Original Article

Association between macronutrients intake and liver dysfunction among tuberculosis patients in rural China

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Background and Objectives: Macronutrients play a vital role in liver dysfunction and affect tuberculosis treatment and prognosis. However, macronutrients intake was inadequate for most tuberculosis patients. This study aimed to clarify the associations between macronutrients intake or energy percentages and liver dysfunction in tuberculosis patients. **Methods and Study Design:** In this cross-sectional study, 2581 active tuberculosis patients aged ≥18 years were included from local tuberculosis clinics in Linyi, China. Macronutrients intake and energy percentages were assessed by 24-hour dietary recalls. The concentration of alanine transferase (ALT) or aspartate transaminase (AST) greater than 40 U/L was defined as liver dysfunction. A restricted cubic spline (RCS) was applied to determine the dose-response relationships. **Results:** Liver dysfunction was assessed for 14.6% (377 patients) of tuberculosis patients. Higher protein (Q2-Q4 in model 1 and 2) or fat intake and fat-to-energy percentages and lower carbohydrate-to-energy percentages (Q4 in model 1) were associated with a decreased incidence of liver dysfunction ($p_{\text{-trend}} < 0.05$). Among those who were male, normal BMI, or consumed energy <1636 kcal/d, inverse associations between protein or fat intake and the risks of liver dysfunction in models were suggested ($p_{\text{-trend}} < 0.05$). Moreover, J-shaped curves in RCS were evident in liver dysfunction tuberculosis patients with protein or fat intake ($p_{\text{-nonlinearity}} < 0.05$). **Conclusions:** Significant linear associations between macronutrients intake or energy percentages and liver dysfunction prevalence were found only in male, normal BMI, or less energy intake patients. The shapes of liver dysfunction-morbidity differed significantly by macronutrients intake or energy percentage.

Key Words: macronutrient intake, macronutrients to energy percentages, liver dysfunction, tuberculosis, RCS

INTRODUCTION

Tuberculosis (TB) is an infectious disease caused by *Mycobacterium tuberculosis*. Despite significant progress in TB control in the past three decades, China remained the third (7.4%) among eight countries with high TB incidence rates, accounting for two-thirds of the estimated incident cases worldwide in 2021.[1,2] Dietary nutrition has an important impact on the development and progression of tuberculosis. In our previous study, it was found that the increased dietary consumption of meat was beneficial in reducing tuberculosis treatment failure rates, which indicated that foods enriched with high-quality proteins might be beneficial in the control of tuberculosis.[3] Macronutrients intake was inadequate for most patients with TB, particularly protein-calorie malnutrition.[4] Macronutrients deficiencies and associated disorders have synergistic relationships with TB infection and its prognosis, exacerbating oxidative and immune dysfunction.[5,6]

Malnutrition has been attributed to an increased risk of the progression of liver dysfunction and consequences such as infection.[7] Macronutrients deficits could increase a patient's risk of being susceptible to hepatocellular diseases, especially protein deficiencies.[8] Various and partly contradictory macronutrients intakes are known to be related to liver dysfunction. For example, in a retrospective study, the proportion of liver injury during TB treatment was higher in the malnourished group than in the well-nourished group ($p = 0.022$).[9] Additionally, previous studies showed that low protein, low polyunsaturated fatty acids (PUFAs), high sugar, and high-fructose corn syrup intake were associated with an increased risk for high liver function index or liver diseases (such as serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST), hepatic steatosis, and non-alcoholic fatty liver disease (NAFLD)).[10-15] Because of damage to intracellular targets, notably lipids, proteins, and DNA, adverse effects were observed in key signaling pathways,

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including oxidative stress, mitochondrial dysfunction, and lipopolysaccharide-induced hepatic inflammation, that could maintain optimal biological functions of the liver.[11,16] Furthermore, several studies have indicated that high dietary intakes of fat could increase serum ALT, AST, and hepatic lipid accumulation, leading to extensive liver inflammation and signs of liver damage.[17,18] Traditionally, liver enzymes, such as ALT and AST, are considered markers of hepatocyte injury and are the most commonly used laboratory indicators of liver diseases.[19] An adequate intake of nutrients is crucial for the integrity of the liver's detoxification mechanism.[5]

Currently, studies have mainly focused on the relationships between dietary protein, fats, or carbohydrates and liver function; however, researches on the association between overall macronutrients intake or energy percentages and liver function remain limited, especially in patients with pulmonary TB. Therefore, this study aimed to identify the associations between macronutrients intake or energy percentages and the incidence of liver dysfunction before TB treatment.

METHODS

Study population

This study utilized data from TB clinics in Linyi, Shandong, China between September 2010 and March 2013. Five TB clinics in Linyi were randomly selected for the study, including in Lanshan, Yinan, Cangshan, Feixian and Pingyi counties. In this survey, 3549 active TB patients completed the interview, and those aged <18 years, had unreliable dietary data (extreme macronutrients intakes and energy intake >5000 kcal or <500 kcal), and lacked ALT or AST data were excluded (n = 162). Furthermore, participants without sociodemographic and confounder data, such as sex, marital status, education, body mass index (BMI), physical activity, smoking, alcohol status, and laboratory features (glucose (GLU), triglycerides (TG), total cholesterol (TCHO), and high-density lipoprotein (HDL) cholesterol) were excluded from this survey (n = 806). Finally, 2581 participants were recruited for analysis (Supplemental Figure 1).

The cross-sectional study was approved by the Ethics Committee of Qingdao Disease Prevention and Control Centre and conducted according to the Declaration of Helsinki guidelines. The study was registered with the Chinese Clinical Trial Registry (No. ChiCTROCC-10 000 994). All patients provided informed written consent.

Ascertainment of outcomes

ALT and AST from participants' fasting blood samples were measured using automatic biochemical analysers by local clinical staff. Liver dysfunction was defined as ALT or AST exceeding the normal upper limit of 40U/L.[20] In particular, when testing blood samples, we calibrated automatic biochemical detectors before each analysis, with the error controlled within 5%.

Assessments of nutrient intakes

Data were obtained through 24-hour dietary recall interviews for 3 consecutive days including 2 weekdays and 1 weekend, which included the date and number of meals, name of dishes, food composition, and weight (g). Data were collected by investigators who are trained and familiar with common local foods Photo sets, measuring utensils (plates and bowls), and food models marked with a specific standard quantity or volume were used as the basic units for measuring intake. The macronutrients and energy intakes were calculated using the China Food Composition Tables and summing the food intake.[21]

Assessments of covariates

Information on demographic and lifestyle factors, including age, sex, education, physical activity, marital status, drinking and smoking, were collected using a structured questionnaire administered by a trained interviewer. In this analysis, education was categorized using survey questions as educational level as follows: illiteracy, primary school, junior high school, and more than high school. Physical activity was based on Chinese adults divided into the following three levels:[22] light, moderate, and heavy. Marital status was classified as single, married, and others, including divorced and widowed, based on the self-report of respondents. Additionally, smoking status and alcohol intake were classified as yes or no according to self-report. Using a standardised and uniform measuring device, the patient maintained the correct posture during measurement and the average of the two measurements was recorded; the height and weight counts were accurate to 0.1 cm and 0.1 kg, respectively. BMI was calculated as weight (kg)/ height^2 (m^2) and classified into underweight (<18.5 kg/m^2), normal weight (18.5-23.9 kg/m^2) and overweight or obesity (≥24.0 kg/m^2) according to Chinese adult standards.[23] GLU, TG, TCHO and HDL concentrations obtained from the patient's fasting venous blood were measured using the automatic biochemical detector.

