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ORIGINAL ARTICLE

Frequency of Smear Positive Pulmonary Tuberculosis in Rheumatoid Arthritis Patients Taking DMARDS at Khairpur Medical College/Hospital Khairpur

ABDUL HAYEE PHULPOTO[1], FARUKH IMTIAZ[2], MUNIR AHMAD CHANNA[3], ABDULLAH KHILJI[4], SYED SOHAIL ABBAS NAQVI[5], SYEDA ABIYA AMBER NAQVI[6]

[1]*Assistant Professor Medicine, Khairpur Medical College, Khairpur Mir's*
[2]*Assistant Professor Community Medicine, Khairpur Medical College, Khairpur Mir's*
[3]*Assistant Professor Medicine, Muhammadi Medical College, Mirpur Khas*
[4]*Associate Professor Anatomy, Khairpur Medical College, Khairpur Mir's*
[5]*Associate Professor Pathology, Khairpur Medical College, Khairpur Mir's*
[6]*Demonstrator Pathology, Khairpur Medical College, Khairpur Mir's*
Corresponding author: Abdul Hayee Phulpoto, Email: Abdulhayee648@gmail.com , Cell: 03337582636

ABSTRACT

Background and Aim: The clinical tuberculosis infection risk increases with rheumatoid arthritis and its medication. Chronic systemic inflammation caused by rheumatoid arthritis is an autoimmune disease may affect various organs and tissues. The present study was aimed to assess the frequency of smear positive pulmonary tuberculosis in rheumatoid arthritis patients taking DMARDS at Khairpur Medical College/ Hospital Khairpur.

Methodology: This cross-sectional study was conducted on 249 smear positive pulmonary tuberculosis in rheumatoid arthritis patients at the Department of Internal Medicine of Khairpur Medical College/Hospital Khairpur from March 2019 to July 2021. All the patients with cough for >3 weeks were enrolled by taking three sputum sample and risk assessment questionnaire. The Mycobacterium tuberculosis bacilli presence was identified based on acid fast staining technique. Tuberculosis incidence, medical records, and clinical manifestation were explored. SPSS version 24 was used for data analysis.

Results: Of the total 249 patients, 226 (90.8%) were male and 23 (9.2%) were females. The overall mean age was 65.73±7.53 years. The incidence of tuberculosis with rheumatoid arthritis was 4-fold. The prevalence of pulmonary tuberculosis and disseminated tuberculosis was 59 (72.8%) and 22 (27.2%) respectively in rheumatoid disease patients. The incidence of tuberculosis with rheumatoid arthritis reduced from 47.6 to 28 per 100 000 with $p<0.001$.

Conclusion: Our study found that pulmonary tuberculosis was more prevalent (72.7%) among adult tuberculosis patients with rheumatoid arthritis. Compared to general population, the tuberculosis incidence among rheumatoid arthritis patients was 4-fold.

Keywords: Smear positive pulmonary tuberculosis, Rheumatoid arthritis, DMARDS

INTRODUCTION

Rheumatoid arthritis (RA) is an autoimmune disease that causes chronic systemic inflammation in a variety of tissues and organs. Over the last decade, the clinical course of patients with active RA that was not controllable with conventional anti-rheumatic drugs has been modified, with good results, due to the introduction of a new class of anti-cytokine drugs, including anti-tumor necrosis factor (TNF) therapy, thereby changing the entire treatment strategy for RA. However, issues of increased infection rates, including tuberculosis, in RA patients have emerged. Extra-pulmonary tuberculosis is a common complication of anti-TNF therapy [1-4]. However, it is unclear whether this high frequency of extra-pulmonary tuberculosis is a feature of RA patients receiving anti-TNF therapy or whether anti-TNF therapy is not a factor in RA patients, as the characteristics of tuberculosis infection in RA patient's not receiving anti-TNF therapy have not been thoroughly studied.

