

# Prevalence and Risk Factors of Diabetes in Patients with Active Pulmonary Tuberculosis: A Cross-Sectional Study in Two Financially Affluent China Cities

Jing Li<sup>1,\*</sup>, Yanhong Zhao<sup>2,\*</sup>, Youli Jiang<sup>3</sup>, Ying Zhang<sup>4</sup>, Peize Zhang<sup>1</sup>, Lingjun Shen<sup>2</sup>, Zijiao Chen<sup>1</sup>

<sup>1</sup>Department of Pulmonary Medicine and Tuberculosis, the Third People's Hospital of Shenzhen, Shenzhen, Guangdong, People's Republic of China; <sup>2</sup>Department of Tuberculosis, the Third People's Hospital of Kunming, Kunming, Yunnan, People's Republic of China; <sup>3</sup>Department of Neurology, People's Hospital of Longhua, Shenzhen, 518109, People's Republic of China; <sup>4</sup>Department of Endocrinology, the Third People's Hospital of Shenzhen, Shenzhen, Guangdong, People's Republic of China

\*These authors contributed equally to this work

Correspondence: Zijiao Chen; Lingjun Shen, Email 785863383@qq.com; m18608770202@163.com

**Background:** Tuberculosis (TB) and diabetes mellitus (DM) present a dual burden to public health. The screening of DM in TB patients may aid in the early detection and management of diabetes, ultimately improving treatment outcomes for those with the comorbidity of TB-DM. We aim to examine the prevalence and identify risk factors of diabetes in individuals with active pulmonary tuberculosis (PTB) in financially affluent China cities.

**Methods:** A cross-sectional survey was conducted in adult patients with highly suspected TB in two cities of China, spanning from May 9, 2023, to June 30, 2023. We compare the clinical characteristics, nutrition status, fasting blood glucose (FBG) level, living style, and knowledge of TB and DM at admission between patients with and without DM. Univariate and multivariate logistic regression analyses were employed to identify risk factors associated with TB-DM comorbidities.

**Results:** Of the 322 patients diagnosed with pulmonary tuberculosis (PTB), 54 individuals (16.8%) had comorbid diabetes mellitus (DM). This included 43 males (13.4%) and 11 females (3.4%). The average age was  $55.44 \pm 12.36$  in DM patients and  $46.09 \pm 16.87$  in non-DM patients. A multivariate logistic regression analysis revealed that male (adjusted odds ratio [aOR]=3.29, 95% confidence interval [CI]: 1.05–10.30), age older than 47 years (aOR = 1.04, 95% CI: 1.01–1.07), having a family history of diabetes (aOR = 5.09, 95% CI: 1.28–20.32), and an elevated random blood glucose level (aOR = 1.6, 95% CI: 1.38–1.86) were risk factors for DM in patients with PTB. Furthermore, it was found that diabetes awareness (aOR = 0.07, 95% CI: 0.03–0.21) and zero, light to moderate alcohol consumption were associated with a lower risk of diabetes.

**Conclusion:** Diabetes is prevalent in patients with active PTB. Screening and raising awareness of DM are recommended, particularly in men after middle age with a family history of diabetes and elevated random blood glucose. Early diagnosis of diabetes and effective diabetes prevention may reduce the dual burden of TB-DM comorbidity.

**Keywords:** tuberculosis, diabetes, risk factors, diabetes awareness, waist-to-hip ratio, alcohol consumption

## Introduction

Tuberculosis (TB) and diabetes mellitus (DM) pose a dual burden to public health worldwide. There were an estimated 10.6 million people living with TB and 537 million adults (20–79 years) with DM in 2021.<sup>1,2</sup> The World Health Organization (WHO) advocates for collaborative efforts towards TB and DM as crucial components of the End TB strategy.<sup>3</sup> China is a country suffering from rapidly emerging type 2 diabetes. It is estimated that approximately one in every eleven adults is currently suffering from diabetes mellitus.<sup>4</sup> Additionally, China is also one of the high TB burden countries. A systematic review reported a near 15% prevalence of DM in TB patients, and a significantly higher

prevalence of comorbidity of DM and pulmonary TB in countries with a high TB burden.<sup>5,6</sup> As a major risk factor of TB, DM affects TB at multiple levels in disease control and treatment efficacy. Many studies demonstrated the unfavorable outcomes of TB in patients with diabetes.<sup>7,8</sup> Screening DM in TB patients may aid in early detection and management of diabetes, preventing delayed diagnosis and diabetes-related complications and improve TB treatment outcomes accordingly.<sup>9</sup>

