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Visceral adiposity index and triglyceride glucose index as effective predictors of insulin resistance and cardiometabolic risk in obese Egyptian children

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Abstract: Childhood obesity is now recognized as one of the most serious health issues worldwide, along with metabolic abnormalities, which are frequent among obese children increasing the risk of chronic diseases in adulthood. Visceral adiposity index (VAI) and triglyceride glucose (TyG) index have recently been identified for detecting type 2 diabetes and cardiometabolic risk in children. This study aimed to estimate VAI and TyG and investigate their possible associations with insulin resistance and cardiometabolic alterations among obese Egyptian children. One hundred pre-pubertal children were enrolled in the study, including 70 obese and 30 normal-weight controls. VA and TyG indices were determined based on biochemical analysis. Obese children showed significantly higher VAI and TyG index values compared to control group. In obese children, VAI exhibited significant positive correlations with cardiac risk ratios I and II, as well as TyG index. The TyG index demonstrated significant positive correlations with total cholesterol, cardiac risk ratios I and II, along with significant negative correlation with high density lipoproteins (HDL). In conclusion, the VA and TyG indices can be suggested as effective predictors of insulin resistance and cardiometabolic risk in obese children. Furthermore, greater VA and TyG indices in obese children suggest a tendency to insulin resistance, type 2 diabetes, and cardiovascular injuries, which should be considered to prevent the occurrence and progression of these complications throughout life.

Keywords: VAI, TyG, insulin resistance, cardiometabolic risk, obesity.

1. INTRODUCTION

Childhood obesity is a global health issue with several negative long-term health consequences in adulthood. Obesity in children is on the rise in many countries highlighting the critical need for early preventive and intervention strategies [1]. Furthermore, childhood obesity has been linked to multiple co-morbidities which include cardiovascular diseases, type 2 diabetes mellitus, as well as metabolic syndrome [2].

In terms of anthropometric measures, clinicians are continually looking for easy and affordable methods to estimate the fat tissue content and the obesity-associated metabolic disorders risk [3]. Along with classic indices, various parameters based on anthropometric measurements and biochemical data have lately been proposed. One of these recommended indices is known as the visceral adiposity index (VAI), which uses a mathematical equation to estimate visceral adipose tissue by combining anthropometric and laboratory data [4]. Previous research has proposed VAI for the prediction of type 2 diabetes, along with metabolic syndrome and hypertension [5-7]. Furthermore, it has been found that high VAI values are related to an elevated type 2 diabetes risk making it an effective method for early identification of the possibility of developing type 2 diabetes [8]. Moreover, prior investigations have demonstrated a substantial

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association of VAI with coronary artery disease [9,10].

The triglyceride glucose (TyG) index represents a unique parameter that combines fasting glucose and triglycerides and has been shown to indicate insulin resistance as well as detect metabolically unhealthy patients [11]. TyG index has recently been considered a helpful determinant for insulin resistance in children [12,13], since it is an easily accessible and economic screening tool [14]. In addition, TyG index has been suggested to be useful to anticipate calcification of coronary arteries in adults and cardiovascular disease risk in children [15,16].

Given the potentially devastating impact of childhood obesity in adult life, it is critical to identify obese children at risk for insulin resistance and cardiometabolic abnormalities in order to prevent the onset and development of these complications in the future. Consequently, the current study aimed to estimate the VA and TyG indices and investigate their possible associations with insulin resistance and cardiometabolic alterations in obese Egyptian children.

2. METHODS

2.1 Subjects:

One hundred pre-pubertal children were enrolled in the study from September 2021 to March 2022 recruited from the National Nutrition Institute's (NNI) obesity clinics in Cairo, Egypt. The children were first divided into two groups: 70 obese children and 30 apparently healthy normal-weight control children of matching age and gender. Obese children had body mass index (BMI) of more than two standard deviations (SD) over the median of World Health Organization (WHO) growth guidelines, whereas normal weight children (BMI -2 to +1 SD) were included in the control group [17]. Obese group was further subdivided into 31 boys and 39 girls. Children with infection, inflammation, chronic illness, primary hyperlipidemia, hypertension, or secondary obesity were excluded.

