ORIGINAL ARTICLE

PULMONARY MANIFESTATIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS VISITING TERTIARY CARE HOSPITAL

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Background: Rheumatoid arthritis is a common problem in elderly individuals. It is reported that lung involvement in these patients is widely present. This study was done with the purpose to assess the burden and characteristics of lung involvement in rheumatoid arthritis patients attending rheumatology clinic. **Methods:** This descriptive cross-sectional study, in which data was retrospectively collected, was carried out from April 2019 to December 2020 at the Rheumatology Department of Jinnah Postgraduate Medical Centre (JPMC), Karachi, Pakistan. All adult rheumatoid arthritis individuals, irrespective of gender or duration of disease, were consecutively enrolled. Information regarding the baseline characteristics, medication history for rheumatoid arthritis, findings of immunological tests along with the frequency of lung involvement and its pattern were observed. **Results:** Of 254 patients, the mean age was 37.46 ±12.39 years. Females were predominantly higher as compared to males, i.e., 232 (91.3%) vs. 22 (8.7%) respectively. Current smoking status was found positive in 7 (2.8%) patients. The mean disease duration was 4.41±3.96 years. Furthermore, frequency of pulmonary manifestation was observed in 45 (17.7%) patients. A significantly higher mean difference of age (*p*-value <0.001) and disease duration (*p*-value <0.001) was observed among patients with and without pulmonary manifestation. Moreover, a significant association of current smoker was also observed with pulmonary manifestation. **Conclusion:** A considerable number of patients with rheumatoid arthritis had pulmonary manifestation. Furthermore, a significant relationship was observed with age, duration of disease, and current smokers.

Keywords: Rheumatoid arthritis; Pulmonary manifestation; Pakistan

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INTRODUCTION

Rheumatoid arthritis, one of the common systemic diseases, which is characterized as inflammatory arthritis affecting multiple joints.[1,2] This condition results in a broad range of intrathoracic lesions. In patients with rheumatoid arthritis, pulmonary involvement and its patterns largely vary. Pulmonary manifestations of rheumatoid arthritis are diverse, with pleural abnormalities and interstitial lung disease being the most common.[3,4] The development of interstitial lung disease in early stages of rheumatoid arthritis is also reported in literature.[5,6] In particular, among patients with active seropositive rheumatoid arthritis, having current status of steroid use, and use of antitumor necrosis factor alpha are largely affected with lung diseases.[6] The current study's rationale is that the burden of rheumatoid arthritis and its complications are increasing. There is a need of studies on the related morbid consequences of rheumatoid arthritis. Published international studies have revealed development of lung diseases in patients with rheumatoid arthritis. However, a thorough literature search of studies from Pakistani has showed dearth of studies on this issue. The goal of this study was to determine the frequency and pattern of lung involvement in people with rheumatoid arthritis.

MATERIAL AND METHODS

The Rheumatology Department of Jinnah Postgraduate Medical Centre (JPMC) conducted a descriptive cross-sectional study from April 2019 to December 2020. Data was retrospectively collected. Ethical approval was received from JPMC's ethical review committee prior to the start of the study. All adult patients with rheumatoid arthritis, regardless of gender and duration of disease were consecutively enrolled in the study. Patients with the human immunodeficiency virus, chronic obstructive pulmonary illness, bronchogenic malignancy, or underlying heart disease were excluded.

The presence of non-specific interstitial pneumonia, pleural effusion, usual interstitial pneumonia, interstitial pneumonia, tuberculosis, and pulmonary embolism were observed as pulmonary manifestation. Furthermore, rheumatoid arthritis treatment histories and immunology test findings were also documented. The SPSS version 23 was used for analysis. Quantitative data such as age and disease duration were expressed as mean standard deviation. While categorical variables such as gender, lung involvement, medication history, and immunological examination findings were expressed as frequencies and percentages. The mean difference of age and duration of disease among patients with and without

pulmonary manifestation were explored using independent t-test. The chi-square test was used to examine the connection between categorical factors and pulmonary manifestation. Significance was defined as a *p*-value ≤0.05.

