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# Association between triglyceride glucose index-related indices with gallbladder disease: a prospective cohort study in rural China

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**This study aimed to examine the association between the triglyceride-glucose (TyG) index, TyG-BMI index, and gallbladder disease (GBD) among Uyghurs in the Xinjiang Production and Construction Corps (XPCC), offering insights for GBD prevention and management. A prospective cohort design was utilized, enrolling 12,794 Uyghur participants from XPCC. The cumulative GBD incidence across quartiles of TyG, TyG-BMI, and BMI categories was estimated using the Kaplan-Meier method. The Cox proportional hazard regression model assessed the association between TyG, TyG-BMI, and GBD incidence, while mediation analysis investigated TyG's potential mediating role in the relationship between BMI and GBD. Participants had a mean age of 37.68 ± 13.96 years, with 51.30% being male. Over a median follow-up of 6.00 years, 466 new GBD cases were identified, yielding a cumulative incidence of 4.3% and an incidence density of 7.68 per 1000 person-years. Women exhibited a higher cumulative incidence of GBD than men. The incidence of GBD gradually rises in both men and women with the increase of age. When the age exceeds 40, the incidence of GBD increases significantly. Following adjustments for gender, age, educational level, exercise frequency, diabetes, HDL-C, and LDL-C levels, individuals in the Q4 TyG index group demonstrated a significantly elevated GBD risk relative to the Q1 group (HR = 1.34, 95% CI:1.01–1.77). Similarly, GBD risk rose progressively across the Q2, Q3, and Q4 TyG-BMI index groups (HR = 1.97, 95% CI:1.23–3.16), (HR = 2.67, 95% CI:1.70–4.19), and (HR = 4.47, 95% CI:2.88–6.93), respectively. Overweight and obesity were also linked to a markedly greater GBD risk compared to normal weight (HR = 1.52, 95% CI:1.09–2.12) and (HR = 3.01, 95% CI:2.22–4.09). Among Uyghurs in the XPCC, elevated TyG and TyG-BMI indices were strongly associated with GBD risk, with TyG-BMI demonstrating the most pronounced association. Early TyG-BMI monitoring may aid in identifying individuals at high risk of developing GBD.**

**Keywords** TyG index, TyG-BMI index, Insulin resistance, Gallbladder disease, Cohort study

Gallbladder disease (GBD) is a prevalent digestive disorder with a significant global incidence, affecting 10% to 15% of adults in certain regions[1]. Common types of GBD include gallstones, cholecystitis, and gallbladder polyps. With improved living standards and dietary shifts, its incidence has shown a continuous upward trend, contributing to increasing disease burden and healthcare costs. Identifying and managing risk factors at an early stage is essential for effective prevention and treatment.

Insulin resistance (IR) is characterized by reduced insulin sensitivity and/or diminished insulin responsiveness[2], leading to metabolic disturbances such as dyslipidemia, hyperglycemia, and hypertension—factors that may elevate GBD risk[3–5]. The hyperinsulinemic-euglycemic clamp technique has been employed in prior studies to assess IR, but its complexity and cost limit its feasibility in large-scale epidemiological research. In 2008, Simental-Mendia et al. introduced the TyG index as a practical surrogate for IR, offering a straightforward

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and accessible calculation method[6,7]. Its validity as an alternative marker for IR has been widely recognized[8,9]. BMI is commonly used to assess overall obesity, and the combination of TyG and BMI has primarily been applied in metabolic and cardiovascular disease research, with limited exploration in the context of GBD.

The prevalence of GBD in the Xinjiang Uyghur population exceeds that observed in the Han ethnic group, exhibiting distinct ethnic disparities[10]. This study prospectively examined the association of TyG and TyG-BMI indices with GBD risk, offering insights to inform preventive and therapeutic strategies.

## Participants and methods

### Participants

The study employed a representative sampling method to select the 51 st Regiment of the Third Division of the XPCC, a region with a high concentration of Uyghur residents, as the survey site. A total of 12,794 Uyghurs aged ≥ 18 years who had resided in the 51 st Regiment for at least one year were randomly selected as survey participants. The baseline survey was conducted between August and September 2016, followed by four subsequent assessments in August to September 2019, August to September 2020, August to September 2021, and August to September 2022. The final outcome survey took place from August to September 2022, ensuring consistency across all assessment phases. Outcome events were systematically collected and evaluated at each follow-up stage. Among the 12,794 initial participants, 858 were excluded due to missing data, severe illness, loss of consciousness, inability to cooperate, unwillingness to participate, migration, or pregnancy. An additional 785 individuals were excluded due to GBD or post-cholecystectomy status. The loss to follow-up rate was 2.60% ($n = 331$). (Fig. 1)

