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Research Article

Estimation of Insulin Resistance in Obese Adults in Baghdad

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Abstract:

Background: Insulin works to control blood sugar levels by sending signals to the liver, muscle and fat cells to bring in sugar out of the blood. Obesity, hyperinsulinemia, hyperglycemia, and hyperlipidemia are only a few of the interconnected metabolic disorders that are frequently linked to these diseases.
Objective: To study the effects and help Triglyceride - Glucose index and Homeometric Assessment Model – IR (TyG & HOMA-IR) of knowing insulin resistance and early detection of prediabetes.
Method: The study was conducted on 160 volunteers, recruited from an age group based on the study data and the preliminary analysis, with ages ranging from (40-70 years). They were grouped into two groups: The first includes 80 individuals, with a body mass index of more than 25Kg/m^2, who suffer from insulin resistance, and the second group includes 80 healthy individuals who do not suffer from insulin resistance and whose body mass index is less than 25Kg/m^2. Measurement of serum glycine using ELISA kits.
Results: After conducting the statistical procedures for the results of the subjects for each of TyG, HOMA - IR, it was found that there was a significant change and p-value (0.00). Both markers of IR (TyG index and HOMA-IR) show that TyG index and HOMA-IR a had significant positive correlation with each of fasting serum glucose, insulin, and blood HbA1c%.
Conclusion: HOMA-IR has had an important role in the evaluation, detection, and prognosis of prediabetes. It also helps detect early complications associated with T2DM and helps determine the best treatment options. It also found that the TyG index beats the HOMA-IR for predicting prediabetes. It has the best potential for early detection and prevention of prediabetes.
Keywords: Collagen; HOMA-IR; Glycine, Insulin resistance; Insulin secretion; TyG index, Type 2 diabetes.

Introduction

Insulin helps control blood sugar levels by sending signals to liver, muscle, and fat cells to bring sugar out of the blood. Therefore, insulin prompts the cells to take up glucose to be used for energy. If the body has enough energy, the insulin signals the liver to absorb glucose and store it as glycogen (1). Insulin resistance (IR), which is characterized as a problem with insulin-mediated regulation of glucose metabolism in tissues, is one of the earliest signs of several conditions that affect people, including type 2 diabetes (T2DM) and cardiovascular disease. Obesity, hyperinsulinemia, hyperglycemia, and hyperlipidemia are only a few of the interconnected metabolic disorders that are frequently linked to these diseases. The causes of IR are hereditary and environmental factors (2).
Insulin resistance is a disruption of metabolism and is a major and well-established risk factor for heart disease (3). Lifestyle factors such as poor diet and improper daily activities are among the most important factors which lead to weight gain and thus lead to obesity (4).
Obesity is considered a pandemic of the current century by international organizations (5).

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One of the complications of IR and diabetes is the occurrence of osteoporosis and bone fractures (6).
Iraqis who appeared to be in good health had a 17% frequency of prediabetes. Prediabetes was more common in people over 40, especially in those who were overweight or obese. Patients with prediabetes had serum levels of proinflammatory and anti-inflammatory cytokines that were elevated (7).
IR plays a role in a variety of metabolic diseases, including T2DM and metabolic syndrome. Inadequate insulin signaling prevents glucose from entering fat cells and skeletal muscle cells. The precise underlying cause of IR is unknown, however various key pathways, such as oxidative stress, inflammation, insulin receptor mutations, endoplasmic reticulum stress, and mitochondrial dysfunction, have been proposed (8).
A statistical procedure called the Homeometric Assessment Model (HOMA) is used to determine IR and pancreatic cell activity. (HOMA - IR). Both are determined using insulin and fasting plasma glucose (FPG), but utilizing different formulas. Although investigations based on a modified version of HOMA using connective peptide concentrate (C-peptide) are shown, they are extremely scarce. The use of HOMA for assessing Cardiovascular Disease (CVD) and Diabetes Mellitus (DM) has been the subject of more than 500 research papers. However, DM is where it is

most frequently employed. In gauging prediabetes, identifying diabetes in the elderly, and detecting all forms of diabetes, HOMA-IR has proven to be more helpful (9).