Statistical analysis

All statistical analyses were conducted in SPSS 21.0 (SPSS Inc., Chicago, IL) and Stata 11.0 (StataCorp LP) software. Characteristics of participants were compared between those with or without liver dysfunction utilizing the Chi-square test for categorical variables, the student's t-test for continuous variables, and the Mann-Whitney test for non-normal distribution. Logistic regressions were used to analyse the associations between macronutrients intakes or energy percentages and liver dysfunction and estimate the crude odds ratio (*OR*s) and 95% confidence intervals (*95% CI*s). Daily intakes of macronutrients were categorized into four levels through quartiles, using the lowest category as the reference. Potential confounders, including age, sex, education, alcohol status, physical activity, marital status, smoking status, GLU, TG, TCHO, and HDL, were incorporated and adjusted into the model. Stratified analyses by sex, energy intake (<1636 kcal/d or ≥1636 kcal/d), BMI, and alcohol status were conducted. When making model adjustments, stratified variables were factored out accordingly. Possible interactions between macronutrients intakes and potential effect modifiers were examined in the logistic regression model by evaluating the multiplicative interactions. In addition, restricted cubic spline (RCS) fitted for logistic regression models was used to analyse the effects of cut-off points of macronutrients intake or energy percentages on liver dys-

function. All reported *p*-values are two-sided, with statistical significance evaluated at 0.05.

RESULTS

General characteristics of participants

Overall, 2581 patients with TB from TB clinics in Linyi City, China, were included, and 377 (14.6%) exhibited liver dysfunction (Supplemental Figure 1). Characteristics of the liver dysfunction events are displayed in Supplemental Table 1. The general characteristics of patients with active TB with and without liver dysfunction were compared (Table 1). Compared to patients with normal liver function, male, lower education level, underweight (BMI <18.5 kg/m^2), and alcohol consumption were all higher in patients with liver dysfunction (all $p < 0.05$). Other demographic characteristics, such as age, physical activity, marital status, smoking status, and laboratory features, were not associated with liver dysfunction. Regarding daily intake of nutrients, patients with had liver dysfunction tended to consume significantly less protein ($p = 0.009$) and fat ($p < 0.001$); however, no significant difference was observed in energy and carbohydrate intake between the liver dysfunction and normal liver function groups (all $p > 0.05$). Furthermore, lower fat-to-energy percentages and higher carbohydrate-to-energy percentages were observed in patients with TB and liver dysfunction.

Macronutrients intake or energy percentages and risk of liver dysfunction

A binary logistic regression was conducted to explore the associations between macronutrients intake or energy percentages and the risk of liver dysfunction in Table 2. Higher protein (≥47.6 g/d) or fat intake (≥20.1 g/d) was associated with a lower risk of liver dysfunction in models 1 and 2 ($p_{\text{-trend}} < 0.05$). Neither total energy nor carbohydrate intake was associated with the risk of liver dysfunction (both $p > 0.05$). Concerning energy percentages,

Table 1. General characteristics of the participants by liver dysfunction among TB patients, n = 2581

	Liver dysfunction		*p*
	Yes (n = 377)	No (n = 2204)	
Age (Years)†	52.0 ± 18.7	50.8 ± 18.4	0.257
Gender, n (%)			0.018
Male	298 (79.0)	1615 (73.3)	
Female	79 (21.0)	589 (26.7)	
Education, n (%)			0.002
Illiteracy	120 (31.8)	559 (25.4)	
Primary school	106 (28.1)	677 (30.7)	
Junior high school	124 (32.9)	686 (31.1)	
More than high school	27 (7.2)	282 (12.8)	
BMI, n (%)			0.017
< 18.5	92 (24.4)	400 (18.1)	
18.5 - 23.9	249 (66.0)	1580 (71.7)	
≥ 24	36 (9.5)	224 (10.2)	
Physical activity, n (%)			0.637
Light	193 (51.2)	1184 (53.7)	
Moderate	176 (46.7)	971 (44.1)	
Heavy	8 (2.1)	49 (2.2)	
Marital status, n (%)			0.728
Single	56 (14.9)	303 (13.7)	
Married	309 (82.0)	1817 (82.4)	
Others	12 (3.2)	84 (3.8)	
Smoking status, n (%)			0.143
Yes	110 (29.2)	564 (25.6)	
No	267 (70.8)	1640 (74.4)	
Alcohol status, n (%)			0.005
Yes	68 (18.0)	280 (12.7)	
No	309 (82.0)	1924 (87.3)	
Laboratory features†			
GLU (mmol/L)	5.04 ± 1.55	5.21 ±1.70	0.065
TG (mmol/L)	1.13 ± 0.77	1.14 ± 2.81	0.941
TCHO (mmol/L)	4.30 ± 1.09	4.37 ± 1.53	0.444
HDL (mmol/L)	1.48 ± 0.67	1.56 ± 2.70	0.582
Daily intake of nutrients			
Total energy (kcal/d)‡	1595 (1242, 2077)	1645 (1305, 2120)	0.146
Protein (g/d)‡	58.2 (44.4, 77.3)	62.6 (48.6, 78.4)	0.009
Fat (g/d)‡	17.4 (11.3, 31.4)	20.8 (13.2, 34.7)	< 0.001
Carbohydrate (g/d)‡	283 (223, 382)	293 (225, 374)	0.625
Protein: energy (%)‡	14.3 (12.5, 16.8)	14.7 (12.7, 17.4)	0.078
Fat: energy (%)‡	9.9 (6.9, 16.0)	11.6 (7.8, 18.2)	< 0.001
Carbohydrate: energy (%)‡	74.3 (67.2, 79.6)	72.2 (65.2, 77.8)	< 0.001

GLU, glucose; TG, triglyceride; TCHO, Total cholesterol; HDL, high-density lipoprotein

†Value is expressed as mean ± standard deviation; n (%) shown frequency counts and (percentages)

‡Values shown as mean ± standard deviation (SD)

Table 2. Association between intake or energy percentages of macronutrients and liver dysfunction among TB patients