Our study aims to understand the prevalence of diabetes in patients with active pulmonary tuberculosis (PTB), as well as to identify risk factors of diabetes in PTB patients in financially affluent Chinese cities. We expect the findings of this study to benefit the design of diabetes screening programs for the early detection and management of diabetes in patients with PTB in cities.

## Methods

### Study Design and Sample Size Estimation

Shenzhen is a special administrative region and enjoys a prime geographic location with high GDP in the past 20 years. It is a big city with estimated 13 million residents in 2022.<sup>10</sup> Kunming is the capital of the Yunnan province with fast financial development. Estimated residents was 4.7 million in 2022.<sup>11</sup> These two cities are characterized by a relatively financial affluence. All patients who are doubted with TB are sent to the designated hospital for further confirmation and care. We conducted a cross-sectional facility-based study targeting adult in-patients suspected of having tuberculosis (TB) at the Third People's Hospital of Kunming and the Third People's Hospital of Shenzhen, both of them are designated hospital for TB.

The prevalence of diabetes among tuberculosis patients is estimated to be 12%. Assuming we want to estimate the true prevalence of diabetes with a 95% confidence level and a 5% margin of error, we use the following formula to calculate the sample size:

$$n = \frac{Z^2 pq}{d^2}$$

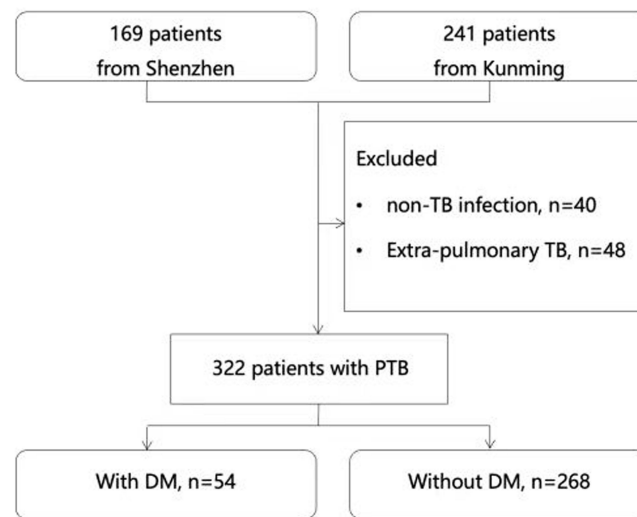
where  $n$  is the sample size,  $Z$  is the quantile of the standard normal distribution corresponding to the confidence level,  $p$  is the expected prevalence,  $q$  is  $1 - p$ , and  $d$  is the allowable margin of error. Substituting the known parameters into the formula, we can get the result below:

$$n = \frac{1.96^2 \times 0.12 \times 0.88}{0.05^2} = 163.9$$

That is to say, we need to survey at least 164 tuberculosis patients to estimate the true prevalence of diabetes with a 95% confidence level and a 5% margin of error. As about 20% of patients came to the designated TB hospital finally ruled out TB, the sample size will be up to 196 cases patients.

### Participants and Screening of DM

The study was conducted from May 1, 2023, to June 30, 2023. We thus included a total of 410 hospitalized patients (169 from Shenzhen, 241 from Kunming respectively). All participants were screened for DM. For every patient, fingerstick blood was attained for random blood glucose test at the day of admission. Fasting blood glucose (FBG) level and Hb1Ac were tested the next day morning after admission. A confirmed diagnosis of diabetes was defined as Hb1Ac level  $>6.5\%$  for both preexisting and newly diagnosed cases.<sup>12</sup> When unequivocal hyperglycemia or borderline elevated Hb1Ac was observed, another blood sample obtained at 2 hours after meal was collected for glycemic monitoring for confirmed diagnosis. To identify the potential factors influencing TB-DM, all participants underwent a nutrition evaluation and diabetes mellitus (DM) screening. The participants were asked to complete a questionnaire on their lifestyle and knowledge of TB and DM at admission. Both non-TB and extrapulmonary TB cases were excluded from the study. Ultimately, a total of 322 patients with active pulmonary TB were included in the analysis. Among them, 54 (16.8%) patients were confirmed to have comorbid PTB-DM, while 268 (83.2%) patients had PTB alone. (Figure 1).



