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Comparison of triglyceride glucose index and other insulin resistance indexes in children with overweight and obesity

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Abstract

Objectives The aim of the study was to determine the correlation between insulin resistance (IR) indexes in children with overweight or obesity.

Methods A total of 276 children with overweight or obesity and 100 normal-weight children were enrolled in the study. IR indexes such as homeostasis model assessment insulin resistance (HOMA-IR), quantitative insulin-sensitivity check index (QUICKI), fasting glucose/insulin ratio (FGIR), Triglyceride glucose index (TyG), and lipid-derived ratios were determined.

Results The mean ages were 13.0 ± 2.6, 13.1 ± 2.7 and 12.72 ± 2.23 (range:6 - 18 years) for children with overweight, obesity and normal-weight, respectively. A statistically significant positive correlation was found between HOMA-IR and TyG index, and a negative correlation between QUICKI, FGIR and TyG index ($r = 0.193$, $P < 0.001$; $r = -0.456$, $P < 0.001$ and $r = -0.392$, $P < 0.001$, respevtively). TyG index, triglyceride (TG)/high-density lipoprotein (HDL), total cholesterol (TC)/HDL, and low-density lipoprotein (LDL)/HDL were higher in children with IR than those without IR ($P < 0.05$). In receiver operating characteristic curves analysis, cut-off points were found to be ≤ 0.31 for QUICKI (94.31% sensitivity and 97.58% specificity), ≤ 6.3 for FGIR (89.1% sensitivity and 93.94% specificity), and > 4.62 for TyG (49.29% sensitivity and 84.85% specificity).

Conclusion HOMA-IR, FGIR, and QUICKI constitute stronger predictors of IR than TyG index in children with overweight and obesity.

Keywords Children, HOMA-IR, İnsulin resistance, Obesity, Overweight, Triglyceride glucose index, QUICKI

Introduction

The prevalence of obesity, a triggering factor for insulin resistance (IR), metabolic syndrome (MS) and type 2 diabetes mellitus is increasing steadily worldwide in both children and adults [1, 2]. Large, prospective longitudinal studies showed a strong association between childhood and adult obesity; children with obesity are about 5 times more likely to have obesity as adults than children without obesity and almost 80% of adolescents with obesity will have obesity as adults [1]. Several specific risk factors attributed to childhood obesity are parental obesity, pregestational and gestational diabetes, maternal smoking, gestational weight gain, premature delivery, rapid infant growth, poor nutrition, low levels of physical activity, inadequate sleep, sedentary behaviors, racial/ethnic differences due to both genetic and nongenetic factors, low family income and puberty [1, 3].

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IR is defined as a condition in which greater concentrations of insulin are needed to determine a physiological effect that was previously induced by lower concentrations. IR is characterized by a decrease in the ability of insulin to stimulate the use of glucose by muscles and adipose tissue and to suppress hepatic gluconeogenesis and release of glucose into circulation, resistance to insulin action on protein and lipid metabolism and on vascular endothelial function and gene expression [3, 4]. Genetic and environmental factors such as insulin receptor mutations, mutations that stimulate autoantibody production against insulin receptors, or mutations that induce the formation of abnormal glucose transporter 4 (GLUT4) molecules or plasma cell membrane glycoprotein- 1 molecules, mutations in the adipocyte-derived hormones or their receptors, obesity, ethnicity, sex, perinatal factors, puberty, polycystic ovary syndrome (PCOS), drugs (glucocorticoids, niacin, cyclosporine, growth hormone and protease inhibitors), sedentary lifestyle, and diet implicated in its etiology [2–5]. Increased free fatty acids, hormones and cytokines released by adipose tissue are involved in the pathogenesis of obesity-related IR [4]. An increased degree of IR is common in children and adolescents and is strongly associated with obesity.

Fasting plasma insulin and glucose, oral glucose tolerance test (OGTT), hyperinsulinemic euglycemic clamp (HEGC), frequently sampled intravenous glucose tolerance test (FSIVGTT), fasting glucose to fasting insulin ratio (FGIR), homeostasis model assessment insulin resistance (HOMA-IR), quantitative insulin-sensitivity check index (QUICKI), adipo-IR, insulin sensitivity index (ISI), Matsuda and Mcauley index (MCAi) are the methods used in assessment of IR [2–6]. The gold standard technique is the HEGC, however it is difficult to perform, invasive, expensive, time-consuming and needs a clinical or research setting [2, 6]. Additionally, the lipid-derived indicators such as triglyceride to high-density lipoprotein (HDL) cholesterol ratio are used for IR in children [7, 8]. Triglyceride glucose index (TyG), is another indicator used in assessment of IR, has been used in children and adolescents [9–12].

