

## Original Article

# Hypertension and its associated risk factors in tuberculosis patients: A hospital based cross-sectional study

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**Background and Objectives:** Tuberculosis (TB) is associated with a number of non-communicable diseases including hypertension. The aim of this study is to determine the prevalence of hypertension in TB patients and investigate its associated risk factors. **Methods and Study Design:** A hospital-based cross-sectional study was conducted in Qingdao, China (2011–2019). Data on demographics, medical history, and lifestyle were collected via questionnaire. Blood pressure was measured at admission. Logistic regression identified hypertension risk factors. **Results:** 2159 TB patients were included in total in the final analysis. Among them, 485 (22.5%) were hypertensive. After adjusting for dietary sodium and potassium intake, marital status, retreatment, physical activity and smoking index, multivariate logistic regression showed that hemoglobin (HGB)  $\geq 143$  (OR, 95% CI: 1.74, 1.08–2.79), age  $>35$  (OR, 95% CI: 2.93, 1.87 ~ 4.59), male gender (OR, 95% CI: 1.77, 1.13–2.77), overweight or obesity (OR, 95% CI: 2.04, 1.42–2.93), heavy drinking (OR, 95% CI: 1.76, 1.19–2.59) and concurrent DM (OR, 95% CI: 1.54, 1.09–2.17) were associated with increased risk of hypertension in TB patients, whereas high education level (OR, 95% CI: 0.47, 0.26–0.85) served as a protective factor. **Conclusions:** Nearly 25% of TB patients have prevalent hypertension at admission. High HGB, being overweight or obese, heavy drinking, male gender and concurrent DM are associated with higher odds of hypertension in TB, while a higher education level serves as a protective factor. Our study provides important evidence for understanding the prevalence of hypertension in TB, underlying the double burden of TB and hypertension.

**Key Words:** tuberculosis, hypertension, prevalence, risk factor, double burden

## INTRODUCTION

The global burden of tuberculosis (TB) is decreasing, yet it continues to be a major health problem in low- and middle-income countries (LMICs).<sup>1</sup> At the same time, with improved socio-economic status, urbanization and changes in lifestyle and dietary habits, many LMICs are also facing a rapid increase of non-communicable diseases (NCDs) such as cardiovascular diseases, cancer, type 2 diabetes mellitus (DM) and hypertension.<sup>2</sup> The double burden of TB and NCDs has aroused intense scientific interests, as well as the attention of international organizations. For instance, DM, estimated to triple the risk of active TB,<sup>3</sup> has recently been identified as a neglected risk factor for the re-emergence of TB by WHO.<sup>4</sup> In agreement, we reported a significantly higher prevalence of DM in TB patients (6.3%) than that in non-TB controls (4.7%) in a representative sample of newly detected TB patients in rural communities in China.<sup>5</sup>

Hypertension, a major risk factor for cardiovascular disease, accounts for one third of deaths worldwide. More

than 75% of cardiovascular deaths occur in LMICs. Cross-sectional studies reported prevalence of hypertension in TB patients ranging from 0.7% to 38.3%.<sup>6</sup> However, few of the studies were designed specifically to assess the association between TB and hypertension, also, hypertension was defined differently in these studies.

In general population, factors such as older age, male gender, cigarette smoking, hyperlipidemia have consistently been reported to be associated with an increased risk of hypertension,<sup>7</sup> while whether these factors also work in TB patients still remains unknown. TB itself may lead to

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increased risk of high blood pressure through directly destructing the parenchyma in the body, affecting the pulmonary vascular structure, as well as the renal tissue that resulting in impaired ability of the kidney to regulate blood pressure.<sup>8</sup> Also, indirect mechanism may work in the process. *Mycobacterium tuberculosis* (MTB) infection triggers immune inflammatory response and the consequent impairment of endothelial function, leading to an increased prevalence of hypertension.

The double burden of rapidly increasing NCDs and still high TB prevalence is a major public health issue in LMICs, including China, in recent years as well as the long run to come. To understand the prevalence of hypertension in TB patients, identifying associated risk factors will help to put forward new strategy to cope with the double burden. Therefore, we carried out this hospital based cross-sectional study, describing the prevalence of hypertension in patients with TB and analyzing associated risk factors.