RESULTS

Of 254 patients, the mean age was 37.46±12.39 years. There were 137 (53.9%) patients with ≤37 years and 117 (46.1%) patients with >37 years of age. Females were predominantly higher as compared to males, i.e., 232 (91.3%) vs. 22 (8.7%) respectively. Current smoking status was found positive in 7 (2.8%) patients. The mean disease duration was 4.41±3.96 years. The frequency of pulmonary manifestation was observed in 45 (17.7%) patients. A significantly higher mean difference of age (*p*-value <0.001) and disease duration (*p*-value <0.001) was observed among patients with and without pulmonary manifestation. Moreover, a significant association of current smoker was also observed with pulmonary manifestation. (Table-1) Among 45 patients with pulmonary manifestation, nonspecific interstitial pneumonia was observed in majority 18 (40%) patients followed by interstitial pneumonitis 12 (26.7%), tuberculosis 7 (15.6), usual interstitial pneumonia 4 (8.9%), whereas pulmonary arterial hypertension and hypersensitivity pneumonitis was observed in 2 (4.4%) each. (Table-2) Immunological test showed that rheumatoid factor was observed in 210 (82.7%), anti-CCP in 123 (48.4%), antinuclear antibody in 10 (3.9%) patients. Furthermore, medication history showed steroid use and hydroxychloroquine use in 252 (99.2%) each. Non-steroidal anti-inflammatory drugs 238 (93.7%), Methotrexate 221 (87%), and Salazopyrin 116 (45.7%) were also found higher. (Table-3)

Table-1: Comparison of pulmonary manifestation with baseline characteristics of the patients (n=254)

Variables	Total	Pulmonary manifestation		
		Yes (n=45)	No (n=209)	*p*-value
Age, years	37.46 ±12.39	43.76 ±12.23	36.11 ±12.01	<0.001†
≤35	137	16 (11.7)	121 (88.3)	0.006‡
>35	117	29 (24.8)	88 (75.2)	
Gender				
Male	22	4 (18.2)	18 (81.8)	>0.999‡
Female	232	41 (17.7)	191 (82.3)	
Disease duration, years	4.41 ±3.96	7.24 ±6.86	3.79 ±3.83	<0.001†
≤3.5	179	27 (15.1)	152 (84.9)	0.090‡
>3.5	75	18 (24.0)	57 (76.0)	
Current Smoker				
Yes	7	4 (57.1)	3 (42.9)	0.006
No	247	41 (16.6)	206 (83.4)	

†ndependent t-test applied, ‡Chi-square test applied, *p*-value <0.05 taken as significant

Table-2: Lung involvement in patients with rheumatoid arthritis (n=45)

	n (%)
Nonspecific interstitial pneumonia	18 (40)
Interstitial Pneumonitis	12 (26.7)
Tuberculosis	7 (15.6)
Usual Interstitial Pneumonia	4 (8.9)
Pulmonary Artery Hypertension	2 (4.4)
Hypersensitivity Pneumonitis	2 (4.4)

Table-3: Immunological tests and medication history among rheumatoid arthritis patients (n=254)

	n (%)
Immunological tests	
Antinuclear antibody	10 (3.9)
ds-DNA	2 (0.8)
Rheumatoid factor	210 (82.7)
Anti Cyclic citrullinated peptide	123 (48.4)
Anti Ribonucleoprotein	2 (0.8)
Anti Ro Systemic lupus erythematosus	4 (1.6)
Anti La	2 (0.8)
Anti Scl 70	1 (0.3)
Medication	
Steroid use	252 (99.2)
Hydroxychloroquine	252 (99.2)
Methotrexate use	221 (87.0)
NSAIDs	238 (93.7)
Sulphasalazine	116 (45.7)
Leflunamide	13 (5.1)
Azathioprine	9 (3.5)
Aspirin	6 (2.4)
Calcium Channel Blocker	4 (1.6)
Sildinafil	4 (1.6)

