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Regular paper

Usefulness of the Triglycerides to High-Density Lipoprotein Cholesterol ratio (TG/HDL-C) in prediction of metabolic syndrome in Polish obese children and adolescents

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The triglycerides to high-density lipoprotein cholesterol ratio (TG/HDL-C) is a useful surrogate marker of insulin resistance and cardiovascular risk factors. We aimed to assess the relationship between the TG/HDL-C ratio and insulin resistance (IR) and its usefulness in prediction of the metabolic syndrome (MS). This retrospective study involved 122 obese children with the mean age of 11.6±3 years and their 58 healthy lean peers. Anthropometric measurements, blood pressure, the plasma lipid profile and oral glucose tolerance test (OGTT) were analyzed. Based on the obtained results, the TG/HDL-C ratio and surrogate insulin resistance indices (HOMA-IR, FGIR, QUICKI, OGIS, Matsuda index) were calculated. The TG/HDL-C ratio positively correlated with weight, waist circumference, waist to hip ratio (WHR), lipid profile, HOMA-IR, fasting insulin and insulin measurements during OGTT, and negatively correlated with FGIR, QUICKI, OGIS, and the Matsuda index. Obese children with the TG/HDL-C ratio≥3 (47.5%) had higher values of WHR and HOMA-IR, and lower ones of FGIR, QUICKI, OGIS, and the Matsuda index when compared to their obese peers with the TG/HDL-C<3. The area under the curve (AUC) calculated for each insulin resistance index in prediction of the metabolic syndrome was the largest for the TG/HDL-C ratio (0.8936, 95% CI:0.809–0.977, *p*=0.000). For 1 unit increase in the TG/HDL-C ratio, the odds for having MS increased by 2.09 times. The TG/HDL-C ratio is a good surrogate marker of insulin resistance in obese children. When comparing the usefulness of some IR markers in prediction of the metabolic syndrome, the TG/HDL-C ratio seems to be the best one and should be used in clinical practice to identify children at risk of metabolic syndrome development.

Key words: TG/HGL-C ratio, insulin resistance, metabolic syndrome, obesity, children

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Abbreviations: AUC, area under the curve; BMI, body mass index; BP, blood pressure; CI, confidence interval; DBP, diastolic blood pressure; %FAT, body fat percentage; FGIR, fasting glucose to insulin ratio; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment for insulin resistance index; IDF, International Diabetes Federation; IOTF, International Obesity Task Force; IR, insulin resistance; LDL-C, Low-density lipoprotein cholesterol; LMS, Least mean squares; MS, metabolic syndrome; NHANES, National Health and Nutrition Examination Survey; OGTT, oral glucose tolerance test; QUICKI, Quantitative insulin sensitivity check index; OGIS, Oral Glucose Insulin Sensitivity Index; OR, odds ratios; ROC, Receiver operating characteristic; SBP, systolic blood pressure; S.D., standard deviation; SDS BMI, standard deviation score Body Mass Index; TC, total cholesterol; TG, triglycerides; WBISI, whole body insulin sensitivity index; WC, waist circumference; WHtR, waist to height ratio; WHR, waist to hip ratio; WHO, World Health Organization

INTRODUCTION

Childhood obesity is an important public health problem worldwide. There are numerous complications associated with excessive fat mass that lead to the deterioration of the health of the whole population. It is well-known that with the increase in the body mass index (BMI) value, the risk of death also increases (Berrington de Gonzalez *et al.,* 2010).

The fundamental disorder related to obesity is insulin resistance (IR), which drives a string of metabolic processes leading to development of proatherogenic lipid profile, type 2 diabetes mellitus and high blood pressure (Nadeau *et al*., 2011). It has been also well-known that insulin resistance, together with other components of the metabolic syndrome, contributes to the development of atherosclerosis.

The gold standard method to measure IR is by use of the hyperinsulinemic euglycemic clamp, rarely performed in children because of its invasiveness, complexity, time-consumption and high costs. In clinical trials indirect methods are often used which are calculated on the basis of timely assessment of fasting glucose and insulin concentration (e.g. FGIR – fasting glucose to insulin ratio, HOMA-IR – homeostasis model assessment for insulin resistance index, QUICKI – Quantitative insulin sensitivity check index) and during the oral test of glucose load (e.g. OGIS – Oral Glucose Insulin Sensitivity Index, Matsuda index) (Ten *et al*., 2004; Levy-Marchal *et al*., 2010). In practice, HOMA-IR is generally used in adults and also approved for children and adolescents. These tests are not standardized in children and are usually performed in hospital settings (Chandrasekhar *et al*., 2014).

