Burden of active pulmonary tuberculosis among patients with diabetes in Dar es Salaam, Tanzania: a cross-sectional study

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ABSTRACT

Objectives We aimed to determine the prevalence, associated factors and describe the chest radiographic findings for active pulmonary tuberculosis (TB) among patients with diabetes mellitus (DM) attending a diabetic clinic in Tanzania.

Design Cross-sectional study.

Setting A diabetic clinic at Temeke Regional Referral Hospital in Dar es Salaam, Tanzania.

Participants Patients with diabetes.

Main outcome measures The prevalence and factors associated with active TB in patients with DM.

Results Among 623 patients with DM screened, 11 (1.8%); 95% CI 0.9 to 3.1, had active TB of which 6 (54.5%) were GeneXpert positive and 5 (45.5%) were diagnosed based on clinical symptoms and suggestive chest radiographs. The risk of active TB was lower in patients aged 45–64 years compared with age below 45 years (adjusted prevalence ratio (aPR) 0.39, 95% CI (0.11 to 0.42), p<0.001) and in patients with normal chest examination findings compared with patients with crackles or bronchial breathing sounds (aPR 0.02, 95% CI (0.01 to 0.15), p<0.01). The predominant chest radiographic findings were opacification 100% mainly in the upper and mid-lung zones.

Conclusion Diabetics should be screened for pulmonary TB, particularly among individuals aged 45 years and below with crackles or bronchial breathing on auscultation of the chest. High index of suspicion could help in the early detection and control of TB.

INTRODUCTION

Patients with diabetes mellitus (DM) are at three times higher risk for acquiring tuberculosis (TB) compared with individuals without DM.1 2 Despite this, there is lack of integration of routine TB screening among patients with DM as it is in the case for HIV.2 4

According to the International Diabetes Federation (IDF), an estimated 463 million people (9.3%) were living with DM in the year 2019.3 It is predicted that without sufficient efforts to address the growing burden, 758 million people (10.2%) will have DM by 2030 and shall further escalate to 700 million (10.9%) by 2045.5 In sub-Saharan Africa (SSA), type 2 DM is more prevalent accounting for more than 90% of diabetes cases.6 The burden of DM in Tanzania for the year 2019 was estimated to be 3.7% in the adult population.5

The increase in the incidence of DM in low-income and middle-income countries poses a significant threat to the control of TB and could hamper efforts towards achieving the Sustainable Development Goal of ending TB by the year 2030.5 Consequently, this has renewed interest in tuberculosis diabetes mellitus (TBDM).5 Studies have shown that about 10–15% of the TB cases are attributable to DM.4 These findings underline that DM is a moderate-to-strong risk factor for active TB.4

Systematic reviews have found the prevalence of TB in DM to be within the range of 0.38–14% with an overall median prevalence of 4.1%.6 6 Despite TBDM comorbidity being a global issue, studies in SSA and more so in Tanzania are limited.4 The few studies conducted in SSA between 2013 and 2018 reported varying prevalence ranging from 3% in South Africa7 to 6.2% in Ethiopia.8 The prevalence of TB in DM in Tanzania for the year 1990 was reported as 5.4%9 which...
dropped to 1.3% in 2014. However, the latter study was limited in having focused only on patients with diabetes presenting with cough.

Although DM is a known risk factor for TB, and Tanzania is one of the countries with a high burden of TB, routine screening for TB among patients with DM is still not a standard of care. The last TB survey among patients with DM was conducted over three decades ago. This study therefore aimed at determining the prevalence of TB and describe the socio-demographic as well as clinical and chest radiographic characteristics of active TB among patients with DM attending a diabetic clinic in Dar es Salaam, Tanzania.

