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Ghada A. Omar
National Institute of Diabetes and Endocrinology, ghadaomar32@yahoo.com

Mona A.E A. Hussein
National Institute of Diabetes and Endocrinology

Wafaa S. Hegab
National Institute of Diabetes and Endocrinology

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Original Article

Assessment of the eligibility of triglyceride–glucose index and triglyceride–high-density lipoprotein cholesterol ratio as applicable insulin resistance indices among overweight/obese Egyptians

Wafaa S. Hegab[a], Ghada A. Omar[b], Mona A.E.A. Hussein[a]

Departments of [a]Internal Medicine and [b]Clinical and Chemical Pathology, National Institute of Diabetes and Endocrinology, Cairo, Egypt

Abstract

Background

Insulin resistance (IR) means the requirement of a higher insulin concentration to produce the expected biological effect. It was proposed that triglycerides–glucose index (TY G) and triglycerides–high-density lipoprotein cholesterol ratio (TG/HDL) were dependable, applicable, and less-expensive markers of IR. However, their results varied significantly among different ethnic groups.

Aim

To assess the eligibility of TY G and TG/HDL as IR indices among overweight and/or obese Egyptians.

Patients and methods

The participants in this cross-sectional study were 328 overweight and/or obese Egyptians. Their fasting blood glucose, TG, HDL, and fasting insulin blood concentrations were estimated. Homeostasis model assessment-insulin resistance (HOMA-IR), TY G, and TG/HDL were calculated.

Results

A statistically significant positive correlation between HOMA-IR and both TY G ($r = 0.688$; $P < 0.001$) and TG/HDL ($r = 0.590$; $P < 0.001$) was identified. Four quartiles had been set up for HOMA-IR across which both indices showed trends of consistent increase. Analysis of the receiver-operating characteristic curves revealed that TY G [area under the curve = 0.858 (95% confidence interval 0.819–0.897) ($P < 0.001$)] is a better marker for IR than TG/HDL [area under the curve = 0.796 (95% confidence interval 0.750–0.843) ($P < 0.001$)] and demonstrated more than or equal to 8.22 and more than or equal to 1.82 as their respective cutoff values.

Conclusion

TY G and TG/HDL demonstrated significant association with HOMA-IR and might be applied as eligible indices of IR among overweight and/or obese Egyptians.

Keywords: Homeostasis model assessment, insulin resistance, triglycerides–glucose index, triglycerides–high-density lipoprotein cholesterol ratio

Introduction

Normally glucose homeostasis is maintained by insulin hormone, which is secreted by pancreatic β-cells in response to the elevation of blood glucose. It binds to muscle, liver, and adipose tissue cell receptors, allowing glucose uptake by these cells [1]. This insulin-receptor binding triggers the

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Correspondence to: Ghada A. Omar, MD, Department of Clinical and Chemical Pathology, National Institute of Diabetes and Endocrinology, 49 Manial Street, Cairo, Egypt.
Tel: +20 122 461 0448;
E-mail: ghadaomar32@yahoo.com

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process of receptor autophosphorylation. This process includes phosphorylation of tyrosine residues of the insulin receptor substrates and phosphatidylinositol 3-kinase with subsequent activation of protein kinase B through a downstream signaling cascade [2]. Any dysfunction in this aforementioned axis results in insulin resistance (IR) with failure of the glucose uptake by the cells and inability to generate energy [3]. The imbalance between insulin demand and insulin production is represented by a vicious circle of IR and hyperinsulinemia, which causes weight gain which, in turn, results in aggravation of IR [4]. That is to say, IR and obesity are markedly interrelated global pandemics [5] with a mutual cause-effect association [6]. Furthermore, the developments of type 2 diabetes mellitus (T2DM) [7], cardiovascular diseases[8] and metabolic syndrome [9] are enhanced by IR.

