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Pulmonary Tuberculosis (PTB) Prevalence & Factors in Diabetic Patients with Poor Glycemic Control In Mwanza.

Sr. Gotfrida Marandu[1*], Gaston Ngonyani[2], Paul Alikado Sabuni[3]

1. Archbishop Anthony Mayala School of Nursing, Catholic University of Health and Allied Sciences, Mwanza, Tanzania.
2. Department of internal Medicine, Catholic University of Health and Allied Sciences-Bugando, Mwanza, Tanzania.
3. Public health Consultant, Muhimbili University of Health and Allied Sciences (MUHAS)

Abstract
Introduction: Tuberculosis (TB) remains a global health threat. Diabetes mellitus (DM) is a critical risk factor for TB, particularly in patients with poor glycemic control.
Objective: To investigate the prevalence and associated factors of newly diagnosed pulmonary tuberculosis (PTB) among poorly controlled diabetic patients in Mwanza, Tanzania.
Methods: A cross-sectional study was conducted in two hospitals, enrolling adult diabetic patients with poor glycemic control. Data were collected through questionnaires, physical examinations, laboratory tests (FBG/RBG, HbA1c, GeneXpert, chest X-ray), and BMI calculation. The primary outcome was newly diagnosed PTB. Statistical analysis was performed using STATA.
Results: Among 97 participants, 59.8% were male, 74.2% were under 60 years old (mean age 48 years), and 81% had HbA1c exceeding 7%. The prevalence of newly diagnosed PTB was 18.6%, of which 12.4% were GeneXpert-positive and 6.2% were clinically/radiologically diagnosed. Obesity was a significant risk factor for PTB (OR=4.4, p=0.006). Overweight and age under 60 also showed higher PTB risk.
Conclusion: Diabetics with poor glycemic control, obesity, overweight, age under 60, and abnormal chest X-rays are at high risk for PTB and require screening. Early detection and control are crucial for preventing TB spread in this vulnerable population.

Key Words: Uncontrolled Diabetes, Obesity, overweight, Tuberculosis (TB), Body Mass Index

Introduction

Tuberculosis (TB) remains a significant global health threat, with an estimated 10.0 million new cases in 2019 (Organization, 2019). Identifying high-risk groups is crucial for targeted prevention and screening. Alongside established risk factors like malnutrition, HIV infection, and smoking, uncontrolled diabetes has emerged as a newly recognized and concerning risk factor for developing active TB (Segura-Cerda, López-Romero, & Flores-Valdez, 2019).

Co-morbidity between TB and diabetes mellitus (DM) is a significant public health issue that is still in its infancy(Khalid, Ahmad, & Qureshi, 2021) and TB is the third most common cause of mortality for people with non-communicable diseases (NCD), notably DM (Bates, Marais, & Zumla, 2015). In the world, for instance, there are more people with TB-DM co-morbidity than TB-HIV (Human Immuno Deficiency) co-infection (Alexander, Gupta, & Mathad, 2019). In other words, TB control is becoming more difficult as DM prevalence rises and vice versa (Kapur & Harries, 2013). This may partly be because patients with significant immunocompromise who have TB and diabetes run the risk of developing uncontrolled hyperglycemia patients with significant immunocompromise who have TB and diabetes run the risk of developing uncontrolled hyperglycemia (Gupta, Koirala, Khardori, & Khardori, 2007).

Dysglycemia in diabetic patients weakens their immune system, creating fertile ground for acute intracellular bacterial infections like TB (Stegenga et al., 2008). This weakened immunity, coupled with the

increased risk of such infections in diabetics explains the higher TB prevalence among them (Pal, Ansari, Hameed, & Fatima, 2016). Studies in South India, the Pacific Islands, and Mexico have confirmed this link, particularly for type 2 diabetes (Bart Jurriaan, 2015; McMurry et al., 2019; Naqshbandi, Harris, Esler, & Antwi-Nsiah, 2008). Consequently, poor glycemic control can lead to higher morbidity and mortality in these patients(Khattab, Khader, Al-Khawaldeh, & Ajlouni, 2010).

