) consecutive patients with RA, who were diagnosed according to ACR 1987 (Amrican CollegeofRheumatology)andACR/EULAR(AmericanCollege of Rheumatology/European League Against Rheumatism) criteria, with an average age of (23-69 years), were involved in this prospective study (7, 8).In addition to 40 control subjects matched for age, height and weight. The patients were attending the outpatient clinic of Rheumatology department in Baghdad medical city for the period between January and May 2012. Each subject was submitted into medical history and clinical examination, physical measurements (height, weight and BMI), assessment of DAS28 (disease activity score) and spirometric examination (pulmonary function test) which included FVC, FEV1, FEV_1%, PEFR and FMF (FEF25-75%) according to ATS/ERS(American Thoracic Society/ European Respiratory Society) standardization (9), using the portable spirometer device, spirodesk (HM-spirowin II mobile wireless monitoring device).

Statistical Analysis: Data were analyzed using SPSS version

*College of Medicine university of Baghdad/ Physiology Department.
** Dept. of Rheumatology College of Medicine university of Baghdad.

18. Statistical methods included: mean ± SD, the independent samples t test (parametric) and Mann- whitney U test (non-parametric) were used to compare results between groups. Pearson s correlations (parametric) and Kruskal-Wallis H (non-parametric) test were used when needed. Results were considered significant at $p<0.05$.

Results:

The results of this study revealed a statistically significant lower values for FVC and FEV_1 for patients with RA as compared with that of controls ($p<0.05$) as in table (1), figure (1).

Table (1): Comparison of spirometric values for patients with RA and control subjects.

Parameter	Patients with RA	Control subjects	P-value
FVC(L)	2.91±0.83	3.38±0.77	0.009*
P%	78.77±16.16	90.93±5.82	0.000*
FEV_1(L)	2.59±0.66	2.83±0.63	0.002*
P%	77.45±16.25	90.7±5.29	0.000*
FEV_1%	82.36±6.98	83.8±3.8	0.166
PEFR(L/s)	5.6±1.79	6.07±1.25	0.195
P%	80.46±19.44	84.77±5.28	0.070
FMF(L/s)	3.2±1.08	3.42±0.79	0.251
P%	95.58±29.25	100.47±15.24	0.254

*P values are considered significant when it is <0.05.

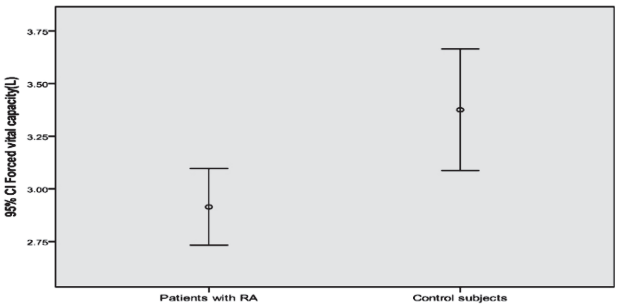

Figure (1): The distribution of FVC values for patients with RA as compared with controls.

Out of eighty two 82 patients with RA, forty two 42 patients (51%) suffered pulmonary involvement, with abnormal spirometric values. These abnormal results are in the form of respiratory restriction in 33 patients (40%), respiratory obstruction 9% (one patient of large airway obstruction and six with small airway obstruction) and mixed abnormality in two patients (2%).There are significant correlations between all of the following: duration of articular disease, age of the patient, disease activity (DAS28) and duration of medication with the reduction of FVC ($P<0.01$), table (2), figures (2-4).

Table (2): The significance of multiple risk factors on the reduction of FVC values.

Risk factor	P value
Duration of articular disease	1.3E-6*
DAS28	1.8E-8*
Duration of drug intake (MTX)	6.1E-7*
Age of the patient	2.2E-4*
Symptomatic patients	4.5E-7*
RF + ve patients	0.236
Smoking	0.778

*P values are considered significant when it is < 0.05

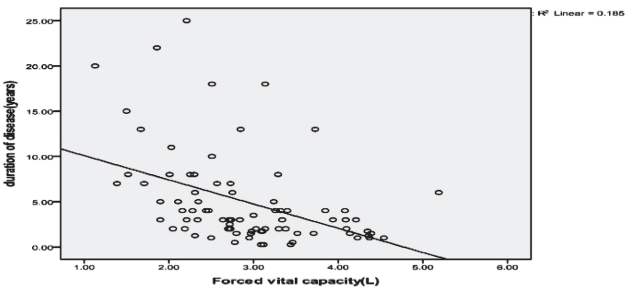

Figure (2): Correlation between disease duration and FVC.