2.2 Sample collection:

Following an overnight fast, a peripheral blood sample of 5 ml was obtained from each subject. Centrifugation at 3000 rpm was done for ten minutes to obtain the serum. Aliquots of serum were used to measure the levels of glucose, triglycerides, HDL, and total cholesterol.

The weight and height were measured, and BMI was determined using the formula: BMI= weight (kg)/height $(m)^2$. The waist circumference was measured, and the waist-to-height ratio was obtained as the waist circumference divided by the height, with a waist-to-height ratio of 0.49 defining central obesity in children [18]. VA and TyG indices were determined by the formulas reported by Amato *et al* [4] and Guerrero-Romero *et al* [19], respectively:

$$\text{VAI (male)} = \frac{\text{Waist circumference}}{39.68 + (1.88 \text{ x BMI})} \text{X} \frac{\text{triglycerides}}{1.03} \text{X} \frac{1.31}{\text{HDL}}$$

$$\text{VAI (female)} = \frac{\text{Waist circumference}}{36.58 + (1.89 \text{ x BMI})} \text{X} \frac{\text{triglycerides}}{0.81} \text{X} \frac{1.52}{\text{HDL}}$$

$$\text{TyG index} = \text{Ln} \left(\text{triglycerides X} \frac{\text{glucose}}{2}\right)$$

A physician performed the clinical examination to confirm that the individuals fulfilled the inclusion and exclusion criteria. The study was carried out in compliance with the Helsinki Declaration Principles and received approval from the National Organization for Teaching Hospitals and Institutes' research ethics committee (IN000110). Each subject's parents provided a written informed consent.

2.3 Biochemical analysis:

Serum glucose, triglyceride, and total cholesterol levels were evaluated using Spinreact (Spain) enzymatic colorimetric kits according to the methods of Trinder [20], Bucolo and David [21], and Meiattini *et al* [22], respectively. Serum HDL was measured using an enzymatic colorimetric kit provided by Spectrum Diagnostics (Egypt) using Grove [23] method. The Friedewald formula was used to calculate the low-density lipoprotein (LDL) [24]. Cardiac risk ratios were calculated as follows: cardiac risk ratio I=total cholesterol / HDL, cardiac risk ratio II=LDL / HDL [25].

2.4 Statistical analysis:

SPSS version 20.0 was used for statistical analysis. All data is presented as mean ± standard error of mean (SEM). The Student T-test was employed to assess normally distributed variables. When necessary, the non-parametric Mann-Whitney U test was performed. Pearson and Spearman's correlation tests were carried out to determine the correlations between the variables. Receiver operating curve (ROC) analysis was performed then the area under the curve (AUC) was determined. The uniform distribution of data was tested. Statistical significance was defined as a P value < 0.05.

3. RESULTS

3.1 Participants' characteristics:

Table (1) shows the demographic and anthropometric data of obese children and controls. No significant difference in age was observed between obese and control groups. Obese children

showed significantly higher weight, BMI, waist circumference, as well as waist-to-height ratio compared to control children. Central obesity was present in all obese children defined as having a waist-to-height ratio higher than 0.49. No significant difference was found in height between the studied groups.

Table (1): Demographic and anthropometric characteristics of obese and control groups:

Parameters	Control group (N=30)	Obese group (N=70)
Age (years)	8.6 ± 0.3 (5-10)	8.7 ± 0.2 (5-10)
Sex (boys/girls)	(18/12)	(31/39)
Weight (kg)	29.6 ± 1.1 (18-40)	55.6 ± 2 *** (28.5-103)
Height (cm)	133.4 ± 1.7 (113.5-149)	136 ± 1.4 (110-157)
BMI (kg/m^2)	16.5 ± 0.3 (13.9-19.8)	29.5 ± 0.6 *** (20-45.3)
Waist circumference (cm)	58.1 ± 0.8 (50-65)	88.6 ± 1.3 *** (67-118)
Waist/height ratio	0.4 ± 0.003 (0.4-0.5)	0.7 ± 0.01 *** (0.5-0.8)

Data are expressed as mean ± SEM, range is stated between parentheses.

BMI: body mass index.

