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Association between the combination of the triglyceride-glucose index and obesity-related indices with hyperuricemia among children and adolescents in China

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Abstract

Background The prevalence of hyperuricemia (HUA) among Chinese children and adolescents is a significant public health concern. Triglyceride-glucose (TyG) is recognized as a reliable biomarker in predicting insulin resistance, a condition associated with various metabolic disorders. Nevertheless, research on the association between TyG and its obesity-related indices with HUA among children and adolescents in China is limited.

Methods This study utilized data from the 2017 Chinese National Nutrition and Health Surveillance of Children and Lactating Mothers. TyG, TyG-BMI, TyG-WC, and TyG-WHtR were calculated based on participants' fasting blood glucose, triglycerides, and measured height, weight, and waist circumference. Multivariable logistic regressions were used to assess the relationships between TyG and its obesity-related indices with HUA in children and adolescents. Receiver Operating Characteristic curves were constructed to compare the predictive power of these indicators. Furthermore, we conducted a stratified analysis based on sex and age. Restricted cubic spline curves were used to illustrate the dose–response relationship of TyG, TyG-BMI, TyG-WC, and TyG-WHtR with HUA in children and adolescents. The sensitivity analysis included 1:1 propensity score matching with a caliper value of 0.02 and adjustments to the diagnostic criteria for HUA.

Results After adjusting for all covariables, multivariable logistic regression analysis indicated that the fourth quartiles of TyG (OR: 1.33, 95% CI: 1.14–1.54, $P < 0.001$), TyG-BMI (OR: 1.43, 95% CI: 1.14–1.79, $P = 0.002$), TyG-WC (OR: 1.76, 95% CI: 1.42–2.19, $P < 0.001$), and TyG-WHtR (OR: 1.92, 95% CI: 1.66–2.21, $P < 0.001$) were significantly associated with higher odds of HUA, compared to the lowest quartile. Stratified analyses identified a significant interaction between sex and TyG-BMI, TyG-WC, and TyG-WHtR. Compared to the first quartile, the highest quartile of TyG-BMI, TyG-WC and TyG-WHtR among male participants exhibited a stronger association with HUA(Male: TyG-BMI: OR = 1.82, 95%CI: 1.28–2.59; TyG-WC: OR = 1.87, 95%CI: 1.31–2.67; TyG-WHtR: OR = 2.07, 95%CI: 1.68–2.54).

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Conclusions This study identified a significant association between TyG and related obesity indices with HUA in children and adolescents in China. Furthermore, stronger associations of TyG-BMI, TyG-WC, and TyG-WHtR with HUA were observed, particularly in males.

Keywords Children, Adolescents, Triglyceride-glucose, Hyperuricemia

Introduction

Hyperuricemia (HUA) is a significant global public health concern, placing substantial economic burdens on patients and healthcare systems [1, 2]. HUA primarily arises from increased uric acid production and reduced renal excretion. Serum uric acid, a byproduct of purine metabolism, exhibits dual roles in human metabolism. Moderate serum uric acid levels can mitigate oxidative stress induced by free radicals and reactive oxygen species, demonstrating strong antioxidant properties [3]. Conversely, elevated serum uric acid levels are strongly associated with higher odds of gout, chronic kidney disease, metabolic syndrome, cardiovascular events, and mortality [2, 4, 5]. Previous studies have demonstrated that HUA in children is associated with metabolic disorders related to purines, genetic syndromes, and obesity [6–8]. Furthermore, a cohort study of US adolescents stratified participants by uric acid levels into quartiles and found a higher prevalence of metabolic syndrome in the top quartile [9]. Elevated childhood uric acid levels are linked to impaired renal urate excretion in individuals with metabolic syndrome [6]. In recent years, the prevalence of HUA has increased substantially, particularly among younger populations [10, 11]. HUA is frequently asymptomatic in its early stages, contributing to underdiagnosis [12]. Therefore, early detection of HUA in children and adolescents and implementing effective preventive strategies are essential.

Previous studies have demonstrated a significant correlation between insulin resistance (IR) and HUA [13, 14]. Additionally, IR may impair renal uric acid excretion in the proximal tubules, contributing to HUA [15, 16]. The hyperinsulinemic-euglycemic clamp (HIEC) method is the gold standard for quantifying and assessing IR [17]. It assesses insulin sensitivity by quantifying the glucose required to maintain euglycemia during continuous insulin infusion. However, it is technically complex, time-intensive, costly, and requires frequent blood sampling, significantly limiting its feasibility in clinical practice. The HOMA-IR index is regarded as a reliable marker for IR in adolescents and post-adolescents [18]. Simental-Mendia et al. reported that the TyG index demonstrated greater sensitivity than the HOMA-IR index in detecting IR in apparently healthy individuals [19]. The TyG index is calculated using the logarithm of the product of fasting triglycerides and glucose levels, which captures the combined effects of hypertriglyceridemia and hyperglycemia and is considered an essential predictor of IR in youth [20]. In states of IR, an increased level of hepatic gluconeogenesis causes increased hepatic glucose production, thereby raising blood glucose levels [21]. Elevated TG levels have been shown to induce IR by increasing hepatic free fatty acid production and disrupting skeletal muscle glucose metabolism [22]. In addition to the TyG index, which demonstrates both high sensitivity and specificity in predicting IR [23, 24], the incorporation of anthropometric indicators such as body mass index (BMI) and waist circumference (WC) has been shown to enhance predictive accuracy in both teenagers and adults [25]. Rilna et al. observed a significant association between high BMI and IR in pediatric populations [26]. Although BMI is a simple measure of weight relative to height and does not directly quantify body fat distribution, it still shows a significant positive correlation with visceral adipose tissue (VAT) content in children and adolescents ($r = 0.72$). Thus, BMI can serve as an indirect indicator of VAT [27]. Given that our study focused on children and adolescents, the waist-to-height ratio (WHtR) may be a more precise measure of abdominal obesity than WC alone [28]. Existing research on the relationship between the TyG index and HUA has primarily focused on adult populations in the United States and China [29, 30]. However, it is significant to note that Chinese adolescents display unique metabolic characteristics throughout their development. Research on the association between TyG-related obesity indices and HUA in Chinese children and adolescents remains limited. Consequently, we utilized a large cross-sectional study that integrated TyG with BMI, WC, and WHtR to examine the relationship between TyG and its obesity-related indicators with HUA in children and adolescents in China. In addition, it aims to provide an accessible and feasible tool for the early identification and prevention of HUA in Chinese children and adolescents.

Materials and methods

Study design and participants

This study utilized the data collected from the Chinese National Nutrition and Health Surveillance of Children and Lactating Mothers in 2017. Based on population distribution, a multi-stage stratified random sampling approach was employed to select 125 monitoring sites

across 31 provincial-level administrative regions in China, including provinces, autonomous regions, and municipalities under direct central government administration. Specifically, 5 monitoring sites were located in large cities, 57 in small and medium-sized cities, 50 in typical rural areas, and 13 in economically underdeveloped regions. At each monitoring site (city/district or county), two towns or streets were randomly selected as research locations, and two village or residential committees were further selected from each town or street as specific investigation units. Two hundred eighty children and adolescents aged 6 to 17 were enrolled at each monitoring site. This surveillance included students from grades 1–6, 7–8, and 10–11, covering ten classes, with 28 students selected for each class, ensuring a balanced sex distribution. Details of the study design are detailed in an earlier publication [31].

Since the participants in this study were children and adolescents aged 6–17 years, individuals younger than 6 years or older than 17 years were excluded from the study. Furthermore, participants with missing physical measurements such as height, weight, WC, or biochemical data such as triglyceride (TG) and fasting blood glucose (FBG) in the survey ($n = 630$) were excluded. Finally, participants with incomplete questionnaires ($n = 4{,}784$) were also excluded, resulting in a final study population of 10,167 participants (Fig. 1).