Tuberculosis increased risk besides rheumatoid arthritis medication might be caused by genetic components, frailty, immunological disturbance, and co-morbidities [5–8]. Sweden based study found that RA patients who were not wide-open had 4-fold increased tuberculosis risk [9]. TB in rheumatoid arthritis (RA) patients is frequently disseminated during TNFi treatment [10, 11], However, TB clinical manifestations during DMARD treatment or in rheumatoid disease patients without specific medication are still poorly documented. To assess the characteristics of tuberculosis in RA patients receiving anti-TNF therapy, the characteristics of tuberculosis in RA patients not receiving anti-TNF therapy must be determined. As a result, the current study sought to clarify the characteristics of tuberculosis in RA patients, with a particular emphasis on the disease's characteristics in those who were not treated with anti-TNF therapy.

METHODOLOGY

This cross-sectional study was conducted on 249 smear positive pulmonary tuberculosis in rheumatoid arthritis patients at the Department of Internal Medicine of Khairpur Medical College/Hospital Khairpur from March 2019 to July 2021. Ethical approval was taken from the institutional ethical committee. All the patients with cough for >3 weeks were enrolled by taking three sputum sample and risk assessment questionnaire. The Mycobacterium tuberculosis bacilli presence was identified based on acid fast staining technique. Tuberculosis incidence, medical records, and clinical manifestation were explored. The tuberculosis clinical diagnosis requires active disease presence such as lesion causing symptomatic disease by

mycobacterium tuberculosis whereas tuberculosis diagnosis in the laboratory requires acid-fast bacilli (AFB) evidence of M. tuberculosis growth on microscopy from casual microorganism in culture medium. Test like tuberculin skin positive test assists in the diagnosis of M. tuberculosis. On a routine basis, Bacille Calmette-Guerin (BCG) vaccination is carried out. Tuberculin skin test does not validate active tuberculosis disease in such circumstances. Instead of purified protein derivative (PPD) test for latent tuberculosis infections, World Health Organization criteria were set for pulmonary tuberculosis diagnosis and treatment explained below; smear-positive pulmonary tuberculosis was considered in cases of a) at least two positive sputum specimens by microscopy for acid-fast bacilli, b) one positive sputum specimen for acid-fast bacilli by microscopy with pulmonary tuberculosis radiographic abnormalities, and c) M. tuberculosis positive culture and one positive sputum specimen by microscopy for acid-fast bacilli. As for the pulmonary tuberculosis treatment outcomes, all the patients were considered cured with a negative smear in th previous month or occasion and completed with no bacteriological proof of cure.

Patients without symptoms such as fever and cough besides negative culture over post three days or negative smears from sputum sample over three days of anti-tuberculosis treatment were discharged from hospital. Relapse was considered in cases where positive culture occurred after therapy completion in patients whose culture-negative results were obtained after antituberculosis drugs. SPSS version 24 was used for data analysis. The results are expressed in frequency and percentages with mean ± S.D. Chi-square test and Student's test were used for statistical analysis. Univariate and multivariate regression was used for rheumatoid arthritis disease risk factors and mortality. All the descriptive statistics were done with a 95% confidence interval and a 5% level of significance.

RESULTS

Of the total 249 patients, 226 (90.8%) were male and 23 (9.2%) were females. The overall mean age was 65.73±7.53 years. The incidence of tuberculosis with rheumatoid arthritis was 4-fold. The prevalence of pulmonary tuberculosis and disseminated tuberculosis was 59 (72.8%) and 22 (27.2%) respectively in rheumatoid patients. The incidence of tuberculosis with rheumatoid arthritis reduced from 47.6 to 28 per 100 000 with p<0.001, average marginal effect 3.4/100 000 per year, 95% CI <4.4, >2.4. Gender distribution is shown in Fiure-1. The demographic and other details are shown in Table-1. Of the total 249 patients, rheumatoid arthritis was in 168 (67.5%) patients and other rheumatoid diseases in 81 (32.5%). The prevalence of polymyalgia rheumatic, ankylosing spondylitis (AS), and Systemic lupus erythematous (SLE) were 16 (19.8%), 11 (13.6%), and 8 (9.9%) respectively. Figure 2 depicts the organ distribution of TB in RD patients who were or were not treated with DMARDs. The positive smear of tuberculosis was present in 244 (98%) cases. In Rheumatoid disease patients, the prevalent TB was pulmonary tuberculosis (72.8%) in rheumatoid disease patients. The prevalence of isolated TB pleurisy, extra-pulmonary forms of TB, and Disseminated TB was 9 (3.6%), 58 (23.2%), and 48 (19.3%) respectively as shown in Figure-3. Mean year-wise cases of tuberculosis are shown in Table-2.

