Triglyceride Parameters (Tgi and Tg/Hdl) Predict Insulin Resistance as Good as Homa-Ir in Obese Adults with Insulin Resistance.

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Abstract
The homeostasis model assessment intended for insulin resistance (HOMA-IR) is broadly used as anindicatorfor insulin resistance (IR) particularly in research. This indicator, however, is difficult to be validfor populations with low incomes in addition to its limited availability. Triglyceride related parameters like triglyceride-glucose index (TGI) and triglyceride high density lipoprotein (TG/HDL) which can be estimated on the other hand from a usual test (lipid profile and glucose) that is less expensive than serum insulin. In predicting the occurrence of IR which is highly desirable for public health due to the association of both obesity and IR with different health issues and complications; so simple tests for the diagnosis of IR are required. Objectives:The aim of this study is to compare (TGI) and (TG/HD) indices with HOMA-IR as a marker of Insulin Resistance (IR) in obese adults. Design and methods:The study was conducted on one hundred obese and non-obese, all non-diabetic, apparently healthy females and males aged 18 to 50 years old from the general population.BMI, waist circumference, blood pressure (BP) were measured and blood samplesfor glucose,HbA1c, triglycerides, HDL cholesterol, and serum insulin were also taken. This data was used in obtaining TG/HDL and TGIformulae;also,HOMA-IR was calculated by: HOMA-IR = {insulin mIU/L} × {glucose mg/dl} / 405. Results: About 50 % of the participants were obese had HOMA–IR level of >2 whereas the other 50% non-obese with HOMA-IR ≤ 2.Pearson's correlation coefficient ofTGI in two groups was (r = 0.34, P- value0.0177) and TG-HDL was (r =0.57, P-value0.0001). The mean of TGIwas(4.93±0.02) in adults with abnormal HOMA-IR and (4.44±0.01) in adults with normal HOMA-IR. Also, TG-HDL mean was (4.72±0.15, 1.80±0.04) in two groups respectively. Area under curve (AUC) for HOMA-IR, TG/HDL and TGI was in order (0.940, 0.803 and 0.721). Conclusions and Recommendations:Both TG/HDLandTGI could be used for IR prediction in obese adults with high significance (p value = 0.0001, p value = 0.0177) and cutoffs (≥ 2.7 and ≥ 4.9) for both parameters respectively. We recommend the use of TG/HDL and TGI in assessing different relations such as obesity with prediabetes, diabetes and cardiometabolic risk among adults. Additionally, it is preferable to increase sample size for better cutoff estimation.
Keywords: insulin resistance, obesity parameter, triglyceride index, triglyceride high density lipoprotein, HOMA-IR.

1. Introduction

Insulin resistance (IR) is a metabolic disturbance in which tissues that depend on insulin be converted intoinsensitive to its hormonal action, resulting in aninequality in carbohydrate, protein, and lipid metabolism. [1]
IR is a situation in which higher insulin levels are needed to maintain normal blood sugar and biological responses. The failure to respond to insulin leads to hyperglycemia and dyslipidemia which mostly manifests as excessive triglycerides (TG) with low levels of good cholesterol [high density lipoprotein–HDL].[2,3]This manifestation had been demonstrated that the TG/HDL ratio be capable of IR prediction.[4-6]
At the same time, it's worth mentioning that the hyper-insulinemic euglycemic clamp technique is the gold standard for IR assessment.[7,8]High test's price and complexity, however, have prohibited its implementation in epidemiological research and routine clinical practice.[9] Instead, HOMA-IR has been authorizedto be employed in children, adolescents &adults, which is used as an IR marker.[10]Even though that HOMA-IR is recommended as an IR suitable marker, lab measurements of insulin level are required, which is expensive for routine practices or not available in health-care services.[11] Therefore, simple markers linked to IR may aid in identifying those who are most susceptible to developing pre-

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diabetes and T2DM.Additionally, IR-free elderly individuals had significantly lower chance of diabetes than those who did; according to Welsh et al.[4]Furthermore, it is anticipated that IR will exacerbate a number of diseases and raise the overall death rate.[12-14]As a result, preventing IR is highly desirable for public health &patient survival and simple tests for the identification of IR are required.[15]

Triglyceride and HDL cholesterol, on the other hand, is a routine affordabletest, as compared to serum insulin and could be found in different general hospitals and outpatient clinics. These two valueshad beenformulated as aratio of TG/HDL.[16]

As the latter, A new formula for Triglyceride-Glucose Index [TGI] has been validated &suggested by Simental-Mendia et al. to assess IR from fasting glucose (FG) & triglycerides (TG). This formula is a possible diagnostic tool when other techniques are not of use. [17,18]

Based on the data above, the study objectivesare to assess the effectiveness of TG/HDL and TGI as predictors of IR and to define the cutoff value in the general obese population with IR.

