

Research Article

Clinical and Demographic Patterns of Pulmonary Tuberculosis in Patients with Diabetes Mellitus: Impact of Diabetes Mellitus on Patient

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Abstract

Background: Tuberculosis (TB) is a communicable infectious disease and one of the leading causes of death. Until the coronavirus pandemic, tuberculosis was the leading cause of death from a single infectious agent, more than HIV/AIDS. Due to urbanization and rapid social and economic development, there is a rapidly increasing diabetes mellitus (DM) epidemic and India has the second largest number of DM patients in the world. There are around 74.2 million DM cases and 40.1 million people with impaired glucose tolerance. Tuberculosis is more common in low- and middle-income countries. The increasing trend of the two diseases poses a major challenge for the tuberculosis control program.

Methods: The main goal of this research was to investigate clinical and demographic patterns of pulmonary tuberculosis in patients with DM. It is a prospective, observational, in-hospital study. We studied 165 PTB patients associated with DM who were at least scanty/1+ positive on smear or had Mycobacterium TB sputum CBNAAT detected.

Results: Of the 165 patients, 127 PTB-DM patients were male and 38 were female. The most common symptom was cough, which occurred in 164 (99.4%) patients. Fever was the second most common symptom in 152 (92.1%) patients and anorexia was the third most common symptom, occurring in 119 (72.1%) patients.

Conclusion: The majority of patients were from IPD 88 (54%), suggesting that PTB-DM cases have a more severe and complicated presentation. Male patients are affected more frequently than female patients. People in the age group 31–60 years often suffer from PTB-DM. Cough, fever, and anorexia are the most common symptoms, while chest pain and breathlessness are more common in the older age group. History of PTB in DM patients is also of concern as the present study shows that there is a possible association with relapse or reactivation of PTB as well as drug resistance of PTB.

Keywords: tuberculosis, diabetes mellitus, PTB-DM, pulmonary, PTB

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1. Introduction

Tuberculosis (TB) is a transmissible infectious disease and one of the leading causes of death [1]. Until the coronavirus (Covid-19) pandemic, TB was the leading cause of death from a single infectious agent, more than HIV/AIDS [1]. TB is caused by *Mycobacterium tuberculosis* (MTB), which is transmitted by inhaling droplet germs from coughing and/or sneezing in untreated pulmonary TB patients [1]. More than 40% of the Indian population is infected with MTB, which means that patients become infected but do not develop the disease [2]. Patients with latent TB have a 10% lifetime risk of developing TB, and patients with an immunocompromised status such as HIV, DM, malnutrition, alcohol abuse, or tobacco use are more prone to developing TB than the general population [1]. The Global Tuberculosis Report 2021 reported an estimated 5.8 million cases of TB worldwide in 2020.

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by insufficient insulin production by the pancreas, or the body's inability to use insulin [3]. Insulin's job is to regulate blood sugar levels in the body. Abnormality in insulin function leads to hyperglycemia and the development of DM.

Moreover, 537 million adults are living with DM and the number is projected to increase to 643 million by 2030 and 784 million by 2045 [4]. Due to urbanization and rapid social and economic development, there is a rapidly increasing DM epidemic and India has the second largest number of DM patients in the world. There are around 74.2 million DM cases and 40.1 million people with impaired glucose tolerance [4]. According to a study by the Indian Council of Medical Research, 11% of the urban population and 3% of the rural population over the age of 15 have DM and about half of 3% of the rural population and a third of 11% of the urban population are not known to have DM.

TB is more common in low- and middle-income countries [1] and 4 in 5 DM patients live in low- and middle-income countries [4]. This poses a major challenge for TB control programs due to the increasing trend of both diseases. DM is a known risk factor for TB and approximately 10% of TB cases worldwide are associated with DM [5]. DM is a chronic metabolic disorder that affects the immune system and leads to an increased susceptibility to TB infection, which poses a two to three times higher risk than people without DM [5]. Patients with TB and DM have a higher risk of treatment failure with drug resistance and an increased risk of death. Medications used to treat TB also increase the risk of glucose intolerance and can cause problems controlling blood sugar in people with DM.