In addition to glycosylated hemoglobin (HbA1c), HOMA indicators are widely based, but adequate standardization is critical for the successful clinical use of HOMA. The accuracy of glucose and insulin values affects how reliable these models can be used. Hypomagnesemia and visceral adipose tissue (VAT) hypomagnesemia are also related to HOMA-IR. That's where people who have T2DM have metabolic syndrome (MS). Patients with a HOMA-IR < 2.5 have a younger mean age, a lower body mass index, and a lower VAT (9).

IR may be easily substituted by the triglyceride-glucose (TyG) index. However, epidemiological data on its association with long-term mortality risk are scant. Increased TyG index had a nonlinear relationship with death from all causes and CVD and represented a more severe IR (10). TyG index = ln [fasting serum triglyceride (mg/dL) FPG (mg/dL) / 2], high values are considered from 8.8 (11). Ease of TyG calculation with minimal time or cost constraints - makes it ideal for a larger population. This could be a feasible approach for large-scale diabetes screening, particularly in developing countries (12). The metabolic pathways for glucose control are now well understood since several amino acids appear to play a significant role in influencing insulin production and likely insulin activity (13). Several factors, including metformin doses, may contribute to glycemic control and signs of obesity (14). Low plasma levels of glucogenic amino acids, especially glycine, have been observed in lean, non-diabetic, insulin-resistant children of diabetic parents who exhibited various degrees of insulin secretion irregularities (15). The development of novel surrogate indicators of IR that are more relevant for clinical screening and large population-based studies was urgently needed. As a result, a variety of surrogate indices have been used to make the determination of IR easier and more accurate. TyG index, Lipid accumulation product (LAP), and Visceral Adiposity Index (VAI), among others, are examples of novel surrogate markers of IR (16). IR has been found to be significantly higher in obese than non-obese diabetic patients and control (17).

The Aim of the Study

Studying Triglyceride - Glucose Index and Home Assessment Form - IR (TyG & HOMA-IR) to see how well it diagnoses insulin resistance and diabetes.

Patients and Method

One hundred and sixty Patients suspected to have DM were selected from the Specialized Center for Endocrinology and Diabetes in Al-Rusafa/Baghdad, the work was carried out during the period from October 2022 to January 2023. BMI of 25 kg/m^2 and/or waist circumference of 102 cm in males and 88 cm in women qualified for the cases for the IR test. Age 40 years or over, plus two or more of the following requirements Fasting glucose 110-125 mg/dl, triglycerides 150 mg/dl HDL cholesterol 40 mg/dl in males and 50 mg/dl in women (18).

The study's 80 individuals with IR (40 men and 40 women) and eighty healthy (40 men and 40 women) controls with an age range 40 to 69 years.

Based on the spectrum of ages of those who suffer from IR. The blood samples were centrifuged at 3000 rpm for 10 minutes to separate and extract the serum, which is used to measure the levels of fasting serum insulin by Cobas E 411 immunoassay analyzer, lipid profile, and serum fasting blood glucose by COBAS C 111 analyzer. The remaining serum was kept at (-20 C^o) to be used for automatic ELISA tests to measure glycine levels. The COBAS C 111 analyzer was used to estimate the HbA1c level.

Version 26 of SPSS was used for statistical analysis. Mean ± standard deviation was calculated for continuous variables and the student t-test was performed to test for difference between two groups. The Chi-square was used to test for association between categorical variables. The relationship between variables was examined using Person's correlation coefficient (r). The P values ($p \leq 0.05$) were considered to be statistically significant. Receiver operator curve analysis (ROC) was used to find the best cut-off, sensitivity, and specificity serum fasting insulin, glycine, HOMA-IR, insulin secretion (IS), and TyG index.

