To use of triglyceride/hdl cholesterol ratio to predict insulin resistance and dysglycemia in overweight and obese children

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Abstract

Aim: Numerous studies have demonstrated a clear relationship between high triglyceride to high-density lipoprotein cholesterol ratio (TG/HDL-C) and decreased insulin sensitivity, nonalcoholic fatty liver disease, and metabolic syndrome. Dysglycemia may result from increased insulin sensitivity. No study has examined the relationship between this ratio and dysglycemia in the literature. In this study, we aimed to determine if the TG/HDL-C ratio of 2.27 would serve as a marker for detecting dysglycemia in the oral glucose tolerance test (OGTT).

Materials and Methods: This study consists of a retrospective and cross-sectional analysis of 101 patients aged 8.93-17.79 years who were assessed for overweight and obesity in pediatric endocrine outpatient clinics and underwent oral glucose tolerance test as a screening tool for prediabetes and/or type 2 diabetes. The patients' anthropometric, physical examination, radiological and laboratory data were collected from the electronic and paper-based patient records.

Results: In overweight and obese children, the TG/HDL-C ratios of 2.27 and higher were correlated with HOMA-IR and insulin levels, similar to previous studies ($p < 0.05$). While basal fasting glucose was significantly higher in patients with dysglycemia ($p < 0.05$), there was no correlation between basal fasting insulin, HbA1C, TG/HDL-C ratio, BMI-SDS and dysglycemia.

Conclusion: Although it was shown in this study that there is a relationship between an increased TG/HDL-C ratio and insulin level, no relationship was found with dysglycemia.

Introduction

Childhood obesity can negatively affect almost every organ system and lead to serious health complications such as dyslipidemia, insulin resistance, hypertension, glucose metabolism disorders, fatty liver disease, and psychological complications [1]. The metabolic deterioration that starts with compensated hyperinsulinemia in obesity can turn into dsyglisemia (impaired fasting glucose [IFG], impaired glucose tolerance [IGT] and type 2 diabetes) with the progression of insulin resistance [2]. Prediabetes is a term used for individuals who do not meet the criteria for diabetes but have abnormal carbohydrate metabolism. Screening for prediabetes and/or type 2 diabetes should be considered after puberty or after the age of ten, whichever occurs first, for individuals with a body mass index (BMI) above 85% percentile and at least one risk factor for diabetes [3]. In general, measurement of fasting plasma glucose (FPG),

plasma glucose levels measured 120 minutes after 75 g oral glucose and glycosylated hemoglobin (HbA1c) levels are administered is appropriate for diagnostic screening [3]. Another laboratory test that should be evaluated in the first examination of obese children is serum lipid levels. Due to its ability to show the interaction between lipoprotein ratios and lipid fractions with greater accuracy, it is used more frequently than isolated lipid values for assessing cardiovascular risk in adults [4].

Several studies in children have demonstrated a clear relationship between the triglyceride/high-density lipoprotein cholesterol ratio (TG/HDL-C) and insulin resistance [5-7]. Giannini et al. suggested if the ratio greater than 2.27 as a critical cut-off point for predicting insulin resistance in children [8].

In this study, we investigated whether a TG/HDL-C ratio of 2.27 would serve as a marker for detecting dysglycemia (IFG, IGT, and/or DM) in the oral glucose tolerance test (OGTT).

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Materials and Methods

During the period March-December 2022, the study was conducted at Malatya Training and Research Hospital and Buca Seyfi Demirsoy Training and Research Hospital Pediatric Endocrinology Clinics with BMI ≥ 85% percentile and at least one diabetes risk factor, the onset of puberty or being older than ten years old, prediabetes and/or type 2 diabetes patients who underwent OGTT as part of a diabetes screening program. A retrospective review was conducted on the records of 101 patients aged 8.93-17.79 years.

This study was conducted in accordance with the principles of the Declaration of Helsinki. The Malatya Turgut Özal University Non-Invasive Clinical Research Ethics Committee approved this study (Ethics Committee date: 5.1.2023 and number: B.117).

Following the ADA 2022 guidelines, at least one of the following factors posed a risk for diabetes in children with a BMI of 85th percentile [3];

1. If the patient's mother has pregnancy-related diabetes or gestational diabetes
2. If the patient's first- or second-degree relative has type 2 diabetes
3. If the patient has arace/ethnicity which is high risk (African American, Asian American, Native American, Latino, Pacific Islander)
4. If the patient has signs of insulin resistance or conditions associated with insulin resistance (dyslipidemia, acanthosis nigricans, polycystic ovary syndrome, hypertension, or low birth weight for gestational age).