MATERIALS AND METHODS
Study design and recruitment
This cross-sectional study was conducted at a diabetic clinic at Temekte Regional Referral Hospital (TRRH) in Dar es salaam, Tanzania, between September 2020 and November 2020. The diabetic clinic enrolls newly diagnosed patients with diabetes and follows-up enrolled patients for routine care including medical check-up and drug refill. Patients attend the diabetic clinic on a monthly basis. The clinic attends to an average of 20 patients per day. Patients attending the diabetic clinic are required to be in a fasting state. On arrival at the clinic, patients receive health education on control of DM and prevention of complications and thereafter have anthropometric measurements taken. Capillary blood samples are collected for assessment of fasting blood glucose (FBG) and thereafter each patient is reviewed by a clinician for a medical consultation and management. The clinical visits end with patients collecting medication refill.

Patients were briefed about the study at the time of provision for diabetes education. All willing patients aged 18 years and above were asked to provide informed consent prior to recruitment into the study. Participants were consecutively recruited into the study by the principal investigator and research assistants who were trained medical doctors. The team completed the data collection tools, screened participants for TB symptoms and performed physical examination. TB screening was performed according to the Tanzania National TB Guidelines that follow the WHO recommendations. In short, following completion of the study questionnaire and physical examination, all recruited participants were instructed on how to provide a spot sputum sample and were given containers for collection of samples for GeneXpert which was performed at a certified laboratory located at the TRRH (procedures elaborated under ‘data collection and measurements’ below). Patients with symptoms suggestive of TB and/or positive GeneXpert were required to undergo chest radiography at the TRRH. TB screening and treatment services in Tanzania are provided through the National TB and Leprosy Control Programme at no cost to the patients. The cost for chest radiographs was covered by the study.

Data collection and measurements
Socio-demographic and clinical characteristics
A structured questionnaire designed by the investigators was used to interview all study participants. The questionnaire was structured into sections covering socio-demographic characteristics (age, sex, level of education, number of rooms and people in the house, number of people per room, housing floor material, cigarette smoking, alcohol consumption) and clinical characteristics (presence of symptoms suggestive of TB, findings on chest examination, BCG scar, duration of diabetes, family history of DM, HIV status and type of antiglycaemic agent used). With regards to cigarette smoking and alcohol consumption, only current practice was recorded. A TB screening tool adopted from the National TB Guideline and included in the questionnaire was used to assess the presence of TB symptoms including: cough >2 weeks, night sweats, weight loss, haemoptysis and fever. In the same screening tool, information on the history of TB contact and previous active TB was also collected.

Anthropometric measurements
Participants’ height (m) and weight (kg) were measured and body mass index (BMI) was calculated using the formula weight/height². The BMI was interpreted as follows: underweight <18.5 kg/m²; normal 18.5–24.9 kg/m²; overweight if 25.0–29.9 kg/m²; obesity if ≥30 kg/m².

Sputum samples
Ensuring that no one is standing in front of the patient in an open area, the patient was instructed to cough deeply and expectorate sputum amounting 3–5 mL into the sputum container. A spot sample was collected per participant. The patient was instructed to avoid contaminating the outside of the container with sputum. If the outside of the container was contaminated the container was discarded and a fresh sputum container was obtained. If the specimen was not suitable the patient was asked to repeat the sputum collection procedure. For patients unable to spontaneously expectorate spot samples, the study team instructed the patients to take several deep breaths, hold their breath for a moment and repeat this several times until coughing was induced. They would then cough deeply and vigorously during expiration. The laboratory technician that performed GeneXpert ensured that the sputum collected was of adequate quality and volume prior to being tested by GeneXpert. A repeated spot sample was requested if the volume of the sample provided was considered to be of inadequate volume or of poor quality (eg, salivary samples).

Blood samples
About 3 mL of venous blood was drawn, collected in plain tubes and serum separated within 8 hours of collection and stored at 20°C before measurement of human glycated haemoglobin (HbA1c). Capillary blood samples were taken for measurement of FBG. The study aimed at observing immediate control that is picked up by FBG as
well as overall glucose control over a 3 months duration by using HbA1c. Capillary blood sample for HIV antibody test was also collected.