Surprisingly, previous studies have shown that the triglycerides (TG) to high-density lipoprotein cholesterol (HDL-C) concentration ratio correlates well with insulin resistance and may be an alternative tool for evaluation of an increased risk of IR development (Giannini *et al*., 2011). Moreover, the TG/HDL-C ratio reflects atherosclerotic lipid changes better than each of the lipoproteinograms interpreted separately, and may be effective in screening for the metabolic syndrome (Olson *et al*., 2012; Liang *et al*., 2015). Due to the fact that measurements of TG and HDL-C concentrations are routine and cost-effective outpatient tests, they would greatly facilitate the assessment of reduced insulin sensitivity. Some studies, however, suggest that the relationships described above do not apply

to all children and all ethnic groups (Giannini *et al*., 2011; Sumner *et al*., 2005; Bridges *et al*., 2016). There is a need for well-planned studies to confirm the usefulness of the TG/HDL-C ratio in identification of children with a high risk of development of insulin resistance and other obesity-related cardiometabolic disturbances.

The aim of this study was to determine the relationship between the TG/HDL-C ratio and surrogate insulin resistance indices and other components of the metabolic syndrome, and to compare it to other indirect IR measurements to establish its usefulness in prediction of MS in Polish obese children and adolescents.

MATERIAL AND METHODS

Study population. A retrospective study was performed on 122 children with simple obesity, 52 girls and 70 boys, whose chronological age ranged between 5.3 and 17.9 years (mean age 11.6±3 years). The control group included 58 children (23 girls, 35 boys) of the same age (mean age 11.7±3 years) with normal somatic parameters. Patients originated from the Department of Paediatrics and Endocrinology at the Medical University of Warsaw. Children with endocrine and genetic obesity, diabetes and hypertension, and those receiving therapy that could affect the lipid and carbohydrate metabolism were excluded from the study. Based on medical documentation data from physical examination, auxological and biochemical parameters were taken into consideration. The project received approval of the Ethical Committee at the Medical University of Warsaw.

In order to evaluate obesity, criteria developed by the International Obesity Task Force (IOTF) were used (Cole *et al*., 2000). The BMI standard deviation score (SDS BMI) expressing the degree of obesity was calculated by means of the LMS method (Cole, 1990). In this study, paediatric metabolic syndrome (MS) was diagnosed according to the 2007 International Diabetes Federation (IDF) consensus for children older than 10 years. The presence of abdominal obesity (WC, waist circumference ≥94 cm in boys and ≥80 cm in girls) and two or more of the following components: elevated values of TG≥150 mg/dl, lower levels of HDL-C<40 mg/dl, increased blood pressure (SBP≥130 mmHg and/or DBP≥85 mmHg), abnormal fasting plasma glucose values (≥100 mg/dl), allow the recognition of MS (Zimmet *et al*., 2007).

Anthropometric measurements. In each patient body height (cm), body weight (kg), waist and hip circumference (cm) and thickness of three skinfolds (mm) using the Harpenden Skinfold Caliper were analyzed. Based on the above measurements, the Body Mass Index (BMI), waist to hip ratio (WHR), waist to height ratio (WHtR) and body fat percentage (%FAT) were calculated. The anthropometric measurements were taken by trained personnel and health examinations were performed by paediatricians.

Blood pressure. Three blood pressure (BP) measurements were used for analysis and the mean value was calculated. Polish reference chart of systolic and diastolic BP depending on gender, age and height was used to evaluated BP in each patient (Ostrowska-Nawarycz *et al*., 2008). Appropriate BP values were defined as mean systolic (SBP) and/or diastolic blood pressure (DBP) values below the 90th percentile. Hypertension was diagnosed when SBP and/or DBP values were above the 95th percentile. Mean blood pressure values between the 90th and 95th percentiles were defined as border values.

Biochemical analysis. Serum concentrations of total cholesterol (TC, mg/dl), high-density lipoprotein cholesterol (HDL-C, mg/dl) and triglycerides (TG, mg/dl) were measured after a 12-hour fast by colorimetric enzymatic method using a Vitros 5600 analyzer (Ortho Clinical Diagnostics). Low-density lipoprotein cholesterol concentration (LDL-C, mg/dl) was calculated based on the Friedewald formula (LDL-C=TC–TG/5–HDL-C). Results of the lipid profile were interpreted according to the American Heart Association (Hayman *et al*., 2007). The TG/HDL-C ratio at a value ≥3 was considered to be closely correlated with IR (McLaughlin *et al*., 2003).