## METHODS

### *Study design and population*

This is a cross-sectional study aiming to examine the prevalence of hypertension in active TB patients. Pulmonary tuberculosis patients admitted in Qingdao Chest Hospital (Qingdao, China) were recruited from July, 2011 to December, 2019.

Trained interviewers administered a standardized questionnaire including information for demographic characteristics, medical history, dietary information, drinking and smoking et al. Pregnant women, patients age < 16 years, have serious comorbidities such as tumor, HIV, severe hepatic and kidney diseases were excluded from the analyses. Furthermore, patients with missing blood pressure values and patients who were hypotensive at study inclusion were excluded from the analyses.

The trial was approved by the Institutional Review Board of Qingdao Center for Disease Control and Prevention and registered with the Chinese Clinical Trial Registry (Registration number: ChicCTR-IPR-15006395). All participants provided informed consent.

### *Assessment of outcome*

Right brachial blood pressure was measured by well-trained co-investigators in the hospital while the subjects were seated at about 8:00 am. Verified medical electronic blood pressure meter with a cuff selected in accord with right-arm circumference was used. Half an hour before the measurement, the subjects were required not to exercise vigorously, not be mentally nervous, empty the bladder, and rest for at least five minutes. Patients with abnormal results were monitored once again under the same condition about one hour later and the mean reading was recorded.

Blood pressure measurement was referred to the Chinese Guidelines for the Prevention and Treatment of Hypertension.<sup>9</sup> Hypertension was defined as systolic blood pressure (SBP)/ diastolic blood pressure (DBP)  $\geq 140/90$  mmHg, as well as those with diagnosed hypertension who took antihypertensive drugs.

### *Assessment of possible associated risk factors*

Subjects' height and weight were measured, and body mass index (BMI) was calculated as weight (kg) divided by the square of height (m). Underweight was defined as BMI < 18.5 kg/m<sup>2</sup>, overweight and obesity as BMI  $\geq 24.0$  kg/m<sup>2</sup>. Standard enzymatic methods were used to measure serum albumin, lipid profile including TC, LDLC, TG and HDLC by using automatic biochemistry analyzer. DM was diagnosed based on self-reported diabetic patients who had already taken anti-diabetic medicines, or on the results of fasting plasma glucose (FPG) at routine admission clinical test according to WHO criteria (1999) for the classification of glucose tolerance.<sup>10</sup>

Smoking index was used to evaluate smoking status, calculated as number of cigarettes smoked per day multiplied by years of smoking.<sup>11</sup> Heavy drinking was defined as  $\geq 14$  drinks/wk in males,  $\geq 7$  drinks/wk in females; one drink contains equivalent to beer (360 mL), 30 mL of distilled spirits.<sup>12</sup> Light physical activity as slightly accelerate the breathing and heartbeat, and moderate to heavy physical activity was defined as activities that significantly accelerate the breathing and heartbeat.<sup>13</sup>

### *Statistical analysis*

Statistical analyses were carried out using SPSS version 23.0. Variables were analyzed for a normal distribution with the Kolmogorov-Smirnov test. For categorical variables, number of cases and percentages were used for the description, while for quantitative variables, mean and the standard deviation were used for which followed a normal distribution, median and interquartile range for which that did not follow a normal distribution. Comparisons of proportions between the qualitative variables were carried out using the Chi-square test, and independent samples T test was used to determine the differences between the groups for data normally distributed and with equal variance.

Potential risk factors were included in the multivariable model for analyzing the possible risk factors of hypertension including age (2 categories:  $\leq 35$  years,  $> 35$  years), sex, concurrent DM, BMI (3 categories: <18.5, 18.5-23.9,  $\geq 24$ ), marital status (2 categories: married, separated/divorced/ widowed or never married), education (4 categories: illiteracy or primary school, middle school, high school, college or university and above), newly treatment/retreatment; smoking index (3 categories: never, < 800, or  $\geq 800$ ), heavy drinking, physical activity (two categories: light, moderate to heavy), HGB (4 categories: < 119, 119~, 131~,  $\geq 143$ ), dietary potassium and sodium intake was categorized into tertiles. In addition, further analysis was stratified by age (categories of < 35;  $\geq 35$  years), concurrent of DM (with/without) and treatment (newly treated/retreated). Two-tailed p value less than 0.05 was considered statistically significant.