Inclusion criteria

- The children whose BMI ≥ 85% percentile and had at least one diabetes risk factor [1 - 4]

- After puberty or after the age of ten, whichever occurs first

- Prediabetes and/or type 2 diabetes patients who underwent OGTT as part of a diabetes screening program

Exclusion criteria

- Patients with a history of drug use or comorbidity

- Patients with chronic diseases, psychiatric diseases or coexisting acut diseases

- Patients who had any lipid metabolism disease in their family

Anthropometric and physical examination, and laboratory data were recorded from file records. Anthropometric evaluations were made in the morning with a thin outfit and shoes removed. The patient's weight was measured with a device of Seca GmbH (Hamburg) with a sensitivity of 0.10 kg and height was measured using a Harpenden stadiometer (Holtain) with a sensitivity of 0.10 cm. Body mass index was calculated with the formula body weight (kg)/square height (m). Body mass index percentiles and standard deviation scores (SDS) were calculated using Turkish children's standards [9]. Puberty was evaluated according to Tanner-Marshall staging. Pubertal onset was considered testicular volume ≥4 ml in boys and Tanner stage ≥ two breasts in girls [10].

Laboratory tests

The patients basal serum lipids levels, liver function tests, glucose and insulin levels measured after 12 hours of fasting, HbA1C levels measured and homeostasis model of assessment for insulin resistance (HOMA-IR) index values were recorded. HOMA-IR was calculated using the ratio of fasting insulin (mIU/ml) x fasting glucose (mmol/L)/22.50, and values above 3.16 in pubertal children and above 2.50 in prepubertal children were considered indicators of insulin resistance [11].

Oral glucose tolerance test

Blood samples were drawn at 08:00 in the morning after a fasting period of 12 hours for glucose and insulin levels, and oral glucose of 1.75 g/kg (maximum 75 g) was given to the patients. Venous blood samples were taken at 0 and 120 minutes for glucose and insulin levels. OGTT was interpreted as; normal fasting glucose (NFG): 0 th minute plasma glucose <100 mg/dl, IFG: 0 th minute plasma glucose 100-125 mg/dl, diabetes: 0th minute plasma glucose ≥126 mg/dl. Normal glucose tolerance (NGT): 120 th minute plasma glucose <140 mg/dl, IGT: 120 th minute plasma glucose 140-199 mg/dl and diabetes 120 th minute plasma glucose ≥ 200 mg/dl.

Radiological evaluation

Evaluation of hepatic steatosis was performed with USG examination. Pediatric radiologists used Samsung RS85 Prestige device (Samsung Medison Co. Ltd., Hongcheon, Korea) a 5 MHz curvilinear transducer in younger children and a 3.5 MHz transducer in older children.

Statistical analysis

A histogram and Kolmogorov–Smirnov test were used to evaluate the assumption of a normal distribution for numerical data. Normally distributed data are presented as the mean ± standard deviation, and nonnormally distributed data are presented as the median (min-max). Percentages (numbers) were used to summarize categorical data. The independent sample T test and Mann–Whitney U tests were used to analyze the numerical data, and the chi-square test was employed to examine the correlation between categorical data. The correlation analysis was conducted using Spearman's correlation. A $p < 0.05$ value was considered statistically significant. IBM SPSS Statistics 20.00 (New York, USA) was used for all analyses.

Results

The mean decimal age of the patients was 13.79±2.24 years. A total of 61.40% of the patients (n: 62) were female, and 94.10% (n: 95) were pubertal. A total of 6.90% (n: 7) of the patients were overweight (BMI: 85-95% percentile), and 93.10% (n: 94) were obese (BMI ≥95% percentile). The mean BMI-SDS of the patients

Table 1. Comparison of the presence of dysglycemia and metabolic parameters.

	Group 1 (n:45)	Group2 (n:56)	p value
Decimal age	13.86±2.35	13.69±2.26	0.709
Pubertal patients	93.30 % (n:42)	98.20 % (n:55)	0.211
BMI-SDS	2.71±0.86	2.68±0.64	0.830
Basal fasting glucose	104(75-192)	97 (76-115)	<0.001
Basal fasting insulin	30(1.20-115.30)	36.10(12.30-130)	0.276
HbA1C	5.79±0.57	5.77±0.43	0.820
HOMA-IR	7.22(0.37-34.20)	8.12 (2.43-35)	0.840
TG	121(41-384)	132.5(28-274)	0.975
HDL	43(29-74)	43.3(32.3-100)	0.684
LDL	88.9(26-146.1)	95.5(19-273)	0.115
Total cholesterol	162(88-228)	170(59-377)	0.280
TG/HDL ratio ≥2.27	69% (n:31)	66.10% (n:37)	0.764
Presence of hepatosteatosis	65 % (n:26/40)	55.30% (n:26/47)	0.359

BMI-SDS: Body mass index standard deviation score TG:Triglyceride HDL: High-density lipoprotein cholesterol LDL: Low density lipoprotein cholesterol TG/HDL: triglyceride/high-density lipoprotein cholesterol. HbA1c: Glycosylated hemoglobin. HOMA-IR: Homeostasis model of assessment for insulin resistance index.

Table 2. In overweight children, correlations of metabolic parameters and insulin with the triglyceride-to-high-density lipoprotein cholesterol ratio.

