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## Original Article

# Prevalence of Various Forms of Active Tuberculosis in Patients with Diabetes

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## ABSTRACT

A diabetic foot ulcer (DFU) is a persistent complication of diabetes mellitus. Diabetes is linked to a two to four-fold higher likelihood of developing peripheral arterial disease (PAD) when compared to individuals without diabetes. **Objective:** To determine the incidence of various forms of active tuberculosis in patients with diabetes. **Methods:** It was a cross-sectional study conducted at the Department of General Medicine from August 2022 to February 2023. 175 patients, including both males and females, participated in this study. Comprehensive demographic information was meticulously documented for each patient following the appropriate consent procedures. These patients had symptoms such as cough with or without phlegm, hemoptysis, persistent fever, and unexplained weight loss, and their ages ranged from 10 to 85 years. Comprehensive medical history, clinical examination, and TB screening tests were conducted and data analysis were done by SPSS version-24 for further analysis. **Results:** The mean age was 51.34 years with a standard deviation of 3.61. Among the patients, 107 (61.14%) were male, and 68 (38.85%) were female. The overall prevalence of active TB was 38 cases, accounting for 21.71% of the total. Among these cases, 18 were pulmonary TB, making up 47.36% of the active TB cases, while 13 were extra-pulmonary TB, constituting 34.21% of the total. Additionally, 5 cases were identified as multidrug-resistant TB, representing 13.15% of the active TB cases. **Conclusions:** In conclusion, our study reveals a higher prevalence of various forms of active tuberculosis in patients with diabetes with pulmonary tuberculosis accounting for 47.35% and extra-pulmonary tuberculosis for 34.21% of cases.

## INTRODUCTION

Mycobacterium tuberculosis infects a quarter of the world's population, solidifying tuberculosis (TB) as a prominent global infectious disease. TB continues to pose a substantial global public health challenge, with an annual death toll exceeding 1.5 million and approximately 10 million new cases reported each year. The death toll from tuberculosis has dropped by 27% since 2000 [1, 2]. People with DM have higher TB rates than the general population, and having DM triples the risk of contracting tuberculosis (TB). In underdeveloped nations, where tuberculosis is rampant and diabetes is on the rise, understanding the connection between the two diseases is crucial [3, 4]. Pakistan saw an increase in the prevalence of diabetes among people 20 and older, from 5% in 1990 to 7% in 2016

[5]. Diminished cellular immunity, impaired alveolar macrophage function, reduced interferon gamma levels, pulmonary microangiopathy, and inadequate micronutrient levels represent some of the proposed pathophysiological mechanisms linking diabetes mellitus (DM) to an increased risk of tuberculosis (TB). In low and middle-income nations, the co-occurrence of TB and DM exemplifies a bidirectional relationship between a communicable and noncommunicable disease, intensifying the dual burden of both conditions [6, 7]. The coexistence of diabetes and active tuberculosis poses a significant public health challenge, warranting investigation into the prevalence of different forms of active tuberculosis in diabetic patients [8-10]. Our study

hypothesized that the prevalence of various forms of active tuberculosis is higher in patients with diabetes compared to the general population without diabetes. Understanding this prevalence is crucial as diabetes can compromise the immune system, increasing susceptibility to tuberculosis. Additionally, diabetes may lead to atypical presentations of tuberculosis, potentially delaying diagnosis and treatment. Exploring the prevalence of various forms of active tuberculosis in diabetic patients can inform targeted interventions to improve the management of these dual conditions and reduce their associated morbidity and mortality.

