Pattern of pulmonary function test in rheumatoid arthritis patients

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ABSTRACT

Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by a painful symmetrical peripheral polyarthritis. Extra-articular involvement in RA is a common condition. Pulmonary involvement occurs in 20 to 67 % of RA patients and it is responsible for about 10-20 % of mortality in RA patients.

Objectives: To evaluate the extent and pattern of pulmonary involvement in RA patients by using spirometry.

Methods: A case control study conducted at the rheumatology unit of Al Sader teaching hospital, forty RA patients [33(82.5%) female and 7(17.5%) male] and sixty apparently healthy subjects {50(83.3%) female and 10(16.7 %) male} were included in the study. All subjects had subjected to a pulmonary function test (PFT) for pulmonary function evaluation using MIR spirolab III. Measured and predicted forced vital capacities (FVC), forced expiratory volume in the first second (FEV1) and FEV1 / FVC ratio were considered as the parameters in this study for both groups.

Results: Nine patients were found to have a restrictive pattern of pulmonary function test, while obstructive pattern was found in only one patient. On the other hand, the pulmonary function tests were normal in all of sixty healthy control. The mean of FEV1 in patient group (2.07 ± 0.56L) and of FEV1% (95.8% ± 25.2) are significantly lower than those in the control group (2.46 ± 0.65 L; 105.3% ± 13.09). In addition, mean FVC in the patient group (2.35 ± 0.62L) and its mean percentage (92% ± 22.68) showed a clear significant reduction compared to those in control group (2.71 ± 0.67 L; 100.53 ± 12.12). No significant difference (P = 0.173) has been observed in FEV1 / FVC ratio between patient (88.17 ± 7.47) and control group (89.87 ± 4.99).

Conclusions: Different pattern of pulmonary function abnormalities could be manifested in RA patients and the restrictive pattern represents the most common feature. Spirometry is indicated as a baseline assessment and for follow up of RA patient to enhance early detection and management of the pulmonary involvement.

Keywords: Rheumatoid arthritis, pulmonary function test.

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انماط فحص وظائف الرئة لدى المرضى المصابين بالتهاب المفاصل الروماتزمي

التهاب المفاصل الروماتزمي هو مرض التهابي مزمن يسبب التهاب المفاصل الطرفية المتناظرة المؤلم. اصابة اعضاء اخرى في الجسم غير المفاصل يعتبر حالة شائعة لدى المصابين بهذا المرض. حيث ان الإصابة الرئوية تحدث في ٢٠ إلى ٦٧٪ من مرضى التهاب المفاصل الروماتزمي، وهي مسؤولة عن حوالي ١٠-٢٠٪ من الوفيات لمرضى التهاب المفاصل الروماتزمي .

الأهداف: لتقييم مدى ونمط الاصابات الرئوية في مرضى التهاب المفاصل الروماتزمي في مدينة بصرة عن طريق فحص وظائف الرئة .

الطريقة: الدراسة هي دراسة مقارنة بين الحالات المرضية والاصحاء واجريت في وحدة الروماتزم في مستشفى الصدر التعليمي في مدينة البصرة وشملت اربعون مريضا بالتهاب المفاصل الروماتزمي {٣٣ (٨٢،٥%) أنثى و ٧(١٧،٥%) ذكور} و ستون شخصا اصحاء {٥٠(٨٣،٣%) أنثى و ١٠(١٦،٧%) ذكور}. وقد خضع جميع الاشخاص المشمولين بالدراسة لاختبار فحص وظائف الرئة لتقييم وظيفة الرئة باستخدام جهاز سبايرولاب حيث تم قياس حجم هواء الزفير الكلي القسري (FVC)، وحجم الزفير القسري في الثانية الأولى (FEV1)، ونسبة القيمتين (FEV1/FVC) لكلا المجموعتين.

النتائج: وجدان تسعة مرضى لديهم نمط تحددي في اختبار وظيفة الرئة، في حين تم العثور على نمط انسدادي في اختبار وظيفة الرئة في مريضة واحدة. من ناحية أخرى، كان اختبار وظيفة الرئة طبيعيا في كل الاشخاص الاصحاء. وكانت قيمة متوسط FEV1 في مجموعة المرضى (٢،٠٧ ±