In Sub-Saharan Africa, where latent TB is prevalent, diabetes significantly increases the risk of active TB (Obels, Ninsiima, Critchley, & Huangfu, 2022). Poor glycemic control further weakens immunity, tripling the risk of active Tb and this is concerning as uncontrolled diabetes is common and can be worsened by infections like TB(Wang et al., 2021). Conversely, TB developing active TB (can complicate diabetes management, shorten the duration of chronic issues, and increase morbidity and mortality risks (Kapur & Harries, 2013). Due to its atypical presentation, TB in immunocompromised patients often goes undetected (Otu et al., 2018).

While limited research has explored the link between poor glycemic management and newly diagnosed PTB, particularly in Sub-Saharan Africa settings like Tanzania, existing studies highlight the high TB prevalence among diabetics regardless of glycemic control levels (Boillat-Blanco et al., 2016; Mtwangambate et al., 2014; Obels et al., 2022). Addressing this knowledge gap is crucial for raising awareness among medical professionals and informing targeted prevention strategies within this high-risk population.

Our study aims to bridge this gap by investigating the prevalence and associated factors of newly diagnosed PTB in poorly controlled diabetic patients admitted to hospitals in Mwanza, Tanzania. By understanding the specific factors contributing to new PTB diagnoses in this population, we can develop more effective prevention and screening strategies for this dual burden of diseases

Materials and Methods

This cross-sectional study recruited adult diabetic patients (≥18 years) admitted to Bugando Medical Center or Sekou-Toure Referral Regional Hospital with uncontrolled glycemia (FBG ≥8 mmol/L or RBG ≥12 mmol/L). Patients with confirmed COVID-19 were excluded. The sample size was calculated using the Kish Leslie formula (1965) based on a 90.5% prevalence of uncontrolled glycemia in diabetics. Consecutive eligible patients were enrolled after informed consent, and questionnaires were administered in Swahili for optimal comprehension.

Structured questionnaires, physical examinations, BMI calculations, and laboratory tests for FBG/RBG, HbA1c, GeneXpert, and chest X-ray were used to collect data. The primary outcome was newly diagnosed pulmonary tuberculosis (PTB).

Sampling procedures

Following informed consent, a structured questionnaire was administered. This comprehensive tool gathered diverse data, including participant identification details, sociodemographic information (age, gender, marital status, education, occupation), medical history (diabetes diagnosis date, medications, complications), and clinical characteristics (physical examinations, vital signs). Throughout the process, the research assistants conducted interviews and reviewed medical records to acquire a thorough understanding of each participant's health status.

Clinical Characteristics and Physical Examination

Clinical symptoms: Participant evaluation for potential TB included assessing for common symptoms using a TB screening tool adapted from the National TB Guideline and incorporated into the questionnaire. This tool covered key symptoms like cough, night sweats, severe weight loss, hemoptysis, and fever, along with a history of TB contact and prior active TB episodes.

Physical examination: All participants underwent a standardized physical examination. Height (m) and body weight (kg) were measured, and palpable lymph nodes were checked. Body mass index (BMI) was then calculated using the formula: Weight / (Height × Height). BMI categories were classified as follows:

normal (18.5-24.9 kg/m²), underweight (<18.5 kg/m²), overweight (25.0-29.9 kg/m²), and obese (>30 kg/m²).

Blood Sample Collection and Analysis

Fasting and Random Blood Glucose (FBG/RBG): Capillary blood samples were collected to measure FBG/RBG using a GlucoPlus glucometer (Canada). FBG levels were categorized as normal (<8 mmol/L) or increased (≥8 mmol/L). Similarly, RBG levels were classified as normal (<12 mmol/L) or elevated (≥12 mmol/L).

Glycated Hemoglobin (HbA1c): Approximately 3 ml of venous blood was collected in plain tubes and centrifuged within 8 hours. Serum was separated and stored at 20°C until HbA1c measurement. Poor glycemic control was defined as HbA1c levels above 7%.

GeneXpert Testing

Sputum Collection and Processing: All participants provided two spontaneous sputum samples, one spot and one morning collection. Each sample was collected and processed according to established protocols for analysis by the Xpert MTB/RIF module XVI (GX-XVI; Cepheid, USA). A disposable pipette was used to add sample reagent at a 2:1 ratio to the sputum in a sterile container. The mixture was then forcefully agitated 10–20 times before incubation. A minimum of 2 mL of the processed sputum was loaded into the cartridge, followed by a 1-hour and 50-minute run on the GX-XVI platform. A trained laboratory technician subsequently read and interpreted the results.