## RESULTS

Between July 2011 and December 2019, 2330 patients newly diagnosed with TB were enrolled in the study. Of these, 146 patients were excluded due to missing blood pressure values, 6 patients were excluded due to aged < 16 years, 2 patients were excluded due to pregnancy at treatment initiation and 17 patients were excluded be-

cause they were hypotensive at treatment initiation. Finally, 2159 patients were included in the final analysis (Figure 1).

#### Baseline characteristics of the participants

Baseline characteristics of TB patients with and without hypertension at admission are presented in Table 1. The proportion of patients with hypertension was 22.5% (485 / 2159). Mean systolic/diastolic blood pressure was  $117 \pm 10.4$  mmHg/ $73.7 \pm 7.39$  mmHg in normotensive patients, and  $144.7 \pm 14.9$  mmHg/ $88.4 \pm 10.1$  mmHg in hypertensive patients. There were more males in patients with hypertension, and hypertensive patients have a higher proportion of retreatment, concurrent DM, high smoking index, heavy drinking and a higher BMI level (Table 1).

#### Risk factors for hypertension in TB patients

In univariate analysis, hypertension prevalence was positively associated with age, BMI, overweight/obesity and HGB. Additionally, individuals with concurrent DM, male gender, heavy drinking, high smoking index, and being married had a higher odds ratio of hypertension (Table 2).

In multivariate model, after adjusted for dietary sodium and potassium intake, marital status, retreatment, physical activity and smoking index, age > 35 (OR, 95%: 2.93, 1.87 ~ 4.59), male gender (OR, 95%: 1.77, 1.13 ~ 2.77), high HGB (OR, 95%: 1.74, 1.08~2.79), overweight/obesity (OR, 95%: 2.04, 1.42~2.93), concurrent DM (OR, 95%: 1.54, 1.09~2.17), heavy drinking (OR, 95%: 1.76, 1.19~2.59) was association with increased risk of having hypertension in TB patients; while both BMI <18.5 (OR, 95% : 0.51, 0.28~0.90) and education level of college/university and above (OR, 95% : 0.47, 0.26~0.85) showed protective effects (Table 2).

In stratified analysis, after adjusted for the same confoundings as in the total analysis, age >35 and over-

weight/obesity showed similar association with hypertension as in the whole TB patients. Low body weight (BMI <18.5) consistently demonstrated a protective effect in patients aged >35, with concurrent DM and new treatment. Furthermore, heavy alcohol consumption significantly increased the risk of hypertension, particularly among retreated patients (Table 3).

#### DISCUSSION

The reported prevalence of hypertension in TB patients varies from 0.7% to 38.3%, and few of the studies were designed specifically to assess the association between TB and hypertension.<sup>6</sup> To our knowledge, the present study is the first of its kind to investigate the prevalence of hypertension and its associated risk factors in TB. The prevalence of hypertension was 22.5%, and high HGB, aging, concurrent DM, overweight/obesity and heavy drinking were identified as major risk factors for hypertension in TB patients.

In a large retrospective cohort study, Chung et al. reported a small but statistically significant higher prevalence of hypertension in the TB cohort at the time of diagnosis than non-TB (38.7% vs. 37.5%,  $p=0.03$ ).<sup>14</sup> Our results showed that the prevalence of hypertension in TB patients was 22.5%, which was comparable to the above results.

With regard to TB leading to hypertension, it has been hypothesized that the triggering of immunological responses can cause an impairment of endothelial function and lead to an increased risk of hypertension.<sup>15,16</sup> In the present study, we identified high HGB increased the odds ratio of hypertension in a dose dependent way in TB. The relationship between high HGB and hypertension had been found in some studies, high HGB concentrations may be a potential risk factor for hypertension.<sup>17</sup> In the state of hypertension, oxidative stress increases due to the increased activation of NADH/NADPH oxidase, and oxi-

