

# Influence of Type 2 Diabetes Mellitus on the Clinical Outcomes in Hospitalized Patients with Active Pulmonary Tuberculosis: A Retrospective, Single-Center, Real-World Study in China

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**Purpose:** To explore the influence of type 2 diabetes mellitus (T2DM) on the clinical outcomes of pulmonary tuberculosis (TB) and the factors that may affect outcomes. In addition, the treatment regimens of active pulmonary TB patients with or without T2DM were described.

**Methods:** This is a retrospective, single-center, real-world study conducted in the Fifth People's Hospital of Suzhou (China), an urban hospital. This study divided 340 inpatients with active TB who received standard anti-tuberculosis treatment into the T2DM and control groups, with 61 patients in the T2DM group and 279 patients in the control group. The outcomes were the time to negative *Mycobacterium tuberculosis* sputum conversion and the rate of negative sputum conversion for tuberculosis bacteria at 2 months.

**Results:** The percentage of patients who received the isoniazid, rifampin, pyrazinamide, and ethambutol (HRZE) regimen was numerically lower in the T2DM vs control group (73.8% vs 79.6%), while the use of the isoniazid, rifapentine, ethambutol, and levofloxacin (HRfELfx) regimen was numerically higher (14.8% vs 9.7%). The median time to negative sputum conversion was longer in the T2DM group (median, 60.00 vs 52.00 days,  $P < 0.001$ ). The rates of negative sputum conversion at 2 months were 85.2% vs 92.8% in the T2DM and control groups ( $P = 0.055$ ). The multivariable Cox regression analysis showed that the male sex (adjusted HR=0.759, 95% CI: 0.585–0.984,  $P = 0.037$ ) and T2DM (adjusted HR=0.721, 95% CI: 0.528–0.986,  $P = 0.040$ ) were independently associated with the time to negative sputum *Mycobacterium tuberculosis* conversion.

**Conclusion:** Patients with TB and T2DM had a longer time to negative sputum *Mycobacterium tuberculosis* conversion. In addition, being male significantly increased the risk of prolonged time to negative sputum *Mycobacterium tuberculosis* conversion.

**Keywords:** tuberculosis, type 2 diabetes mellitus, anti-tuberculosis drugs, treatment regimens, prognosis

## Introduction

Pulmonary tuberculosis (TB) refers to the clinical syndrome associated with the infection of the respiratory system caused by *Mycobacterium tuberculosis* (*M. tuberculosis*).<sup>1,2</sup> The World Health Organization estimated that, in 2022, 10.6 million people developed TB, and 1.3 million died from the disease globally.<sup>2</sup> In 2021, China reported approximately 590,000 new cases of TB, with a mortality rate of 2.1 per 100,000. China has the world's third-largest number of TB cases.<sup>3</sup> *M. tuberculosis* is spread through the air from one person to another when bacteria are aerosolized from a person with pulmonary TB.<sup>2</sup> TB is a global public health issue that poses a serious threat to public health.

Type 2 diabetes mellitus (T2DM) is a chronic condition with a worldwide prevalence of 6.1%;<sup>4</sup> the prevalence in China is among the highest worldwide, at 12.4%.<sup>5</sup> T2DM is associated with low-grade systemic inflammation and

immune dysfunction,<sup>6,7</sup> increasing the risk of opportunistic infections.<sup>8</sup> T2DM is closely related to the incidence of pulmonary TB.<sup>9,10</sup> Patients with T2DM have a 2-3-time increased risk of developing TB than non-T2DM patients.<sup>11</sup> Globally, the incidence of diabetes-associated TB is increasing, with nearly 17% of TB cases in China being attributed to T2DM.<sup>12</sup> The prevalence of T2DM in China has continuously increased in the last decades due to the aging population, urbanization, and lifestyle changes.<sup>13</sup> Hence, it is expected that the burden of TB will follow the T2DM burden, posing a double-threat to public health, especially in countries with high prevalences of both diseases.

Previous studies demonstrated that T2DM has a significant influence on the treatment outcomes of TB, resulting in a delayed time to negative sputum culture conversion, increased risk of treatment failure, TB relapse, and death.<sup>14–18</sup> A meta-analysis showed that, compared with non-T2DM patients, patients with pulmonary TB and T2DM had a lower rate of negative sputum culture conversion at 2 months and higher rates of treatment failure and death,<sup>17</sup> but that meta-analysis included only one study from mainland China. The available studies based on the Chinese population mainly focused on the prevalence, clinical characteristics, and outcomes of patients with pulmonary TB complicated by T2DM.<sup>19–22</sup> A study demonstrated that T2DM was an independent risk factor for tuberculosis.<sup>23</sup> A study in China indicated that T2DM had an adverse effect on the treatment outcomes of drug-sensitive pulmonary TB and suggested that all patients in the intensive phase applied the standard treatment regimen, which included the combination of isoniazid (H), rifampicin (R), pyrazinamide (Z), and ethambutol (E) (HRZE);<sup>22</sup> however, the patients in that study were treated between 2008 and 2010. Adjustment may be necessary based on tolerance; Z and R can lead to liver toxicity and may be replaced with Lfx and Rft. Therefore, the isoniazid (H), rifapentine (Rft), ethambutol (E), and levofloxacin (Lfx) (HRftELfx) regimen is also an option. Since patients with T2DM exhibit individual differences in response to anti-TB drugs, it is necessary to personalize treatment regimens by considering the individualized factors of patients in the clinical practice. However, the influence of T2DM on the treatment outcomes of patients with pulmonary tuberculosis diagnosed by sputum culture and other factors (such as other clinical parameters affected by the disease) that influence the treatment outcomes still lack evidence.