Chest radiography

All CXR images were independently interpreted by two blinded radiologists or physicians. This maintained unbiased evaluation by ensuring evaluators were unaware of participants' clinical symptoms or GeneXpert results. Each radiologist independently wrote a report documenting their findings and agreement on the presence or absence of CXR features suggestive of PTB. Air space infiltrates/consolidation, lung cavitation, fibrosis, miliary nodules, and granuloma were among the CXR characteristics used to identify pulmonary tuberculosis

Statistical Analysis

Data analysis was conducted using STATA version 15 statistical software. To identify factors associated with newly diagnosed pulmonary tuberculosis (PTB), logistic regression analysis was employed. This method was chosen due to its suitability for modeling the binary outcome variable (new PTB diagnosis) and exploring the relationship with independent variables. Odds ratios (ORs) with 95% confidence intervals were estimated for each statistically significant factor to quantify the strength and direction of the association. Continuous data were appropriately summarized using means and standard deviations, following tests for normality. For categorical variables, frequencies and proportions (percentages) were used to describe their distribution.

Ethical consideration.

Ethical approval was granted by the joint Catholic University of Health and Allied Sciences (CUHAS)/ Bugando Medical Centre (BMC) Review Board (IRB) under protocol number (CREC/659/2023) and the Sekou-Toure Regional Ethics Committee granted ethical clearance under reference FA137/264/01M/56. Informed consent was obtained from all participants before any study procedures commenced. Participants were provided with detailed information about the study, and their right to withdraw at any time without penalty. Written informed consent forms were signed by each participant or their legal guardian, ensuring their voluntary participation and understanding of the study.

Results

Socio-demographic characteristics

Table 1 summarizes the sociodemographic characteristics of the enrolled participants. Among the 120 participants, 58 (59.8%) were male and 72 (74.2%) were younger than 60 years old, with the mean age of 48 ± 14 years. A majority, 73 (75.3%), were married, and 58 (59.8%) reported farming as their primary

occupation. The most frequent reason for hospital admission, reported by 87 (89.7%) of participants, was severe cough (**Table 1).**

Table 1. Demographic and clinical characteristics of the participants

Variable	Number (n=97)	Percentage (%)
Age		
Below 60	72	74.2
60 and above	25	25.8
Gender		
Male	58	59.8
Female	39	40.2
Marital status		
Single	24	24.7
Married	73	75.3
Education		
No education	32	33
Basic education (Primary & Seco. level of education)	63	65
Tertiary	2	2
Occupation		
Unskilled worker	23	23.7
Farmer	58	59.8
Skilled worker	16	16.5
History of cough		
Yes	87	89.7
No	10	10.3
History of TB		
Yes	13	13.4
No	84	86.6
History of night sweat		
No	79	81.4
Yes	18	18.6
Hospitals		
BMC	53	54.6
SRRH	44	45.4

Hints: BMC=Bugando Medical Centre; SRRH= Sekou-Toure Referral Regional Hospital

Glycemic Control and Body Mass Index among the participants.

Upon admission, 106 (88.3%) of participants had elevated random or fasting blood glucose levels, suggesting poorly controlled blood sugar. Only 23 (19.1%) had HbA1c levels below 7%, indicating good control, while 97 (91.5%) exceeded 7%, suggesting poor control. Among those with poor control, 35 (36%) were overweight, 31(32%) were obese, and 31(32%) had normal BMI values,

Prevalence and Associated Factors of New TB Diagnoses in Diabetics with Poor Glycemic Control

Among diabetic patients with poor glycemic control, 22 (18.6%) were newly diagnosed with pulmonary tuberculosis (PTB). Notably, 12 (12.4%) of these cases were GeneXpert-positive, and 8 (6.6%) had abnormal chest X-rays with at least two clinical symptoms (fever, cough, night sweats, or unintended weight loss). All (100%) of the 22 newly diagnosed PTB cases were connected to a TB clinic and initiated anti-TB treatment. Univariate analysis revealed obesity as a significant risk factor for PTB, with a p-value of 0.006, an odds ratio (OR) of 4.4, and a confidence interval (CI) of 1.5-12.7 ***(Table 2).***

Table 2: Prevalence and Associated Factors of New TB Diagnoses in Diabetics with Poor Glycemic Control

Variable	Gene expert		Univariate		Multivariate	
	Negative (n=85)	**Positive (n=12)**	**OR [95%CI]**	**p-value**	**OR [95%CI]**	**p-value**
Age						
< 60 years	62 (86.1)	10 (13.9)	0.5(0.1-2.6)	0.447		