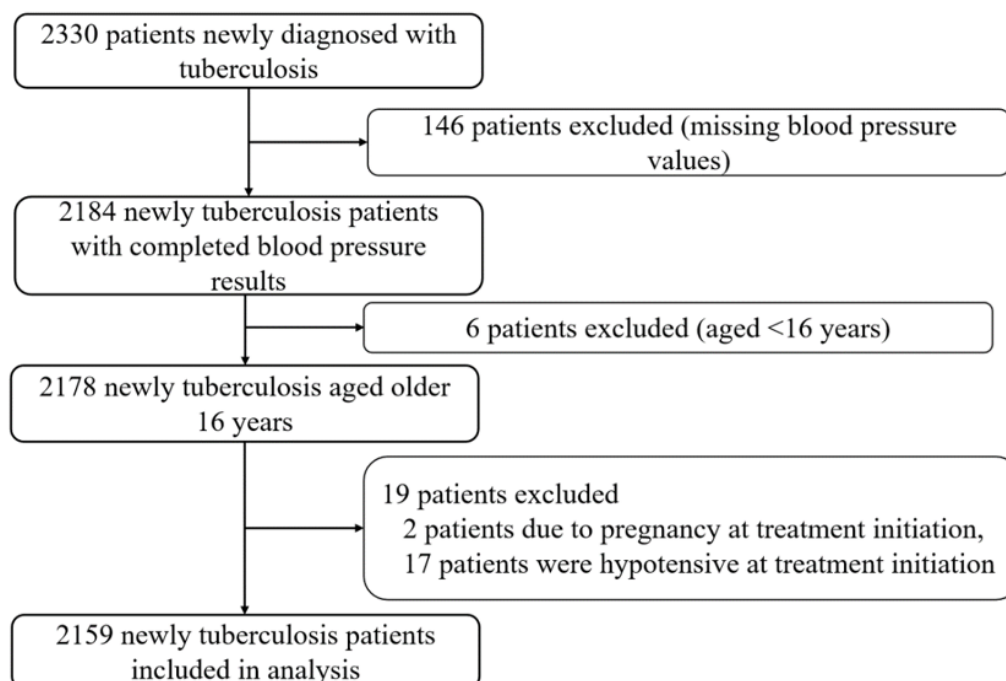


Figure 1. Flow chart of the screening process for the selection of eligible participants

**Table 1.** Baseline Characteristics of normotensive and hypertensive tuberculosis patients (n=2159)

	Normal BP, n=1674	Hypertension, n=485	p-value
Age (years)	41.9±16.4	55.2±14.6	<0.001
≤35	923 (57.3)	104 (22.1)	<0.001
>35	718 (43.7)	337 (76.6)	
Male	1149 (68.7)	395 (81.4)	<0.001
BMI (kg/m <sup>2</sup> )	21.2±3.18	22.8±3.39	<0.001
<18.5	283 (19.9)	28 (7.9)	<0.001
18.5-23.9	881 (62.0)	197 (55.8)	
≥24	256 (18.1)	128 (36.3)	
SBP (mmHg)	117±10.4	144.7±14.9	<0.001
DBP (mmHg)	73.7±7.39	88.4 ± 10.1	<0.001
Married	1075 (67.7)	403 (86.7)	<0.001
Education level			
Illiteracy/primary school	228 (15.4)	136 (33.9)	<0.001
Middle school	349 (23.6)	120 (29.9)	
High school	383 (25.9)	93 (23.2)	
College/university	518 (35.0)	52 (13.0)	
Retreatment	298 (19.0)	125 (27.5)	<0.001
TC	4.20±1.01	4.70±1.15	<0.001
TG	1.04±0.62	1.42±1.27	<0.001
HDLc	1.23±0.62	1.36±0.54	<0.001
LDLC	2.53±0.82	2.72±0.89	<0.001
HGB	130±18.6	132±21.6	0.010
<119	375 (25.0)	95 (21.5)	0.004
119~	389 (26.0)	91(20.6)	
131~	377 (25.2)	116 (26.3)	
≥143	358 (23.9)	139 (31.5)	
Concurrent diabetes	526 (31.4)	259 (53.4)	<0.001
Physical activity			0.002
Light	890 (66.8)	249 (73.2)	0.022
Moderate to heavy	443 (33.2)	91 (26.8)	
Smoking Index			<0.001
0	879 (56.1)	194 (45.8)	<0.001
<800	471 (30.1)	134 (31.6)	
≥800	217 (13.8)	96 (22.6)	
Heavy drinking	291 (17.4)	154 (31.8)	<0.001
Sodium (mg/d)	11126±1264	11069±10319	0.244
Potassium (mg/d)	1478 (711)	1453 (664)	0.691

BP, blood pressure; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; TC, total cholesterol; TG, triglyceride; HDLC, high density lipoprotein cholesterol; LDLC, low density lipoprotein cholesterol; HGB, hemoglobin; M, median; Q, interquartile range.

