

Effect of age on presentation with diabetes: Comparison of nondiabetic patients with new smear-positive pulmonary tuberculosis patients

Jagdish Rawat, Girish Sindhwani, Debasish Biswas¹

Departments of Pulmonary Medicine and ¹Microbiology, Himalayan Institute of Medical Sciences, Dehradun, Uttarakhand, India

ABSTRACT

Background: Diabetes mellitus (DM) has been reported to modify the presenting features of pulmonary tuberculosis (PTB), but data regarding the effect of diabetes on the presentation of PTB are highly variable. **Objective:** To determine whether DM alters the demographic, clinical, and radiological manifestations of tuberculosis and whether the effect of diabetes varies with the age group of PTB patients. **Materials and Methods :** This prospective observational study was conducted on new smear-positive PTB patients with DM (PTB-DM group) and non-diabetic PTB patients (PTB group). Patients of both groups were again divided into six age groups (15–29, 30–39, 40–49, 50–59, 60–69, and >70 years) to analyze and compare the impact of age on clinicoradiological presentations of PTB. **Results:** Patients in the PTB-DM group were significantly older (53.34 ± 14.06 year) in comparison to their nondiabetic counterparts (PTB group) (44.35 ± 18.14 year) ($P < 0.001$). The former group also had a lower male:female ratio, although the difference was not statistically significant (1.16:1 vs. 2.05:1, $P = 0.101$). Tuberculin positivity was significantly higher in the PTB group, compared with patients in the PTB-DM group ($P < 0.004$). The proportion of patients with lower lung field involvement ($P = 0.003$) and cavitations ($P = 0.005$) was also higher in the former group compared with the latter. **Conclusion:** Diabetic patients with tuberculosis were relatively older, had lower tuberculin positivity, and higher proportion of lower lung field involvement and cavitation in comparison to nondiabetic patients.

KEY WORDS: Comparative study, diabetes mellitus, pulmonary tuberculosis, radiology

Address for correspondence: Dr. Jagdish Rawat, Department of Pulmonary Medicine, Himalayan Institute of Medical Sciences, Dehradun, Uttarakhand - 248140, India. E-mail: drjagdishrawat@yahoo.com

INTRODUCTION

Diabetes mellitus (DM) is known to be an important predisposing factor in the development of pulmonary tuberculosis (PTB). The frequency of tuberculosis in diabetics is reported to be four times higher than in nondiabetics.^[1] The global burden of diabetes is increasing, and recent estimates indicate that India is poised to become the diabetes capital of the world. There were an estimated 20–30 million people in India with diabetes

in 2000 (estimates vary with study methodology)^[2,3] and projections suggest that the prevalence will rise to almost 80 million people by 2030.^[3] It is possible that in areas of high diabetes prevalence, the impact of the diabetes epidemic on tuberculosis could be as great as that of human immunodeficiency virus (HIV).^[4] However, the overall importance of diabetes as a risk factor for tuberculosis is still largely unknown, although a recent analysis in Mexico concluded that, in the population studied, 25% of PTB was attributable to diabetes.^[4]

The impact of age on the clinicoradiological presentation of PTB in diabetic patients is important because misinterpretation of the clinicoradiological findings might delay diagnosis and initiation of treatment, thus risking the dissemination of *Mycobacterium tuberculosis* to others. In the Indian context, there is no such comparative study on patients with PTB with diabetes which explore the impact of age on demographic, clinical, and radiological presentations. Some studies conducted

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outside India reported atypical radiological patterns of PTB among diabetic patients,^[5-10] but only few^[11,12] of these studies analyzed the possible effect of age. In order to identify age-related changes in patients with PTB with DM, this study was designed to compare the effect of age on demographic, clinical, and radiological features and compare these features with nondiabetic tubercular patients.