Hence, this study explored the influence of T2DM on the clinical outcomes of pulmonary TB and the factors that may affect clinical outcomes. In addition, the treatment regimens of active pulmonary TB patients with or without T2DM were described.

## Methods

### Study Design and Patients

This retrospective, single-center, real-world study included inpatients diagnosed with active pulmonary TB according to the Diagnostic Criteria for Pulmonary TB (WS288-2017)<sup>24,25</sup> and received anti-TB treatment between April 1, 2019, and May 31, 2020, at the Tuberculosis Department of the Fifth People's Hospital of Suzhou. This study adhered to the Declaration of Helsinki and was approved by the Ethics Review Committee of the Fifth People's Hospital of Suzhou (approval #K-2023-001-002). The requirement for individual informed consent was waived by the committee because of the retrospective nature of the study. The investigators were committed to maintaining strict confidentiality of all patient data.

The inclusion criteria were 1)  $\geq 35$  years of age, male or female, 2) diagnosed with active pulmonary TB according to the Diagnostic Criteria for Pulmonary TB (WS288-2017),<sup>24,25</sup> 3) microscopy positive for sputum smear or culture positive for *Mycobacterium tuberculosis*, and 4) inpatients with a documented anti-tuberculosis treatment history. The exclusion criteria were 1) known or suspected infection with rifampicin mono-resistant *M. tuberculosis* (RMR-TB), multidrug-resistant *M. tuberculosis* (MDR-TB), and extensively drug-resistant *M. tuberculosis* (XDR-TB), 2) concomitant non-tuberculous mycobacterial lung disease, 3) type 1 diabetes mellitus, 4) severe cardiac, hepatic, or end-stage renal disorders, history of neoplasm malignant, or any other terminal conditions, or 5) incomplete data or lost to follow-up. Patients with HIV were not explicitly excluded, but at the study hospital, patients with HIV, irrespective of the TB status, are treated in the Infectious Diseases Department, not the Tuberculosis Department.

MDR-TB was defined as *M. tuberculosis* resistant to at least two first-line anti-TB drugs, including isoniazid and rifampicin. XDR-TB was defined as *M. tuberculosis* resistant to first-line anti-TB drugs isoniazid and rifampicin and additionally resistant to at least one fluoroquinolone antibiotic and at least one other group A anti-TB drug (levofloxacin/moxifloxacin, bedaquiline, linezolid).

## Data Collection and Outcome

All data in this study were collected from the patient's medical records, and the baseline serum biomarkers were extracted from the results on the first day after admission. Patients with T2DM were defined as<sup>19</sup> the population meeting the Guideline for the Prevention and Treatment of T2DM in China,<sup>13,19</sup> or those treated with antidiabetic agents. Based on the status of baseline T2DM, the patients were divided into the T2DM and control groups.

The routine follow-up methods during the study period were Ziehl-Neelsen staining to detect acid-fast bacilli in sputum smears and liquid culture for culturing *M. tuberculosis*. Patients' sputum smears for acid-fast bacilli and sputum *M. tuberculosis* culture were collected before treatment. Sputum smears for acid-fast bacilli were examined every 2 weeks after anti-TB treatment, and sputum *M. tuberculosis* culture was examined monthly; some patients provide their samples at the Fifth People's Hospital of Suzhou, China, while others do so at designated local hospitals. The results of sputum sample tests were recorded in the electronic medical system. The time to negative sputum culture conversion was defined as the interval between the start of anti-TB treatment and the first time that *M. tuberculosis* could not be detected in two consecutive sputum samples recorded in days. The rate of negative sputum culture conversion at 2 months was defined as the proportion of patients who achieved negative conversion of *M. tuberculosis* in sputum samples within the first two months of anti-TB treatment. The standard of sputum conversion was defined as negative for acid-fast bacilli in sputum smear test for 2 consecutive months without recurrence or negative for *M. tuberculosis* in sputum culture.