Ethical approval and consent to participate

Ethical approval for this study was granted by the Institute of Nutrition and Health Ethics Committee of the Chinese Center for Disease Control and Prevention (CDC) (Ethics number: 201614). Additionally, all participating provinces, autonomous regions, and

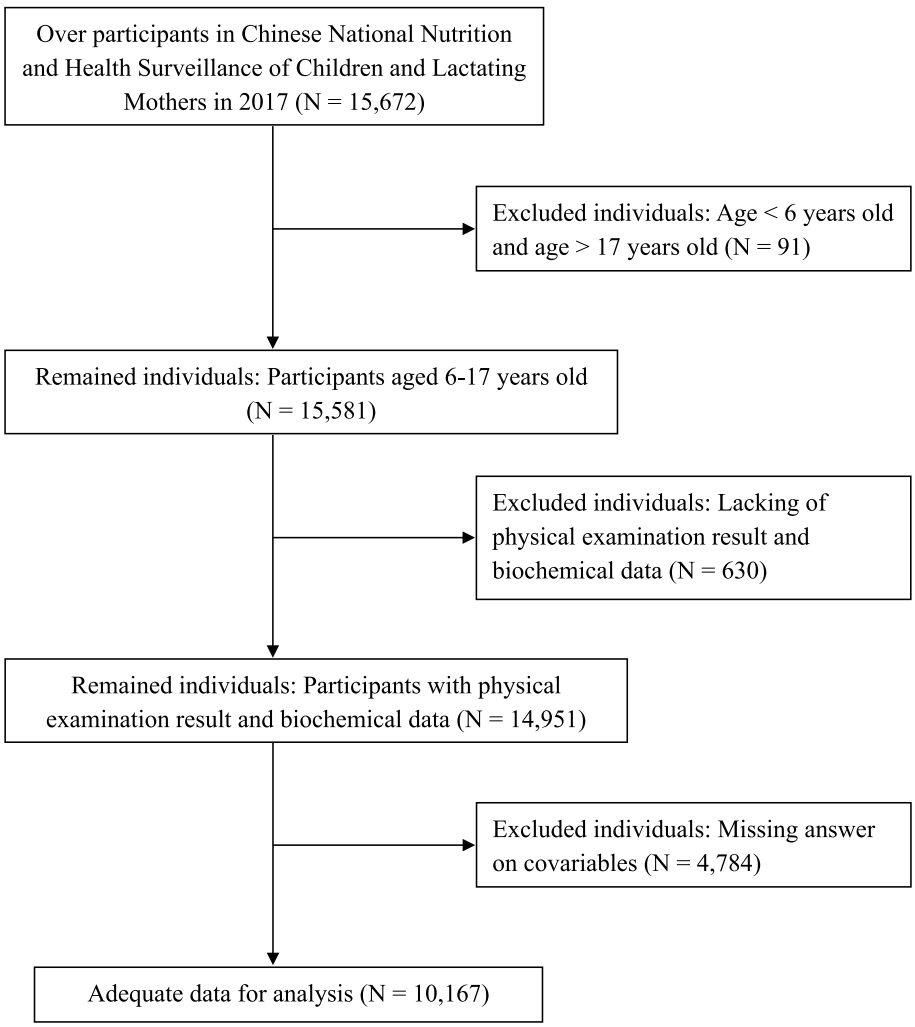

Fig. 1 The flow chart of participants in the study

municipalities independently conducted ethical review procedures. In this surveillance, written informed consent was obtained from the legal guardians of children aged 5–11, while for adolescents aged 12–17, consent was jointly provided by both the adolescents and their legal guardians. This process ensured compliance with ethical regulations.

Definitions and calculations of TyG-related obesity indices

The TyG-related obesity indices comprises the TyG, TyG-BMI, TyG-WC, and TyG-WHtR. These indices are calculated by detecting FBG and TG and measuring height, weight, and WC. Six milliliters of venous blood samples were collected after an overnight fast to measure FBG, TG, and other routine biochemical indicators. The provincial CDC coordinated centralized testing following the Chinese CDC's quality control and operational technical standards. Participants were instructed to remove their shoes, coats, and hats during the measurements. Height was measured using a standardized TZG height-measuring device at each monitoring site, with a maximum measurable height of 2.0 m and a minimum scale of 0.1 cm, validated by the quality inspection department. Weight was measured using a calibrated electronic scale with a minimum scale of 0.1 kg and a maximum capacity of 150 kg, which was also inspected by the quality inspection department. WC was measured using a standardized tape of the same brand and model, with a length of 1.5 m and a minimum scale of 0.1 cm.

The TyG-related obesity indices were calculated as follows:

(1) $TyG = LN(FBG(mg/dl) * TG(mg/dl)/2)$
(2) $BMI = Weight(kg)/(Height(m))^2$

$$TyG\text{-}BMI = TyG * BMI(kg/m^2)$$

(3) $TyG\text{-}WC = TyG * WC(cm)$
(4) $TyG\text{-}WHtR = TyG * WC(cm)/Height(cm)$

Definition of HUA

According to the criteria described in the Dietary Guidelines for Patients with HUA and Gout (WS/T 560–2017), men and women with serum uric acid levels of ≥ 420 μmol/L and ≥ 360 μmol/L, respectively, were classified as having HUA, while the remaining individuals were categorized into the non-HUA group.

Assessment of covariables

The following covariables were included in the study: sex, age, systolic blood pressure (SBP), diastolic blood pressure (DBP), total cholesterol (TC), creatinine (CREA), passive smoking, alcohol consumption, daily moderate-to-vigorous physical activity (MVPA) time, family histories of asthma, hypertension, and diabetes, as well as daily sugar-sweetened beverage (SSB) intake. Sex was categorized as either male or female. SBP and DBP were measured using an Omron HBP1300 electronic sphygmomanometer with a 0–300 mmHg measurement range and an accuracy of ± 1 mmHg. The arm cuff was wrapped around the upper arm, approximately 1–2 cm above the inside of the elbow joint. Measurements were taken three times, with a one-minute interval between each measurement, and the average value of these three measurements was recorded. TC and CREA analyses were performed on fasting venous blood samples. Passive smoking, alcohol consumption, daily MVPA time, daily SSB intake, and family histories of asthma, hypertension, and diabetes were assessed using standardized questionnaires administered by the Chinese CDC project team. Passive smoking and alcohol consumption were assessed by asking participants about the number of days per week they were exposed to secondhand smoke and whether they had consumed alcohol in the past 30 days, respectively. These responses were subsequently categorized as "No" or "Yes". MVPA time was defined as any daily activity causing temporary shortness of breath or noticeable perspiration, such as running, biking, swimming, playing, or performing household chores. Participants were asked to self-report their daily MVPA time. MVPA time was categorized into < 1 h, 1 to < 2 h, and ≥ 2 h. SSB intake were collected using the food frequency questionnaire method. Participants were asked to recall their consumption of foods listed in the table over the past week and to estimate the daily frequency and average quantity consumed. SSBs included fruit and vegetable drinks, carbonated beverages, tea beverages, milk-based drinks, vegetable protein drinks, cereal drinks, energy drinks, coffee, and other sugar-sweetened beverages. Participants were asked whether any of the family members, including parents and grandparents, had asthma, hypertension, or diabetes.

Statistical analyses

Continuous variables following a normal distribution are presented as mean ± standard deviation (x ± s), whereas non-normally distributed variables are reported as median (interquartile range, IQR). Categorical variables are expressed as percentages (n, %). The independent T-test and Pearson's chi-squared test were used to compare baseline characteristics of children and adolescents in the HUA and non-HUA groups. TyG, TyG-BMI, TyG-WC, and TyG-WHtR were categorized into quartiles. Multivariable logistic regression models were utilized to evaluate the association between TyG-related obesity

indices and HUA in children and adolescents. Model 1 was unadjusted; Model 2 adjusted for sex and age; Model 3 was further adjusted for SBP, DBP, TC, CREA, passive smoking, alcohol consumption, daily MVPA time, family histories of asthma, hypertension, and diabetes, as well as daily SSB intake, based on adjustments made in Model 2. Additionally, a stratified analysis was conducted according to sex and age. RCS curves were employed to investigate the dose–response relationships between TyG, TyG-BMI, TyG-WC, and TyG-WHtR with HUA in children and adolescents. In sensitivity analysis, a 1:1 PSM was conducted using the nearest neighbor method with a caliper value of 0.02. Standardized Mean Differences (SMD) were employed to evaluate the balance of covariables before and after PSM. The diagnostic criteria for HUA were adjusted to 5.5 mg/dL, 6 mg/dL, and 7 mg/dL [9].

