Parameters that Increase Risk of Interstitial Lung Disease in Rheumatoid Arthritis Patient

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Abstract

Background: Several studies have been focused on interstitial lung disease among patients with established rheumatoid arthritis, with fluctuating incidence and prevalence depending on the methods used.

Patients and Methods: A case- control study design was used in this study performed on 100 cases with RA (50 cases with ILD). Data were analyzed by using Statistical Package of Social Sciences (SPSS) version18. Categorical variables were presented as frequencies and percentages. Continuous variables were presented as means with their confidence interval (CI) and standard deviation. The Pearson's chi-square test was used to determine the associations between categorical variables. A p-value of < 0.05 was considered as statistically significant

Keywords: Rhenmatoid arthritis, interstitial lung disease, HRCT.

Introduction

1.1 Background

Interstitial Lung Disease (ILD) is a progressive fibrotic disease of the lung parenchyma occurs in association with several rheumatic diseases including rheumatoid arthritis (RA). An association a between positive rheumatoid factor and ILD in RA is well established. ILD is the only complication of RA reported to be increasing in prevalence worldwide, as well as, it has been shown to be approximate of 6% for all RA deaths[1&2] Several studies revealed a high post-mortem occurrence of RA ILD, which has been subsequently supported by high-resolution computed tomography (HRCT) to be out of 25% for all RA patients[3&4]

1.2 Rheumatoid Arthritis (RA)

Rheumatoid arthritis (RA) is one of the most important chronic inflammatory disorders that affect the joints and musculoskeletal systems. It is associated with swelling, stiffness, pain and may lead to substantial loss of functioning and mobility in severe cases[1].

1.3 Pulmonary Involvement in Rheumatoid Arthritis Patients

RA is an autoimmune disease in which the body attacks its own tissue and it may affect the lungs. Since, 1948, Ellman and Ball described three cases with classic manifestations of RA and extensive pulmonary involvement[5]

However, the nature of the relationship between inflammation in lungs and joints is still unclear. Several studies have been focused on ILD among patients with established RA, with fluctuating incidence and prevalence depending on the methods used [1,4, 6,7, 8,9,10,11] .

The incidence of RA associated lung disease has been increasing, as a result of improved availability of diagnostic tests [10]. there is limited data on obstructive pulmonary disease in RA, however, a study done by Geddes et al found that 32% of patients with established RA had an obstructive lung disease, based on standard pulmonary function tests[4] Intrapulmonary rheumatoid nodules is typical pleuropulmonary manifestations for RA, meanwhile, pulmonary complications are common and responsible for 10 to 20% of all mortality[12&13] have respiratory symptoms patients However, approximately one-third of the RA and two-thirds had significant [1] on high-resolution computed tomography[14] radiographic abnormalities ILD presentations vary from asymptomatic to severe, rapidly progressive shortness of breath as well as respiratory failure and death. According to presentation ILD can be classified into acute presenting symptoms, chronic slowly progressive symptoms. Meanwhile, ILD can be presented with an abnormal chest radiograph or abnormal pulmonary function test but with no symptoms[15] progressive dysponea with or However, ILD most common presentation is slow without cough.

1.5 Diagnosis of Interstitial Lung Disease

Symptoms of ILD are major stone in diagnosis. Patients usually presented with increasing exertional breathlessness, dry cough as well as increasing fatigue which becomes an invariable feature once hypoxia develops [15]. Meanwhile, Physical signs of ILD include bi-basal lung crackles, initially fine and heard in late inspiration, progressing to louder coarser crepitation audible throughout inspiration. Finally, finger clubbing which is relatively uncommon occurring in less than 20% of patients. However, central cyanosis may accompany resting hypoxia which can lead to low oxygen saturations at rest. Hypercapnia is the end-stage of advanced ILD.

Normal chest radiography did not exclude RA-ILD. However established disease will usually be visible as reticular shadowing accompanied by increasingly nodular opacification of the lower lobes[16]. or coin lesion ,or lobar collapse is pathognomonic An isolated nodule High resolution CT of the thorax provides much more definitive information and is required to make a confident diagnosis of ILD. Furthermore, it establishes the type of ILD assesses disease and finally excludes of other pathologies that might mimic ILD[17] Serological test represented by Cyclic Citrullinated Peptides (CCP) antibodies is likely to be positive in ILD and may precede the onset of RA especially in smokers[18&19]. the development of RA include There are ranges of lung abnormalities during airways disease and might suggest the lung as a site of initiation of RA [20&21].

1.6 Aim of the study

This study has been carried out to determine the risk of developing of interstitial lung disease in RA patients.

1.7 Patients and method

2.1 Study Design

This was a hospital based case-control study which conducted to determine the association of RA patients by socio-demographic characteristics and other study variables performed on 100 cases with RA (50 cases of them diagnosed to have ILD by chest physicion based on clinical data radiological, PFT, histological), at Baghdad Medical City from September2013 to September 2014

2.2 Data Collection

The Inclusion and exclusion criteria for the cross-sectional study groups were as follows:

a) Inclusion criterion: RA patient with &without ILD with age group 20-above 60 years.

:b) Exclusion criterion

1. IHD& Heart failure.
2. Chronic lung disease as asthma, COPD.
3. Drugs as biological agent, MTX.
4. Other CTD as SLE, Mixed CTD.

2.3 Study Instruments

Structured questionnaire consists of duration of RA, serology test, presence of subcutaneous nodules and pulmonary nodules..

2.4 Data Analysis

Statistical analysis was carried out using SPSS version 18. Categorical variables were presented as frequencies and percentages. Pearson's chi square (x2) test and fisher exact test were used to find the association between the categorical variables. A p-value of ≤ 0.05 was considered as significant.

