



DIABETES MELLITUS AMPLIFIES THE RISK OF PULMONARY TUBERCULOSIS: FINDINGS FROM A RETROSPECTIVE STUDY

Pulmonary Medicine

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ABSTRACT

Background: Tuberculosis (TB) remains a major public health concern in India, particularly among individuals with comorbid conditions such as diabetes mellitus (DM), which is rapidly increasing nationwide. Diabetes is recognized as an important risk factor for TB, influencing disease occurrence and outcomes. This study aimed to compare the prevalence of pulmonary tuberculosis (PTB) among diabetic and non-diabetic patients and to estimate the relative risk of TB associated with diabetes. **Methods:** A hospital-based retrospective observational study was conducted at a tertiary care centre. Medical records of 761 patients presenting with symptoms suggestive of PTB were reviewed. Patients were categorized into diabetic ($n = 128$) and non-diabetic ($n = 633$) groups. Sputum samples from both groups were processed prospectively for Mycobacterium tuberculosis detection and rifampicin resistance using the GeneXpert MTB/RIF assay, along with smear microscopy. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated as estimates of relative risk for tuberculosis among diabetic and non-diabetic groups. **Results:** Tuberculosis was confirmed in 41 diabetic patients (32.0%) and 115 non-diabetic patients (18.2%). The prevalence of TB was significantly higher among diabetic patients. Male predominance was observed in both diabetic TB (82.9%) and non-diabetic TB (73.9%) groups, with no statistically significant sex-based difference. The mean age of diabetic TB patients was 50 ± 16 years, compared to 48 ± 17 years in non-diabetic TB patients. No rifampicin resistance was detected among diabetic TB patients, while three cases were identified in the non-diabetic group. The relative risk of TB among diabetic patients was 1.82 (95% CI: 1.31–2.53; $p = 0.0003$). **Conclusion:** Diabetes mellitus is associated with a significantly increased risk of tuberculosis. These findings highlight the need for integrated TB–DM screening and management strategies to improve early diagnosis and outcomes among diabetic patients.

KEYWORDS

Pulmonary Tuberculosis, Diabetes Mellitus, HIV.

INTRODUCTION

Tuberculosis (TB) remains a major global public health challenge, with an estimated 10.7 million people falling ill with TB in 2024, corresponding to 131 incident cases per 100 000 population, according to the most recent World Health Organization (WHO) Global Tuberculosis Report. TB continues to cause substantial mortality, with approximately 1.23 million deaths worldwide in 2024, making it one of the leading causes of death from a single infectious agent (1). Current TB control strategies primarily emphasize early detection and effective treatment of infectious cases to interrupt transmission, yet high disease burden persists, especially among individuals with conditions that compromise immune function, including human immunodeficiency virus (HIV) infection, diabetes mellitus (DM), malnutrition, and tobacco smoking (2,3).

Among these risk factors, the association between tuberculosis and diabetes mellitus has emerged as a major challenge to global TB control. Diabetes is now recognized as an important driver of TB incidence, particularly in low- and middle-income countries where the prevalence of diabetes is rapidly increasing alongside endemic TB (4). Multiple epidemiological studies and systematic reviews have consistently demonstrated that individuals with diabetes have a two- to three-fold higher risk of developing active TB compared with non-diabetic individuals (5,6).

The increased susceptibility to TB among patients with diabetes is attributed to chronic hyperglycaemia-induced impairment of both innate and adaptive immune responses, including reduced macrophage activation, altered cytokine production, and defective T-cell-mediated immunity (7). In addition, hyperglycaemia is believed to create a favourable environment for the growth and persistence of Mycobacterium tuberculosis (8). Importantly, the association between TB and diabetes is bidirectional: TB infection can worsen glycaemic control, while diabetes adversely affects TB disease severity, treatment response, and outcomes, including higher rates of treatment failure, relapse, mortality, and drug-resistant TB (9,10).