DISCUSSION

Rheumatoid arthritis is a disease that targets the joints and leads to gradual destruction of bones and joints secondary to the production of autoantibody. The magnitude of rheumatoid arthritis is much lower in developed countries however, in developing countries it is still not properly reported as data on this topic is scarce. Individuals with Rheumatoid arthritis commonly present with joint disease, however, there are number of other presentations including eye diseases, vasculitis, subcutaneous nodule formation and lung disease. Patients with rheumatoid arthritis with pulmonary manifestation are at increased risk of morbidity and mortality. This study was conducted at a large tertiary care facility in metropolitan city of Karachi, Pakistan to assess the pulmonary manifestation among rheumatoid arthritis patients presented to the out-patient department. For this purpose, individuals who were diagnosed case of rheumatoid arthritis irrespective of age, duration of study, and gender were included. The findings of the study reported that the frequency of pulmonary manifestation was observed in 17.7% patients. A relatively higher prevalence of lung involvement in rheumatoid arthritis individuals is reported in a previous study by Habib et al.[7] According to findings of Habib et al, lung involvement was observed in 45% of the patients. However, in a large longitudinal study conducted in United Kingdom, the prevalence of lung disease was reported to be 7.7% in rheumatoid arthritis individuals.[8] Another study has reported lung involvement in 1–40% patients with rheumatoid arthritis.[9] There is wide variation in the magnitude of lung involvement in patients with rheumatoid arthritis in different studies as mentioned above and this may be due to change in geographical conditions, duration of disease and exposure to smoking. The current study finding also revealed a significantly higher mean difference of age, duration of disease, and current smoking among patients with and without pulmonary manifestation. However, this study reported an insignificant association of gender with pulmonary manifestation. Individuals with cigarette smoking tend to have higher pulmonary manifestations as compared to non-smokers with RA.[10–14] These findings support the fact that smoking results in the increasing complications of the rheumatoid arthritis. In particular, those who are heavy smokers or smoking for longer period of time, could have more negative consequences. Though, in the current study, the frequency of smokers was relatively small, still it showed a higher prevalence in rheumatoid arthritis patients with pulmonary manifestations. Cigarette smoking is connected to greater rheumatoid arthritis titers and plays an important role in antibody production.[15,16] Smoking may have a pertinent contribution in RA-ILD by enhancing citrullination of lung proteins and thus develops anti-CCP antibodies.[17,18] In population like Pakistan, where prevalence of smoking is highly prevalent, a special attention is required among these patients to prevent the severity of the disease. The current study has disclosed that out of forty-five patients with pulmonary manifestation, nonspecific interstitial pneumonia was observed in majority 40% patients followed by interstitial pneumonitis 26.7%, tuberculosis 15.6, usual interstitial pneumonia 8.9%, whereas pulmonary arterial hypertension and hypersensitivity pneumonitis was observed in 4.4% each.[14,19]

Contrary to the current study findings, a higher mean age was reported in previous study. However, like our study, females were predominantly higher.[12] Several other studies have reported use of Methotrexate as a risk factor for development of pulmonary disease in rheumatoid arthritis patients.[20–24]

In the current study, there were some limitations. First, this study was retrospective in nature and was carried out in a limited number of sample size. Second, certain important predictor variables like comorbid status, pulmonary function test, and severity of the pulmonary manifestation were not reported in the current study. Further large scale multicenter analytical studies are recommended that not only include important predictor variables but also reported long term follow-up findings of the patients as well. Despite the limitations of the current investigation, it is significant since it is the first study from Pakistan to report the burden of pulmonary manifestations in rheumatoid arthritis individuals, as well as the disease pattern.

CONCLUSION

A considerable number of individuals with rheumatoid arthritis had pulmonary manifestation. Furthermore, a significant relationship was observed with age, duration of disease, and current smokers.

AUTHORS' CONTRIBUTION

Conceptualization: Assadullah Dahani, Nasrullah Aamer, Nand Lal Seerani. Data Collection: Assadullah Dahani, Furqan Khan. Analysis: Assadullah Dahani, Muhammad Tariq Karim, Shafique Rehman Arain, Nasarullah Aamer, Furqan Khan. Methodology: Assadullah Dahani, Mohammad Tariq Khan, Nand Lal Seerani, Furqan Khan. Supervision: Shafique Rehman Arain. Writing – original draft: Assadullah Dahani. Writing –review & editing: Shafique Rehman Arain, Nasrullah Aamer, Nand Lal Seerani, Mohammad Tariq Khan

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