The aim of this study is establishing the correlation between insulin resistance indexes and determining the role of these indexes in assessment of IR in children with overweight and obesity.

Methods

A total of 276 children with overweight or obesity and 100 normal-weight healthy children admitted to outpatient pediatric clinics between January 2022 and November 2023 were enrolled in this single-center retrospective study. The patients with chronic diseases such as diabetes mellitus, dyslipidemia, metabolic dysfunction-associated steatotic liver disease (MASLD), hematological diseases, infectious diseases, endocrinological disorders and who were treated with drugs such as corticosteroids, nonsteroidal antiinflammatory drugs, psychotropic medications such as risperidone, antiepileptics such as valproate, and hormones were excluded from the study.

Body Mass Index (BMI) is calculated by dividing an individual's weight in kilograms (kg) by the square of his/her height in meters (m2). For children and teens, BMI is age- and gender-specific and is often referred to as "BMI-for-age" and is expressed, not as an absolute value, but as a percentile.

Children were divided into groups according to BMI. BMI percentiles were assessed using the reference tables of Neyzi et al. [13] as normal weight (BMI < 85 th percentile), overweight (BMI 85 - 94 th percentile) and obesity (BMI ≥ 95 th percentile).

All of the patients had complete blood count, biochemical tests such as alanine aminotransferase (ALT), aspartate aminotransferase (AST), fasting glucose, insulin, urea, creatinine, total cholesterol, triglyceride, HDL-cholesterol, and LDL-cholesterol tests, glycated hemoglobin (HbA1c), and thyroid function tests. The results were identified from medical records.

Biochemical tests were measured with colorimetric method and insulin was measured in the an auto-analyzer (Roche Brand, Cobas 8000 model, USA) by chemiluminescence immunoassay method.

IR was calculated using the homeostasis model assessment (HOMA) method as per the following equation: insulin resistance (HOMA-IR) = fasting insulin [mIU/L] x fasting glucose [mg/dL]/405). Patients with HOMA-IR levels > 3.16 were considered as having IR [14]. QUICKI was calculated from fasting plasma glucose (FPG) and fasting immunoreactive insulin (FIRI) levels, according to the report by Katz et al. with the formula: QUICKI = 1/(log [FIRI in mU/l] + log [FPG in mg/dl]) [15]. TyG index was calculated according to the formula: Ln [fasting triglycerides (mg/dL) × fasting plasma glucose (mg/dL)/2] [16].

Authors declared that the research was conducted according to the principles of the World Medical Association Declaration of Helsinki "Ethical Principles for Medical Research Involving Human Subjects", (amended in October 2013). Ethical approval was not required because the study was retrospective in accordance with the Regulation on Clinical Research (April 13, 2013, number: 28617).

Statistical analysis

Statistical analysis was performed using SPSS 15.0 software (SPSS Inc., Chicago, IL, U.S.A.). Results were

expressed as numbers and percentages for categorical variables and mean ± SD, minimum, maximum, and median for numerical variables. The Chi-square test was used for the comparison of rates in independent groups. As the numerical variables did not meet the normal distribution, comparisons of two independent groups were made by using the Mann Whitney U test. Relationships between numerical variables were examined with Spearman Correlation Analysis since the parametric test condition was not met. Cut-off value analyzes were performed with ROC curve analysis.

Sample size was calculated with G*Power Version 3.1.6 program. It was anticipated that the difference in insulin index levels between the 3 planned independent groups would be statistically significant with a medium effect size (Effect size f= 0.25 Ref: Cohen, J. (1988)). The minimum sample size was determined as 252 patients in total, 82 in groups, with a 5% margin of error within a 95% confidence interval. The study was planned to be completed with 100 patients in each group and a total of 300 patients.

P values of <0.05 were considered statistically significant.