Pharmacological interactions further complicate the management of

TB–DM comorbidity. Rifampicin, a key first-line anti-tubercular drug, is a potent inducer of hepatic enzymes and is known to reduce the efficacy of several oral hypoglycaemic agents, thereby destabilizing glycaemic control during TB treatment (11). These interactions necessitate close monitoring and integrated management of both conditions.

Recognizing the growing dual burden, the WHO and the International Union Against Tuberculosis and Lung Disease have proposed a “Collaborative Framework for Care and Control of Tuberculosis and Diabetes”, which emphasizes bidirectional screening, coordinated clinical management, and strengthened surveillance of TB–DM comorbidity (12). This integrated approach is particularly relevant in regions such as South Asia, where both TB and diabetes are highly prevalent.

In this context, the present study was undertaken to determine the comparative incidence of pulmonary tuberculosis (PTB) among diabetic and non-diabetic subjects and to estimate the relative risk of TB associated with diabetes in this region. The findings are expected to contribute to a better understanding of TB–DM interaction and support evidence-based strategies for improved prevention and management of tuberculosis among diabetic patients.

MATERIALS AND METHODS

Study Design and Setting

This was a hospital-based retrospective observational study conducted at a tertiary care teaching hospital in Andhra Pradesh. The study protocol was reviewed and approved by the Institutional Ethics Committee (IEC No: 1205/2025), and the study was conducted in accordance with the principles of the Declaration of Helsinki. A total of 761 patients who presented to the hospital with clinical suspicion of pulmonary tuberculosis (PTB) were included in the study. Medical records of these patients were retrospectively reviewed for the period from January 2022 to December 2024. Patients of all age groups and both sexes who underwent sputum examination for PTB were eligible for inclusion. Patients with incomplete clinical or laboratory records were excluded from the analysis.

Data Collection

Relevant data were extracted from hospital medical records and laboratory registers using a standardized data collection proforma. The variables collected included socio-demographic characteristics, diabetic status, anti-tubercular treatment (ATT) history, sputum smear microscopy results, and GeneXpert MTB/RIF assay findings. Diabetes mellitus was defined based on documented medical diagnosis and/or ongoing treatment with oral hypoglycaemic agents or insulin, as recorded in patient case files (13).

Based on diabetic status, patients were categorized into two groups: a) Diabetic group, and b) Non-diabetic group. For further analysis, patients diagnosed with tuberculosis were classified as Diabetic Tuberculosis (DMTB) and Non-Diabetic Tuberculosis (NDTB) groups.

Sputum samples collected from all study participants were subjected to Ziehl-Neelsen (ZN) staining for detection of acid-fast bacilli (AFB). Smears were examined and graded according to National Tuberculosis Elimination Programme (NTEP) guidelines (14). Further all sputum samples were processed prospectively for the detection of Mycobacterium tuberculosis (MTB) and rifampicin resistance using the GeneXpert MTB/RIF assay (Cepheid, Sunnyvale, CA, USA). The assay was performed according to the manufacturer's instructions. This automated, cartridge-based nucleic acid amplification test detects MTB complex DNA and mutations associated with rifampicin resistance within two hours (15). The GeneXpert MTB/RIF assay is recommended by the World Health Organization as an initial diagnostic test for pulmonary tuberculosis, especially in high-burden settings (16).

Statistical Analysis

Data were entered into Microsoft Excel and analysed using OpenEpi statistical software. Continuous variables were summarized as mean $\pm$ standard deviation (SD), while categorical variables were expressed as frequencies and percentages. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated as estimates of relative risk for tuberculosis among diabetic and non-diabetic groups. The Chi-square test was used to assess associations between categorical variables, and the Student's t-test was applied to compare means between groups where appropriate. A p value < 0.05 was considered statistically significant.