### Data collection

(1) Questionnaire survey: A standardized training team administered a structured questionnaire to participants, including basic information, lifestyle habits, and personal and familial medical histories. (2) Physical examination: Anthropometric and physiological assessments adhered to standardized protocols, including measurements of height, weight, waist circumference, hip circumference, and blood pressure. Height and weight were obtained using a calibrated measuring instrument, while waist circumference was recorded with a flexible measuring tape. Blood pressure was assessed three times with an electronic sphygmomanometer [HBP-9020, Omron (China) Co., Ltd.], and the mean value was calculated. (3) For laboratory analyses, a 5 ml fasting venous blood sample was drawn from the antecubital vein in the morning, and biochemical markers such as FPG, TG, TC, LDL-C, and HDL-C were quantified using an OLYMPUS 2007 fully automated biochemical analyzer.

### Diagnostic criteria for GBD

*Diagnostic criteria for gallstones*

According to the 2016 EASL Clinical Practice Guidelines[11], routine abdominal B-ultrasound identified gallstones based on three characteristic findings: (1) a stable, hyperechoic mass within the gallbladder lumen; (2) a well-defined acoustic shadow posterior to the hyperechoic mass; (3) positional mobility of the hyperechoic mass, shifting according to gravitational changes. In cases where cholecystectomy was performed due to gallstones, the surgical report should explicitly state "cholecystectomy for gallstones."

*Diagnostic criteria for cholecystitis*

According to the Consensus on Diagnosis and Treatment of Chronic Cholecystitis and Gallstones in China (2018)[12], routine abdominal B-ultrasound examination identified characteristic features indicative of cholecystitis. (1) Acute cholecystitis: The gallbladder appeared enlarged with indistinct contours. The gallbladder wall exhibited diffuse thickening, characterized by hyperechoic bands interspersed with hypoechoic bands, producing a distinctive "double-sided shadow" effect. In cases of pus accumulation, the lumen contained sparse, or dense variably sized echogenic spots without acoustic shadowing or sedimentation bands. (2) Chronic cholecystitis: The gallbladder was enlarged, with a coarsely thickened wall and widened echogenic bands. Contractile function was impaired, and in severe cases, significant wall thickening was observed, along with mucosal cavity reduction, gallbladder atrophy, and filled stones. These features corresponded to the "wall-echo-shadow (WES) sign."

*Diagnostic criteria for gallbladder polyps*

The 2017 European Multi-Society Joint Guidelines defined diagnostic criteria based on routine abdominal B-ultrasound imaging[13]. Characteristic features included an elevated lesion arising from the gallbladder wall and extending into the lumen, devoid of acoustic shadowing, and demonstrating no positional mobility. The echogenicity predominantly appeared as medium to low, with an absence of posterior acoustic shadowing. The lesion may present with a pedunculated morphology or exhibit no pedunculated characteristics.

*Definition of related indicators*

(1) Hypertension[14]: Defined as SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg, a documented history of hypertension, or antihypertensive use within the past two weeks.

(2) Smoking[15]: A smoking habit of at least one cigarette per day, either continuously or cumulatively, for six months or longer.

(3) Alcohol Consumption[16]: Alcohol consumption at a frequency of at least once per week, either continuously or cumulatively, for a minimum of six months.

(4) BMI Classification ($kg/m^2$)[17]: Categories include underweight (< 18.5), normal weight (18.5–23.9), overweight (24.0–27.9), and obesity (≥ 28.0).

