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Triglyceride-Glucose (TyG) Index in a Pediatric Non-Diabetic Cohort-Surrogate Marker of Insulin Resistance?

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Abstract: The incidence of diabetes and obesity has reached epidemic levels. Although insulin resistance is the key pathophysiological mechanism, several surrogate biomarkers of insulin resistance such as Homeostatic Model Assessment for Insulin Resistance (HOMA-IR), have been proposed. In recent years, research on triglyceride-glucose (TyG) index as a useful marker for identifying cardio-metabolic risk, particularly in adults, has been on the rise. However, there is a paucity of data on the role of the TyG index in children and adolescents and the association of the TyG index with HOMA-IR and DEXA (dual-energy X-ray absorptiometry), especially in North America. Therefore, this study aims to investigate the role of the TyG index in children and adolescents, and explore the relationship between the TyG index and HOMA-IR and DEXA in North American children and adolescents. Forty-four lean and obese children and adolescents were recruited after obtaining informed consent, anthropometric and laboratory assessments. TyG index was significantly higher in obese children and adolescents than in their lean counterparts ($p < 0.001$) and correlated significantly with glucose, BMI, DEXA, triglycerides and HOMA-IR. Thus, this pilot study shows that the TyG index may serve as an excellent surrogate for assessing cardio-metabolic risk in pediatrics.

Keywords: TyG index; insulin resistance; children; pediatric; marker

1. Introduction

The incidence of diabetes and obesity in children have reached alarming proportions [1]. The main pathophysiological mechanisms underlying metabolic syndrome, obesity and diabetes is insulin resistance [2]. In recent years, several surrogate biomarkers of insulin resistance such as fasting insulin levels, HOMA-IR derived from the product of glucose etc., have been proposed. The triglyceride-glucose (TyG) index has emerged as a useful marker for identifying cardio-metabolic risk, particularly in adults, and it is increasingly being studied in children [3–5]. The TyG index is derived from fasting triglyceride (TG) and glucose levels and appears to be better than HOMA-IR since it also includes the dyslipidemia component of cardio-metabolic disorders. The TyG index has been validated against the gold standard of hyperinsulinemic-euglycemic clamp technique for defining insulin resistance [6,7]. Indeed, it has been shown to be a good correlate of non-alcoholic fatty liver disease in children and is associated with higher risk of subclinical cardiovascular conditions, such as increased carotid intima-media thickness (cIMT) or arterial stiffness [8,9]. However, few studies have explored the role of the TyG index in children and adolescents, and the association of the TyG index with HOMA-IR and DEXA, especially in North America.

Therefore, this study investigated the role of the TyG index as a non-invasive and cost-effective tool in children and adolescents, and its association with HOMA-IR and DEXA.

2. Subjects and Methods

This cross-sectional study analyzed the clinical data of children and adolescents enrolled in our pediatric hospital from January 2013 to July 2015to investigate biomarkers of insulin resistance. The study was approved by Baylor Institutional Review Board (IRB). A total of 44 participants, ages 8–14 yrs were enrolled after obtaining informed consent. Anthropometric variables were recorded, including pubertal stage, blood pressure and lean body mass by dual-energy X-ray absorptiometry (DEXA). Subjects were divided into 2 groups: Obese and Lean. Overweight was defined as having a body mass index (BMI) equal to or above the 85th percentile and below the 95th percentile for children and adolescents of the same sex and age. Obesity was defined as having a BMI equal to or greater than the 95th percentile for children and adolescents of the same sex and same age. None of the participants had diabetic ketoacidosis. The TyG index was calculated as ln (fasting glucose (mg/dL) × triglycerides (mg/dL))/2 and the HOMA (homeostatic model assessment) index as fasting insulin (μU/mL) × fasting glucose (mmol/L)/22.5. Glucose, Hemoglobin A1C, Insulin and C-peptide levels were obtained on a fasting sample by routine clinical laboratory testing and none of the subjects had or was treated for any endocrine-related diseases such as diabetes mellitus, non-alcoholic fatty liver disease, dyslipidemia, hypertension, thyroid disease or growth hormone deficiency.