Daily intake of macronutrients	Liver dysfunction		*OR* (95% *CI*)		
	Yes	No	Model 1	Model 2	Model 3
Total energy (kcal/d)					
Q1 < 1300	104 (16.1)	541 (83.9)	1.000	1.000	1.000
Q2 1300 - 1636	95 (14.7)	553 (85.3)	0.894 (0.660, 1.209)	0.928 (0.684, 1.260)	0.936 (0.689, 1.272)
Q3 1636 - 2114	86 (13.4)	557 (86.6)	0.803 (0.590, 1.094)	0.830 (0.607, 1.136)	0.851 (0.621, 1.166)
Q4 > 2114	92 (14.3)	553 (85.7)	0.865 (0.638, 1.173)	0.895 (0.656, 1.221)	0.913 (0.667, 1.250)
p trend			0.566	0.705	0.795
Protein (g/d)					
Q1 < 47.6	120 (18.6)	526 (81.4)	1.000	1.000	1.000
Q2 47.6 - 62.0	90 (13.9)	559 (86.1)	0.706 (0.524, 0.951)	0.730 (0.541, 0.986)	0.733 (0.542, 0.991)
Q3 62.0 - 78.2	80 (12.5)	561 (87.5)	0.625 (0.460, 0.850)	0.664 (0.485, 0.908)	0.680 (0.496, 0.931)
Q4 > 78.2	87 (13.5)	558 (86.5)	0.683 (0.506, 0.923)	0.709 (0.522, 0.962)	0.723 (0.532, 0.984)
p trend			0.010	0.037	0.055
Fat (g/d)					
Q1 < 12.8	124 (19.2)	521 (80.8)	1.000	1.000	1.000
Q2 12.8 - 20.1	106 (16.3)	545 (83.7)	0.817 (0.614, 1.087)	0.837 (0.627, 1.118)	0.830 (0.621, 1.110)
Q3 20.1 - 34.3	64 (10.0)	578 (90.0)	0.465 (0.336, 0.643)	0.487 (0.350, 0.676)	0.493 (0.355, 0.686)
Q4 > 34.3	83 (12.9)	560 (87.1)	0.623 (0.460, 0.843)	0.661 (0.486, 0.899)	0.660 (0.484, 0.899)
p trend			< 0.001	< 0.001	< 0.001
Carbohydrate (g/d)					
Q1 < 225.0	97 (15.0)	548 (85.0)	1.000	1.000	1.000
Q2 225.0 - 291.8	100 (15.5)	546 (84.5)	1.035 (0.764, 1.401)	1.041 (0.767, 1.413)	1.033 (0.760, 1.403)
Q3 291.8 - 374.2	84 (13.0)	561 (87.0)	0.846 (0.617, 1.159)	0.868 (0.632, 1.192)	0.886 (0.644, 1.220)
Q4 > 374.2	96 (14.9)	549 (85.1)	0.988 (0.727, 1.342)	0.965 (0.706, 1.318)	0.979 (0.714, 1.342)
p trend			0.610	0.710	0.808
Protein: energy (%)					
Q1 < 12.7	104 (16.1)	543 (83.9)	1.000	1.000	1.000
Q2 12.7 - 14.7	97 (15.1)	547 (84.9)	0.926 (0.685, 1.251)	0.922 (0.681, 1.247)	0.929 (0.685, 1.259)
Q3 14.7 - 17.3	100 (15.5)	544 (84.5)	0.960 (0.712, 1.294)	0.983 (0.728, 1.329)	0.988 (0.730, 1.337)
Q4 > 17.3	76 (11.8)	570 (88.2)	0.696 (0.506, 0.957)	0.730 (0.530, 1.006)	0.736 (0.533, 1.015)
p trend			0.121	0.212	0.199
Fat: energy (%)					
Q1 < 7.7	114 (17.7)	530 (82.3)	1.000	1.000	1.000
Q2 7.7 - 11.3	107 (16.6)	539 (83.4)	0.923 (0.691, 1.233)	0.978 (0.729, 1.311)	0.964 (0.716, 1.297)
Q3 11.3 - 18.0	80 (12.4)	566 (87.6)	0.657 (0.482, 0.895)	0.696 (0.509, 0.952)	0.694 (0.507, 0.952)
Q4 > 18.0	76 (11.8)	569 (88.2)	0.621 (0.454, 0.850)	0.673 (0.490, 0.925)	0.664 (0.482, 0.914)
p trend			0.004	0.015	0.015
Carbohydrate: energy (%)					
Q1 < 65.5	81 (12.6)	563 (87.4)	1.000	1.000	1.000
Q2 65.5 - 72.4	82 (12.7)	565 (87.3)	1.009 (0.726, 1.401)	0.987 (0.709, 1.374)	0.999 (0.717, 1.392)
Q3 72.4 - 78.2	96 (14.9)	548 (85.1)	1.218 (0.886, 1.674)	1.179 (0.856, 1.623)	1.179 (0.855, 1.628)
Q4 > 78.2	118 (18.3)	528 (81.7)	1.553 (1.143, 2.111)	1.419 (1.039, 1.938)	1.436 (1.049, 1.965)
p trend			0.012	0.068	0.066

†Model 1 was not adjusted

‡Model 2 was adjusted by age, gender, education, BMI and alcohol status

§Model 3 was further adjusted by physical activity, marital status, smoking status, GLU, TG, TCHO and HDL

fat-to-energy percentages (≥11.3%) were negatively associated with the risk of liver dysfunction (p_{-trend} < 0.05) in the three models. A significant positive connection was identified in the highest carbohydrate-to-energy percentages (≥78.2%) for higher liver dysfunction risk before adjusting for covariates (p_{-trend} = 0.012).

Association between protein intake and liver dysfunction by stratified analyses

Stratified analyses for associations between protein intake and the odds of liver dysfunction according to sex, energy intake, BMI, and alcohol status are shown in Table 3. Higher Q3 intake of protein could decrease liver dysfunction in these patients in the <1636 kcal/d energy intake groups (*OR* Q3 vs Q1 (*95% CI*): 0.555 (0.349, 0.881), 0.592 (0.371, 0.947), and 0.594 (0.370, 0.953), respectively, all p_{-trend} < 0.05) in all models. In the male or normal BMI (18.5-23.9 kg/m^2) group, protein intake was associated with the odds of liver dysfunction (all p_{-trend} < 0.05) in model 1. However, in females, higher energy intake and other BMI groups, protein intake was not associated with the odds of liver dysfunction (p_{-trend} > 0.05). Based on alcohol consumption, no association was observed between protein intake and liver dysfunction was observed; all interactions between protein intake and sex, energy intake, BMI groups, or alcohol status were not significant (all $p_{-interaction}$ > 0.05).

Association between fat intake and liver dysfunction by stratified analyses

A similar stratified analysis was conducted to explore the association between fat intake and the odds of liver dysfunction, as presented in Table 4. Among males, low energy intake (<1636 kcal/d), normal BMI (18.5-23.9 kg/m^2), and non-drinker patients, significant protective effects for liver dysfunction were observed in fat intake more than 20.1 g/d (all p_{-trend} < 0.005). Additionally, no interactions were found between fat intake and sex, energy intake, BMI groups, or alcohol status (all $p_{-interaction}$ > 0.05).

The results indicated that no significant associations were observed between carbohydrate intake and liver dysfunction, as demonstrated in the stratified analyses, and relevant data are displayed in Supplemental Table 2.

Cut-off points of macronutrients intake and energy percentages for liver dysfunction

As shown in Figure 1, the RCS model was used to further analyse the dose-response relationships between the odds of liver dysfunction and macronutrients intake or energy percentages. For protein or fat intake in patients with TB, J-shaped associations were verified for the odds of liver dysfunction (both $p_{-nonlinearity}$ < 0.05). The RCS fitted the logistic regression model when daily protein intake consumed was between 72.1 g and 77.7 g (*OR* (*95% CI*) = 0.46 (0.28-0.77), and the ORs of liver dysfunction decreased gradually; similarly, the risk of liver dysfunction decreased slightly with 34.3-49.7 g/d fat intake (*OR* (*95% CI*) = 0.43 (0.28-0.67)). There was no dose-response relationship between carbohydrate intake or macronutrients to energy percentages and the odds of liver dysfunction (all $p_{-nonlinearity}$ > 0.05).

DISCUSSION

The current results showed that higher protein or fat intake was associated with a decreased risk of liver dysfunction. Associations with more pronounced effects were noted between liver dysfunction and lower energy intake, normal BMI, and male sex. Additionally, RCS model showed J-shaped associations between protein or fat intake and ORs of liver dysfunction for patients with TB, thereby supporting the notion of providing nutritional support to improve the cure rate and quality of life of those with liver dysfunction in TB.

