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REGULAR ARTICLE

Associations of several anthropometric indices with insulin resistance in children: The Children Study

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Abstract

Aim: To compare the associations of several anthropometric indices (i.e. waist circumference [WC], waist-to-height ratio, body mass index (BMI) and waist-to-hip ratio) with the insulin resistance (IR) proxy measures in Greek schoolchildren.

Methods: A random sample of 248 children was used. Fasting plasma glucose and serum insulin levels were measured. IR was estimated through homeostasis model assessment (HOMA), glucose-to-insulin ratio and quantitative insulin sensitivity check index.

Results: Insulin levels and IR indices were significantly related to BMI, WC and waist-to-height ratio. Glucose-to-insulin ratio and quantitative insulin sensitivity check index were inversely correlated with all anthropometric indices, while insulin levels and HOMA were positively associated with these indices. Generally, all significant correlations were weak to moderate ($0.217 \leq r \leq 0.513$). BMI, WC and waist-to-height ratio displayed similar correlation with insulin levels ($r = 0.431$, $r = 0.427$ and $r = 0.354$, respectively) and IR indices. Similar results were found using multiple linear regression analysis.

Conclusion: Based on the current findings, BMI, waist-to-height ratio and WC are higher, associated with the IR proxy measures compared with waist-to-hip ratio, among Greek pupils. Therefore, all these simple adiposity-related indices could be used, alternatively, in clinical practice as a simple tool for identification of children at risk for developing IR.

INTRODUCTION

Several studies have demonstrated that the prevalence of obesity in children and adolescents is increasing worldwide at an alarming rate (1). Moreover, it has been reported that obesity is associated with increased prevalence of cardiovascular (CVD) risk factors among children and adolescents (2). More particularly, previous studies have shown that visceral adiposity is more predictive of CVD risk and its risk factors (i.e. hypertension, hyperlipidemia and abnormal glucose tolerance) compared to total adiposity (3). For this reason, an assessment tool for total obesity, for example body mass index (BMI), may not provide the best estimates of metabolic and CVD risk. Therefore, the need for an index that could detect central obesity was presented. Unfortunately, there is no standard and widely accepted measure of abdominal obesity; waist circumference-to-hip circumference ratio (WHR), waist circumference (WC) and waist circumference-to-height ratio (WHtR) have been proposed as indices of visceral adiposity (4,5). However, none of the above-mentioned obesity indices is considered as the best one for predicting CVD risk, as the results of previous studies are inconsistent.

Large studies conducted in adults have proposed that WHtR (6) or WC (7) are better predictors than BMI in detecting CVD risk factors, while some others have demonstrated that WHR is the best predictor (8). Regarding studies carried out among children, investigators in Cyprus (9), Japan (10) and China (11) concluded that both WC and WHtR are better predictors of total cholesterol, triglyceride, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol and systolic and diastolic blood pressure levels than BMI, with a small superiority of WHtR. Also, Kahn et al., using cross-sectional US survey data in a population based sample, reported that WHtR identifies better than BMI youths with adverse CVD risk factors (5).

Several studies have investigated which is the best obesity-related predictor of CVD risk factors (i.e. BMI, WHR, WC, WHtR, % fat), both in adults and children. However, limited data have been reported regarding the association of various anthropometric indices with insulin resistance (IR) proxy measures and plasma glucose levels (5,11–15). In particular, Yan et al. have investigated the correlation among BMI, WC and WHtR and fasting serum insulin, plasma glucose and HOMA (11), among children and adolescents; Kahn et al. examined the better anthropometric indicator (between BMI and WHtR) of fasting plasma glucose levels in youths (5) and Misra et al. compared the correlation of BMI, WC and subscapular skinfold thickness with fasting hyperinsulinemia (14). Moreover, to our knowledge, no similar study has been conducted in a European population neither in adults nor in children.

Therefore, the aim of this study is to identify which obesity-related measure is strongly associated with fasting plasma glucose levels and IR proxy measures in Greek schoolchildren. In this context, the associations of BMI, WC, WHR and WHtR with fasting plasma glucose and serum insulin levels, HOMA, FGIR and QUICKI indices will be assessed.

