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The associations of insulin resistance, obesity, and lifestyle with the risk of developing hyperuricaemia in adolescents

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Abstract

Background Hyperuricaemia is common among obese children and adolescents, and is closely related to insulin resistance. The aim of this study was to explore the relationships between youth insulin resistance and hyperuricaemia, as well as their relationships with lifestyle factors in youths, to provide early guidance on the risk factors for hyperuricaemia in adolescents.

Methods This study included 233 adolescents aged 10 to 20 years. Insulin resistance was evaluated via the homeostasis model assessment-insulin resistance (HOMA-IR) method. Binary logistic regression analysis was used to assess the associations of HOMA-IR with hyperuricaemia status and serum uric acid (UA) levels. The participants were subsequently divided into two groups, the noninsulin resistant group (HOMA-IR ≤ 3.2) and the insulin resistant group (HOMA-IR > 3.2), to further explore the factors that may affect the serum UA level. Finally, the predictive ability of different indicators of hyperuricaemia was evaluated via the ROC curve.

Results Binary logistic regression analysis revealed a significant increase in the risk of developing hyperuricaemia for individuals with elevated HOMA-IR ($p < 0.001$) and insulin resistance ($p < 0.01$). Spearman's correlation analysis revealed a significant positive linear correlation between HOMA-IR and serum UA levels ($r = 0.4652$, $p < 0.001$). Among insulin-resistant adolescents, UA levels were positively correlated with weight ratings, frequency of staying up late, and sugary beverages intake. Notably, individuals who engaged in 1–3 h of weekly exercise had the lowest UA levels. The area under the ROC curve for HOMA-IR was 0.847 (cut-off value = 2.165, $p < 0.001$), and the optimal prediction model included HOMA-IR, BMI z-score, and other lifestyle factors (AUC: 0.870, $p < 0.001$)).

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Conclusion HOMA-IR was identified as an independent risk factor for the development of hyperuricaemia and could be used as a sensitive indicator for the prediction its development in adolescents. In insulin-resistant adolescents with hyperuricaemia, maintaining normal weight, engaging in physical exercise for 1–3 h per week, avoiding staying up late and limiting sugary beverages intake are recommended to reduce the prevalence of hyperuricaemia among adolescents.

Keywords Hyperuricaemia, HOMA-IR, Adolescent, Insulin resistance, BMI

Introduction

Hyperuricaemia is caused by a disorder in purine metabolism, which includes excessive production of purines and reduced excretion, resulting in an imbalance in uric acid (UA) levels [1]. Purine metabolism is influenced by various factors such as heredity, diet, exercise and unhealthy lifestyles [2]. Hyperuricaemia has the potential to directly trigger both gout and kidney ailments while also showing a strong correlation with diabetes and insulin resistance. Additionally, it is closely associated with hyperlipidaemia, chronic kidney disease, hypertension and atherosclerotic disease [3, 4]. In recent years, the prevalence of hyperuricaemia has increased, especially among the younger population. A previous study revealed that the prevalence of adult hyperuricaemia in China increased from 11.1% from 2015 to 2016 to 14.8% from 2018 to 2019 [5]. The prevalence of hyperuricaemia among children and adolescents in China is 23.3%, reaching 55.12% in some areas [6, 7]. Hyperuricaemia among adolescents often goes unnoticed due to the perception that gout primarily affects adults and because of the asymptomatic nature of hyperuricaemia for most individuals.

Insulin resistance (IR) is characterized by a decrease in the tissue responsiveness to insulin, which servie as the underlying mechanism for diabetes. It is a crucial factor contributing to several metabolic disorders, including elevated levels of uric acid [8]. The homeostasis model Assessment of insulin resistance (HOMA-IR) has been extensively used to assess insulin resistance in adolescent populations in both epidemiological studies and clinical settings [9–11]. In most cases, patients with chigh HOMA-IR have no specific symptoms, but they are often accompanied by diseases such as obesity, diabetes and atherosclerosis [12, 13]. Compensatory hyperinsulinaemia and insulin resistance can reduce urinary excretion of UA, leading to hyperuricaemia [3]. Studies showed that UA causes endothelial dysfunction and vascular damage by promoting oxidative stress and vascular inflammation. In addition, UA may directly affect intracellular insulin signaling pathways, thereby inducing insulin resistance. Synergistic interaction of elevated UA and HOMA may promote vascular injury [14, 15]. Research findings indicate that patients with hyperuricaemia exhibit a notable increase in the levels of HOMA-IR, which is positively associated with serum UA levels. Furthermore, HOMA-IR independently contributes to the risk of developing hyperuricaemia [16–18]. Most adolescents with hyperuricaemia have no apparent symptoms and there are no clear medication guidelines for treating this population. Therefore, these patients are mostly treated with diet and weight control. Additionally, insulin resistance is a major health outcome associated with metabolic syndrome, making lifestyle interventions critical for adolescents as well [19]. When HOMA-IR is combined with dietary patterns and lifestyles assessments, its efficiency in assessing IR in adolescents may be improved [20]. Timely detection and intervention in IR may help prevent diabetes and related metabolic diseases.