Presence of at least one of the following elements according to American Association of Clinical Endocrinology (AACE) definition of IR CVD, hypertension, PCOS, NAFLD, or acanthosis diagnosis Nigerians family history of CVD, hypertension, or T2DM gestational diabetes or a past sweat glucose intolerance that isn't a white sedentary life type BMI 25 kg/m^2 and/or waist measurements of at least 102 cm for men and 88 cm for women 40 years of age and at least two of the following requirements Triglycerides > 150 mg/dL HDL > 40 mg/dL and > 50 mg/dL in men and women 130/85 mmHg or lower blood pressure 120 minutes after a glucose challenge or a fasting glucose of 110–125 mg/dl (Diabetes is not included in the AACE IRS range of 140-200 mg/dl.) (18). The International Diabetes Federation (IDF) definition of metabolic syndrome (MS) is the only one of the three that requires a high value of waist circumference for it to diagnose MS, and it is this definition that has the strongest connection to IR. Waist circumference is the key marker for IR and can therefore be used to identify MS early on (19). Permission to conduct the research was granted by the Iraqi Ministry of Health at the Specialized Center for Endocrinology and Diabetes, Baghdad, Rusafa.

Results

Table 1 shows that the two study groups were not significantly different when compared by their mean age. The IR group had a significantly higher BMI (32.1±3.7) than those without IR (21.3±1.76). P<

0.05. The same is true for waist circumference (113.4±8.91) vs. (76.8±11.06) respectively.

Table (1): Comparison of the groups by Mean ± SD of Age, BMI, and waist circumference.

Parameter	Individual without IR (N= 80) mean ± SD	Individual with IR (N= 80) mean ± SD	*p*-Value
Age (years)	53.6±8.63	53.27±8.83	0.82 (N.S)
BMI (Kg/M$^{2)}$	21.3±1.76	32.14±3.7	0.000 (S)
Waist Circumference(cm)	76.8± 11.06	113.4± 8.91	0.000 (S)

To confirm the diagnosis of IR the following test Blood HbA1c, serum fasting glucose, fasting insulin, Lipid profile, triglyceride-glucose index, HOMA-IR, insulin secretion, and TG/HDL ratio are dependent and on American Association of Clinical Endocrinology (AACE) criteria. All results in Table (2) match definition of the insulin resistance as well as its absence.

Table (2): Comparison of the two study groups by Mean ±SD of the results of blood tests.

Markers	Healthy individuals without IR (N= 80) mean ± SD	Individuals with IR (N= 80) mean ± SD	*p*-Value
Fasting Serum Glucose (mg/dl)	71.3±9.74	120.9±4.76	0.000 (s)
Blood HbA1c (%)	4.8±0.52	6.3±0.23	0.000 (s)
Fasting Serum Insulin (µU/Ml)	6.8±1.31	20.8±24	0.000 (s)
Total Serum Cholesterol (mg/dl)	135.9±10.24	174.2±43.40	0.000 (s)
Serum Triglyceride (mg/dl)	76.4±8.21	217.8±72.31	0.000 (s)
Serum LDL cholesterol (mg/dl)	72.5±11.63	97.3±38.17	0.000 (s)
Serum HDL cholesterol (mg/dl)	47.7±5.43	35.0±6.80	0.000 (s)
HOMA-IR	1.16±0.10	7.2±1.11	0.000 (s)
TyG Index	4.3±0.09	5.1±0.14	0.000 (s)
Insulin secretion	0.1±0.30	0.2±0.07	0.000 (s)

Pearson‘s correlation for both markers of IR (TyG index and HOMA-IR) how that TyG index and HOMA-IR a had a significant positive correlation with each of fasting serum glucose, insulin, and blood HbA1c% (p≤ and diabetes finding of studied in Healthy 0.05) (r = 0.63, r = 0.35, r = 0.41) (r = 0.65, r = 0.30, r = 0.32). Both IR markers TyG index and HOMA-IR show a significant negative correlation with serum glycine (p≤ and diabetes finding of studied in Healthy 0.05) (r = -0.21, r = -0.24) respectively. IR markers were not significantly correlated with insulin secretion (*p*> and diabetes finding of studied in Healthy 0.05) table (3) shows.

Table (3): Correlation of TyG index and HOMA-IR with the results of blood tests in the IR group.