Results

The mean ages were 13.0 ± 2.6, 13.1 ± 2.7 and 12.72 ± 2.23 (range:6–18 years), and male: female ratios were 1.14, 0.6 and 1.04 for the children with overweight, children with obesity and normal-weight healthy children, respectively. The characteristics and laboratory findings of the groups are shown in Table 1.

Statistically significant differences were observed in fasting glucose, HOMA-IR, ALT, HDL, TG, total cholesterol, LDL, TG/HDL, total cholesterol/HDL, LDL/HDL, TyG index, QUICKI and FGIR ($P<0.05$) (Table 1). In subgroup analysis, significant differences were obtained in parameters except AST and total cholesterol levels between controls and children with overweight and those with obesity (Table 2). When the children with overweight and children with obesity were compared, significant differences were obtained in insulin, HOMA-IR, TG, TG/HDL, TyG index, QUICKI and FGIR (Table 2).

Statistically significant positive correlations were observed between HOMA-IR and BMI, insulin, fasting glucose, ALT, TG, LDL, total cholesterol, TG/HDL, total cholesterol/HDL, LDL/HDL ve TyG index (Table 3). In addition, a statistically significant positive correlation was found between HOMA-IR and TyG index, and a negative correlation was found between QUICKI, FGIR and TyG index ($r=0.193$, $P<0.001$, $r=-0.456$, $P<0.001$ and $r=-0.392$, $P<0.001$, respectively) (Table 3).

When TyG index and lipid-derived indices were compared between children with/without IR, TyG index, TG/HDL, total cholesterol/HDL, and LDL/HDL ratios were higher in children with IR than those without IR (Table 4).

In receiver operating characteristic (ROC) curves analysis, cut-off points were found to be ≤ 0.31 for QUICKI (94.31% sensitivity and 97.58% specificity), ≤ 6.3 for FGIR (89.1% sensitivity and 93.94% specificity), and >4.62 for TyG index (49.29% sensitivity and 84.85% specificity). All the p-values were less than 0.001 (Fig. 1).

ROC curves analysis revealed that cut-off points for girls were ≤ 0.31 for QUICKI (95.83% sensitivity and 97.47% specificity), ≤ 6.2 for FGIR (92.5% sensitivity and 93.67% specificity), and >4.54 for TyG index (64.17% sensitivity and 77.22% specificity), and cut-off points for boys were ≤ 0.31 for QUICKI (92.31% sensitivity and 97.67% specificity), ≤ 6.9 for FGIR (94.51% sensitivity and 93.02% specificity), and >4.66 for TyG index (48.35% sensitivity and 86.05% specificity).

Discussion

IR indexes reflect the basal insulin secretion by pancreatic β cells and the hepatic insulin sensitivity/resistance due to the fact that fasting induces a steady basal state where insulin and glucose plasma levels should be maintained in the normal ranges in a healthy human [3]. However, these indexes carry disadvantages such as insensitivity, changes in β-cell function over time, lack of standardization, and lack of universal cut-off points for IR [2].

HOMA-IR is widely used for detection of IR and related diseases such as type 2 diabetes mellitus, MS, cardiovascular diseases, and MASLD [17]. Similarly, TyG index has been known to excellent marker for detection of IR-related diseases [16, 18, 19], even better than HOMA-IR [19, 20]. Matsuda uses parameters derived from OGTT to calculate the whole body insulin sensitivity index and the index has been validated for children with a high correlation with HEGC [6]. OGTT does not indicate whether elevated glucose levels depend on IR or β-cell dysfunction, but HOMA can estimate both insulin sensitivity and β-cell function [5, 21].

Although the insulin indexes have been well defined in adults and different studies have tried to identify HOMA cut-off values for children and adolescents, appropriate reference values are still lacking [6, 22]. Shashai et al. [23] conducted a study on children and adolescents to define the specific percentiles of HOMA-IR in relation to age, gender, and BMI and to establish reliable cut-offs to distinguish between low and high cardiometabolic risk. They stated that the values higher than 1.68 in normal-weight children defined as "nonphysiological state" and the cut-off rised to 3.42 in children with overweight/obesity [23] A higher value of HOMA-IR corresponds

