

Correspondence: Fikriatul Fadhillah, Department of Pulmonology and Respiratory Medicine, Faculty of Medicine, Hasanuddin University, Perintis Kemerdekaan Street, Km. 10, Tamalanrea Indah 90245, Makassar, South Sulawesi.
Tel.: +62 852-2273-2723-
E-mail: dr.fikrimarala@gmail.com

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The effect of type 2 diabetes mellitus on clinical symptoms, sputum molecular test results, and lesions in thoracic photos of pulmonary tuberculosis patients

Fikriatul Fadhillah,¹ Erwin Arief,^{1,2}
Nur Ahmad Tabri,^{1,2} Irawaty Djaharuddin,^{1,2}
Arif Santoso,^{1,2} Jamaluddin Madolangan^{1,2}

¹Department of Pulmonology and Respiratory Medicine, Faculty of Medicine, Hasanuddin University, Makassar;

²Wahidin Sudirohusodo Hospital, Makassar, Indonesia

ABSTRACT

Pulmonary tuberculosis (TB) remains a major global health issue, particularly in developing countries. Type 2 diabetes mellitus (T2DM) has been linked to increased susceptibility and more severe TB presentations, though evidence on its impact remains inconsistent. This prospective cohort study, conducted at RSUP Dr. Wahidin Sudirohusodo Makassar from August to November 2024, evaluated 90 bacteriologically confirmed pulmonary TB patients, with and without T2DM. Clinical symptoms, sputum molecular test (RMT) results, and radiographic lesion extent were assessed. TB patients with T2DM showed significantly more severe symptoms ($p=0.002$), more extensive lung lesions ($p=0.008$), and a lower rate of RMT positivity ($p=0.033$). These findings suggest that T2DM is associated with more severe disease manifestations and broader lung involvement but reduced molecular test positivity in pulmonary TB patients.

Introduction

Pulmonary tuberculosis (TB) remains a significant global health burden, particularly in countries with moderate to high disease prevalence.¹⁻⁶ Infection with *Mycobacterium tuberculosis* (MTB) involves a complex interaction between the pathogen and the host immune system, particularly through phagocytosis by alveolar macrophages.^{2,7-9} Although macrophages play a central role in bacterial clearance, successful eradication of MTB is highly dependent on the host's immunological and metabolic status.⁷⁻¹⁰ When MTB survives within macrophage vacuoles, inflammatory responses are triggered, leading to both systemic and local clinical symptoms.¹¹⁻¹³

On the other hand, type 2 diabetes mellitus (T2DM), characterized by chronic hyperglycemia, contributes to immune dysregulation and oxidative stress.^{12,14-16} The accumulation of advanced glycation end-products, along with increased activation of inflammatory pathways such as NF-

κB, impairs macrophage function and enhances apoptosis of immune cells.¹⁷ These alterations hinder the body's ability to control MTB infection, potentially leading to higher bacterial viability and proliferation within lung tissue.^{18,19}

The coexistence of T2DM and pulmonary TB has been associated with more severe clinical manifestations, higher mycobacterial burden, and extensive structural damage observable on chest radiographs.^{14,20-26} Systemic symptoms such as fever, weight loss, and night sweats tend to be more pronounced, alongside local respiratory symptoms including cough, dyspnea, and hemoptysis.²⁷⁻³⁰ Radiologically, this combination often presents with more extensive parenchymal destruction and fibrosis.^{17,31,32}

This study aims to investigate the effect of T2DM on clinical symptoms, molecular test (RMT) positivity, and radiographic lesions in patients with pulmonary TB. Understanding this relationship may inform more tailored diagnostic and therapeutic strategies for the growing population of TB patients with coexisting diabetes.

The general objective of this study is to evaluate the impact of T2DM on clinical symptoms, sputum acid-fast bacilli (AFB) positivity, and the extent of lung lesions observed in chest X-ray imaging among TB patients. Specifically, the study aims to determine how T2DM affects the severity of clinical symptoms in TB patients, assess its influence on the rate of AFB sputum positivity, and evaluate its impact on the extent of lung lesions as visualized on chest X-rays. By addressing these objectives, this research seeks to provide valuable insights into the relationship between T2DM and the clinical progression of TB.