MATERIALS AND METHODS

We included consecutive new sputum smear-positive PTB patients who were aged 15 years or more and who presented to the outpatient and inpatient departments of pulmonary medicine from a period of December 2007 to November 2008, at Himalayan Institute of Medical Sciences, Utrakhand, Dehradun. Diagnosis of PTB was made on the basis of clinical presentations, chest radiographic findings, and microscopic detection of Acid Fast Bacilli in sputum samples.

All patients with confirmed tuberculosis were screened for DM by measuring fasting glucose concentration. No antidiabetic agents were received within 48 h before collection of blood samples, and DM was diagnosed if the fasting blood glucose concentration was more than 126 mg/dl.^[13] Serological testing for HIV was done in all patients with PTB at the integrated counseling and testing centre, located within hospital. We excluded mixed form of tuberculosis (PTB plus extra PTB), retreatment cases of PTB, and HIV seropositive to allow better data comparison.

Every posteroanterior chest roentgenogram was reviewed by either pulmonologist or radiologist. Chest radiographs of difficult images were jointly interpreted by both reviewers. The tubercular lesion was classified according to the site of lesion (unilateral or bilateral) and extent of lesion. Extent of lesion was again divided into three categories, viz, minimal lesion (i.e., disease with a combined area of less than that of the right upper lobe), moderately advanced lesion (i.e., disease with a combined area of less than that of the right lung but more than that of the right upper lobe), and far advanced lesion (i.e., disease with a combined area of more than that of the right lung). Lesions were considered to be located in the upper and lower fields depending on whether the majority of the lesion was present in the upper or lower half, respectively. A cavitation was considered to be present only when its diameter was larger than 2 cm.

A total of 156 patients were included in this study. For further analysis patients were divided into two groups: PTB with DM (PTB-DM group) and nondiabetic patients with PTB (PTB group). Patients were again subdivided into six age groups (15–29, 30–39, 40–49, 50–59, 60–69, and >70 years) in order to assess and compare impact of age on demographic, clinical, and radiological features of both groups of patients.

Statistical analysis

The SPSS (Statistic package for social sciences) program for windows 7.0 was used for the statistical analyses. Chi-square test, Fisher's Chi-square test, and univariate arranged Chi-square test were used for comparing the qualitative data. Numerical variables were compared between the two groups by using the unpaired *t* test. Statistical analysis was two-tailed and *P* value of less than 0.05 was considered significant.

RESULTS

A total of 156 patients were included in this study, out of which 104 patients were in PTB group and 52 patients in PTB-DM group. The age distribution of patients in the two groups is shown in Table 1.

Patients in the PTB-DM group were significantly older (53.34 ± 14.06 years) in comparison to PTB group (44.35 ± 18.14 years) ($P < 0.001$) and had a lower male:female ratio (1.16:1 vs. 2.05:1, $P = 0.101$).

The influence of age on symptoms of PTB-DM and PTB group is shown in Table 2. No significant difference was found in symptoms of all six age groups except for the frequency of hemoptysis, which decreased in both groups as age increased. Tuberculin positivity was significantly higher in the PTB group, compared with patients in the PTB-DM group ($P < 0.004$). Moreover, patients with age more than 60 years had significantly lower proportion of tuberculin positivity in the PTB group, compared with those aged lower than 60 years ($P = 0.008$). On the other hand, this difference was not significant in the PTB-DM group ($P = 0.89$), thereby signifying that diabetes has an age-independent effect on tuberculin response.

The proportion of patients with lower lung field involvement and cavitations was significantly higher in the PTB-DM group, compared with patients in the PTB group ($P = 0.003$ and $P = 0.005$, respectively). While in nondiabetic tubercular patients the proportion of patients with lower lung field involvement and cavitations was significantly different between patients younger and older than 60 years ($P = 0.01$ and $P = 0.003$, respectively), the same difference was not observed in the PTB-DM group ($P = 0.62$ and $P = 0.52$, respectively). The age-wise distribution of lower zone involvement and cavitations in the two groups of patients is shown in Figures 1 and 2.