Table 1 The characteristics and laboratory parameters of the children

	Normal weight	Overweight	Obese	P
	(*n* = 100)	(*n* = 133)	(*n* = 143)	
Age (years; mean ± SD)	12.7 ± 2.2	13.0 ± 2.6	13.1 ± 2.7	0.143
	8–17 (12)*	6–17 (13)*	6–17 (14)*	
Gender(Male/female)	1.04 (51/49)	1.14 (71/62)	0.6 (54/89)	0.35
BMI(kg/m2)	20.4 ± 1.6	24.3 ± 2.3	29.0 ± 4.3	< 0.001
	17–24 (20)*	19–29 (25)*	20–45 (28)*	
Glucose (74–109 mg/dL)	90.5 ± 7.1	92.7 ± 7.2	93.9 ± 8.2	0.005
	74–109 (91)*	73–111 (92)*	75–125 (94)*	
FPI (2.6—24.9 mU/L)	14.2 ± 11.6	17.2 ± 9.6	24.6 ± 18.1	< 0.001
	3–86 (11.5)*	4–47 (14)*	4–105 (20)*	
HbA1 C(< 5.7%)	5.29 ± 0.21	5.36 ± 0.27	5.44 ± 1.15	0.070
	4.6–5.9 (5.3)*	4.3–6.1 (5.4)*	2.3–18.2 (5.3)*	
HOMA-IR	2.73 ± 1.3	3.98 ± 2.35	6.48 ± 11.1	< 0.001
	0.10–5.80 (2.45)*	0.2–12 (3.3)*	0.3–28 (4.6)*	
ALT (0–41 IU/L)	14.6 ± 7.6	19.8 ± 11.6	22.8 ± 24.0	< 0.001
	6–55 (12)*	6–87 (17)*	5–271 (19)*	
AST (0–50 IU/L)	19.7 ± 4.7	20.5 ± 7.7	22.4 ± 13.5	0.194
	11–34 (19)*	10–65 (19)*	11–145 (20)*	
TG(0–200 mg/dL)	80.9 ± 34.7	107.1 ± 55.6	126.0 ± 69.2	< 0,001
	35–231 (73.5)*	41–398 (89)*	36–550 (108)*	
HDL (35–55 mg/dL)	54.5 ± 12.1	48.5 ± 9.6	47.2 ± 9.8	< 0.001
	30–88 (54.5)*	29–71 (48)*	28–78 (47)*	
Total cholesterol (50–200 mg/dL)	155.6 ± 29.6	159.3 ± 30.8	162.6 ± 29.8	0.156
	71–229 (152.5)*	43–238 (162)*	84–254 (160)*	
LDL (0–100 mg/dL)	84.4 ± 24.5	92.0 ± 23.6	93.8 ± 35.8	0.014
	29–147 (80.5)*	24–167 (91)*	27–400 (88)*	
TG/HDL	1.58 ± 0.82	2.39 ± 1.65	2.92 ± 2.15	< 0.001
	0.41–4.8 (1.47)*	0.66–11.3 (1.85)*	0.48–17.1 (2.31)*	
TC/HDL	2.92 ± 0.67	3.38 ± 0.93	3.55 ± 0.89	< 0.001
	1.62–4.76 (2.86)*	1.10–6.77 (3.25)*	2.01–6.59 (3.44)*	
LDL/HDL	1.62 ± 0.58	1.96 ± 0.68	2.06 ± 1.09	< 0.001
	0.55–3.33 (1.56)*	0.61–4.41 (1.95)*	0.75–12.5 (1.98)*	
TyG index	4.40 ± 0.20	4.55 ± 0.23	4.62 ± 0.25	< 0.001
	4.96 (4.39)*	4.01–5.28 (4.54)*	3.37–5.49 (4.6)*	
FGIR	9.04 ± 4.78	6.98 ± 3.64	5.40 ± 3.50	< 0.001
	3.46–31 (8.17)*	2.06–23.5 (6.6)*	0.90–22.5 (4.6)*	
QUICKI	0.33 ± 0.03	0.31 ± 0.02	0.30 ± 0.03	< 0.001
	0.29–0.40 (0.33)*	0.27–0.38 (0.31)*	0.24–0.39 (0.3)*	

ALT Alanine aminotransferase, *AST* Aspartate aminotransferase, *BMI* Body mass index, *FPI* Fasting plasma insulin, *FGIR* Fasting glucose/insulin ratio, *HbA1c* Glycated haemoglobin, *HDL* High-density lipoprotein, *HOMA-IR* Homeostatic model assessment insulin resistance, *LDL* Low-density lipoprotein, *TC* Total cholesterol, *TG* Triglyceride, *TyG* Triglyceride glucose index, *QUICKI* Quantitative insulin-sensitivity check index

P < 0.05 is statistically significant

ANOVA test

* max.-min., median

to a more severe IR [23]. Shashaj et al. [23] reported that children with overweight/obesity had higher HOMA-IR levels compared with normal-weight peers at any age. Similarly, our children with overweight or obesity had significantly higher HOMA-IR levels than the normal-weight children.