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٠.٥٥) لتر ومتوسط نسبة FEV1% (٩٥،٨±٢٥,٢%) وهو اقل من المجموعة المقارنة للأشخاص الاصحاء (٢.٤٦ ± ٠.٦٥ لتر) بمتوسط نسبة FEV1% (١٠٥,٣± ١٣,٩%). بالإضافة إلى ذلك، أظهر متوسط FVC في مجموعة المرضى (٢,٣٥±) لتر بمتوسط نسبة ٩٢% بانخفاض واضح مقارنة مع مجموعة المقارنة للأشخاص الاصحاء الذين كان متوسط قيمة FVC (٢.٧ ± ٠.٦٧ لتر) ومتوسط نسبة FVC% عند (١٠٠،٥٣%). هناك اختلافات طفيفة (غير معنوية) في نسبة FEV1 / FVC بمتوسط قيمة ٨٨.١٧% في مرضى التهاب المفاصل الروماتزمي و ٨٩.٨٧% في المجموعة المقارنة للأشخاص الاصحاء.

الاستنتاجات: انماط مختلفة من اصابات الرئة يمكن أن تظهر لدى مرضى التهاب المفاصل الروماتزمي ويمثل النمط المحدد الاصابة الأكثر شيوعا. ونتيجة لذلك يوصى بأجراء فحص وضائف الرئة باعتباره فحص اساسي لمرضى التهاب المفاصل الراتزمي لتعزيز الكشف المبكر للإصابات الرئوية.

الكلمات المفتاحية: التهاب المفاصل الروماتزمي، فحص وظائف الرئة

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by a painful symmetrical peripheral polyarthritis. It affects multiple body organs in addition to joints' surrounding tissues and it is a leading cause of joints deformities and disabilities. Rheumatoid arthritis can develop at any age with increased incidence between 35 and 55 years of age.[1] The prevalence of RA is approximately 0.5-1% worldwide with some variability among different populations,[2] in Iraq it is prevalence is 1%.[3] Highest prevalence was recorded in Pima Indians and Chippewa Indians, whereas the lowest in Japan and China.[4,5] 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.[6] Extra-articular involvement in RA is common. It was recorded in 51% of 587 RA Italian patients, and the manifestation was more common in males patients, in positive antinuclear antibody and in rheumatoid factor positive patients.[7] In addition to rheumatoid nodules, other organs could be involved in the disease process includeing heart, lung, blood vessels, peripheral nerves as well as hematological involvement. The occurrence of extra-articular pulmonary manifestation of RA ranges from 20 % in some studies to as high as 67% in others.[8,9] Respiratory airways, pleura, lung parenchyma and vascular compartment all may be attacked by RA.[10] In the majority of RA patients, arthritis develops first, whereas in others, pulmonary involvements could proceed or simultaneously occur with arthritis.[11] Different forms of interstitial lung disease (ILD) occur in RA patients. They are a group of heterogenous paranchymal lung disorders characterized by their clinical, pathological and radiological features.[12] The most commonly observed ILD in RA patients are usual interstitial pneumonia, nonspecific interstitial pneumonia and inflammatory airway disease with organizing pneumonia pattern.[11] It has been estimated that pulmonary complications are responsible for 10-20% mortality in RA patients which is mostly caused by ILD.[13]

OBJECTIVES

The aim of this study is to evaluate the extent and abnormality of pulmonary function test in RA patients by using spirometry.

SUBJECTS AND METHODS

This study is a case control study done at the rheumatology unit in Al Sader teaching hospital during the period from June 2011 to October 2011. Spirometry was used as a diagnostic test to evaluate the type and the severity of pulmonary involvement in RA patients. After detailed and thorough medical history and physical examination, forty newly and previously diagnosed patients of both genders (82.5% female and 17.5% male) who met RA 2010 classification criteria as described by American College of Rheumatology were included in our study.[14] Patients age is ranging

from 13 to 67 (mean 48.5) years. Another sixty healthy subjects (83.3% female and 16.7% male) were included in the study as a control group, their age ranges from 13 to 64(mean 46.1) years. Both groups were matched for height, weight and race. Patients with history of smoking, drug intake, past medical history of respiratory, cardiac and other chronic diseases were excluded from the study. All subjects had further subjected to a pulmonary function test (PFT) for their pulmonary function evaluation using spirolab- III (MIR-Italy). The test was carried out in a sitting position according to the standard protocol with the best record out of three attempts was considered for further data analysis. Measured and predicted forced vital capacity (FVC), forced expiratory volume in the first second (FEV1) and FEV1 / FVC of RA and control groups were analyzed in our study. Data analysis were carried out using SPSS software version V.20, t test and Fisher exact test were and the data were expressed as mean ± standard deviation (mean ± SD), P ≤ 0.05 was considered significant.