Obese subjects also underwent an oral glucose tolerance test (OGTT with 1.75 g glucose solution per 1 kg body weight, maximum 75 g of glucose). Glucose concentrations were determined in blood serum by glucose oxidase colorimetric method using a Vitros 5600 analyzer. Serum concentrations of insulin were measured by an immunoassay using an IMMULITE 2000 Xpi Analyzer (Siemens). Hyperinsulinism has been identified as fasting insulin level ≥15 μIU/ml, and/or maximum level of OGTT≥150 μIU/ml, and/or insulin level at 120 minutes during OGTT≥75 μIU/ml (Ten *et al*., 2004). Homeostasis model assessment for insulin resistance index (HOMA-IR), fasting glucose to insulin ratio (FGIR), quantitative insulin sensitivity check index (QUICKI), oral glucose insulin sensitivity index (OGIS) and the Matsuda index were calculated to determine the status of insulin resistance (Ten *et al*., 2004). HOMA-IR≥3.16 shows evidence of insulin resistance (Keskin *et al*., 2005).

Statistical analysis. Data obtained from patients in the study and control groups are expressed as mean with standard deviation (S.D.) or median with minimum and maximum values. The anthropometric and biochemical measurements in both groups were compared by using the T-test for parameters in a normal distribution, and in case of non-normal distribution by the Mann-Whitney test. Correlations between the variables were assessed using the Spearman coefficient. Receiver operating characteristic (ROC) curve was drawn and the area under the curve (AUC) was calculated for the TG/HDL-C ratio and other surrogate insulin resistance (IR) indices in order to discriminate which of the mentioned above parameters is more useful in prediction of the metabolic syndrome (MS). Using logistic regression analysis, the odds for MS were calculated. Values are presented as odds ratios (OR) with 95% confidence interval (Cl). The data analyses were carried out using the statistical package SPPS 19 software. A p value<0.05 was considered as the indicator of statistical significance.

RESULTS

Anthropometric and clinical data describing and comparing the obese and control group children are presented in Table 1.

In the obese group children, 26 (21.3%) had an elevated concentration of total cholesterol (TC>200 mg/dl). Incorrect concentration of high-density lipoprotein cholesterol (HDL-C<40 mg/dl) was detected in 43 (35.2%) obese patients. High concentration of LDL cholesterol (LDL-C≥130 mg/dl) was found in 18 (14.8%) children and high amount of triglycerides (TG≥110 mg/dl) was found in 76 (62.3%) individuals in the same group.

Abnormal glucose tolerance was diagnosed in 26 (21.3%) obese children. Increased fasting insulin (≥15 μIU/ml) was found in 55 (45%) of the obese children. In the oral glucose tolerance test (OGTT), increased values of insulin (≥150 μIU/ml) were found at 30 minutes in 19 (15.5%) patients, at 60 minutes in 21 (17.2%) patients, at 90 minutes in 18 (14.7%) patients. Insulin

Table 1. Comparison of anthropometric and biochemical parameters between the obese and control children groups

Variable	Control group (n=58)	Obese group (n=122)
Age (years)	11.7±3.0	11.6±3.01
Height (cm)	159.0 (128.1–186.5)	156.0 (110.0–187.1)
Body weight (kg)	46.77±12.9	72.34±24.11***
BMI (kg/m2)	18.7 (12.7–23.1)	28.8 (20.7–43.8)***
SDS BMI	0.1 (–2.2–1,4)	2.7 (2.0–4.8)***
WC (cm)	64.32±6.62	90.27±12.27***
HC (cm)	84.5 (61.0–97.0)	102.0 (72.0–131.0)***
WHR	0.79 (0.64–0.87)	0.9 (0.71–1.04)***
WHtR	0.4±0.02	0.58±0.05***
% FAT	19.8 (9.6–31.8)	33.5 (20.2–53.1)***
fasting glucose (mg/dl)	80.5 (68.0–114.0)	82.0 (59.0–106.0)
TC (mg/dl)	157.5±22.4	176.9±30.03***
HDL–C (mg/dl)	54.0 (33.0–92.0)	42.0 (25.0–92.0)***
LDL–C (mg/dl)	85.1±24.2	105.8±27.2***
TG (mg/dl)	74.0 (23.0–167.0)	123.0 (39.0–458.0)***
TG/HDL–C	1.3 (0.9–4.3)	2.9 (0.5–14.3) ***

Data are presented as mean ± standard deviation (S.D.) or median with minimum and maximum values, as appropriate. BMI, Body Mass Index; WC, Waist circumference; HC, Hip circumference, WHR–Waist to hip ratio; WHtR, Waist to height ratio; % FAT, % of body mass; TC, Total cholesterol; TG, Triglycerides; HDL–C, High–density lipoprotein cholesterol; LDL–C, Low–density lipoprotein cholesterol; TG/HDL–C, Triglycerides to high–density lipoprotein cholesterol ratio. ***p<0.001, **p<0.01, *p<0.05

level exceeding 75 μIU/ml at 120 minutes was detected among 55 (45%) patients. The median HOMA-IR value was 2.89. Insulin resistance (HOMA-IR≥3.16) was diagnosed among 43.2% of obese children. The median FGIR, QUICKI, OGIS and Matsuda index values were 5.8; 0.14; 425.65; and 3.29, respectively.