ductive stress can damage endothelial cells.<sup>18</sup> Hepatocyte growth factor (HGF), which is known as an angiogenic growth factor, plays an important role in endothelial maintenance and endothelial repair.<sup>19</sup> However, other studies have reported HGF as a possible biochemical index of vascular damage due to hypertension.<sup>20</sup> High plasma concentration of HGF indicates the presence of aggressive vascular remodeling. It is noteworthy that HGF is constitutively produced by human bone marrow and indirectly stimulates the growth of undifferentiated hematopoietic cells and erythroid progenitor cells, serving as a potential source of HGB.<sup>21</sup> Consequently, the plasma concentration of HGF may be intricately related to hemoglobin levels in patients with hypertension.

However, few studies have reported the relationship between high HGB and TB till now. When TB patients are complicated with hypertension, on one hand, hypertension will cause the patient's HGB to increase;<sup>22</sup> on the other hand, the clinical symptoms of TB patients may be more serious, such as leading to dyspnea, and HGB plays an important physiological role in the combination, utilization, transportation and release of oxygen in the body.

When patients have difficulty breathing and oxygen supply is insufficient, hemoglobin level may rise to provide sufficient oxygen to ensure tissue needs.<sup>17</sup> While, more research is needed on the relationship between TB complicated with hypertension and the possible intermediating effect of high HGB.

In line with previous reported risk factors of hypertension in general population, patients with concurrent overweight/obesity, heavy drinking and DM had significantly higher prevalence of hypertension.<sup>23,24</sup> Overweight/obesity and heavy drinking are established modifiable risk factors for hypertension in general population. Studies in various populations demonstrate a direct, nearly linear association of BMI with blood pressure. About 40% of adults with hypertension in the United States are overweight/obesity, and over one-third of the overweight/obesity population has hypertension (SBP/DBP >140/90 mmHg or treatment with antihypertensive medication), compared to less than one-fifth of normal-weight individuals. Clinical studies have repeatedly demonstrated that weight loss reduces the risk for hypertension and BP in adults with hypertension.<sup>25</sup> Some evidence has

**Table 2.** Logistics regression of risk factors for hypertension in TB

	Univariable OR (95% CI)	<i>p</i> -value	Multivariable OR (95% CI)	<i>p</i> -value
Age (years)	1.05 (1.04~1.06)	<0.001	1.05 (1.03, 1.06)	<0.001
≤35	Ref		Ref	-
>35	4.71 (3.71~5.98)	<0.001	3.21 (2.16~4.76)	<0.001
Male	2.00 (1.56~2.58)	<0.001	1.83 (1.16, 2.89)	0.009
BMI (kg/m <sup>2</sup> )	1.16 (1.12~1.20)	<0.001	1.16 (1.11~1.21)	<0.001
18.5-23.9	Ref		Ref	-
<18.5	0.44 (0.29~0.67)	<0.001	0.46 (0.27~0.79)	0.005
≥24	2.24 (1.72~2.91)	<0.001	2.14 (1.54~2.95)	<0.001
Married	3.11 (2.33~4.14)	<0.001	1.24 (0.76, 2.02)	0.398
Education level				
Illiteracy/primary	Ref	<0.001	Ref	-
Middle school	0.57 (0.43~0.78)	<0.001	0.73 (0.49~1.09)	0.124
High school	0.41 (0.30~0.56)	<0.001	0.92 (0.60~1.43)	0.733
College/university and above	0.17 (0.12~0.24)	0.001	0.49 (0.29~0.84)	0.009
Retreatment	1.50 (1.17~1.92)	<0.001	0.80 (0.57, 1.13)	0.212
HGB	1.01 (1.00~1.01)	0.010	1.01 (1.00, 1.02)	0.003
<119	Ref	-	Ref	-
119~	0.92 (0.67~1.27)	0.626	1.15 (0.72~1.81)	0.561
131~	1.22 (0.89~1.65)	0.214	1.74 (1.12~2.69)	0.013
≥143	1.53 (1.14~2.07)	0.005	2.29 (1.50~3.50)	<0.001
DASH score	0.96 (0.93~0.98)	0.001	1.00 (0.96, 1.04)	0.936
<20	Ref	-	Ref	-
20~	0.69 (0.53~0.91)	0.009	0.93 (0.65, 1.33)	0.678
≥24	0.74 (0.56~0.97)	0.031	0.95 (0.66, 1.38)	0.788
Concurrent DM	2.50 (2.04~3.07)	<0.001	1.50 (1.10~2.03)	0.011
Physical activity				
Light	Ref	-	Ref	-
Moderate to heavy	0.73 (0.56~0.96)	0.023	0.85 (0.61, 1.17)	0.316
Smoking index				
0	Ref		Ref	
<800	1.29 (1.01~1.64)	0.038	0.68 (0.46, 1.01)	0.056
≥800	2.16 (1.63~2.85)	<0.001	0.60 (0.38, 0.95)	0.029
Heavy drinking	2.21 (1.76~2.78)	<0.001	1.81 (1.32~2.49)	<0.001
Sodium				
1 <sup>st</sup> tertile	Ref	-	Ref	-
2 <sup>nd</sup> tertile	1.08 (0.74~1.58)	0.679	1.03 (0.67~1.60)	0.870
3 <sup>rd</sup> tertile	1.15 (0.83~1.59)	0.385	1.07 (0.74~1.56)	0.725
Potassium				
1 <sup>st</sup> tertile	Ref	-	Ref	-
2 <sup>nd</sup> tertile	1.11 (0.79~1.55)	0.540	1.18 (0.80~1.75)	0.400
3 <sup>rd</sup> tertile	0.97 (0.69~1.38)	0.859	0.87 (0.58~1.30)	0.495