Table 1: Distribution of study population in various age groups

Age groups	PTB-DM (n = 52)	PTB (n = 104)
15–29 year	3	29
30–39 year	4	18
40–49 year	12	10
50–59 year	14	17
60–69 year	12	19
>70 year	7	11

PTB-DM: Pulmonary tuberculosis- Diabetes mellitus

Table 2: Differences in clinical features and Mantoux test among patients with PTB-DM and PTB group

Symptoms	15–29 years (%)	30–39 years (%)	40–49 years (%)	50–59 years (%)	60–69 years (%)	>70 years (%)	P value
Cough							
PTB	28 (96.5)	16 (88.8)	7 (70.0)	16 (94.2)	16 (84.2)	10 (90.9)	
PTB-DM	2 (66.6)	3 (75.0)	11 (91.6)	13 (92.8)	11 (91.6)	6 (85.7)	0.855
P value	0.041	0.465	0.189	0.886	0.546	0.732	
Fever							
PTB	28 (96.5)	18 (100)	10 (100)	14 (82.3)	18 (94.7)	11 (81.8)	
PTB-DM	3 (100)	3 (75.0)	10 (83.6)	12 (85.7)	12 (100)	5 (71.4)	0.055
P value	0.743	0.029	0.175	0.800	0.419	0.732	
Hemoptysis							
PTB	14 (48.2)	6 (33.3)	3 (30.0)	3 (17.6)	3 (15.7)	0	
PTB-DM	1 (33.3)	1 (25.0)	2 (16.6)	2 (14.2)	2 (16.2)	0	0.083
P value	0.621	0.746	0.457	0.800	0.948		
Mantoux							
PTB	20 (68.9)	11 (61.1)	6 (60.0)	11 (64.7)	8 (42.1)	3 (27.2)	
PTB-DM	1 (33.3)	1 (25.0)	5 (41.6)	4 (28.5)	4 (33.3)	2 (28.5)	0.004
P value	0.216	0.189	0.391	0.045	0.625	0.952	

PTB-DM: Pulmonary tuberculosis- Diabetes mellitus

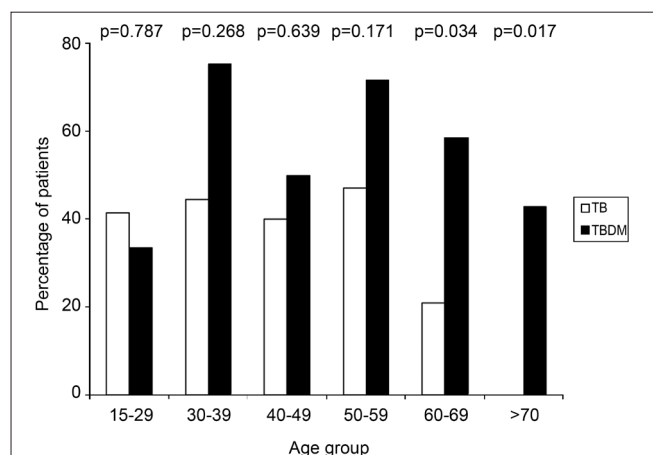


Figure 1: Comparison of cavitory lesions between PTB patients with and without DM

DISCUSSION

In this study, we have explored the differences in the clinicoradiological features of PTB between diabetic and nondiabetic patients. We report that diabetic tubercular patients are relatively older and have higher proportion of lower lung field involvement and cavitations, compared with their nondiabetic counterparts. Moreover, the effect of age on tuberculin positivity, cavitations, and lower lung involvement is less marked in diabetic patients.