All statistical analyses were performed using R software (version 4.3.2). A *P*-value of less than 0.05 was considered statistically significant.

Results

Baseline characteristics of the participants

A total of 10,167 participants were enrolled in this study, consisting of 5038 males (49.6%) and 5129 females (50.4%), with a mean age of 11.3 ± 3.2 years. The prevalence of HUA among participants was 22.8%. Participants in the HUA group demonstrated significantly higher TyG, TyG-BMI, TyG-WC, and TyG-WHtR values than those in the non-HUA group ($P < 0.001$). Compared to children and adolescents without HUA, those in the HUA group had significantly higher TG, FBG, age, WC, SBP, DBP, TC, and CREA levels. Furthermore, participants in the HUA group had significantly increased rates of passive smoking, alcohol consumption, and daily SSB intake exceeding 100 ml. There were no statistically significant differences observed between the non-HUA and HUA groups in terms of sex, MVPA time, family history of asthma, and family history of hypertension. Detailed baseline characteristics of the participants are presented in Table 1.

Association between TyG-related obesity indices and HUA

Multivariable logistic regression models were utilized to investigate the associations between TyG, TyG-BMI, TyG-WC, and TyG-WHtR with HUA in children and adolescents. After adjusting for all covariables, compared to the lowest quartile, the third and fourth quartiles of TyG were associated with HUA (OR(95%CI): 1.16 (1.00–1.35), $P = 0.045$; OR(95%CI): 1.33 (1.14–1.54), $P < 0.001$). The highest quartile of TyG-BMI was significantly associated with HUA (OR(95%CI): 1.43 (1.14–1.79), $P = 0.002$). Furthermore, the third and fourth quartiles of TyG-WC and TyG-WHtR were also significantly associated with HUA (TyG-WC: OR(95%CI): 1.52 (1.26–1.83), $P < 0.001$; OR(95%CI): 1.76 (1.42–2.19), $P < 0.001$; TyG-WHtR: OR(95%CI): 1.20 (1.04–1.39), $P = 0.015$; OR(95%CI): 1.92 (1.66–2.21), $P < 0.001$). (Table 2).

Figure 2 illustrates the predictive capabilities of TyG-related obesity indices for HUA odds in children and adolescents based on ROC curves. The area under the curve (AUC) values for TyG, TyG-BMI, TyG-WC, and TyG-WHtR indicated strong predictive performance for HUA odds in children and adolescents (TyG: 0.747, 95%CI: 0.735–0.758; TyG-BMI: 0.744, 95%CI: 0.733–0.756; TyG-WC: 0.746, 95%CI: 0.734–0.757; TyG-WHtR:0.737, 95%CI: 0.726–0.748).

Stratified analysis

This study further analyzed the relationship between the TyG-related obesity indices and HUA in children and adolescents, stratified by sex and age. Figures 3, 4, 5, and 6 depicts statistically significant interactions between sex and TyG-BMI, TyG-WC, and TyG-WHtR. Specifically, compared to the first quartile, the highest quartile of TyG-BMI, TyG-WC and TyG-WHtR among male participants demonstrated a stronger association with HUA(Male: TyG-BMI: OR = 1.82, 95%CI: 1.28–2.59; TyG-WC: OR = 1.87, 95%CI: 1.31–2.67; TyG-WHtR: OR = 2.07, 95%CI: 1.68–2.54. Female: TyG-BMI: OR = 1.71, 95%CI: 1.26–2.32; TyG-WC: OR = 1.84, 95%CI: 1.38–2.45; TyG-WHtR: OR = 2.06, 95%CI: 1.68–2.53). The relationship between TyG and HUA was observed exclusively in the highest quartile of female participants(OR = 1.41, 95%CI: 1.15–1.74). Furthermore, significant interactions between age and TyG-BMI were observed (6 ~ < 12: OR = 2.48, 95%CI: 1.73–3.56; 12 ~ 17: OR = 1.45, 95%CI: 1.01–2.08).

The dose–response relationships between TyG-related obesity indices and HUA based on RCS

RCS curves were used to examine the dose–response relationships between TyG, TyG-BMI, TyG-WC, TyG-WHtR, and HUA in children and adolescents. Based on the fully adjusted model, positive linear relationships were observed between TyG, TyG-BMI, TyG-WC, and TyG-WHtR with HUA (P-nonlinear value > 0.05)(Figures 7, 8, 9, and 10).

Sensitive analysis

To assess the stability of our findings, Table 3 presents a comparative analysis before and after PSM, showing that the standardized mean differences (SMD) of most covariables reduced to less than 0.1 after matching. After PSM, compared with those in the lowest quartile, TyG (OR(95%CI): 1.32 (1.10–1.58), $P = 0.003$),

Table 1 Baseline characteristics of participants

Variables	Total participants($n=10,167$)	non-HUA($n=7845$)	HUA($n=2322$)	*P* value
Male, n(%)	5038 (49.6)	3924 (50.0)	1114 (48.0)	0.084
Age, Mean ± SD	11.3 ± 3.2	10.9 ± 3.1	12.8 ± 2.8	< 0.001***
TG, Mean ± SD	0.9 ± 0.6	0.9 ± 0.7	1.0 ± 0.5	< 0.001***
FBG, Mean ± SD	5.2 ± 0.6	5.1 ± 0.5	5.3 ± 0.6	< 0.001***
TyG, Mean ± SD	8.1 ± 0.4	8.1 ± 0.4	8.2 ± 0.4	< 0.001***
TyG-BMI, Mean ± SD	151.1 ± 38.1	146.1 ± 35.7	167.9 ± 41.1	< 0.001***
TyG-WC, Mean ± SD	517.6 ± 101.1	502.4 ± 90.5	569.2 ± 116.8	< 0.001***
TyG-WHtR, Mean ± SD	3.5 ± 0.5	3.5 ± 0.5	3.6 ± 0.6	< 0.001***
WC, Mean ± SD	63.2 ± 11.1	61.8 ± 10.1	69.0 ± 12.4	< 0.001***
SBP, Mean ± SD	111.9 ± 11.7	111.1 ± 11.3	115.1 ± 12.6	< 0.001***
DBP, Mean ± SD	66.1 ± 8.7	65.8 ± 8.7	66.6 ± 8.5	< 0.001***
TC, Mean ± SD	4.0 ± 0.8	4.0 ± 0.8	4.1 ± 0.8	< 0.001***
CREA, Mean ± SD	53.9 ± 14.3	52.1 ± 12.3	62.4 ± 17.0	< 0.001***
Passive smoking, n(%)				< 0.001***
No	5702 (56.1)	4475 (57.0)	1227 (52.8)	
Yes	4465 (43.9)	3370 (43.0)	1095 (47.2)	
Alcohol consumption, n(%)				< 0.001***
No	8903 (87.6)	7066 (90.1)	1837 (79.1)	
Yes	1264 (12.4)	779 (9.9)	485 (20.9)	
Daily MVPA, n(%)				0.976
< 1 h	5204 (51.2)	4018 (51.2)	1186 (51.1)	
1 ~ < 2 h	3531 (34.7)	2725 (34.7)	806 (34.7)	
> = 2 h	1432 (14.1)	1102 (14.0)	330 (14.2)	
Family history of asthma, n (%)				0.417
No	9684 (95.3)	7465(95.2)	2219(95.6)	
Yes	483 (4.7)	380(4.8)	103(4.4)	
Family history of hypertension, n (%)				0.165
No	6477 (63.7)	5026(64.1)	1451(62.5)	
Yes	3690 (36.3)	2819(35.9)	871(37.5)	
Family history of diabetes, n (%)				0.023*
No	8779 (86.3)	6807(86.8)	1972(84.9)	
Yes	1388 (13.7)	1038(13.2)	350(15.1)	
Daily SSB intake, n (%)				< 0.001***
< 100 ml/d	6500 (63.9)	5196 (66.2)	1304 (56.2)	
≥ 100 ml/d	3667 (36.1)	2649 (33.8)	1018 (43.8)	

* $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$

TyG-BMI (OR(95%CI): 1.50 (1.14–1.98), $P = 0.004$), TyG-WC (OR(95%CI): 1.60 (1.23–2.09), $P < 0.001$), TyG-WHtR (OR(95%CI): 2.03 (1.71–2.42), $P < 0.001$) continued to show significant associations with HUA among children and adolescents Table 4. The diagnostic thresholds for HUA were lowered to 5.5 mg/dL, 6 mg/dL, and 7 mg/dL, respectively, and the associations remained consistent. (Tables S1-S3).