**Figure 1** Flowchart of the study.

## Key Definitions

Our study collected information on various demographic characteristics, including sex, age, education level, marital status, lifestyle, social insurance coverage, etc. Additionally, we gathered information on medical history, family history of diabetes, diabetes screening tests, and nutrition status. Alcohol consumption was categorized based on the WHO's definition, with a standard drink being defined as 10 grams alcohol in China.<sup>13</sup> Individuals consuming less than a standard drink in the past month were classified as non-alcohol users, 1–3 drinks as mild-alcohol users, 4–6 drinks as moderate-alcohol users, and >6 drinks in a month as heavy-alcohol users. According to the guideline for nutrition screening launched in 2023,<sup>14</sup> the nutritional impairment status of an individual is defined as follows: 1) Absent: BMI greater than 18.5, no significant change in body weight in the past three months, no significant change in food intake in the past week. 2) Mild: Body weight loss greater than 5% in the past three months, food intake reduced by 25%–50% in the past week. 3) Moderate: Body weight loss greater than 5% in the past two months, food intake reduced by 51%–75% in the past week. 4) Severe: Body weight loss greater than 5% in the past month and greater than 15% in the past three months, BMI less than 18.5 with poor general clinical condition, food intake reduced by 76%–100% in the past week. Following WHO's recommendations, Waist-to-Hip Ratio (WHR)  $\geq 0.85$  for females and  $\geq 0.90$  for males were used to define abdominal obesity.<sup>15</sup> In addition, our questionnaire covered questions on individuals' disease awareness.

## Statistical Analysis

We conducted an extensive statistical analysis in SPSS version 25 to explore diabetes risk factors among tuberculosis patients while assessing their nutritional status. Beginning with a detailed descriptive analysis of patient characteristics and clinical data, we reported numerical variables as means with standard deviations (SDs) and medians with interquartile ranges (IQRs). Categorical variables were expressed in frequencies and percentages. We employed the chi-square ( $\chi^2$ ) test to uncover distinctions in categorical variables. To investigate potential diabetes risk factors, we performed meticulous univariate logistic regression analyses, retaining variables with  $\chi^2$ -test outcomes of  $P < 0.05$  for further scrutiny. Building on these findings, we subjected significant results from the univariate analysis to a binary stepwise logistic regression, systematically assessing variable roles within the risk factors. All presented outcomes were derived from two-tailed tests, adhering to established scientific research standards. Significance levels were conservatively set at  $p < 0.05$ , aligning seamlessly with accepted norms of scientific discourse.

## Results

### Basic Characteristics Between the Two Groups

Baseline demographic and clinical characteristics of the 322 patients included in the study were presented in Table 1. The DM group had a median age of  $55.44 \pm 12.36$  years and was consisted of 43 (79.6%) males. In the non-DM group, the