**Laboratory investigations**

**FBG**
The FBG was assessed using a glucometer (GlucoPlus, Canada). FBG levels of <7 mmol/L were considered normal and ≥7 mmol/L were considered elevated.13

**Glycated haemoglobin**
Assessment of human HbA1c was performed at Muhimbili University of Health and Allied Sciences Genetic Laboratory. Serum samples were tested for HbA1c by ELISA using human-specific HbA1c ELISA kit according to the manufacturer’s instructions (Qayee Bio-Technology, Shanghai, China). HbA1c levels were categorised as follows: controlled glycaemia 12.5–800 ng/mL and poorly controlled glycaemia >800 ng/mL.

**GeneXpert**
All participants underwent spontaneous sputum collection that was analysed using Xpert MTB/RIF module XVI (GX-XVI; Cepheid, USA) using standard procedures. Briefly, using a disposable pipette reagent was added to the sputum sample at a ratio of 2:1, shook vigorously 10–20 times and incubated. A minimum amount of 2 mL was loaded into the cartridge and ran for 1 hour and 50 min. Once the run was complete the results were printed out and read. Analysis was performed at an accredited government laboratory at TRRH.

**HIV testing**
The SD Bioline third generation (Standard Diagnostics, Republic of Korea) rapid HIV test was used for assessing the presence of HIV-1/2 specific antibodies in whole blood samples.

**Chest radiography**
Chest radiography imaging was done in order to describe chest radiographic findings in patients with pulmonary TB. Chest radiographic imaging was therefore performed on all participants whose sputum samples were positive on GeneXpert and/or had clinical symptoms suggestive of pulmonary TB. Two independent radiologists who were blinded to patients’ symptoms interpreted the chest X-rays (CXR) and produced independent radiographic reports documenting findings and conclusions with the possible outcomes being CXR suggestive or not suggestive of TB. The agreed radiographic features of pulmonary TB were the presence of one or more of the following features on CXR; air space infiltrates/consolidation, lung caviation, fibrotic bands, miliary nodules, granuloma, superior mediastinal and hilar lymphadenopathy and pleural effusion.

**TB case definition**
TB was defined according to Tanzania National TB Guidelines.12 Active pulmonary TB was defined as presence of symptoms suggestive of TB being at least 2 weeks history of any of the following: cough, haemoptysis, fever, night sweats or unexplained weight loss and detection of Mycobacterium tuberculosis by GeneXpert OR presence of symptoms suggestive of TB and CXR findings suggestive of TB. GeneXpert testing was performed by a certified laboratory technician.

**Statistical analysis**
Data were entered in KoboTool box software (Cambridge, Massachusetts, USA), extracted in the form of Microsoft Excel, and imported into Stata V.15 statistical software (StataCorp. 2017. Stata Statistical Software: Release 15, College Station, Texas, USA: StataCorp) for cleaning and analysis. Descriptive statistics were conducted to describe the socio-demographic and clinical characteristics of the study participants. Frequencies were estimated for categorical variables and median and IQRs were used to summarise the numerical variables. The prevalence of TB disease was calculated as the total number of TB cases divided by the total number of patients with DM. We used a modified Poisson regression model with a robust SE and log link function estimated prevalence ratios (PR) and 95% CIs for the association between independent variables and the outcome variable (active TB).14 Modified Poisson regression was used due to the non-convergence of the log-binomial regression model.14 Multivariable modified Poisson regression was used to ascertain predictors of active TB while controlling for confounders and effects of multiple predictors where variables with a p value of <0.2 in bivariate analysis were included in the multivariable model. All parameters were checked for multicollinearity before being included in the multivariable model. All tests were two-sided and the significance level was set at 5%. A parsimonious model was selected based on the lowest Akaike information criteria.

**RESULTS**

**Socio-demographic characteristics of study participants**
During the study period of September 2020 to November 2020, 851 patients with diabetes attended the diabetic clinic and a total of 623 patients with diabetes were recruited into the study (figure 1). The median age of study participants was 50.0 years±IQR (36–61). The majority of study participants were in the age category of 45–64 years 273 (43.8%) with the highest proportion being women 331 (53.1%; table 1).