Discussion

This study utilized data from the 2017 Chinese National Nutrition and Health Surveillance of Children and Lactating Mothers to examine the association between TyG-related obesity indices and HUA in children and adolescents. Elevating TyG, TyG-BMI, TyG-WC, and TyG-WHtR were associated with higher odds of HUA.

Table 2 Associations between TyG-related obesity indices and HUA

Variables	Model 1		Model 2		Model 3	
	OR(95%CI)	*P* value	OR(95%CI)	*P* value	OR(95%CI)	*P* value
TyG						
Quartile 1	ref.					
Quartile 2	1.19 (1.04–1.37)	0.013*	1.10 (0.95–1.27)	0.205	1.04 (0.90–1.21)	0.575
Quartile 3	1.47 (1.29–1.69)	< 0.001***	1.31 (1.14–1.51)	< 0.001***	1.16 (1.00–1.35)	0.045*
Quartile 4	1.96 (1.71–2.23)	< 0.001***	1.77 (1.54–2.03)	< 0.001***	1.33 (1.14–1.54)	< 0.001***
TyG-BMI						
Quartile 1	ref.					
Quartile 2	1.75 (1.48–2.06)	< 0.001***	1.29 (1.09–1.53)	0.003**	1.15 (0.96–1.37)	0.126
Quartile 3	2.85 (2.44–3.34)	< 0.001***	1.58 (1.33–1.89)	< 0.001***	1.16 (0.96–1.40)	0.131
Quartile 4	5.24 (4.50–6.10)	< 0.001***	2.81 (2.37–3.33)	< 0.001***	1.43 (1.14–1.79)	0.002**
TyG-WC						
Quartile 1	ref.					
Quartile 2	1.62 (1.37–1.92)	< 0.001***	1.14 (0.96–1.36)	0.135	1.16 (0.97–1.39)	0.110
Quartile 3	3.10 (2.65–3.62)	< 0.001***	1.68 (1.41–2.01)	< 0.001***	1.52 (1.26–1.83)	< 0.001***
Quartile 4	5.38 (4.62–6.26)	< 0.001***	2.81 (2.36–3.35)	< 0.001***	1.76 (1.42–2.19)	< 0.001***
TyG-WHtR						
Quartile 1	ref.					
Quartile 2	1.02 (0.89–1.17)	0.744	1.06 (0.92–1.23)	0.392	1.04 (0.89–1.20)	0.638
Quartile 3	1.16 (1.01–1.33)	0.038*	1.24 (1.08–1.43)	0.003**	1.20 (1.04–1.39)	0.015*
Quartile 4	1.97 (1.73–2.24)	< 0.001***	2.10 (1.84–2.41)	< 0.001***	1.92 (1.66–2.21)	< 0.001***

Model 1 unadjusted;

Model 2 adjusted for sex and age;

Model 3 adjusted for sex, age, SBP, DBP, TC, CREA, passive smoking, alcohol consumption, daily MVPA, family history of asthma, family history of hypertension, family history of diabetes, and daily SSB intake

* $P < 0.05$; **$P < 0.01$; ***$P < 0.001$

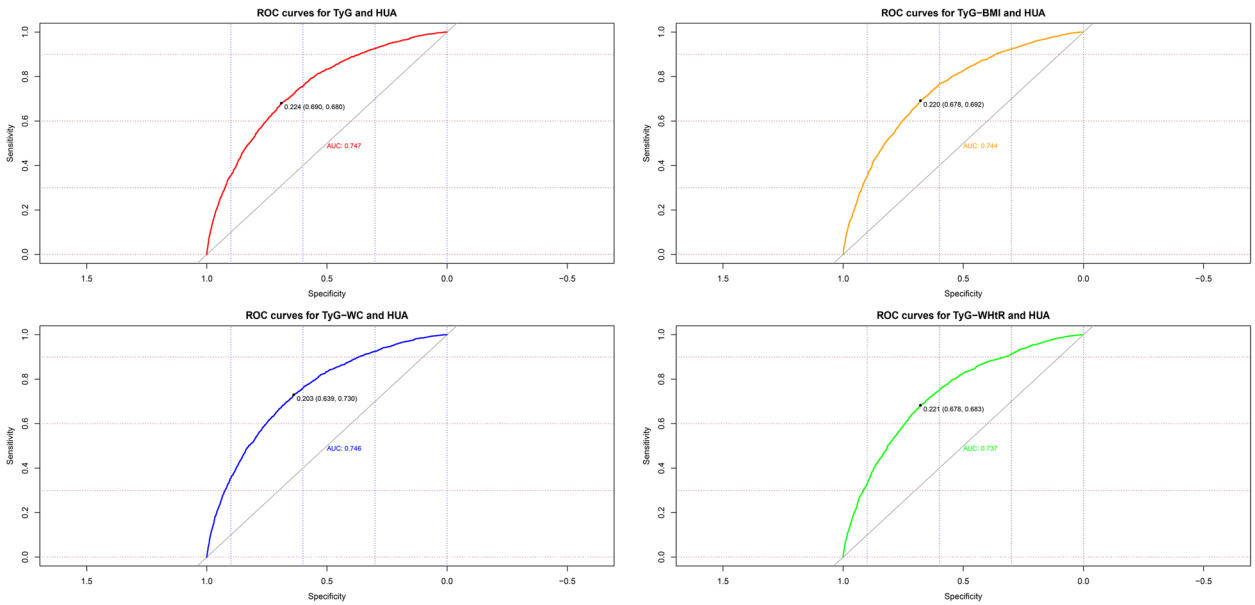

Fig. 2 The receiver-operating characteristic curve of TyG-related obesity indices for predicting HUA

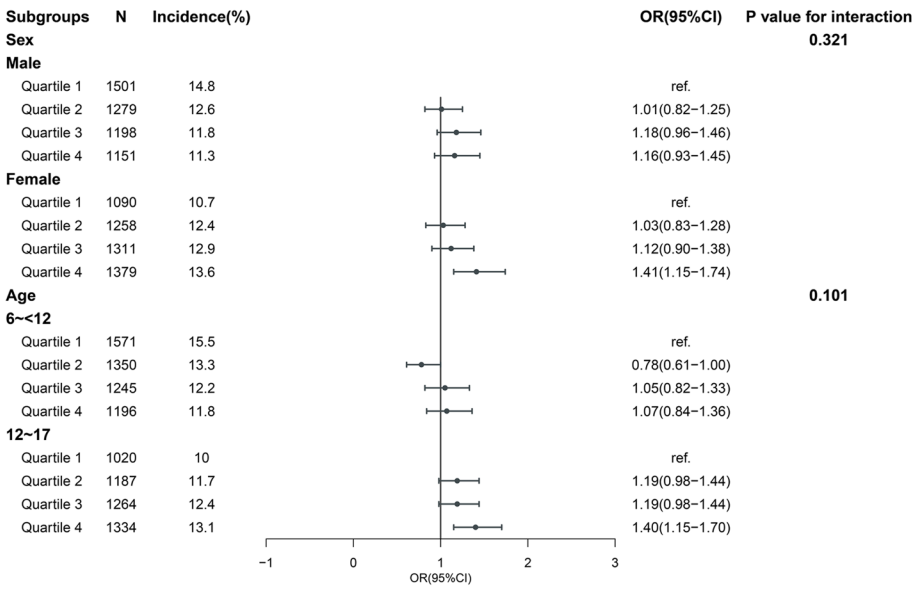

Fig. 3 OR forest map of HUA in children and adolescents in stratified analysis (TyG group)