Materials and Methods

Study design

This study is an analytical observational study with a prospective cohort approach aimed at assessing the effect of T2DM on i) clinical outcomes (symptoms) and severity of TB; ii) sputum AFB conversion; and iii) the extent of lung lesions on chest X-ray imaging.

Study location and time

The study was conducted at RSUP Dr. Wahidin Sudirohusodo Makassar. Data collection, including chest X-ray images, sputum smears for AFB, and blood samples for confirming T2DM, was carried out on the same day patients visited the emergency department or outpatient clinic. The study was planned to be conducted from August to November 2024.

Study population

The target population of this study includes all TB patients at RSUP Dr. Wahidin Sudirohusodo Makassar. The accessible population consists of TB patients at the hospital, both with and without T2DM. For the group with TB and T2DM, the study will evaluate the effects of T2DM diagnosis on i) clinical outcomes (symptoms) and severity of TB based on Bandim score; ii) sputum AFB conversion; and iii) the extent of lung lesions on chest X-ray. Basic characteristics will also be compared between the TB with T2DM group and the TB without T2DM group.

Sample size and sampling method

The minimum sample size required is 80 patients, with 40 patients in the TB + T2DM group and 40 patients in the TB non-T2DM group, ensuring a homogeneous or linear result.

Inclusion criteria

The inclusion criteria represent the sample of patients eligible for this study, as follows: i) patients aged ≥ 18 years; ii) confirmed bacteriologically and drug-sensitive pulmonary TB patients under anti-TB regimen 2(HRZE)/4(HR)3 (for newly positive sputum AFB); iii) patients with T2DM: TB patients who met the above criteria and are diagnosed with DMT2 according to operational definitions and were receiving treatment at RSUP Dr. Wahidin Sudirohusodo Makassar; iv) patients who consented to undergo chest X-ray and sputum AFB testing for TB diagnosis; v) patients with TB and no cognitive impairment who could complete the clinical severity questionnaire.

Exclusion criteria

Exclusion criteria include: i) patients with comorbidities that could affect the clinical severity of TB and the results of chest X-ray, such as cardiovascular diseases (coronary artery disease, heart valve disorders, heart failure, *etc.*), pulmonary diseases (asthma, chronic obstructive pulmonary disease, malignancy, *etc.*), or immunological disorders (systemic lupus erythematosus, *etc.*), regardless of their treatment status;³³ ii) pregnant TB patients;³⁴ iii) TB patients with HIV co-infection; iv) extra-pulmonary TB patients; v) drug-resistant TB patients; vi) patients unwilling to undergo chest X-ray and blood sampling for T2DM evaluation.

Study procedure

Patients who meet the inclusion criteria will be enrolled until the minimum sample size of 80 patients is reached. Eligible patients will undergo three tests: i) sputum AFB test; ii) blood test for T2DM evaluation; and iii) chest X-ray. Patients diagnosed with TB and negative AFB results, but with radiological findings supporting TB diagnosis, will be categorized as TB non-RMT (-). All diagnostic tests will be performed at the time of patient admission to the hospital, with no follow-up assessments.

Statistical analysis

Descriptive statistics will be used to present basic patient characteristics, including age, sex, socioeconomic status, and family history of T2DM. Categorical data will be presented as frequencies (n) and percentages (%), while numerical data will be shown as means $\pm$ standard deviations. Comparison of baseline characteristics between the two main groups (TB + T2DM and TB non-T2DM) will be performed to evaluate any significant differences. A linear regression test will be used to examine the effects of T2DM on i) symptom severity; ii) AFB test results; and iii) extent of lung lesions. Comparative tests such as Chi-square (Pearson χ^2) for categorical data and independent *t*-tests or Mann-Whitney U tests for numerical data will be performed as needed.