**Table I** Sociodemographic Characteristics of PTB Patients with and without Diabetes

	<b>Total</b>	<b>With-DM</b>	<b>Without-DM</b>	<b>P-value</b>
	<b>N=322</b>	<b>n (%)</b>	<b>n (%)</b>	
<b>Gender</b>				0.006
Male	203	43(21.1%)	160(78.8%)	
Female	119	11(9.2%)	108(90.6%)	
<b>Age (year, mean±SD)</b>	47.39±16.64	55.44±12.36	46.09±16.87	0.000
<b>Occupation</b>				0.462
Full-time	88	11(12.5%)	77(87.5%)	
Part-time	46	7(15.2%)	39(84.8%)	
Retired	30	10(29.4%)	22(73.3%)	
Farmer	90	17(16.0%)	75(83.3%)	
Unemployed	68	13(16.3%)	55(80.9%)	
<b>Living alone</b>				0.034
Yes	48	3(6.3%)	45(93.8%)	
No	274	51(18.6%)	223(81.4%)	
<b>Marital status</b>				0.031
Single	50	2(4.0%)	48(96.0%)	
Married	258	49(19.0%)	209(81.0%)	
Not available	14	3(21.4%)	11(78.6%)	
<b>Education</b>				0.033
Primary school	111	24(21.6%)	87(78.4%)	
Junior Middle school	105	18(17.1%)	87(82.9%)	
Senior Middle school	52	10(19.2%)	42(80.8%)	
College	54	2(3.7%)	52(96.3%)	
<b>Social Insurance Coverage</b>				0.534
Yes	309	51(16.5%)	258(83.5%)	
No	13	3(23.1%)	10(76.9%)	
<b>Smoking</b>				0.164
Non-smoker	177	27(15.3%)	150(84.7%)	
Current smoker	145	27(18.6%)	70(81.4%)	
<b>Alcohol consumption*</b>				0.002
Non	209	34(16.3%)	175(83.7%)	
Light	79	13(16.5%)	66(83.5%)	
Moderate	29	3(10.3%)	26(89.7%)	
Heavy	5	4(80.0%)	1(10.0%)	

(Continued)

**Table 1** (Continued).

	<b>Total</b>	<b>With-DM</b>	<b>Without-DM</b>	<b>P-value</b>
	<b>N=322</b>	<b>n (%)</b>	<b>n (%)</b>	
<b>Cough</b>				0.335
Yes	259	46(17.8%)	213(82.2%)	
No	63	8(12.7%)	55(87.3%)	
<b>Fever</b>				0.527
Yes	56	11(19.6%)	45(80.4%)	
No	266	43(16.2%)	223(83.8%)	
<b>BCG vaccinated</b>				0.372
Yes	100	14(14.0%)	86(86.0%)	
No	222	40(18.0%)	182(82.0%)	

**Notes:** \*Alcohol consumption: A standard drink is defined as 10 grams alcohol in China. Individuals having less than a standard drink in the past month was classified as non-alcohol user, 1~3 drinks as mild-alcohol user, 4~6 drinks as moderate-alcohol user, and more than 6 drinks in a month as heavy-alcohol user.

median age was  $46.09 \pm 16.87$  years and 160 (59.7%) of them were male. A significant gender and age difference between the two groups was observed ( $P < 0.001$ ). It was also noted that patients in the DM group had a higher alcohol consumption and lower education level ( $P < 0.05$ ). No significant differences were observed between the two groups in marital status, cough, fever, and BCG vaccination coverage ( $P > 0.05$ ).

## Nutrition Status and Disease Awareness Between the Two Groups

In the DM group, the mean body weight was  $58.32 \pm 10.27$  kg. The mean waist circumference was  $80.26 \pm 13.69$  cm, with 50% (27/54) participants attaining a normal WHR. In the non-DM group, the mean body weight was  $54.55 \pm 10.63$  kg. The mean waist circumference was  $76.66 \pm 9.91$  cm and the proportion of normal WHR was 69.4% (186/268). In comparison, body weight, waist circumference, and waist-hip ratio ( $P < 0.05$ ) showed a statistically significant difference between the two groups. The mean random blood glucose (RBG) was 12.28 mmol/L in DM group and was 6.53 in non-DM group. The fasting blood glucose (FBG) was 8.12 mmol/L in DM group and was 5.10 in non-DM group. In addition to the RBG and FBG, family history of diabetes and DM awareness were different between the two groups ( $P < 0.05$ ). Of note, the nutritional impairment score and BMI on admission showed no difference between the two groups ( $P = 0.184$ ). (Table 2)

## Risk Factors of Diabetes in Patients with Active PTB

Multivariable logistic regression analysis results are shown in Table 3. The OR value shows that male has a 3.29 times higher risk of developing DM than female. Patients with a family history of diabetes also have a higher risk than those without (aOR = 5.09, 95% CI: 1.28–20.32). And for every year of age increase, the risk of diabetes increases by 1.04 times. For every unit increase in random blood glucose, the risk of diabetes increases by 1.6 times. Diabetes awareness is a protective factor for lowering the occurrence of diabetes (aOR = 0.07, 95%:0.03–0.21). Compared to patients with heavy alcohol consumption, zero and light to moderate alcohol consumption are protective factors for DM (Figure 2).