Pastucha et al. [24] reported that the presence of IR according to QUICKI < 0.357 was identified in 86% and

Table 2 Subgroup analysis of the study groups

	Normal weight vs overweight group	Normal weight vs children with obesity group	Children with obesity vs children with overweight
	P	*P*	*P*
Age	0.163	0.056	0.501
BMI	< 0.001	< 0.001	< 0.001
FPI	0.001	< 0.001	< 0.001
Glucose	0.027	0.001	0.276
HBA1 C	0.021	0.078	0.830
HOMAIR	< 0.001	< 0.001	< 0.001
ALT	< 0.001	< 0.001	0.072
AST	0.944	0.147	0.107
HDL	< 0.001	< 0.001	0.246
TG	< 0.001	< 0.0010.001	
Cholesterol	0.145	0.059	0.722
LDL	0.006	0.019	0.620
TG/HDL	< 0.001	< 0.001	0.002
Cholesterol/HDL	< 0.001	< 0.001	0.081
LDL/HDL	< 0.001	< 0.0010.657	
TyG index	< 0.001	< 0.001	0.004
QUICKI	< 0.001	< 0.001	< 0.001
FGIR	< 0.001	< 0.001	< 0.001

ALT Alanine aminotransferase, *AST* Aspartate aminotransferase, *BMI* Body mass index, *FPI* Fasting plasma insulin, *FGIR* Fasting glucose/insulin ratio, *HbA1c* Glycated haemoglobin, *HDL* High-density lipoprotein, *HOMA-IR* Homeostatic model assessment insulin resistance, *LDL* Low-density lipoprotein, *TG* Triglyceride, *TyG* Triglyceride glucose index, *QUICKI* Quantitative insulin-sensitivity check index

Mann Whitney U test

$P < 0.05$ is statistically significant

according to HOMA-IR > 3.16 in 53% of their children with obesity. 53.3% of our children with overweight and 75.5% of those with obesity had HOMA-IR > 3.16 levels, while 48.1% of our children with overweight and 74.1% of children with obesity had QUICKI ≤ 0.3 levels. Basal insulin and glucose levels, HOMA-IR and QUICKI were significantly higher in children with MS than the children without MS. We could not evaluate MS due to retrospective nature of this study.

Chandrasekhar et al. [25] reported that children with obesity had significantly higher fasting insulin levels, HOMA-IR, FGIR and QUICKI when compared to controls. HOMA-IR had more AUC (0.760) followed by FGIR (0.721) when compared to QUICKI (0.240), thus HOMA-IR was found to be a stronger predictor of IR when compared to FGIR and QUICKI in children with obesity [25]. Although no significant difference was observed in AUC (HOMA-IR: 0.996, FGIR: 0.980, QUICKI: 0.986, TyG index:0.717) in our study, HOMA-IR, FGIR, and QUICKI constitute stronger predictors of IR than TyG index in children with overweight and obesity according to the present study.

Obesity leads to elevated levels of TC, TG, and LDL and reduced levels of HDL, which are risk factors for IR. It has been reported that lipid related derived indices have a higher predictive diagnostic value than conventional lipid indices alone [8]. You-xiang et al. [8] demonstrated that the diagnostic value of the nomogram model including lipid related derived indices such as TG/HDL, TC/HDL, and LDL/HDL screened by the LASSO-logistic regression combination was better than a single indicator for predicting the risk of IR in children and adolescents with obesity. García et al. [26] and Giannini et al. [7] reported that although efficiency low, single lipid-derived indexes such as TC/HDL or TG/HDL could discriminate IR in children and adolescents. In this study, we observed a statistically significant positive correlation between lipid-derived indices and HOMA-IR, and TyG index and a negative correlation between FGIR, QUICKI and TyG index of children with overweight and obesity.