*** Significantly different from the control group at P < 0.001

3.2 Metabolic characteristics and cardiac risk ratios:

As demonstrated in table (2), obese children had significantly higher fasting glucose, triglycerides, total cholesterol, LDL, and significantly lower HDL levels compared to control children. Also, obese children exhibited significantly higher cardiac risk ratio I and II when compared with control.

Table (2): Metabolic characteristics and cardiac risk ratios of obese and control groups:

Parameter	Control group	Obese group
Glucose (mg/dl)	87.4 ± 1.9 (70-109.3)	94.5 ± 1.6 ** (69-118.7)
Triglycerides (mg/dl)	81.8 ± 4 (36.7-127.5)	128.6 ± 7 *** (49.4-385.3)
HDL (mg/dl)	56.5 ± 2.6 (34.8-88.4)	46.3 ± 1.6 ** (10.8-74.1)
Total cholesterol (mg/dl)	133.6 ± 4.5 (79.3-176.1)	148.9 ± 4.3 * (87.7-270)
LDL (mg/dl)	60.7 ± 4.3 (29.2-116.7)	76.9 ± 4.4 * (11.4-191)
Cardiac risk ratio I (total cholesterol /HDL)	2.5 ± 0.1 (1.7-4.6)	3.6 ± 0.2 *** (1.4-10.6)
Cardiac risk ratio II (LDL/HDL)	1.1 ± 0.1 (0.3-1.9)	1.9 ± 0.1 *** (0.2-5.5)

Data are expressed as mean ± SEM, range is stated between parentheses.

HDL: high-density lipoprotein cholesterol; LDL: low-density lipoprotein cholesterol.

*, **, *** Significantly different from the control group at P < 0.05, 0.01, and 0.001, respectively.

3.3 Results of VAI and TyG index:

The obese group showed significantly higher VAI and TyG compared to control group as shown in figure (1) and (2), respectively. Obese girls exhibited significantly higher VAI compared with obese boys (Figure 3). ROC curve analysis of VAI was performed for discrimination between obese boys and girls and VAI demonstrated a fair area under the curve (AUC = 0.796), at cut off value of 1.2 had sensitivity 94.9% and specificity 61.3% (Figure 4). The VAI showed significant positive correlations with cardiac risk ratio I (correlation coefficient (r) = 0.68, P <0.001), cardiac risk ratio II (r = 0.54, P <0.001) and TyG index (r = 0.7, P <0.001) in obese children (Figure 5). Furthermore, TyG index exhibited significant positive correlations with total cholesterol, cardiac risk ratio I, and cardiac risk ratio II, along with significant negative correlation with HDL (Table 3).

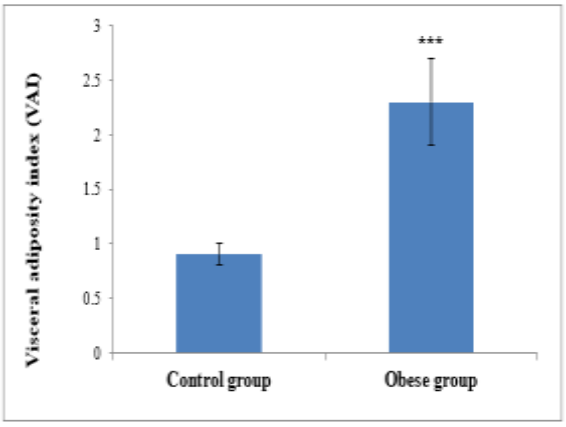

Figure 1. Visceral adiposity index (VAI) in studied groups. Data are expressed as mean ± SEM, *** Significant difference from the control group at P < 0.001