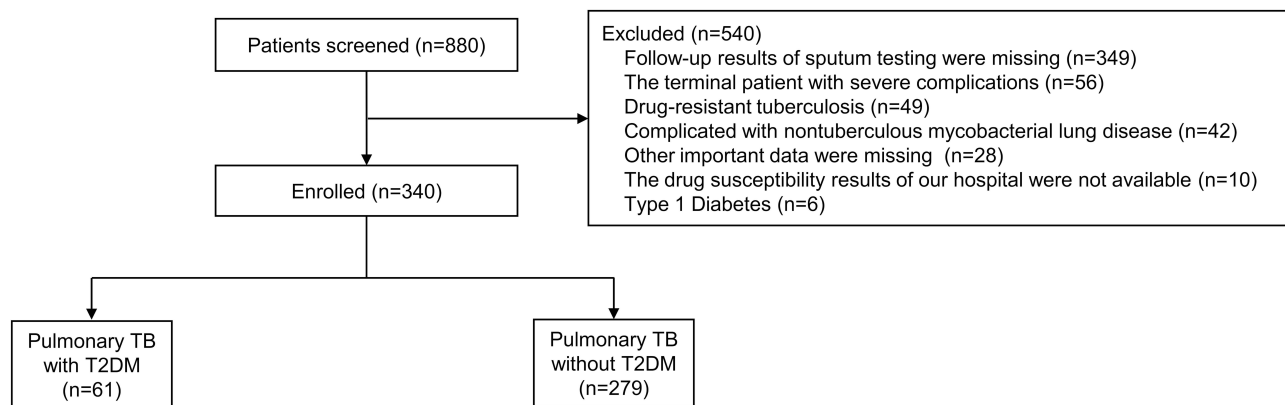
## Statistical Analysis

Statistical analyses were performed using SPSS 26.0 (IBM, Armonk, NY, USA) and R (Version 4.2.3). The continuous variables were tested for normal distribution using the Kolmogorov–Smirnov test. Normally distributed continuous variables were described using means  $\pm$  standard deviations, and those not normally distributed were described using medians (Q1, Q3). The categorical variables were described using frequency and percentage for a descriptive statistical summary. Cox regression analysis was used to investigate the factors associated with the time to negative sputum culture conversion in patients with active pulmonary TB. All factors that may affect the clinical outcome of pulmonary TB were tested using univariable analyses for the time to sputum conversion, including age, sex, body mass index (BMI,  $\geq 18.5$  or  $< 18.5$  kg/m<sup>2</sup>), T2DM, hypertension (systolic blood pressure  $\geq 140$  mmHg and/or diastolic blood pressure  $\geq 90$  mmHg), pulmonary bacterial infection, pulmonary fungal infection (including pulmonary aspergillosis and pulmonary candidiasis), prior TB treatment (yes or no), smoking status (non-smoking or smoking: Non-smoking individuals are defined as patients who have never smoked or those who have smoked in the past but have quit for more than six months. Smoking individuals are defined as patients who continue to smoke at the time of hospitalization, excluding those who have previously smoked but have successfully quit), alcohol use status (non-alcohol use or alcohol use: Individuals who use alcohol are defined as patients who continue to consume alcohol at the time of hospitalization, with a weekly alcohol intake exceeding 140 grams of pure alcohol. Individuals who do not use alcohol are defined as patients who have never consumed alcohol or those who have consumed alcohol in the past but have abstained for more than six months), hemoglobin ( $> 115$  or  $\leq 115$  g/L), neutrophils ( $\leq 6.30$  or  $> 6.30 \times 10^9$ /L), and albumin ( $\geq 35$  or  $< 35$  g/L). All indicators that were significant in the univariable analyses were included in the multivariable analysis. All statistical tests were two-sided. P-value  $< 0.05$  was considered statistically significant.

## Results

### Characteristics of the Patients

This study identified 880 potentially eligible patients, but 540 were excluded, leaving 340 patients with pulmonary TB: 61 patients (17.9%) had concurrent T2DM (T2DM group), and 279 patients (82.1%) did not have T2DM (control group) (Figure 1). Compared with the non-T2DM group, the patients in the T2DM group were older (median, 54.00 vs 46.00 years,  $P=0.011$ ) and showed higher frequencies of males (85.2% vs 59.5%,  $P<0.001$ ), hypertension (34.4% vs 10.8%,  $P<0.001$ ), pulmonary fungal infection (4.9% vs 0.4%,  $P=0.019$ ), smoking (34.4% vs 16.1%,  $P<0.001$ ), alcohol use (27.9% vs 14.0%,  $P=0.001$ ), and high neutrophils (neutrophils  $> 6.30 \times 10^9$ /L, 29.5% vs 9.3%,  $P<0.001$ ). Demographic data and other baseline characteristics of the patients are shown in Table 1.

**Figure 1** Patient flowchart.

Abbreviations: TB, tuberculosis; T2DM, type 2 diabetes mellitus.

## Tuberculosis Treatment Regimens

In the T2DM group, 45 patients (73.8%) received the HRZE regimen, nine (14.8%) received the HRft ELfx regimen, and four (6.6%) received the rifampicin (R), pyrazinamide (Z), ethambutol (E), and levofloxacin (Lfx)/moxifloxacin (Mfx) [RZELfx (Mfx)] regimen. In the control group, 222 patients (79.6%) received the HRZE regimen, 27 (9.7%) received the HRft ELfx regimen, and 18 (6.5%) received the RZELfx (Mfx) regimen (Table 2). There were no significant differences in TB treatment regimens between the T2DM group and the control group.