RESULTS

A total of 761 patients presenting with symptoms suggestive of pulmonary tuberculosis (PTB) were included in the retrospective analysis. Among them, 128 patients (16.82%) were known diabetics, while 633 patients (83.18%) were non-diabetic. All sputum samples from both groups were processed prospectively for Mycobacterium tuberculosis (MTB) detection and rifampicin resistance using the GeneXpert MTB/RIF assay. Of the 128 diabetic patients, 41 (32.0%) were confirmed positive for tuberculosis, while 87 (68.0%) were negative. In contrast, among the 633 non-diabetic patients, 115 (18.2%) were TB positive and 518 (81.8%) were TB negative. The prevalence of tuberculosis was thus significantly higher among diabetic patients compared to non-diabetic patients (32.0% vs 18.2%).

Among the diabetic TB-positive patients ($n = 41$), 34 (82.9%) were males and 7 (17.1%) were females. In the non-diabetic TB-positive group ($n = 115$), 85 (73.9%) were males and 30 (26.1%) were females (Figure 1). Although males predominated in both groups, the difference in sex distribution between diabetic TB and non-diabetic TB patients was not statistically significant ($p = 0.244$). The male-to-female ratio was 4.8:1 in the diabetic TB group and 2.8:1 in the non-diabetic TB group, indicating a stronger male predominance among diabetic TB patients.

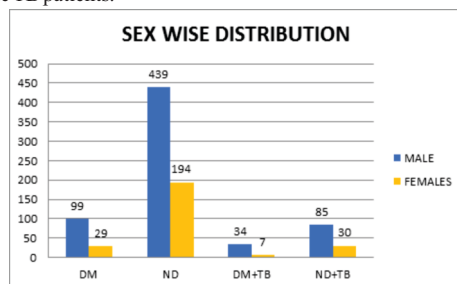


Figure-1: Sex Wise Distribution Among 761 Patients in the Study.

The age of TB-positive patients ranged from 11 to 90 years. The mean age of diabetic TB patients was 50 ± 16 years, while that of non-diabetic TB patients was 48 ± 17 years. The difference in mean age between the two groups was not statistically significant (t-test, $p > 0.05$). Age-wise analysis revealed that TB was most commonly observed in the 41–50 year age group among diabetic patients, whereas in the non-diabetic group, the 51–60 year age group showed the highest number of TB cases (Figure 2). This suggests an earlier occurrence of TB among patients with diabetes.

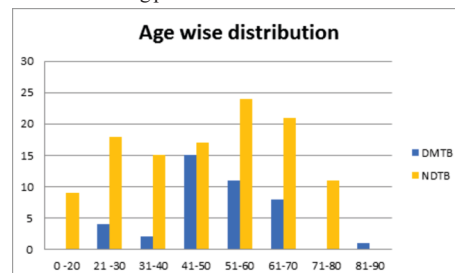


Figure 2: Age Wise Distribution Among Diabetic with TB and Non-Diabetic with TB patients.

Rifampicin resistance was not detected in any of the diabetic TB patients. Among non-diabetic TB patients, 3 cases (2.6%) showed rifampicin resistance as detected by GeneXpert MTB/RIF assay. Due to the small number of resistant cases, statistical comparison between groups was not performed. A significantly higher proportion of diabetic patients had already been initiated on anti-tubercular treatment (ATT) prior to microbiological confirmation when compared to non-diabetic patients. Among diabetic patients, 83 were already receiving ATT, whereas only 45 were not on treatment. In contrast, among non-diabetic patients, 85 were on ATT and 548 were not. This difference was highly statistically significant ($p < 0.0000001$, Chi-square test), indicating a tendency toward earlier or empirical initiation of ATT among diabetic patients (Table 1).

Table-1: ATT Initiated in Patients with Diabetic.

ATT	Yes	No	P Value
Diabetic patients	83	45	<0.0001
Non-Diabetic patients	85	548	

The relative risk (RR) of developing tuberculosis among diabetic patients was 1.82 (95% CI: 1.31–2.53, $p = 0.0003$), indicating that diabetic patients had an 82% higher risk of tuberculosis compared to non-diabetic patients. This statistically significant association confirms diabetes mellitus as an important risk factor for tuberculosis in the study population. Although males constituted the majority of TB cases in both groups, diabetes emerged as an independent factor associated with increased TB prevalence.