Results

Subject characteristics

This study involved 90 respondents, evenly divided into two groups: 45 patients with pulmonary TB without T2DM and 45 patients with pulmonary TB and T2DM. This balanced distribution aimed to minimize selection bias and enable valid comparisons between the two groups. Based on demographic and clinical characteristics, the severity of clinical symptoms was found to be higher in the pulmonary TB with T2DM group. Patients in this group exhibited more severe symptoms compared to those without T2DM. Hyperglycemia in T2DM patients contributed to increased symptom severity—such as cough, shortness of breath, and weight loss—due to impaired immune function, as reported in several previous studies (Table 1).

As shown in Table 1, out of the 90 samples in this study, the majority were male, comprising 64 individuals (71.1%), while 26 were female (28.9%). The mean age of the patients was 48.91 ± 13.32 years. Results from the GeneXpert MTB/RIF (RMT) test showed that 52 patients (57.8%) tested negative, while 38 patients (42.2%) tested positive. Regarding smoking status, 42 patients (46.7%) were non-smokers, while 48 patients (53.3%) were smokers. The evaluation of thoracic lesion extent revealed that 19 patients (21.1%) had minimal lesions, whereas 71 patients (78.9%) had extensive lesions.

According to Table 2, in the group of TB patients without T2DM, the most frequently reported clinical symptom was productive cough, observed in 42 patients (93.3%).

Shortness of breath was reported in 33 patients (73.3%), while fever occurred in 23 patients (51.1%). A total of 30 patients (66.7%) experienced weight loss, and chest pain was reported in 3 patients (6.7%). In the group of TB patients with T2DM, productive cough was also the most dominant symptom, occurring in 43 patients (95.5%). Shortness of breath was more prevalent compared to the non-T2DM group, affecting 42 patients (93.3%). Fever was also more frequently reported, found in 37 patients (82.2%). A total of 40 patients (88.9%) experienced weight loss, while chest pain was more commonly observed in this group, affecting 21 patients (46.7%).

According to the study data in Table 3, the distribution of lesion locations in TB patients varied between those with and without T2DM. In the TB without T2DM group, lesions were most frequently found from the apex to the base of the lungs (57.8%), followed by the apex alone (26.7%). In contrast, in the TB with T2DM group, lesions were most commonly located in the basal area (66.7%), followed by the medial to basal regions (22.2%). Lesions extending from the apex to the base were found in only 8.9% of TB patients with T2DM, significantly lower than in the non-T2DM group. Medial lesions were not observed in either group.

Differences in symptom severity of pulmonary tuberculosis without and with type 2 diabetes mellitus

The available data in Table 4 indicate that the severity of symptoms in pulmonary TB patients differs between those with and without T2DM. Among TB patients without

Table 1. Characteristics of research subjects.

Variable	Frequency (n=90)	Percentage (%)
Sex		
Male	64	71.1
Female	26	28.9
Age (mean $\pm$ SD), years	48.91 $\pm$ 13.32	
RMT test results		
Negative	52	57.8
Positive	38	42.2
Smoking status		
Non-smoker	42	46.7
Smoker	48	53.3
Extent of thoracic lesion		
Minimal lesion	19	21.1
Extensive lesion	71	78.9

SD, standard deviation; RMT, sputum molecular test.

Table 2. Clinical symptoms in pulmonary tuberculosis without and with type 2 diabetes mellitus.

Variable	TB without T2DM (n=45) n (%)	TB with T2DM (n=45) n (%)
Clinical symptoms		
Productive cough	42 (93.3)	43 (95.5)
Dyspnea	33 (73.3)	42 (93.3)
Chest pain	3 (6.7)	21 (46.7)
Fever	23 (51.1)	37 (82.2)
Weight loss	30 (66.7)	40 (88.9)

TB, tuberculosis; T2DM, type 2 diabetes mellitus.