METHODS

Study population

Between October 2005 and March 2006, 522 children (52% of those were girls) aged 10–12 years were recruited from primary schools in the island of Crete, Greece. Among those, full data about their anthropometric and biochemical characteristics, dietary habits, physical activity, cardiorespiratory fitness and serum insulin levels had been recorded for a subgroups (n = 248 children). Therefore, only 248 children were included in our analyses for this study.

In the present study, school was used as the main sampling unit. Sampling of schools was random and multistage and was made from two counties in the eastern part of Crete. In these two counties there is only one urban municipality where the capital of Crete, that is the city of Heraklion, is located (population size >180 000) and several rural municipalities with many small villages (population size of each municipality <5000). From the city of Heraklion, 20 schools were randomly selected. Among the total number of rural municipalities, seven were randomly selected and among each one of these seven municipalities, one school was randomly selected. The number of schools selected from the urban and rural regions was determined by the distribution of pupils in these regions (65% in urban and 35% in rural regions).

All children in the same class were invited to participate in the study to avoid ethical problems. An extended letter explaining the aims of the current study and a consent form was provided to each parent in these schools. Those parents agreed to participate in the study had to sign the consent form and return it back to school. Approval to conduct the study was granted by the Ethical Committee of Harokopio University of Athens and the Greek Ministry of Education.

Anthropometric measurements

Weight was measured to the nearest 10 g using a Seca digital scale (Seca@Alpha, Model 770, Hamburg, Germany). Subjects were weighed without shoes and in the minimum clothing possible, that is their underwear, in the fasting stage. Standing height was measured without shoes to the nearest 0.5 cm with the use of a commercial stadiometer. BMI was calculated as weight in kilograms to height-squared in square metre ratio. Children were classified as 'normal weight', 'overweight' and 'obese', according to the IOTF's age and sex-specific BMI cut-off points (16). Moreover, we measured WC at the level of umbilicus and hip circumference at the level of greater trochanters and pubic symphisis to the nearest 0.1 cm by using a nonelastic tape (Hoechstmass, Sulzbach Germany). WHR and WHtR were calculated.

Identification of pubertal staging was also assessed (17). Pubertal stage was recorded by a researcher of the same sex as the child, after brief observation. Breast development in girls and genital development in boys was used for pubertal classification.

Biochemical assessment

After a 12-h overnight fast, venous blood samples (10 mL of whole blood) were obtained from each child. Blood was centrifuged for plasma separation at 3000 rpm for 15 min using a bench centrifuge, and 1.5 mL aliquots were pipetted into plastic Eppendorf tubes. The aliquots were then stored at –80°C until further analyses. Plasma glucose was determined in duplicate using commercially available enzymatic colorimetric assays (Sigma Diagnostics, St. Louis, MO, USA) on an automated ACE analyser (Sciapparelli Biosystems, Inc., Fairfield, NJ, USA). Serum insulin was determined in duplicate by immunofluorescence using an automated immunoassay analyser AIA- 600 II (Tosoh Corporation, Tokyo, Japan). IR was estimated through homeostasis model assessment (HOMA) (18), fasting glucose to insulin ratio (FGIR) and quantitative insulin sensitivity check index (QUICKI) (19). These indices were calculated using fasting plasma glucose (G_F) and fasting serum insulin (I_F), as follows:

$$\begin{aligned}\text{HOMA} &= [I_F(\mu\,\text{units/mL}) * G_F(\text{mmol/L})]/22.5\\ \text{FGIR} &= G_F(\text{mg/dL})/I_F(\mu\,\text{units/mL})\\ \text{QUICKI} &= 1/[\log I_F(\mu\,\text{units/mL}) + \log G_F(\text{mg/dL})].\end{aligned}$$

The aforementioned ones are valid tools for assessing IR among obese children and adolescents (20).

Dietary assessment

A combination of a 24-h recall and a 3-day food diary was used to collect information regarding children's dietary intake (21). It has been shown that the minimum number of days needed to obtain the intake of a nutrient varies. In that context, fewer days are needed for energy and macronutrient intake compared to other nutrients, such as vitamin A or B12. A reliable estimate of energy intake, which tends to show less day-to-day variation than other nutrients, can be obtained over a shorter period of time (a few days) compared to for example vitamin A (several weeks), for which intake is much more variable from day-to-day (22). However, for most nutrients a total of 3–5 days are enough for accurate intake estimation. Furthermore, it is a common practice in most epidemiological studies to obtain one or two 24-h recalls from all subjects to assess their diets and then obtain three or four 24-h recalls just from a sub-population of the study to correct for the day-to-day variability (23).