DM patients who develop pulmonary TB often present with an atypical radiographic presentation with sputum AFB results. Thus, the main objective of this study is to analyze the clinical and demographic pattern in PTB with DM in relation to the patient's blood glucose level.

2. Methods

2.1. Study design

This study is a hospital-based prospective observational study.

2.2. Sample size

165 patients with pulmonary TB associated with DM with at least scanty/1+ smear positive or MTB detected on sputum CBNAAT were included in the current study.

2.3. Screening of patients

All known DM patients show signs and symptoms of TB. All newly diagnosed DM patients were referred by the medical department for screening for pulmonary TB. In DM patients, chest X-rays indicate consolidation. See Figure 1 for details.

2.4. Inclusion criteria

1. All DM patients with signs and symptoms of TB and AFB-positive sputum.
2. In all DM patients, consolidation was noted on chest X-ray and sputum was determined to be AFB positive or sputum CBNAAT showed MTB detected.
3. All sputum-positive patients recently detected as DM patients.
4. All newly diagnosed DM patients presented to the Department of Pulmonary Medicine for TB screening who were found to be AFB-positive in sputum.

2.5. Exclusion criteria

1. All DM patients younger than 12 years.
2. All DM patients with an HIV-positive status.

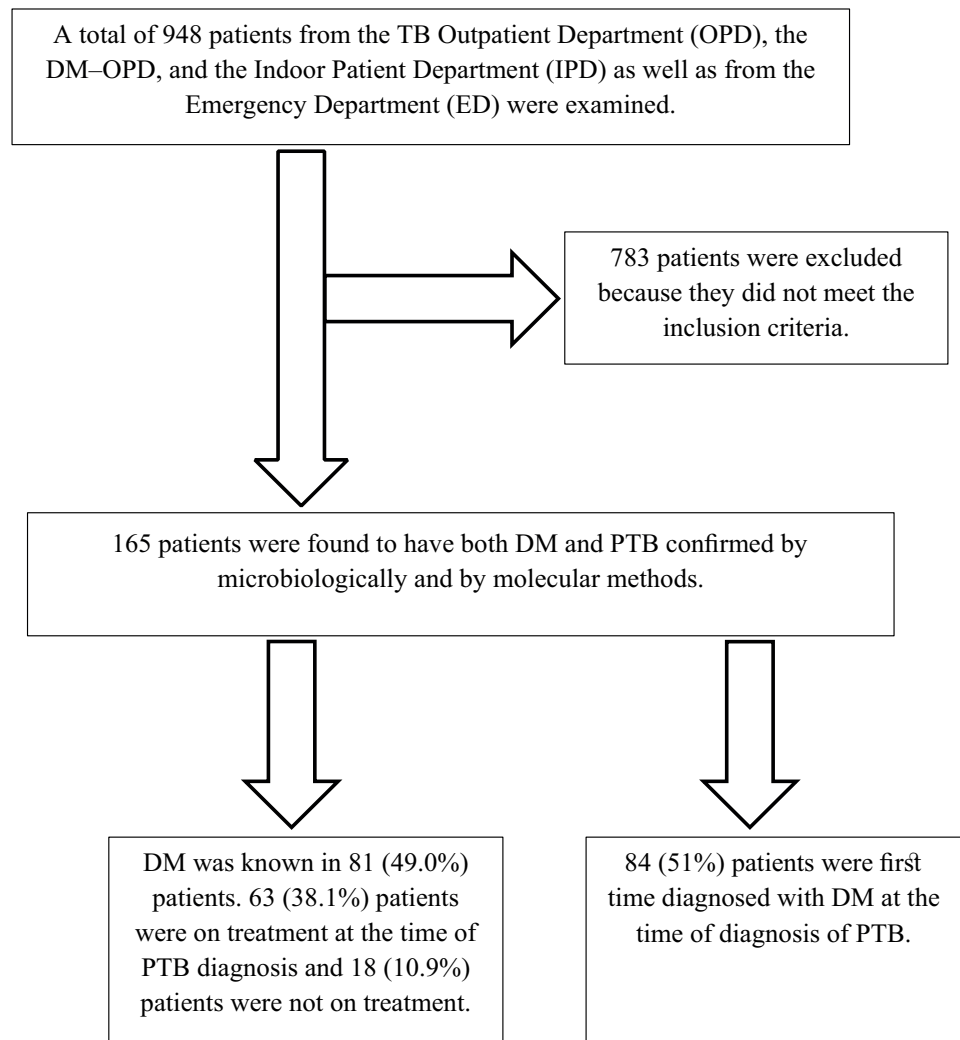


Figure 1

3. Screening patients whose sputum AFB is negative and MTB was not detected on sputum CBNAAT.

2.6. Data collection and analysis

After obtaining written informed consent to be included in the study and ensuring appropriate privacy and confidentiality, all patients underwent a standard interview. A complete medical history was taken and a comprehensive general and systemic examination was performed. The collected data were analyzed in Microsoft Excel 2016.

2.7. Informed consent

Informed consent was obtained from participants in our study in local Gujarati language.

3. Results

A total of 165 patients with pulmonary TB and DM were included in this study. Of the 165 patients, 77 (46.7%) patients came from the outpatient department and 88 (53.3%) patients from the inpatient department.

3.1. Sex distribution of patients