Research has indicated a correlation between increased insulin levels and the likelihood of developing hyperuricaemia. By addressing insulin resistance, it is possible to mitigate the risk of developing hyperuricaemia and gout [21]. However, data on the association between insulin resistance and the risk of developing hyperuricaemia in adolescents are limited. The objective of this study was to examine the correlation between HOMA-IR and the risk of developing hyperuricaemia in adolescents aged 10–20 years in Taizhou, and to evaluate whether HOMA-IR can be used to predict the development of hyperuricaemia. Moreover, in the present study, we evaluated the relationships between BMI, dietary patterns, lifestyle, and UA levels in the HOMA-IR subpopulation of adolescents.

Methods

Study population and design

In this study, 858 adolescent patients aged 10–20 years with hyperuricaemia were followed up at Taizhou Hospital of Zhejiang Province from July 1, 2022 to July 15, 2023. Of these, 187 patients willingly agreed to participate in our study. We recruited 193 students from schools as representatives of normouricaemia. The participants were asked to fill out a structured questionnaire covering their medical history, dietary habits and lifestyles. Blood samples were subsequently taken after an overnight fast. Body mass index (BMI), a standard measure of weight and height, was determined by dividing weight (kg) by the square of height (m). The levels of UA, estimated glomerular filtration rate (eGFR), glucose (GLU), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) were measured with an AU5800 automatic analyser

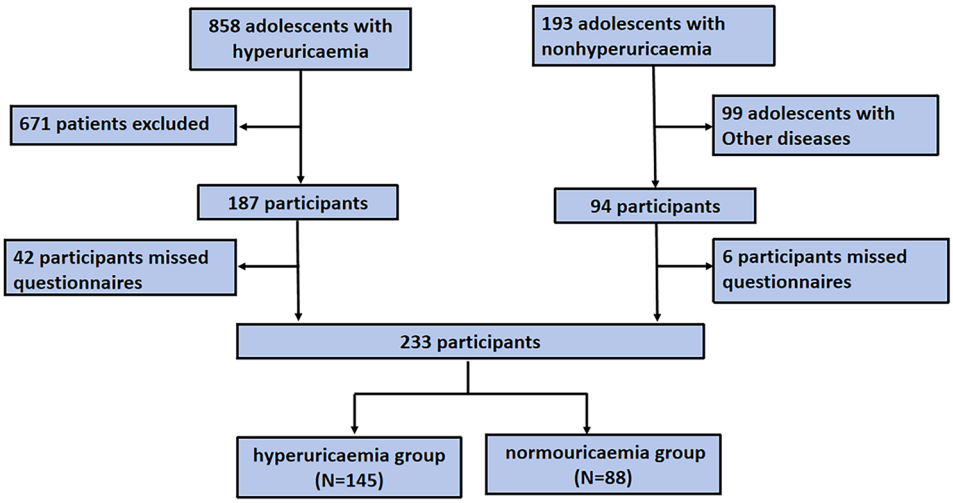

Fig. 1 Flowchart of the study

(Beckman, USA). Insulin levels were measured with a fully automated chemiluminescent immunoassay system (Abbott, USA). The inclusion criteria were as follows: (1) aged between 10 and 20 years; (2) the normouricaemia group had no history of self-reported or clinical diagnosis of hyperuricaemia or gout; (3) the UA levels in hyperuricaemia patients were ≥420 μmol/L in males and ≥360 μmol/L in females for two separate fasting blood tests (nonconsecutive days) while consuming a normal purine diet, respectively [15]. The exclusion criteria were as follows: (1) took urate-lowering drugs in the past 1 month. (2) had signs of acute infection or previous diagnosis of serious metabolism-related diseases, including diabetes and cardiovascular disease. Ultimately, a total of 233 individuals were included in the study (Fig. 1). The study was approved by the Ethics Committee of Taizhou Hospital of Zhejiang Province (Approval number: K20220625), and all participants or their legal guardians (for participant under the age of 18) provided written informed consent.