## Discussion

Our study found that about 15% of PTB patients also had DM, with a majority being middle-aged males. Excessive alcohol use, a family history of diabetes, elevated random blood glucose, and lack of awareness of diabetes were the risk factors for these co-morbid patients.

**Table 2** Nutrition Status and Disease Awareness of PTB Patients with Diabetes and Without Diabetes

	Total	With-DM	Without-DM	P-value
	N(%) / Mean $\pm$ SD	N(%) / Mean $\pm$ SD	N(%) / Mean $\pm$ SD	
<b>Vegetarian</b>				0.437
Yes	12	3(25.0%)	9(75.0%)	
No	310	51(16.5%)	259(83.5%)	
<b>BMI</b>				0.437
<18.5	91	12(13.2%)	79(86.8%)	
18.5–23.9	185	31(16.8%)	154(83.2%)	
$\geq 24$	19	5(26.3%)	14(73.7%)	
24–26.9	21	4(19.0%)	17(81.0%)	
27–29.9	6	2(33.3%)	4(66.7%)	
<b>Nutritional impairment score<sup>#</sup></b>				0.184
Normal	222	41(18.5%)	181(81.5%)	
Mild	39	2(5.1%)	37(94.9%)	
Moderate	3	1(33.3%)	2(66.7%)	
Severe	58	10(17.2%)	48(82.8%)	
<b>History of diabetes</b>				0.000
Newly diagnosed	15	15(27.8%)	/	
Known diabetes	39	39(72.2%)		
<1 year	11	11(20.4%)	/	
1–3 years	7	7(13.0%)	/	
3–10 years	13	13(24.0%)	/	
>10 years	8	8(14.8%)	/	
<b>Family history of Diabetes</b>				0.000
Yes	26	13(50.0%)	13(50.0%)	
No	296	41(13.9%)	255(86.1%)	
<b>TB awareness</b>				0.684
Yes	219	38(17.4%)	181(82.6%)	
No	103	16(15.5%)	87(84.5%)	
<b>DM awareness</b>				0.000
Yes	243	21(8.6%)	222(91.4%)	
No	79	33(41.8%)	46(58.2%)	

(Continued)

Table 2 (Continued).

	Total	With-DM	Without-DM	P-value
	N(%) / Mean $\pm$ SD	N(%) / Mean $\pm$ SD	N(%) / Mean $\pm$ SD	
<b>Waist-to-Hip Ratio*</b>				0.001
Normal	213	27(12.7%)	186(87.3%)	
Abnormal	109	27(24.8%)	82(75.2%)	
<b>Weight(kg, mean<math>\pm</math>SD)</b>	55.19 $\pm$ 10.645	58.32 $\pm$ 10.27	54.55 $\pm$ 10.63	0.017
<b>Height(cm, mean<math>\pm</math>SD)</b>	163.60 $\pm$ 7.90	164.91 $\pm$ 8.48	163.34 $\pm$ 7.78	0.186
<b>Upper arm circumference(cm, mean<math>\pm</math>SD)</b>	24.80 $\pm$ 3.37	25.04 $\pm$ 3.00	24.75 $\pm$ 3.44	0.556
<b>Waist circumference(cm mean<math>\pm</math>SD)</b>	77.26 $\pm$ 10.69	80.26 $\pm$ 13.69	76.66 $\pm$ 9.91	0.024
<b>Hip circumference(cm mean<math>\pm</math>SD)</b>	89.85 $\pm$ 8.49	91.19 $\pm$ 6.94	89.58 $\pm$ 8.76	0.203
<b>Haemoglobin (g/L, mean<math>\pm</math>SD)</b>	126.54 $\pm$ 21.15	129.09 $\pm$ 20.45	126.03 $\pm$ 21.29	0.332
<b>Serum proteins (g/L, mean<math>\pm</math>SD)</b>	37.46 $\pm$ 5.88	35.79 $\pm$ 8.51	37.80 $\pm$ 5.15	0.023
<b>Random blood glucose(mmol/L, mean<math>\pm</math>SD)</b>	7.50 $\pm$ 3.83	12.28 $\pm$ 5.86	6.53 $\pm$ 2.28	0.000
<b>Fasting blood glucose(mmol/L, mean<math>\pm</math>SD)</b>	5.61 $\pm$ 3.45	8.12 $\pm$ 3.42	5.10 $\pm$ 3.23	0.000