2. Subjectsand Methods

This study was conducted as case-controlwith one hundred apparently healthy obese and non-obese individuals with an average age of (18-50) years; attend Al-Yarmouk teaching hospital in Baghdad in a period from October 2022 to January 2023.

Anthropometric measurements and routine blood tests were donefor all participants. The information was gathered through medical history as well as accurate blood pressure measurements with stethoscopes and mercury sphygmomanometers. A digital balance was used to determine weight, and a vertical tape measure calibrated in centimeters was used to determine waist circumference (WC) and height. Body Mass Index had been calculated by the following formula: [Weight (kg) / Height (m)2].

For obesity classification, two parameters must be available: BMI of ≥ 30 kg/m2, and WC ≥ 94 cm in males or ≥ 80 cm in females according to the International Diabetes Federation (IDF) and The American Association of Clinical Endocrinologists (AACE)[19-22].

After an overnight fast of 8 hours or more, blood samples collection was carried outat 8:00 - 10:00 in the morning, FG, HbA1c,TGs, and HDL cholesterol levels were measured. The Siemens'serum insulin IMMULITE 1000 Immunoassay System was usedin calculationof HOMA-IRby multiplying fasting insulin (mIU/l) and FG (mg/dl) divided by 405.The score of HOMA-IR > 2 was categorized as IR, while a score of 2or less was considered as insulin sensitive.

The TGI calculation was done using the following equation:

TGI= ln {Fasting triglyceride(mg/dl) x Fasting glucose (mg/dl)} / 2. [7, 18]

TG/HDL was calculated dividing TG by HDL-C. [16]

3. Results

A total of 100 subjects, comprising 50 non-obese and 50 obese subjects with insulin resistance, all appeared to be healthy (52% female and 47% male; average age, 18 to 50 years).The averages of (BMI) and (WC) for non-obese was[22.84 ±0.22kg/m2 , 83.76 ±0.85 cm] and for obese [32.02 ±0.69 kg/m2, 106.62 ±1.68 cm] respectively; with p- value 0.0001 for both of them. The biochemical characteristics for the first group (FBG= 82.40±1.48 mg/dl, HbA1c=4.41 ±0.06, TG=96.36 ±2.02mg/dl, HDL=50.11 ±1.03mg/dl) and for the second one (FBG=111.84 ±1.57 mg/dl, HbA1c=5.67 ±0.09, TG=175.26 ±3.66mg/dl, HDL=38.41 ±0.84mg/dl). The average of HOMA-IR, TG/HDL and TGI is presented in table (1).

Table (1) sample average of HOMA-IR, TG/HDL and TGI in an obese and non-obese group.

Average ± SE			
Parameter	HOMA-IR	TGI	TG/HDL
Non-obese	1.230 ±0.03	4.48 ±0.01	1.80 ±0.04
Obese	2.38 ±0.04	4.93 ±0.02	4.72 ±0.15
T-test	0.091	0.0383	0.315
P-value	0.0001**	0.0001**	0.0001**

Values expressed by the average and standard errors.
T-Test was used to compare between means in two groups.
** (P≤0.01) considered highly significance.

The relationship between HOMA-IR, TG/HDL and TGI was calculated and showed a positive correlation as assessed by coefficient-r to be (r= 0.57 **, P-value=0.0001) for TG/HDL and (r= 0.34 *, P-value=0.0177) for TGI.

Receiver operating characteristic (ROC) and the area under the curve (AUC) is used to prove the ability of the test to obtain aproper cutoff valueand to compare the diagnostic tests'accuracy where an AUC of 1 is considered as anideal diagnostic test.[23]In general, thecloser AUC to 1 is a better overall diagnostic performance of the test; Fig. (1).By Using youden Index(*J*), the cutoff value on the ROC curve which corresponds to *J*, that is, at which (sensitivity + specificity − 1) is maximized, is taken to be the optimal cut-off point.Table (2).[24,25]