The dieticians of the research group collected information using a 24-h recall during the first day of the morning visit at each school. During the interview, each child was familiarized with portion sizes and the relevant procedures in order to successfully complete a food record at home in the forthcoming days, most preferably one Sunday and two weekdays. When food records were returned at school, a team member received and checked the records for any

miss-recorded or missing information. Food intake data were analysed using the Nutritionist V diet analysis software (First Databank, San Bruno, CA, USA), which was extensively amended to include traditional Greek foods and recipes, as described in Food Composition Tables and Composition of Greek Cooked Food and Dishes (24) and the databank was updated with nutritional information of chemically analysed commercial food items widely consumed by school children in Greece. The distribution of usual intakes was estimated by using the National Research Council method (NRC method) (25,26), which attempts to remove the effects of day-to-day variability (within subject) in dietary intakes. More specifically, the equation used for the calculation of adjusted (usual) intake was the following:

$$[(\text{Subject's mean} - \text{group mean}) \times SD_{\text{between-person}}/SD_{\text{observed}}] + \text{group mean}.$$

Statistical analysis

Normally distributed continuous variables are expressed as mean values ± standard deviation and skewed variables are reported as median (25th, 75th interquartiles). Normality of distribution was evaluated through the Kolmogorov–Smirnov test. I_F and HOMA were non-normally distributed and were log-transformed. Differences in anthropometric measures, G_F levels, FGIR and QUICKI between genders were examined using Student's *t*-test, while in I_F levels and HOMA were evaluated using Mann–Whitney. Correlations between anthropometric variables and G_F levels, FGIR and QUICKI were tested by the use of Pearson's correlation coefficient, while the relationship between anthropometric indices and I_F and HOMA were assessed using Spearman correlation coefficient. For each of the following indices: G_F, I_F, HOMA, QUICKI and FGIR (as dependent variables), we applied four multiple regression models. In each model, we included one of the four anthropometric indices as well as age, sex, pubertal stage total energy, simple carbohydrate and fat intake as independent variables. We used the adjusted R^2 of each one model (variance explained by each one model) in order to determine which of the anthropometric indices is strongly associated with proxy IR measures even after controlling for potential confounders. We ran different analyses for the several anthropometric markers as independent variables in order to avoid problems of collinearity, because all these anthropometric markers were strongly correlated. To evaluate whether sex modifies the effect of anthropometric indices on all biochemical measurements, an interaction term was entered in the regression model. Because no significant interaction was observed, they were not included in the final models. p-values <0.05 from two-sided hypotheses are considered as statistically significant. All statistical calculations were performed using STATA 8.0 (STATA Corp, College Station, TX, USA).

RESULTS

Among 248 pupils, 55% were normally weighted, 31% were overweight and 14% were obese. The prevalence of obesity was higher among boys compared to girls although this did not reach statistical significance (17.6% and 12.8%, respectively, $p = 0.459$). Table 1 illustrates descriptive characteristics of the anthropometric characteristics, G_F levels, I_F levels and IR indices for the total study population and by gender. It was observed that boys had greater WC, WHR, WHtR and they were less insulin resistant compared to girls (lower values of HOMA and higher values of FGIR).

Univariate correlation coefficients between anthropometric indices and glycemic control indices are presented in

Table 1 Anthropometric indices, fasting glucose and insulin levels as well as insulin resistance indices of study population