Definition

Hyperuricaemia was diagnosed via two separate fasting blood tests (nonconsecutive days) that revealed UA levels≥420 μmol/L in males and ≥360 μmol/L in females. On the basis of the assessment of excessive weight and obesity in students and teenagers (Chinese standard, WS/T 586–2017), the weight status of adolescents was categorized into normal, overweight and obesity. The following formula was used to calculate Z-score: (Sample value - mean of the reference population for age and sex)/standard deviation of the reference population. Z-scores for BMI, SBP, and DBP were calculated on the basis of Chinese children's references updated in 2017 [22]. The HOMA-IR value was calculated via the following formula: HOMA-IR=GLU (mmol/L) × insulin (mIU/L)/22.5. Insulin resistance was determined as a HOMA-IR greater than 3.2, according to a cross-sectional study conducted among the paediatric and adolescent population in China [20]. The EGFR value was determined via the CKD-EPI formula [23]. According to the hypertension criteria for metabolic syndrome, elevated blood pressure was defined as a reading of 130/85 mmHg or higher [24]. Each dietary variable was classified into three categories: none (0–3 times per month), sometimes (1–2 times per week), and often (3 or more times per week). Each serving of food was defined as 300 g, and each serving of milk or sugary beverages was defined as 250 mL. Sugary beverages include those containing energy-dense sweeteners such as sucrose, high-fructose corn syrup, or fruit juice concentrate. Staying up late was defined as going to bed after 11 PM with a total sleep duration of less than 6 h, and it was categorized into three levels on the basis of weekly frequency: none, 1–2 days, and ≥3 days. Weekly exercise time was similarly categorized into three levels: < 1 h, 1–3 h, and >3 h.

Statistical analysis

The subjects were divided into a hyperuricaemia group and the normouricaemia group. For basic characteristics, the chi-square test was used to analyse categorical variables, whereas the t-test was used to examine continuous variables. Univariate and multivariate analyses were conducted via binary logistic regression to assess the risk factors associated with hyperuricaemia. The correlation between the two variables was examined via the Pearson's correlation test. The analysis of insulin resistance subgroups involved the use of the chi-square test and one-way ANOVA (noninsulin resistance and insulin resistance). The ROC curve analysis was used to determine the ability of HOMA-IR and other indicators to predict hyperuricaemia. Statistical analysis was performed via R statistics (version 4.3.1) and SPSS software

(version 25.0). $p<0.05$ was considered to indicate statistical significance.

Results

Characteristics of participants

The characteristics of the participants in the hyperuricaemia group and normouricaemia group are presented in Table 1. Compared with those in the normouricaemia group, adolescents in the hyperuricaemia group had a higher BMI z-score, significantly greater odds of hyperuricaemia family history of and UA-lowering drugs use, and predominantly unhealthy dietary patterns and lifestyles ($p<0.01$). In the target population of adolescents aged 10 to 20 years, alcohol consumption was rare did not significantly differ between groups; therefore, alcohol consumption status was not included in the analysis.

Table 1 Characteristics of study population

Characteristics	Level	Overall (*n* = 233)	Normouricaemia (*n* = 88)	Hyperuricaemia (*n* = 145)	*p*-value
Demographic factors					
Gender - n (%)[b]	Female	20 (8.6)	10 (11.4)	10 (6.9)	0.348
	Male	213 (91.4)	78 (88.6)	135 (93.1)	
Age (years)[a]		16.48 (2.21)	16.61 (1.87)	16.39 (2.40)	0.462
Family history of hyperuricaemia - n (%)[b]	No	181 (77.70)	83 (94.30)	98 (67.60)	< 0.001
	Yes	52 (22.30)	5 (5.70)	47 (32.40)	
Use of UA-lowering drugs - n (%)[b]	No	189 (81.10)	88 (100.00)	101 (69.70)	< 0.001
	Yes	44 (18.90)	0 (0.00)	44 (30.30)	
SBP z-score[a]		0.68 (1.13)	0.29 (0.93)	0.94 (1.18)	< 0.001
DBP z-score[a]		0.17 (1.00)	0.50 (0.93)	-0.05 (0.99)	< 0.001
Blood pressure - n (%)[b]	Normal	160 (76.90)	69 (84.10)	91 (72.20)	0.068
	Elevated	48 (23.10)	13 (15.90)	35 (27.80)	
BMI (kg/m^2)[a]		24.55 (5.62)	21.11 (3.63)	26.64 (5.59)	< 0.001
BMI z-score[a]		1.39 (1.80)	0.26 (1.15)	2.08 (1.78)	< 0.001
Weight ratings - n (%)[b]	Normal	116 (49.80)	70 (79.50)	46 (31.70)	< 0.001
	Overweight	37 (15.90)	11 (12.50)	26 (17.90)	
	Obesity	80 (34.30)	7 (8.00)	73 (50.30)	
Dietary patterns					
Seafood - n (%)[b]	None	92 (39.50)	29 (33.00)	63 (43.40)	0.157
	Sometimes	100 (42.90)	39 (44.30)	61 (42.10)	
	Often	41 (17.60)	20 (22.70)	21 (14.50)	
Fruits - n (%)[b]	None	41 (17.60)	15 (17.00)	26 (17.90)	0.036
	Sometimes	109 (46.80)	50 (56.80)	59 (40.70)	
	Often	83 (35.60)	23 (26.10)	60 (41.40)	
Vegetables - n (%)[b]	None	13 (5.60)	7 (8.00)	6 (4.10)	0.420
	Sometimes	36 (15.50)	12 (13.60)	24 (16.60)	
	Often	184 (79.00)	69 (78.40)	115 (79.30)	
Milk - n (%)[b]	None	35 (15.00)	14 (15.90)	21 (14.50)	0.037
	Sometimes	59 (25.30)	30 (34.10)	29 (20.00)	
	Often	139 (59.70)	44 (50.00)	95 (65.50)	
Sugary beverages - n (%)[b]	None	93 (39.90)	49 (55.70)	44 (30.30)	< 0.001
	Sometimes	95 (40.80)	33 (37.50)	62 (42.80)	
	Often	45 (19.30)	6 (6.80)	39 (26.90)	
Lifestyles					
Weekly exercise time - n (%)[b]	< 1 h	39 (16.70)	7 (8.00)	32 (22.10)	0.001
	1–3 h	145 (62.20)	68 (77.30)	77 (53.10)	
	> 3 h	49 (21.00)	13 (14.80)	36 (24.80)	
Weekly staying up late days - n (%)[b]	None	38 (16.30)	17 (19.30)	21 (14.50)	0.009
	1–2 days	125 (53.60)	55 (62.50)	70 (48.30)	
	≥ 3 days	70 (30.00)	16 (18.20)	54 (37.20)	