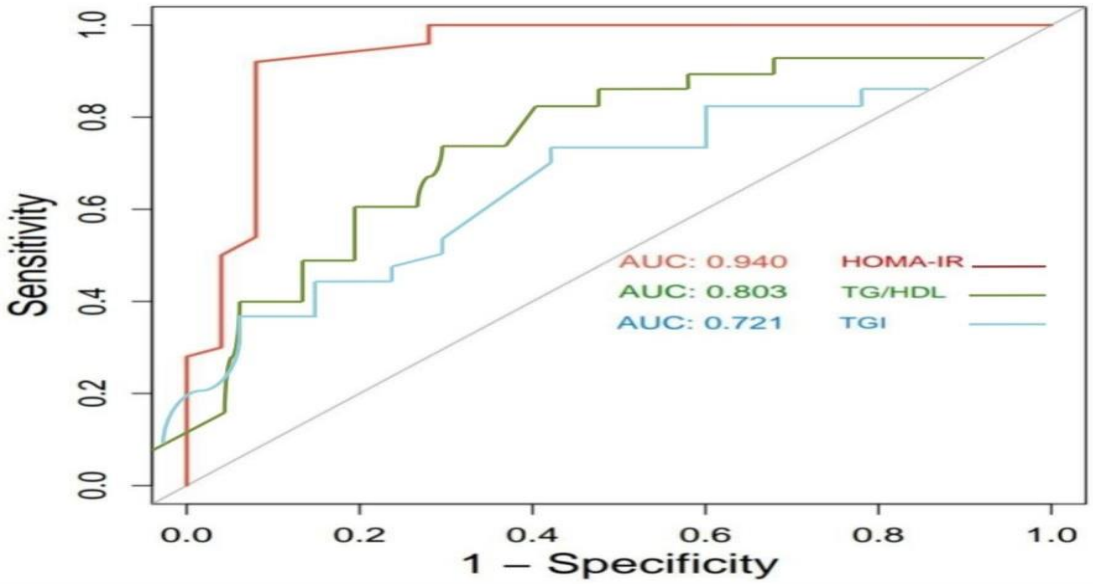

Fig. (1) ROCcurves for HOMA, TG/HDL and TGI in the target population; AUC= area under the curve; X =1-specificity& Y=sensitivity.

According to table (2);comparing with (*J*), the best TG/HDL value for the diagnosis of insulin resistance was 2.7, while The TGI with a value of 4.9.

Table (2) the cutoffs of target parameters on ROC. curve obtained by youden index (J).

Parameter	AUC	Cutoffs	Youden Index (J)
HOMA-IR	0.940	2	0.97
TG/HDL	0.803	2.7	0.92
TGI	0.721	4.9	0.89

By eye balling target sample, The TG/HDL failed to detect 8% of the subjects with insulin resistance as defined by HOMA-IR; on the other hand, itfound no IR in the participants who were classified as normal by HOMA-IR.

While The TGI detected insulin resistance in 37% of the subjects; and detected no IR in all the participants who were classified as normal by HOMA-IR.

4. Discussion

The assessment of IR is a goal that persists to gain importance in epidemiologicalandclinical research, owing to the possible role of this condition in the Pathophysiology of Metabolic Syndrome, as well as its risk in developing Diabetes type two and cardiovascular diseases.[26]

While Routine measurements of serum insulin are difficult to obtain in developing countries with limited health-care systems; The TGI had just recently been introduced as a useful substitute in clinical settings, and it had received widespread acceptance because of its high predictive potential in comparison with otherIR indices.[27]

Many studies demonstrated that TGI is a good predictor of IR compared to other parameters; [28-30]also tried to highlight the relationship with HOMA-IR by using ROC curve; with AUC for TGI around (0.709) and (0.80).

The results of this studyshow TGI closely resembles the HOMA-IR technique in the evaluation of IR (r=0.34**,p value=0.0177), indicating that it can be helpful to identify IR among people with obesity. TheTGI cutoff value of 4.9 with AUC (0.72); is almost corresponds to the studies of Simental-Mendía et al. and Guerrero-Romero et al. [18, 29];whichhad been suggest that TGI could be useful for identifying subjects with reduced insulin sensitivity but with a cutoff around 4.65 and 4.55respectively. This difference could be account for involving younger adults, larger sample size or different score of HOMA-IRin those studies.

Regarding TG/HDL ratio a nonlinear relationship with IR had been discovered; Indeed, Rongpeng Gong and his colleagues; in cross-sectional study in US population;discovered that (A non-linear interaction between TG/HDL ratio and IR was found, with a point of 1.06).[31] In addition to other studies mentioned that the ratio ofTG/HDL could be a clinically useful tool for assessing IR withTG/HDL around (2.2 and 1.36) seen in IR children with and without obesity. [29, 32]

Notably The results of this study in table (2) indicate that the TG/HDL ratio is positively correlated with HOMA-IR; had a cutoff value ≥ 2.7 in obese adults.

The summary of the clinical significance of this study as follows: the study sample is 50% obese and 50% normal weight levels and ROC curve was done to aid in the prediction of diagnostic value for both TG/HDL ratio and TGI in targetsample and significancewas conducted for both parameters in relation to HOMA-IR.

To the best of our knowledge, this report revealsan independent association of the TG/HDL, TGI and obesitywith IR; additionally, the results of this study

will help future research to establish predictive cutoffs for triglycerides markers.

5. Conclusions

Both TG/HDL andTGI could be used for IR prediction in obese adults with high significance (p value = 0.0001, p value = 0.0177) and cutoffs (TG/HDL ≥ 2.7 and TGI ≥ 4.9) indicate an insulin resistance.

6. Recommendations

We recommend the use of TG/HDL andTGIto find relations between obesity and prediabetes, diabetes and cardiometabolic risk among adults. Additionally, it is preferable to increase sample size in same target population for better cutoff estimation.

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