Parameter	TyG index N= 80, r =	*p*-Value	HOMA-IR N= 80, r =	P-Value
Fasting Serum Glucose (mg/dl)	0.63	0.000 (S)	0.65	0.000 (S)
Blood HbA1c (%)	0.41	0.000 (S)	0.32	0.02 (S)
Fasting Serum Insulin (µU/Ml)	0.35	0.001(S)	0.30	0.01 (S)
Serum Glycine (Pg/ml)	-0.21	0.05 (S)	-0.24	0.03 (S)
Insulin secretion	0.06	0.54 (N.S)	0.04	0.71 (N.S)

Although it was not among the objectives of the study to specify the use of serum glycine as a diagnostic tool for IR, it showed high sensitivity and specificity when compared with the approved indicators for diagnosis (HOMA-IR & TyG index). As shown in the table (4).

Table (4): Area under curve, Sensitivity, Specificity, and cut-off value for serum glycine, HOMA-IR, insulin secretion, TyG index, and fasting insulin.

Marker	AUC	Sensitivity %	Specificity %	Cut-off
HOMA-IR	1	100%	100%	3.32
Insulin secretion	0.932	83.8%	92.5%	0.135
TyG index	1	100%	100%	4.63
Fasting insulin	1	100%	100%	10.05

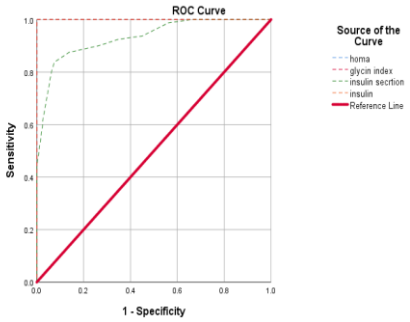

Figure (1): ROC curve for serum fasting insulin, HOMA-IR, TyG index, and insulin secretion.

Discussion:

Weight gain is the most important factor for diabetes related to IR. In overweight people, adipose tissue produces high levels of non-esterified fatty acids, glycerol, hormones, and pro-inflammatory cytokines that may lead to the development of IR (20).

The non-significant findings revealed that age is not only associated with insulin resistance and mitochondrial myopathy but also with changes in body composition, which may be involved in the development of age-related insulin resistance. The

effect of age was also eliminated by selecting the ages of the control group, close to the ages of the patients (21).

Adipose tissue and some viscera may develop an excess of glucose as a result of IR. In this situation, fat tissue acts as an endocrine organ and secretes inflammatory cytokines (adipocytokines), which block the insulin signal, increase (IR), and result in a certain level of tissue inflammation (22).

However, in addition to the previously noted reduction in beta-oxidation brought on by hyperinsulinemia, which prevents lipolysis, there is also an increase in fatty tissue as a result of the accumulation of glucose in the adipocytes. The release of very-low-density lipoproteins (VLDLs), which result in dyslipidemia, the synthesis of triglycerides in the liver, and abdominal obesity are all made more likely by these processes (23).

Modifications in redox balance, oxidative stress, inflammation, and insulin sensitivity appear to be linked, at least in part, with mitochondrial dysfunction playing a crucial supporting role that may worsen these abnormalities. Additionally, recognized as modulators of the metabolic pathways influencing insulin action are nutrients, substrates, and systems engaged in host-nutrient interactions, including gut bacteria (24).

The results of indirect laboratory measurements and indices are erratic and unreliable. However, an accurate and simple method of identifying IR is through skin manifestations. Clinicians should always keep in mind that skin conditions associated with IR may be an indication of a metabolic imbalance that puts the patient at risk for or who already has diabetes. At the same time, clinicians should not only be aware of them but also take action by determining the patient's current metabolic status and, if necessary, providing them with counseling regarding lifestyle interventions like eating well, exercising, quitting smoking, and losing weight (25). HbA1c and FPG revealed a substantial connection to HOMA – IR for both sexes (26). Both HOMA-IR and TyG index were found to have high accuracy, represented by good sensitivity, and specificity of up to 100%, and this confirmed the diagnosis for the group's individuals with high insulin resistance. According to studies, the TyG index accurately predicted insulin resistance and reflected glycemic management. Despite this, it cannot be adopted as a diagnostic tool because the sample collected is a region of confidence intervals that cannot be adopted. The TyG index and HOMA-IR were strongly associated with this study (27).

Conclusion

This study has highlighted the following outcomes:

HOMA-IR has had an important role in the evaluation, detection, and prognosis of prediabetes. It also helps detect early complications associated with T2DM and helps determine the best treatment options. It also found that the TyG index beats the HOMA-IR for predicting prediabetes. It has the best potential for early detection and prevention of prediabetes.