Table 1 (continued)

Characteristics	Level	Overall (*n* = 233)	Normouricaemia (*n* = 88)	Hyperuricaemia (*n* = 145)	*p*-value
Biomarkers					
UA (μmol/L)[a]		448.35 (118.74)	345.38 (50.01)	510.84 (103.88)	< 0.001
eGFR (ml/ (min·1.73 m^2))[a]		127.96 (16.56)	131.48 (13.64)	125.83 (17.81)	0.011
GLU (mmol/L)[a]		4.70 (0.42)	4.63 (0.27)	4.74 (0.48)	0.036
HbAc1 (%)[a]		5.37 (0.35)	5.32 (0.24)	5.39 (0.40)	0.105
Insulin (μU/mL)[a]		13.67 (10.04)	7.40 (3.43)	17.48 (10.80)	< 0.001
TC (mmol/L)[a]		4.09 (1.17)	3.98 (0.73)	4.15 (1.37)	0.294
HDL-C (mmol/L)[a]		1.34 (0.30)	1.48 (0.31)	1.25 (0.27)	< 0.001
LDL-C (mmol/L)[a]		2.37 (0.67)	2.08 (0.54)	2.54 (0.69)	< 0.001
HOMA -IR[a]		2.91 (2.30)	1.53 (0.73)	3.75 (2.52)	< 0.001
HOMA-IR - n (%)	<= 3.2	160 (68.70)	83 (94.30)	77 (53.10)	< 0.001
	> 3.2	73 (31.30)	5 (5.70)	68 (46.90)	

[a]Data were expressed as the mean ± SD

[b]Data were expressed as the number (proportion)

BMI, Body mass index; eGFR, Estimated glomerular filtration rate; UA, Uric acid; GLU, Glucose; HbA1c, Glycated hemoglobin; TC, Total cholesterol; HDL-C, High-density lipoprotein cholesterol; LDL-C, Low-density lipoprotein cholesterol; HOMA-IR, Homeostasis model assessment of insulin resistance

The participants in the hyperuricaemia group also had an increased likelihood of developing metabolic conditions such as high blood pressure, dyslipidaemia, and insulin resistance ($p < 0.001$). The HOMA-IR was 2.45 times greater in individuals with hyperuricaemia than in individuals with normouricaemia.

The relationship between HOMA-IR and hyperuricaemia

Univariable logistic regression analysis revealed that BMI, weekly exercise time, weekly staying up late days, sugary beverages intake and metabolism-related indicators (blood pressure, GLU, eGFR, insulin, HDLC, LDLC, and HOMA-IR) were associated with the risk of developing hyperuricaemia (All $p < 0.05$, Table 2). Insulin resistance status significantly increased the risk of developing hyperuricaemia regardless of adjustment for confounders when a HOMA-IR cut-off value of 3.2 was used to define insulin resistance ($p < 0.001$, Table 3). Even after controlling for other variables, HOMA-IR was significantly independently associated with the risk of developing hyperuricaemia (all $p < 0.05$, Table 3).

The effects of insulin resistance on the risk of developing hyperuricaemia and UA levels

The participants were divided into two cohorts on the basis of a HOMA-IR threshold of 3.2 in order to investigate the impact of HOMA-IR on the risk of developing hyperuricaemia and UA levels. Spearman analysis revealed a positive correlation between HOMA-IR and UA levels ($r = 0.4652$, $p < 0.001$). According to the data presented in Fig. 2, compared with those without insulin resistance, individuals with insulin resistance had a significantly greater prevalence of hyperuricaemia and greater UA levels ($p < 0.001$).