**Prevalence of active TB**
Out of the 623 participants with DM included in the study, 11 (1.8%; 95% CI 0.9 to 3.1) were diagnosed with active TB in which 6/11 (54.5%) were diagnosed via GeneXpert testing.
and 5/11 (45.5%) were diagnosed via clinical symptoms supported by chest radiography. We found that participants below the age of 45 had a higher burden of active TB 8/11 (72.7%).

**Clinical characteristics of participants with active TB**

Table 2 shows the clinical characteristics of the study participants with active TB. The median duration of DM was 4.0 years±IQR (2–8). Of note, 2 (18.2%) patients with TB by GeneXpert were clinically asymptomatic. In terms of glycaemic level, all 11 patients with TB had controlled glycaemia. All patients with TB were HIV negative.

**Chest radiographic findings of active TB in patients with DM**

CXR findings suggestive of TB were detected in 10 of the 11 patients diagnosed with TB of which 9 were lung findings and 1 was lymphadenopathy. Among those with lung findings, most patients had involvement of both lungs or the right lung, each accounting for 4/9 (44.4%). The upper and middle lobes were the most commonly affected, each accounting for 6/9 (66.7%). Radiographic patterns largely revealed findings of opacification 9/9 (100%) and cavitiation 4/9 (44.4%) (online supplemental figure 1).

**Risk factors associated with active TB in patients with DM**

In univariate analysis, normal auscultatory findings on chest examination (crude PR (cPR) 0.01, 95% CI 0.00 to 0.25), receiving metformin treatment (cPR 0.08, 95% CI 0.01 to 0.64) and not receiving insulin therapy (cPR 0.16, 95% CI 0.04 to 0.60) were associated with a lower risk of TB disease. Conversely, being underweight (cPR 6.79, 95% CI 1.74 to 26.50) was associated with an increased risk of TB disease. Following adjustment in multivariate model, age 45–64 years (adjusted PR (aPR) 0.39,95% CI 0.11 to 0.42) and >65 years (aPR 0.34, 95% CI 0.15 to 0.96), respectively, and normal findings on chest examination (aPR 0.02, 95% CI 0.01 to 0.15) were associated with a lower risk of TB disease (table 3). Other factors such as cigarette smoking, HbA1c level and HIV status were not significantly associated with TB disease.

**DISCUSSION**

Understanding the magnitude and determinants of TB among patients with DM is critical in efforts to control the burden of TB. The prevalence of active pulmonary TB among patients with DM in Dar es salaam, Tanzania, was found to be 1.8%. TB had a higher burden of 72.7% among those below 45 years. Patients with diabetes with TB presented with crackles or bronchial breathing on chest examination.

The prevalence of TB among patients with DM found in our study was higher than the national estimate of 237 per 100 000 (0.23%) in the general population, although it was within the range of 0.1–6.2% among patients with DM that has been reported in previous studies. The reported lower prevalence in our study compared with the study done by Swai et al in Tanzania is consistent with the overall drop in TB infection in the country due to impactful strides in TB control having achieved the

Figure 1 Flow diagram of recruitment process and results of patients with DM screened for active TB. CXR, chest X-rays; DM, diabetes mellitus; TB, tuberculosis; TBDM, tuberculosis diabetes mellitus.
2020 WHO global TB milestone of 20% reduction in new TB cases.17

TB risk has been found to vary within populations. Studies have revealed that adults below 45 years are at a higher risk of TB infection compared with older persons.18 The present study is in agreement with these findings; younger patients with DM were found to have significantly increased risk of having active TB. Studies have also shown male patients with DM to have a higher risk of TB compared with women.18 Although sex was not significantly associated with TB in our study, the majority of patients with TB were men. It is reasonable to speculate that this could be due to increased engagement in social activities among the younger and male individuals which predisposes them to a higher risk of TB transmission.