Systolic blood pressure (SBP) above the 95th percentile was detected among 6.1% of the obese children; diastolic blood pressure (DBP) above the 95th percentile was among 14.2% of patients.

The International Diabetes Federation (IDF) criteria for metabolic syndrome (MS) were analysed in 84 obese children older than 10 years. The diagnosis of MS was made in 17 children, which accounted for 20.2% of the group. Characteristics of anthropometric and biochemical parameters, blood pressure in obese children with or without the metabolic syndrome IDF criteria are presented in Table 2.

The median value of the TG to HDL-C concentration ratio in obese children and adolescents was higher than in their healthy peers (2.9 *vs.* 1.3, p=0.000). The TG/HDL-C ratio ≥3 was found in 58 obese children (47.5%) and they had higher values of WHR, HOMA-IR, and lower of FGIR, QUICKI, OGIS, and the Matsuda index when compared to their obese peers with the TG/HDL-C<3 (Table 3). In children with the metabolic syndrome (MS), the median TG/HDL-C value was 5.33, in comparison to obese children who did not meet the criteria of MS; their TG/HDL-C was 2.74 (p=0.000) (Fig. 1). There were no significant differences in HOMA-IR, QUICKI, and the OGIS values between these groups. Only the FGIR and Matsuda index were significantly different (p=0.044 ; 0.036, respectively) (Table 2).

Among the obese children, the TG/HDL-C ratio was positively correlated with weight (r=0.202, p=0.028), WC (r=0.236, p=0.01), WHR (r=0.192, p=0.037), TC (r=0.221, p=0.016), TG (r=0.936, p=0.000), and HDL-C (r=–0.760, p=0.000). No statistically significant correlations were found between the TG/HDL-C ratio and fasting or OGTT glucose levels. However, the TG/HDL-C ratio was correlated with fasting insulin (r=0.266, p=0.004), and insulin measurements during OGTT: at 30 minutes (r=0.192, p=0.039), at 60 minutes (r=0.192, p=0.04), at 90 minutes (r=0.178, p=0.05), at 120 minutes (r=0.196, p=0.035) and also with HOMA-IR (r=0.261, p=0.004), FGIR (r=–0.254, p=0.006), QUICKI (r=–0.262, p=0.004), OGIS (r=–0.204, p=0.028) and the Matsuda index (r=–0.34, p=0.002). A statistically significant positive correlation was found with SBP (r=0.198, p=0.05), but not with DBP.

Figure 2 shows the ROC curve analysis for each insulin resistance indicator as a predictor of the metabolic

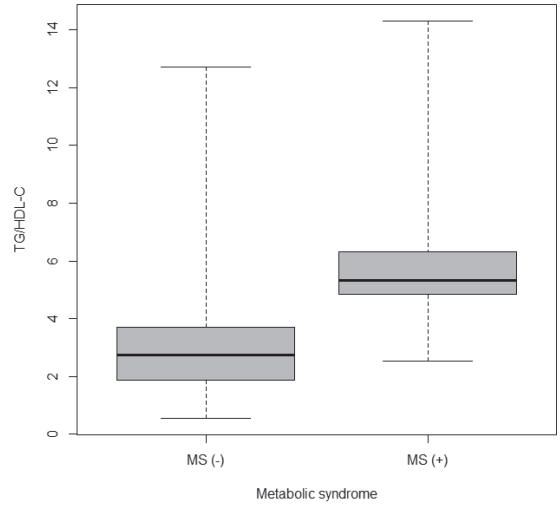

Figure 1. Comparison of median TG/HDL-C values in obese children with metabolic syndrome and their peers, who did not meet the criteria of the metabolic syndrome.

Table 2. Comparison of anthropometric and biochemical parameters, surrogate insulin resistance measurements, and blood pressure in the obese children >10 years old with and without metabolic syndrome criteria.