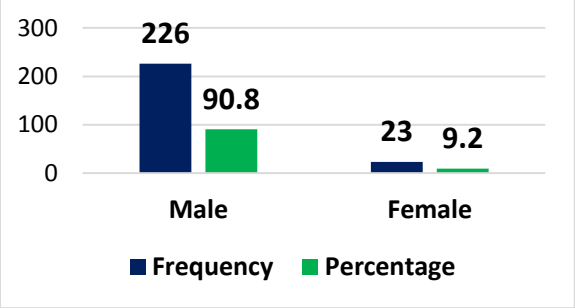

Figure 1: Gender distribution

Table 1: Patient's demographic details.

Parameters	Rheumatoid Arthritis (168)	Rheumatoid Disease (81)
Age (mean ± S.D) years	68.81±8.92	62.65±6.14
Disease Duration (SD) years	16 (12)	9 (10)
Smoking Habits 160, n (%) Current Smokers No Smoking Ex-Smokers	 23 (13.7%) 56 (33.3%) 28 (16.7%)	 13 (16%) 32 (39.5%) 8 (9.9%)
Co-morbidities 247, n (%) Pulmonary Diseases Diabetes Kidney Disease	 49 (29.2%) 21 (12.5%) 17 (10.1%)	 19 (23.5%) 14 (17.3%) 7 (8.6%)
Medication for RD DMARDS Glucocorticoids TNFi	 105 (62.5%) 105 (62.5%) 18 (10.7%)	 34 (42%) 49 (60.5% 3 (3.7%)

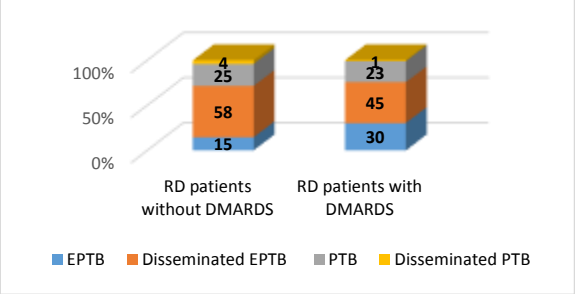

Figure 2: Tuberculosis Organ distribution in rheumatoid arthritis patients

Table 2: Mean year-wise TB cases

TB Cases	2019-2020	2020-21	2019-2021
Rheumatoid Diseases	24.53 (20-30)	16.62 (14-19)	21.83 (15-30)
RD with DMARDS		3.83 (1-5)	
RD without DMARDS		13.72 (11-15)	19.69 (13-29)
Rheumatoid Arthritis	16.95 (15-20)	12.9 (10-14)	14.87 (11-15)
RA with DMARDS		3.26 (1-5)	
RA without DMARDS		9.65 (8-10)	12.94 (9-15)

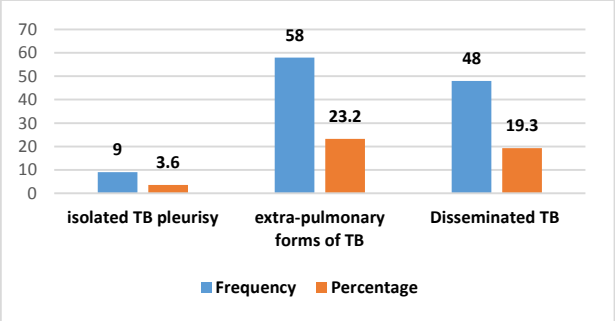

Figure 3: Prevalence of different forms of TB (n=249)