**Table 1** Characteristics of the Patients

Indicators	T2DM (n=61)	Control (n=279)	P
Age, median (Q1, Q3)	54.00 (48.00, 61.00)	46.00 (39.00, 61.00)	0.011
Age, years, n (%)			0.706
<65	49 (80.3)	218 (78.1)	
≥65	12 (19.7)	61 (21.9)	
Sex, n (%)			<0.001
Male	52 (85.2)	166 (59.5)	
Female	9 (14.8)	113 (40.5)	
BMI (kg/m <sup>2</sup> ), n (%)			0.360
<18.5	7 (11.5)	45 (16.1)	
≥18.5	54 (88.5)	234 (83.9)	
Hypertension, n (%)	21 (34.4)	30 (10.8)	<0.001
Chronic pulmonary diseases, n (%)	5 (8.2)	11 (3.9)	0.178*
Pulmonary bacterial infection, n (%)	38 (62.3)	175 (62.7)	0.950
Cardiac insufficiency, n (%)	2 (3.3)	4 (1.4)	0.294*
Hepatitis, n (%)	0	11 (3.9)	0.225*
Neoplasm, n (%)	2 (3.3)	8 (2.9)	0.696*
Pulmonary fungal infection, n (%)	3 (4.9)	1 (0.4)	0.019*
Autoimmune diseases, n (%)	0	2 (0.7)	>0.999*
Prior TB treatment, n (%)			0.606
No	55 (90.2)	245 (87.8)	
Yes	6 (9.8)	34 (12.2)	
Smoking status, n (%)			<0.001
Non-smoking	20 (32.8)	164 (58.8)	
Smoking	21 (34.4)	45 (16.1)	
Unknown	20 (32.8)	70 (25.1)	

(Continued)

**Table 1** (Continued).

Indicators	T2DM (n=61)	Control (n=279)	P
Alcohol use status, n (%)			0.001
Non-alcohol use	25 (41.0)	184 (65.9)	
Alcohol use	17 (27.9)	39 (14.0)	
Unknown	19 (31.1)	56 (20.1)	
Laboratory test results, n (%)			
Hemoglobin (g/L)			0.843
≤115	9 (14.8)	44 (15.8)	
>115	52 (85.2)	235 (84.2)	
Neutrophils (10 <sup>9</sup> /L)			<0.001
≤6.30	43 (70.5)	253 (90.7)	
>6.30	18 (29.5)	26 (9.3)	
Albumin (g/L)			0.363
<35	14 (23.0)	50 (17.9)	
≥35	47 (77.0)	229 (82.1)	

**Notes:** \*Fisher's exact test. Other categorical variables were analyzed using the chi-square test.

**Abbreviations:** T2DM, type 2 diabetes mellitus; Q, quartile; BMI, body mass index; TB, tuberculosis.

**Table 2** Tuberculosis Treatment Regimens

Treatment Regimens, n (%)	T2DM (n = 61)	Control (n = 279)
HRZE	45 (73.8)	222 (79.6)
HRft ELfx	9 (14.8)	27 (9.7)
RZELfx (Mfx)	4 (6.6)	18 (6.5)
HEZLfx (Mfx)	2 (3.3)	2 (0.7)
HRZLfx (Mfx)	0	2 (0.7)
Other treatments	1 (1.6)	4 (1.4)

**Note:** Fisher's exact test for trend: P=0.405.

**Abbreviations:** T2DM, type 2 diabetes mellitus; H, isoniazid; R, rifampicin; Z, pyrazinamide; E, ethambutol; Rft, rifapentine; Lfx, levofloxacin; Mfx, moxifloxacin.

## Time to Negative Sputum Conversion

The median time to negative sputum conversion for all patients was 53.00 days (CI: 50.80–55.20). According to the Kaplan–Meier curves, before 60 days, patients with T2DM, patients with age <65 years, female patients, patients with high albumin ( $\geq 35$  g/L) and patients with low neutrophils ( $\leq 6.30 \times 10^9$ /L) were more likely to get negative sputum conversion than patients without T2DM, patients with age  $\geq 65$  years, male patients, patients with low albumin (<35 g/L) and patients with high neutrophils ( $> 6.30 \times 10^9$ /L), respectively (Figure 2).

## Rates of Negative Sputum Conversion at 2 months After Anti-Tuberculosis Treatment

The rates of negative sputum conversion at 2 months were 85.2% vs 92.8% in the T2DM and control groups (P=0.055), 94.0% vs 82.2% for patients aged <65 and  $\geq 65$  years (P=0.001), 88.5% vs 96.7% for male and female patient (P=0.010), 92.3% vs 85.0% for patients without any prior TB treatment and patients having TB treatment before (P=0.131), 84.4% vs 93.1% for patients with albumin <35 and  $\geq 35$  g/L (P=0.024), 88.5% vs 92.0% for patients with BMI <18.5 and  $\geq 18.5$  kg/m<sup>2</sup> (P=0.418) and 93.6% vs 77.3% for patients with neutrophils  $\leq 6.30 \times 10^9$ /L and  $> 6.30 \times 10^9$ /L (P=0.001) (Figure 3).