RESULTS

(Table-1), a total of 100 individuals of both sex were selected in our study, 40 RA patients and 60 healthy individuals. As illustrated in (Table-1) there was no significant difference in sex distribution between RA patients and control groups (P = 0.56). The mean age of RA group (48.5 ± 10.4 year) was not significantly different (P = 0.205) from the mean age of control group (46.1 ± 8.2 year). Moreover, no significant difference (P = 0.344) was observed between the mean height of RA group (159.5 ± 7.3 cm) and control group (161 ± 8.1cm).

Table 1. General characteristics of RA and control groups.

Group	Gender		Age (Year)	Height (Cm)
RA (n=40)	7(17.5%) male	33(82.5%) female	48.5±10.4	159.5±7.3
Control (n=60)	10 (16.7%)	50 (83.3%)	46.1±8.2	161±8.1
P value	P =0.560		0.205	0.344
Applied test	**Fisher exact test**		**T test**	**T test**

(Table-2), the mean and standard deviation of FEV1 and FVC (measured and predicted), FEV1%, FVC% and FEV1/FVC % of both groups are shown in (Table-2). No significant difference has been observed with regard to predicted mean values of FEV1 and FVC between the RA and control groups, this indicates that the two groups were well matched. A highly significant (P = 0.002) lower values of FEV1 has been observed in RA group (2.07 ± 0.56L) compared with control group (2.46 ± 0.65 L). Also the FEV1% (FEV1 measured / FEV1 predicted × 100) was significantly lower (P = 0.015) in RA group (95.8 ± 25.2%) compared with control group (105.3 ± 13.09%). The FVC in RA group (2.35 ± 0.62 L) is significantly lower (P = 0.005) than that in control group (2.73 ± 0.67 L). Moreover, the FVC% is significantly reduced (P = 0.02) in RA group (92.28 ± 22.68) compared with control group (100.53 ± 12.12). No significant difference (P = 0.173) has been observed in FEV1/FVC% between RA group (88.17 ± 7.47) and control group (89.87 ± 4.99).

Table 2. Results of FEV1, FEV1%, FVC, FVC% and FEV1/FVC% in RA and control groups (mean± SD)

|	RA (N=40)	Control (N=60)	P value
FEV1(L)	2.07 ± 0.56	2.46 ± 0.65	0.002
FEV1 predicted (L)	2.19 ± 0.35	2.57 ± 1.96	0.230
FEV1 % (FEV1/FEV1 predicted)	95.8 ± 25.2	105.3 ± 13.09	0.015
FVC (L)	2.35 ± 0.62	2.73 ± 0.67	0.005
FVC predicted (L)	2.56 ± 0.44	2.71 ±. 62	0.200
FVC % (FVC /FVC predicted)	92.28 ± 22.68	100.53 ± 12.12	0.020
FEV1/FVC%	88.17 ± 7.47	89.87 ± 4.99	0.173
T-test was applied			

(Table-3, figure-1) show abnormal pulmonary function test in 10 of RA patients (25%), obstructive pulmonary disease observed in one patient (FEV1 / FVC% < 70%) while restrictive pulmonary disease in nine patients (FVC measured / FVC predicted % < 80%). Pulmonary function test was normal in all of 60 healthy control subjects i.e. all have FEV1 / FVC % > 70% and FVC % > 80%.[15]

Table 3. Results of pulmonary function test in RA and control groups.