The Association of RA Patients with Duration of RA, DAS 28

Serology Test, Presence of Subcutaneous Nodule and Pulmonary

Nodules

Table-1: shows the association of RA patients with and without ILD with duration of RA, DAS 28, serology test, presence of subcutaneous nodules and pulmonary nodules. There was significant association between RA patients and serology test, RA patients with ILD were seven times more likely to have a positive test. There was

significant association between RA patients and presence of pulmonary nodules; RA patients without ILD were nine times more likely to do not have pulmonary nodules by chest x-ray.

Variables	RA patients With ILD %	RA patients without ILD %	X2	OR 95% C.I	P value
Duration of RA					
<6 years	11 (22.0)	17 (34.0)			
6-12 years	14 (28.0)	19(38.0)	5.72	0.88(0.31-2.45)	0.126
13-18years	11 (22.0)	8 (16)		0.47(0.14-1.54)	
>18years	14 (28.0)	6 (12)		0.28(0.08-0.94)	
DAS 28					
Mild disease activity	16 (32.0)	24 (48.0)			
Moderate disease activity	23 (46.0)	21 (42)	3.94	0.61(0.26-1.45)	0.139
Sever disease activity	11 (22)	5 (10.0)		0.30(0.09-1.04)	
Serology Test					
Positive	35 (70.0)	21 (42.0)	**7.95**	**3.22 (1.41-7.35)**	**0.005***
negative	15 (30.0)	29 (58.0)			
Presence of subcutaneous nodule					
Yes	20 (40.0)	14 (28.0)	1.60	1.71 (0.74-3.96)	0.205
no	30 (60.0)	36 (72.0)			
Presence of pulmonary nodule					
Yes	9 (18.0)	0 (0.0)	**9.89**	**2.22 (1.77-2.78**)	**0.002***
no	41 (82.0)	50 (100.0)			

p value ≤ 0.05 is significant*

Discussion

Rheumatoid arthritis is traditionally considered a disease that involves the joints. Nevertheless, up to 50% of the patients have some type of extra articular manifestations, such as serositis, pneumonitis, peripheral neuritis ,nodules, and sclerosis. Pulmonary involvement is a frequent and among the most severe extra-articular manifestations of RA ranking as the second cause of mortality in this patient population [22]

This current study reported no significant association between presence of ILD and duration of RA, however, it has not agreed with Vergnenègre and his co-workers in France 1997, meanwhile, it is agreed with Bongartz et al in 2010 in America revealed that there was not significant association between presence of ILD and duration of RA [1&22].

There was no significant association between DAS 28 and presence of ILD in current study which agreed with Harlow and its co-workers research in USA 2013, who reported that, there were no significant differences between parameters diseases activity like ESR and DAS 28 by RA patients with or without ILD[24]

The present study findings found that, there was significant association between presence of ILD in RA patients and positive serological test. RA patients were ten times more likely to suffer from ILD. This finding was in agreement with study in America in 2012 by Fischer and his co-workers who found that, serological test for Rheumatoid factor were in higher rate for RA patients with ILD[1]

Meanwhile, the present study reported that RA patients with ILD were eight times more likely to have subcutaneous nodules which were the similar to Bongartz et al in 2010 in America who found that RA patients without ILD were two times more likely to have subcutaneous nodules[1]

In addition, Saag et al. 1997 in USA found that smoking cigarette more than 25 pack-years were significantly associated with higher titer or Rheumatoid factor as well as presence of subcutaneous nodules in RA patient with ILD [25] .

Conclusion

RA patients were (ten times) more likely to suffer from ILD Meanwhile, this study reported that RA patients without ILD were (nine times) more likely to do not have pulmonary nodules.

Recommendation

Further studies will be required to establish the exact relationship between the ILD and RA, and to throw further light on the pathophysiological mechanism involved.

Conflict of Interests.

There are non-conflicts of interest .

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الخلاصة

الخلفية :لقد ركزت دراسات عديدة في أمراض الرئة الخلالي بين المرضى المصابين بالتهاب المفاصل الرثياني الراسخة، ومع حدوث تقلبات اعتماداً على الأساليب المستخدمة.

الهدف :قد أجريت هذه الدراسة لتحديد خطر الإصابة بأمراض الرئة الخلالي حسب الخصائص الاجتماعية الديمغرافية لمرضى الرثياني ومتغيرات الدراسة الأخرى.

المرضى والطرق :تم تصميم دراسة الحالة التحكم في هذه الدراسة ،وقد تم تحليل البيانات باستخدام الحزمة الإحصائية للعلوم الاجتماعية (SPSS) الإصدار 18 ، وعرضت المتغيرات قاطعة الترددات و النسب المئوية، وعرضت المتغيرات المستمرة كوسيلة مع أصدقائهم 95% فاصل الثقة (CI) والانحراف المعياري .بيرسون تشي اختبار مربع (x2) تم استخدامه لتحديد الروابط بين المتغيرات الفئوية .واعتبرت قيمة$p < 0.05$ كما إحصائيا.

الاستنتاج : نتيجة الدراسة الحالية ذكرت ان أعلى معدل 15 مرة من أمراض الرئة الخلالي في مرضى التهاب المفاصل الرثياني الذين يعيشون قرب المنطقة من المولدات الكهربائية او المصانع، كذلك، المدخنين الحاليين في هذه الدراسة كانت أعلى مرتين للاصابه بأمراض الرئة الخلاليه بين مرضى التهاب المفاصل، فضلا عن غير المدخنين كانت أعلى بثلاث مرات عدم تقديم أمراض الرئة الخلالي.

الكلمات الدالة: التهاب المفاصل الرثوي، امراض الرئة الخلالية ، مفراس الصور.