## Multivariable Analysis

The multivariable Cox regression analysis showed that male sex (adjusted HR=0.759, 95% CI: 0.585–0.984, P=0.037) and T2DM (adjusted HR=0.721, 95% CI: 0.528–0.986, P=0.040) independently increased the risk of the time to negative sputum *M. tuberculosis* conversion, which could prolong the time to negative conversion (Table 3).

## Discussion

This retrospective study explored the influence of T2DM on the clinical outcomes of pulmonary TB and the factors that may affect outcomes. Furthermore, the treatment regimens of active pulmonary TB patients with or without T2DM were described. The results suggest that patients with pulmonary TB and T2DM had a longer time to negative sputum *M. tuberculosis* culture conversion than those without T2DM. Male sex was also independently associated with a longer time to negative sputum *M. tuberculosis* culture conversion. These findings highlight the importance of strengthening monitoring and individualized treatment strategies in treating TB and adjusting the treatment regimens to improve clinical outcomes.

Previous studies showed that T2DM is associated with a poor prognosis of TB. Indeed, Wang et al<sup>21</sup> showed that T2DM was associated with a poor TB prognosis and that the association of T2DM remained significant even after adjusting for age and sex. A longitudinal study showed that T2DM was an important predictor of death in patients with TB; the effect did not appear to be related to increased TB severity but to an impaired response to treatment.<sup>14</sup> A systematic review of 33 early studies showed that T2DM increased the risk of relapse and death in patients with TB.<sup>17</sup> A

