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Royal Medical Services, Amman, Jordan

Corresponding author: Deifallah Mohammad Alsharari. Royal Medical Srevices. Amman, Jordan. Mobile: 00962772256994. E-mail: alsharari76@yahoo.com. ORCID ID: https://orcid.org/0000-0002-8334-4030

Rheumatoid Arthritis Interstitial Lung Disease: Measuring and Predictive Factors Among Patients Treated in Rehabilitation Clinics at Royal Medical Services

Deifallah Mohammad Alsharari, Laith Abdulsalam Obeidat, Hayat Khuzai Khasawneh, Moh'd Rami Hani Alhmar, Raja Mohammad Khasawneh, Zeyad Sulieman Bataineh, Ahmad Abdelqader Aldhoun

ABSTRACT

Introduction: Autoimmune diseases have increasing importance in modern medicine and cover increasing areas of medicine including rheumatoid arthritis interstitial lung disease. **Aim:** The main aims of this study are to evaluate the association of some autoimmune variables in patients with rheumatoid arthritis interstitial lung disease. **Methods:** A retrospective study was conducted from files of patients with rheumatoid arthritis interstitial lung disease. A total of 210 files of intended patients were included in this study. The study was conducted in rehabilitation clinics at Royal Medical Services. Study variables include some demographic variables such as age, and gender; clinical variables such as disease related factors such as duration, diagnostic criteria; predictive factors such as rheumatoid factors, smoking, and MTX treatment. Data were collected and entered into excel spreadsheet to create raw data. The analysis of data was carried out using the software SPSS version 21. Descriptive statistical parameters were used to describe data including means and standard deviations for continuous variables. Frequency and percentages were used to describe categorized variables such as gender. The relationships between study variables were computed using independent T test, and One Way ANOVA test. Significance was determined if $\alpha \leq 0.05$. **Results:** The prevalence of RA-ILD was 3.70%. The study participants were subdivided into two groups according to MTX treatment, non-exposed group and exposed group. There were significant relationships between MTX treatment and study variables including gender, age of (rheumatoid arthritis) RA onset, smoking, and rheumatoid factor (RF). The progression of RA-ILD was impacted by gender, age of (rheumatoid arthritis) RA onset, smoking, rheumatoid factor (RF), and MTX treatment. **Conclusion:** Patients with RA and RA-ILD follow similar clinical characteristics in other studies except MTX treatment, but this can't be generalized because of small number of RA-ILD patients.

Keywords: rheumatoid arthritis, rheumatoid factor, interstitial lung disease, smoking, age

1. INTRODUCTION

Rheumatoid arthritis (RA) is an autoimmune disease that influences up to1% of general population at global level [1-3]. It is mainly a cause of chronic pain and inflammation in synovial joints [4, 5], besides to interstitial lung disease (ILD) [6]. ILD is the most known clinical pulmonary presentation of RA in about 10% of patients [7]. ILD is a fibrotic disease affecting the lung parenchyma and associated with increasing rates of death [8]. Patients are mainly affected by RA-associated ILD (RA-ILD) patterns such as interstitial pneumonia as well as nonspecific interstitial pneumonia [9-11].

Recently, several risk factors of RA-ILD have been reported including: smoking, gender (mainly male), human leukocyte antigen haplotype (HLA), rheumatoid factor and anticyclic citrullinated protein antibodies (ACPAs) [3, 12, 13].

Avouac et al [14] conducted a study to distinguish the presentation of 3 flowing markers for the conclusion and the development of interstitial lung disease (ILD) related with rheumatoid joint inflammation (RA). Markers included were lung epithelial-derived surfactant protein D (SPD), chemok-

ine CCL-18 and Krebs von den Lungen-6 glycoprotein (KL-6). The results indicated that KL-6 is an appropriate marker for the diagnosis and development of RA-ILD. RA-ILD shares some genetic and phenotypic similarities with other fibrotic diseases including idiopathic pulmonary fibrosis, supporting the use of the same drugs in these conditions [15, 16].

