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Waist-to-height ratio as a clinical predictor for cardiovascular risks and insulin resistance in children and adolescents with exogenous obesity

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Abstract

Background: Obesity is one of the most challenging clinical syndromes associated with deleterious health problems. Waist-to-height ratio (WHtR), a newer index for abdominal fat assessment, can be a superior tool in the evaluation of cardiometabolic risk. This study aimed to determine the relation between WHtR and lipid cardiovascular risk ratios and insulin resistance (IR) in children and adolescents with exogenous obesity.

Results: This analytical cross-sectional study included 80 children and adolescents with exogenous obesity, compared to 80 age- and sex-matched healthy non-overweight non-obese controls. Fasting lipid profile (total cholesterol (TC), triglyceride (TG), high-density lipoprotein (HDL) and low-density lipoprotein (LDL)), fasting insulin, and fasting blood glucose were done and lipoprotein risk ratios were calculated; TC/HDL, LDL/HDL, non-HDL/HDL, and TG/HDL. In addition, homeostatic model assessment for IR (HOMA IR), triglyceride glucose index (TyG), TyG-BMI, and TyG-WC were calculated. The study group included 55 (34.4%) males and 105 (65.6%) females with a mean age of 13.6 ± 2.22 years. Obese group had significantly higher TC, TG, LDL, non-HDL, LDL/HDL, TC/HDL, non-HDL/HDL, and TG/HDL, with significantly lower HDL. In addition, they had significantly higher FBG, HOMA IR, TyG, TyG-BMI, and TyG-WC indices compared to the control group. There were statistically significant correlations between WHtR and lipid profile, lipid risk ratios and indices of IR. WHtR was found to be an independent predictor of IR by linear regression analysis.

Conclusion: WHtR can be an excellent, easy, and reliable clinical predictor for cardiovascular risk and IR in children and adolescents with exogenous obesity.

Keywords: Exogenous obesity, Insulin resistance, Cardiovascular risks, Waist-to-height ratio, Lipoprotein risk ratios

Background

Obesity represents one of the most serious public health problems of the twenty-first century and can be defined as a state of excessive body adiposity occurring when energy intake chronically exceeds energy expenditure [1]. Moreover, obesity is one of the most complex and

challenging clinical syndromes worldwide that can affect children and adults and has an association with numerous deleterious health outcomes as type 2 diabetes mellitus (T2DM), dyslipidemia, hyperinsulinemia, polycystic ovary syndrome, hypertension, coronary heart diseases, as well as many psychosocial and social problems [2–5].

Anthropometric measures such as weight, height, and circumferences are often used in clinical practice due to their low cost and high convenience. Anthropometric measures of abdominal obesity (as waist circumference (WC), Waist-to-hip ratio (WHR)) appear to be strongly associated with metabolic and cardiovascular risk

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factors [6, 7]. However, waist-to-height ratio (WHtR), a newer index for abdominal fat assessment, has emerged to be a superior tool in the evaluation of cardiometabolic risks [8].

Coronary risk assessment based exclusively on low-density lipoprotein (LDL) cholesterol is not optimal. Several lipoprotein ratios or “atherogenic indices” were identified and proved to be better predictors for cardiovascular disease (CVD) than conventional lipid parameters [9, 10]. Total cholesterol/high-density lipoprotein cholesterol ratio (TC/HDL); known as the atherogenic or Castelli index and LDL/HDL ratio can be also used [9, 11]. In addition, the use of a simple non-HDL calculation in a lipid profile testing, with determination of the new risk factors, can provide a better assessment of the CVD risk [12–14].

Insulin resistance (IR) or impaired insulin sensitivity is considered an important risk factor for metabolic syndrome, T2DM, and CVD. Thus, early detection of IR can help to prevent the manifestation of clinical diseases. Currently, there are various indirect and direct methods to assess IR; the standard method was the euglycemic-hyperinsulinemic clamp technique, originally developed by DeFronzo. However, it is a complex, costly, and time-consuming method, making it difficult to be used for routine clinical practice. Therefore, a number of indices for the measurement of IR have been suggested. Triglyceride glucose index (TyG) and TyG-related indices (TyG-BMI and TyG-WC) were found to be excellent surrogate markers of IR [15–17].

The aim of this study is to determine the relation between WHtR and lipid cardiovascular risk ratios (LDL/HDL, TC/HDL, non-HDL/HDL, and TG/HDL ratios) and IR (measured by homeostatic model assessment for IR (HOMA-IR), TyG index, TyG-BMI, and TyG-WC) in children and adolescents with exogenous obesity.