Yoon et al. [19] reported that TyG index had a positive correlation with fasting glucose, HOMA-IR, HbA1c, total cholesterol, TG, and LDL, and a negative correlation with HDL after controlling for sex, age and BMI standard

Table 3 Relationship between insulin indexes and demographic and laboratory parameters

	HOMA-IR		QUICKI		FGIR	
	r	P	r	P	r	P
Age	0.059	0.253	− 0.193	< 0.001	− 0.231	< 0.001
BMI	0.211	< 0.001	− 0.426	< 0.001	− 0.357	< 0.001
FPI	0.505	< 0.001	− 0.737	< 0.001	− 0.572	< 0.001
Glucose	0.213	< 0.001	− 0.391	< 0.001	− 0.083	0.107
HBA1 C	0.060	0.244	− 0.206	< 0.001	− 0.134	0.009
ALT	0.158	0.002	− 0.256	< 0.001	− 0.192	< 0.001
AST	0.086	0.096	− 0.072	0.164	− 0.015	0.776
HDL	− 0.032	0.538	0.242	< 0.001	0.241	< 0.001
TG	0.205	< 0.001	− 0.403	< 0.001	− 0.355	< 0.001
Total cholesterol	0.138	0.007	− 0.151	0.003	− 0.135	0.009
LDL	0.163	0.002	− 0.153	0.003	− 0.106	0.040
TG/HDL	0.204	< 0.001	− 0.400	< 0.001	− 0.340	< 0.001
Total cholesterol/HDL	0.143	0.005	− 0.330	< 0.001	− 0.304	< 0.001
LDL/HDL	0.159	0.002	− 0.246	< 0.001	− 0.194	< 0.001
TyG index	0.193	< 0.001	− 0.456	< 0.001	− 0.392	< 0.001

ALT Alanine aminotransferase, *AST* Aspartate aminotransferase, *BMI* Body mass index, *FPI* Fasting plasma insulin, *FGIR* Fasting glucose/insulin ratio, *HbA1c* Glycated haemoglobin, *HDL* High-density lipoprotein, *HOMA-IR* Homeostatic model assessment insulin resistance, *LDL* Low-density lipoprotein, *TG* Triglyceride, *TyG* Triglyceride glucose index, *QUICKI* Quantitative insulin-sensitivity check index

Spearman Correlation Analysis

P < 0.05 is statistically significant

Table 4 Lipid-derived indexes in patients with/without insulin resistance

	IR (+)	IR (-)	*P*
TyG Index	4.62 ± 0.25	4.43 ± 0.21	< 0.001
	4.01–5.49 (4.61)*	3.37–4.92 (4.44)*	
TG/HDL	2.86 ± 2.12	1.76 ± 0.92	< 0.001
	0.48–17.1 (2.22)*	0.41–6.94 (1.61)*	
Total cholesterol/HDL	3.52 ± 0.92	3.07 ± 0.78	< 0.001
	1.77–6.77 (3.41)*	1.1–5.68 (3.04)*	
LDL/HDL	2.01 ± 0.99	1.78 ± 0.62	0.014
	0.71–12.5 (1.92)*	0.55–3.8 (1.77)*	

HDL High-density lipoprotein, *LDL* Low-density lipoprotein, *TG* Triglyceride, *TyG* Triglyceride glucose index

P < 0.05 is statistically significant

Mann–Whitney U test

* min.-max., median

deviation scores (SDS). In ROC analysis, the TyG index (AUC:0.839) showed a better performance compared to HOMA-IR (AUC:0.645) in identifying children and adolescents with type 2 diabetes mellitus (P < 0.001). When compared, our children had higher AUC of HOMA-IR than TyG index (0.996 vs 0.717) in our study. The lower AUC of TyG index than HOMA-IR in our study population may be explained by the fact that more than one measurement method other than BMI was not used and that central obesity could not measured using waist circumference and waist-to-height ratio, which are suggested to be better indices than BMI [11, 27]. In addition, failure to identify factors other than obesity that may be associated with IR in children, such as dietary patterns and lifestyle, daily screen time (television, computer, games) and daily time spent in activities (running, cycling, playing ball) may play a role in the lower AUC of TyG index. Peplies et al. [28] reported that after adjusting for other variables, the longer daily time spent in active activities was associated with lower TyG index values in preadolescent children. Vieira-Ribeiro et al. [29] suggested that more than one indicator should be used whenever possible for an early and more reliable diagnosis of adiposity alterations in children.