Variable	Total (n=84)	MS (–) (n=67)	MS (+) (n=17)
Age (years)	13.0 (10.1–17.9)	13.0 (10.1–17.7)	13.5 (12.0–17.9)*
Height (cm)	162.3±11.09	160.8±10.94	168.4±9.75*
Body weight (kg)	83.6±19.84	81.4±20.5	92.2±14.52*
BMI (kg/m2)	30.8 (23.5–43.8)	30.4 (23.5–43.8)	31.7 (26.8–38.9)
SDS BMI	3.7 (2.1–9.2)	3.6 (2.1–9.2)	4.0 (2.3–6.8)
WC (cm)	95.5±10.46	94.4±10.92	100.0±6.99*
HC (cm)	108.1±11.11	107.0±11.6	112.1±7.98*
WHR	0.88±0.06	0.88±0.06	0.89±0.04
WHtR	0.58±0.05	0.58±0.05	0.59±0.04
%FAT	34.8 (20.2–53.1)	34.3 (25.9–53.1)	36.5 (20.2–49.0)
TC (mg/dl)	176.2±31.59	175.2±32.1	179.7±30.33
HDL–C (mg/dl)	42.9±9.6	45.4±8.89	33.5±5.44***
LDL–C (mg/dl)	104.8±28.43	104.3±27.72	106.5±31.75
TG (mg/dl)	129.0 (39.0–458.0)	116.0 (39.0–318.0)	168.0 (101.0–458.0)***
TG/HDL–C	3.16 (0.55–14.31)	2.74 (0.55–12.72)	5.33 (2.53–14.31)***
Fasting glucose (mg/dl)	83.0 (59.0–106.0)	82.0 (59.0–101.0)	84.0 (73.0–106.0)
Fasting insulin (μIU/ml)	15.3 (4.0–51.0)	14.5 (4.0–51.0)	19.0 (9.5–38.9) *
HOMA	3.1 (0.69–11.21)	2.89 (0.69–11.21)	3.98 (1.83–9.92)
QUICKI	0.14 (0.12–0.18)	0.14 (0.12–0.18)	0.13 (0.12–0.15)
OGIS	410.5±71.10	417.14±70.02	385.7±71.71
FGIR	5.53 (1.75–17.5)	5.76 (1.75–17.5)	4.46 (2.39–8.65) *
Matsuda	3.02 (0.73–11.91)	3.27 (0.73 –11.91)	2.23 (1.11–4.68)*
SBP (mmHg)	117.4±10.25	115.5±9.75	123.3±9.76**
DBP (mmHg)	72.0 (55.0–100.0)	73.0 (55.0–90.0)	71.0 (67.0–100.0)

Data are presented as mean ±standard deviation (S.D.) or median with minimum and maximum values, as appropriate. MS, Metabolic syndrome; BMI, Body Mass Index; SDS BMI, Standard deviation score of Body Mass Index; WC, Waist circumference; HC, Hip circumference; WHR, Waist to hip ratio; WHtR, Waist to height ratio; % FAT, % of body mass; TC, Total cholesterol; TG, Triglycerides; HOMA–IR, Homeostasis model assessment for insulin resistance index; QUICKI, Quantitative insulin sensitivity check index; OGIS, Oral glucose insulin sensitivity index; FGIR, Fasting glucose to insulin ratio; SBP, Systolic blood pressure; DBP, Diastolic blood pressure. ***p<0.001, **p<0.01, *p<0.05

syndrome. AUC for the TG/HDL-C ratio was the largest: 0.893, 95% Cl: 0.809–0.977 (Table 4), indicating the superiority of the insulin resistance parameter to others for risk prediction of MS development. Moreover, for 1 unit increase in the TG/HDL-C, the odds for having the metabolic syndrome increased by 2.09 times (OR 2.09, 95% CI: 1.37–3.20, p=0.001).

DISCUSSION

The growing number of children and adolescents with overweight and obesity is an unsettling problem on a global scale. According to the World Health Organization report, in 2014 the number of children under the age of 5 years affected by overweight or obesity reached 41 million. Prevalence of obesity is much higher in the developed countries (WHO, 2016). When compared to other European countries, the incidence of obesity and overweight in Poland is at an average level.