≥ 60 years	23 (92)	2 (8)				
Gender						
Male	52 (89.7)	8(15.4)	1.5(0.5 - 5.2)	0.462		
female	33 (84.6)	4 (12.1)				
History of TB						
No	73 (87.1)	11 (12.9)	0.6(0.07-4.7)	0.587		
Yes	12 (92.3)	1 (7.7)				
Hx of night sweat						
No	70 (88.6)	9 (11.4)				
Yes	15 (83.3)	3 (16.7)	1.6(0.4-6.4)	0.542		
BMI						
Normal	29 (93.5)	2 (6.5)				
Overweight	35 (100)	0				
Obese	21 (67.7)	10 (32.3)	4.4(1.5-12.7)	**0.006***	3.8(1.1-13.7)	**0.037***
Marital status						
Single	22 (91.7)	2 (8.3)				
Married	63(86.3)	10 (13.7)	1.7(0.4-8.6)	0.493		
Education						
None	30 (93.8)	2 (6.2)				
Primary	53 (84.1)	10 (15.9)				
Tertiary	2 (100)	0	1.9(0.5-7.2)	0.301		
Occupation						
Unskilled worker	21 (91.3)	2 (8.7)				
Farmer	50 (86.2)	8(13.8)	1.2(0.5 - 3.2)	0.672		
Skilled worker	14 (87.5)	2(12.5)				
History of cough						
Yes	76 (87.4)	11(12.6)	1.3(0.15-11.1)	0.810		
No	9 (90)	1 (10)				
Type of medication						
Insulin	27 (91.7)	3 (8.3)				
Oral	58 (86.7)	9 (13.4)	0.7(0.2-2.8)	0.636		
Type of DM						
Type one	23 (95.8)	1 (4.2)				
Type two	62 (84.9)	11 (15.1)	4.1(0.5-33.3)	0.190		

*Hints: *P < 0.05 significant level, **P < 0.01 significant level.*

Chest X-ray Findings in Participants with Newly Diagnosed PTB

Among the 29 participants who underwent chest X-rays, 14 (48.3%) had normal findings, while 15 (51.7%) showed abnormalities. Notably, 9 (31.0%) exhibited lower lobe opacities, 3 (10.3%) had upper lobe opacities, 2 (6.9%) displayed cavitations, and 1 (3.5%) presented with unilateral effusion. Interestingly, 9 of the 15 participants with abnormal chest X-rays also tested positive for Mycobacterium tuberculosis using the GeneXpert assay.

Discussion

Diabetic patients with poor glycemic control exhibited a significantly elevated risk of PTB, with nearly 19% diagnosed in our study at Bugando Medical Center and Sekou-Toure Referral Regional Hospital. Notably, 12% of these cases were GeneXpert-positive, solidifying the diagnosis based on clinical symptoms and suggestive chest X-rays. This observed prevalence is considerably higher than those reported by (Ji et al., 2020; Mtwangambate et al., 2014).This discrepancy could be partially attributed to the use of GeneXpert, a highly sensitive and specific diagnostic tool recommended by the ADA and CDC for high-risk populations like diabetics with poor glycemic control. Compared to the traditional AFB smear microscopy employed in the previous studies, GeneXpert's accuracy significantly increases the likelihood of identifying early-stage PTB cases, potentially contributing to the observed difference in prevalence (Yu, Kong, Ye, & Wang, 2020).

Our findings highlight the critical role of GeneXpert screening in resource-limited settings with a high burden of both diabetes and TB. Implementing such targeted screening protocols could pave the way for earlier diagnosis and treatment of PTB in this vulnerable population, ultimately improving clinical outcomes and potentially reducing TB transmission. In addition, our study focused specifically on diabetic patients with poor glycemic control (HbA1c > 7%). This differs from (Mtwangambate et al., 2014) inclusion of all

diabetes patients, regardless of glycemic status. This selection bias limits direct comparison but suggests a potential link between poor glycemic control and increased PTB risk. This suggested more evidence on broader diabetic populations. Also, disparity likely reflects several factors, including variations in geographic TB prevalence, patient populations, diagnostic methods, and potentially, the impact of glycemic control.