There are few studies which have examined cut-off values of TyG index in the pediatric population [10, 29–31]. Brito et al. [30] examined the predictive capacity TyG index throughout eight study and stated that the TyG index was positively associated with other IR indexes in prediction of IR risk and other cardiometabolic risk factors in children and adolescents. Considering all cut-off points established by the included studies, they reported that the lowest cut-off point was 4.65 and the highest was 8.66. Reckziegel et al. [10] reported that TyG cut-off point was ≥ 7.94 (AUC:0.64) in overall, ≥ 7.94 and ≥ 7.91

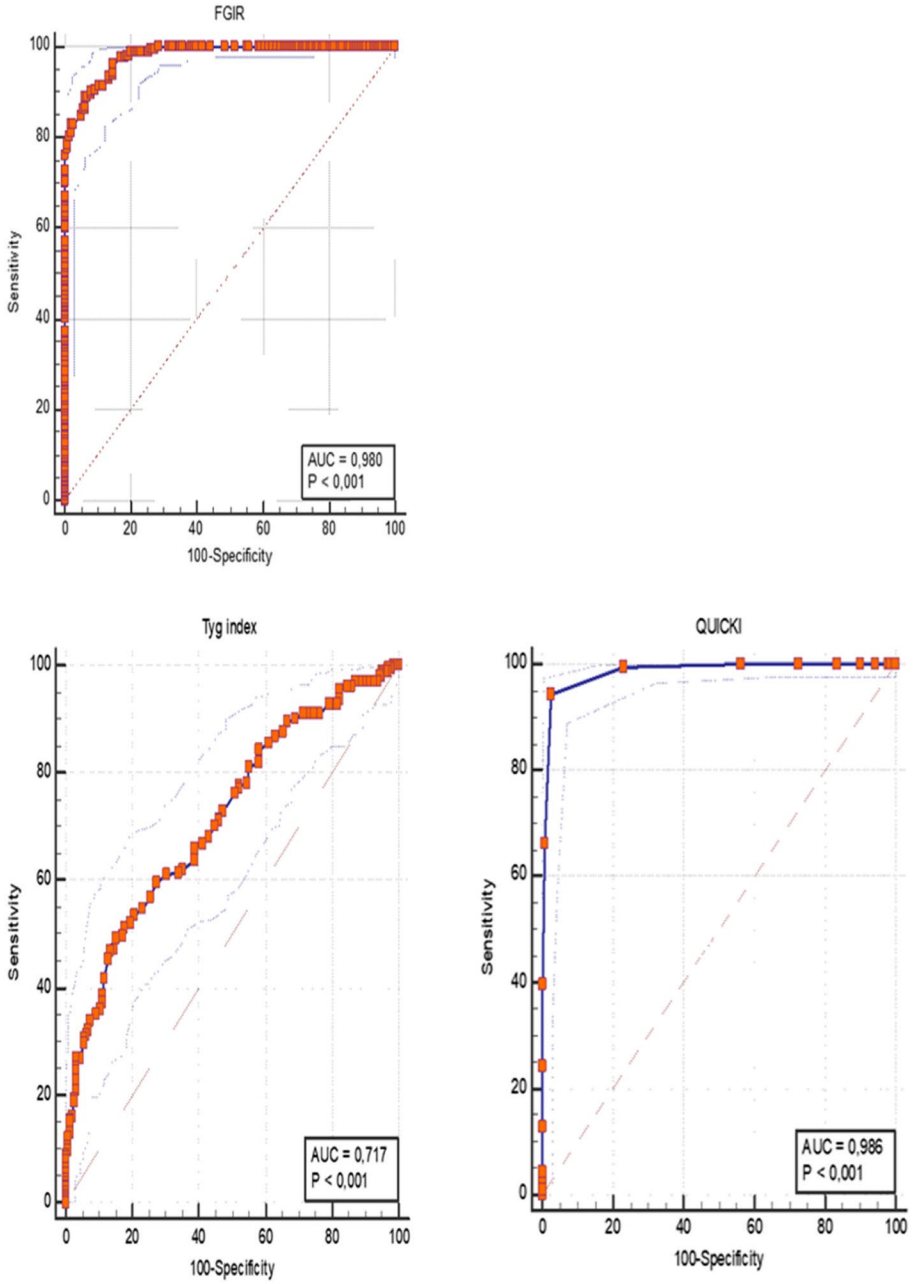

Fig. 1 The receiver operating characteristic (ROC) curve analysis of FGIR, QUICKI and TyG index