Of the 165 cases, 127 PTB–DM patients were male and 38 were female as shown in Table 1.

3.2. Age

As shown in Table 1, the mean age of the patients in this study was 46.5 years and the standard deviation (SD) was 14.79 years. For males, the average year with SD was 48.15 ± 14.02 years and for women the mean year with SD was 41.18 ± 16 years. In this study, we found that female patients were younger compared to male patients.

TABLE 1: Demography and DM status.

No. of patients (%)			Male	Female	Total
			127 (77.0)	38 (23.0)	165 (100.0)
Average Age (Yr ± SD)			48.15±14.02	41.18±16	46.55±14.79
Average Weight (Kg ± SD)			45.29±7.91	38.5±6.64	43.73±8.16
Past history of PTB	Yes (%)		45 (27.3)	9 (5.4)	54 (32.7)
	No (%)		82 (49.7)	29 (17.6)	111 (67.3)
Family history of PTB	Yes (%)		6 (3.7)	8 (4.8)	14 (8.5)
	No (%)		121 (73.3)	30 (18.2)	151 (91.5)
DM patients	Known case	On treatment (%)	55 (33.3)	8 (4.8)	63 (38.1)
		Not on treatment (%)	17 (10.3)	1 (0.6)	18 (10.9)
		Total (%)	72 (43.6)	9 (5.4)	81 (49.0)
New case (%)			55 (33.4)	29 (17.6)	84 (51.0)
Type of DM	Type I		49 (29.7)	24 (14.5)	73 (44.2)
	Type II		78 (47.3)	14 (8.5)	92 (55.8)
	Total		127 (77.0)	38 (23.0)	165 (100.0)

3.3. Average weight

The average weight with SD in this study was 43.73 ± 8.16 as shown in Table 1.

3.4. Past history

In this study, of the 165 patients with PTB–DM, 54 (32.7%) had a history of PTB and were receiving TB treatment from either the government or the private sector. Of the 54 patients who had received TB treatment in the past, 45 had taken the treatment once, 6 had taken it twice, 2 had taken it three times, and 1 patient had taken it four times.

3.5. Family history

In this study, 14 (8.5%) patients had a family history of pulmonary TB and a history of close contact (Table 1).

3.6. Status of DM at the time of diagnosis of PTB

As seen in Table 1, of the 165 patients, 81 (49.0%) were previously diagnosed with DM who were either on treatment or had discontinued treatment; 63 (38.1%) patients were on regular treatment; and 18 (10.9%) patients were receiving treatment but not on treatment at the time of PTB diagnosis and were no longer receiving treatment.

Furthermore, 84 (51.0%) patients were unaware they had DM for the first time during screening.

Gender distribution of known and new cases are reported in Table 1.