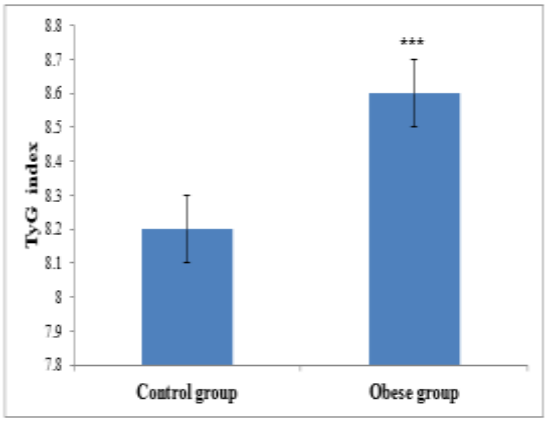

Figure 2. Triglyceride glucose (TyG) index in studied groups.
Data are expressed as mean ± SEM, *** Significant difference from the control group at P < 0.001

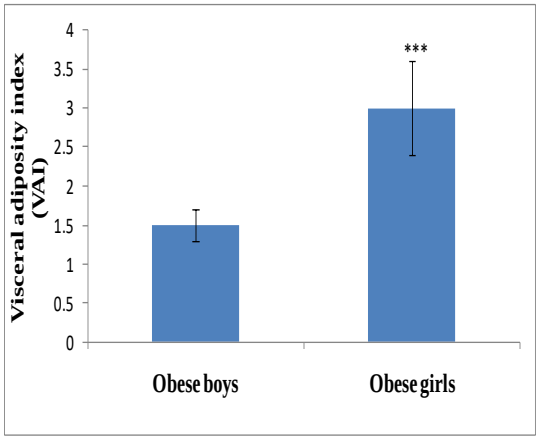

Figure 3. Visceral adiposity index (VAI) in obese boys and girls.
Data are expressed as mean ± SEM, *** Significant difference from obese boys' group at P < 0.001

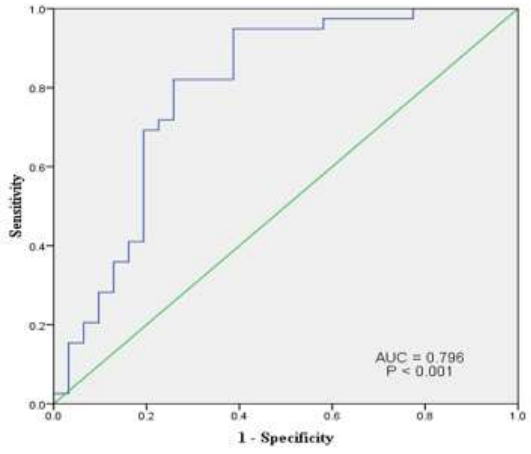

Figure 4. ROC curve of visceral adiposity index (VAI) for discrimination between obese boys and girls.

4. DISCUSSION

Obesity in children is a global public health issue with increasing trends. According to recent estimates, around 37 million children worldwide are overweight or obese [26]. As reported by UNICEF, Egypt presently has one of the highest rates of childhood obesity in the world, with approximately two million overweight children [27]. Worryingly, the implications of obesity developing in the early life might exceed those of obesity developing at adulthood [28]. Further, several comorbidities, including metabolic and cardiovascular conditions, as well as neurological, hepatic, and renal abnormalities have been linked to childhood obesity [29].

Indeed, chronic metabolic conditions including resistance to insulin and type 2 diabetes are frequently associated with visceral obesity [30,31]. In this respect, the VAI, which is derived from lipid and anthropometric data, has been demonstrated to be related to visceral adipose tissue and a good predictor of insulin resistance [4,8]. In the present study, obese children had significantly higher VAI compared to control ones. This finding is consistent with previous research by Ismail *et al* [32], Yin *et al* [33], and Al-Daghri *et al* [34] who found that obese children had significantly higher VAI than control children. Furthermore, obese girls exhibited significantly higher VAI than obese boys, and VAI had a fair AUC in ROC analysis for discriminating between obese boys and girls in the present study, which is in line with the findings of Radetti *et al* [35] who found that VAI levels were significantly higher in girls with severe obesity. Similarly, it has recently been demonstrated that obese children having nonalcoholic fatty liver disease showed significantly higher VAI values [36].