The impact of lifestyles and beverage intake on the risk of developing hyperuricaemia and UA levels in individuals with and without insulin resistance

To investigate the factors impacting the correlation between HOMA-IR and the risk of developing hyperuricaemia, a subgroup analysis was performed on individuals with and those without insulin resistance. Spearman's correlation analysis revealed a positive association between BMI and UA levels ($r = 0.5346$, $p < 0.001$). We conducted analyses to examine the impact of weight ratings, lifestyles, and dietary patterns on UA levels among different subgroups. There was a positive association between weight ratings, weekly staying up late, frequency of sugary beverages intake, and UA levels. Higher values of these factors correspond to higher UA levels, particularly in individuals with insulin resistance. Notably, the lowest UA levels were observed when the weekly exercise time ranged from 1 to 3 h (Fig. 3). The UA level and the prevalence of HUA in patients with or without insulin resistance were compared, and the results showed that the UA level and the prevalence of HUA were significantly increased when the weight ratings was obesity, the weekly staying up late days and the intake of sugary beverages were no matter how much, and the difference was most obvious when the weekly exercise time was 1–3 h (Supplement Tables 1 and 2).

ROC curve analysis of the risk of developing hyperuricaemia

The AUC for HOMA-IR in predicting the risk of developing hyperuricaemia was 0.847 ($p < 0.001$), the Youden index was 0.595, the optimal cut-off value was 2.165, and the predictive performance was better than that of BMI z-score (Fig. 4). The best predictive model was predictive Model 2, which consisted of HOMA-IR, BMI z-score,

Table 2 Odds ratios for hyperuricaemia associated with related factors derived via univariable logistic regression

Variable	Level	OR (95% CI)	*p*-value
Demographic factors			
Gender	Female	1.00	
	Male	1.73 (0.68, 4.40)	0.242
Age (years)		0.96 (0.84, 1.08)	0.46
BMI (kg/m^2)		1.27 (1.19, 1.37)	< 0.001
BMI z-score		2.22 (1.78, 2.84)	< 0.001
Weight ratings	Normal	1.00	
	Overweight	3.60 (1.66, 8.25)	0.002
	Obesity	15.87 (7.12, 40.66)	< 0.001
SBP z-score		1.77 (1.34, 2.40)	< 0.001
DBP z-score		0.55 (0.40, 0.75)	< 0.001
Blood pressure	Elevated	2.04 (1.02, 4.27)	0.049
Dietary patterns			
Seafood	None	1.00	
	Sometimes	0.72 (0.39, 1.30)	0.28
	Often	0.48 (0.23, 1.03)	0.059
Fruits	None	1.00	
	Sometimes	0.68 (0.32, 1.41)	0.308
	Often	1.51 (0.67, 3.33)	0.315
Vegetables	None	1.00	
	Sometimes	2.33 (0.64, 8.81)	0.199
	Often	1.94 (0.62, 6.27)	0.249
Milk	None	1.00	
	Sometimes	0.64 (0.27, 1.49)	0.309
	Often	1.44 (0.66, 3.08)	0.351
Sugary beverages	None	1.00	
	Sometimes	2.09 (1.17, 3.79)	0.014
	Often	7.24 (2.97, 20.51)	< 0.001
Lifestyles			
Weekly exercise time	< 1 h	1.00	
	1–3 h	0.25 (0.10, 0.57)	0.002
	> 3 h	0.61 (0.21, 1.67)	0.342
Weekly staying up late days	None	1.00	
	1–2 days	1.03 (0.49, 2.14)	0.936
	≥ 3 days	2.73 (1.17, 6.46)	0.02
Biomarkers			
UA (μmol/L)		1.04 (1.03, 1.05)	< 0.001
eGFR (ml/ (min·1.73 m^2))		0.98 (0.96, 1.00)	0.013
GLU (mmol/L)		2.07 (1.06, 4.21)	0.039
Insulin (μU/mL)		1.31 (1.22, 1.44)	< 0.001
TC (mmol/L)		1.13 (0.90, 1.42)	0.293
HDL-C (mmol/L)		0.06 (0.02, 0.17)	< 0.001
LDL-C (mmol/L)		3.30 (2.05, 5.56)	< 0.001
HOMA-IR		3.60 (2.51, 5.48)	< 0.001

OR: Odds ratios; 95% CI: 95% confidence intervals. BMI, Body mass index; eGFR, Estimated glomerular filtration rate; UA, Uric acid; GLU, Glucose; HbA1c, Glycated hemoglobin; TC, Total cholesterol; HDL-C, High-density lipoprotein cholesterol; LDL-C, Low-density lipoprotein cholesterol; HOMA-IR, Homeostasis model assessment of insulin resistance

Table 3 Association of HOMA-IR with the risk of developing hyperuricaemia according to multivariable logistic regression

Variables	Model 1[a]		Model 2[b]		Model 3[c]	
	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
HOMA-IR	3.60 (2.51, 5.48)	< 0.001	2,70 (1.76, 4.36)	< 0.001	3.92 (2.25, 7.45)	< 0.001
Subgroups (HOMA-IR)						
≤ 3.2	1.00		1.00		1.00	
> 3.2	14.66 (6.14, 43.51)	< 0.001	3.74 (1.30, 12.47)	0.020	5.14 (1.49, 20.33)	0.013