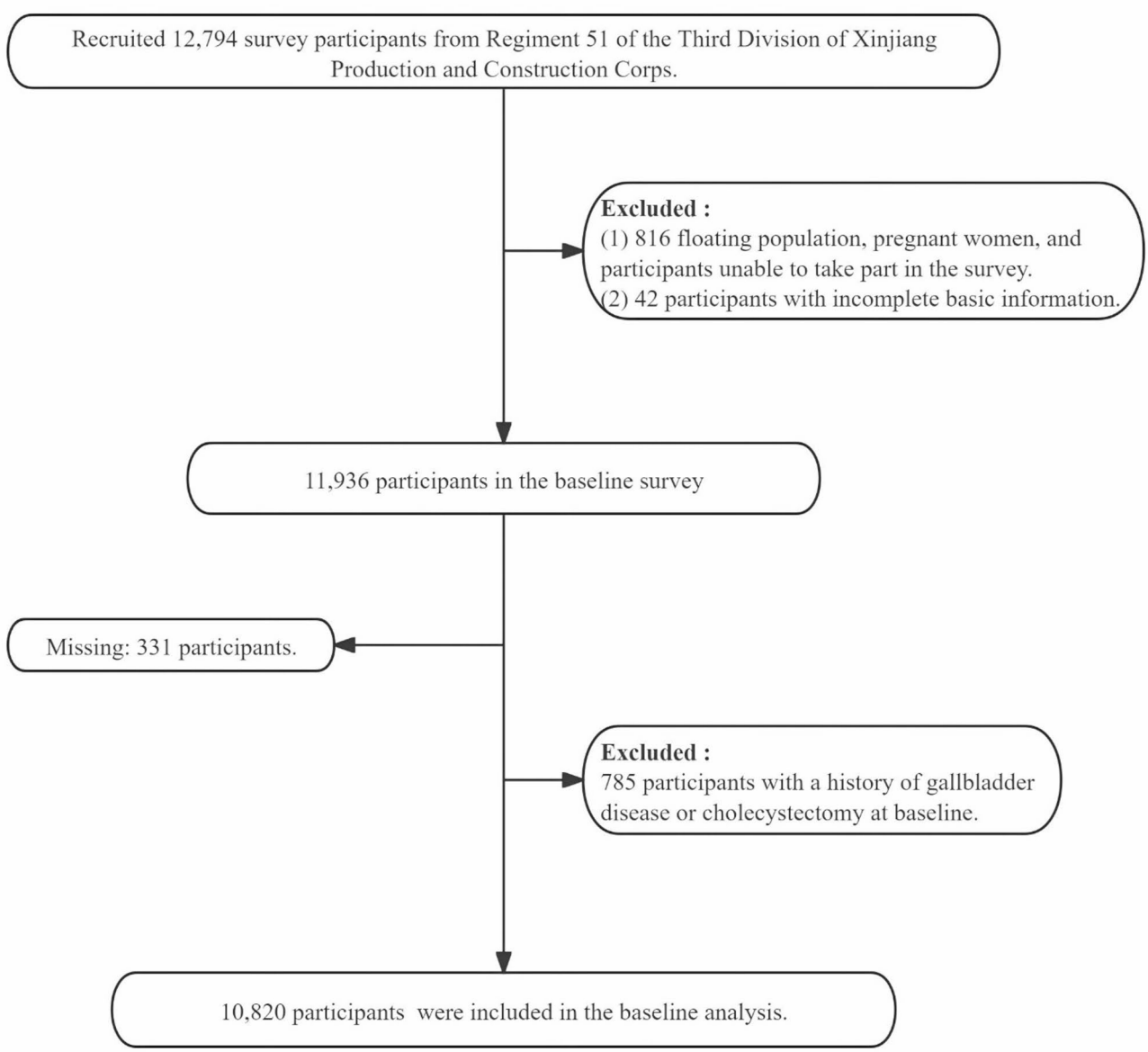


**Fig. 1**. Flow chart of the inclusion and exclusion criteria of the rural Xinjiang population. GBD, gallbladder disease.

(5) Exercise Frequency : Classified as regular exercise (≥ 3 sessions per week, ≥ 30 min per session), occasional exercise (< 3 sessions per week, < 30 min per session), or minimal exercise (< 1 session per week).

(6) Type 2 Diabetes[18]: Diagnosis based on medical records, insurance data, or physical examination findings, including FPG ≥ 7.0 mmol/L.

(7) Dyslipidemia[19]: HDL-C < 1.00 mmol/L or LDL-C ≥ 3.40 mmol/L.

*Calculation of related indicators*

(1) BMI = weight (kg)/height ($m^2$).

(2) TyG Index = ln [TG (mg/dL) × FPG (mg/dL)/2]

(3) TyG-BMI Index = TyG × BMI.

## Statistical analysis

Data analysis was conducted using SPSS 26.0 and R 4.4.2. Continuous variables were presented as mean ± standard deviation and compared using the independent sample t-test, while categorical variables were expressed as frequency and constituent ratio, with inter-group comparisons performed using the test. BMI was categorized into four groups based on the quartiles of the TyG index and TyG-BMI index: <18.5 (underweight), 18.5- (normal weight), 24.0- (overweight), and ≥ 28.0 (obese). The Kaplan-Meier method estimated the cumulative incidence of GBD events across these index groups, and the Log-rank test assessed differences in cumulative GBD incidence among quartile groups. The Cox proportional hazards regression model evaluated associations

between index groups and GBD risk, yielding HR and 95% CI. Covariates and traditional risk factors with $P < 0.05$ in the univariate analysis were incorporated into the multivariate Cox model.