With higher fat mass accumulation, a higher frequency of atherogenic lipid profile, diabetes mellitus, metabolic syndrome and arterial blood pressure is found. Excessive weight gain in childhood increases the chance of becom-

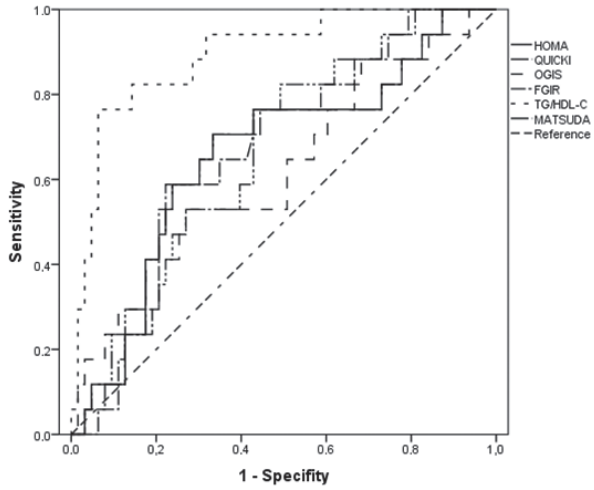

Figure 2. Receiver operating characteristic (ROC) curves for TG/HDL-C and other surrogate insulin resistance indices in prediction of the metabolic syndrome.

Table 3. Comparison of anthropometric and biochemical parameters, surrogate insulin resistance measurements and blood pressure in group of obese children divided according to the TG/HDL-C value

Variable	Obese children		
	Total (n=122)	TG/HDL–C<3 (n=64)	TG/HDL–C≥3 (n=58)
Height (cm)	156.0 (110.0–187.1)	155.1 (120.0–177.2)	156.0 (110.0–187.1)
Body weight (kg)	72.34±24.11	68.78±24.04	74.25±22.95
BMI (kg/m²)	28.8 (20.7–43.8)	27.55 (20.7–43.6)	29.2 (23.4–42.7)
SDS BMI	2.7 (2.0–4.8)	2.73 (2.0–4.77)	2.7 (2.18–3.96)
WC (cm)	90.27±12.27	87.79±12.54	92.02±11.20
HC (cm)	101.43±14.01	100.21±14.48	101.74±13.17
WHR	0.89±0.05	0.88±0.06	0.91±0.05**
WHtR	0.58±0.05	0.58±0.05	0.59±0.04
% FAT	33.5 (20.2–53.1)	32.75 (25.9–46.3)	34.8 (20.2–49.0)
Fasting glucose (mg/dl)	83.6±10.3	83.58±11.36	83.81±9.3
Fasting insulin (uIU/ml)	14.0 (4.0–51.0)	12.3 (4.0–51.0)	15.4 (6.5–48.0)**
TC (mg/dl)	176.9±30.03	172.9±28.44	181.55±31.23
HDL–C (mg/dl)	42.0 (25.0–92.0)	50.5 (37.0–92.0)	36.0 (25.0–56.0)***
LDL–C (mg/dl)	105.8±27.2	103.0±25.8	109.16±28.5
TG (mg/dl)	123.0 (39.0–458.0)	100.5 (39.0–150.0)	162.0 (103.0–458.0)***
HOMA–IR	2.89 (0.69–11.21)	2.63 (0.69–11.21)	3.22 (1.17–10.55)*
QIUCKI	0.14 (0.12–0.18)	0.14 (0.12–0.18)	0.14 (0.12–0.16)***
OGIS	425.65 (250.34–725.96)	432.63 (250.34–643.94)	417.94 (289.6–725.96)
Matsuda	3.29 (0.73–17.86)	3.58 (0.73–17.86)	3.0 (1.04–9.44)*
FGIR	5.8 (1.7–18.8)	6.21 (1.75–18.84)	5.23 (1.85–13.69)**
SBP (mmHg)	113.5 (96.0–140.0)	110.0 (100.0–140.0)	118.5 (96.0–134.0)
DBP (mmHg)	70.0 (55.0–100.0)	60.0 (60.0–100.0)	70.0 (55.0–96.0)

Data are presented as mean ±standard deviation (S.D.) or median with minimum and maximum values, as appropriate. BMI, Body Mass Index; SDS BMI, Standard deviation score of Body Max Index; WC, Waist circumference; HC, Hip circumference; WHR, Waist to hip ratio; WHtR, Waist to height ratio; % FAT, % of body mass; TC, Total cholesterol, TG, Triglycerides; HDL–C, High–density lipoprotein cholesterol; LDL–C, Low–density lipoprotein cholesterol; HOMA–IR, Homeostasis model assessment for insulin resistance index; QUICKI, Quantitative insulin sensitivity check index; OGIS, Oral glucose insulin sensitivity index; FGIR, Fasting glucose to insulin ratio; SBP, Systolic blood pressure; DBP, Diastolic blood pressure. ***p<0.001, **p< 0.01, *p< 0.05

ing obese in adulthood and can lead to cardiovascular diseases (Litwin, 2014). Kasley and coworkers (Kasley *et al.*, 2014) have demonstrated that the health consequences of childhood obesity may be present even after weight loss.