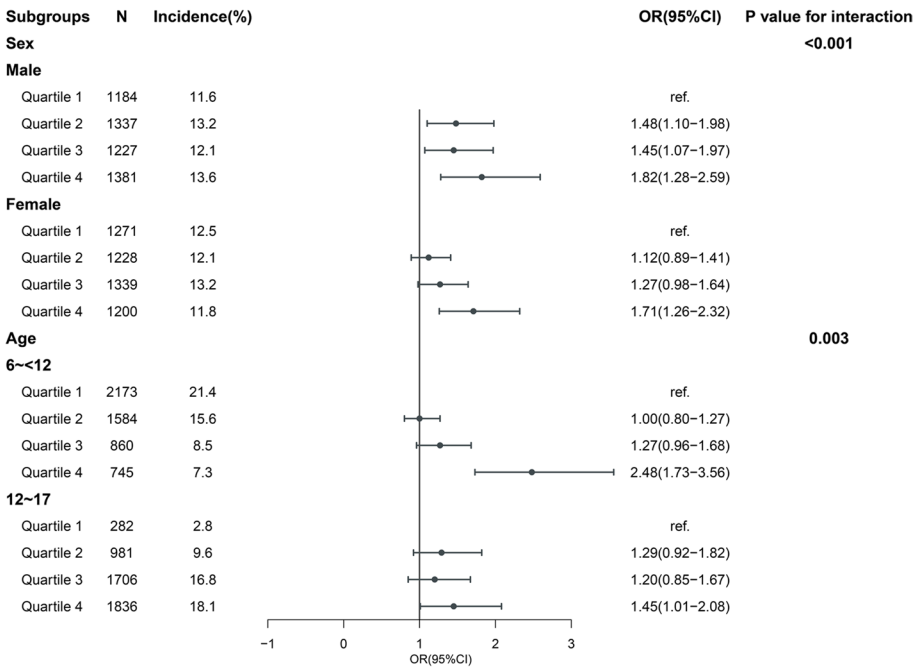

Fig. 4 OR forest map of HUA in children and adolescents in stratified analysis (TyG-BMI group)

Stratified analysis further revealed that males exhibited higher odds of HUA.

The prevalence of HUA among children and adolescents varied geographically, with reported rates of 30.2% in the United States [8] and 9.4% in South Korea [32]. This study determined that the prevalence of HUA among children and adolescents was 22.8%, closely aligning with findings from prior Chinese studies [33, 34]. A recent study reported an overall prevalence of HUA of 55.12% (8766/15,739) among children and adolescents receiving hospital treatment. High prevalence of HUA may be attributed to the adoption of lower diagnostic thresholds used for HUA [35]. However, most studies used varying diagnostic thresholds for HUA across

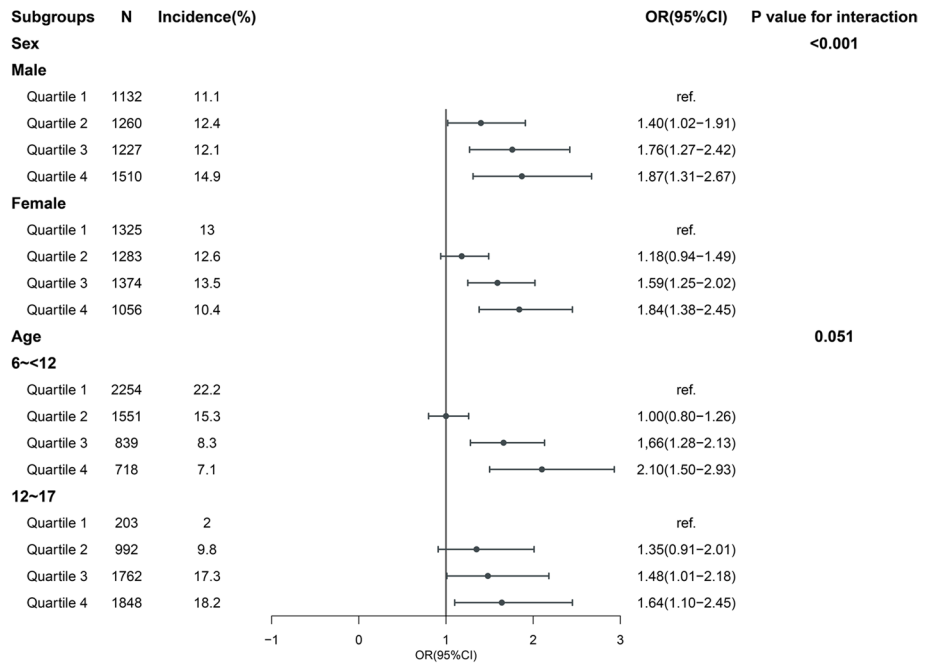

Fig. 5 OR forest map of HUA in children and adolescents in stratified analysis (TyG-WC group)

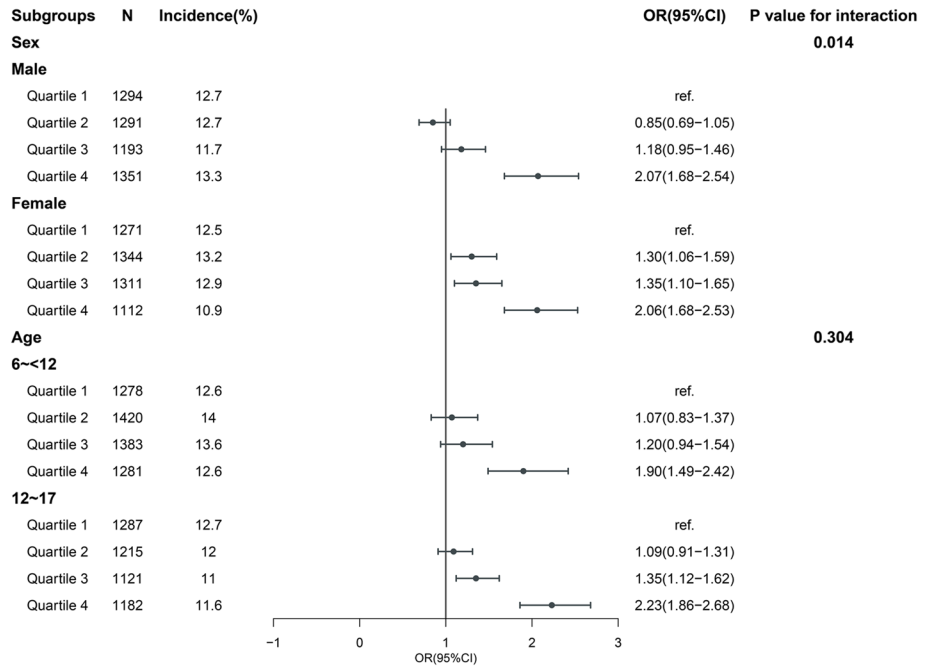

Fig. 6 OR forest map of HUA in children and adolescents in stratified analysis (TyG-WHtR group)

diverse populations, and no universally accepted diagnostic criteria for HUA in children have been established. Accordingly, the sensitivity analysis adjusted the diagnostic thresholds to 5.5 mg/dL, 6 mg/dL, and 7 mg/dL, respectively, with consistent results.

Numerous studies have examined the association between TyG and HUA across various populations. Previous research has reported a significant positive correlation between TyG levels and HUA in hypertensive adults, with the OR of HUA increasing by 104% for each