3. Results

The characteristics and complete data of the 24 lean and 20 obese children/adolescents are presented in Table 1. Notably, 11 of the lean children were in Tanner stage 1 and the rest were in Tanner stage 3 or 4. In the obese group, 11 of the obese children were in Tanner stage 1 and the rest were in Tanner stage 3 or 4. As expected, BMI was significantly higher in obese children and they had higher triglyceride and fasting insulin and C-peptide levels. HOMA-IR was significantly elevated in obese group compared to the lean group. Importantly, since insulin and C-peptide values are difficult to obtain, we calculated the TyG index, which is only derived from glucose and triglyceride concentrations. The results indicated that the TyG index was significantly higher in obese non-diabetic children compared to lean non-diabetic children ($p < 0.0001$, Figure 1).

Next, we determined the correlation of the TyG index with the known parameters of BMI, Insulin, DEXA as well as HOMA. It was observed that the TyG index correlated significantly with BMI, r = 0.67, $p = 0.01$; fasting insulin: r = 0.61, $p < 0.05$; with DEXA: r = 0.51, $p < 0.05$ and HOMA, r = 0.59 and $p = 0.045$.

Table 1. Subject characteristics and laboratory parameters.

	LEAN (n = 24)	OBESE (n = 20)
AGE (years)	11.17 ± 2.20	10.25 ± 2.17
GENDER (M/F)	15/9	9/11
HEIGHT (cm)	151.14 ± 18.47	147.41 ± 12.96
WEIGHT (kg)	45.12 ± 17.79	59.54 ± 19.05 *
BMI (kg/m^2)	18.39 ± 2.26	26.81 ± 4.77 **
Lean Body Mass by DEXA (kg)	33.05 ± 11.12	35.68 ± 11.21
Glucose (mg/dL)	90.05 ± 5.71	89.58 ± 7.59
HbA1C (%)	5.33 ± 0.20	5.38 ± 0.17
Triglycerides (mg/dL)	66.13 ± 38.92	111.5 ± 60.73 **
Insulin (mU/L)	9.56 ± 5.91	24.65 ± 13.09 **
C-peptide (ng/mL)	0.83 ± 0.32	1.50 ± 0.82 *
Glucose (mg/dL)	89.28 ± 7.84	92.24 ± 6.80
HOMA Index	1.84 ± 0.89	5.67 ± 3.25 **
TyG Index	3.39 ± 0.22	3.65 ± 0.23 **