The mediation effect of the TyG index on the relationship between BMI and GBD was assessed using the causal mediation analysis method developed by Imai et al.[20].Incorporating adjustments for confounding variables, including age, gender, educational level, exercise frequency, hypertension, HDL-C, and LDL-C. A statistically significant mediation effect ($P < 0.05$) indicated the TyG index functioned as a mediating variable in the BMI-GBD association. Statistical significance was defined as $P < 0.05$ across all analyses.

## Results

### Baseline characteristics

The study comprised 10,820 participants (mean age: 37.68 ± 13.96 years), of whom 51.3% were male. Significant differences were observed between the GBD and non-GBD groups concerning educational level, exercise frequency, smoking status, diabetes, hypertension, HDL-C, LDL-C, BMI, TyG index, TyG-BMI index, and BMI classification ($P < 0.001$). No statistically significant association was identified between GBD incidence and alcohol consumption history, family history of cardiovascular disease, or diabetes ($P > 0.05$) (Table 1).

### Incidence of GBD

The median follow-up duration was 6.00 years, during which 466 individuals experienced their first GBD event. The cumulative incidence reached 4.3%, with an incidence density of 7.68 per 1,000 person-years. Women exhibited a higher cumulative incidence of GBD than men. (Fig. 2). The incidence of GBD gradually rises in both men and women with the increase of age. When the age exceeds 40, the incidence of GBD increases significantly. (Fig. 2). A progressive rise in cumulative GBD incidence was observed across TyG and TyG-BMI quartiles. Specifically, the incidence rates across TyG quartiles (Q1–Q4) were 3.1%, 2.9%, 3.8%, and 7.52%, respectively, with an upward trend from Q3 onward. Similarly, TyG-BMI quartile (Q1–Q4) analysis revealed

| Variable | Gallbladder | | Total population($n$=10820) | $t/\chi^2$ value | $P$ value |
|---|---|---|---|---|---|
| | Yes($n$=466) | No($n$=10354) | | | |
| **Gender(%)** | | | | 81.21 | <0.001 |
| Male | 144(30.9) | 5408(52.2) | 5552(51.3) | | |
| Female | 322(69.1) | 4946(47.8) | 5268(48.7) | | |
| **Age(year), mean±SD** | 49.89±13.20 | 37.13±13.74 | 37.68±13.96 | −19.67 | <0.001 |
| **Educational Attainment (%)** | | | | 128.47 | <0.001 |
| Below Primary School | 321(68.9) | 9033(87.2) | 9354(86.5) | | |
| Primary/Junior High School | 130(27.9) | 1194(11.5) | 1324(12.2) | | |
| Senior High School and Above | 15(3.2) | 127(1.2) | 142(1.3) | | |
| **Exercise Frequency (%)** | | | | 14.72 | 0.001 |
| Regular Exercise | 41(8.8) | 1540(14.9) | 1581(14.6) | | |
| Occasional Exercise | 16(3.4) | 245(2.4) | 261(2.4) | | |
| Almost No Exercise | 409(87.8) | 8569(82.8) | 8978(83.0) | | |
| **Smoking (%)** | 46(9.9) | 1812(17.5) | 1858(17.2) | 18.25 | <0.001 |
| **Drinking (%)** | 15(3.2) | 539(5.2) | 554(5.1) | 3.62 | 0.057 |
| **FHCVD (%)** | 56(12.0) | 1291(12.5) | 1347(12.4) | 0.08 | 0.773 |
| **FHDM (%)** | 23(4.9) | 372(3.6) | 395(3.7) | 2.29 | 0.131 |
| **Diabetes (%)** | 84(18.0) | 569(5.5) | 653(6.0) | 123.46 | <0.001 |
| **Hypertension (%)** | 210(45.1) | 2773(26.8) | 2983(27.6) | 74.64 | <0.001 |
| **HDL-C(mmol/L) (%)** | 205(44.0) | 3456(33.4) | 653(33.8) | 22.44 | <0.001 |
| **LDL-C(mmol/L) (%)** | 105(22.5) | 1597(15.4) | 1702(15.7) | 17.00 | <0.001 |
| **BMI (kg/m$^2$) (%)** | | | | −15.30 | <0.001 |
| Normal Weight | 2(0.4) | 275(2.7) | 277(2.6) | | |
| Underweight | 54(11.6) | 3695(35.7) | 3749(34.6) | | |
| Overweight | 114(24.5) | 3320(32.1) | 3434(31.7) | | |
| Obese | 296(63.5) | 3064(29.6) | 3360(31.1) | | |
| **BMI (kg/m$^2$),mean±SD** | 30.52±6.17 | 25.87±4.63 | 26.07±4.80 | −20.88 | <0.001 |
| **TyG, mean±SD** | 9.02±0.98 | 8.60±0.71 | 8.61±0.73 | −12.44 | <0.001 |
| **TyG-BMI, mean±SD** | 276.77±69.81 | 223.36±49.08 | 225.66±51.31 | −22.49 | <0.001 |