	Boys (n = 109)	Girls (n = 139)	Total (n = 248)
Age (years)	10.45 ± 0.38	10.47 ± 0.35	10.46 ± 0.36
Anthropometric measures			
Height (m)	1.44 ± 0.06	1.44 ± 0.07	1.44 ± 0.07
Weight (Kg)	43.00 ± 9.81	41.03 ± 10.16	41.89 ± 10.02
BMI (kg/m^2)	20.45 ± 3.81	19.56 ± 3.93	19.95 ± 3.89
WC (cm)	71.78 ± 9.83	68.12 ± 9.97**	69.73 ± 10.04
HIP (cm)	82.20 ± 8.64	81.43 ± 9.67	81.77 ± 9.21
WHR	0.87 ± 0.06	0.84 ± 0.05**	0.85 ± 0.06
WHtR	0.49 ± 0.06	0.47 ± 0.06**	0.48 ± 0.06
Biochemical measurements			
Fasting glucose levels (mg/dL)	4.78 ± 0.78	4.67 ± 0.61	4.72 ± 0.67
Fasting Insulin levels (μ unit/mL)†	4.80 (3.20, 7.10)	6.30 (4.40, 8.60)**	5.80 (3.60, 8.00)
HOMA†	0.79 (0.51, 1.16)	0.98 (0.69, 1.33)*	0.89 (0.55, 1.30)
FGIR	15.24 ± 8.49	12.32 ± 8.08*	13.61 ± 8.37
QUICKI	0.40 ± 0.05	0.39 ± 0.04	0.40 ± 0.04

Data are presented as mean ± standard deviation.

*$p < 0.05$ and **$p < 0.001$ for sex differences.

†Data are presented as median (25th, 75th percentile).

BMI = body mass index; WC = waist circumference; HIP = hip circumference; WHR = waist to hip ratio; WHtR = waist to height ratio; HOMA = homeostasis model assessment; FGIR = fasting glucose to insulin ratio; QUICKI = quantitative insulin sensitivity check index.

Table 2 Correlation coefficients between anthropometric indices and glucose, insulin levels and insulin resistance indices

	BMI	WC	WHR	WHtR
Fasting glucose levels (mg/dL)				
Total population	0.067	0.074	−0.016	−0.070
Boys	0.100	0.059	−0.096	0.034
Girls	0.016	0.070	0.035	0.090
Fasting insulin levels (μ unit/mL)†				
Total population	0.431**	0.427**	0.125	0.354**
Boys	0.447**	0.484**	0.171	0.397**
Girls	0.513**	0.490**	0.217*	0.443**
HOMA§				
Total population	0.390**	0.400**	0.127	0.337**
Boys	0.387**	0.434**	0.145	0.356**
Girls	0.461**	0.460**	0.239*	0.428**
FGIR				
Total population	−0.367**	−0.348**	−0.097	−0.287**
Boys	−0.399**	−0.438**	−0.227*	−0.383**
Girls	−0.399**	−0.358**	−0.099	−0.293*
QUICKI				
Total population	−0.376**	−0.375**	−0.139	−0.329**
Boys	−0.356**	−0.379**	−0.170	−0.333**
Girls	−0.449**	−0.454**	−0.224*	−0.408**

For abbreviations, see footnote to Table 1.
*$p < 0.05$ for correlation coefficients; **$p < 0.001$.
†Spearman correlation coefficient was calculated.

Table 2. No anthropometric index was significantly correlated with G_F levels, while I_F and IR indices were significantly related to BMI, WC and WHtR. FGIR and QUICKI indices were inversely correlated with all anthropometric indices, while I_F and HOMA were positively associated with these indices. I_F and all IR indices were similarly correlated with BMI and WC, and these correlations were a little higher compared to that observed between I_F, all IR indices and WHtR. Generally, all significant correlations were weak to moderate ($0.217 \leq r \leq 0.513$).

Results of the multiple linear regression for each one of dependent variables are presented in Table 3. The results confirmed our findings in the univariate analysis, because models including WC, BMI and WHtR explained higher proportion of variance of I_F and all IR indices compared to that explained by model with WHR.

DISCUSSION

The purpose of this study was to determine which of the following anthropometric indices – WC, WHtR, WHR and BMI – are strongly associated with glucose levels and IR proxy measures among Greek schoolchildren population. Our findings showed that BMI, WC and WHtR are statistically significantly correlated with proxy IR measures, while no anthropometric index is significantly associated with G_F levels.