A key role in the induction of the above-mentioned changes is played by visceral fat mass and insulin resistance (IR). Central obesity is the most unfavourable because adipocytes are more hormonally and metabolically active, and regulate numerous signal pathways. Insulin resistance disturbs glucose homeostasis, which is associated with reducing the sensitivity of the target tissues to insulin, despite its normal or increased serum levels. Moreover, IR increases the glycogenolysis process in the liver, and impacts lipoprotein metabolism which together with other components of the metabolic syndrome contribute to the development of atherosclerosis (Ten, 2004; Levy-Marchal *et al.*, 2010). Many studies have confirmed the association of IR with ischemic heart disease and cardiovascular mortality (Laakso *et al.*, 1991). An epidemiological study showed that more than half of obese children have impaired insulin signalling (according to the National Health and Nutrition Examination Survey, NHANES – 52.1%, in the Polish study – 58%) (Lee *et al.*, 2006; Skowrońska *et al.*, 2007). Therefore, an early detection of children with IR and their treatment can effectively delay further development of unfavourable metabolic and hemodynamic disturbances.

Methods used to diagnose insulin resistance are based on simultaneous measurements of glucose and insulin.

Table 4. Area under the curve (AUC) for the TG/HDL-C ratio and other surrogate insulin resistance indices in prediction of the metabolic syndrome.

Variable	AUC	95% CI	*p*-value
HOMA-IR	0.6592	0.5109–0.8075	0.045
QUICKI	0.6592	0.5109–0.8075	0.045
OGIS	0.6209	0.4656–0.7762	0.128
FGIR	0.6681	0.5338–0.8024	0.034
TG/HDL-C	0.8936	0.8098–0.9773	0.000
Matsuda	0.6639	0.5305–0.7972	0.039

HOMA-IR- Homeostasis model assessment for insulin resistance index, QUICKI, Quantitative insulin sensitivity check index; OGIS, Oral glucose insulin sensitivity index; FGIR, Fasting glucose to insulin ratio; TG/HDL-C, Triglycerides to high-density lipoprotein cholesterol ratio; AUC, area under the curve; CI, confidence interval

The "gold standard" of IR measurement is a metabolic euglycemic clamp, but this method is laborious and expensive, so it is mainly used for scientific purposes only. The most commonly used method for the diagnosis of IR is the homeostasis model assessment for insulin resistance index (HOMA-IR). This index correlates well with the metabolic euglycemic clamp (Bonora *et al*., 2000) and is more reliable than other surrogate IR markers, such as FGIR and QUICKI (Keskin *et al*., 2005). But there is no cut-off point for estimation of IR in children. HOMA-IR values vary depending on sex, age and pubertal stage. In a few studies, different cut-off points have been demonstrated (Keskin *et al*., 2005; Reinehr *et al*., 2004; Shashaj *et al*., 2016).

Unexpectedly, the triglyceride to high-density lipoprotein cholesterol concentration ratio (TG/HDL-C) was found to be associated with insulin resistance. McLaughlin and co-workers (McLaughlin *et al*., 2003) suggested that this indicator could be an alternative tool for insulin resistance diagnosis. In that study, it was found that the TG/HDL-C ratio≥3 correlated well with the insulin resistance. A strong correlation between the TG/HDL-C and HOMA-IR was confirmed in a cross – sectional study of the Korean population (Kang *et al*., 2012; Park *et al*., 2016) and in indigenous Argentinean children (Hirschler *et al*., 2013). Similar results were obtained in groups of overweight and obese children (Bridges *et al*., 2016; Iwani *et al*., 2017), in which the relationship between the TG/HDL-C ratio and the hiperinsulinemic - euglicemic clamp (Giannini *et al*., 2011), and other indirect measurements of insulin resistance, such as QUICKI (Olson *et al*., 2012) and WBISI (whole body insulin sensitivity index) (Giannini *et al*., 2011), were documented. Moreover, Giannini and co-workers (Giannini *et al*., 2011) found that this association is significant only in obese Caucasian children, but not in Hispanic or African American children, so the TG/ HDL-C ratio may be ethnically dependent. Most often, this is explained by racial differences in the lipid profile (Sumner *et al.,* 2005). In our study, which included Polish obese children and adolescents, the TG/HDL-C ratio significantly correlated with HOMA–IR and also with other surrogate insulin resistance indices (QUICKI, FGIR, OGIS, Matsuda), as well as with fasting insulin and OGTT insulin levels.