for girls and boys, respectively, diagnosing IR in 54.3% of the children. Vieira-Ribeiro et al. [29] obtained cut-off points of TyG ≥7.88 (AUC:0.63) in Brazilian children age 4 to 7 years, finding 42.3% of IR, while it was ≥8.33 overall; ≥8.33 and ≥8.47 for boys and girls, respectively in study conducted by Angoorani et al. [18] and ≥7.96 (AUC:0.65) with 65% sensitivity and 58% specificity in the study of Dikaiakou et al. [31]. The variations among studies may be related to various characteristics of the population studied such as age group, different ethnic groups, puberty stage, sample size, and different reference standards.

In our study, the cutt-off point for TyG index was >4.62 (AUC:0.717) with 49.29% sensitivity and 84.85% specificity overall, and it was >4.54 for girls (64.17% sensitivity and 77.22% specificity), and >4.66 for boys (48.35% sensitivity and 86.05% specificity). In the clinical setting, this means that a TyG index greater than 4.62 should be

considered as having a higher risk for IR development, when compared to those with lower TyG values. As suggested by Vieira-Ribeiro et al. [29], if IR risk is identified by TyG, another more precise and more specific method can be used to confirm the diagnosis.

Puberty as an unchangeable risk factor, is a physiological condition responsible for IR. Hormonal changes in puberty is linked to a marked decrease (25–50%) of insulin sensitivity. d'Annunzio et al. [32] reported that the HOMA-IR index slightly increases with Tanner's stage and no significant correlation was observed between HOMA-IR, QUICKI and BMI-SDS or chronologic age throughout puberty. One of the limitations of our study was inability to determine changes in IR indexes according to puberty stage due to retrospective nature of this study.

Limitations of the study were being a single-center retrospective study with a small number of children, inability to perform the anthropometric measurements other than BMI such as waist circumference, whether there was fluctuations of TyG and other indexes similar to HOMA-IR with weight loss or gain. The indexes such as OGTT, HEGC, ISI, and FSIVGTT could not be performed in our hospital.

In conclusion, we think that our study, which compares all four IR indexes, namely HOMA-IR, QUICKI, FGIR and TyG index, in children and adolescents, will contribute to the literature, especially considering the few existing studies on IR markers in this age group. It is essential to prevent development and occurrence of IR in children and adolescents with overweight/obesity due to increased metabolic and cardiovascular risks. Therefore, early identifying IR is important, and practical, easy, cost-effective, non-invasive, accessible, reliable, accurate and valid screening tests adjusted for ethnic groups, genders, and pubertal stages were needed. Further studies were required for determining the multi-center validation of cutt-off values for IR indexes in childhood.

Abbreviations

ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
BMI	Body mass index
FGIR	Fasting glucose/insulin ratio
FPI	Fasting plasma insülin
FSIVGTT	Frequently sampled intravenous glucose tolerance test
HbA1c	Glycated haemoglobin
HDL	High-density lipoprotein
HEGC	Hyperinsulinemic euglycemic clamp
HOMA-IR	Homeostasis model assessment insulin resistance
IR	Insulin resistance
LDL	Low-density lipoprotein
MASLD	Metabolic dysfunction-associated steatotic liver disease
MS	Metabolic syndrome
OGTT	Oral glucose tolerance test
TC	Total cholesterol
TG	Triglyceride
TyG	Triglyceride glucose index
QUICKI	Quantitative insulin-sensitivity check index

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Written informed consent was obtained from the parents.

Author contributions
Conceptualization: D.K; Methodology: D.K; Formal analysis and investigation: D.K, M.K.K; Data collecting: D.K, M.K.K; Writing—original draft preparation: D.K; Writing—review and editing: D.K, M.K.K.

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Data availability
All data generated or analysed during this study are included in this published article.

Declarations

Ethics approval and consent to participate
Authors declared that the research was conducted according to the principles of the World Medical Association Declaration of Helsinki "Ethical Principles for Medical Research Involving Human Subjects", (amended in October 2013). No ethical approval is required because of retrospective nature of the study.

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