DISCUSSION

RA is thought to be associated with an increased risk of tuberculosis, which may be attributed to immunosuppressive therapy and the diseases own immunological dysfunction [12]. Although the incidence of tuberculosis has not been shown to increase after conventional immunosuppressive treatment in the United States [13], other studies have suggested that corticosteroids and TNF antagonists (but not MTX) increase the risk of opportunistic infections, including tuberculosis [14, 15]. Our findings show that corticosteroids are commonly given to RA patients in Japan who develop tuberculosis.

The annual incidence of tuberculosis (TB) in patients with RDs was four times that of the general population. This finding is persistence with the findings of a RA cohort study from Spain, Korea and Sweden [16-18]. During our study period, the prevalence of tuberculosis fell by nearly half. The decreasing incidence of tuberculosis in Rheumatoid disease patients in spite of increased clinical TNFi reflects the cohort effect of older generations, but it also demonstrates the effectiveness of LTBI screening and treatment, as well as patient selection. Due to the high cost of TNFi, it was initially used by young and working people.

Tuberculosis higher prevalence in rheumatoid disease patients are mainly due to old age generation suffers more from both RD and TB. However, rheumatoid disease patients are more susceptible to tuberculosis in addition to DMARDs and TNFi usage [19, 20]. Prior to admission, the patient's corticosteroid doses were increased above administrated rheumatoid arthritis about three times. However, several complications with infection may result from corticosteroids administration for the long term. No evidence has been found regarding tuberculosis relapse increases risks with DMARDs. Therefore, instead of increasing corticosteroids dose, DMARDs could provide effective results and physicians should know the antituberculosis drugs worsening effect for the utilization of rheumatoid arthritis. Advance research should be carried out to propose effective strategies for rheumatoid arthritis treatment while receiving anti tuberculosis treatment. People with RDs may be able to work for longer if advanced medicines assist in maintaining efficient capability [21, 22]. In the future, potential occupational exposure must be considered, particularly in the treatment of TNFi patients. Population transition from TB low-incidence area to highly infected areas may become infected. Physicians should be aware of the risk of tuberculosis in immigrants from high-incidence areas.

TB contacts, underweight people, dialysis patients, health-care workers, TNFi patients, and immigrants from countries with a high burden of tuberculosis, diabetes patients, smokers, and radiological findings of fibrotic lesions in individual have all been linked to an increased risk of TB [23, 24]. If clinicians suspect LTBI or active TB, these risk factors should be useful.

Pulmonary tuberculosis is the most common type of tuberculosis in the general population, accounting for more than 80% of cases, while disseminated tuberculosis is uncommon (5–10% of cases) [25, 26]. Patients with RA who are treated with TNFi are more likely to develop disseminated or extra-pulmonary tuberculosis [27]. Rheumatoid disease patients had disseminated disease in a 19.3% cases, which was consistent with the another study results comprising 20 rheumatoid arthritis patients [28]. Because of the diversity of rheumatoid disease patients, our concentrated on clinical data for RA patients, which may have limited the scope of our study. Our study period may have been limted to demonstrate the effect of DMARDs on TB rates, but the incidence trend was still downward. Notification rates for clinically diagnosed TB cases may differ between clinics. Unfortunately, our analysis took a long time, but these data still provide clinically relevant information on the risk and manifestation of tuberculosis in patients with RD.

CONCLUSION

Our study found that pulmonary tuberculosis was more prevalent (72.7%) among adult's tuberculosis patients with rheumatoid arthritis. Compared to general population, the tuberculosis incidence among rheumatoid arthritis patients was 4-fold.

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