[a]No adjustment

[b]Adjusted for gender, age, and BMI z-score

[c]Adjusted for gender, age, BMI z-score, elevated blood pressure, weekly exercise time, weekly staying up late days, sugary beverages, eGFR, HDL-C, LDL-C

HOMA-IR, Homeostasis model assessment of insulin resistance; OR: Odds ratios; 95% CI: 95% Confidence intervals

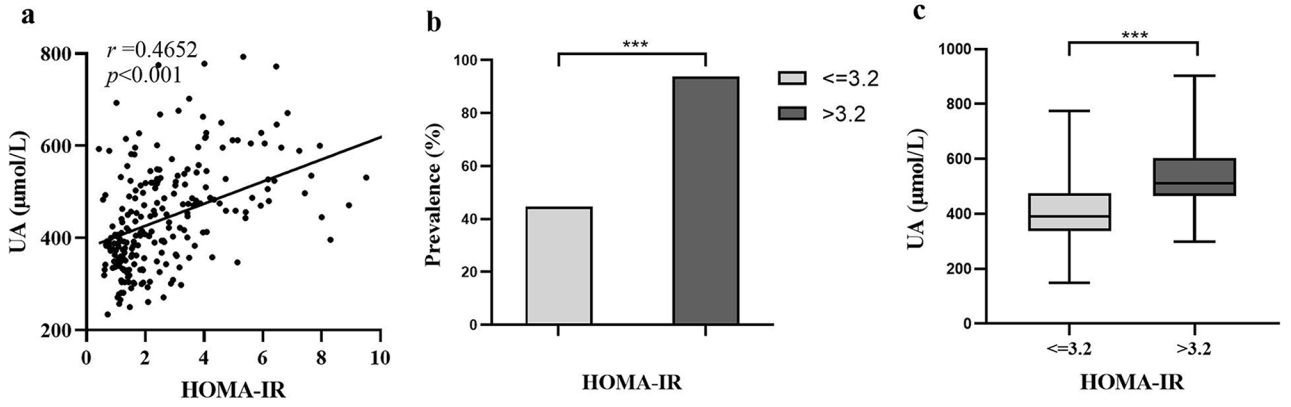

Fig. 2 Comparison of the prevalence of hyperuricaemia and UA levels between participants with and without insulin resistance. (**a**) Spearman linear correlation analysis between HOMA-IR and UA levels; (**b**) comparison of the prevalence of hyperuricaemia; (**c**) comparison of UA levels. Data were expressed as medians (upper and lower quartiles) or proportions (%). HOMA-IR, homeostasis model assessment of insulin resistance; UA, uric acid