## METHODS

This study was conducted at the Department of General Medicine from August 2022 to February 2023. A sample size of 150 patients was determined using the WHO online calculator, incorporating a 5% margin of error and a 95% confidence interval, while considering a TB prevalence of 7.2% [11]. Patients of both genders having age of 18 to 60 with a diagnosis of DM and were already receiving medication for diabetes were included. Patients with a recent diagnosis of diabetes, those on steroids or other immunosuppressant's and those who have been taking antibiotics within the past 15 days were not included in our study. All participants in the study gave their informed consent after being fully briefed on the study's design. Patients were classified as having tuberculosis based on the presence or absence of certain symptoms. A patient with TB positive symptoms will exhibit at least three of the following: a cough that has persisted for > 2 weeks, fever, appetite loss, night sweats, and extreme fatigue. Sputum analysis was explored for patients with three or more complaints. For the purpose of observing AFB (stands for Acid-Fast Bacilli), by light microscopy with Ziehl-Neelson (ZN) staining, three sputum samples (morning-spot) were taken. In the Ziehl-Neelsen staining procedure, clinical specimens from diabetic patients were smeared on microscope slides, subjected to Carbol Fuchsin staining and gentle heating, followed by decolorization with Ziehl-Neelsen Decolorizer. Counterstaining with Methylene Blue, air-drying, and microscopic examination facilitated the identification of acid-fast bacilli indicative of active tuberculosis. If a patient showed both positive TB symptoms and if any of their samples displayed positive ZN staining, individuals were categorized as having tuberculosis. Patients were judged to be TB-negative if they showed no signs of TB and had negative ZN staining in all of their samples. SPSS version 25, statistical software, was used to enter and analyse the acquired data. Frequencies and percentages were calculated for qualitative variables like gender, TB positive, and TB

negative. Age, gender, and diabetes type served as stratification variables to mitigate their moderating effects, with the chi-square test applied post-stratification. A significance level of 0.05 was utilized for statistical inference.

## RESULTS

The table 1 provides information on several variables among the demographic groups of patients with type-II diabetes. The mean age was 51.34 years with a standard deviation of 3.61. Among the patients, 107 (61.14%) were male, and 68 (38.85%) were female. Regarding their medical history, 116 (70.3%) had a history of BCG vaccination, while 59 (33.71%) did not. Additionally, 50 patients (28.57%) had a familial history of TB, while 125 (71.42%) did not. In terms of diabetes type, 37 (21.14%) had Type-I diabetes, and 138 (78.85%) had Type-II diabetes.

**Table 1:** The demographic distribution of individuals with diabetes

Measurements	Category	Frequency (%)
Age	Mean ± SD	51.34±3.61
Gender	Male	107(61.14%)
	Female	68(38.85%)
History of BCG vaccination	Yes	116(70.3%)
	No	59(33.71%)
Familial history of TB	Yes	50(28.57%)
	No	125(71.42)
Type of Diabetes	Type-I	37(21.14%)
	Type-II	138(78.85%)
Mean duration of diabetes	Mean±SD	12.11±1.67

Table 2 presents the different categories of tuberculosis observed in individuals with diabetes. The overall prevalence of active TB was 38 cases, accounting for 21.71% of the total. Among these cases, 18 were pulmonary TB, making up 47.36% of the active TB cases, while 13 were extra-pulmonary TB, constituting 34.21% of the total. Additionally, 5 cases were identified as multidrug-resistant TB, representing 13.15% of the active TB cases, and 2 cases were classified as miliary TB, making up 5.26% of the total cases.

**Table 2:** Various categories of tuberculosis found in individuals with diabetes

Variables	Frequency (%)
Overall Prevalence of Active TB	38(21.71)
Pulmonary TB	18(47.36)
Extra Pulmonary TB	13(34.21)
Multidrug-Resistant TB	05(13.15)
Milliary TB	02(5.26)

Table 3 outlines the characteristics of individuals who are impacted by both active tuberculosis and diabetes mellitus. Among them, 145 cases (82.85%) were identified with pulmonary localization, while 30 cases (17.14%) had extra-pulmonary TB. When assessing chest X-ray findings, 85 individuals (48.57%) exhibited cavities, while 90 (51.43%) did not have cavities. In terms of sputum smear results, 125 cases (71.24%) tested positive for AFB, and 50 cases (28.57%) were AFB negative. Regarding radiographic presentation, 135 cases (77.14%) displayed typical features, while 40 cases (22.85%) exhibited atypical characteristics.