BMI, body mass index; HGB, hemoglobin; DM, diabetes mellitus

emerged demonstrating that subjects who are overweight, in close contacts with TB patients, because obesity and the accompanying metabolic syndrome are typically associated with increased prevalence of DM that can triple the risk of active TB.<sup>26</sup> Our data show that overweight/obesity is associated with increase in the prevalence of hypertension in TB, which is in accordance with the association in the general population.

Heavy drinking ranks among the top five risk factors for disease, as well as being a causal factor in more than 200 disease and injury conditions, including TB and hypertension, worldwide. We found a positive relationship between heavy drinking and prevalence of hypertension, which was in line with many studies.<sup>27</sup> It has been estimated that approximately 10% of all TB cases are attributable to alcohol use. Heavy drinking or a clinical diagnosis of alcohol use disorder increases the risk of developing active TB by 3.5 times, as excessive consumption impairs immune response to MTB and compromises treatment effectiveness.<sup>28</sup> In view of the high

prevalence of heavy drinking and TB with hypertension, drinking in moderation and abstainers should be important strategies for reducing hypertension and the related disease burden.

Although extensive epidemiological evidence indicates that sodium and potassium intake are significantly associated with hypertension in the general population,<sup>29</sup> this study found no significant association between sodium/potassium intake and hypertension risk among TB patients. To date, research on the relationship between sodium/potassium intake and hypertension in TB populations has been scarce. The observed null association may be explained by the fact that TB patients frequently present with hyponatremia and electrolyte disturbances—metabolic abnormalities that may alter sodium-potassium homeostasis regulation compared to healthy populations,<sup>30</sup> thereby attenuating or masking the influence of dietary sodium/potassium on blood pressure. Food frequency questionnaire (FFQ) was used to assess sodium