To our knowledge, there are only few studies that have examined the associations between anthropometric measures of obesity and IR or G_F levels in children or adolescents. Our findings are partially in line with those of other researchers. For instance, Yan et al. reported that WC, WHtR and BMI showed similar correlation with I_F and HOMA and that WC was the best predictor of G_F among Chinese children (11), while Kahn et al. demonstrated that no anthropometric index was a statistically significant predictor of G_F in youth

Table 3 Variance of glucose levels and insulin resistance indices explained of various anthropometric measures

Dependent variable	Anthropometric index as independent factor	β ± SE†	p-value	Adjusted-R^2
Fasting glucose levels (mg/dL)	BMI (kg/m^2)	0.26 ± 0.16	0.117	0.001
	WC (cm)	0.10 ± 0.06	0.109	0.001
	WHR	−6.21 ± 10.6	0.559	−0.004
	WHtR	15.8 ± 9.90	0.112	0.001
Fasting insulin levels (μ unit/mL)§	BMI (kg/m^2)	0.07 ± 0.01	<0.001	0.235
	WC (cm)	0.03 ± 0.004	<0.001	0.256
	WHR	2.66 ± 0.79	0.001	0.084
	WHtR	4.18 ± 0.64	<0.001	0.214
HOMA§	BMI (kg/m^2)	0.07 ± 0.01	<0.001	0.200
	WC (cm)	0.03 ± 0.004	<0.001	0.221
	WHR	2.78 ± 0.86	0.001	0.066
	WHtR	4.29 ± 0.69	<0.001	0.186
FGIR	BMI (kg/m^2)	−0.84 ± 0.15	<0.001	0.176
	WC (cm)	−0.33 ± 0.06	<0.001	0.180
	WHR	−26.9 ± 11.1	0.018	0.060
	WHtR	−43.4 ± 9.19	<0.001	0.139
QUICKI	BMI (kg/m^2)	−0.005 ± 0.0008	<0.001	0.178
	WC (cm)	−0.002 ± 0.0003	<0.001	0.196
	WHR	−0.179 ± 0.06	0.004	0.061
	WHtR	−0.27 ± 0.05	<0.001	0.160

†After controlling for age, sex, pubertal stage, total energy, carbohydrate and fat intake.
§Log-transformed values were used.

(5). Moreover, investigators who compared the correlations of BMI and WC with insulin levels and HOMA-IR suggested that WC is the best predictor and that it could be included in clinical practice as a simple tool to help identify children at risk (27,28). More similar studies among children have been conducted to investigate which anthropometric index is the best indicator of classical CVD risk factors (i.e. hypertension, hyporcholesterolaemia, hypertriglyceridemia etc). Their results are partially in accordance. For example, Savva et al. demonstrated that WC and WHtR are better predictors of lipids and blood pressure than BMI among Greek-Cypriot children 10–14 years old (9). Hara et al. reported that WHtR is the most significant predictor for total cholesterol levels, triglyceride levels, low-density-lipoprotein cholesterol levels and atherogenic index in children aged 9–13 years (10). Finally, Yan et al. concluded that WHtR and BMI is a better indicator of lipids and blood pressure, respectively, compared to WC among Chinese children aged 7–18 years (11).

Among adults, only one study was found to compare the correlations between anthropometric measures of obesity and IR in a group of Indigenous Australians. The results of this study revealed that both BMI and WC are better predictors of IR compared to WHR (13). More studies have tried to identify the best obesity-related indicator in predicting type 2 diabetes mellitus among adults and WC has emerged as the best predictor compared to BMI, WHR and WHtR (15,29,30).

There is an unanimous agreement that obesity-associated metabolic complications in children, as in adults, (i.e. abnormal lipid or insulin concentration) are associated with an upper body or centralized deposition of excess body fat than with total obesity (28,31). In particular, the link between central adiposity and elevated fasting insulin could be attributed to the low hepatic insulin clearance due to high exposure of liver to free fatty acids from abdominal adiposity (32). Furthermore, the increased intramyocellular fat accumulation, induced by high levels of circulating free fatty acids derived from the abdominal adipose tissue, could be another explanatory mechanism for the association observed in the present study between IR and central adiposity (33).

According to the aforementioned ones, it can be concluded that WC, BMI and WHtR are similarly correlated and explicitly strongly associated with proxy IR measures compared to WHR among Greek schoolchildren. This implies that all these simple obesity indices could be used, alternatively, in clinical practice as a simple tool for identification of children at risk for developing IR and type 2 diabetes mellitus. Of course, further studies to investigate the association between several anthropometric indices and IR among children are required, because data regarding this issue are limited. Moreover, further research should be conducted in order to propose appropriate WC, WHtR and BMI cut-offs for using in clinical practice.

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