T2DM (n=45), the majority (29 individuals) experienced mild symptoms, while 16 had severe symptoms. In contrast, TB patients with T2DM (n=45) exhibited a much higher tendency toward severe symptoms, with 40 patients affected, and only 5 reporting mild symptoms. Statistical analysis revealed a significant association between T2DM and symptom severity ($p=0.002$). The odds ratio (OR) of 0.519 [95% confidence interval (CI): 0.053-5.112] suggests that TB patients without DM tend to have a lower risk of experiencing severe symptoms compared to those with DM. However, the wide CI indicates variability in the risk estimate (Table 4).

Association of pulmonary tuberculosis without and with type 2 diabetes mellitus and sputum molecular test results

The relationship between lesion extent in clinical TB without T2DM and bacteriological TB without T2DM with RMT results is presented in Table 5. From Table 5, in the group of TB patients without T2DM, 21 individuals (46.7%) showed negative RMT results, while 24 individuals (53.3%) had positive results. The p-value of 0.033 indicates that the difference between the groups with and without T2DM in

terms of RMT results is statistically significant. The OR of 0.395 with a 95% CI (0.167-0.935) suggests that TB patients with T2DM are approximately 60% less likely to obtain a positive RMT result compared to patients without T2DM. Since the CI does not include the value 1, this result is considered statistically significant. On the other hand, in the group of TB patients with T2DM, only 31 patients (68.9%) had negative RMT results, while 14 patients (31.1%) had positive results.

Difference in the size of lesions between pulmonary tuberculosis without and with type 2 diabetes mellitus

This study evaluates the difference in the size of lesions between pulmonary TB without T2DM and pulmonary TB with T2DM. The results of this analysis are presented in Table 6. The results of this study in Table 6 show that the pattern of thoracic lesion distribution in TB patients differs between those with T2DM and those without. Patients with both TB and T2DM are more likely to have extensive lesions, with 86.7%, compared to 71.1% in TB patients without T2DM. On the other hand, minimal lesions are more

Table 3. Lesion location in pulmonary tuberculosis without and with type 2 diabetes mellitus.

Variable	TB without T2DM (n=45) n (%)	TB with T2DM (n=45) n (%)
Lesion location		
Apex	12 (26.7)	1 (2.2)
Apex to medial	4 (8.9)	0 (0)
Apex to basal	26 (57.8)	4 (8.9)
Medial	0 (0)	0 (0)
Medial to basal	1 (2.2)	10 (22.2)
Basal	2 (4.4)	30 (66.7)

TB, tuberculosis; T2DM, type 2 diabetes mellitus.

Table 4. Association of symptom severity in pulmonary tuberculosis without and with type 2 diabetes mellitus.

	Severity of symptoms		p	OR (95% CI)
	Mild	Severe		
Pulmonary TB without DM (n=45)	29	16	0.002*	0.519 (0.053-5.112)
Pulmonary TB with DM (n=45)	5	40		

TB, tuberculosis; DM, diabetes mellitus; OR, odds ratio; CI, confidence interval. *Chi square.

Table 5. Association of pulmonary tuberculosis without and with type 2 diabetes mellitus and sputum molecular test results.

	RMT negative	RMT positive	p	OR (95% CI)
Pulmonary TB without T2DM (n=45)	21 (46.7%)	24 (53.3%)	0.033*	0.395 (0.167-0.935)
Pulmonary TB with T2DM (n=45)	31 (68.9%)	14 (31.1%)		

TB, tuberculosis; T2DM, type 2 diabetes mellitus; RMT, sputum molecular test; OR, odds ratio; CI, confidence interval. *Chi square.

Table 6. Differences in lesion extent between pulmonary tuberculosis without and with type 2 diabetes mellitus.