Table 1  Socio-demographic characteristics of the study participants, N=623

| Variables          | Categories                  | n (%) |
|--------------------|-----------------------------|-------|
| Age (years)        | 18–44                       | 240 (38.5) |
|                    | 45–64                       | 273 (43.8) |
|                    | ≥65                         | 110 (17.7) |
| Sex                | Male                        | 292 (46.9) |
|                    | Female                      | 331 (53.1) |
| Marital status     | Single                      | 241 (38.7) |
|                    | Married/cohabiting          | 382 (61.3) |
| Education          | No education                | 110 (17.7) |
|                    | Primary                     | 306 (49.1) |
|                    | Secondary                   | 180 (28.9) |
|                    | College/university          | 27 (4.3) |
| Occupation         | Employed                    | 52 (8.3) |
|                    | Unemployed                  | 571 (91.7) |
| Residence          | Temekwe                     | 513 (82.3) |
|                    | Outside Temekwe             | 110 (17.7) |
| Cigarette smoking  | Yes                         | 9 (1.4) |
|                    | No                          | 619 (99.4) |
| Alcohol consumption| Yes                         | 148 (23.8) |
|                    | No                          | 475 (76.2) |
| Number of people in house | One                    | 17 (2.7) |
|                    | Two                         | 83 (13.3) |
|                    | Three or more               | 523 (83.9) |
| Number of sleeping rooms | One                      | 56 (9.0) |
|                    | Two                         | 172 (27.6) |
|                    | Three or more               | 395 (63.4) |
| Number of people per room | One                    | 90 (14.4) |
|                    | Two                         | 435 (69.8) |
|                    | Three or more               | 98 (15.7) |
| House floor material | Carpet/ ceramic/ cement | 568 (91.2) |
|                    | Dung/earth/sand             | 55 (8.8) |

Table 2  Clinical characteristics of participants with active TB (n=11)

| Variables                      | Categories                   | n (%) |
|--------------------------------|------------------------------|-------|
| Family history of DM           | Yes                          | 6 (54.5) |
|                                | No                           | 5 (45.5) |
| Cough for 2 weeks or more      | Yes                          | 6 (54.5) |
|                                | No                           | 5 (45.5) |
| Fever                          | Yes                          | 2 (18.2) |
|                                | No                           | 10 (90.9) |
| Night sweats                   | Yes                          | 5 (45.5) |
|                                | No                           | 6 (54.5) |
| Weight loss                    | Yes                          | 8 (72.7) |
|                                | No                           | 3 (27.3) |
| Haemoptysis                    | Yes                          | 0 (0.0) |
|                                | No                           | 0 (0.0) |
| Findings on chest examination  | Yes                          | 8 (72.7) |
|                                | No                           | 3 (27.3) |
| BMI                            | Underweight                  | 4 (36.4) |
|                                | Normal                       | 5 (45.5) |
|                                | Overweight/obesity           | 2 (18.2) |
| BCG scar                       | Present                      | 9 (81.8) |
|                                | Absent                       | 2 (18.2) |
| Fasting blood glucose          | Elevated                     | 10 (90.9) |
|                                | Normal                       | 1 (9.1) |
| HbA1c                          | Controlled                   | 11 (100) |
|                                | Poorly controlled            | 0 (0.0) |
| HIV status                     | Positive                     | 0 (0.0) |
|                                | Negative                     | 11 (100) |
| Duration of diabetes           | ≤5 years                     | 8 (72.3) |
|                                | >5 years                     | 3 (27.3) |
| Previous TB contact            | Yes                          | 4 (36.4) |
|                                | No                           | 7 (63.6) |

There is an ongoing debate concerning the atypical radiographic presentation of TB in patients with diabetes. Some scientists reported that TB affects mostly the lower lung zones9 19 20 while others state that there was no difference with the lower lung zones only being affected in older patients.21 Our study findings support that TB mostly affects the upper and mid-lung zones. We also found bilateral involvement of the lungs and this finding is supported by Patel et al.19 Previous studies showed that diabetic individuals presented mostly with cavitation in the lungs.9 19 Our study revealed that TB in patients with diabetes presented predominantly with opacifications, similar to a study done by Bacakoglu et al.21 A similar radiographic presentation of TB in patients with diabetes versus patients without diabetes could easily result in...
### Table 3  Socio-demographic characteristics associated with active TB