Other studies had also highlighted that a higher TG/HDL-C ratio is associated with an unfavourable cardiometabolic profile (Berrington *et al.,* 2010; Olson *et al,* 2012; Kang *et al*., 2012; Iwani *et al.,* 2017). With increasing percentiles of the TG/HDL-C ratio, apart from HOMA-IR, the values of BMI, waist circumference, fasting plasma glucose, total cholesterol level, and systolic and diastolic blood pressure were rising (Di Bonito *et al*., 2012; Hirschler *et al,* 2015; Iwani *et al*., 2017). Our research also provides evidence of the association between the TG/HDL-C ratio and central obesity assessed by using waist circumference, lipid profile and systolic blood pressure; however we did not find a correlation with carbohydrate glucose metabolism. Di Bonito and co-workers (Di Bonito *et al*., 2012) had shown that the TG/HDL-C ratio is a predictor of left ventricular hypertrophy, independently of visceral adiposity and high blood pressure, and may be useful in the risk assessment of cardiometabolic factors also in non-obese patients.

We did not obtain a clear TG/HDL-C cut-off value for the definition of insulin resistance in childhood. Di Bonito and co-workers (Di Bonito *et al*., 2012) had shown that in the group of obese children, the TG to HDL-C ratio≥2 increased the risk of insulin resistance by 1.5 to 10-fold, and so did the high blood pressure and metabolic syndrome when compared to those with the TG/HDL-C<2.0. In another study, Giannini and co-workers (Giannini *et al*., 2011) suggested a 2.27 value as a cut-off point for predicting severe IR in Caucasian obese children. On the other hand, Olson and co-workers (Olson *et al.,* 2012) found that the TG/HDL-C≥3.0 is more specific for IR and favours the occurrence of higher HOMA-IR and BMI, blood pressure, glucose level and small dense LDL particles, and lower QUICKI and HDL-C concentration in 32 children with the TG/HDL-C≥2.0 among a group of 40 children deemed insulin resistance (HOMA>2.45). In our study, we adopted the TG/HDL-C cut-off point≥3.0, and these children were characterized by a higher waist to hip ratio and increased insulin resistance.

McLaughlin and co-workers (McLaughlin *et al*., 2005), in their study involving 258 nondiabetic, overweight adults, had shown that the TG/HDL-C ratio above 3.5 is a good indicator of the metabolic syndrome (MS). This relationship was also observed in a children population. In the Quijada study (Quijada *et al*., 2008), 95% of children with MS had an elevated TG/HDL-C to 3.5 or more. As we found in our study, the median TG/HDL-C ratio value in children under the age of 10 years who fulfilled the IDF criteria was 5.33, and in their peers who did not meet the MS criteria it was 2.74. On the other hand, there was no significant difference in HOMA-IR values and others surrogate insulin resistance indices between both groups. Dhuper and co-workers (Dhuper *et al*., 2007) reported an elevated prevalence of MS in children with a high TG and low HDL-C concentration. They did not find a correlation between the presence of MS and HOMA-IR. Likewise, the Liang study (Liang *et al*., 2015) had shown the superiority of the TG/HDL-C ratio to the HOMA – IR index in screening metabolic syndrome in children, even after consideration of such factors as gender, age and the pubertal stage. The cut-off values for predicting MS were: for the TG/HDL-C>1.25 (sensitivity 80%, specificity 75%), and for HOMA – IR>4.59 (58.7% and 65.5%, respectively). Our study confirmed that the TG/HDL ratio is a meaningful parameter in prediction of MS. The area under the ROC curve of TG/HDL-C was the largest when compared to FGIR, QUICKI, OGIS and MATSUDA indices. The odds ratio (OR) for having MS was 2.09. As a result, this parameter can be used as a screening tool for metabolic syndrome in paediatric obese patients.

There are a lot of surrogate indices used in the assessment of insulin resistance. Complex formulas and the necessity to use parallel assessment of glucose and insulin concentrations in order to calculate the IR markers are not helpful in daily clinical routine. The generally available lipid profile test allows doctors to use the TG/HDL-C ratio in clinical practise for identification of patients with insulin resistance and unfavorable metabolic profile. As shown in our study, the TG/HDL-C ratio seems to be a good predictor of the metabolic syndrome in obese children and adolescents.

CONCLUSIONS

This study has shown that the TG/HDL-C ratio is an inexpensive marker of insulin resistance. It may help to identify children who benefit the most from early interventions. Thanks to that, the development of IR-related diseases, such as type 2 diabetes or the metabolic syndrome, may be delayed or eliminated. In addition, the above results suggest that the TG/HDL-C ratio can be used to identify children at risk of the metabolic syn-

drome development. Obviously, more studies are needed on a larger number of patients to confirm the above relationships and determine the correct cut-off for this indicator value.

Conflict of interests

The authors declare no conflict of interests.

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