**Notes:** #Nutritional impairment score: 1) Absent: -BMI greater than 18.5. -No significant change in body weight in the past 3 months. -No significant change in food intake in the past week. 2) Mild: -Body weight loss greater than 5% in the past 3 months. -Food intake reduced by 25%-50% in the past week. 3) Moderate: -Body weight loss greater than 5% in the past 2 months. -Food intake reduced by 51%-75% in the past week. 4) Severe: -Body weight loss greater than 5% in the past month. -Body weight loss greater than 15% in the past 3 months. -BMI less than 18.5 with poor general clinical condition. - Food intake reduced by 76%-100% in the past week. \*Waist-to-Hip Ratio: WHR  $\geq$  0.85 for females and  $\geq$ 0.90 for males were categorized as abnormal abdominal obesity.

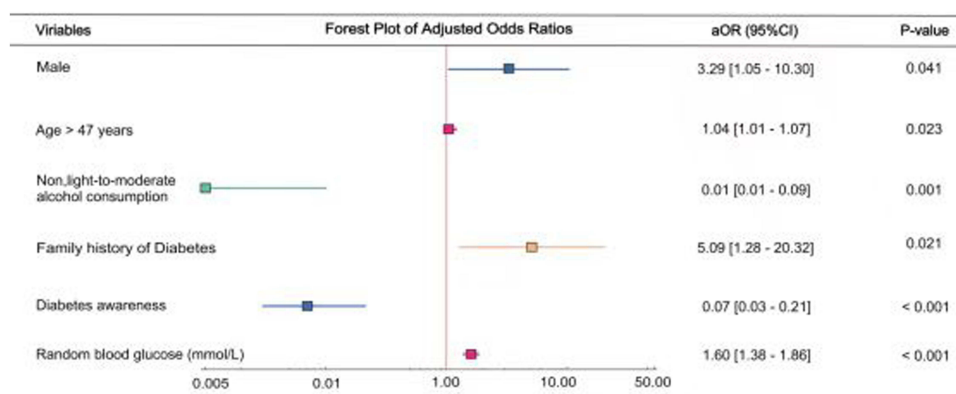
Table 3 Multivariable Analysis of the Predictors of DM

Characteristics	OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value
Male			3.29(1.05–10.30)	0.041
Age>47 years			1.04(1.01–1.07)	0.023
Weight	1.08(1.01–1.15)	0.018		
Non, Light-to-moderate alcohol consumption			0.01(0.01–0.10)	0.000
Family history of Diabetes	5.26(1.23–25.0)	0.000	5.09(1.28–20.32)	0.021
Diabetes awareness	0.08(0.03–0.23)	0.000	0.07(0.03–0.21)	0.000
Random blood glucose (mmol/L)	1.59(1.36–1.87)	0.000	1.60(1.38–1.86)	0.000

As a risk factor of TB, the prevalence of DM in TB patients has been widely researched. A systematic review from South Asia showed a 21% pooled prevalence of diabetes in TB patients.<sup>8</sup> A cross-sectional study from Yemen showed that DM was prevalent in 18% of the TB patients.<sup>16</sup> Other studies indicated that up to about one-third of TB patients in India and Brunei Darussalam also had diabetes.<sup>17,18</sup> The percentage differences among them might be due to the socio-economic characteristics of the studied population in each study. Notably, there has been a drastic rise in the prevalence of DM worldwide, particularly in South Asia, over the past three decades.<sup>19</sup> We believe that the increasing trend of TB-DM will persist until the risk factors of DM are addressed.