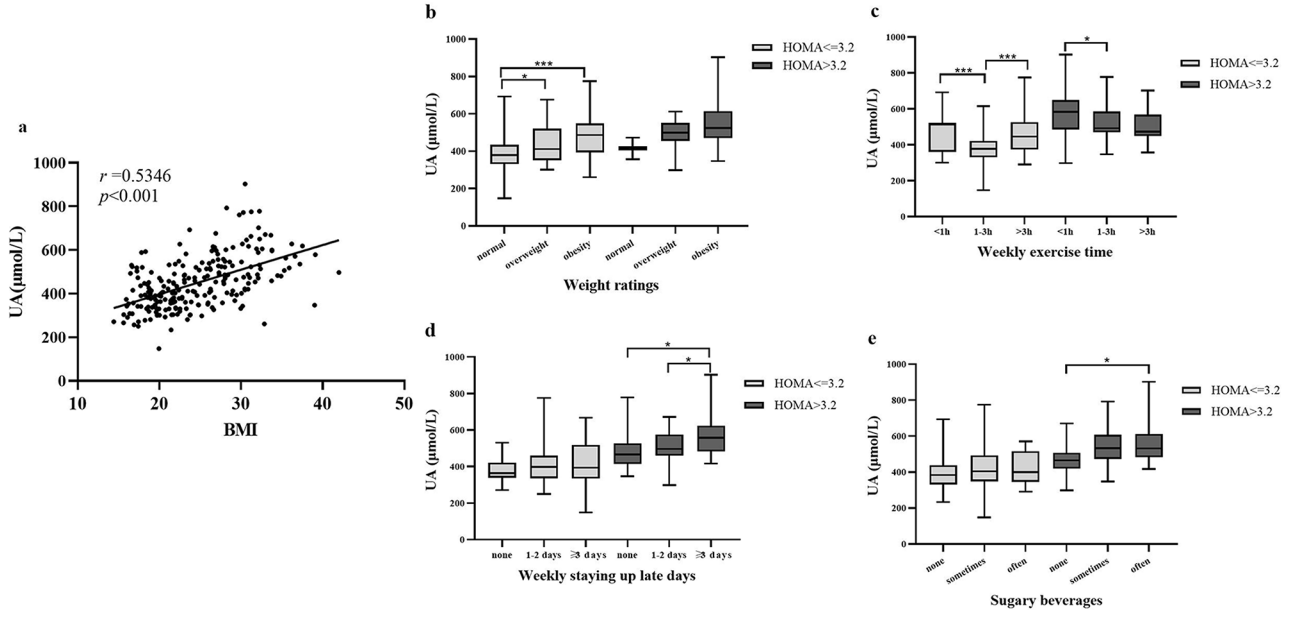

Fig. 3 UA levels in subgroups with and without insulin resistance. (**a**) Spearman linear correlation analysis between BMI and UA levels; (**b**-**e**) comparison of UA levels. Data are expressed as medians (upper and lower quartiles) or proportions (%). BMI, body mass index; UA, uric acid; HOMA-IR, homeostasis model assessment of insulin resistance

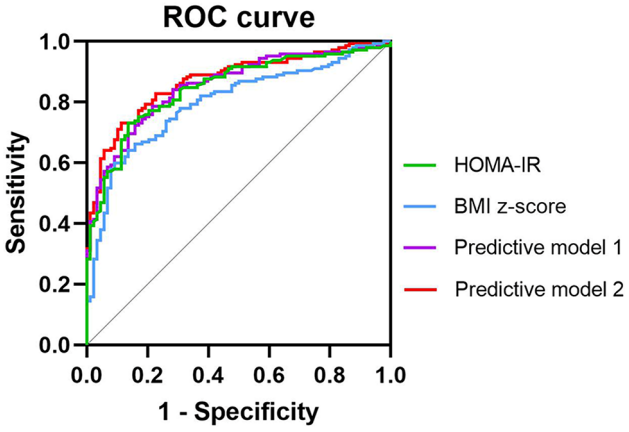

Fig. 4 ROC curves of HOMA-IR and other indicators for predicting the risk of developing hyperuricaemia in the general population. BMI, body mass index; HOMA-IR, homeostasis model assessment of insulin resistance. Predictive model 1: HOMA-IR and BMI z-score. Predictive model 2: HOMA-IR, BMI z-score, weekly exercise time, weekly staying up late days, sugary beverages

weekly staying up late days, weekly exercise time, and sugary beverages intake (AUC: 0.870, $p<0.001$) (Table 4).

Discussion

The global incidence of hyperuricaemia has been increasing, with research indicating a higher prevalence among adolescents than among adults [6, 25, 26]. Influenced by oestrogen and lifestyle, both in children and adults, the prevalence of hyperuricaemia is much greater in males (42.3%) than in females (8%), which is consistent with the findings of the present study [7, 27]. This suggests that hyperuricaemia in adolescents has emerged as a significant suboptimal health condition requiring increased attention. This study investigated the correlation between HOMA-IR and the risk of developing hyperuricaemia in adolescents. Our findings indicated that HOMA-IR can predict the risk of developing hyperuricaemia in adolescents, is an independent risk factor for hyperuricaemia and is closely associated with UA levels. UA levels were positively correlated with weight ratings, the frequency of staying up late, and sugary beverages intake among insulin-resistant adolescents. Notably, individuals who participated in 1–3 h of weekly exercise demonstrated the lowest UA levels.

There is a strong correlation between insulin levels and UA levels in the body, and insulin may increase urate reabsorption by stimulating UA transporters in the proximal renal tubules [28]. Additionally, the compensatory mechanism of hyperinsulinemia causes the kidneys to produce low–PH urine [29]. Elevated insulin levels reduce urate excretion in the kidneys, leading to increased serum UA levels in patients with insulin resistance syndrome. Fructose in sugary beverages and fruits not only promotes the generation of UA by depleting ATP and increasing AMP levels, but also indirectly induces hepatic insulin resistance through mechanisms such as promoting de novo lipogenesis, reducing fatty acid oxidation, and decreasing insulin receptor expression. These mechanisms may be more pronounced in the paediatric population, thereby further increasing uric acid levels [30]. Hyperuricaemia can increase the risk of cardiovascular disease. Research results showed that patients with hyperuricaemia have increased SBP and decreased DBP, so the pulse pressure difference is increased, which may increase the risk of cardiovascular disease [14]. HOMA-IR, as a simple method for assessing insulin sensitivity, has been shown to have strong associations with hyperuricaemia and gout in adolescents [31, 32]. In this study, HOMA-IR was also found to be a risk factor for the development of hyperuricaemia in adolescents and was closely related to UA levels.