The reference method for IR assessment, the hyperinsulinemic euglycemic glucose clamp technique, cannot be used as a routine tool because of being a very tedious and expensive method. Therefore, more convenient measures were introduced including homeostasis model assessment-insulin resistance (HOMA-IR) [10] and the quantitative insulin-sensitivity check index [11]. These common methods of IR assessment require the estimation of fasting insulin (FI), which demands laboratory facilities that are neither easily available nor affordable, especially in developing countries [12]. The aforementioned obstacles, together with the lack of standardization of insulin assay issues [13], led to the evolution of a trend adopting much easier, more applicable, and economical assessments of IR[14] depending on the routine measurements of fasting blood glucose (FBG), triglycerides (TG), and high-density lipoprotein cholesterol (HDL). These parameters gained attention owing to the assumption that high TG and low HDL are significant contributors to the development of IR, and mutually IR increases TG as a result of increasing fatty acid synthesis [15]. Accordingly, TY G [16,17] and TG/HDL [18,19] were proposed as substituting IR indices. However, these indices had controversial roles in accordance with ethnicity among various populations [20,21]. Thus, the current piece of work aimed to assess the eligibility of TY G and TG/HDL as IR indices among overweight and/or obese Egyptians.

Procedures

A total of 328 overweight and/or obese Egyptians participated in this cross-sectional study. They were recruited from the National Institute of Diabetes and Endocrinology during the period from November 2021 to February 2022. This work was officially approved by an Ethics Committee (adapting the Declaration of Helsinki principles), and a knowledgeable written consent was signed by all participants before enrollment. All of the enrolled participants (156 males and 172 females) met the inclusion criteria, which included being Egyptian patients, aged more than or equal to 40 years old, who were overweight or obese with BMI 25.0–29.9 kg/m^2 or more than or equal to 30 kg/m^2, respectively. BMI was calculated using the adult BMI calculator (kg/m^2) [22]. Exclusion criteria included the consumption of exogenous insulin therapy [23].

Blood samples were withdrawn from all of the participants into serum separator vacutainers after an overnight fasting of 12 h with no caloric intake. After clotting and centrifugation, the serum was used for the estimation of FBG, TG, HDL, and FI using Cobas 8000 modular analyzer series (Roche Diagnostics 9115 Hague Rd, Indianapolis, Indiana, USA). In the current paper, the following published formulas were used to calculate the recruited IR indices: HOMAIR as [FI (μIU/ml)×FBG (mg/dl)/405] [10], TY G as Napierian logarithmic (ln) [fasting TG (mg/dl)×FBG (mg/dl)/2] [24], and the ratio of TG (mg/dl) and HDL (mg/dl) [25].

Statistics

SPSS version 13 for Windows (SPSS Inc., Chicago, Illinois, USA) and Microsoft Excel 2010 were utilized to analyze the acquired data statistically. Mean ± SEM and frequencies (%) were used for quantitative and categorical data, respectively. Correlations were assessed using Pearson's correlation coefficient test (r). After setting up quartiles for HOMA-IR, two-at-a-time comparisons of the mean values of the relevant parameters were made using the analysis of variance post-hoc test (Games-Howell test), and the presence of a trend of the relevant indices was assessed using the linear term of the between quartiles analysis of variance contrast study. After taking into account sex and age, binary logistic regression analysis revealed that each of TY G and TG/HDL indices was associated with HOMA-IR, and the corresponding odds ratios (expB) values were given. The most appropriate cutoff points of these indices were determined via the receiver-operating characteristic (ROC) curve. P values less than 0.05 were regarded as significant.

Results

The characteristics of the collective study group are shown in Table 1, with 156 (47.6%) males and 172 (52.4%) females. Overweight patients comprised 183 (55.79%), whereas obese ones constituted 145 (44.21%).

Table 2 and Fig. 1 summarize the highly significant positive correlations of TY G (r = 0.688; P < 0.001) and TG/HDL (r = 0.590; P < 0.001) with HOMA-IR.

Table 3 and Fig. 2 represent the setup of four quartiles (each recruiting 82 participants) for HOMA-IR parameter (as here we applied no cutoff in assessing IR). They show the presence of highly significant, consistently increasing linear trends regarding BMI, TY G, and TG/HDL means (P < 0.001).