Methods

Study population

This cross-sectional study included 80 children and adolescents with exogenous obesity. Patients were recruited from the Pediatric Endocrine Unit, in the period from May 2018 to May 2019. Subjects were eligible if they had exogenous obesity, were between 10 and 19 years, had a body mass index more than or equal to 95% for age and sex plotted on Egyptian growth charts [18] and showing pubertal signs; Tanner stage 2 or more. Subjects with a history of diabetes mellitus, hypothyroidism or other endocrinal disorders, or prepubertal, or those taking any lipid altering drugs or corticosteroids or having obesity due to any endocrinal or syndromic etiology were excluded from the study. Eighty healthy non-overweight

non-obese age- and sex-matched controls were recruited from the general outpatient clinics.

All procedures performed in this study, involving human participants were in accordance with the ethical standards of Cairo University and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Informed consent was obtained from every individual participant or their legal guardians included.

Data collection

All patients and controls were subjected to full history taking laying stress on age, gender, the presence of any associated conditions or complications.

Thorough clinical examination and the following measurements were carried out: height, weight, BMI, waist circumference (WC-measured in centimeters to the nearest 0.1 cm, with a flexible tape, at the level of umbilicus, at the end of expiration with person breathing silently. Hip circumference (HC-measured in centimeters to the nearest 0.1 cm at the level of the greater trochanters, using a flexible tape), waist-hip ratio (WC/HC-calculated as WC divided by HC), and waist-to-height ratio (WHtR-calculated by dividing WC/height).

- Laboratory investigations including fasting lipid profile including: serum cholesterol (TC), triglycerides (TG), high-density lipoproteins (HDL) and low-density lipoproteins (LDL), and fasting blood glucose (FBG).
- Fasting blood glucose was assessed using GOD-PAP enzymatic colorimetric method. Test Kit Catalog No. 250001/250002 (Salucea Inc.). Total cholesterol was assessed using CHOD-PAP Enzymatic-Colorimetric method in Serum Test Kit Catalog No.230001/230002 (Salucea Inc.). Serum triglycerides was assessed using Quantitative Enzymatic-Colorimetric Determination of Triglycerides in Serum Test Kit Catalog No. 2100 (STANBIO LABORATORY- An EKF Diagnostics Company). LDL Cholesterol was assessed using Direct Enzymatic colorimetric Test Kit REF: NS280001 R1 30 ml/R2 10 ml (Salucea Inc.). HDL Cholesterol was assessed using Test Kit Ref: No. 0599 (Stanbio Laboratory (an EKF Diagnostics Company). Serum insulin was assessed using Enzyme Immunoassay Test Kit Catalog No. E29-072 (Immunospec Corporation).
- Lipoprotein risk ratios were calculated as follows: LDL/HDL was calculated by dividing LDL (mg/dl) by HDL (mg/dl); it should be < 3 in males, < 2.5 in females, TC/HDL by dividing TC (mg/dl) by HDL (mg/dl); it should be below < 4.5 in males, < 4 in females [9], and non-HDL/HDL by dividing non-

HDL (mg/dl) by HDL (mg/dl); it should be less than 2.845. TG/HDL was calculated by dividing TG (mg/dl) by HDL (mg/dl) [19].

- Insulin resistance (IR) was calculated according to Matthews et al. (1985) using the following equation: $HOMA-IR = \text{fasting blood glucose (mg/dl)} \times \text{fasting insulin } (\mu\text{IU/ml})/405$. Cut-off point ≥ 3.16 for HOMA-IR was considered to be risky for insulin resistance [20, 21].
- The TyG index was calculated using the formula: $\ln [TG \text{ (mg/dL)} \times \text{fasting glucose (mg/dL)} / 2]$ [22].
- TyG-BMI: TyG index \times BMI and TyG-WC: TyG index \times WC [16].

Statistical analysis

Data were analyzed using the statistical package SPSS version 22. Data was summarized as mean and standard deviation for quantitative variables and as frequencies (number of cases) and relative frequencies (percentages) for categorical variables. Unpaired *t* test was used for comparisons between groups. Chi square (C2) test was performed to compare categorical data. Exact test was used instead when the expected frequency is less than 5. *P* values less than 0.05 were considered as statistically significant. Spearman's correlation coefficient was used to test non-parametric variables and Pearson's correlation coefficient to test parametric variables. linear regression analysis was performed between WHtR and HOMA-IR.

Results

The study group included 160 pubertal children and adolescents; 55 (34.4%) males and 105 (65.6%) females with a mean age of 13.6 ± 2.22 years (ranged from 10.2–18.52 years). They were divided into two groups; group (1) included 80 obese children and adolescents, group (2) included 80 healthy non-obese non-overweight children and adolescents as control.