**Table 3.** Stratified multivariable analysis of risk factors of hypertension in TB

	Age ≤35	Age >35	TB-non DM	TB-DM	Newly treated	Retreated
Male	4.29 (1.79, 10.28)	1.13 (0.73, 1.68)	1.94 (0.91, 4.15)	1.29 (0.73, 2.29)	1.72 (0.96, 3.08)	0.96 (0.35, 2.61)
Age>35	/	/	2.27 (1.18, 4.39)	3.05 (1.55, 6.02)	3.26 (1.95, 5.48)	3.47 (1.25, 9.64)
Concurrent DM	1.42 (0.62, 3.21)	1.35 (0.91, 1.99)	/	/	1.54 (1.03, 2.31)	1.53 (0.79, 3.11)
BMI	/	/	/	/	/	/
18.5-23.9	Ref	Ref	Ref	Ref	Ref	Ref
<18.5	0.48 (0.16, 1.39)	0.46 (0.27, 0.85)	0.52 (0.26, 1.04)	0.36 (0.15, 0.84)	0.43 (0.23, 0.81)	0.45 (0.16, 1.26)
≥24	3.06 (1.72, 5.46)	1.80 (1.24, 2.64)	3.16 (1.93, 5.19)	1.57 (1.03, 2.39)	2.04 (1.41, 2.97)	2.68 (1.40, 5.12)
HGB	/	/	/	/	/	/
<119	Ref	Ref	Ref	Ref	Ref	Ref
119~	0.84 (0.42, 1.68)	0.81 (0.47, 1.42)	1.33 (0.62, 2.87)	0.91 (0.49, 1.69)	9.90 (0.51, 1.60)	1.22 (0.42, 3.52)
131~	1.62 (0.83, 3.18)	1.38 (0.79, 2.38)	2.01 (0.95, 4.27)	1.58 (0.87, 2.84)	1.59 (0.92, 2.77)	1.17 (0.42, 3.27)
≥143	1.96 (1.01, 3.83)	1.49 (0.87, 2.58)	1.19 (0.89, 4.11)	1.91 (1.09, 3.35)	1.46 (0.83, 2.58)	2.15 (0.82, 5.62)
Heavy drinking	1.44 (0.34, 6.17)	1.55 (0.99, 2.41)	1.38 (0.76, 2.52)	1.55 (1.01, 2.36)	1.63 (1.05, 2.53)	2.50 (1.03, 6.04)

The table above aggregates the salient characteristics identified in the analysis.

†Adjusted for dietary sodium and potassium intake, education level, marital status, retreatment, physical activity and smoking index. DM, diabetes mellitus; BMI, body mass index; HGB, hemoglobin; TB, tuberculosis.

and potassium intake. This method may be subject to recall bias and measurement error, particularly in accurately capturing the use of condiments and sodium content in processed foods, potentially leading to misclassification of actual intake levels and thereby affecting the power of the association analysis between sodium, potassium, and hypertension. Future studies may employ more accurate sodium/potassium measurement methods in larger TB patient cohorts to investigate the potential impact of TB-specific pathological mechanisms on the sodium-potassium-blood pressure relationship.

There are several strengths in our study. Firstly, we compared or adjusted for potential mechanistic correlates of hypertension in TB patients-such as high glycosylated hemoglobin, overweight/obesity, alcohol abuse, and diabetes. This allows us to investigate the risk factor for high blood pressure in TB patients more specifically. Secondly, our study provides comprehensive analyses of prevalence and risk factors of hypertension in a large population of newly diagnosed TB patients in Qingdao and contributes to the ongoing discussion on the association between chronic communicable disease and chronic non-communicable disease. Furthermore, the TB patients included in this study consists of different types of TB, both TB with and without DM and newly treated and retreated TB. The potential confounders in the relationship between TB and hypertension, such as DM, lifestyle factors/socioeconomic factors were adjusted.

Also, this study has several limitations. The major weakness is this cross-sectional study cannot exclude potential recall bias and unable to explain causal relationship between diseases. Compared with the natural TB cohort, more patients with DM were included. Due to the close relationship between hypertension and DM, the prevalence of hypertension in TB in the present study may be higher than that of the natural cohort, therefore, the interpretation of this result should be cautious. Furthermore, the study did not incorporate the assessment of n-3 polyunsaturated fatty acid (n-3 PUFA) intake due to extremely low intake frequency in the participants. Future research will further explore the role of these possibly relevant factors on hypertension prevalence in TB patients. Also, the serum lipid levels were measured on a single day. Therefore, the intra-individual variation of lipid profiles was not taken into consideration in this study. Finally, the subjects included were active TB patients from Qingdao, China, a coastal city with an economic level higher than the average level in the country. Therefore, caution should be taken when extrapolates our results to patients from other settings. Future studies should expand the geographical coverage to examine the cross-regional applicability of the findings.

### Conclusion

The findings demonstrated a 22.5% prevalence of hypertension in tuberculosis patients. Risk factors for hypertension included elevated HGB levels, advanced age, male gender, overweight/obesity, heavy drinking, and concurrent DM, whereas higher educational attainment was associated with protective effects. From a clinical perspective, our result provides important evidence for understanding the correlation of hypertension with TB, which

may impact significantly on the prognosis of TB. The underlying biological mechanism warrants further investigation.

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### CONFLICT OF INTEREST AND FUNDING DISCLOSURES

The authors have no competing interests to declare.

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