Our finding of the negative association between protein intake and liver dysfunction is consistent with previous studies, such as a large-scale, community-based prospective cohort of Korean adults,[24] randomised controlled trials among patients with long-chain fatty acid oxidation disorders,[25] and participants with morbid obesity.[26] Additionally, results from an animal experiment on rats revealed that higher protein intake in the diet resulted in lower liver weight and less fat deposition in the liver.[27] The reason might be that amino acids, such as methionine, N-acetylcysteine, and glycine, could mitigate or prevent oxidative stress and damage in the liver to humans and other animals.[28] Our RCS model predicted that the risk of liver dysfunction might decline apparently by consuming dietary protein of 72.1-77.7 g/day, which was consistent with a study that investigated the quantitative relationship between dietary protein intake and liver disease.[29] Previous studies have indicated that inadequate protein intake is prevalent in patients with TB.[3,30] For example, protein intake in patients with TB (44.6 g/day in males and 35.9 g/day in females) was significantly lower than the Dietary Reference Intake in the normal population (65 g/day in males and 55 g/day in females),[3] which was also lower than the cut-off in our RCS models. Therefore, recommending increased protein intake for patients with TB.

In our study, a negative association was found between the prevalence of liver dysfunction and fat intake, which was consistent with previous cohort studies.[31,32] The possible underlying mechanisms are as follows: docosahexaenoic acid contained in dietary fat reduces endoplasmic reticulum stress in hepatocytes through the activation of AMP-activated protein kinase and protects against hepatic steatosis by enhancing oxidation resistance, relieving hepatic inflammation, and preventing hepatic lipogenesis.[33] Similarly, n-3 PUFA can inhibit nuclear factor-kappa B from translocating to the nucleus and activating the transcription of pro-inflammatory cytokines, thereby protecting against liver injury by inhibiting oxidative stress and inflammation.[34,35] However, conflicting results exist from other studies. After an average follow-up time of 26.6 years, there was a null association between total fat intake and hepatocellular carcinoma cancer (HCC) in 160 cases.[36] Some studies have suggested that high-fat intake could worsen NAFLD, possibly because excess saturated fatty acids and trans fatty acids might impact hepatocyte steatosis through chylomicron uptake and fatty decomposition of adipose tissue and de novo hepatic adipogenesis.[37-39] Our result was inconsistent with these results, which could be due to two factors as following: On the one hand, in China's dietary fat structure, vegeta-

Table 3. Stratified analyses for the association between protein intakes and odds of liver dysfunction among TB patients

Stratified groups/ Quantile of protein intake	Liver dysfunction		Model 1		Model 2		Model 3	
	Yes	No	*OR* (95% *CI*)	p_{trend}	*OR* (95% *CI*)	p_{trend}	*OR* (95% *CI*)	p_{trend}
Gender								
Male				0.011		0.051		0.077
Q1	94 (31.5)	368 (22.8)	1.000		1.000		1.000	
Q2	68 (22.8)	397 (24.6)	0.671 (0.476, 0.945)		0.697 (0.493, 0.984)		0.693 (0.490, 0.981)	
Q3	64 (21.5)	431 (26.7)	0.581 (0.411, 0.822)		0.637 (0.448, 0.907)		0.661 (0.463, 0.944)	
Q4	72 (24.2)	419 (25.9)	0.673 (0.480, 0.943)		0.713 (0.506, 1.004)		0.730 (0.516, 1.032)	
Female								
Q1	26 (32.9)	158 (26.8)	1.000	0.642	1.000	0.670	1.000	0.602
Q2	22 (27.8)	162 (27.5)	0.825 (0.449, 1.517)		0.826 (0.446, 1.530)		0.813 (0.436, 1.517)	
Q3	16 (20.3)	130 (22.1)	0.748 (0.385, 1.454)		0.753 (0.382, 1.484)		0.722 (0.364, 1.431)	
Q4	15 (19.0)	139 (23.6)	0.656 (0.334, 1.288)		0.661 (0.334, 1.309)		0.638 (0.320, 1.269)	
$p_{interaction}$				0.310		0.382		0.576
Energy								
< 1636 kcal/d								
Q1	116 (58.6)	507 (46.4)	1.000	0.014	1.000	0.041	1.000	0.048
Q2	52 (26.3)	338 (31.0)	0.672 (0.472, 0.959)		0.703 (0.491, 1.005)		0.706 (0.493, 1.011)	
Q3	25 (12.6)	197 (18.0)	0.555 (0.349, 0.881)		0.592 (0.371, 0.947)		0.594 (0.370, 0.953)	
Q4	5 (2.5)	50 (4.6)	0.437 (0.171, 1.120)		0.470 (0.183, 1.211)		0.483 (0.187, 1.245)	
≥ 1636 kcal/d				0.903		0.942		0.964
Q1	4 (2.2)	19 (1.7)	1.000		1.000		1.000	
Q2	38 (21.2)	221 (19.9)	0.817 (0.263, 2.533)		0.795 (0.254, 2.486)		0.809 (0.257, 2.549)	
Q3	55 (30.7)	364 (32.7)	0.718 (0.235, 2.188)		0.729 (0.237, 2.245)		0.756 (0.244, 2.347)	
Q4	82 (45.8)	508 (45.7)	0.767 (0.254, 2.311)		0.767 (0.252, 2.332)		0.790 (0.258, 2.418)	
$p_{interaction}$				0.643		0.722		0.707
BMI								
< 18.5 kg/m^2				0.589		0.685		0.701
Q1	29 (31.5)	126 (31.5)	1.000		1.000		1.000	
Q2	27 (29.3)	95 (23.8)	1.235 (0.686, 2.223)		1.267 (0.694, 2.315)		1.274 (0.694, 2.338)	
Q3	14 (15.2)	81 (20.3)	0.751 (0.374, 1.507)		0.832 (0.408, 1.699)		0.846 (0.410, 1.744)	
Q4	22 (23.9)	98 (24.5)	0.975 (0.528, 1.802)		1.143 (0.601, 2.174)		1.151 (0.602, 2.201)	
18.5 - 23.9 kg/m^2				0.011		0.013		0.017
Q1	82 (32.9)	365 (23.1)	1.000		1.000		1.000	
Q2	54 (21.7)	399 (25.3)	0.602 (0.415, 0.874)		0.608 (0.418, 0.883)		0.607 (0.417, 0.883)	
Q3	57 (22.9)	409 (25.9)	0.620 (0.430, 0.895)		0.627 (0.432, 0.910)		0.636 (0.437, 0.927)	
Q4	56 (22.5)	407 (25.8)	0.612 (0.424, 0.885)		0.601 (0.414, 0.873)		0.609 (0.418, 0.888)	

Q1: protein intake < 47.6; Q2: protein intake 47.6 - 62.0; Q3: protein intake 62.0 - 78.2; Q4: protein intake > 78.2

†Model 1 was not adjusted

‡Model 2 was adjusted by age, gender, education, BMI and alcohol status

§Model 3 was further adjusted by physical activity, marital status, smoking status, GLU, TG, TCHO and HDL

Table 3. Stratified analyses for the association between protein intakes and odds of liver dysfunction among TB patients (cont.)