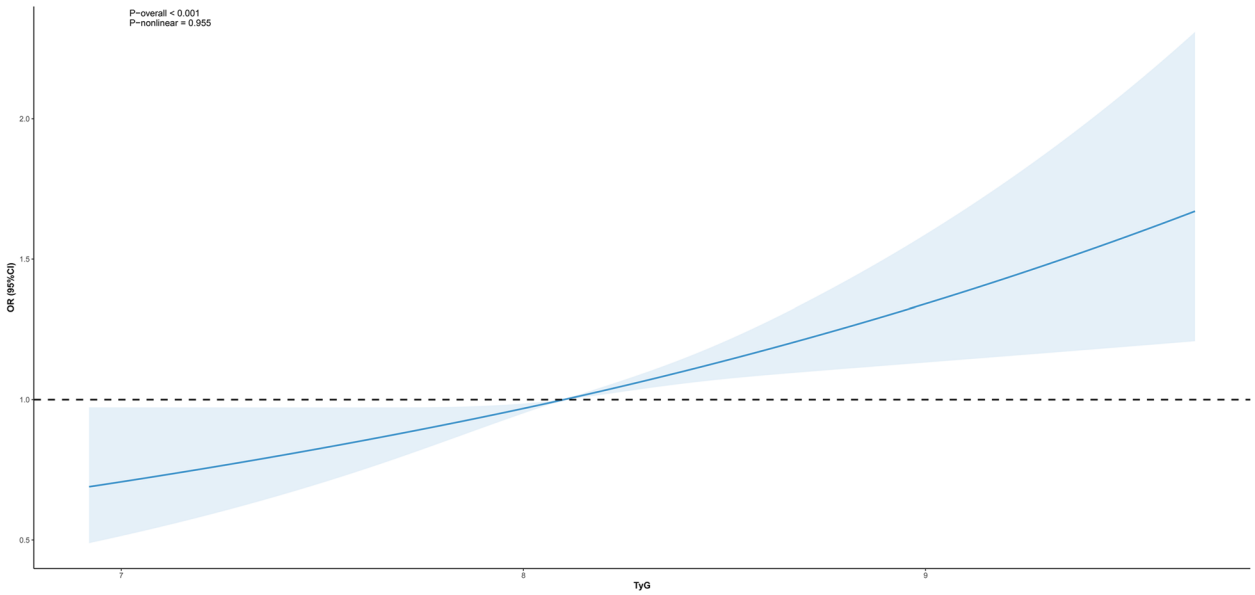

Fig. 7 RCS linear regression analysis of TyG and HUA (The blue shaded sections represent 95% confidence intervals; the dashed line represents that OR is 1)

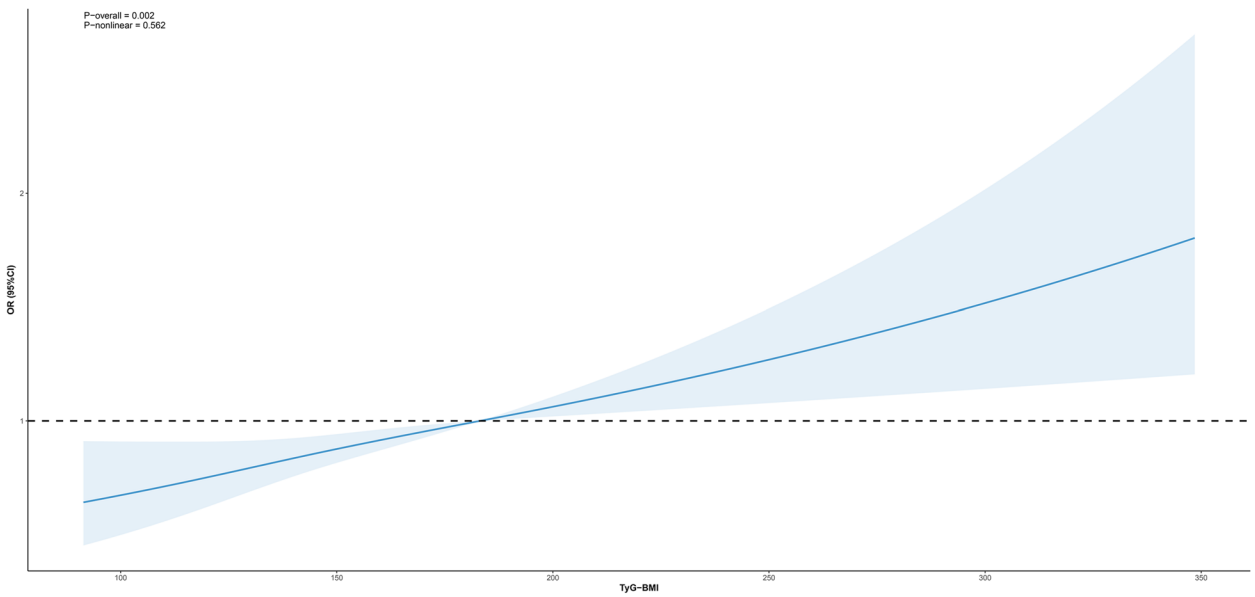

Fig. 8 RCS linear regression analysis of TyG-BMI and HUA (The blue shaded sections represent 95% confidence intervals; the dashed line represents that OR is 1)

unit increase in the TyG index [36]. A cross-sectional and longitudinal study conducted in Tianjin, China, demonstrated that elevated TyG levels were associated with higher odds of HUA in patients with diabetic nephropathy [37]. Similarly, other studies have investigated the distribution patterns of TyG and its correlation with HUA in pediatric populations. The TyG index distribution in children and adolescents demonstrated a consistent linear trend, aligning with findings from existing study [38]. A study on short-stature children and adolescents aged 3–18 reported a significant positive correlation between the TyG index and HUA level [39]. Moreover, HUA exhibited a positive association with the TyG index when serum uric acid levels exceeded 6.55 mg/dL. Our

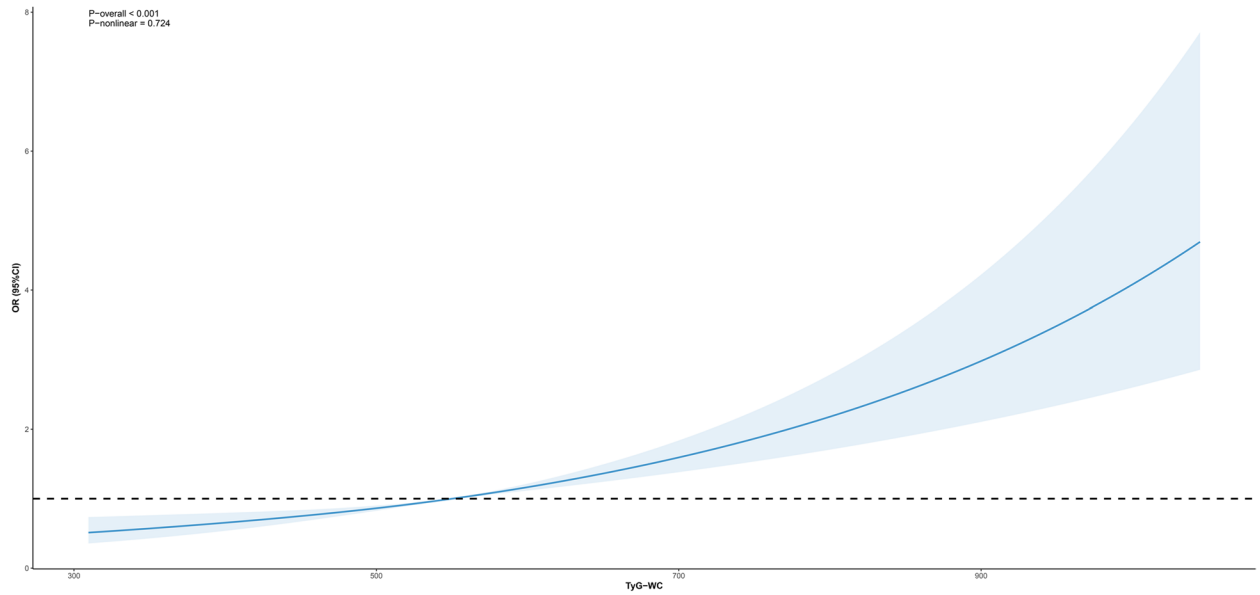

Fig. 9 RCS linear regression analysis of TyG-WC and HUA (The blue shaded sections represent 95% confidence intervals; the dashed line represents that OR is 1)