Thoracic lesion	TB with T2DM (n=45)	TB without T2DM (n=45)	p	OR (95% CI)
Minimal lesion	6 (13.3%)	13 (28.9%)	0.008*	2.591 (1.240-5.412)
Extensive lesion	39 (86.7%)	32 (71.1%)		

TB, tuberculosis; T2DM, type 2 diabetes mellitus; OR, odds ratio; CI, confidence interval. *Fisher's exact test.

commonly found in TB patients without T2DM (28.9%) compared to those with T2DM (13.3%). Statistically, this difference is significant ($p = 0.008$), with an OR of 2.591 (95% CI: 1.240-5.412). This means that TB patients without T2DM have a 2.59 times higher risk of having minimal lesions compared to TB patients who also suffer from T2DM.

Discussion

Severity of symptoms of pulmonary tuberculosis without and with type 2 diabetes mellitus

This study of 90 participants (45 with pulmonary TB alone and 45 with TB-T2DM) demonstrated that TB-T2DM patients had more severe symptoms (cough, dyspnea, weight loss). Hyperglycemia in T2DM impairs immune functions (e.g., neutrophils, macrophages, T-cells), worsening the immune response to MTB infection and delaying sputum conversion.^{2,8,26,33,34} Chronic inflammation and oxidative stress also contribute to greater lung damage, reflected radiologically as larger lesions or cavities.^{14,35,36}

The severity of symptoms was significantly different between groups: most TB-only patients had mild symptoms, while the TB-T2DM group predominantly had severe symptoms. This supports findings that TB-T2DM patients suffer worse outcomes and slower responses due to immune dysfunction.^{2,31,37,38} Dysregulated cytokines like tumor necrosis factor- α and interferon- γ , persistent hyperglycemia, and diabetic angiopathy contribute to poor prognosis.^{33,39,40}

The relationship between pulmonary tuberculosis without and with type 2 diabetes mellitus and sputum molecular test results

The study also revealed a significant difference in RMT results between the TB-only and TB-T2DM groups (53.3% vs. 31.1%, $p=0.033$). TB-T2DM patients had a lower chance of obtaining a positive RMT result (OR=0.395, 95% CI: 0.167-0.935). This may be due to T2DM-induced immune dysfunction affecting sputum quality and bacillary load, thus impacting RMT sensitivity.^{18,19,33} Furthermore, TB-T2DM patients often present with atypical radiological findings, which may affect test performance.^{2,20} These results emphasize the need for a personalized diagnostic approach, including repeated evaluations for TB-T2DM patients.^{8,41,42}

The difference in lesion size of pulmonary tuberculosis without and with type 2 diabetes mellitus

The study also found that TB-T2DM patients had larger lung lesions compared to TB-only patients. This supports the hypothesis that hyperglycemia exacerbates tissue damage by impairing immune responses, disrupting granuloma formation, and enhancing inflammation.^{14,20,28} Additionally, abnormal angiogenesis in TB-T2DM patients could contribute to further lung damage. These findings call for more intensive monitoring and aggressive treatment strategies, including regular radiological evaluations and strict glucose control, to improve disease outcomes.⁴³

Limitations

This study involved 90 respondents (45 TB without T2DM and 45 TB-T2DM). Although the balanced group distribution helps minimize selection bias, the relatively small sample size reduces statistical power and makes the results less generalizable to a broader population. The limited sample and relatively short study duration are additional constraints. Nevertheless, this study generally provides insights into the relationship between the extent of thoracic lesions and positive RMT results in both TB patients with T2DM and without T2DM.

Conclusions

This study demonstrates that T2DM affects several clinical aspects in patients with pulmonary TB. First, patients with DM tend to have more severe clinical symptoms compared to TB patients without DM. Second, T2DM influences the sputum RMT results, where TB patients without DM show a higher rate of positive RMT results compared to TB patients with T2DM. Third, TB patients with T2DM have larger lung lesions compared to those without T2DM.

For further research, it is recommended to conduct studies with a larger sample size and longer duration to obtain more representative data on the prognosis of TB patients with T2DM. Additionally, more uniform supportive examinations, such as using HbA1c as a parameter to compare the size of lesions on chest radiographs, could help establish a deeper connection between symptom severity, RMT results, and the radiological findings.

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