Stratified groups/	Liver dysfunction		Model 1		Model 2		Model 3	
Quantile of protein intake	Yes	No	*OR* (95% *CI*)	p_{trend}	*OR* (95% *CI*)	p_{trend}	*OR* (95% *CI*)	p_{trend}
BMI								
≥ 24 kg/m^2				0.529		0.641		0.534
Q1	9 (25.0)	35 (15.6)	1.000		1.000		1.000	
Q2	9 (25.0)	65 (29.0)	0.538 (0.196, 1.480)		0.557 (0.195, 1.590)		0.496 (0.166, 1.483)	
Q3	9 (25.0)	71 (31.7)	0.493 (0.180, 1.352)		0.546 (0.191, 1.561)		0.495 (0.170, 1.445)	
Q4	9 (25.0)	53 (23.7)	0.660 (0.239, 1.827)		0.737 (0.257, 2.112)		0.703 (0.240, 2.059)	
$p_{interaction}$				0.061		0.129		0.172
Alcohol status								
Yes				0.080		0.093		0.133
Q1	29 (42.6)	75 (26.8)	1.000		1.000		1.000	
Q2	14 (20.6)	71 (25.4)	0.510 (0.249, 1.043)		0.488 (0.237, 1.006)		0.477 (0.226, 1.007)	
Q3	12 (17.6)	55 (19.6)	0.564 (0.265, 1.203)		0.572 (0.263, 1.243)		0.608 (0.274, 1.348)	
Q4	13 (19.1)	79 (28.2)	0.426 (0.206, 0.880)		0.445 (0.213, 0.930)		0.475 (0.223, 1.013)	
No				0.112		0.199		0.282
Q1	91 (29.4)	451 (23.4)	1.000		1.000		1.000	
Q2	76 (24.6)	488 (25.4)	0.772 (0.555, 1.074)		0.795 (0.570, 1.110)		0.806 (0.577, 1.126)	
Q3	68 (22.0)	506 (26.3)	0.666 (0.475, 0.935)		0.693 (0.491, 0.978)		0.716 (0.506, 1.014)	
Q4	74 (23.9)	479 (24.9)	0.766 (0.549, 1.068)		0.790 (0.563, 1.108)		0.807 (0.574, 1.135)	
$p_{interaction}$				0.461		0.633		0.629

Q1: protein intake < 47.6; Q2: protein intake 47.6 - 62.0; Q3: protein intake 62.0 - 78.2; Q4: protein intake > 78.2

[†]Model 1 was not adjusted

[‡]Model 2 was adjusted by age, gender, education, BMI and alcohol status

[§]Model 3 was further adjusted

Table 4. Stratified analyses for the association between fat intakes and odds of liver dysfunction among TB patients

Stratified groups/	Liver dysfunction		Model 1		Model 2		Model 3	
Quantile of fat intake	Yes	No	*OR* (95% *CI*)	p_{trend}	*OR* (95% *CI*)	p_{trend}	*OR* (95% *CI*)	p_{trend}
Gender								
Male				< 0.001		< 0.001		< 0.001
Q1	100 (33.6)	350 (21.7)	1.000		1.000		1.000	
Q2	81 (27.2)	413 (25.6)	0.686 (0.496, 0.951)		0.721 (0.519, 1.001)		0.711 (0.511, 0.989)	
Q3	49 (16.4)	437 (27.1)	0.392 (0.271, 0.568)		0.425 (0.292, 0.617)		0.430 (0.296, 0.627)	
Q4	68 (22.8)	415 (25.7)	0.573 (0.408, 0.805)		0.626 (0.444, 0.883)		0.626 (0.442, 0.884)	
Female				0.245		0.257		0.275
Q1	24 (30.4)	171 (29.0)	1.000		1.000		1.000	
Q2	25 (31.6)	132 (22.4)	1.349 (0.737, 2.470)		1.362 (0.739, 2.510)		1.310 (0.705, 2.436)	
Q3	15 (19.0)	141 (23.9)	0.758 (0.383, 1.500)		0.765 (0.383, 1.530)		0.758 (0.378, 1.518)	
Q4	15 (19.0)	145 (24.6)	0.737 (0.373, 1.458)		0.751 (0.374, 1.508)		0.712 (0.352, 1.444)	
$p_{interaction}$				0.497		0.581		0.714
Energy								
< 1636 kcal/d				< 0.001		0.001		0.001
Q1	98 (49.5)	401 (36.7)	1.000		1.000		1.000	
Q2	64 (32.3)	336 (30.8)	0.779 (0.551, 1.102)		0.813 (0.572, 1.157)		0.816 (0.573, 1.164)	
Q3	27 (13.6)	265 (24.3)	0.417 (0.265, 0.656)		0.440 (0.278, 0.696)		0.439 (0.277, 0.696)	
Q4	9 (4.5)	90 (8.2)	0.409 (0.199, 0.841)		0.411 (0.199, 0.847)		0.407 (0.197, 0.842)	
≥ 1636 kcal/d				0.080		0.153		0.192
Q1	26 (14.5)	120 (10.8)	1.000		1.000		1.000	
Q2	42 (23.5)	209 (18.8)	0.927 (0.541, 1.589)		0.929 (0.540, 1.597)		0.903 (0.522, 1.562)	
Q3	37 (20.7)	313 (20.7)	0.546 (0.317, 0.940)		0.577 (0.333, 1.000)		0.583 (0.335, 1.015)	
Q4	74 (41.3)	470 (42.3)	0.727 (0.445, 1.186)		0.782 (0.475, 1.285)		0.757 (0.457, 1.253)	
$p_{interaction}$				0.601		0.565		0.534
BMI								
< 18.5 kg/m^2				0.174		0.222		0.193
Q1	35 (38.0)	121 (30.3)	1.000		1.000		1.000	
Q2	23 (25.0)	93 (23.3)	0.855 (0.473, 1.545)		0.847 (0.463, 1.550)		0.829 (0.450, 1.530)	
Q3	13 (14.1)	98 (24.5)	0.459 (0.230, 0.914)		0.483 (0.239, 0.977)		0.466 (0.228, 0.953)	
Q4	21 (22.8)	88 (22.0)	0.825 (0.450, 1.513)		0.936 (0.498, 1.759)		0.935 (0.493, 1.775)	
18.5 - 23.9 kg/m^2				0.003		0.004		0.004
Q1	77 (30.9)	356 (22.5)	1.000		1.000		1.000	
Q2	70 (28.1)	394 (24.9)	0.821 (0.577, 1.170)		0.810 (0.567, 1.159)		0.797 (0.556, 1.142)	
Q3	46 (18.5)	425 (26.9)	0.500 (0.338, 0.740)		0.499 (0.335, 0.742)		0.496 (0.333, 0.739)	
Q4	56 (22.5)	405 (25.6)	0.639 (0.440, 0.928)		0.643 (0.440, 0.939)		0.632 (0.432, 0.926)	

Q1: fat intake < 12.8; Q2: fat intake 12.8 - 20.1; Q3: fat intake 20.1 - 34.3; Q4: fat intake > 34.3

[†]Model 1 was not adjusted

[‡]Model 2 was adjusted by age, gender, education, BMI and alcohol status

[§]Model 3 was further adjusted by physical activity, marital status, smoking status, GLU, TG, TCHO and HDL

Table 4. Stratified analyses for the association between fat intakes and odds of liver dysfunction among TB patients (cont.)

Stratified groups/	Liver dysfunction		Model 1		Model 2		Model 3	
Quantile of fat intake	Yes	No	*OR* (95% *CI*)	p_{trend}	*OR* (95% *CI*)	p_{trend}	*OR* (95% *CI*)	p_{trend}
BMI								
≥ 24 kg/m^2				0.074		0.154		0.188
Q1	12 (33.3)	44 (19.6)	1.000		1.000		1.000	
Q2	13 (36.1)	58 (25.9)	0.822 (0.342, 1.975)		0.875 (0.345, 2.216)		0.867 (0.323, 2.324)	
Q3	5 (13.9)	55 (24.6)	0.333 (0.109, 1.018)		0.388 (0.122, 1.234)		0.382 (0.114, 1.286)	
Q4	6 (16.7)	67 (29.9)	0.328 (0.115, 0.939)		0.373 (0.126, 1.103)		0.374 (0.120, 1.169)	
$p_{interaction}$				0.061		0.142		0.178
Alcohol status								
Yes				0.078		0.089		0.060
Q1	30 (44.1)	79 (28.2)	1.000		1.000		1.000	
Q2	15 (22.1)	72 (25.7)	0.549 (0.273, 1.102)		0.545 (0.269, 1.102)		0.501 (0.242, 1.038)	
Q3	9 (13.2)	61 (21.8)	0.389 (0.172, 0.879)		0.388 (0.170, 0.885)		0.371 (0.160, 0.860)	
Q4	14 (20.6)	68 (24.3)	0.542 (0.266, 1.105)		0.562 (0.271, 1.166)		0.502 (0.236, 1.067)	
No				< 0.001		0.001		0.003
Q1	94 (30.4)	442 (23.0)	1.000		1.000		1.000	
Q2	91 (29.4)	473 (24.6)	0.905 (0.659, 1.241)		0.919 (0.668, 1.264)		0.918 (0.666, 1.265)	
Q3	55 (17.8)	517 (26.9)	0.500 (0.350, 0.714)		0.516 (0.360, 0.740)		0.530 (0.369, 0.762)	
Q4	69 (22.3)	492 (25.6)	0.659 (0.471, 0.923)		0.696 (0.495, 0.980)		0.704 (0.500, 0.993)	
$p_{interaction}$				0.526		0.694		0.682