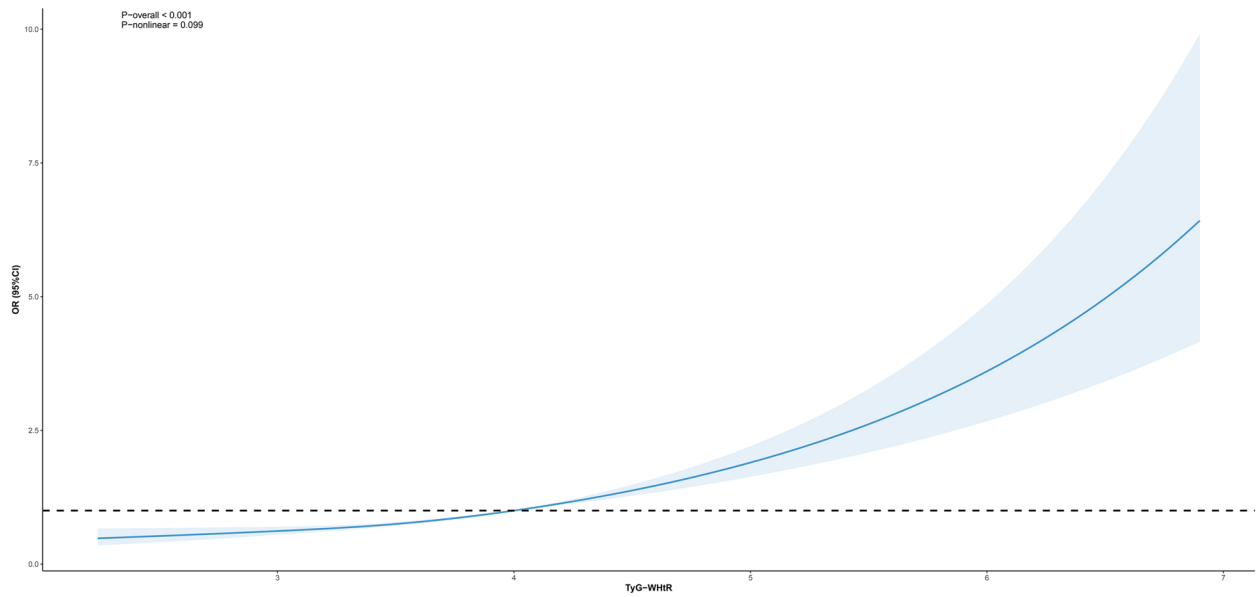

Fig. 10 RCS linear regression analysis of TyG-WHtR and HUA (The blue shaded sections represent 95% confidence intervals; the dashed line represents that OR is 1)

study suggests that TyG, TyG-BMI, TyG-WC, and TyG-WHtR are reliable predictors of HUA. This conclusion is supported by high AUC values, which align with findings from a study conducted on Korean children and adolescents [40]. As Mazidi et al. demonstrated, the association between TyG and serum uric acid is partially mediated by BMI and WC [41]. Hao et al. reported that the TyG-WC index is a superior indicator of centripetal obesity and IR compared to other indicators. Intermediate TyG-WC levels may indicate a balanced state of energy metabolism, whereas elevated TyG-WC levels may impair insulin sensitivity, leading to HUA by increasing uric acid levels [42]. One study demonstrated a strong association between uric acid levels and abdominal obesity [43]. Akiko et al.

Table 3 Baseline characteristics of HUA and Non-HUA groups before and after matching ($N_1 = 10,165$, $N_2 = 4420$)

Variables	Unmatched population				Matched population			
	Non-HUA($n = 7845$)	HUA($n = 2322$)	SMD	*P* value	Non-HUA($n = 2210$)	HUA($n = 2210$)	SMD	*P* value
Sex, n(%)			0.041	0.084			0.229	0.037
Male	3924 (50.0)	1114 (48.0)			1073 (48.6)	1114 (50.4)		
Female	3921(50,0)	1208(52.0)			1137 (51.4)	1096 (49.6)		
Age, Mean ± SD	10.9 ± 3.1	12.8 ± 2.8	0.646	< 0.001***	12.8 ± 3.1	12.7 ± 2.8	0.044	0.140
SBP, Mean ± SD	111.1 ± 11.3	115.1 ± 12.6	0.338	< 0.001***	114.6 ± 11.2	114.5 ± 12.3	0.010	0.747
DBP, Mean ± SD	65.8 ± 8.7	66.6 ± 8.5	0.089	< 0.001***	66.5 ± 8.3	66.4 ± 8.5	0.004	0.895
TC, Mean ± SD	4.0 ± 0.8	4.1 ± 0.8	0.091	< 0.001***	4.1 ± 0.8	4.1 ± 0.8	0.030	0.324
CREA, Mean ± SD	52.1 ± 12.3	62.4 ± 17.0	0.693	< 0.001***	60.8 ± 13.7	60.9 ± 13.6	0.012	0.692
Passive smoking, n(%)			0.084	< 0.001***			0.031	0.319
No	4475 (57.0)	1227 (52.8)			1219 (55.2)	1185 (53.6)		
Yes	3370 (43.0)	1095 (47.2)			991 (44.8)	1025 (46.4)		
Alcohol consumption, n(%)			0.307	< 0.001***			0.015	0.646
No	7066 (90.1)	1837 (79.1)			1796 (81.3)	1783 (80.7)		
Yes	779 (9.9)	485 (20.9)			414 (18.7)	427 (19.3)		
Daily MVPA, n(%)			0.005	0.976			0.027	0.676
< 1 h	4018 (51.2)	1186 (51.1)			1154 (52.2)	1140 (51.6)		
1 ~ < 2 h	2725 (34.7)	806 (34.7)			770 (34.8)	764 (34.6)		
> = 2 h	1102 (14.0)	330 (14.2)			286 (12.9)	306 (13.8)		
Family history of asthma, n (%)			0.019	0.417			0.018	0.607
No	7465 (95.2)	2219 (95.6)			2117 (95.8)	2109 (95.4)		
Yes	380 (4.8)	103 (4.4)			93 (4.2)	101 (4.6)		
Family history of hypertension, n (%)			0.033	0.165			0.007	0.827
No	5026 (64.1)	1451 (62.5)			1387 (62.8)	1395 (63.1)		
Yes	2819 (35.9)	871 (37.5)			823 (37.2)	815 (36.9)		
Family history of diabetes, n (%)			0.053	0,023*			0.010	0.765
No	6807 (86.8)	1972 (84.9)			1892 (85.6)	1884 (85.2)		
Yes	1038 (13.2)	350 (15.1)			318 (14.4)	326 (14.8)		
Daily SSB intake, n (%)			0.208	< 0.001***			0.003	0.952
< 100 ml/d	5196 (66.2)	1304 (56.2)			1259 (57.0)	1262 (57.1)		
≥ 100 ml/d	2649 (33.8)	1018 (43.8)			951 (43.0)	948 (42.9)		

* $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$

utilized computed tomography and observed that adipose tissue distribution in various anatomical regions significantly influences uric acid metabolism. Greater visceral and hepatic fat content is linked to increased HUA risk. Consequently, TyG-WC and TyG-WHtR are strongly associated with both IR and HUA. The potential underlying mechanism may involve visceral obesity and hyperinsulinemia caused by fatty liver, which hinders uric acid excretion and promotes its systemic accumulation [44].

Stratified analysis demonstrates a significant interaction between sex and TyG-BMI, TyG-WC, and TyG-WHtR, revealing that elevated TyG-BMI, TyG-WC, and TyG-WHtR levels are linked to higher odds of HUA in male children and adolescents. However, high TyG levels in female children and adolescents were similarly associated with increased odds of HUA, which is consistent with previous research findings [45]. Pre-adolescent girls have lower waist fat percentages but higher peripheral fat percentages compared to males. The sex differences in fat distribution during adolescence are pronounced, becoming more evident during late adolescence [46]. In males, WC and WHtR serve as more effective indicators of VAT accumulation. Males are more likely to accumulate metabolically active VAT, which is characterized by a heightened inflammatory response and closely associated with

Table 4 Associations between TyG-related obesity indices and HUA after PSM

Variables	Model 1		Model 2		Model 3	
	OR(95%CI)	*P* value	OR(95%CI)	*P* value	OR(95%CI)	*P* value
TyG						
Quartile 1	ref.					
Quartile 2	1.07 (0.90–1.28)	0.442	1.09 (0.91–1.29)	0.205	1.06 (0.89–1.27)	0.510
Quartile 3	1.20 (1.01–1.43)	0.036*	1.22 (1.03–1.45)	0.022*	1.16 (0.97–1.38)	0.108
Quartile 4	1.54 (1.30–1.82)	< 0.001***	1.57 (1.33–1.87)	< 0.001***	1.32 (1.10–1.58)	0.003**
TyG-BMI						
Quartile 1	ref.					
Quartile 2	1.10 (0.90–1.35)	0.361	1.25 (1.01–1.55)	0.043**	1.18 (0.95–1.48)	0.137
Quartile 3	1.18 (0.97–1.43)	0.097	1.48 (1.19–1.84)	< 0.001***	1.26 (1.00–1.60)	0.053
Quartile 4	1.76 (1.45–2.13)	< 0.001***	2.21 (1.78–2.74)	< 0.001***	1.50 (1.14–1.98)	0.004**
TyG-WC						
Quartile 1	ref.					
Quartile 2	0.92 (0.75–1.14)	0.457	1.10 (0.88–1.38)	0.400	1.08 (0.86–1.35)	0.524
Quartile 3	1.17 (0.96–1.42)	0.121	1.52 (1.21–1.90)	< 0.001***	1.45 (1.15–1.83)	0.002**
Quartile 4	1.63 (1.34–1.98)	< 0.001***	2.14 (1.71–2.68)	< 0.001***	1.60 (1.23–2.09)	< 0.001***
TyG-WHtR						
Quartile 1	ref.					
Quartile 2	1.06 (0.90–1.26)	0. 479	1.07 (0.90–1.26)	0.392	1.07 (0.91–1.27)	0.413
Quartile 3	1.17 (0.98–1.38)	0.078	1.17 (0.99–1.39)	0.071	1.20 (1.01–1.43)	0.037*
Quartile 4	1.92 (1.62–2.27)	< 0.001***	1.92 (1.62–2.26)	< 0.001***	2.03 (1.71–2.42)	< 0.001***