Group 1 (obese group) included 80 obese patients; 30 (37.5 %) males and 50 (62.5 %) females with a mean age of 13.39 ± 2.06 years, while group 2 (control group) included 80 healthy children and adolescents; 25 (31.25 %) males and 55 (68.75%) females with a mean age of 13.83 ± 2.36 years. The two groups were age- and sex-matched (*P* values 0.104, 0.496 respectively). The obese group has significantly higher body mass index (BMI), waist circumference (WC), hip circumference (HC), waist-hip ratio (WHR), and waist-to-height ratio (WHtR) (Table 1).

Regarding the laboratory findings; the obese group has significantly higher TC, TG, LDL, non-HDL, LDL/HDL, TC/HDL, non-HDL/HDL, and TG/HDL, with significantly lower HDL. In addition, they had significantly

Table 1 Demographic and clinical data of the study groups

Variables	Obese (n = 80) Mean \pm SD	Control (n = 80) Mean \pm SD	P value
Age (years)	13.39 \pm 2.06	13.83 \pm 2.36	0.21
BMI	37.96 \pm 6.3	21.19 \pm 2.66	< 0.001*
WC (cm)	96 \pm 10.35	54.14 \pm 3.15	< 0.001*
HC (cm)	100.64 \pm 9.12	67.39 \pm 3.39	< 0.001*
WHR	0.94 \pm 0.08	0.8 \pm 0.05	< 0.001*
WHtR	0.64 \pm 0.07	0.37 \pm 0.04	< 0.001*
Sex:			0.41
Male	30 (37.5%)	25 (31.25%)	
Female	50 (62.5%)	55 (68.75%)	

BMI body mass index, WC waist circumference, HC hip circumference, WHR waist-hip ratio, WHtR waist-to-height ratio

**P* value < 0.05 is considered significant

higher FBG, HOMA-IR, TyG, TyG-BMI, and TyG-WC indices compared to the control group (Table 2). Moreover, all obese subjects had high HOMA-IR values, however, only 22.5% (18 out of 80) of the control group had their HOMA-IR values above the cut-off point (≥ 3.12).

There was significantly positive correlation between waist-height ratio and BMI, WC, WHR, TC, TG, LDL, non-HDL, LDL/HDL ratio, TC/HDL ratio, non-HDL/HDL ratio, and TG/HDL ratio in addition to, FBG, and HOMA-IR, TyG index, TyG-BMI, and TyG-WC.

Table 2 Laboratory data of the study groups

Variables	Obese (n = 80) Mean \pm SD	Control (n = 80) Mean \pm SD	P value
TC (mg/dl)	189.94 \pm 37.62	138.6 \pm 19.8	< 0.001*
TG (mg/dl)	117.95 \pm 35.82	79.83 \pm 14.86	< 0.001*
LDL (mg/dl)	121.1 \pm 27.7	79.5 \pm 11.15	< 0.001*
HDL (mg/dl)	46.54 \pm 13.97	54.41 \pm 7.43	< 0.001*
Non-HDL (mg/dl)	143.4 \pm 36.7	84.18 \pm 25.22	< 0.001*
FBG (mg/dl)	104.89 \pm 14.05	86.45 \pm 9.82	< 0.001*
HOMA-IR	6.8 \pm 1.16	3.31 \pm 0.9	< 0.001*
TyG index	8.56 \pm 0.28	8.06 \pm 0.31	< 0.001*
TyG-BMI index	289 \pm 20.68	192.64 \pm 12.04	< 0.001*
TyG-WC index	898.8 \pm 105.74	454.96 \pm 26.08	< 0.001*
	Median (range)		
LDL/HDL ratio	2.6 (0.54–6.68)	1.51 (0.77–3.7)	< 0.001*
TC/HDL ratio	3.99 (1.58–11.14)	2.67 (1.38–5.68)	< 0.001*
Non-HDL/HDL ratio	2.99 (0.79–10.14)	1.67 (0.38–4.68)	< 0.001*
TG/HDL ratio	2.58 (1.08–6.95)	1.5 (0.64–3.41)	< 0.001*

TC Total cholesterol, TG triglycerides, HDL high-density lipoprotein-cholesterol, LDL low-density lipoprotein-cholesterol, FBG fasting blood glucose, HOMA-IR homeostasis model assessment for insulin resistance, TyG index triglycerides/glucose index

**P* value < 0.05 is considered significant

Table 3 Correlation between waist-height ratio (WHtR) and the clinical and laboratory parameters in the study