Q1: fat intake < 12.8; Q2: fat intake 12.8 - 20.1; Q3: fat intake 20.1 - 34.3; Q4: fat intake > 34.3

[†]Model 1 was not adjusted

[‡]Model 2 was adjusted by age, gender, education, BMI and alcohol status

[§]Model 3 was further adjusted by physical activity, marital status, smoking status, GLU, TG, TCHO and HDL

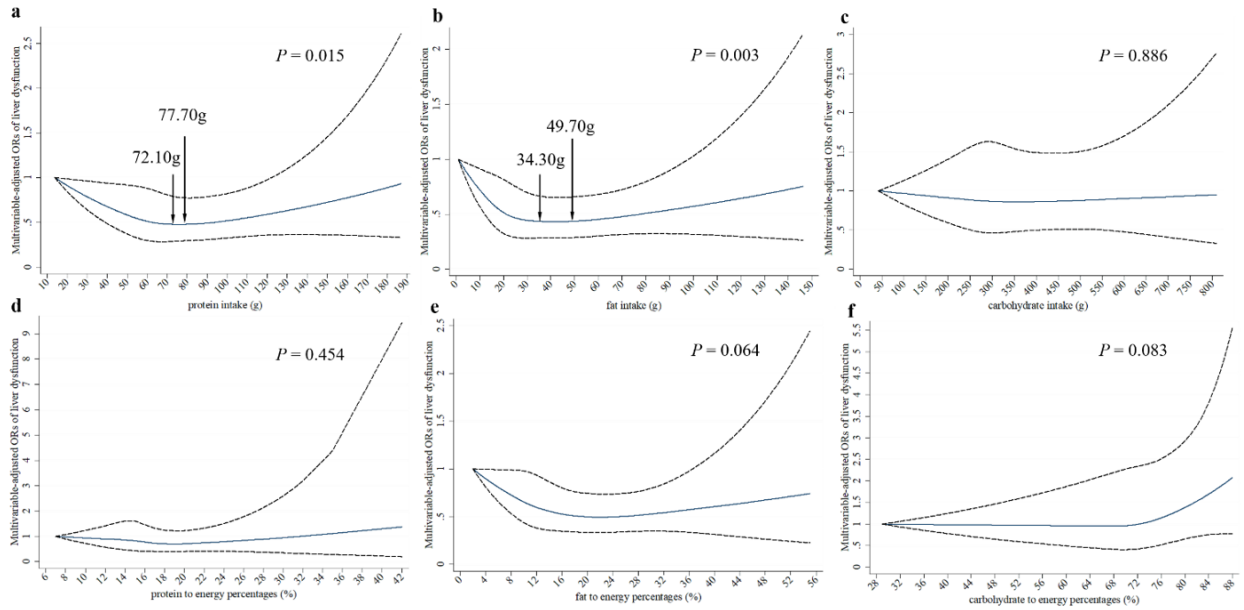


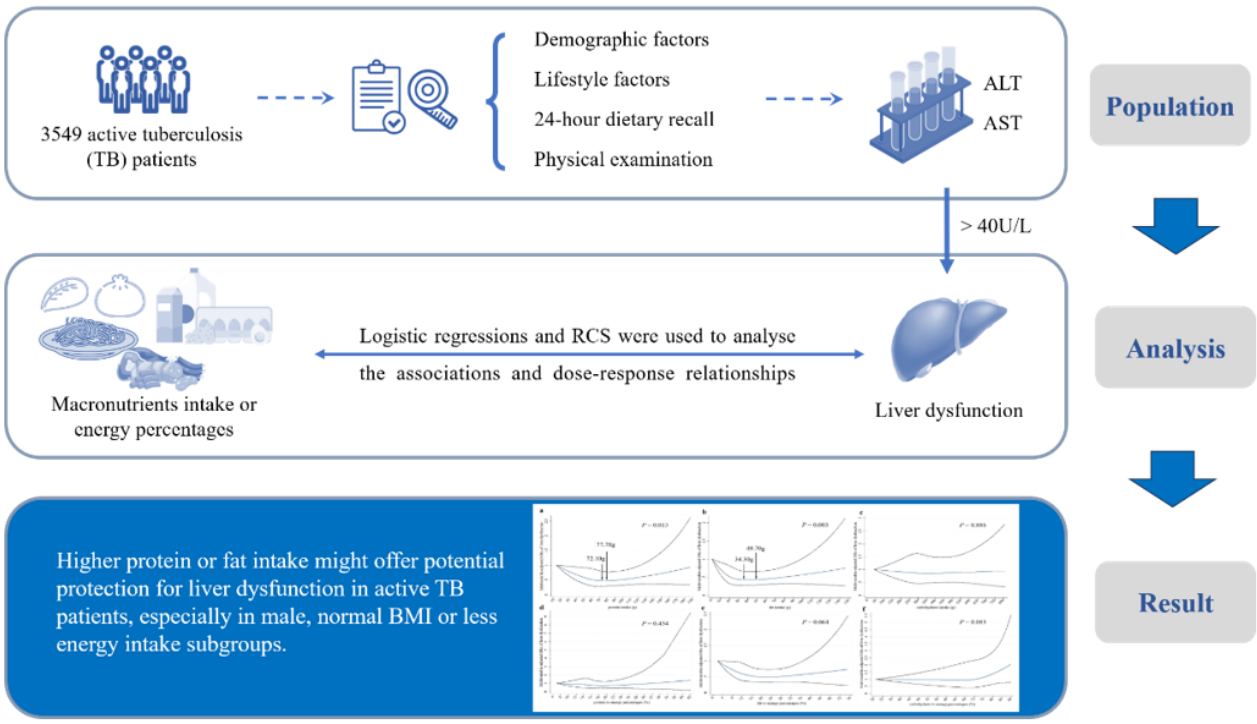
Figure 1. RCS model of the *OR*s of liver dysfunction with macronutrients intake (a: protein intake, b: fat intake, c: carbohydrate intake) or energy percentages (d: protein-to-energy percentages, e: fat-to-energy percentages, f: carbohydrate-to-energy percentages). Adjusted for age (years), gender (male, or female), BMI, education, alcohol drinking, physical activity, marital status, smoking status, GLU, TG, TCHO and HDL. The solid lines represent the *OR*s, and dashed lines represent the 95% *CI*s.