**Table 1**. Baseline characteristics of xinjiang's rural population according to the incidence of gallbladder disease. HDL-C stands for high-density lipoprotein cholesterol; LDL-C stands for low-density lipoprotein; BMI stands for body mass index; TyG refers to triglyceride-glucose index; TyG-BMI refers to the product index of triglyceride-glucose and body mass index; FHCVD represents family history of cardiovascular disease; FHDM represents family history of diabetes mellitus.

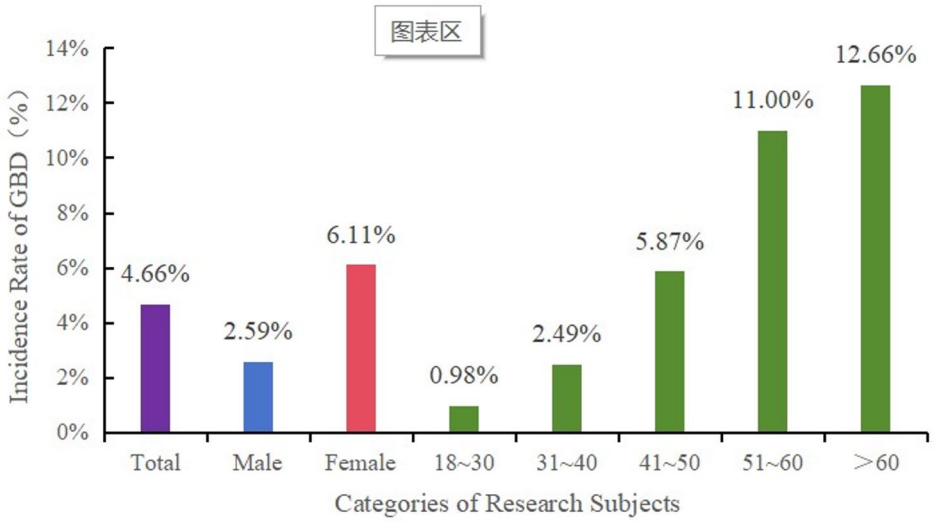


**Fig. 2**. Cumulative incidence Rates of Research Subjects by Different Genders and Ages.

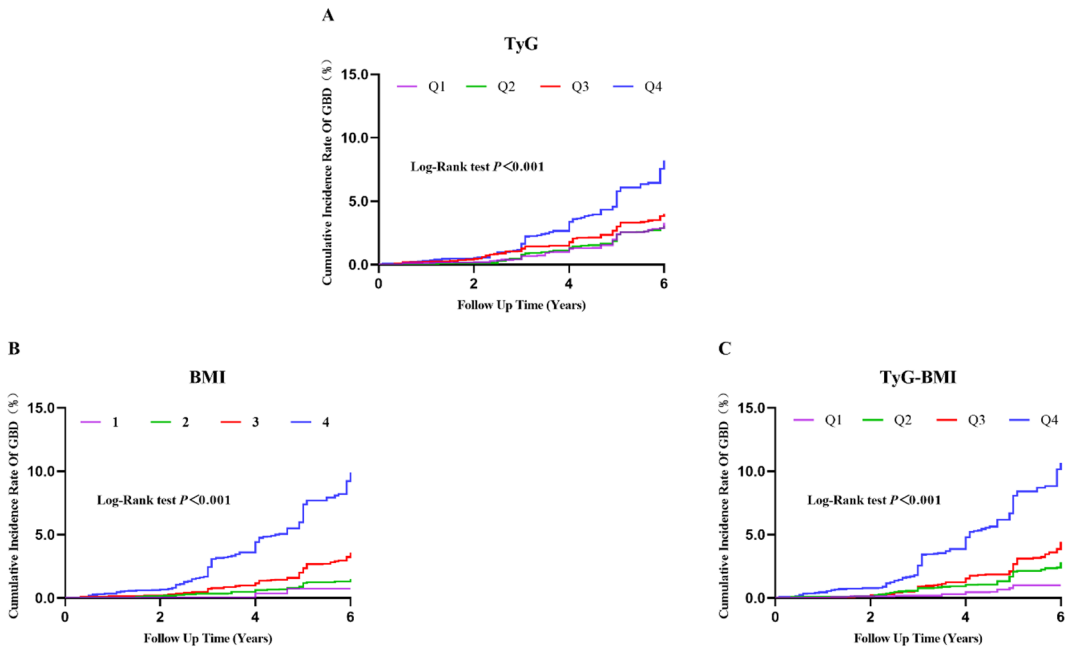


**Fig. 3**. The cumulative incidence rate of gallbladder disease for each index. TyG index,triglyceride-glucose index (A); BMI,body mass index (B); TyG-BMI,triglyceride glucose-body mass index (C); Q1,Quartile1;Q2,Quartile2;Q3,Quartile3;Q4,Quartile4; 1,Normal Weight;2,Underweight;3,Overweight;4,Obese.

cumulative incidence rates of 0.9%, 2.5%, 4.3%, and 9.5%, demonstrating a consistent increase.Among different BMI categories (underweight, normal weight, overweight, obese), the cumulative incidences of GBD are 0.88%, 1.44%, 3.31%, and 8.81% respectively. (Fig. 3)

## Association of TyG and TyG-BMI indices with the risk of GBD

The Cox regression model was employed to assess the link between both indices and GBD risk, stratified by quartiles and BMI categories. Univariate Cox analysis identified gender, age, educational level, exercise frequency, diabetes, HDL-C, LDL-C, TyG index, overweight, obesity, and TyG-BMI index as significant factors associated with GBD. Multivariate Cox proportional hazard regression analysis, adjusted for gender, age, educational level, exercise frequency, diabetes, HDL-C, and LDL-C, revealed a markedly elevated GBD risk in the TyG index Q4 compared to Q1. A progressive increase in GBD risk was observed across the Q2, Q3, and Q4 TyG-BMI index