| Variable                      | cPR (95% CI)     | P value  | aPR (95% CI)    | P value |
|-------------------------------|------------------|----------|-----------------|---------|
| **Age**                       |                  |          |                 |         |
| 18–44                         | 1                | 1        |                 |         |
| 45–64                         | 0.21 (0.05 to 1.02) | 0.053   | 0.39 (0.11 to 0.42) | 0.001 |
| 65 and above                  | 0.27 (0.33 to 2.15) | 0.215   | 0.34 (0.15 to 0.96) | 0.048 |
| **Sex**                       |                  |          |                 |         |
| Male                          | 1                | 1        |                 |         |
| Female                        | 0.32 (0.09 to 1.24) | 0.099   | 0.25 (0.01 to 7.81) | 0.431 |
| **Marital status**            |                  |          |                 |         |
| Single                        | 1                | 1        |                 |         |
| Married/cohabiting            | 0.52 (0.16 to 1.72) | 0.288   | 0.12 (0.01 to 1.39) | 0.09   |
| **Alcohol consumption**       |                  |          |                 |         |
| No                            | 1                |          |                 |         |
| Yes                           | 2.73 (0.82 to 9.10) | 0.101   | 1.42 (0.45 to 4.46) | 0.55   |
| **House floor material**      |                  |          |                 |         |
| Dung/earth/sand               | 1                |          |                 |         |
| Carpet/ceramic/cement         | 0.43 (0.09 to 2.03) | 0.284   |                 |         |
| **Residence**                 |                  |          |                 |         |
| Outside Temeke                | 1                |          |                 |         |
| Temeke                        | 0.57 (0.15 to 2.17) | 0.405   |                 |         |
| **People per room**           |                  |          |                 |         |
| One                           | 1                |          |                 |         |
| Two                           | 0.72 (0.15 to 3.52) | 0.685   |                 |         |
| Three or more                 | 0.92 (0.13 to 6.65) | 0.931   |                 |         |
| **Family history of DM**      |                  |          |                 |         |
| No                            | 1                |          |                 |         |
| Yes                           | 2.11 (0.64 to 6.99) |         |                 |         |
| **DM duration**               |                  |          |                 |         |
| ≤5 years                      | 1                |          |                 |         |
| >5 years                      | 0.44 (0.05 to 3.35) | 0.443   |                 |         |
| **Findings on chest examination** |              |          |                 |         |
| Crackles/bronchial breath sounds | 1            |          |                 |         |
| None                          | 0.01 (0.00 to 0.25) | <0.01   | 0.02 (0.01 to 0.15) | <0.01 |
| **Metformin use during diabetes treatment** | |          |                 |         |
| No                            | 1                |          |                 |         |
| Yes                           | 0.08 (0.01 to 0.64) | 0.017   | 0.18 (0.02 to 1.43) | 0.105 |
| **Insulin use during diabetes treatment** | |          |                 |         |
| Yes                           | 1                |          |                 |         |
| No                            | 0.16 (0.04 to 0.60) | 0.007   | 0.31 (0.04 to 2.71) | 0.29   |
| **BMI status**                |                  |          |                 |         |
| Normal                        | 1                |          |                 |         |
| Obesity/overweight            | 0.63 (0.07 to 5.49) | 0.677   | 3.72 (0.57 to 24.2) | 0.17   |
| Underweight                   | 6.79 (1.74 to 26.50) | 0.006   | 1.17 (0.33 to 4.15) | 0.805 |
| **FBG**                       |                  |          |                 |         |
| Normal                        | 1                |          |                 |         |
| Elevated                      | 2.26 (0.29 to 17.87) | 0.438   |                 |         |

Continued
misdiagnosis of TB for pneumonia,\(^9\) therefore warranting high suspicion for TB by a clinician at all times.

In contrast to a study done by Berkowitz et al in South Africa that revealed a high prevalence of HIV among patients with TB with diabetes,\(^2\) our study did not observe a similar finding. The perceived difference can be attributed to the global decline in new HIV infections over the past decade.\(^22\) In addition, there is a higher HIV prevalence of 19% among adults in South Africa compared with the meagre 4.8% in Tanzania.\(^22\) However, larger studies such as population-based studies are needed to ascertain the role of HIV and DM comorbidity on the risk of TB.