ble oils were the primary source of total fat, accounting for approximately ≥ 40%; animal oil and meat intakes accounted for approximately one-third or less of total fat.[40] On the other hand, the study's participants consumed low total dietary fat daily (median 20.10 and mean 27.5 g/day, respectively), which is significantly below the average 76.9 g of fat ingested daily by the rural Chinese population.[41] Moreover, dietary total fat intake of up to 90 g/day has a significant protective effect on HCC, considerably higher than the protective effect of dietary fat intake in liver function suggested by our RCS model.[42] This may be caused by differences in the eating habits of Chinese and Americans or different properties of the diseases. Research has shown that dietary fat provides 35% of total dietary energy for Americans and only 22% for Chinese.[43-45]

Regarding carbohydrates, only the unadjusted carbohydrate-to-energy percentages was positively associated with the incidence of liver dysfunction in our study. A few studies exist on the relationship between carbohydrate intakes or to energy percentages and the incidence of hepatic dysfunction, and the results of a study on cornstarch showed that a high-cornstarch diet (36%) significantly increased blood GLU and liver glycogen content of tilapia compared with a low (0) and medium-cornstarch (18%) diet.[46] Another research indicated that reducing the proportion of carbohydrate intake was also positive for controlling the disease in patients with NAFLD.[47] However, a meta-analysis of four cohort studies and three case-control studies showed that daily carbohydrate intake (*RR* = 1.09, *95% CI* = 0.84-1.32) was not significantly associated with the risk of HCC in the general population.[48] Additionally, higher intake of whole grains and dietary fibre was associated with lower mortality rates from liver cancer (*HR* Q5 vs Q1 = 0.69, *95% CI* = 0.53-0.90) and liver disease (*HR* Q5 vs Q1 = 0.37, *95% CI* = 0.29-0.48).[49] This could still be due to differences in the type of carbohydrate intake.

Furthermore, consensus exists that gradual weight loss through energy reduction improves serum liver enzymes, liver fat, liver inflammation, and the degree of fibrosis.[50] Previous studies have suggested that intrahepatic fat content loss and improved liver profile were achieved in adults with NAFLD by reducing energy intake and improving diet quality.[51,52] This was consistent with our results, which suggested an inverse association between dietary protein or fat intake and the odds of liver dysfunction in patients with lower energy intake.[53] We found a stronger inverse association between fat consumption and liver dysfunction risk in males than in females. This result was similar to the results of the previous study.[54] The possible reasons include the following: i) males had a higher fat intake than females due to eating out of home and dietary food intakes;[55-57] ii) the small sample size of females in this study (668 (25.9%)) might have led to a weakening of the final results; and iii) drinking is considerably higher in males than females.[58] However, our results showed that non-drinkers experience more significant benefits than drinkers regarding liver dysfunction in patients with TB, evaluated based on serum concentrations of ALT or AST. The evidence suggested that alcohol consumption played a role in all types of liver disease, such as excess alcohol related to liver mortality in 240 thousand adults in the United States. However, no apparent thresholds were observed for the impacts of alcohol consumption on the liver.[59,60] Our study was limited to determining whether the patients consume alcohol without specifying the exact quantity of intake.

The strengths of this study include the large-scale epidemiological study, which investigated the relationship between macronutrients intake and liver dysfunction before TB treatment and considered the effect of macronutrients to energy percentages on liver dysfunction among



Graphical abstract

patients with TB. We also conducted the RCS model among participants tested for cut-off values of macronutrients intake or energy percentages.

Our study had a few limitations, which are common to observational studies. Owing to the nature of cross-sectional studies, the temporal sequences may not be clear. However, this study could provide clues about the cause for the benefits of increasing nutritional education and supplementing appropriate protein and fat on the treatments and prognosis of TB patients with liver dysfunction. In addition, observational studies cannot be free from some residual confounding factors, although we adjusted for many potential risk factors of liver dysfunction, including age, sex, education, alcohol intake, physical activity, marital status, smoking status, GLU, TG, TCHO, and HDL. We focused only on pure nutrients, and no data on dietary types were considered. Finally, all participants in this study were patients with TB in China rural, which limits its generalisability.

Conclusion

In conclusion, our study demonstrated that higher protein or fat intake might protect against liver dysfunction in TB patients who were male, had normal BMI or had less energy intake, within a certain range. However, further studies, such as prospective cohort studies in various geographic regions, are warranted to confirm the results. Our study has important implications, providing constructive suggestions to public administrative departments regarding people's dietary habits.

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The content of the manuscript has previously appeared preprint (https://doi.org/10.21203/rs.3.rs-2669723/v1). However, we have revised, collated and analysed some of the data, which is inconsistent with the partial results of the submitted preprint.

CONFLICT OF INTEREST AND FUNDING DISCLOSURE

The authors declare no conflict of interest.

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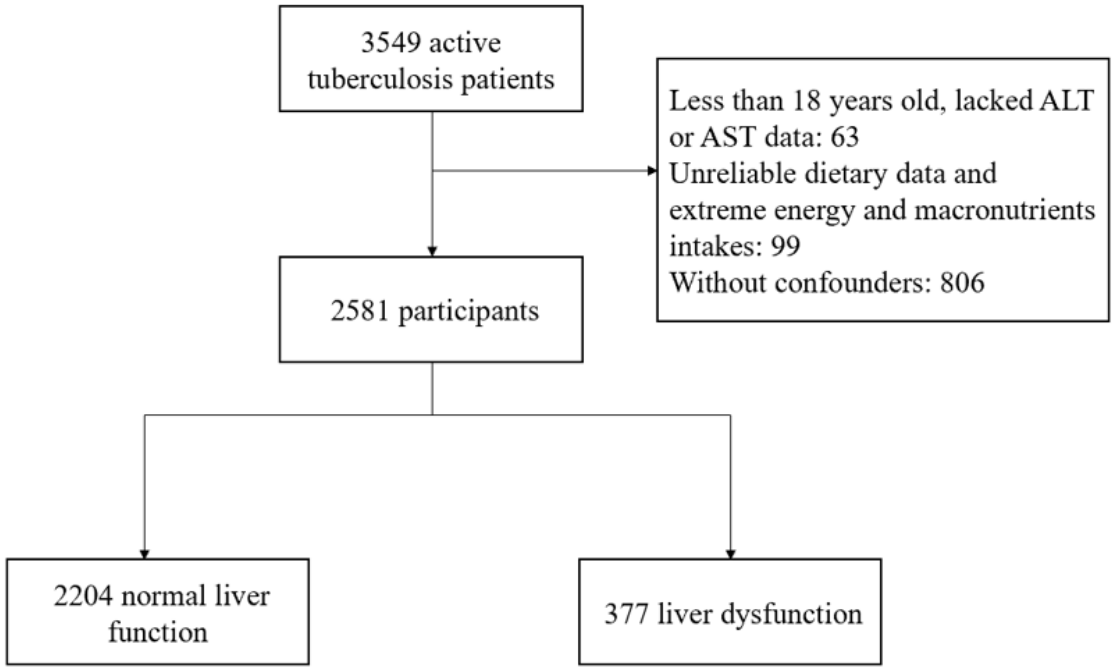
Supplementary Tables and Figures



Supplementary Figure 1. The cross-section flowchart

Supplementary Table 1. General characteristics of the participants by liver dysfunction among TB patients, n = 2581

	Liver dysfunction (N = 377)		Normal liver function (N = 2204)	
	N	Value†	N	Value†
ALT, (U/L)	377	40.00 (29.50)	2204	14.00 (13.00)
AST, (U/L)	377	42.00 (20.00)	2204	18.00 (12.00)
AST/ ALT	373	1.17 (1.75)	2160	1.25 (1.21)
GGT (U/L)	376	33.00 (32.00)	2201	22.00 (16.00)

ALT, alanine aminotransferase; AST, aspartate aminotransferase; AST/ ALT, aspartate aminotransferase/ alanine aminotransferase; GGT, gamma-glutamyl transpeptidase

†Numerical variables are presented as median (IQR).