| Variables | Model 1 | | Model 2 | | Model 3 | |
|---|---|---|---|---|---|---|
| | HR(95%CI) | *P* value | HR(95%CI) | *P* value | HR(95%CI) | *P* value |
| TyG index | | | | | | |
| Q1(≤8.14) | 1 | | 1 | | 1 | |
| Q2(8.14~) | 0.97(0.71~1.31) | 0.82 | 0.72(0.53~0.98) | 0.037 | 0.75(0.55~1.03) | 0.074 |
| Q3(8.59~) | 1.25(0.94~1.68) | 0.129 | 0.87(0.65~1.17) | 0.349 | 0.95(0.71~1.28) | 0.737 |
| Q4(≥8.99) | 2.56(1.98~3.31) | <0.001 | 1.48(1.14~1.93) | 0.004 | 1.34(1.01~1.77) | 0.04 |
| BMI | | | | | | |
| Normal Weight | 1 | | 1 | | 1 | |
| Underweight | 0.50(0.12~2.05) | 0.335 | 0.59(0.14~2.43) | 0.465 | 0.74(0.18~3.05) | 0.637 |
| Overweight | 2.41(1.74~3.33) | <0.001 | 1.66(1.19~2.30) | 0.003 | 1.52(1.09~2.12) | 0.012 |
| Obese | 6.87(5.14~9.18) | <0.001 | 3.59(2.65~4.85) | <0.001 | 3.01(2.22~4.09) | <0.001 |
| TyG-BMI index | | | | | | |
| Q1(≤188.15) | 1 | | 1 | | 1 | |
| Q2(188.15~) | 2.95(1.85~4.70) | <0.001 | 2.17(1.35~3.47) | 0.001 | 1.97(1.23~3.16) | 0.005 |
| Q3(218.99~) | 5.23(3.37~8.10) | <0.001 | 3.05(1.95~4.79) | <0.001 | 2.67(1.70~4.19) | <0.001 |
| Q4(≥255.92) | 12.18(8.01~18.50) | <0.001 | 5.53(3.58~8.54) | <0.001 | 4.47(2.88~6.93) | <0.001 |

**Table 2**. Cox proportional hazards regression Analysis. Model 1: Without adjustment for confounding factors;. Model 2: Adjusted for gender and age;. Model 3: On the basis of Model 2, adjusted for educational level, exercise frequency, diabetes, HDL-C level, and LDL-C level. (TyG index, triglyceride-glucose index; BMI, body mass index; TyG-BMI, triglyceride glucose-body mass index; HR Hazard Ratio).