Noteworthy in our study is that majority of the patients with diabetes with TB were on insulin and not metformin therapy. Metformin therapy showed protective effects against TB acquisition but only at a univariate level. We believe this could be due to confounding effect and the small number of respondents with TB who used metformin probably affected the PR. A national-based study conducted in Taiwan revealed that the patients who are on metformin had a lower risk of TB with the recommendation that newly diagnosed patients with diabetes should be prescribed metformin due to its increased TB protective effects.\(^23\) A large systematic review study revealed that the protective effect of metformin is through multiple effects on the immune system; it enhances the host cell production of mitochondrial oxygen species and enhances acidification of mycobacterial phagosome and inhibits intracellular growth of Mycobacterium through the adenosine monophosphate-activated protein kinase pathway.\(^24\)

Our study findings revealed discordant glycaemic levels obtained by FBG and HbA1c tests. An explanation for this could be due to the nature of the two tests. High HbA1c represents the glycation of proteins in the body secondary to high blood glucose\(^25\) that takes an unknown period.\(^25\) Blanco et al in their study conducted in Tanzania echoed this phenomenon as they found that FBG tests at the time of TB detection were preferable to HbA1c testing as HbA1c testing failed to detect patients with hyperglycaemia and consequently those at risk of adverse outcomes due to TB.\(^26\)

Our study patients with diagnosed TB routinely in all patients with diabetes and not only in symptomatic patients as compared with previous studies.\(^5\)\(^15\)\(^27\)\(^28\) This was an important aspect of the study as we were also able to diagnose TB in a few asymptomatic patients thus underscoring the significance of routine screening of TB in diabetes. Furthermore, glycaemic levels were based on FBG and HbA1c according to WHO, IDF and American Diabetes Association diagnostic guidelines.\(^5\)\(^13\)\(^29\)

We acknowledge that our study had limitations. As our study targeted patients who attended a diabetic clinic, we risked missing undiagnosed or non-adherent patients with diabetes. Since we used consecutive enrolment of study participants at the diabetic clinic those who perceived themselves at risk might have selected themselves for the study. We did not do sputum induction using hypersonic saline in our study and this could have underestimated the TB prevalence among patients with diabetes found in our study. Although, despite this, our study was still able to detect prevalent TB cases in patients with diabetes at levels that are higher than that reported in the general population. Due to the low outcome of active TB that resulted in low precision and the cross-sectional study design, the observed association between independent variables and the outcome of active TB in our study should not be interpreted as a cause-and-effect relationship. Furthermore, our study was confined to a single hospital, and therefore, the findings should be cautiously generalised. In order to accurately determine how control of diabetes may influence the development of TB we propose larger prospective studies to evaluate the link between glucose control and TB development. We also propose further study on the use of chest CT in evaluating possible radiological features of pulmonary TB.

Our study findings indicate that although there is a decline in the burden of TB in the diabetic population, the prevalence is still much higher than in the general population, signalling the need for routine screening of TB in patients with diabetes, especially those aged less than 45 years and presenting with crackles or bronchial breathing on chest examination.

| Variable                  | cPR (95% CI)       | P value | aPR (95% CI)       | P value |
|---------------------------|--------------------|---------|--------------------|---------|
| Previous TB contact       |                    |         |                    |         |
| No                        | 1                  |         | 1                  |         |
| Yes                       | 2.89 (0.83 to 10.07)| 0.095   | 5.58 (1.00 to 33.31)| 0.05    |
| BCG scar                  |                    |         |                    |         |
| Absent                    | 1                  |         |                    |         |
| Present                   | 0.86 (0.18 to 4.03)| 0.846   |                    |         |

Bold values indicate the significance of the p-value.

\(^1\) reference group; \(^aPR\), adjusted prevalence ratio; \(^BMI\), body mass index; \(^cPR\), crude prevalence ratio; \(^DM\), diabetes mellitus; \(^FBG\), fasting blood glucose; \(^TB\), tuberculosis.
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