	R	P
BMI-SDS	0.115	0.250
Basal fasting glucose	-0.198	0.047
Basal fasting insulin	0.265	0.007
HbA1C	0.078	0.461
HOMA-IR	0.200	0.045

BMI-SDS: Body mass index standard deviation score HbA1C: Glycosed hemoglobin HOMA-IR: Homeostasis model of assessment for insulin resistance index.

was 2.69±0.74. The median HOMA-IR score of the patients was 7.63 (min: 0.37, max: 34.99). When insulin resistance was evaluated according to puberty status, insulin resistance was found in 93.10 % (n: 94) of patients.

OGTT results were typical in 55.40% (n: 56) of patients. Of 45 patients with dysglycemia, 20% (n: 9) had IFG, 33.30% (n: 15) had IGT, 35.60% (n: 16) had IFG and IGT together, and 11.10% (n: 5) had diabetes mellitus.

As a result of the OGTT, patients with dysglycemia were assigned to Group 1, and patients with normal glucose levels were assigned to Group 2. There was no statistically significant difference between the two groups in decimal age, puberty status, BMI-SDS, basal insulin, HbA1C, HOMA-IR score, TG/HDL-C ratio ≥2.27 and presence of hepatosteatosis, but basal fasting glucose was significantly higher in group 1. Table 1 presents the results in detail.

The number of patients with a ratio of 2.27 and above was 67.30% (n: 68). The ratio greater than 2.27 was found to have a statistically significant correlation with HOMA-IR and insulin levels, while BMI-SDS was not correlated with HbA1c. The results are presented in detail in Table 2.

Liver ultrasonography was performed in 87 of our patients. Steatosis was detected in 59.80% (n: 52) of them. The ratio was 2.27 and above in 73.10% (n: 38) of the patients with steatosis. The ratio was 2.27 and above in 60% (n: 21) of 35 patients without steatosis (p=0.200).

Discussion

The TG/HDL-C ratio, which predict the increased risk of metabolic and cardiovascular complications, has recently been used in adolescents and children [12]. Studies in children have shown that the ratio is associated with insulin resistance, metabolic syndrome, and cardiometabolic complications [5-7,13-15]. In their study, Giannini et al. concluded that a cutoff value 2.27 for the ratio was significant in predicting insulin resistance in children [8]. However, Bridges et al. did not find evidence in their study that the ratio was an indicator of insulin resistance [16]. In this study, we found that the ratio of 2.27 and above was correlated with HOMA-IR and insulin levels in overweight and obese children, similar to the literature.

The main risk factor for nonalcoholic fatty liver disease is insulin resistance. The ratio has been defined as an index that can be used instead of insulin resistance. Nobili et al. [17] found a positive correlation between an increased ratio and nonalcoholic fatty liver disease in children. Ala Üstünyol et al. determined a cutoff value and found that the ratio of 2.27 and above was associated with hepatosteatosis [18]. Between the ratio of 2.27 and above and hepatosteatosis ,there was no statistically significant difference in our study.

The ADA 2022 guidelines recommend screening overweight and obese children at risk for dysglycemia by measuring FPG, and plasma glucose levels two hours after 75 grams of oral glucose or HbA1c levels [3]. Joyce M et al. stated that the random glucose level in overweight and obese children is more important than HbA1C in detecting dysglycemia [19]. Vajravelu M. E et al. in their prospective study, showed that glucose and HbA1C, which were randomly checked for the prediction of dysglycemia, had similar performance [20]. In our study, while the fasting glucose values of patients with dysglycemia were significantly higher, there was no statistically significant difference in HbA1c levels between patients with and without dysglycemia.

High serum TG levels interfere with muscle glucose metabolism and decrease insulin sensitivity [21]. Eventually, patients may develop dysglycemia due to their decreased insulin sensitivity. No study in the literature examines the relationship between dysglycemia and the TG/HDL-C ratio. In our study, a TG/HDL-C ratio of 2.27 and above was not correlated with the detection of dysglycemia. When 3.72 was taken as the cutoff value for the ratio, there was 91% specificity and 37.20% sensitivity, and when 3.90% was taken as the cutoff value, there was 95.90% specificity and 34.90% sensitivity. These results may help predict dyslipidemia. There is a need for more studies to be conducted on this topic with more patient groups.

One of the most significant limitations of our study is the small number of patients involved. OGTT reproducibility in adolescents is poor, with a compatibility rate of less than 30% between tests conducted a few weeks apart. Therefore, OGTT results may not be reliable.

Conclusion
This study is the first of research on the relationship between TG/HDL-C ratio (2.27) and dysglycemia. We did not find a correlation between this rate and dysglycemia. Based on the findings of our study, an increase in the TG/HDL-C ratio was related to insulin levels and an increase in the HOMA-IR score. It is necessary to conduct studies with a larger number of patient groups.

Ethical approval
The Malatya Turgut Özal University Non-Invasive Clinical Research Ethics Committee approved this study (Ethics Committee date: 5.1.2023 and number: B.117).

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