Group	Diagnosis					P value
	Normal	Obstructive	Restrictive			
RA (n=40)	30 (75%)	1(2.5%)	**9 (22.5%)**			0.000
			Mild **6 (15%)**	**Moderate** **2 (5%)**	**Sever** **1(2.5)**	
Control (n=60)	60 (100%)	0 (0%)	0 (0%)			
Total	90 (90%)	1(1%)	9 (9%)			
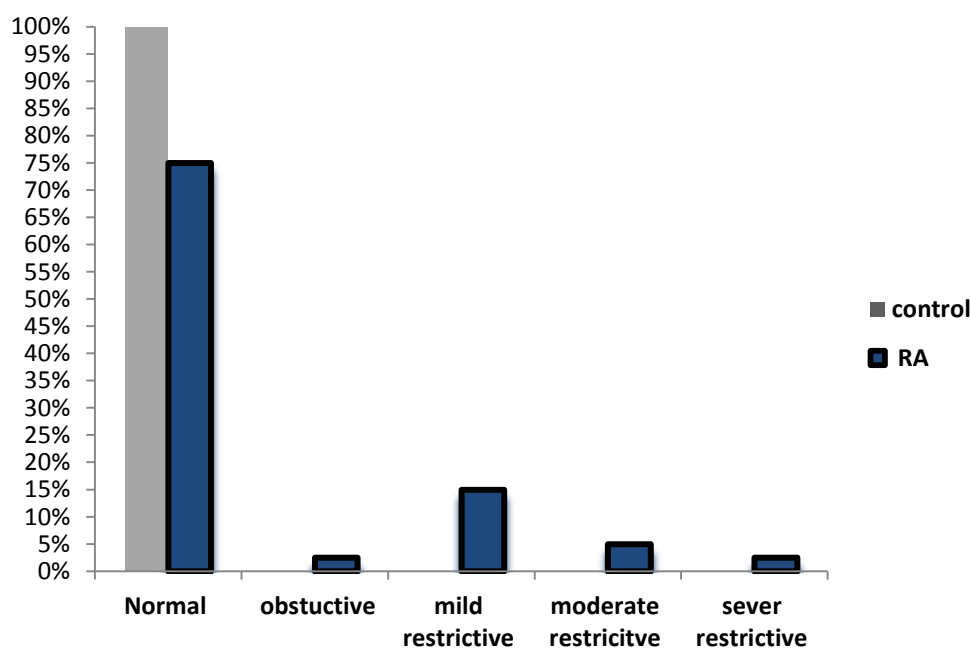
Fig 1. Results of pulmonary function test in RA and control group.

DISCUSSION

The results of this study show that the number of RA female patients exceed that of male patients seen within same time frame with a ratio reached to as high as 4.7:1. Although this results is a little higher value than what has been reported in the other populations,[3] it is consistent with worldwide reports that demonstrate a tendency of RA disease for female gender. It has been found that rheumatoid arthritis improves during treatment with estrogen-containing oral contraceptives, pregnancy and with estrogen replacement therapy which suggest the role of sex hormone in developing RA in such a higher rate in females.[16] Abnormal pulmonary function test has been found in 25% of RA patients. A restrictive pulmonary features found in nine patients (22.5%), ranging from mild features in six patients (15%) moderate severity in two patients (5%) to severe restrictive features in one patient (2.5%). Only one patient (2.5%) showed obstructive pulmonary features. Our results show a tendency of RA as a systemic inflammatory condition to attack pulmonary tissues as an early common extra articular target of the disease process. A comparable data has

been reported by a study in which abnormal pulmonary function test has been observed in 30% of 246 RA patients.[17] In addition, the overall patients data compared to the matched control group shows a significant decrease in the average FEV1and FVC among RA patients with no significant changes in FEV1/FVC. These results indicate a restrictive lung pattern of interstitial lung disease that does not affect the bronchial resistance and tone but lung volumes. Our finding of abnormal pulmonary function tests in RA patients rises the question of time at which pulmonary tissues are attacked by RA autoantibodies. It has been found by data from other studies that systemic inflammation and autoimmunity may precede the presentation of RA as a classifiable disease.[18] Deane et al 2010 found elevated levels of autoantibodies, cytokines and chemokines in a stored blood samples obtained from 73 military cases with seropositive RA in the preclinical stage of RA.[19] Whereas van de Sande et al 2011 could not find any histological or magnetic resonance imaging (MRI) evidence of synovial inflammation in the knee of individuals with seropositive RA-related autoantibodies without

clinically-evident synovitis.[20], Demoruelle and his colleagues recently observed a higher prevalence of inflammatory airways disease using computed tomographic imaging in arthritis-free with seropositive RA-related autoantibodies compared to a seronegative matched controls.[21] In a consistent cross sectional study for characterizing pulmonary involvement in 63 RA patients by spirometer, x-ray and high resolution computed tomography (HRCT) of thorax, Mohd et al 2009 found a restrictive pattern of pulmonary disease in 66.7% of the patients. The most common HRCT findings were reticulation (46%), ground glass opacities (38.1%) and bronchiectasis (28.6%).[22] The limitations in our study includes small sample size, the inability to show the disease activity in correlation with pulmonary involvement by using rheumatoid factor, anti-citrullinated peptides (CCP) antibody levels and x-ray changes as well as diffusion lung capacity for carbon monoxide (DL_{CO}) test as an indicator of the severity of respiratory membrane involvement.

In conclusion, the lung is a potential target organ of the RA inflammatory disease process that could precede the onset of the synovial joint involvement. Different pattern of pulmonary function abnormalities could be manifested in RA patients and a restrictive pattern represents the most common feature. Spirometry test is indicated as a baseline assessment and follow up for RA patient to enhance early detection and management of the pulmonary involvement.

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