Clinically RA-ILD is distinguished in 2% to 10% of patients with RA, yet detailed assessments fluctuate because of the heterogeneity of RA, hereditary weakness, and variations in the definition of disease and diagnostic approaches [17-21]. The lifetime danger of creating ILD in patients with RA is accounted for to be 6%–15% [22]. ILD may go before the advancement of articular signs [18].

Hyldgaard et al [19] found that 14% of patients with RA-ILD had been determined to have ILD, 1-5 years before the occurrence of RA. The danger of creating ILD increments with delayed length of RA. A few hazard factors for improvement of ILD in patients with RA have been recognized [23]. The most reliably revealed hazard factors incorporate more established age and male gender [24], cigarette smoking [25], positive anti- cyclic citrullinated peptide antibodies (against CCP) or IgM rheumatoid factor [26], and, in certain investigations, RA disease progression [22]. Smoking is the main preventable hazard factor [23].

Methotrexate (MTX) is presently immovably settled universally as the stay medicine for the executives of RA, suggested to be used in the first place, to which other regular manufactured medicines are used [27, 28].

2. AIM

The main aims of this study are to evaluate the association of some demographic and immunological variables in patients with rheumatoid arthritis interstitial lung disease.

3. METHODS AND SUBJECTS

Study design and setting

A retrospective study design was followed to collect data from files of patients with rheumatoid arthritis (RA). The study was conducted in rehabilitation clinics at Royal Medical Services.

Study sample

A total of 250 files for patients with RA were reviewed. A total of 40 files were excluded due to lack of information. The remaining 210 files were included in the study.

Study variables

Study variables included: gender, age, age of onset of RA, smoking, rheumatoid factor, exposure to MTX treatment, and ILD diagnosis.

Study procedure

The study was approved by ethical committee at royal medical services. Files of patients were reviewed and the data were extracted from files of all patients. The excel spreading sheets were used for data entry. Data was analyzed using SPSS version 21. Data were coded to better analyzed by the SPSS. As an example, the variable gender can be answered either male, or female. Male was given number 1, female number 2, and so on. Descriptive statistics were used to describe study variables. Frequencies and percentages were used to present categorical variables, whereas means, and standard deviations were used to present non-categorical variables. The relationships between variables were evaluated based on T – independent test, and One Way ANOVA test. Significance was considered if $\alpha<0.05$.

4. RESULTS

The data presented in table (1) showed that study participants were 210. A total of 137 (65.24%) were males. The mean age was 64.5±14.3 years. The age of patients at the onset of RA was mainly <50 (43.81%). Smoking was reported by the majority of participants (60.95%). About 64% of patients were positive for RF. About 57% of patients were exposed to MXT treatment. ILD diagnosis was identified in about 4% of patients.

Variable	Description
Gender (N, %):	
- Males	137 (65.24%)
- Females	73 (34.76%)
Age (M±SD) years	64.5±14.3
Age of RA diagnosis (N, %):	
- <50	92 (43.81%)
- 50-60	54 (25.71%)
- >60	64 (30.48%)
Smoking (N, %):	
- Yes	128 (60.95%)
- No	82 (39.05)
RF (N, %):	
- Positive	135 (64.29%)
- Negative	75 (35.71%)
MTX treatment (N, %):	
- Yes	120 (57.14%)
- No	90 (42.86%)
ILD- assessment:	
- Yes	9 (4.29%)
- No	201 (95.71%)

Table 1. Demographic variables of study participants

The relationship between MTX treatment and study variables

As shown in table (2) and figures (1-4), there was a significant relationship between exposure to MTX treatment and gender ($p=0.038$). males were more likely to be exposed to MTX treatment. Age of RA onset was also significantly related with the exposure to MTX treatment ($p<0.001$). Smoking status was significantly associated with the exposure to MTX treatment ($P=0.042$). It seems that smokers were more likely not to be exposed to MTX treatment. RF positivity was significantly associated MTX exposure ($p<0.001$). Patients who were positive for RF were more likely to be exposed to MTX treatment.