Variables	WHtR	
	r value	P value
BMI	0.79	< 0.001*
WC	0.97	< 0.001*
WHR	0.79	< 0.001*
TC	0.68	< 0.001*
TG	0.57	< 0.001*
LDL	0.7	< 0.001*
HDL	- 0.4	< 0.001*
Non-HDL	0.74	< 0.001*
HOMA IR	0.81	< 0.001*
LDL/HDL ratio	0.77	< 0.001*
TC/HDL ratio	0.72	< 0.001*
Non-HDL/HDL ratio	0.74	< 0.001*
TG/HDL ratio	0.68	< 0.001*
FBG	0.55	< 0.001*
TyG index	0.8	< 0.001*
TyG-BMI index	0.92	< 0.001*
TyG-WC index	0.99	< 0.001*

BMI body mass index, WC waist circumference, WHR waist-hip ratio, WHtR waist-to-height ratio, TC total cholesterol, TG triglycerides, HDL high-density lipoprotein-cholesterol, LDL low-density lipoprotein-cholesterol, FBG fasting blood glucose, HOMA IR homeostasis model assessment for insulin resistance, TyG index triglycerides/glucose index. Pearson's correlation test (parametric variables) or Spearman's correlation (non-parametric variables) for the correlation between variables, considering significance when $p < 0.05$ (5%)

*P value < 0.05 is considered significant

However, there was a significant negative correlation with HDL (Table 3).

Linear regression analysis was done and proved that WHtR is an independent predictor of IR assessed by HOMA-IR in this study (adjusted $R^2 = 0.65$, $p < 0.001$) (Fig. 1)

Discussion

Obesity in childhood and adolescence is associated with well-known comorbidities. Moreover, regional body fat distribution has an important influence on metabolic and cardiovascular risk factors. Increased visceral fat accumulation is considered a risk factor for CVD, dyslipidemia, hypertension, stroke, and T2DM [23, 24].

In the current study, the measures of visceral obesity (WC, WHR, and WHtR) were significantly higher in obese patients compared to the control group. Moreover, obese children had significantly higher TC, TG, LDL, and non-HDL compared to the control group. This is in line with other studies that found that obesity especially the central obesity was associated with unfavorable lipid profile [25–28].

Estimation of cardiovascular risk is the cornerstone of cardiovascular prevention. Many lipoprotein ratios were

defined in an attempt to optimize the predictive capacity of the lipid profile [9]. In our study, lipoprotein risk ratios (LDL/HDL, TC/HDL, non-HDL/HDL, and TG/HDL ratio) were significantly higher in obese children and adolescents compared to the control group. This in agreement with other authors who found that obesity is associated with increased risk for CVD and these ratios had greater predictive value for CVD than conventional lipid parameters used independently [9, 10, 28].

There is a well-known association between obesity and T2DM especially the visceral obesity [29–31]. Visceral obesity plays an important role in the development of T2DM by mobilizing free fatty acids and certain inflammatory cytokines causing IR [30]. Studies have shown that IR is a risk factor for the development of T2DM and CVD in children and adolescents [32, 33].

In this work, fasting blood glucose (FBG), IR assessed by HOMA-IR, TyG index, TyG-BMI, and TyG-WC were significantly higher in the obese group compared to the control group. This is in line with Hussain et al. [30] who found increased incidence of T2DM in obese patients. Also, Hajian-Tilaki and Heidari [34] found a significant correlation between FBG and WHR and explained this by central obesity which correlates with the development of subsequent metabolic abnormalities and cardiovascular morbidity.

In the current study, there were significantly positive correlations between WHtR and BMI, WC, WHR, TC, TG, LDL, non-HDL, LDL/HDL ratio, TC/HDL ratio, non-HDL/HDL ratio, and TG/HDL ratio in addition to, FBG, HOMA-IR, TyG index, TyG-BMI, and TyG-WC. However, there was significant negative correlation with HDL. This agrees with Miralles et al. [8] who analyzed the correlation of WHtR with the other anthropometric variables, and observed a positive significant correlation with BMI, WC, BF%, lipid profile and TG/HDL and significant negative correlation with HDL. Moreover, Jamar et al. [35] found that among anthropometric obesity indicators, WHtR was most closely associated with occurrences of IR and predicted the onset of diabetes in obese individuals as compared with other parameters (BMI, WC, WHR, neck circumference, and body shape index).

Several studies have been recently conducted to demonstrate the accuracy of WHtR in identifying the risks for CVD in obese children and adolescents from healthy youth population; defining cut-offs and centiles for this easily calculated parameter [36–38]. It is also ideal and non-invasive tool in terms of interpretation and measurement to be used in clinical practice.