3.7. Type of DM

In this study, 73 (44.2%) type I DM patients and 92 (55.8%) type II patients were affected. Table 1 contains the details and sex-wise distribution.

3.8. Duration of DM

Among the known cases of DM, 41 (24.8%) patients had a duration of 0–3 years; 14 (8.5%) patients of 4–6 years; 6 (3.6%) patients of 7–9 years; 13 (7.9%) patients of 10–12

years; 6 (3.6%) patients of 13–15 years; and 1 patient had a duration of >15 years. Table 2 shows the distribution in DM patients by DM duration among known cases.

TABLE 2: Duration of DM among known TB cases.

Duration in range (yr)	No. of patients
0–3	41
4–6	14
7–9	6
10–12	13
13–15	6
>15	1
Average duration with SD	5.56 ± 4.37

Highest numbers of patients (41) had a duration of 0–3 years from the first diagnosis put on treatment. The average duration of DM in these patients was 5.56 years.

3.9. Range of RBS at time of PTB diagnosis

As shown in Table 3, the mean RBS value at the time of diagnosis was 208.7 mg/dl in 165 patients with PTB–DM – 61 (37%) patients with PTB–DM had an RBS in the range of 151–200 mg/dl whereas 51 (30.9%) patients had an RBS in the range of 201–250 mg/dl at the time of diagnosis.

TABLE 3: RBS at time of diagnosis.

Range of RBS	No. of patients
<100	1
101–150	23
151–200	61
201–250	51
251–300	15
301–350	7
351–400	4
> 400	3
Average RBS with SD	208.72 ± 64.5

3.10. Age-wise patient distribution according to DM status

Most patients were registered in the age group of 41–50 years, which corresponds to 40 (24%). Moreover, a total of 110 (67%) patients were aged 30–60 years, accounting for 2/3 of all patients enrolled in this study.

TABLE 4: Age-wise distribution of DM patients.

Age		Sex	
Ranges (yr)	Number of patients	Male	Female
13–20	5	1	4
21–30	23	15	8
31–40	34	26	8
41–50	40	31	9
51–60	36	31	5
61–70	18	16	2
71–80	8	6	2
81–90	1	1	0
Total	165	127	38

3.11. Presenting complaints

Of the 165 patients with PTB–DM, the most common symptom was cough, occurring in 164 (99.4%) patients. Fever was the second most common symptom noted in 152 (92.1%) patients. Anorexia was the third most common symptom, occurring in 119 (72.1%) patients. PTB in DM is therefore mainly manifested by cough, fever, and anorexia. The proportion is shown in Table 5.

Other symptoms included chest pain in 68 (41.2%) patients and shortness of breath in 56 (33.9%) patients. Both symptoms are common in patients over 40 years of age. A proportion of cases with weight loss was noted in 48 (29.1%) patients, suggesting that although the patient has anorexia, the patient may not experience weight loss due to DM. The least common symptom was hemoptysis in 15 (9.1%) patients.

TABLE 5: Symptomatology of PTB patients with DM ($n = 165$).

Symptoms	Known case of DM ($n = 81$)			New case of DM ($n = 84$)	Total (%)
	On treatment ($n = 63$)	Not on treatment ($n = 18$)	on Total ($n = 81$)		
Cough	62 (37.6)	18 (10.9)	80 (48.5)	84 (51.0)	164 (99.4)
Breathlessness	23 (13.9)	12 (7.3)	35 (21.2)	21 (12.7)	56(33.9)
Chest pain	29 (17.6)	6 (3.6)	35 (21.2)	33 (20)	68(41.2)
Hemoptysis	3 (1.8)	2 (1.2)	5 (3.0)	10 (6.0)	15 (9.0)
Fever	57 (34.5)	17 (10.3)	74 (44.8)	78 (47.3)	152 (92.1)
Anorexia	42 (25.5)	10 (6.0)	52 (31.5)	67 (40.6)	119 (71.1)
Weight loss	14 (8.5)	2 (1.2)	16 (9.7)	32 (19.4)	48 (29.1)

4. Discussion

Out of the 165 cases, 127 patients with PTB–DM were male and 38 were female. The number of male patients in this study was high. The male-to-female ratio observed in the present study was 3.6:1. The reason for the male predominance found in our study was the social stigma surrounding PTB in society. Additionally, increased outdoor and occupational exposure, as well as work-related stress, make males more susceptible to PTB–DM. Male patients also have easier access to healthcare facilities, and in some cases, there is a gender bias within families.