The impact of study variables on ILD diagnosis:

Variable		Non exposed		Exposed		P value
		N	%	N	%	
Gender:						0.038
-	Male	59	65.56%	83	69.17%	
-	Female	31	34.44%	37	30.83%	
Age of RA diagnosis:						
-	<50	36	40.00%	54	45%	<0.001
-	50-60	23	25.56%	30	25%	
-	>60	31	34.44%	36	30%	
Smoking:						0.042
-	Yes	61	67.78%	73	60.83%	
-	No	29	32.22%	47	39.17%	
RF:						<0.001
-	Positive	52	57.78%	79	65.83%	
-	Negative	38	42.22%	41	34.17%	

Table 2. The relationship between MTX treatment and study variables

		Sum of Squares	df	Mean Square	F	Sig.
Gender	Between Groups	1.136	1	1.136	5.084	0.025
	Within Groups	46.488	208	0.223		
	Total	47.624	209			
RA_ age	Between Groups	7.063	1	7.063	10.117	0.002
	Within Groups	145.204	208	0.698		
	Total	152.267	209			
Smoking	Between Groups	1.434	1	1.434	6.143	0.014
	Within Groups	48.547	208	0.233		
	Total	49.981	209			
RF	Between Groups	1.199	1	1.199	5.306	0.022
	Within Groups	47.015	208	0.226		
	Total	48.214	209			
MTX	Between Groups	1.727	1	1.727	7.228	0.008
	Within Groups	49.701	208	0.239		
	Total	51.429	209			

Table 3. The impact of study variables on ILD diagnosis

Using One Way ANOVA, the impacts of study variables on ILD were evaluated. As seen in table (3), all variables including gender, age of RA diagnosis, smoking, RF, and MTX treatment were statistically significant with ILD diagnosis ($p<0.05$, for mentioned variables).

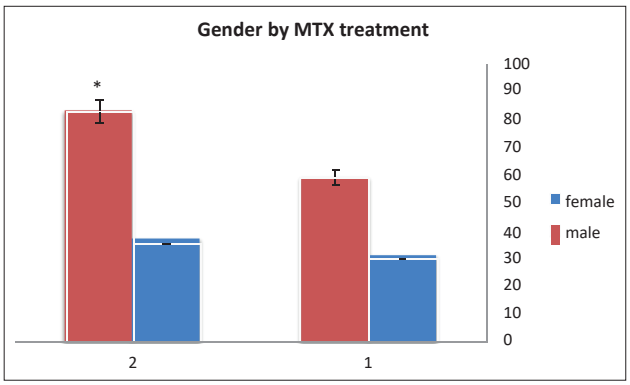

Figure 1. The relationship between gender and the exposure to MTX treatment. * denotes significance. 1: non-exposed, 2: Exposed.

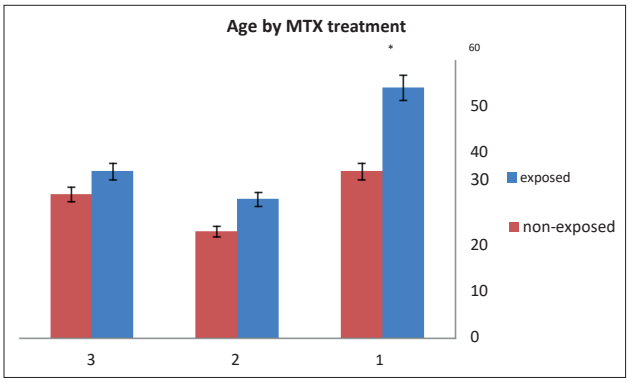

Figure 2. The relationship between age and the exposure to MTX treatment. * denotes significance. 1: <50, 2: 50-60, 3>60.