In our study, we found that most TB-DM patients were men aged 47 years old or older, consistent with the results from the studies in Brunei and Yemen, which also reported a higher prevalence of TB-DM in males than in females.<sup>16,17</sup>





**Figure 2** Adjusted odds ratios of risk factors of DM in patients with PTB.

Additionally, findings of numerous studies in Denmark, Pakistan, and India showed a higher prevalence of TB-DM among those aged  $\geq 45$  years old.<sup>20–22</sup> We attributed the higher prevalence of DM in older people to a decreased immunity and age-related frailty, making this population more vulnerable to developing TB.

Of note, we found that about one-third of TB-DM patients were newly diagnosed with DM. They had no history of diabetes and lacked awareness of the disease. It is reported that about 8.1% people in China has undiagnosed diabetes.<sup>23</sup> Most of these patients are unaware of DM. As the family history of diabetes is a risk factor for TB-DM patients,<sup>16</sup> education on tuberculosis and diabetes is pivotal in raising awareness in the public, particularly those with a family history of the diseases, in prevention, early diagnosis, and treatment. Enhancing the awareness of DM and living a healthy lifestyle help people from suffering of type 2 DM, so as to reduce the complications of diabetes and the incidence of tuberculosis.

As consumptive disease, TB often leads to malnutrition which in turn aggravates TB itself. Diabetes is a metabolic disease often leads to unbalanced nutrition. In our study, we found that the nutritional impairment score, BMI and Upper arm circumference were similar in patients with and without DM on admission. All these commonly used indicators for reflecting nutritional status were no difference. But we noticed that elevated WHR is more commonly seen in patients with DM-TB, though the correlation between WHR and DM was weak and there was no independent correlation in multiple linear regression analysis. Waist-to-hip ratio (WHR) adjusted for body mass index (BMI) had been used as an index of abdominal obesity and been demonstrated to be associated with the development of DM and coronary heart diseases.<sup>24</sup> Abdominal adiposity was more commonly seen in patients with diabetes in our study. Further assessment of the mechanism between abdominal adiposity and the onset of DM is needed. Additionally, we found that no or light-to-moderate alcohol consumption decreased the risk of DM, while alcohol abuses increased it. This finding is similar to the Meta-analysis which reported a threshold in women and non-Asian populations, alcohol intake of  $< 63$  g/day, below which are associated with reductions in the risk of type 2 diabetes, but risks increasing above this threshold.<sup>25</sup> As men consume more alcohol than women in populations and the benefit of moderate alcohol consumption only be demonstrated in women but not overall,<sup>26,27</sup> and alcohol abuse was proved to be a risk factor for incidence and re-infection of TB,<sup>28</sup> we thus believe that the effect of alcohol consumption in the development of DM should be further validated in large populations.

There were several limitations in our study. Firstly, the data in the study were limited and collected from only two hospitals specializing in TB. Therefore, the results may only reflect the current situation in large cities in China and may be limited by the geographical area. Secondly, we did not assess lifestyle, dietary habits, physical exercise, and environmental factors, which could introduce selection bias and potentially overlook additional factors contributing to the development of DM-TB. Thirdly, due to a small number of patients with extra-pulmonary TB, we were unable to address the risk factors of DM in these patients.

In conclusion, we found that about one-fifth of PTB patients have diabetes. The risk factors are male, age  $\geq 47$  years, excessive alcohol use, family history of DM, and an elevated random glucose level. Awareness of DM and zero-to-light alcohol consumption may lower the risk of developing DM. Raising disease awareness, effective prevention, and early diagnosis of diabetes aids in the reduction of the dual burden of TB-DM comorbidity, particularly in men after middle age.



## Data Sharing Statement

All original data used in the study has been de-identified and are available from the corresponding author on request.

## Declarations

This study is approval by the Ethical Committee of the third people's hospital of Shenzhen and the Ethical Committee of the third people's hospital of Kunming. All participants in this study provided written consent to participate. Both hospitals assure that no personal information of any patients was involved in using these statistics. Furthermore, the study adheres to the Declaration of Helsinki guidelines regarding confidentiality and ethical standards.

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## Disclosure

The authors declare no conflicts of interest in this study.

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