| Variable | ADE | *P* Value | ACME | *P* Value | Total Effect | *P* Value | Proportion of Mediation Effect (%) |
|---|---|---|---|---|---|---|---|
| BMI | $1.43*10^{-4}$ | <0.001 | $2.33*10^{-5}$ | <0.001 | $1.66*10^{-4}$ | <0.001 | 13.70 |

**Table 3**. Mediation effect analysis of the association between TyG, BMI, and gallbladder disease Risk. ADE: Average Direct Effect; ACME: Average Causal Mediation Effect Proportion of Mediation Effect = Average Causal Mediation Effect/Total Effect

groups. Additionally, overweight and obesity were associated with a significantly higher GBD risk relative to normal weight (Table 2).

### Mediation effect of TyG index on the association between BMI and GBD

After adjusting for age, gender, educational level, exercise frequency, hypertension, HDL-C, and LDL-C, analysis indicated that the TyG index served as a potential mediating variable in this association, accounting for 13.70% of the total effect (Table 3).

## Discussion

This study represents the first prospective cohort analysis examining the association between TyG index, TyG-BMI index, and GBD in the Uyghur population within the XPCC in China. Multivariate Cox regression analysis identified TyG index and TyG-BMI index as independent risk factors for GBD. Compared with the Q1 group, the TyG index Q4 group exhibited a significantly higher risk of GBD. Similarly, an elevated risk of GBD was observed across the Q2, Q3, and Q4 groups of the TyG-BMI index, respectively. Overweight and obese individuals demonstrated a markedly higher risk of GBD compared to those with normal weight. These findings indicate that TyG-BMI may serve as a valuable reference metric for assessing GBD risk in this population.

IR is an independent risk factor for GBD, under IR conditions, hepatic lipid synthesis exhibits hyperactivation[21], with fatty acid synthase gene expression increasing by 2.4 to 2.9 times[22]. SREBP1c activation occurs independently of insulin signaling through ER stress, mTORC1, and FoxO1, leading to enhanced lipid synthesis[23] and a marked rise in hepatic plasma fatty acids and triglycerides. Excessive lipid accumulation in the liver activates specific protein kinases, which impair insulin receptor function and further aggravate IR[24]. IR represents a significant risk factor for GBD, contributing to compensatory hyperinsulinemia, excessive lipid synthesis, obesity, dysregulated lipid metabolism, inflammation, oxidative stress, and alterations in gut microbiota[25]. Among these, lipid metabolism disorders promote gallstone formation by disrupting cholesterol metabolism, while chronic inflammation and oxidative stress[26] compromise gallbladder epithelial integrity, inducing or exacerbating gallbladder inflammation. Gut microbiota imbalances may interfere with bile acid metabolism, further contributing to GBD pathogenesis[27]. Previously, the hyperinsulinemic-euglycemic clamp technique had been employed for IR diagnosis; however, its high cost and time-consuming nature limit its application to specialized research rather than large-scale epidemiological studies. In contrast, the TyG index offers a practical alternative, characterized by simplicity, low cost, and accessibility, making it well-suited for clinical assessments and extensive epidemiological investigations[7]. A multicenter cross-sectional study involving

a health examination cohort of over 500,000 participants identified a significant association between the TyG index and GBD risk[28]. Each unit increase in the TyG index corresponded to a 1.25-fold rise in GBD risk (95% CI: 1.13–1.37), while a standard deviation change was linked to a 1.24-fold increase (95% CI: 1.16–1.32). A similar cross-sectional study in the US reported a significant link between elevated TyG index levels and higher GBD prevalence[29]. Additionally, Chang Fu et al.[30] demonstrated a strong positive relationship between TyG-BMI, TyG-WC, and TyG-WHtR and GBD in the American adult population. A cohort study utilizing a public database further corroborated that a progressive rise in the TyG index was associated with an incremental increase in GBD risk[31]. This study represents the first prospective cohort analysis to establish a significant link between the TyG index, TyG-BMI index, and GBD risk in the rural Uyghur population of Xinjiang.