It has been shown that the mean FVC is lower in clinically positive patients, and this difference is considered statistically significant ($P< 0.05$). Patients who has + ve RF have lower mean value for the FVC as compared with RF – ve. But this difference is statistically non-significant (P value > 0.05). Regarding patients with heavy smoking, they have lower FVC mean value as compared with non-smoker patients but this difference is considered statistically non-significant ($P>0.05$). Nine patients (11%), 2 males and 7 females were asymptomatic with abnormal spirometric results. The abnormalities of PFT results are in the form consisting with respiratory restriction. They are six patients with mild restriction and three patients with moderate restriction. As compared with pulmonary symptomatic patients, the spirometric values FVC, FEV_1 is shown to be higher in asymptomatic patients and this difference is considered as statistically significant ($P<0.05$). Regarding the other spirometric values, the differences are statistically not significant, table (3).

Table (3): Comparison of PFT data among asyptomatic and symptomatic patients with abnormal spirometric results.

PFTs	Asymptomatic + abnormal PFTs No.(9)	Symptomatic + abnormal PFTs No.(27)	P value
FVC	2.86±0.97	2.26±0.63	0.043*
P%	73±6.67	63.22±14.01	0.035*
FEV_1	2.29±0.64	1.83±0.48	0.033*
P%	71.78±8.83	61.37±13	0.023*
FEV_1/FVC	80.88±7.44	80.77±9.29	0.869
PEFR	5.27±1.95	4.69±1.22	0.648
P%	74.44±20.35	68.63±11.20	0.380
FMF	2.75±0.74	2.52±0.95	0.511
P%	84.22±27.77	79.48±26.54	0.635

*P values are considered significant when it is < 0.05.

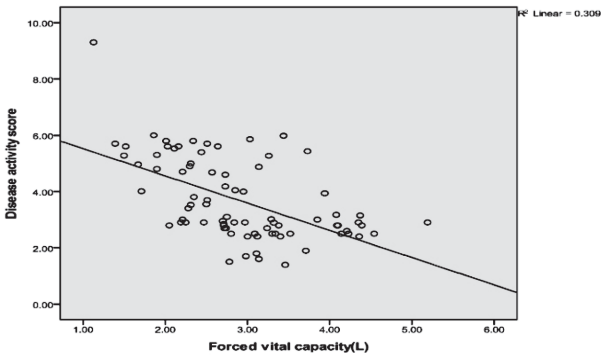

Figure (3): Correlation between DAS28 and FVC.

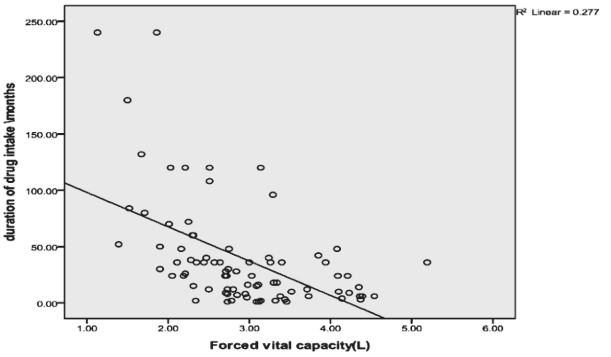

Figure (4): Correlation between duration of drug intake (MTX)

6 out of 82 patients with RA (7%) have early pulmonary involvement and half of them are asymptomatic. The abnormal spirometric results are in the form restriction (4 mild and 1 moderate) and one case of large airway obstruction. Risk factors were not correlated with abnormal spirometry (P<0.05).