metabolic dysfunction [47]. An elevated TyG-WC index in men was associated with higher odds of HUA, possibly due to men's greater visceral and hepatic adipose tissue accumulation. Central obesity, characterized by increased VAT accumulation, is strongly associated with increased metabolic risk and all-cause mortality [48]. Scholars have reported that the TyG index is more predictive of T2DM risk in females, possibly due to sex-specific differences in glucose metabolism and IR [49]. However, elevated TyG index in women has also been linked to increased odds of HUA. In women, adipose tissue tends to be predominantly stored in peripheral or subcutaneous tissue. In contrast, the TyG index is derived exclusively from the FBG and TG levels, and does not account for fat distribution. Salisbury et al. attributed the observed sex-based differences in hepatic metabolism to variations in RNA modification. The modification of hepatic lipid metabolism was regulated by m^6A, resulting in consistently higher fasting TG levels in female mice than their male counterparts under various dietary conditions [50]. Although these findings are derived from animal studies, they may provide insights into the association between the TyG index and HUA in women in our study.

A review has highlighted age- and sex-specific differences in the dynamic changes of uric acid levels in children and adolescents. Blood uric acid levels gradually rise in children and adolescents, starting from birth and continuing through the completion of elementary school. In males, blood uric acid levels rise rapidly, whereas in females, they continue to increase at a slower rate [8]. This difference is likely attributable to the relatively higher muscle mass observed in males. Muscle mass is a well-established primary source of purines in the body, and skeletal muscle mass strongly correlates with HUA risk in obese youth [51]. Furthermore, pre-adolescent girls exhibit significantly higher estrogen levels than boys of the same age. In adolescent females, estrogen levels significantly enhance uric acid excretion [52, 53]. Blood uric acid levels progressively rise from infancy through adolescence. However, in males, testosterone drives a more pronounced rise in uric acid levels during adolescence [54]. Furthermore, our study identifies a significant interaction between age and TyG-BMI. Childhood obesity is strongly associated with VAT accumulation, which is more susceptible to glucose and lipid metabolism disruptions, contributing to IR [55]. The effects of obesity on IR may be partially alleviated during adolescence due to increased growth hormone secretion, which stimulates lipolysis and muscle mass growth [56]. Therefore, the diagnostic criteria for HUA should account for age- and sex-specific differences.

The sequence of causal relationships between IR and HUA remains controversial. A study utilizing a cross-hysteresis pathway analysis approach suggested that elevated uric acid levels may precede the onset of IR [57]. Another study indicated that uric acid may contribute to IR by activating the NLRP3 inflammasome [58]. IR has been shown to induce HUA, as elevated insulin levels impair insulin sensitivity by altering receptor function and enhancing lipid synthesis. Consequently, this exacerbates IR, which, in turn, leads to increased uric acid levels, thus creating a vicious cycle within the body [59]. However, another Mendelian randomization study indicated a bidirectional causal link between hyperinsulinemia and HUA. Conversely, HUA was not found to induce hyperinsulinemia [60]. The underlying mechanisms linking TyG and HUA remain incompletely understood. TyG index has been identified as a reliable indicator of IR and pancreatic beta-cell dysfunction in children and adolescents [23, 61]. IR is typically characterized by impaired insulin signaling and receptor dysfunction. In response to the effects of IR, beta-cells increase insulin secretion to maintain euglycemia, resulting in compensatory hyperinsulinemia. Hyperinsulinemia-induced renal vasodilation increases the glomerular filtration rate, which is associated with reduced endothelial nitric oxide production and increased oxidative stress. Moreover, glomerular pressure overload can induce structural changes and increase uric acid excretion, contributing to HUA [62]. IR has been shown to also upregulate the expression of urate transporter 1 (URAT1) and downregulate ATP-binding cassette subfamily G member 2 (ABCG2) through enhanced sodium reabsorption in the proximal renal tubules, consequently reducing sodium and urate excretion, thereby elevating uric acid levels [16, 63].

One notable strength of this study is that we used the data from 2017 Chinese National Nutrition and Health Surveillance of Children and Lactating Mothers, which is nationally representative. Considering the growth, developmental characteristics, and lifestyle behaviors of children and adolescents, adjustments were made for variables such as passive smoking, alcohol consumption, daily MVPA time, and daily SSB intake. Sensitivity analysis included performing 1:1 PSM and modifying the HUA diagnostic threshold, both of which yielded consistent results. However, this study has several limitations. Firstly, excluding ninth- and twelfth-grade students in this study may limit its ability to accurately represent the characteristics of children and adolescents. The pressures of transitioning to a new academic stage may lead these students to deviate from their usual dietary intake, body measurements, lifestyle habits, and other health indicators. Secondly, the high heritability of HUA is well-documented, with specific genes identified that may influence its prevalence [64]. However, due to limitations, neither family history of HUA nor genetic factors were included as covariables. Finally, as a cross-sectional study, this research cannot establish causal relationships between TyG-related obesity indices and HUA. Longitudinal follow-up studies are recommended to investigate the effects of dynamic changes in TyG indices on uric acid levels.

Conclusion

Our study revealed that TyG, TyG-BMI, TyG-WC, and TyG-WHtR exhibited a linear and positive correlation with HUA in children and adolescents. Monitoring TyG obesity-related indices could serve as practical biomarkers for identifying HUA in children and adolescents. Moreover, males exhibited stronger associations among TyG-BMI, TyG-WC, and TyG-WHtR with HUA. Incorporating these readily available indices into routine metabolic assessments could facilitate the development of sex-specific prevention protocols in HUA.

Abbreviations

TyG	Triglyceride-glucose
BMI	Body mass index
WC	Waist circumference
WHtR	Waist-to-height ratio
HUA	Hyperuricemia
HIEC	Hyperinsulinemic-euglycemic clamp
TG	Triglyceride
FBG	Fasting blood glucose
CDC	Center for Disease Control and Prevention
SBP	Systolic blood pressure
DBP	Diastolic blood pressure
TC	Total cholesterol
CREA	Creatinine
MVPA	Moderate-to-vigorous physical activity
IQR	Interquartile range
RCS	Restricted cubic splines
ROC	Receiver operating characteristic curve
AUC	Area under the curve
PSM	Propensity score matching
SD	Standard deviations
OR	Odds ratios
CI	Confidence interval
SMD	Standardized mean differences

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12944-025-02547-0.

Additional file 1.

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Authors' contributions

RQZ, TL, DL and XMD were involved in conception and design, and data interpretation for this article. JWP, TL, DL and XMD were involved in data collection for this article. RQZ, QQW and HYZ were involved in manuscript drafting. RQZ

was involved in data analysis for this article. RQZ, JWP, TL, DL, XFC and XMD were involved critical review in for this article.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
Approval for this study was obtained from the Ethics Committee of the Institute of Nutrition and Health, Chinese Center for Disease Control and Prevention (Ethics number: 201614). Written informed consent was obtained from the legal guardians of children aged 5–11, while for adolescents aged 12–17, consent was jointly provided by both the adolescents and their legal guardians. This process ensured compliance with ethical regulations.

Consent for publication
All the authors gave their consent to publication.

Competing interests
The authors declare no competing interests.

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