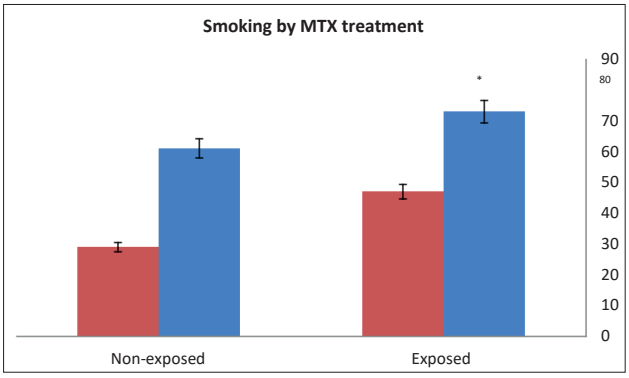

Figure 3. The relationship between smoking and the exposure to MTX treatment. * denotes significance. Blue color: Smoking, red color: non-smoking.

5. DISCUSSION

The results of the present study showed that about two thirds of patients were males. This result supported previous studies which showed males were more likely to be involved in RA disease [18, 24]. Age is a risk factor for RA in this study since about 56% of patients were over 50 years. Other studies have reported similar trends that involved age as a risk factor for RA [18, 24]. Smoking was reported by about 61% of patients with RA. Several studies have shown that smoking is a risk factor for the occurrence and the progression of RA [23-25].

The positivity of RF was found in about 64% of patients with RA. However, this result supports similar findings of other studies [24, 26].

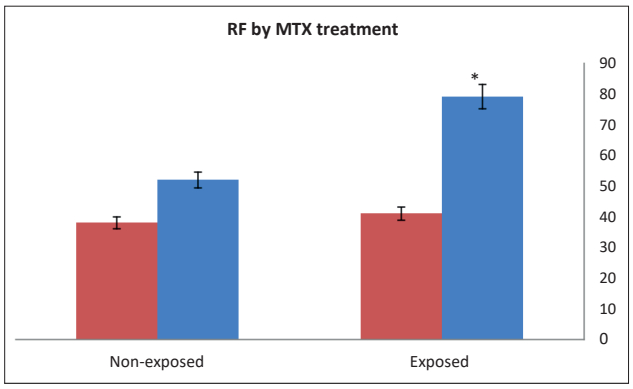

Figure 4. The relationship between RF and the exposure to MTX treatment. * denotes significance. Blue color: positive for RF, red color: negative for RF

The results showed that about 57% received MTX treatment. MTX is considered the prime treatment option for RA [27, 28]. Our findings are close to the results of the study of Kiely et al [29], who reported that about 58% of patients with RA received MTX treatment.

The prevalence of ILD in this study was 4.29%, which is slightly higher than that reported by Kiely et al [29], who found the prevalence of ILD as 3.7%. Other studies reported the prevalence of ILD to be up to 10% among patients with RA [7].

Taking into consideration the use of MTX treatment, the results showed that there are significant relationships between gender, age of RA diagnosis, smoking, and RF ($p<0.05$, for mentioned variables) (table 2). In general, this indicates that patients who require the treatment by MTX have more severe status. Similar trends were reported by the study of Kiely et al [29].

The results of the present study showed that ILD was impacted by male gender ($p=0.025$), age of RA diagnosis ($p=0.002$), smoking ($p=0.014$), RF (p=0.022), and MTX treatment ($p=0.008$). Although 9 cases (3.7%) of patients with RA developed ILD, it seems that the progression of RA-ILD was significantly precipitated by the mentioned variables. These results agree with other studies [26, 29-31], except for the MTX treatment that does not agree with previous studies [29, 32, 33]. However, we cannot generalize these findings due to small number of cases with RA-ILD.

6. CONCLUSION

The present study showed that the prevalence of RA-ILD is 3.7%. The progression of RA-ILD significantly depends on gender male, age of RA onset, smoking, RF, and MTX treatment.

- **Conflict of interest**: All authors have no conflict of interest.
- **Data availability**: All data are available and used in the study
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