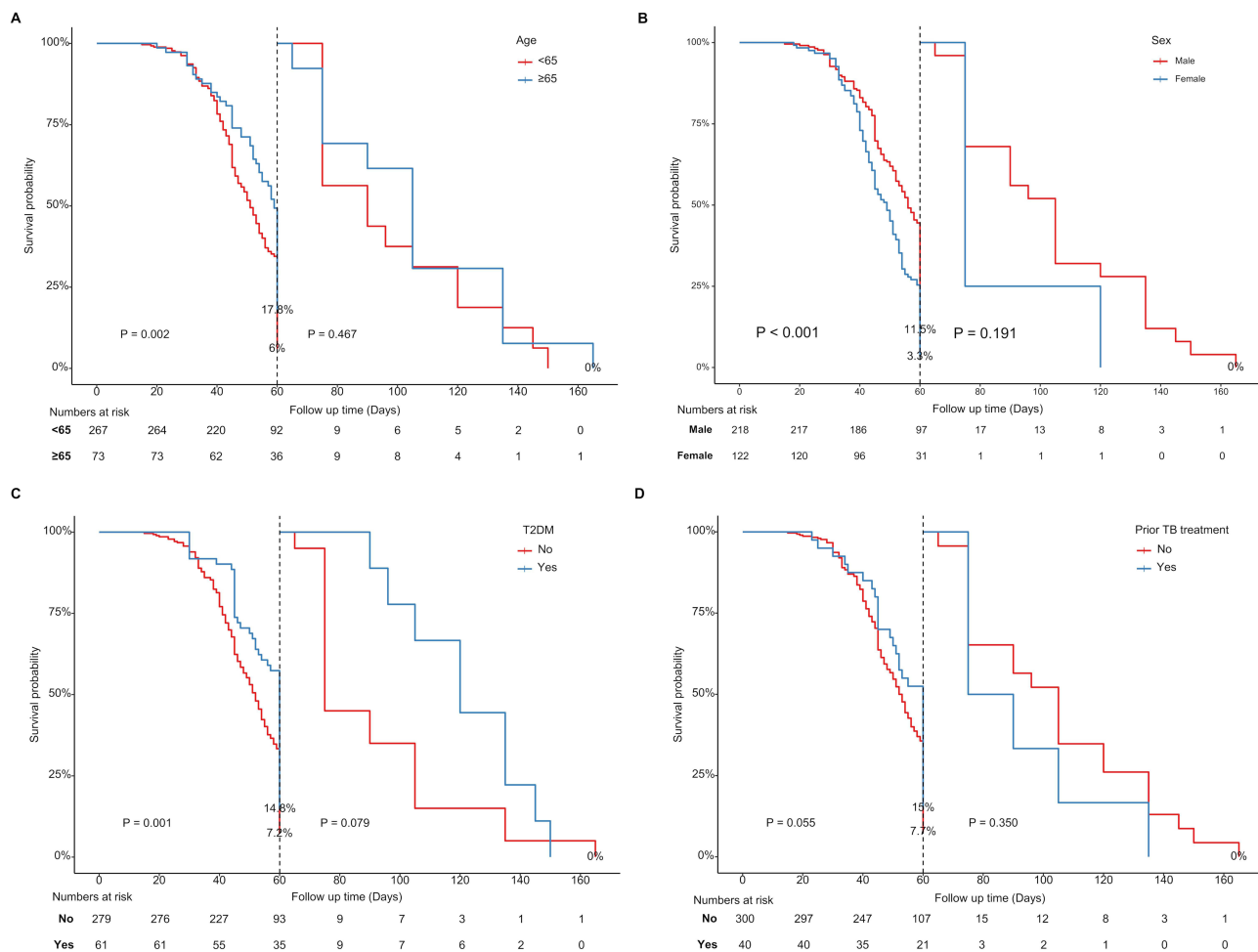
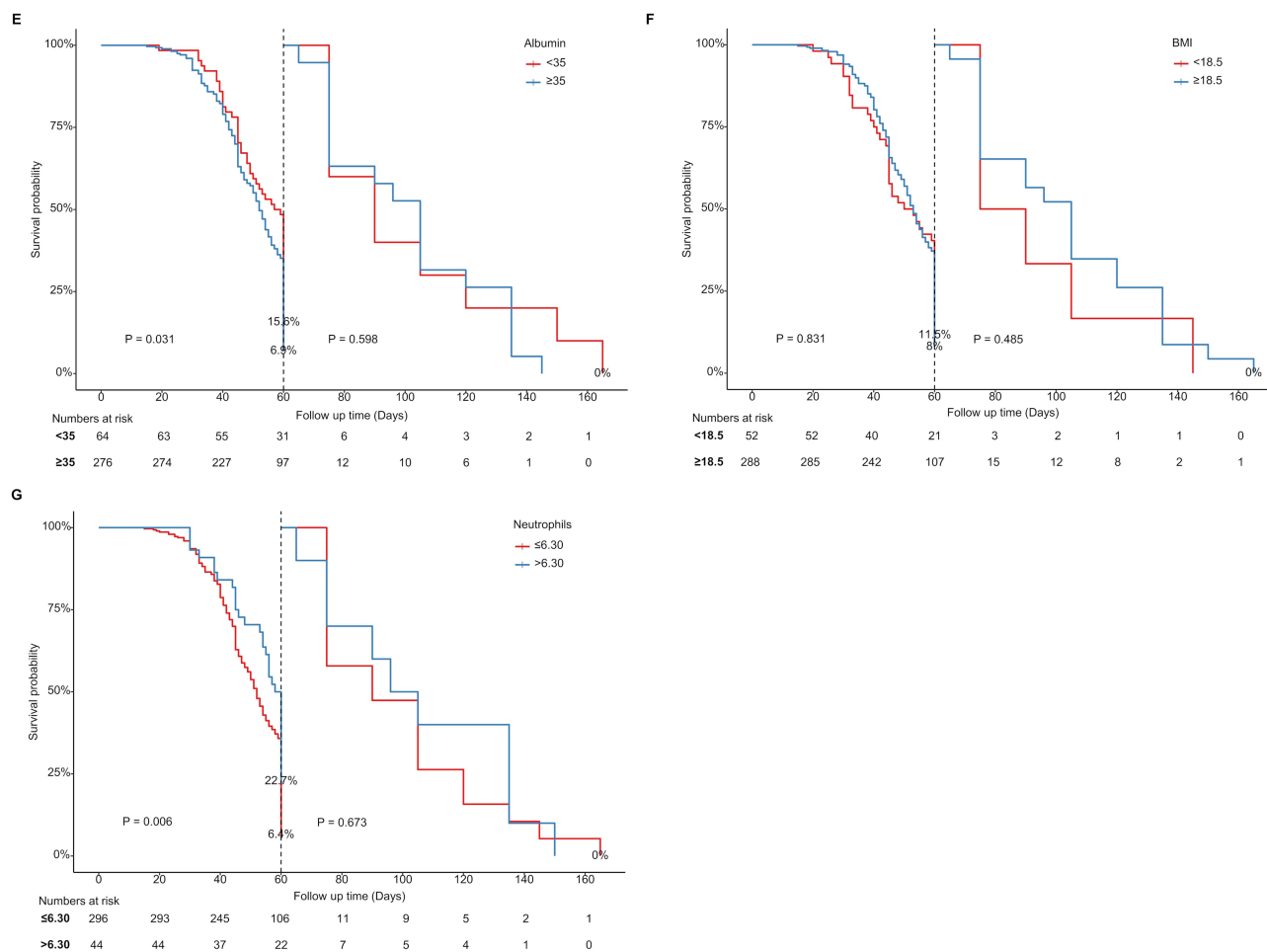