Fig. 3 and Table 4 display the outcome of the ROC curve analysis for TY G and TG/HDL versus HOMA-IR (with a cutoff ≥2.6). The TY G showed a significant area under the curve (AUC)=0.858 (95% confidence interval 0.819–0.897) (P < 0.001). The TG/HDL also showed a significant but a lower AUC = 0.796 (95% confidence interval 0.750–0.843) (P < 0.001). This suggests that TY G is a better marker

for IR than TG/HDL. The ROC curves exhibited more than or equal to 8.22 and more than or equal to 1.82 as IR cutoff values concerning TY G and TG/HDL, respectively (based on sensitivity and specificity).

Table 5 shows cross-tabulation between HOMA-IR (cutoff ≥2.6) and TY G and TG/HDL (with cutoffs derived from ROC analysis ≥8.22 and ≥1.82) respectively). Binary logistic regression indicates a highly significant association between HOMA-IR and each of TY G (odds ratio = 4.635; $P < 0.001$), with an accuracy index of 79.5%, and TG/HDL (odds ratio = 1.995; $P < 0.001$), with an accuracy index of 68.6%. This suggests that IR in the participants with TY G at more than or equal to 8.22 is about 4.6 times more than those with TY G at less than 8.22, whereas it is about 2.0 times more in the participants with TG/HDL more than or equal to 1.82 than those with TG/HDL at less than 1.82.

Table 1: Characteristics of the collective study group (*n*=328)

Parameters	Mean±SEM
Age (years)	52.3±0.5
BMI (kg/m^2)	29.74±0.17
FBG (mg/dl)	127.5±2.97
FI (mIU/l)	13.1±0.42
TG (mg/dl)	113.9±5.65
HDL (mg/dl)	42.8±0.63
HOMA-IR	4.7±0.20
TY G	8.4±0.06
TG/HDL	2.6±0.12

FBG, fasting blood glucose; FI, fasting insulin; HDL, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment of insulin resistance; TG/HDL, triglycerides to high-density lipoprotein cholesterol ratio; TG, triglycerides; TY G, triglycerides glucose index.

Table 2: Triglycerides glucose index and triglycerides to high-density lipoprotein cholesterol ratio correlations with homeostasis model assessment of insulin resistance

	HOMA-IR	
Parameters	*r*	*P*
TY G	0.688	<0.001*
TG/HDL	0.590	<0.001*

HOMA-IR, homeostasis model assessment of insulin resistance; *r*, correlation coefficient; TG/HDL, triglycerides to high-density lipoprotein cholesterol ratio; TY G, triglycerides glucose index. *Significant (*P*<0.0 5).

Discussion

Although the usefulness of the TY G and the TG/HDL was confirmed as applicable IR measures [26], it had been suggested that they might be ethnicity dependent [27,28]. Moreover, it was proven that obesity and IR had been related in a mutual-causal relationship [29,30]. Consequently, the current work aimed to assess the eligibility of TY G and TG/HDL as markers of IR among overweight and/or obese Egyptians.

According to the findings of this cross-sectional study, each of TY G and TG/HDL demonstrated a positive correlation with HOMA-IR in overweight and/or obese Egyptians. These outcomes clarified the validity of employing TY G and TG/HDL to indicate IR. The aforementioned findings are in agreement with other studies, which demonstrated that these indices were considered as reliable representative markers for IR in both healthy and T2DM cases [31–34]. However, they were opposed by other studies among African-Americans [35], African-American women [36], and South Asians [27], indicating their unreliability as good indicators for IR measurement.

In addition, this current study indicated that the means of the TY G and TG/HDL increased progressively across HOMA-IR setup quartiles, suggesting the presence of highly significant, consistently increasing linear trends. This was reinforced by previously performed studies [24,37]. Furthermore, the outcome of the ROC curve analysis displayed that TY G and TG/HDL were good indicators of IR. The AUC values of both parameters were greater than 0.75, which is considered as an acceptable representative of the test performance [38]. However, the TY G was a better marker for indicating IR than TG/HDL owing to the fact that it had a higher value of AUC. Such findings were in consistence with some studies, which stated that although TG/HDL was a reliable indicator of IR, the TY G had been a more effective representative marker for IR regardless of the studied population [34,39,40].