This study showed that male gender predominates among PTB group, a finding that has already been reported in several studies.^[14-20] One possible explanation for this male predominance may be that in most countries young male usually have more social, cultural, and labor activities than women, which predispose them to a higher transmission rate of *M. tuberculosis*. Our study did not fully support the above mentioned theory, because if sociocultural factors were the only reason of the male predominance among tuberculosis patients, then this predominance would also be expected to occur in diabetic tuberculosis patients,

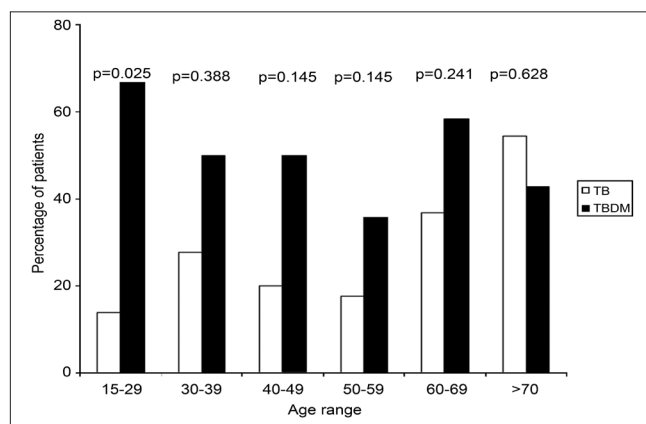


Figure 2: Comparison of lower zone involvement in PTB patients with and without DM

although we observed a steady decline in the percentage of male in the PTB-DM group. Our observation that low male:female ratio occurs in PTB-DM group is consistent with Pérez-Guzmán *et al.*,^[12] One possible hypothesis for this gender difference is that Type II DM might be more prevalent in females with age more than 50 years. Other causes might be possible for this gender differences which need further study.

Our study showed that there is no influence of age on symptomatology of both groups except hemoptysis which is more common in younger patients of both group. Similar observations have been reported by other studies.^[21,22] These finding might be due to better immunity in younger individuals in comparison to elderly so that there is higher frequency of lung cavitations which caused more hemoptysis in this population.

Our data suggest that lower lung lesion increased while cavitations decreased with progression of age in nondiabetic group, while higher proportion of lower lung lesion and cavitations was found in all ages in PTB-DM group. The finding of PTB group is consistent with those of Pérez-Guzmán *et al.*,^[11] Cavalcanti *et al.*,^[23] and our

previous study.^[16] It has been suggested that the higher frequency of lower lung lesion in PTB may be due to immunological abnormalities, higher frequency of primary tuberculosis, higher VA/VQ ratio in lower zone, and higher partial pressure of oxygen in the lower lobe in elderly. Therefore, age-induced change should favor multiplication of *M. tuberculosis* in lower lung zone.

In this study, we found that in PTB group cavitations were significantly higher in younger patients, while in PTB-DM group the age-dependent difference in the occurrence of cavitations was not observed. These findings in PTB-DM group may be explained by the fact that the mean age of tuberculosis in PTB-DM group is significantly higher. Many studies have found that with progression of age, patients' perception of his symptoms become blunted, leading to late presentation and increased progression of the disease. This consequently leads to increased occurrence of cavitations in this group. Further work has to be done to better explain this interesting phenomenon.

We conclude that PTB with DM was associated with lower male:female ratio, low tuberculin positivity, and high proportion of lower lung field involvements in comparisons to nondiabetic patients. No significant difference was found in symptoms among both groups. Hence, PTB with DM resembles elderly tuberculosis and age-related changes in presentation observed in nontubercular patients are less distinct among diabetic tubercular patients.

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Announcement

Workshop on Intensive Respiratory Critical Care

The Indian Chest Society is organizing Workshops on "Intensive Respiratory Critical Care" in the month of September/October 2011 at various places across the country. The workshop is for the benefit of Post Graduate students, Practicing Chest Physicians and others who are interested in acquiring knowledge in Respiratory Critical Care along with hands on training. The course is limited to only 25 delegates per center. For further details of centers please refer to Indian Chest Society website or contact at following address:

Dr. Vijayalakshmi Thanasekaraan, Course Director, No.3, Third Cross Street, West C.I.T. Nagar, Chennai – 600035.
 E-mail: drvthanasekaraan@yahoo.com Mobile: 09840112099