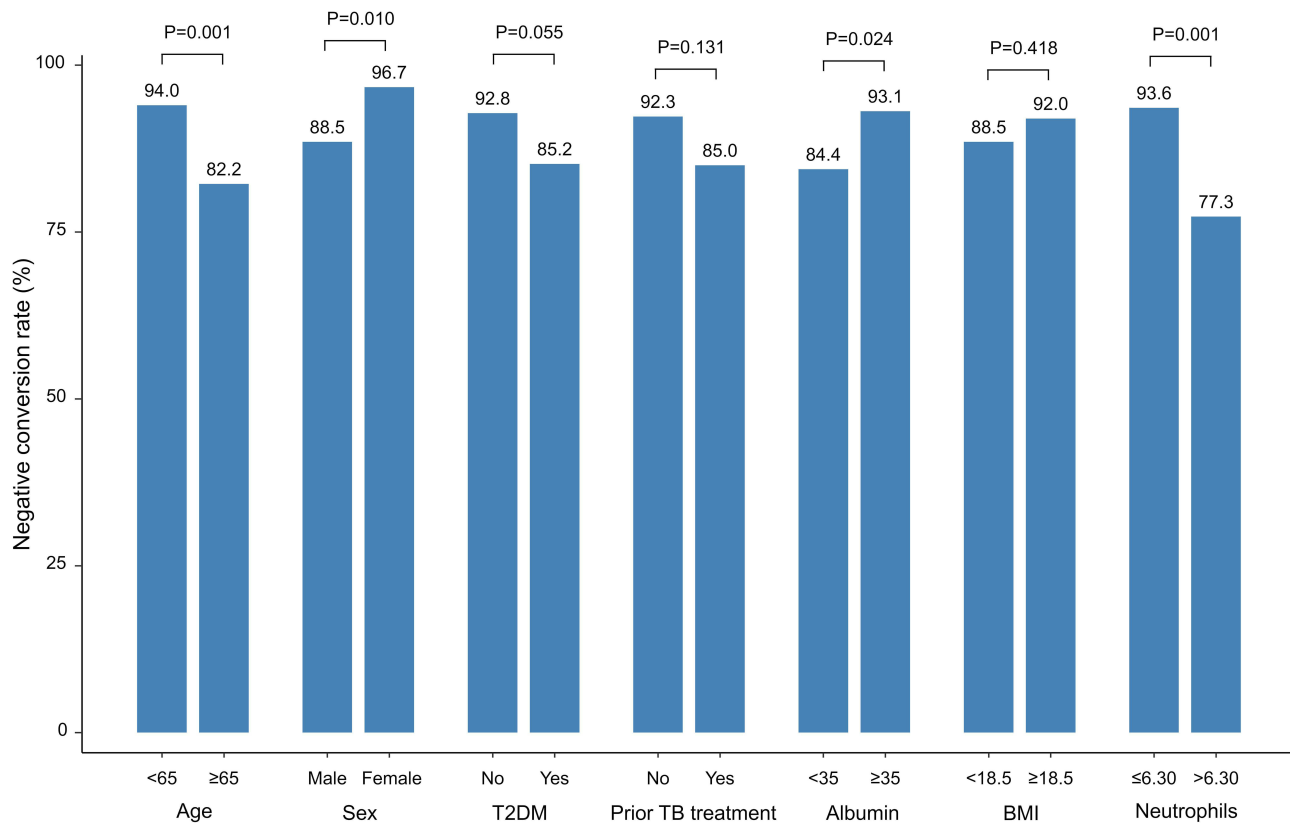
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**Figure 2** Kaplan–Meier curves for the rate of negative sputum conversion after anti tuberculosis treatment in different subgroups. (A) Age; (B) Sex; (C) type 2 diabetes mellitus (T2DM); (D) Prior TB treatment; (E) Albumin; (F) Body mass index (BMI); (G) Neutrophils.

more recent meta-analysis of 65 studies from South Asia showed that patients with T2DM and TB were at higher risk of treatment failure and death than patients with TB alone.<sup>18</sup> The present study showed that patients with T2DM and TB had a longer time to negative sputum *M. tuberculosis* culture conversion than those with TB alone. T2DM and TB interact at multiple levels. Suboptimal glycemic control is associated with a higher risk of TB and poorer response to anti-TB treatments. In addition, TB also causes hyperglycemia, complicating glycemic control. The anti-TB drugs can also interact with the hypoglycemic drugs, potentially leading to both poor glycemic control and suboptimal *M. tuberculosis* killing.<sup>15</sup> On the other hand, T2DM does not appear to be associated with a higher *M. tuberculosis* resistance to treatments,<sup>26</sup> suggesting that the worse prognosis is not due to resistance to antibiotics.