Finally, our findings showed that the values of TY G of 8.22 and of TG/HDL of 1.82 were proposed as cutoff values for

Table 3: Comparison between means of different parameters across homeostasis model assessment of insulin resistance four quartiles

Parameters	Mean±SEM				ANOVA	
	Q1 (*n*=82)	Q2 (*n*=82)	Q3 (*n*=82)	Q4 (*n*=82)	Between quartiles	
					Combined	Linear term (contrast)
HOMA-IR	0.99±0.016	1.97±0.113	5.76±0.098	9.92±0.147	<0.001*	<0.001*
BMI (kg/m^2)	28.2±0.25	28.8±0.29	30.5±3.05	31.5±2.82	<0.001*	<0.001*
TY G	7.4±0.06	8.1±0.1	8.7±0.11	9.6±0.09	<0.001*	<0.001*
TG/HDL	1.2±0.09	2.0±0.16	2.9±0.21	4.5±0.25	<0.001*	<0.001*

ANOVA, analysis of variance; HOMA-IR, homeostasis model assessment insulin resistance; TG/HDL, triglycerides to high-density lipoprotein cholesterol ratio; TY G, triglycerides glucose. *Significant (*P*<0.05).

Table 4: Area under curve of triglycerides glucose and triglycerides to high-density lipoprotein cholesterol ratio versus homeostasis model assessment insulin resistance (cutoff ≥2.6)

IR indices	AUC (95% CI)	*P*	Sensitivity	Specificity	Cut-off
TY G	0.858 (0.819-0.897)	<0.001*	0.75	0.85	8.22
TG/HDL	0.796 (0.750-0.843)	<0.001*	0.68	0.70	1.82

AUC, area under the curve; CI, confidence interval; IR insulin resistance; TG/HDL, triglycerides to high-density lipoprotein cholesterol ratio; TY G, triglycerides glucose index. *Significant (*P*<0.0 5).

Table 5: Binary logistic regression of triglycerides glucose index and triglycerides to high-density lipoprotein cholesterol ratio with the homeostasis model assessment insulin resistance (cutoff ≥2.6)

Cut-off	HOMA-IR			Odds ratio (95% CI)	*P*	Accuracy index
	IR	Non-IR	Total			
TY G						
≥8.22	136	22	158	4.635 (3.346-6.421)	<0.001*	79.5%
<8.22	45	125	170			
Total	181	147	328			
TG/HDL						
≥1.82	122	44	166			
<1.82	59	103	162	1.995 (1.68-2.37)	<0.001*	68.6%
Total	181	147	328			

CI, confidence interval; HOMA-IR, homeostasis model assessment; IR, insulin resistant group; non-IR, noninsulin resistant group; OR odds ratio (ExpB adjusted for age and sex); TG/HDL, triglycerides to high-density lipoprotein cholesterol ratio; TY G, triglycerides glucose index. *Significant (*P*<0.05).

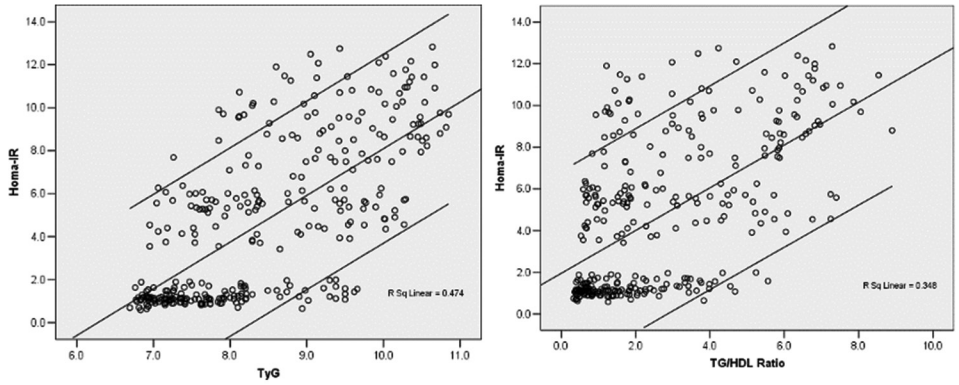

Figure 1: TY G and TG/HDL positive correlations with HOMA-IR. HDL, high-density lipoprotein; HOMA-IR, homeostasis model assessmentinsulin resistance; TG, triglycerides; TY G, triglycerides–glucose index.