HOMA-IR was significantly correlated with the risk of developing hyperuricaemia. We categorized HOMA-IR into two subgroups based on insulin resistance status to investigate the factors influencing these associations. To assess their impact on hyperuricaemia, we subsequently analysed several indicators, namely weight ratings, weekly exercise time, weekly staying up late days, and sugary beverages consumption. Studies have shown that lifestyle and dietary patterns are closely related to UA levels [33]. The study of Jae Hyun Jung et al. reported that obesity is most strongly associated with elevated insulin resistance in patients diagnosed with hyperuricaemia, and that BMI and WC are significantly positively correlated [34]. A cross-sectional study in China revealed that diabetic patients with elevated UA levels who experienced shorter sleep durations had an increased likelihood of developing hyperuricaemia [35]. Studies by

Table 4 Predictive value of HOMA-IR and other indicators for the risk of developing hyperuricaemia in adolescents

Variables	AUC (95% CI)	Cut-off	Sensitivity	Specificity	Youden index	*p*-value
HOMA-IR	0.847 (0.797, 0.897)	2.165	0.731	0.864	0.595	< 0.001
BMI z-score	0.798 (0.741, 0.855)	1.738	0.600	0.909	0.509	< 0.001
Predictive model 1[a]	0.854 (0.806, 0.902)	0.510	0.786	0.784	0.570	< 0.001
Predictive model 2[b]	0.870 (0.825, 0.915)	0.629	0.731	0.886	0.617	< 0.001

BMI, Body mass index; HOMA-IR, Homeostasis model assessment of insulin resistance

[a]Predictive model 1: HOMA-IR and BMI z-score

[b]Predictive model 2: HOMA-IR, BMI z-score, weekly exercise time, weekly staying up late days, sugary beverages

Wei-Ting Lin et al. have shown that adolescents who frequently consume beverages with added sugar have an increased likelihood of developing insulin resistance and elevated levels of UA, which are associated with obesity [36]. According to the expert consensus in China, moderate exercise can help lower uric acid, but it is advisable to avoid strenuous exercise. Vigorous exercise may cause an increase in the metabolism of purines in muscles, leading to an increase in serum uric acid levels [37], which is consistent with our findings. We performed a subgroup analysis to examine the impact of weight ratings, exercise, staying up late, and frequency of sugary beverages consumption on the relationships of HOMA-IR with UA levels and the risk of developing hyperuricaemia. These factors have a significant influence, especially in the presence of insulin resistance. Among them, food did not play a significant role, possibly because most teenagers eat in school cafeterias, which are relatively fixed and healthy. HOMA-IR performs well as a single predictor of hyperuricaemia risk. We also constructed a predictive model that included HOMA-IR, BMI z-score, and several lifestyle factors. Research has shown that improving dietary habits and lifestyles can lower blood glucose levels and serum uric acid levels in paediatric populations [38]. Therefore, combining lifestyle assessment with assessment of hyperuricaemia risk in adolescents can improve assessment efficiency.

Nevertheless, it is crucial to recognize the limitations of this investigation. First, the recruitment of participants was limited to a specific district, resulting in a relatively small sample size. Second, there is a lack of standardized consensus regarding the threshold of HOMA-IR used to define insulin resistance in adolescents due to potential variations in factors such as age, race, and geographical region [39, 40]. Additionally, owing to the observational design, this study does not provide sufficient evidence to establish a direct causal relationship between HOMA-IR and the risk of developing hyperuricaemia. Therefore, further research is necessary to validate the association between insulin resistance and UA levels while expanding upon our findings across diverse geographical regions and special populations.

Conclusions

In summary, this study revealed that the HOMA-IR is significantly positively correlated with the risk of developing hyperuricaemia in adolescents and has good predictive value for this disease. UA levels were positively correlated with weight ratings, the frequency of staying up late, and sugary beverages intake among insulin-resistant adolescents. Notably, individuals who engaged in 1–3 h of weekly exercise presented the lowest UA levels. Therefore, we recommend that adolescent patients with hyperuricaemia take measures to maintain a healthy weight, engage in physical exercise for 1–3 h per week, avoid staying up late and consuming sugary beverages, and receive personalized prevention and treatment on the basis of scientific evidence.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12902-024-01757-4.

Supplementary Material 1

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Author contributions
Linyan Cheng, Jinhu Zhou and Yufen Zheng helped design and conceive the study. Ying Zhao, Na Wang, Minya Jin, Wen Mao, Guangjun Zhu and Donglian Wang performed the experiments. Linyan Cheng, Ying Zhao and Jinhu Zhou analysed the data. Linyan Cheng and Yufen Zheng prepared the main manuscript text. Bo Shen and Na Wang helped revise the paper. Junbo Liang and Bo Shen conducted project management and supervision. All authors read and approved the final manuscript.

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Data availability
The data that support the findings of this study are not publicly available due to their containing information that could compromise the privacy of research participants. The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
This study was performed in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Taizhou Hospital of Zhejiang Province (Approval number: K20220625). All participants or their legal guardians (for participant under the age of 18) provided written informed consent.

Consent for publication
Not applicable.

Clinical trial number
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Competing interests
The authors declare no competing interests.

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