**Table 3:** Characteristics of individuals affected by both active tuberculosis and diabetes mellitus

Variables	Category	Frequency (%)
Localization	Pulmonary	145(82.85)
	Extra pulmonary	30(17.14)
Cavity on Chest X-ray	Yes	85(48.57)
	No	90(51.43)
Sputum smear	AFB+	125(71.24)
	AFB-	50(28.57)
Radiographic presentation	Typical	135(77.14)
	Atypical	40(22.85)

## DISCUSSION

This study examined the rate of tuberculosis in diabetics. Tuberculosis and diabetes are strongly related illnesses, and both are increasing in prevalence. Infections of the lungs are typically caused by the bacterium *Mycobacterium*; however, the disease can extend to other organs. Among the many illnesses that can be particularly dangerous for people with diabetes, TB stands out as a major threat. Diabetic patients have a prevalence of tuberculosis that is three- to five-fold higher than that of the general population. Since tuberculosis and diabetes share symptoms including fatigue, weight loss, and anorexia, it can be challenging to manage people with both conditions at the same time [12, 13]. In our study overall prevalence of active TB was 38 cases, accounting for 21.71% of the total. Among these cases, 18 were pulmonary TB, making up 47.36% of the active TB cases, while 13 were extra-pulmonary TB, constituting 34.21% of the total. Additionally, 5 cases were identified as multidrug-resistant TB, representing 13.15% of the active TB cases, and 2 cases were classified as miliary TB, making up 5.26% of the total cases. Our results are similar to findings of Basit et al., who found that among the 550 survey participants, 19 individuals (13%) were diagnosed with active TB. Among these TB cases, 58% were attributed to pulmonary TB, 42% to extra-pulmonary TB, and 6% to multi-drug resistant TB (MDR-TB). These findings underscore the heightened risk of MDR-TB and pulmonary tuberculosis among individuals

with diabetes, with pulmonary TB being notably more prevalent than extra-pulmonary TB [14]. Since both TB and diabetes are more common in poor nations, and since anti-TB drugs tend to affect glycemic control, it's possible that this is why there's such a significant positive correlation between the two diseases [15]. Supporting these results are studies looking into the DM-TB link, which have shown that diabetes triples the risk of tuberculosis, especially in locations where the disease is prevalent [16, 17]. Kermansaravi et al., reported comparable results with our findings, among the 400 diabetic patients, 24 individuals (6%) were initially suspected for PTB. However, subsequent laboratory preclinical assessments confirmed the presence of smear-positive pulmonary TB in 4 cases. Furthermore, the results of the PPD test showed that 257 patients (64.25%) had a negative response (induration of 0-4 mm). Among the entire cohort, 118 patients (29.5%) displayed an intermediate positive result, indicated by an induration size between 5-9 mm, while 25 patients (6.25%) tested positive, with an induration size falling within the range of 10-14 mm [18]. Masood et al., also reported that among the diabetic patients, 63 individuals (21.7%) were diagnosed with type 1 diabetes mellitus (DM), while 227 individuals (78.3%) had type 2 DM. When inquired about tuberculosis (TB) symptoms, 32 patients (11.0%) reported positive symptoms, while the remaining 258 patients (89%) reported negative symptoms. However, upon conducting additional sputum analysis, TB was confirmed in only 12 patients (4.1%) [19]. Ali et al., reported that the mean duration of diabetes was 11.5±9.19 years. Among the participants, active tuberculosis was detected in only 30 cases (15%). Out of these cases, 17 (56.7%) were diagnosed with pulmonary tuberculosis, while the remaining 13 (43.3%) had extra-pulmonary tuberculosis. Additionally, 18 patients (60%) had smear-positive TB, while 12 patients (40%) had smear-negative TB [20]. Tuberculosis incidence is notably elevated in individuals with diabetes, and non-diabetics also experience a relatively high occurrence of extra-pulmonary TB. Post-primary tuberculosis predominantly affects the upper and apical lung lobes. Intestinal tuberculosis ranks as the most prevalent form of extra-pulmonary TB. Within the diabetic population, multi-drug resistant TB (MDR-TB) is alarmingly prevalent. Urgent and comprehensive measures are imperative, as failure to address this issue promptly could lead to a severe and escalating public health crisis in the future. Patients with DM-TB have additional factors beyond their glucose levels that must be taken into account in order to provide effective therapy and maintenance.

## CONCLUSIONS

In conclusion, our study reveals a higher prevalence of various forms of active tuberculosis in patients with diabetes with pulmonary tuberculosis accounting for 47.35% and extra pulmonary tuberculosis for 34.21% of cases.

## Authors Contribution

Conceptualization: MT, AW

Methodology: MT

Formal Analysis: RR

Writing-review and editing: NA, SZ, FB

All authors have read and agreed to the published version of the manuscript.

## Conflicts of Interest

The authors declare no conflict of interest

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