While our study found that 91.5% of participant had poor glycemic control (HbA1c > 7%). This magnitude was greater than those reported in previous studies, Ethiopia 73.8% (Abera, Demesse, & Boko, 2022), Tanzania 75.2% (Mtwangambate et al., 2014), and United state 69% (Milo & Connelly, 2019). This discrepancy could be due to several factors, including differences in participant demographics, diagnostic criteria, or underlying healthcare access and diabetes management practices.

Furthermore, the distribution of BMI among participants with poor glycemic control in our study (36% overweight, 32% obese, 32% normal) warrants further investigation. While similar data is not readily available from the other studies mentioned, understanding the potential link between BMI and glycemic control in this high-risk group could inform targeted interventions for improved overall health outcomes. Our study revealed a concerningly high 18.6% prevalence of newly diagnosed pulmonary tuberculosis (PTB) among diabetic patients with poor glycemic control. This finding aligns with similar studies conducted in other regions, such as the work by (Wu et al., 2016) in China, who observed a comparable rate of 17.5%. This suggests a potential consistency in the elevated risk of PTB among poorly controlled diabetics across diverse geographic locations.

However, the prevalence of diabetes among TB patients appears to vary significantly across regions. For instance, studies conducted in Asia and the Middle East have documented a wider range, with prevalence figures ranging from 9.5% to 44% (Anyanwu, Ajumobi, Afolabi, Usman, & Kehinde, 2022; Ugarte-Gil et al., 2020) Similarly, a multi-center study in Texas, USA, and Mexico reported prevalence rates of 39% and 36%, respectively (Barber, 2020). These higher prevalence figures in certain regions could potentially be attributed to a higher background prevalence of diabetes within the general population.

Our study unveiled a concerningly high prevalence of chest X-ray abnormalities (51.7%) among diabetic patients diagnosed with pulmonary tuberculosis (PTB). This finding adds to a growing body of evidence suggesting atypical X-ray presentations in diabetic PTB patients, emphasizing the importance of considering glycemic control in TB diagnosis.

Further analysis of specific X-ray findings revealed intriguing divergences. Although lower lobe opacities were the most common abnormality (31.0%), unexpectedly, cavitations were present in only 6.9% of participants compared to 10.3% with upper lobe opacities. This suggests potential variations in disease progression or presentation in this population, and warrants further investigation.

Significantly, our study demonstrated a strong correlation between chest X-ray abnormalities and GeneXpert positivity. Nine out of 15 participants with abnormal X-rays tested positive for Mycobacterium tuberculosis, highlighting the potential value of X-ray in guiding GeneXpert testing and diagnosis in diabetic PTB patients.

These findings underscore the need for further research to understand the mechanisms behind atypical X-ray presentations in diabetic PTB, and their impact on diagnosis and treatment strategies. Study from three southern California community-based organizations (Huang, Wang, Lai, & Chang, 2017) investigating the influence of glycemic control on radiological manifestations, offer valuable insights in this direction. By improving our understanding of these unique X-ray features, we can enhance early diagnosis and effective management of PTB in diabetic patients

Conclusion

Diabetics with poor glycemic control harbor a hidden TB threat, with 18.6% in our study newly diagnosed. This demands active case finding and targeted TB interventions for this vulnerable group. Obesity, identified as a risk factor, suggests comprehensive metabolic management may be key. While younger age needs

further study, it hints at potentially crucial age-specific strategies. Missing 18 TB cases through routine screening highlights the vital role of proactive case finding, emphasizing the need for strengthened screening and diagnostic efforts to safeguard this population.

List of Abbreviations

APC: Antigen Presenting Cells
BMI: Body mass index
CXR: Chest radiography
DM: Diabetes Mellitus
FBG: Fasting Blood Glucose
HbA1c: Glycated haemoglobin
HIV: Human Immunodeficiency Virus
PTB: Pulmonary tuberculosis
SRRH: Sekou Toure Regional Referral Hospital
SSA: Sub-Saharan Africa
TB: Tuberculosis

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Authors' contributions
Authors' contributions GM and GN wrote the first draft of the manuscript. PAS and GM contributed to the writing of the paper and provided vital feedback. GM, PAS and GN contributed to data acquisition. PAS ran the analyses with input from GM, and GN. All authors contributed to the study design and interpretation of analyses. All authors critically reviewed and revised the manuscript and approved the final version

Conflict of Interest

Authors declare no conflict of interest.

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