DISCUSSION

The burden of diabetes mellitus (DM) is increasing rapidly in India, with prevalence historically higher in economically and epidemiologically advanced states. Recent national estimates, however, indicate a faster rise in diabetes prevalence in less developed states, which together account for a large proportion of India's population (17). This epidemiological transition has important implications for tuberculosis (TB) control, as India continues to bear the highest global burden of TB. Consequently, bidirectional screening for TB and DM is now strongly recommended under the National Tuberculosis Elimination Programme (NTEP) and by the World Health Organization (WHO) (18,19).

The increased incidence of tuberculosis among patients with diabetes is well established. Although the precise mechanisms underlying this association remain incompletely understood, both innate and adaptive immune dysfunctions have been described in individuals with diabetes, particularly in those with poor glycaemic control. Chronic hyperglycaemia impairs macrophage activation, chemotaxis, phagocytosis, cytokine signalling, and T-cell-mediated immunity, thereby facilitating progression from latent TB infection to active disease (20).

In the present study, a significantly higher prevalence of tuberculosis was observed among diabetic patients (32%) compared to non-diabetic patients (18%), reinforcing diabetes as an important risk factor for TB. These findings are consistent with reports from South

India. Raghuraman et al. from Puducherry reported a TB prevalence of 29% among diabetic patients (21). Studies from Kerala documented prevalence rates ranging from 21% to 23% among known and newly diagnosed diabetic TB patients (22). Similar prevalence has been reported from Karnataka (25.3%) using biochemical diagnostic criteria for diabetes (23) and from Tamil Nadu (25.3%) (24).

In contrast, studies from North India have generally reported lower prevalence of diabetes among TB patients, ranging from 13% to 15.3% (25–28). These regional differences suggest a higher burden of TB–DM comorbidity in southern India, likely reflecting variations in baseline diabetes prevalence, urbanization, lifestyle factors, and health-care access. Internationally, lower prevalence has been reported from China (6.3%) and Spain (5.9%), highlighting the influence of population-level diabetes epidemiology on TB burden (29,30).

The most commonly affected age group among diabetic TB patients in the present study was 41–50 years, consistent with earlier Indian studies and reports from the United States (22,23,31). This overlap may reflect the convergence of peak type 2 diabetes prevalence and increased TB susceptibility in middle-aged adults. Male predominance was observed in both diabetic TB and non-diabetic TB groups, similar to earlier studies (32,33). The higher TB prevalence among men may be influenced by additional risk factors such as smoking, alcohol use, occupational exposure, and delayed health-seeking behaviour.

The relative risk (RR) of tuberculosis among diabetic patients in this study was 1.82 (95% CI: 1.31–2.53), indicating an 82% higher risk compared to non-diabetic individuals. This finding aligns with previous reports. A nationwide cohort study from Australia reported an RR of 1.78 for TB among patients with diabetes (34), while several cohort studies and meta-analyses have reported RRs ranging from 1.5 to 3.0 across different populations (35,36).

Emerging evidence indicates that poor glycaemic control significantly increases TB risk. Leung et al. demonstrated that individuals with glycated haemoglobin (HbA1c) $\geq 7\%$ had a markedly increased risk of TB, whereas those with HbA1c $< 7\%$ did not exhibit excess risk (37). Furthermore, diabetes has been associated with adverse TB treatment outcomes, including delayed sputum conversion, increased relapse, higher mortality, and a greater likelihood of drug-resistant TB (38).

CONCLUSION

The present study demonstrates a significantly higher prevalence and risk of tuberculosis among diabetic patients, with diabetes conferring a 1.82-fold increased risk compared to non-diabetic individuals. These findings emphasize diabetes mellitus as an important and growing contributor to the tuberculosis burden in India. Although the immunopathological mechanisms underlying this susceptibility remain incompletely defined, the evidence underscores the need for integrated TB–DM care, including routine TB screening among diabetic patients, optimal glycaemic control, early microbiological diagnosis, and close clinical monitoring. Strengthening collaborative TB–DM strategies is essential for achieving national and global TB elimination goals.

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