Potential limitations of our study must be considered. First, this is a cross-sectional rather than a population-based study, which may lead to over-estimation of the prevalence of insulin resistance in obese children. Moreover, this

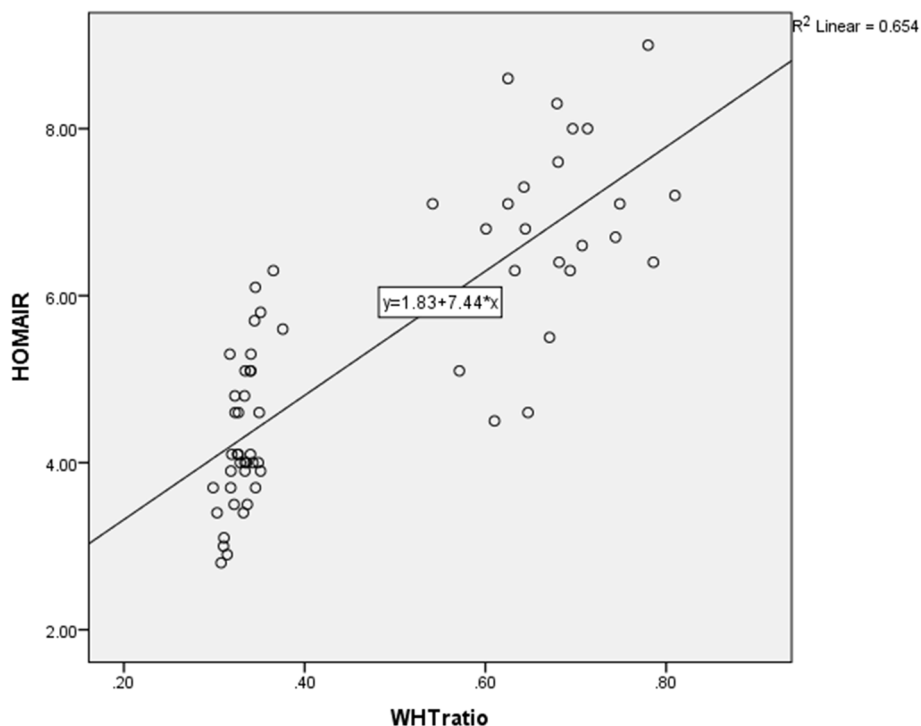


Fig. 1 Linear regression analysis between WHtR and HOMA-IR. R^2 = regression determinant coefficient ($R^2 = 0.65$, $p < 0.001$)

work was a cross-sectional study and might lack adequate evidence of the predictive values of WHtR. Although, this value is not diagnostic; it can be predictor for the screening for IR among obese children and adolescents. Additionally, being based on convenient consecutive sampling this study may lack clear generalizability, however, while applying consecutive sampling, each consecutive eligible patient who presents for care within the defined study time period is approached for enrollment, thus, consecutive sampling provides some structure and additional rigor that reduces the bias in sampling. Finally, blood pressure measurements for the studied subjects were not included in the study.

Conclusion

Waist-to-height ratio (WHtR) can be an excellent, easy and reliable clinical predictor for cardiovascular risk and insulin resistance in children and adolescents with exogenous obesity.

Abbreviations

BMI: Body mass index; CVD: Cardiovascular disease; FBG: Fasting blood glucose; HDL: High-density lipoproteins; HC: Hip circumference; IR: Insulin resistance; LDL: Low-density lipoproteins; T2DM: Type 2 diabetes; TC: Total cholesterol; TG: Triglycerides; TyG index: Triglycerides glucose index; TyG-BMI index: Triglycerides glucose body mass index; TyG-WC index: Triglycerides glucose waist circumference index; WC: Waist circumference; WHtR: Waist-to-height ratio; WHR: Waist-hip ratio.

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Authors' contributions

HS and AI conceived and designed the study plan and wrote the manuscript. AI initiated the study idea, edited initial drafts, contributed to analyzing and presenting data, and collated the final draft in consultation with the other coauthor. HS and SA recruited the subjects, processed samples, contributed to acquisition of data, data monitoring and initial data analysis, supervised the final statistical analysis, and reviewed and edited the manuscript. The authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analyzed during this study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The study protocol was approved by the ethical committee of Cairo University Hospital Research Committee. Ethics committee reference number was not available at the time this work was done. A written informed consent was taken from the parents of the study participants. The study and data collection were conformed to all local laws and were compliant with the principles of the Declaration of Helsinki.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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