In this study, the mean age of the patients was 46.5 years with an SD of 14.79. The mean age of males in this study was 48.15 years, with an SD of 14.02, while in females was 41.18, with an SD of 16. Female patients were younger than male patients.

In the present study, the age group between 41 and 60 years was most frequently affected, with 74 (44.8%) patients suffering from PTB–DM. The high incidence of PTB with DM in this age group could be due to undiagnosed early-stage DM or because DM is diagnosed in patients who, for some reason, are not receiving regular treatment. The age group of 21–40 years has the second highest number of patients, with 57 (34.5%) individuals suffering from PTB–DM. In >60 years, only 27 (16.4%) patients had PTB–DM. This finding implies that DM predisposes individuals to PTB at a younger age.

The mean weight observed in this study was 43.73, with an SD from 8.16. Female patients weigh less than male patients.

Among the patients with DM and PTB, 54 had a history of PTB and received treatment for it. Of them, 9 patients had multiple treatment histories. This could indicate that due to DM there is insufficient elimination of TB bacteria through treatment, reactivation of dormant bacteria, or a higher susceptibility to reinfection with TB bacteria compared to the general population.

We found that 14 patients had a family history of exposure to TB bacteria. Family history is also one of the risk factors for developing TB in DM patients as this population is more susceptible.

In the present study, a total of 81 (49%) patients had DM, while 84 (51%) were diagnosed with PTB at the time of diagnosis. Out of the known cases, 18 patients were not receiving treatment since their diagnosis, while 63 patients were receiving treatment. However, despite being on treatment, 55 patients had uncontrolled DM. Based on this data, it is suggested that poor glycemic control is the main reason for the development or reinfection of TB in these patients.

Our study includes only 165 patients and requires more participants to get an accurate result of such a study. We did not compare this study to nondiabetics. A case control study in TB patients will be helpful.

5. Conclusion

We found that uncontrolled DM is a risk factor for the development or reactivation of PTB.

In the present study, the majority of patients were from IPD (88 (53.3%)), suggesting that PTB–DM cases have a more severe and complicated presentation. Male patients are more commonly affected than female patients. People in the age group 31–60 years often suffer from PTB–DM. Cough, fever, and anorexia are the most common symptoms, while chest pain and breathlessness are more common in the older age group.

The history of PTB in DM patients is also important as the present study shows that it may be related to recurrence or reactivation of PTB.

Most patients with a known case of DM have a duration of 0 to 3 years. Patients newly diagnosed with DM are therefore more likely to develop PTB in the first few years of DM. In the highest number of patients, DM duration ranged from 0 to 3 years in known cases and was found in 41 (24.8%) patients. This suggests that patients with a known case of DM are at high risk of developing PTB, with the likelihood being highest in the early years of DM. This may be because in the initial phase, the patient may be in the rejection phase of the DM diagnosis and not taking the treatment properly, or taking an insufficient dose due to side effects of the drug, or the existing dose may not be able to initially control sugar, or that he is only on a diabetic diet.

Given the heavy burden of DM patients in this country and worldwide, and the fact that many of them are unaware of their DM status and many are undertreated, as a systemic approach, every patient with DM should be screened for PTB, and for such patients a programmatic approach to HIV–TB program should be taken.

Acknowledgements

Not applicable.

Ethical Considerations

Approval was obtained from the Institutional Ethical Committee for Human Research, Medical College and SSG Hospital, Baroda, India. Approval Number is ECR/85/Int/Gj/2013/RR-16.

In addition, written informed consent was taken for enrolment in the study from all patient and maintaining adequate privacy and confidentiality.

Competing Interests

None declared.

Availability of Data and Material

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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