Supplementary Table 2. Stratified analyses for the association between carbohydrate intake and odds of liver dysfunction among TB patients

Stratified groups/ Quantile of fat intake	Liver dysfunction		Model 1		Model 2		Model 3	
	Yes	No	*OR* (95% *CI*)	*p trend*	*OR* (95% *CI*)	*p trend*	*OR* (95% *CI*)	*p trend*
Gender								
Male				0.392		0.579		0.671
Q1	71 (23.8)	385 (23.8)	1.000		1.000		1.000	
Q2	79 (26.5)	374 (23.2)	1.145 (0.807, 1.627)		1.146 (0.805, 1.631)		1.142 (0.801, 1.628)	
Q3	65 (21.8)	420 (26.0)	0.839 (0.583, 1.207)		0.889 (0.616, 1.284)		0.918 (0.634, 1.329)	
Q4	83 (27.9)	436 (27.0)	1.031 (0.731, 1.458)		1.044 (0.735, 1.483)		1.070 (0.750, 1.527)	
Female				0.774		0.764		0.696
Q1	26 (32.9)	163 (27.7)	1.000		1.000		1.000	
Q2	21 (26.6)	172 (29.2)	0.765 (0.414, 1.414)		0.760 (0.410, 1.411)		0.724 (0.387, 1.357)	
Q3	19 (24.1)	141 (23.9)	0.845 (0.449, 1.591)		0.841 (0.445, 1.588)		0.812 (0.427, 1.543)	
Q4	13 (16.5)	113 (19.2)	0.721 (0.355, 1.464)		0.711 (0.347, 1.457)		0.692 (0.336, 1.426)	
p interaction				0.085		0.097		0.180
Energy								
< 1636 kcal/d				0.776		0.773		0.780
Q1	92 (46.5)	532 (48.7)	1.000		1.000		1.000	
Q2	82 (41.4)	443 (40.6)	1.070 (0.775, 1.479)		1.055 (0.762, 1.461)		1.055 (0.760, 1.463)	
Q3	24 (12.1)	117 (10.7)	1.186 (0.725, 1.940)		1.196 (0.729, 1.963)		1.194 (0.724, 1.970)	
Q4	-	-	-		-		-	
≥ 1636 kcal/d				0.267		0.247		0.222
Q1	5 (2.8)	16 (1.4)	1.000		1.000		1.000	
Q2	18 (10.1)	103 (9.3)	0.559 (0.182, 1.718)		0.523 (0.168, 1.625)		0.444 (0.141, 1.396)	
Q3	60 (33.5)	444 (39.9)	0.432 (0.153, 1.223)		0.385 (0.134, 1.105)		0.353 (0.122, 1.024)	
Q4	96 (53.6)	549 (49.4)	0.560 (0.200, 1.563)		0.474 (0.167, 1.344)		0.437 (0.152, 1.252)	
p interaction				0.729		0.329		0.362
BMI								
< 18.5 kg/m^2				0.170		0.148		0.159
Q1	26 (28.3)	104 (26.0)	1.000		1.000		1.000	
Q2	23 (25.0)	97 (24.3)	0.948 (0.507, 1.773)		0.899 (0.475, 1.704)		0.905 (0.469, 1.746)	
Q3	15 (16.3)	107 (26.8)	0.561 (0.281, 1.118)		0.559 (0.278, 1.127)		0.587 (0.289, 1.190)	
Q4	28 (30.4)	92 (23.0)	1.217 (0.666, 2.225)		1.281 (0.681, 2.410)		1.337 (0.705, 2.539)	
18.5 - 23.9 kg/m^2				0.778		0.625		0.674
Q1	62 (24.9)	397 (25.1)	1.000		1.000		1.000	
Q2	69 (27.7)	396 (25.1)	1.116 (0.771, 1.615)		1.123 (0.773, 1.631)		1.107 (0.761, 1.610)	
Q3	61 (24.5)	389 (24.6)	1.004 (0.687, 1.468)		1.014 (0.691, 1.489)		1.026 (0.697, 1.511)	
Q4	57 (22.9)	398 (25.2)	0.917 (0.624, 1.349)		0.869 (0.587, 1.286)		0.869 (0.584, 1.294)	

Q1: carbohydrate intake < 225; Q2: carbohydrate intake 225 - 291.8; Q3: carbohydrate intake 291.8 - 374.2; Q4: carbohydrate intake > 374.2

†Model 1 was not adjusted

‡Model 2 was adjusted by age, gender, education, BMI and alcohol status

§Model 3 was further adjusted by physical activity, marital status, smoking status, GLU, TG, TCHO and HDL

Supplementary Table 2. Stratified analyses for the association between carbohydrate intake and odds of liver dysfunction among TB patients (cont.)

Stratified groups/	Liver dysfunction		Model 1		Model 2		Model 3	
Quantile of fat intake	Yes	No	*OR* (95% *CI*)	p_{trend}	*OR* (95% *CI*)	p_{trend}	*OR* (95% *CI*)	p_{trend}
BMI								
≥ 24 kg/m^2				0.809		0.879		0.843
Q1	9 (25.0)	47 (21.0)	1.000		1.000		1.000	
Q2	8 (22.2)	53 (23.7)	0.788 (0.281, 2.208)		0.869 (0.301, 2.507)		0.789 (0.267, 2.329)	
Q3	8 (22.2)	65 (29.0)	0.643 (0.231, 1.789)		0.691 (0.241, 1.976)		0.619 (0.207, 1.848)	
Q4	11 (30.6)	59 (26.3)	0.974 (0.373, 2.545)		1.006 (0.373, 2.716)		0.891 (0.319, 2.487)	
$p_{interaction}$				0.162		0.264		0.346
Alcohol status								
Yes				0.163		0.160		0.170
Q1	20 (29.4)	65 (23.2)	1.000		1.000		1.000	
Q2	17 (25.0)	68 (24.3)	0.813 (0.391, 1.687)		0.766 (0.366, 1.606)		0.862 (0.401, 1.850)	
Q3	7 (10.3)	63 (22.5)	0.361 (0.143, 0.813)		0.365 (0.144, 0.929)		0.400 (0.154, 1.041)	
Q4	24 (35.3)	84 (30.0)	0.929 (0.472, 1.826)		0.961 (0.485, 1.906)		1.146 (0.557, 2.357)	
No				0.893		0.855		0.881
Q1	77 (24.9)	483 (25.1)	1.000		1.000		1.000	
Q2	83 (26.9)	478 (24.8)	1.089 (0.779, 1.522)		1.096 (0.783, 1.536)		1.071 (0.764, 1.502)	
Q3	77 (24.9)	498 (25.9)	0.970 (0.690, 1.362)		0.987 (0.701, 1.390)		0.985 (0.698, 1.391)	
Q4	72 (23.3)	465 (24.2)	0.971 (0.687, 1.372)		0.945 (0.664, 1.344)		0.928 (0.651, 1.324)	
$p_{interaction}$				0.151		0.084		0.069

Q1: carbohydrate intake < 225; Q2: carbohydrate intake 225 - 291.8; Q3: carbohydrate intake 291.8 - 374.2; Q4: carbohydrate intake > 374.2

[†]Model 1 was not adjusted

[‡]Model 2 was adjusted by age, gender, education, BMI and alcohol status

[§]Model 3 was further adjusted by physical activity, marital status, smoking status, GLU, TG, TCHO and HDL