BMC Public Health

RESEARCH Open Access

Abstract

Background Tuberculosis (TB) and diabetes mellitus (DM) are known to influence each other, with insulin resistance playing a pivotal role. The relationship between the triglyceride-glucose (TyG) index and its derived indices with the incidence of TB infection across varying glucose metabolic statuses is not well defined.

Methods This cross-sectional study utilized data from the 2011–2012 National Health and Nutrition Examination Survey. Weighted multivariable regression analysis was employed to explore the correlation between TyG and associated parameters with the incidence of TB infection within different categories of glucose metabolism. Interaction analyses and restricted cubic splines were utilized to assess potential heterogeneity in these associations and to explore the link between TyG and its derivatives with the occurrence of TB infection.

Results

†Min Qi and Runjuan Qiao contributed equally to this work.

*Correspondence:
Jian-Qing He
jianqing_he@scu.edu.cn

Full list of author information is available at the end of the article

Background

Fig. 1 Flowchart of the sample selection from National Health and Nutrition Examination Survey (NHANES) 2011–2012

circumference (cm), and BMI were recorded. Disease status, including diabetes, hypertension, and chronic kidney disease (CKD), was also documented. Fasting venous blood samples were collected and measured in the laboratory. e NHANES study protocol speci es that laboratory assessments requiring blood samples are conducted exclusively with participants aged 12 years and older. Eligible subjects must have fasted for a period of at least 8.5 h up to, but not exceeding, 24 h prior to the morning blood draw.

Assessment of TyG-related index

We selected the TyG index as the primary exposure variables, calculated using the formulation: Ln [triglycerides (mg/dl) × fasting glucose (mg/dl)/2]. Triglycerides concentration was measured via the Roche Modular *P* and Roche Cobas 6000 analyzers. Fasting plasma glucose levels were determined using the Roche/Hitachi Cobas C 501 analyzer based on the hexokinase-mediated reaction.

And TyG related parameters were calculated as follows: TyG-WC = TyG×waist circumference (cm), TyG-BMI = TyG×BMI (kg/m^2), WHtR = waist circumference (cm)/height (cm), TyG-WHtR = TyG×WHtR.

De nition of glucose metabolism status

DM was de ned by self-reported doctor-diagnosed diabetes, medication or insulin use for diabetes, or glycated hemoglobin (HbA1c) ≥ 6.5%, fasting blood glucose ≥ 7.0 mmol/L or 2 h oral glucose tolerance test (OGTT) glucose levels ≥ 11.1 mmol/L.

Impaired fasting glucose (IFG) was identi ed in participants whose fasting blood glucose levels were between 5.6 and 6.9 mmol/L but not meet the diagnostic criteria for diabetes and 2 h OGTT glucose levels < 7.8 mmol/L.

Impaired glucose tolerance (IGT) was de ned by fasting blood glucose levels < 5.6 mmol/L and 2 h OGTT glucose levels between 7.8 and 11.0 mmol/L, without fulfilling the criteria for a diabetes diagnosis.

Normal glucose tolerance (NGT) was de ned by fasting blood glucose levels < 5.6 mmol/L and 2 h OGTT glucose levels < 7.8 mmol/L.

Assessment of LTBI

For the assessment of LTBI, participants in the NHANES study underwent a skin test using a commercially available antigen, PPD, speci cally tubersol. A precise volume of 0.1 ml (equivalent to 5 international units) of the designated PPD was administered by trained NHANES technicians. ese technicians, blinded to the participant's medical history and potential TB contact, measured the skin reaction 46–76 h post-administration. Additionally, NHANES participants underwent an IGRA test, the QuantiFERON-TB Gold In-Tube (QFT-GIT), an FDA-approved method for detecting TB infection. e QFT-GIT utilized specialized blood collection tubes, including a Nil control tube (negative control), a TB Antigen tube, and a Mitogen tube (positive control), for the collection

Table 1 Weighted baseline characteristics in di□erent glucose metabolic groups

Variable	All participants	DM	IFG	IGT	NGT	*P* value
Age (year), mean (SD)	46.14(0.82)	58.47(0.80)	51.59(1.45)	53.88(1.19)	43.46(0.90)	< 0.0001
HbA1c, mean (SD)	5.63(0.02)	7.22(0.07)	5.65(0.03)	5.51(0.04)	5.38(0.01)	< 0.0001
BMI (kg/m2), mean (SD)	28.58(0.23)	32.97(0.34)	31.18(0.44)	29.12(0.54)	27.71(0.20)	< 0.0001
Glucose(mg/dl), mean (SD)	98.56(0.88)	148(L598 0 0 e))Tj ET EMC /P<</Lang(en-US)/MCID 4Tj 5(588)1a>>B)31.18(0.4404504 8				653.364013671