Authors' declaration: We hereby confirm that all the figures and tables in the manuscript are mine/ours. Besides, figures and images which are not mine/ours have been given permission for re-publication attached with the manuscript.

Authors have been sign on an ethical consideration's approval, and the project was approved by the local ethical committee in College of medicine of Baghdad University according to the code number (ISU.17.10.22), (24.10.22).

Conflicts of Interest: None

Authors' contributions:

Study conception & design: (Maysaa J. Majeed). Literature search: (Bareq E. Taha). Data acquisition: (Bareq E. Taha). Data analysis & interpretation: (Bareq E. Taha & Maysaa J. Majeed). Manuscript preparation: (Bareq E. Taha). Manuscript editing & review: (Maysaa J. Majeed).

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تقدير مقاومة الأنسولين لدى البالغين البدينين في بغداد

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الخلفية: يعمل الأنسولين على التحكم في مستويات السكر في الدم عن طريق إرسال إشارات إلى خلايا الكبد والعضلات والدهون لإخراج السكر من الدم. إن السمنة وفرط أنسولين الدم وارتفاع السكر في الدم وفرط شحميات الدم ليست سوى عدد قليل من الاضطرابات الأيضية المترابطة التي ترتبط في كثير من الأحيان بهذه الأمراض. يتم استخدام إجراء إحصائي يسمى نموذج تقييم المقاييس المنزلية لتحديد مقاومة الأنسولين ونشاط خلايا البنكرياس. يتم تحديد كلاهما باستخدام الأنسولين وجلوكوز بلازما الصيام ولكن باستخدام صيغ مختلفة. على الرغم من أن التحقيقات المستندة إلى نسخة معدلة من باستخدام تركيز الببتيد الضام معروضة، إلا أنها نادرة للغاية.
الهدف: دراسة لمعرفة مقاومة الأنسولين والكشف المبكر عن مقدمات السكري باستخدام المعادلات الحسابية لمقاومه الانسولين ومؤشر الدهون الثلاثية مع السكر.
الموضوعات، والمواد، والطريقة: التصميمات المقطعية التحليلية والفوجية هما نوعان من التصاميم الإحصائية. وقد أجريت الدراسة على 160 متطوعًا، تم تجنيدهم في بداية الدراسة واختيارهم من فئة عمرية بناءً على بيانات الدراسة والتحليل الأولي، تتراوح أعمارهم بين (40-70 عامًا). تم تقسيمهم إلى مجموعتين: المجموعة الأولى تضم 80 فردًا، بعد اعتماد متوسط مؤشر كتلة الجسم لأكثر من 25، والذين يعانون من مقاومة الأنسولين، والمجموعة الثانية تضم 80 فردًا سليمًا لا يعانون من مقاومة الأنسولين وجسمهم. مؤشر الكتلة أقل من 25. تم تحديد نسبة الجلوكوز في الدم، ونسبة الدهون، و HbA1Cباستخدام Cobas c111 على عينات مصل من كلا المجموعتين. تم تحديد أنسولين الصيام باستخدام Cobas E411 ومصل الجلايسين باستخدام مجموعات .ELISA
النتائج: بعد إجراء الإجراءات الإحصائية لنتائج الموضوعات لكل من TyG، HOMA-IR، وجد أن هناك تغيرًا معنويًا وقيمة 0) p،.(00
الخلاصة: HOMA-IR كان له دور مهم في تقييم واك,تشاف والتنبؤ بمرض السكري. كما أنه يساعد في اكتشاف المضاعفات المبكرة المرتبطة بـ T2DM ويساعد في تحديد أفضل خيارات العلاج. ووجد أيضًا أن مؤشر TyG يتفوق على HOMA-IR للتنبؤ بمقدمات السكري. لديه أفضل إمكانات للكشف المبكر والوقاية من مقدمات السكري.
الكلمات المفتاحية: مقاومة الأنسولين، داء السكري من النوع 2، مؤشر TyG، الجلايسين، الكولاجين، إفراز الأنسولين، علاقة حساب مقاومه الانسولين.