The four-drug regimen HRZE is commonly used in anti-tuberculosis treatment. A previous randomized controlled trial showed that patients treated with HRC (isoniazid, rifampin, and ciprofloxacin) had a longer time to negative *M. tuberculosis* negative conversion and a higher proportion of TB recurrence than those treated with HRZE.<sup>27</sup> Moreover, due to the caution for patients with T2DM in the pyrazinamide (Z) monograph due to changes in pharmacokinetics,<sup>28</sup> the proportion of patients with diabetes mellitus using Z is low, and thus, the difference in treatment regimens between the two groups may be related to the poorer prognosis. However, no differences in treatment regimens were observed between the two groups in this study. Furthermore, many studies have shown that long-term T2DM can alter various clinical manifestations of pulmonary TB, such as increasing the range of pulmonary TB lesions and the occurrence of pulmonary cavities and increasing the risk of treatment failure, death, recurrence, and drug resistance, affecting prognosis.<sup>17,18</sup>



**Figure 3** Subgroup analysis of the rate of negative sputum conversion at 2 months after anti-tuberculosis treatment.

In the present study, male sex was also independently associated with a prolonged time to negative conversion. A retrospective study, combined with a meta-analysis, showed that males with TB had higher 9-month mortality rates and lower 2-month negative culture rates than females after adjustment for confounding factors.<sup>29</sup> This association can be due

**Table 3** Univariable and Multivariable Analyses of the Time to Sputum Conversion in Patients with Pulmonary Tuberculosis

Variables	Univariable		Multivariable	
	HR (95% CI)	P	HR (95% CI)	P
Age, years				
<65	1		1	
≥65	0.702 (0.539–0.913)	0.008	0.769 (0.580–1.021)	0.070
Sex				
Female	1		1	
Male	0.654 (0.521–0.819)	<0.001	0.759 (0.585–0.984)	0.037
BMI, kg/m <sup>2</sup>				
≥18.5	1			
<18.5	1.001 (0.745–1.345)	0.995		
T2DM	0.649 (0.489–0.860)	0.003	0.721 (0.528–0.986)	0.040
Hypertension	0.664 (0.490–0.900)	0.008	0.805 (0.576–1.125)	0.203
Pulmonary bacterial infection	0.878 (0.702–1.098)	0.254		
Pulmonary fungal infection	0.463 (0.170–1.266)	0.134	0.662 (0.232–1.883)	0.439

(Continued)

**Table 3** (Continued).

Variables	Univariable		Multivariable	
	HR (95% CI)	P	HR (95% CI)	P
Prior TB treatment				
No	1			
Yes	0.804 (0.578–1.119)	0.196		
Smoking status				
Non-smoking	1		1	
Smoking	0.793 (0.596–1.056)	0.113	0.995 (0.662–1.495)	0.980
Unknown	0.775 (0.600–1.000)	0.050	0.755 (0.498–1.144)	0.185
Alcohol use status				
Non-alcohol use	1		1	
Alcohol use	0.782 (0.581–1.053)	0.105	0.999 (0.671–1.488)	0.995
Unknown	0.951 (0.729–1.241)	0.712	1.340 (0.883–2.033)	0.169
Laboratory test results				
Hemoglobin (g/L)				
>115	1			
≤115	1.131 (0.843–1.518)	0.411		
Neutrophils ( $\times 10^9/L$ )				
≤6.30	1		1	
>6.30	0.687 (0.498–0.948)	0.022	0.840 (0.598–1.180)	0.314
Albumin (g/L)				
≥35	1			
<35	0.769 (0.583–1.014)	0.062		

**Abbreviations:** HR, hazard ratio; CI, confidence interval; BMI, body mass index; T2DM, type 2 diabetes mellitus; TB, tuberculosis.

to various factors, including higher frequencies of T2DM, smoking, and alcohol use than females<sup>30</sup> but also higher sputum *M. tuberculosis* load and more severe lung lesions.<sup>31,32</sup>

Furthermore, the Kaplan-Meier curves for the rate of negative sputum conversion after 2 months of anti-TB treatment in different subgroups of this study suggested that, before 60 days, albumin <35 g/L was associated with a reduced rate of negative sputum conversion, but albumin was not identified as being associated in the univariable Cox analysis, possibly because of the differences between the two statistical methods. Nevertheless, malnutrition is known to be associated with worse TB outcomes because of secondary immune dysfunction.<sup>33,34</sup>

This study has limitations. Firstly, it was a retrospective study, limiting the level of evidence that can be derived. The data were limited to those available in the patient charts. In addition, no data pertaining to T2DM, including glycemic control or medication, were collected. Therefore, it is difficult to analyze the influence of glycemic control status on the clinical outcomes of patients with T2DM. Even though longitudinal data were collected, the lack of long-term follow-up data made it impossible to assess the long-term outcomes, such as the maintenance of therapeutic effects and TB recurrence. Secondly, it was a single-center study with a small sample size. The results may be subject to a selection bias, affecting the accuracy of the conclusions. Therefore, future studies with larger sample sizes and multiple centers are warranted. The duration and severity of pulmonary TB and T2DM and the diversity of comorbidities may affect the treatment response, but the available data did not allow the analysis of these factors in detail.

## Conclusion

This study suggests that patients with pulmonary TB and T2DM had a longer time to negative sputum *M. tuberculosis* conversion, and male sex was also associated with the prolonged time. Thus, enhanced monitoring and personalized treatment may be needed for pulmonary TB patients with comorbid T2DM and male TB patients in order to improve clinical outcomes for these patients.

## Data Sharing Statement

The authors confirm that the data supporting the findings of this study are available within the article.

## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis, and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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## Disclosure

The authors declare no conflicts of interest.

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