Original Article:

Effect of Type 2 Diabetes Mellitus on Clinical and Radiological Presentation and Drug Resistance in Pulmonary Tuberculosis

Authors
Sukriti Arora, MBBS Student,
Bharti Chogtu, Department of Pharmacology,
Rahul Magazine, Department of Pulmonary Medicine,
Kasturba Medical College, Manipal, Manipal University, Karnataka 576104, India.

Address for Correspondence
Dr. Rahul Magazine,
Department of Pulmonary Medicine,
Kasturba Medical College, Manipal,
Manipal University,
Karnataka - 576104, India.
E-mail: rahulmagazine@gmail.com

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Abstract: Studies suggest that tuberculosis (TB) patients with diabetes mellitus (DM) present atypically. This study was done to assess symptoms, radiological findings and multidrug resistance in TB patients with or without diabetes. A prospective study on 100 TB patients was carried out in a tertiary care hospital. The clinical presentation of patients in two groups did not vary. Bilateral and lower lobe involvement was seen more in diabetics. Lung cavitation and multidrug resistance was predominant in non-diabetics. Though clinical presentations remain the same, radiological findings vary in diabetics. This information can help in better understanding and thereby better treatment outcomes in patients with TB and DM.

Key Words: Tuberculosis, diabetes mellitus, radiological findings

Introduction:
Diabetes Mellitus (DM) and tuberculosis (TB) represent a critical intersection between communicable and non-communicable diseases in developing countries. Studies examining the incidence of TB show that patients with DM have 1.5 times higher risk of developing TB than the non-diabetic ones.[1] A systematic review of 13 studies suggested that diabetic patients had about a 3-fold risk of developing TB when compared to those without diabetes.[2] The association between these two diseases may become even more important, as the prevalence of diabetes is on rise.[3]

Two factors responsible for treatment failure in TB with DM are chronic hyperglycemia disabling the immunity to mycobacterial TB [4] and suboptimal plasma levels of antitubercular drugs in diabetics as compared to non-diabetics.[5] Evidence concerning radiological appearances in TB patient groups with and without concurrent DM is conflicting. Some studies suggest that TB patients with DM are more likely to present with atypical images [6] whereas others suggest there are no differences in the radiological findings.[7] Diabetes cause changes in the clinical manifestations of TB, often exacerbating them. Effects of DM on the treatment and outcomes of TB infection show varied results.[8] An association between DM and multi-drug resistant TB (MDR-TB) has been shown in some studies [9], while others suggest that there exists no association.[10] Since the nature of relationship between DM and TB has been evaluated but not fully understood, the study assessed the clinical presentation, chest X-Ray findings and multi-drug resistance in TB patients with and without DM.

Materials and Methods
A prospective study was performed in diagnosed cases of pulmonary TB with or without concurrent diabetes mellitus in a tertiary care hospital in South India after approval from the Institutional ethics committee. The patients were enrolled as per the inclusion criteria and a written informed consent was taken. Patients of tuberculosis of both sexes aged over 12 years with or without diabetes were included in the study. The investigator visited the pulmonary medicine wards and recorded the baseline investigations like hemoglobin, ESR and sputum status of patients diagnosed with pulmonary TB. The presenting symptoms, radiological findings, and presence or absence of MDR tuberculosis in TB patients without DM was compared with those with concurrent DM.

Results:
A total of 100 patients with pulmonary tuberculosis were included in the study. The following results were obtained:

1. Socio-demographic Parameters: The patients were in the age group of 16-89 years. Of these, patients in the age group of 41-60 years constituted 47% of the study population. The
number of male patients (67%) was almost double that of females (33%). Most of the patients were agriculturists (39), 7 were drivers and of the 33 females, 27 were homemakers.

2. Baseline Investigations: 56% of the patients had hemoglobin less than 12g%. 89% of the patients had high ESR values. Deranged renal function tests were noted in 19% of the patients. A high proportion (~50%) of the patients was found to have abnormal liver function tests. The random blood glucose of diabetics and non-diabetics is shown in Fig 1. WBC count was increased in 60% of patients.

3. Treatment category: Out of the 44 patients with concurrent diabetes, 32 were on Category I DOTS, 8 on Category II and 4 were prescribed MDR TB treatment (Fig. 2). Out of the 56 non-diabetic patients, 31 were on Category I, 15 on Category II and 10 on treatment for MDR-TB (Fig. 3).

4. Clinical Features: Presenting symptoms of diabetics and non-diabetics with pulmonary tuberculosis is shown in the following Figures 4, 5.

5. Radiological Findings:
   Bilateral lung involvement was seen more in diabetics as compared to non-diabetics (Figure 6).