** $p < 0.0001$ compared to lean; * $p < 0.01$ compared to lean. Data are expressed as the mean ± S.D.

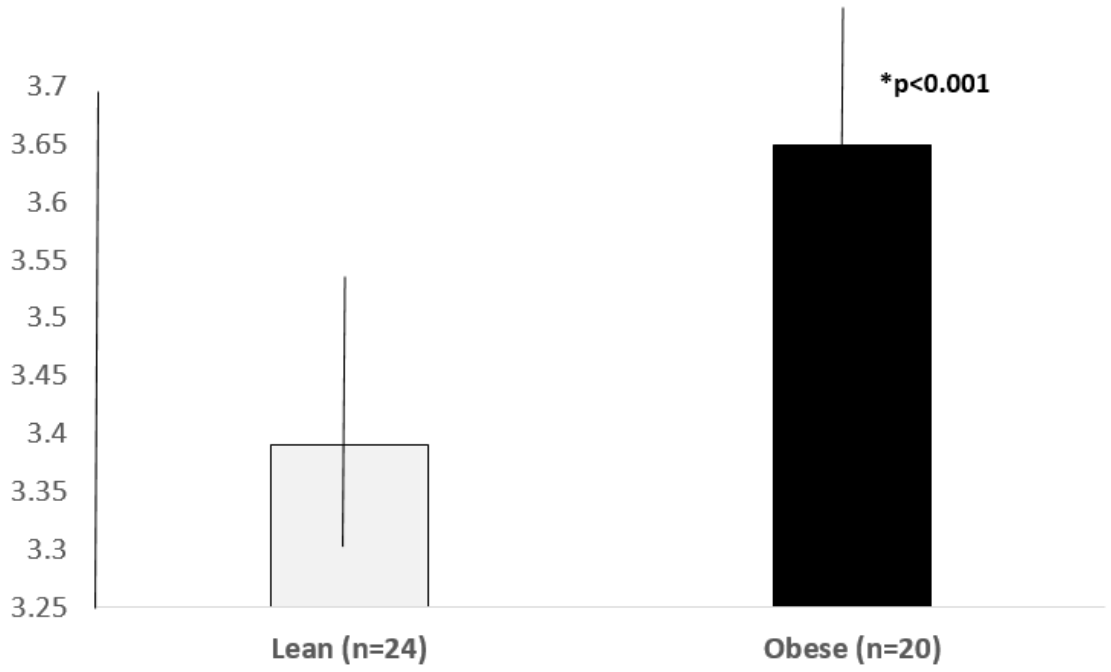

Figure 1. TyG index in lean vs obese non–diabetic children.

4. Discussion

In this report, we show that TyG index is an important marker of obesity, dyslipidemia and insulin resistance and may be used as a non-invasive, cost-effective, and simple marker to calculate the cardio-metabolic risk of pediatric populations.

Although HOMA is recognized mainly as a marker of insulin resistance, the TyG index shows better performance because it is also a marker of obesity and dyslipidemia, making it a superior predictive tool for assessing cardio-metabolic risk.

Song et al. [8] reported the utility of TyG index and modified TyG indices in predicting nonalcoholic fatty liver disease (NAFLD) in 3728 youth aged 10–19 years, from Korea. All TyG and modified TyG indices exhibited progressively increasing odds rations as well as 95% confidence intervals in the prediction of NAFLD across all TyG tertiles (all $p < 0.001$). Chang et al. [9] further reported similar findings as Song et al. regarding the predictive power of the original and modified TyG indices for NAFLD detection in 1233 obese children aged 6–18 years from Taiwan.

In another Korean study comprising 7400 children and adolescents, Yoon et al. [10] demonstrated that the TyG index could effectively predict metabolic perturbations that could contribute to future cardiovascular disease. Multiple linear regression analysis in their study revealed that the TyG index was significantly associated with waist circumference, systolic and diastolic blood pressure, glucose, HDL and TG ($p < 0.001$), all of which are features of the metabolic syndrome. A recent review of prospective studies investigating the role of the TyG index as a biomarker of cardio-metabolic risk worldwide [11] showed that, although the studies obtained promising results, the utility of TyG index in predicting the risk in children and adolescents in North America has not been clarified, which represents a key novelty of this study.

The findings of this small sample-size study in North America, together with results from other studies in children, suggest that the TyG index may be an excellent predictor of future complications in children. Identifying children with a high TyG index will allow clinicians to implement early lifestyle and dietary interventions to reduce long-term health risks. Further longitudinal studies are advocated to explore the predictive value of the TyG index for future cardiovascular and metabolic diseases in children, assess the effect of Tanner stage and racial disparities in the pediatric population, and derive cut-offs for cardio-metabolic risk.

Author Contributions

S.D. generated the idea for this publication. D.K. and X.C. undertook the analysis and preparation of data and tables. All generated the manuscript and reviewed revisions. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement

This study was approved by the Baylor College of Medicine Institutional Review Board, H29575.

Informed Consent Statement

All volunteers provided written informed consent.

Data Availability Statement

The data is available for review upon request.

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Conflicts of Interest

None of the authors reports any conflicts of interest.

Use of AI and AI-Assisted Technologies

These were not used by the authors submitting this paper.

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