Table 2 Weighted baseline characteristics in TB infection and non-infection group

Variable, mean (SD)	All participants (*n* = 4823)

Table 3 Multiple logistic analysis of TyG and related parameters and the occurrence of TB infection in di□erent glucose metabolic status

TyG and related index	Glucose metabolic status	OR (95%CI)	*P* value	*P* for interaction
TyG				0.61
	DM	1.50(0.69,3.23)	0.28	
	IFG	57.10(1.17,2785.66)	**0.04**	
	IGT	2.91(0.41, 20.67)	0.27	
	NGT	2.17(1.40,3.35)	**0.002**	
TyG-WC				0.7
	DM	1.00(1.00,1.01)	0.48	
	IFG	1.02(1.00, 1.05)	**0.05**	
	IGT	0.99(0.98, 1.01)	0.49	
	NGT	1.01(1.00,1.01)	**0.01**	
TyG-BMI				0.49
	DM	1.01(0.98,1.03)	0.6	
	IFG	1.10(0.91, 1.32)	0.3	
	IGT	1.01(0.91, 1.12)	0.88	
	NGT	1.02(1.00,1.04)	**0.04**	
TyG-WHtR				0.8
	DM	2.00(0.69,5.86)	0.19	
	IFG	872.94(43.31,17592.72)	**< 0.001**	
	IGT	0.33(0.04, 2.81)	0.29	
	NGT	2.12(0.90,4.98)	0.08	

DM, diabetes mellitus; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; NGT, normal glucose tolerance

Adjusted variables: age, HbA1c, fasting glucose, albumin, creatinine, triglycerides, cholesterol, races, educational levels, alcohol consumption, CKD, hypertension