Furthermore, VAI showed significant positive correlation with TyG index, a predictor of insulin resistance, among the obese children of the current study. Similarly, Vizzuso *et al* [37] observed a significant correlation between VAI and TyG index in obese children and adolescents. The role of visceral fat has lately been a focus of intense research. Excess visceral fat has been shown to cause increased adipocytokine production, aggravation of inflammatory activity, and deterioration of insulin sensitivity [38,39]. Furthermore, insulin resistance possesses an inflammatory basis, and once insulin resistance develops in visceral adipose tissue, this pathological state has the potential to spread throughout the body [40]. Concerning the reasons of insulin resistance in visceral adipose tissue, earlier research has shown that fat and sugar rich foods cause adipocyte swelling and inflammation, which enhance the macrophages infiltration [41,42]. Accordingly, localized inflammation starts, which

promotes obesity along with insulin resistance [43]. The current study's positive correlation between VAI and TyG index suggested that any increase in visceral adiposity may be accompanied by increased insulin resistance in studied obese children, as represented by increased TyG index which is a prognostic tool for insulin resistance. Such findings indicate the negative health impacts of excess visceral fat including metabolic problems and insulin resistance, which raise the likelihood of developing type 2 diabetes in the studied obese children.

Table (3): Correlation between TyG index and the measured parameters in the obese group:

Parameters	TyG index	
	Correlation coefficient (r =)	P-value
Total cholesterol	0.27	0.02 *
Cardiac risk ratio I	0.3	0.02 *
Cardiac risk ratio II	0.25	0.03 *
HDL	-0.26	0.03 *

HDL: high-density lipoprotien cholesterol

* Significant correlation at P < 0.05

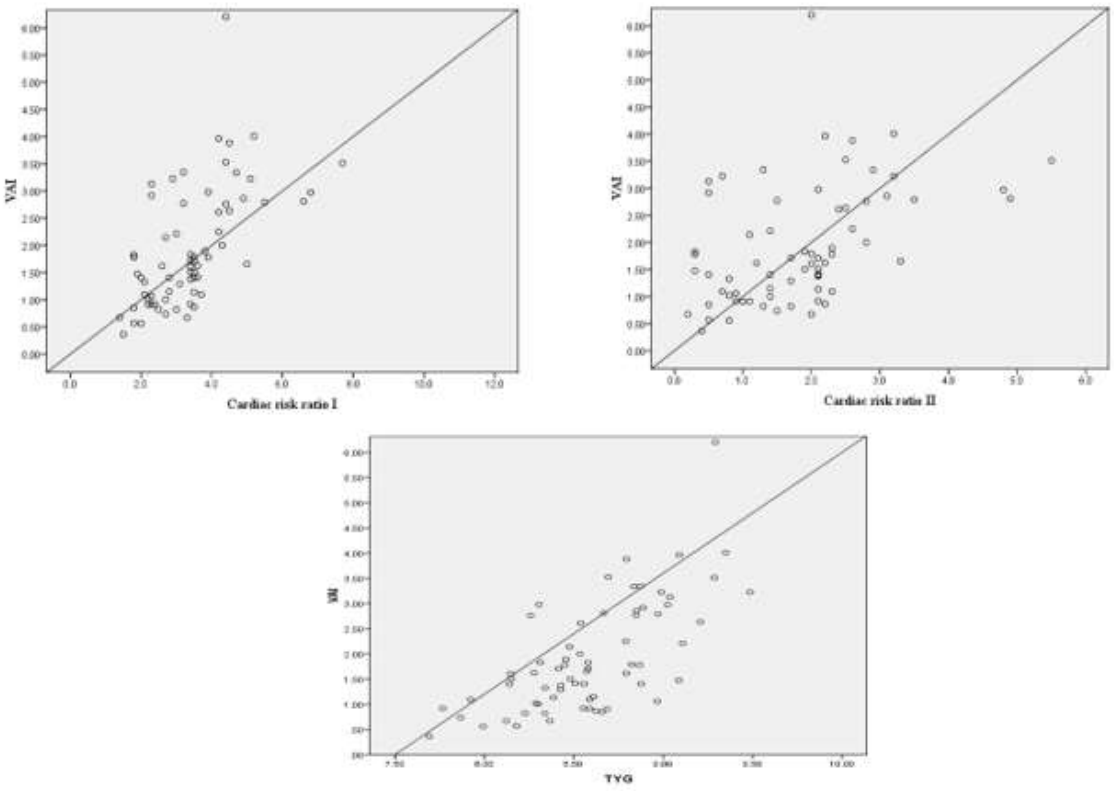

Figure 5. Correlation between visceral adiposity index (VAI), cardiac risk ratio I, cardiac risk ratio II and triglyceride glucose index (TyG) showing positive correlations.