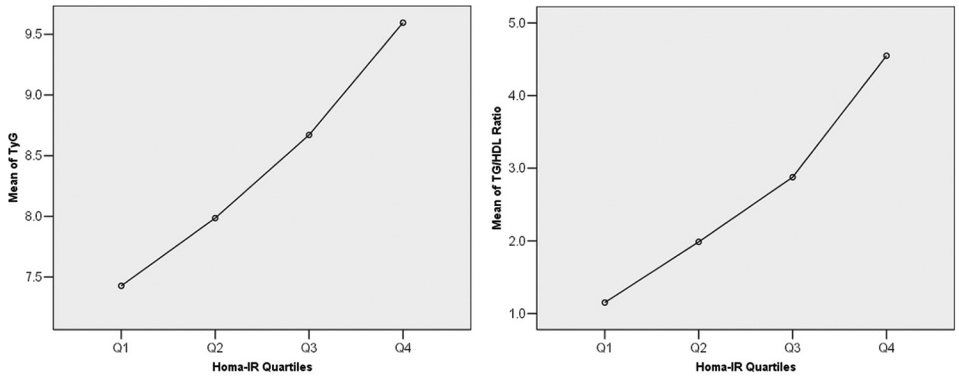

Figure 2: Consistently increasing means of TY G and TG/HDL across HOMA-IR four quartiles. HDL, high-density lipoprotein; HOMA-IR, homeostasis model assessment-insulin resistance; TG, triglycerides; TY G, triglycerides–glucose index.

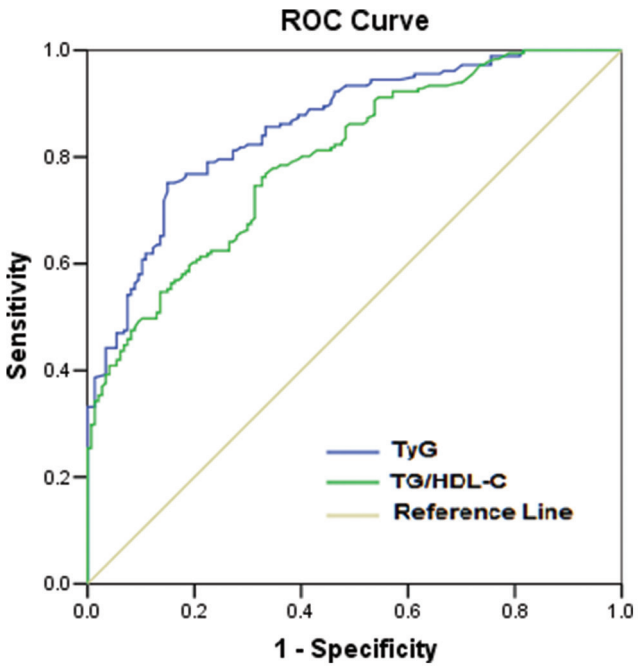

Figure 3: ROC curves related to TY G and TG/HDL. HDL, high-density lipoprotein; TG, triglycerides; TY G, triglycerides–glucose index.ROC, receiver-operating characteristic.

identifying the existence of IR among overweight and/or obese Egyptians. It is worthy to note that the cutoff values for TY G and TG/HDL varied significantly in different studies, as the one in a Venezuelan population[41] and in the systemic review of four different studies that were conducted among various ethnic groups [42], indicating that cutoff values varied by ethnicity.

Conclusions

TY G and TG/HDL demonstrated significant association with HOMA-IR. They are eligible as IR indices among overweight and/or obese Egyptians. Both can be used as acceptable, applicable, and affordable measures of IR, provided that the TY G is a more efficient marker than TG/HDL. Nevertheless, despite their effectiveness, they still require further evaluation in future studies recruiting larger numbers of participants and verifying their correlation with the gold standard method of IR detection (hyperinsulinemic euglycemic glucose clamp), as the HOMA-IR, which was used for the verification of their association with IR, adopts an indirect technique. It is also recommended to perform other studies to establish further validated and defined cutoff values in different categories of the population, such as prediabetic, metabolic syndrome, and T2DM patients, as these will be markedly required for usage in clinical practice.

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Conflicts of interest

There are no conflicts of interest.

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