The findings of this study revealed a significantly higher cumulative incidence of GBD among adult females in the Uyghur rural population of Xinjiang compared to males. Extensive research, both domestically and internationally, has consistently demonstrated a greater susceptibility to GBD in females than in males[32–34], suggesting that gender disparities in GBD prevalence are independent of racial or geographical factors. Prior studies have attributed this pattern to the physiological influence of estrogen in women[35]. Estrogen levels exhibit considerable fluctuations due to age, menstrual cycle variations, and different physiological states[36]. Notably, pregnancy induces a sharp rise in estrogen levels, whereas menopause leads to a substantial decline. Evidence indicates that estrogen receptors are definitely expressed in the bile duct, with both estrogen receptor α and estrogen receptor β present in biliary cells[37]. Estrogen modulates cholesterol metabolism by activating estrogen receptor α and estrogen receptor β[38], inhibiting cholesterol 7-alpha hydroxylase (CYP7A1) expression through multiple signaling pathways[39–41], and reducing bile acid synthesis. This process lowers cholesterol solubility in bile, increases cholesterol saturation[42], and contributes to GBD onset. Additionally, estrogen elevates the cholesterol-to-phospholipid ratio in liver and gallbladder cell membranes, diminishing membrane fluidity and obstructing bile outflow[35], leading to cholestasis and further promoting GBD development. Its influence on gallbladder motility[43] further delays gallbladder emptying and weakens contraction function, impairing bile excretion and causing cholesterol stone formation. Furthermore, the high fertility rate among Uyghur women in Xinjiang is associated with an elevated GBD risk, as multiparity has been linked to increased susceptibility. The data in this study corroborate this association, demonstrating a significantly higher GBD incidence in women compared to men.

Prior research has demonstrated a marked increase in GBD incidence with advancing age[44], highlighting a distinct age-related risk pattern. The findings of this study align with those observed in previous investigations.

Obesity has been identified as a significant risk factor for GBD, with a well-established association between obesity and GBD onset[44]. IR contributes to weight gain through secondary hyperinsulinemia and serves as a fundamental mechanism underlying obesity-related disorders[45]. In this study, 63.5% of individuals with GBD were classified as obese. TyG demonstrated a partial mediation effect in the relationship between obesity and GBD, indicating that obesity elevates GBD risk by inducing IR, lipid metabolism disturbances, and chronic inflammation[46]. Epidemiological data highlight a concerning trend of increasing obesity rates in Xinjiang[47]. Greater attention should be directed toward obesity management, emphasizing early health education, structured dietary habits, proactive weight control, and preventive strategies to mitigate GBD onset and progression.

A key strength of this study lies in its large prospective cohort design, enabling the examination of the time-dependent relationship between TyG index, TyG-BMI index, and GBD. Additionally, this is the first investigation of the association between both indices and GBD within the Uyghur population of Xinjiang. However, several limitations should be acknowledged. The broad definition of GBD prevents a separate analysis of the association and relative strength of the links between gallstones, cholecystitis, and gallbladder polyps these indices. Moreover, the early diagnosis of GBD remains challenging due to its prolonged insidious onset and complex etiology. Extending the follow-up period is necessary to further validate these results. Furthermore, this study primarily focuses on the Uyghur population residing in rural areas of the XPCC. Variations in genetic background, diet, lifestyle, and cultural practices across different regions and populations may limit the generalizability of the findings.

## Conclusions

In summary, both the TyG index and TyG-BMI index exhibit significant associations with GBD risk in the Uyghur population of the XPCC. Compared to the TyG index, the TyG-BMI index demonstrates a stronger correlation with GBD. In large-scale epidemiological investigations, assessing the TyG-BMI index holds substantial value for the early identification of individuals at high risk for GBD.

## Data availability

The dataset used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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MHZ: Investigation, Conceptualization, Data curation, Methodology, Software, Visualization, Writing-original draft.JG: Conceptualization, Data curation, Investigation, Writing-original draft. JS: Conceptualization, Data curation, Investigation, Writing-original draft. ZHH: Conceptualization, Data curation, Investigation, Writing-review & editing.SLL: Conceptualization, Data curation, Investigation, Writing-review & editing.SJZ: Investigation, Methodology, Resources, Writing-review & editing.WHZ: Conceptualization, Data curation, Investigation, Writing-review & editing.JL: Conceptualization, Datacuration, Investigation, Writing-review & editing. JY: Conceptualization, Data curation, Investigation, Writing-review & editing.WXW: Conceptualization, Methodology, Supervision, Writing-review & editing.SXG: Investigation, Supervision, Writing-review & editing.XYP: Funding acquisition, Investigation, Project administration, Resources, Supervision, Writing-review & editing.

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## Declarations

## Competing interests
The authors declare no competing interests.

## Ethics approval and consent to participate
The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Institutional Ethics Review Board (IERB) of the First Affiliated Hospital of Shihezi University School of Medicine (IERB no.: SHZ2010LL01). Informed consent was obtained from all subjects involved in the study.

## Additional information
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