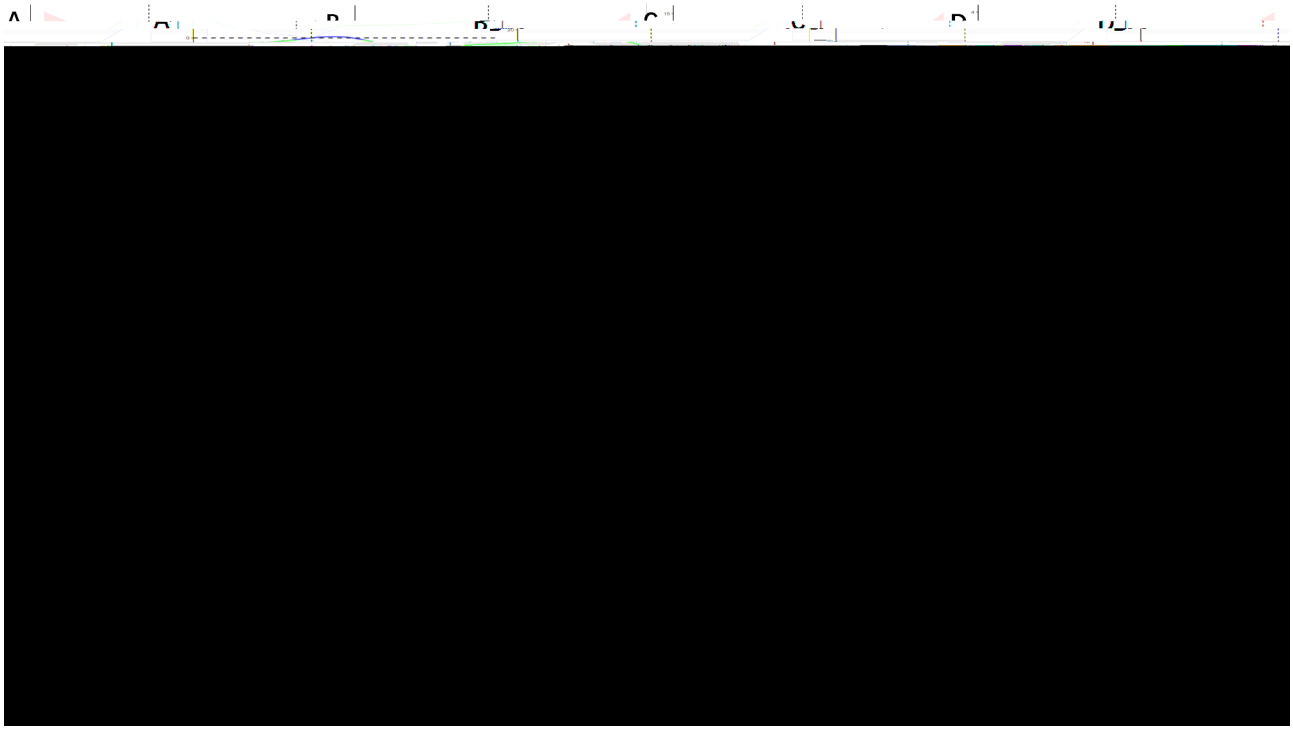

Fig. 2 Restricted cubic spline plot of TyG and its derivative parameters with the occurrence of tuberculosis infection under di□erent glucose metabolism statuses. Panels **A**–**D** represent the RCS curves of TyG index in individuals with di□erent glucose metabolic statuses, respectively. Similarly, panels **E**–**H** represent TyG-BMI, panels **I**–**L** represent TyG-WC, panels **M**–**P** represent TyG-WHtR

adjusting for confounding factors, including age, HbA1c, fasting glucose, albumin, creatinine, triglycerides, cholesterol, races, educational levels, alcohol consumption, CKD, hypertension, the relationship between the TyG index and its related parameters with the likelihood for TB infection was found to be approximately linear (all *p* values for non-linearity > 0.05).

Relationship of TyG index with the likelihood of TB infection

Our analysis revealed that the TyG index was signi - cantly elevated in the TB infection group (4.29 vs. 4.18, $P = 0.01$). To further investigate this association, we conducted a sensitivity analysis by converting the TyG index from a continuous to a categorical variable based on quartile distribution (Table 4). In the NGT group, the multivariable adjusted OR and 95%CI for TB infection across ascending TyG index quartiles were as follows: 1.00 (reference), 1.87 (1.24– 2.83), 1.89 (1.35–2.64), and 2.45 (1.31–4.60), respectively; In the IGT group, the adjusted OR for the TyG index quartiles were 1.00 (reference), 2.70 (0.90– 8.06), 29.42(4.72–183.19), and 761.33 (10.54–54999.02), respectively. No signi cant association between the TyG index and TB infection was observed in the DM and IFG groups in our study.

Discussion

In this cross-sectional analysis of 4823 adults, several signi cant associations between the TyG index and TB infection were identi ed, which are as follows: (1) in individuals with NGT, we observed a correlation between TB infection and levels of TyG, TyG-WC and TyG-BMI; (2) In IFG participants, an association was found between TB infection and TyG, TyG-WC, TyG-WHtR; (3) a higher TyG index was independently linked to an increased likelihood of TB infection in individuals with NGT and IGT. ese ndings are of considerable interest. e TyG index, along with its related parameters, as a predictive tool for TB infection in individuals with NGT or in a prediabetic state. However, this predictive value does not extend to those with established DM.

TB infection and hyperglycemia share a complex and interconnected relationship. Firstly, due to stress, prolonged in ammation [16], glucose metabolic status and IR caused by TB infection [17], many patients without previous DM history have been observed to develop hyperglycemia at the onset of TB treatment [18]. Secondly, a hyperglycemic state can impair immune function, which may manifest as compromised neutrophil activity, a suppressed antioxidant system, and diminished humoral immunity [19]. Such immunological dysregulation can increase susceptibility to infection. Moreover, DM is known to elevate the risk of TB infection [6], the development of multi-drug-resistant tuberculosis [20], and is correlated with adverse treatment outcomes [21], higher rates of treatment failure, and delayed sputum conversion [22].

Aside from DM, evidence suggests that elevated fasting plasma glucose levels also contribute to the burden of TB infection [23], which is consistent with our study that participants with TB infection had higher levels of HbA1c, fasting glucose, along with a greater prevalence of disrupted glucose metabolism. Pre-DM, marked by an intermediate state of hyperglycemia and characterized by IR, is increasingly recognized globally, particularly in TB endemic regions [6]. e prevalence of pre-DM is estimated about 15–30% [24, 25]. A prospective cohort study in South Africa, enrolled non-DM pulmonary tuberculosis patients, revealed an IR prevalence of 25.4% [26]. IR is associated with low-grade systemic in ammation, stemming from factors such as adipokine deregulation and adipose tissue in ammation, which signi cantly in uence in innate immunity [27]. is in ammation results in increased circulating levels of innate immune mark-

and mycobacterial growth restriction. However, an animal study noted that in the setting of IR, macrophage obtained a unique M2-like phenotype, enhancing glycolysis [29], which may dampen in ammatory responses and suppress the antibacterial actions necessary for pathogens clearance in polymicrobial sepsis. ese complicated e ects of IR on innate immunity can impact the elimination and reactivation of Mycobacteria tuberculosis (*M.tb*

investigate additional factors in uencing the relation-