Additionally, the current study revealed that VAI showed significant positive correlations with cardiac risk ratio I and cardiac risk ratio II in obese children. Such observation agreed with a previous study in which VAI correlated positively with total cholesterol, LDL, triglycerides and triglycerides/HDL ratio in obese children [37]. The VAI has been proposed as a cost-effective and easy tool for early identification of cardiovascular diseases [44]. A recent study found that VAI was associated with angina, coronary heart disease, and hypertension [45]. Large amounts of free fatty acids produced by excess visceral fat and chronic inflammation may increase lipogenesis, gluconeogenesis, and insulin resistance, resulting in higher blood lipid levels, glucose intolerance, hypertension, and eventually atherosclerosis [46,47]. Besides, reactive oxygen species and inflammatory cytokines linked to visceral adipose tissue cause lower nitric oxide levels that increase the arterial stiffness risk [48]. Even though atherosclerotic cardiovascular abnormalities are infrequent in children, atherogenic mechanisms that

cause cardiovascular disease could start during childhood and develop throughout life [49]. As a result, developing heart-healthy behaviors and controlling cardiovascular risk in early childhood can prevent or postpone the progression of atherosclerosis and lower the cardiovascular diseases risk during later life. Therefore, VAI may be recommended as a useful predictor of insulin resistance, future type 2 diabetes, and cardiovascular diseases risk in obese children.

In the present study, TyG index was significantly higher in obese children than control group demonstrating that these obese children have higher insulin resistance and are more prone to future type 2 diabetes, which is consistent with previous studies that found significantly higher TyG index in obese children [50] and adolescents [51]. In addition, the TyG index is currently gaining attention as a promising predictor of cardiometabolic risk in young children and adolescents [52]. In that context, the current study found that TyG index had significant positive correlations with total cholesterol, cardiac risk ratios I and II, along with significant negative correlation with HDL. Similar results were reported by de Brito et al [15] who found that obese children with elevated TyG index exhibited higher total cholesterol, LDL, cardiac risk ratio I and II, along with lower HDL. Besides, it has been revealed that higher TyG is linked to increased blood pressure in children [53]. Meanwhile, central obesity, high blood pressure, and elevated blood lipid levels have been associated with elevated TyG index in Brazilian children [15]. One possible underlying cause for TyG index's association with the risk factors of cardiovascular disease is that insulin resistance is a main contributor to cardiovascular diseases, as well, TyG index functions as a useful marker for insulin resistance, which could be an indirect explanation for this relationship [52].

5. CONCLUSIONS

Our findings showed that VA and TyG indices can be proposed as useful indicators for insulin resistance and cardiometabolic risk in obese children. Furthermore, obese children have deteriorating physical and biochemical characteristics that predispose them to insulin resistance, type 2 diabetes, and cardiovascular disease in the future. Therefore, identifying high-risk obese children in a timely manner is crucial for preventing the onset and progression of these issues later in life.

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Conflicts of Interest: The authors declare that they have no conflicts of interest.

Ethical Statement: The study was approved by the research ethics committee of the National Organization for Teaching Hospitals and Institutes (approval number IN000110). Written informed consent was obtained from the parents of each participant.

Author Contribution: Shimaa M. Abdou: methodology, data collection, statistical analysis, and writing the manuscript; **Awatif M. Abd El-Maksoud:** supervision, visualization, validation, and editing the manuscript; **Gihan F. Ahmed:** supervision, clinical examination of participants and gaining ethical approval; **Heba G. Abd El-Aziz:** supervision, visualization, validation, editing and revising the manuscript. All authors have read and approved the final manuscript.

List of Abbreviations: BMI: body mass index; HDL: high-density lipoproteins; LDL: low-density lipoprotein; TyG index: triglyceride glucose index; VAI: visceral adiposity index.

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