Discussion:

Pulmonary involvement in patients with RA is found to be common and it influences the prognosis of RA patients and increases theincidence of mortality (10,11). In this study pulmonary evaluation included mainly the use of spirometerwhich is considered as an important, more available and low risk tool for screening, detecting and classifying pulmonary involvement and for indicating for further investigations when needed.

Purely restrictive results are found to be (40%) in 33 patients, which are the most frequent abnormality reported in this study. It was similar to the study of Yu-Qiong et al, 2012who found that 43% RA patients were diagnosed as ILD; although, the method of detection was by HRCT (12). Whereas, this result differs from the results observed by Bilgici et al who reported a rare pure restrictive defect with PFTs; although, 48% of patients with abnormal HRCT findings had combined ventilatory impairment. These findings suggest the possible development of a restrictive defect over time (13). Spirometric restrictive defect could be related to the involvement of the lung by the disease effect, chest wall restriction due to musculoskeletal or pleural involvement and neuromuscular disease affecting respiratory mechanics, after exclusion of the poor effort of the patient (14).

Regarding obstructive lung involvement, purely obstructive pulmonary function test results (large or small airways) in the present study is (8%), one female patient (1%) with large airway obstruction and six (7%) female patients with small airway obstruction. This result goes with that of Pappas study who reported (11%) of cases with obstructive lung disease (4). While it differs from Biederer study (37%) and Kanatstudy (42%) (15,16).The discrepancy between the results in this study and the others may be partly accounted for the different criteria used to assess small airways involvement in these studies, in this study abnormal values are considered as below 80% of the predicted values.

Multiple risk factors were assessed to find the correlation with pulmonary involvement for patients with RA. It has been found that various risk factors like: the duration of articular disease, DAS28 (disease severity), age of the patients and the duration of medication are significantly correlated with abnormal spirometric values (low FVC), While smoking and positive RF show no significant correlation. As compared to other studies, the duration of articular disease, age of the patients were associated with pulmonary involvement in Mori study and Yu-Quing study (17,12).While the age and disease severity (DAS28) was not associated in Gabbay study (18). On the contrary in this study, high titer of RF was considered as an associated risk factor in Bilcigstudy (13).

Smoking is one of the strongest risk factors in many studies as in Gochuicostudy(3). While in this study and in Gabbay smoking showed no significant association (18). Although smoking is known as a major risk factor for obstructive airway disease, the exact mechanism for the development of this obstruction in RA is not yet known. On the other hand, studies in non-smokers with RA show that smoking increases obstructive pulmonary involvement but donot play a big part in the process (19,20). Kanat reported no significant correlation between symptoms and cigarette smoking(16). While, in this study, although the number smoker patients was only ten (1 mild smoker and 9 heavy smokers), there was significant correlation between the presence of pulmonary symptoms and smoking. Thus, smoking might contribute to the occurrence of pulmonary symptoms (21, 16). Although pulmonary involvement in RA may cause respiratory symptoms such as chronic cough, dyspnea, and sputum production, some patients may have no symptoms at all (21,22). In this study, consecutive RA patients who were asymptomatic with abnormal spirometric values are found to be nine (11%); while (40%) are symptomatic. In the study of Perez (70%) of the patients were symptomatic (21). The commonest respiratory symptom is dyspnea which is consistent with perez and Kanat study (21,16). Despite that the duration of articular disease correlate significantly with the appearance of symptoms, some patients with positive pulmonary involvement remain asymptomaic even for longer duration of articular disease, thus screening of asymptomatic

patients with RA should be considered especially for prolonged disease duration. The spirometric values for asymptomatic patients with positive spirometry are higher than those who have symptoms and this is significant only for FVC and FEV_1 which goes with pulmonary involvement in the form of respiratory restriction; and this is not the case for Perez and Kanat studies which reported higher obstructive defects (21,16).

Conclusions:

In conclusion the results of this study offer evidence that Pulmonary involvement is common in Iraqi patients with RA, mostly in the form of respiratory restriction and was found to be asymptomatic in some patients and even it occurs early in the disease process. Moreover, spirometry is considered as a valuable tool for screening pulmonary involvement in patients with RA. The presence of various risk factors like (high disease activity, advanced age of the patient and long duration of the disease) represent a strong indication for pulmonary involvement screening and early detection.

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