   - **Lobar Involvement**: Lower lobe involvement was more in diabetics as shown in Figure 7.
   - **Lung Cavitation**: Lung cavitation was more in nondiabetics as compared to diabetics as shown in Figure 8.
Discussion:
Co-morbidity with TB and DM is associated with deterioration in both disease conditions. It is therefore important that poor glycemic control in patients suffering from chronic infectious diseases like TB be taken care of. Also, TB, a chronic infection, can be associated with reactionary hyperglycemia secondary to increased production of counter-regulatory stress hormones like epinephrine, glucagon, cortisol, and growth hormone that act synergistically.[11] DM alters the clinical presentation of TB and its outcomes like delayed sputum conversion, treatment failure and increased mortality.[12] DM increases the risk of TB, and on the other hand affects anti-tubercular treatment adversely.[13] Increased blood glucose levels also decrease the mobility, adhesion, and bactericidal phagocytosis of white blood cells.[14] DM by suppressing immunity decreases ability to produce immunoglobulin and lymphocyte function of T cells. B cells, and antibodies.[15] TB patients with DM have a higher risk of death when compared to TB without DM.[13]

This prospective study was performed to assess the clinical and radiological manifestations and drug resistance in a total of 100 diagnosed cases of Pulmonary TB with and without co-existent Type 2 Diabetes Mellitus in each group being 44 and 56 respectively. The sputum status of 96 of these patients was positive for acid-fast bacilli whereas the bacilli were demonstrated in the bronchial lavage fluid of 4 patients.

Patients were in the age group of 16-89 years. Those in the age group of 41-60 years comprised 47% of the study population. Also, 26 patients belonged to the age group of 20-40 years, indicating that a large proportion of the working population is affected by the disease. This results in loss of productive days directly due to the disease. Of the patients, 67% were males, most of them agriculturists and daily wage workers. This is in consistence with the fact that overcrowded houses and poor ventilation increase both the likelihood of exposure to tubercular bacilli and progression to disease.

The baseline investigations showed that 56% of the patients had hemoglobin levels less than 12 gm%. Anemia was observed in 32-94% of patients with tuberculosis.[16] Malnutrition is severe in patients of tuberculosis with anemia as compared to those without anemia.[17] Most of them (89%) had raised ESR. These findings reassert that active TB is mostly associated with very high ESR values (>100 mm/hr) as stated in a study conducted in South Africa.[18]

The treatment group of Category I includes the newly diagnosed sputum smear positive or sputum smear negative pulmonary TB patients. Cases of sputum positive relapse, sputum positive failure or re-treatment after default are included in category II. Patients in whom the tubercular isolates are multiply resistant to isoniazid and rifampicin, the most powerful first line anti-TB drugs are labeled as MDR-TB patients. It was observed in our scenario that most of the diabetic patients (73%) were receiving Cat I DOTS, 18% on Cat II and there were 4 cases of MDR TB. Of the non-diabetics, 55% were receiving Cat I DOTS, Cat II was being given to 27% and 10% were multi-drug resistant. A study conducted in Saudi Arabia proposed that pulmonary TB-DM patients had a lower prevalence of resistance to any anti-tubercular drug (6.4% vs. 16.0%).[8] A study done in Texas and Mexico on the contrary found that type 2 diabetes mellitus patients with TB were more prone to drug resistance.[19] Sputum smear-positive PTB is more common in TB patients with DM,[20] while no difference in type of TB at diagnosis has also been reported.[21] In sputum smear conversion at 2 months, no significant difference was found in positive TB patients with and without DM was noted and there was no difference in the rates of treatment success between the two groups.[22] So authors are of the opinion that presence of DM does not adversely affect the outcomes in TB.

The presentation of TB in diabetic subjects may not always be different as they manifest themselves with the common symptoms in diabetic subjects as in any other individual without DM. In agreement with this statement, patients from both groups presented with similar symptoms; fever with cough being the commonest symptom. 26 out of the 44 diabetic patients manifested dry cough whereas 13 had cough with expectoration. This was comparable to the non-diabetic group in which the number of patients presenting with dry cough and cough with expectoration was 33 and 12 respectively. Loss of weight and loss of appetite was seen more frequently in the non-diabetic patients (33.9% vs 22.7%). A possible explanation of this finding may be that obesity and weight gain are important determinants of insulin resistance.

A study done in Thailand including 227 patients with TB proclaimed that significantly higher proportion of TB patients with DM presented with anorexia and haemoptysis whereas cough was predominant in patients without DM.[23] In another study, no significant difference between symptoms was seen between patients of TB with or without diabetes.[24] In the present study, 46.1% of the non-diabetic patients and 28.9% of the diabetic patients were found to have sputum positive failure or relapse. Treatment outcome was similar in the two groups.[30] In a study of 192 patients, diabetes was not a significant risk factor for diabetes, and that all diabetic patients were screened for TB when symptomatic.[32] It is conceivable that without active intervention the burgeoning diabetes epidemic will adversely impact TB control in India.
A better understanding of the differences in clinical and radiological manifestations would help in managing TB with concomitant diabetes in a rational way and lead to better treatment outcomes.

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Conflict of Interest:
The authors declare that there exists no conflict of interest in the making of this paper.

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