Concordance between homeostatic model assessment and triglyceride glucose index in assessing insulin resistance among HIV-infected patients

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ABSTRACT

الأهداف: تقييم التوافق بين مؤشر الجلوكوز ثلاثي الجليسريد (TyG) وتقييم النموذج الاستتبابي لمقاومة الأنسولين (HOMA–IR) في تقييم مقاومة الأنسولين (IR) لدى الأشخاص المصابين بفيروس نقص المناعة البشرية (PLWH). بالإضافة إلى ذلك، كنا نهدف إلى تقدير القيمة الفاصلة لمؤشر TyG في الأشخاص المصابين بفيروس نقص المناعة البشرية/الإيدز.

المنهجية: اشتملت هذه الدراسة الرصدية بأثر رجعي السجلات الطبية للمرضى الذين تم تشخيص إصابتهم بفيروس نقص المناعة البشرية في مستشفى التدريب والأبحاث من يناير 201 إلى يناير 2024. بناءً على مستويات HOMA–IR لديهم، تم تقسيم مرضى PLWH إلى مجموعتين: المجموعة أ (المرضى الذين لا يعانون من الأشعة تحت الحمراء) والمجموعة ب (المرضى الذين يعانون من الأشعة تحت الحمراء).

النتائج: في هذه الدراسة، تم فحص مقاومة الأنسولين لدى 147 شخصًا مصابًا بفيروس نقص المناعة البشرية (PLWH) تتراوح أعمارهم بين 18– 68 عامًا. أظهرت نتائجنا وجود علاقة خطية إيجابية كبيرة بين HOMA– IR و TyGindex (r=0.628، p<0.001). لقد وجدنا أن القيمة الفاصلة لمؤشر TyG للتنبؤ بـIR لدى الأشخاص المصابين بفيروس نقص المناعة البشرية (PLWH) تبلغ 8.25.

الخلاصة: حددت دراستنا العلاقة بين مؤشر TyG ومؤشر HOMA IR في الأشخاص المصابين بفيروس نقص المناعة البشرية/الإيدز. قد يكون مؤشر TyG بمثابة بديل فعال لـ HOMA–IR لتقييم مقاومة الأنسولين لدى الأشخاص المصابين بفيروس نقص المناعة البشرية/الإيدز.

Objectives: To evaluate the concordance between the triglyceride glucose (TyG) index and the homeostatic model assessment of insulin resistance (HOMA-IR) in assessing insulin resistance (IR) in people living with HIV (PLWH). Additionally, we aimed to estimate a cut-off value for the TyG index in PLWH.

Methods: This retrospective, observational study included medical records of patients diagnosed with HIV at Sakarya Training and Research Hospital from January 2019 to January 2024. Based on their HOMA-IR levels, PLWH patients were divided into 2 groups: Group A (patients without IR) and Group B (patients with IR).

Results: In this study, insulin resistance was investigated in 147 people living with HIV (PLWH) between the ages of 18-68. Our results showed a significant positive linear relationship between HOMA-IR and the TyG index (r=0.628, p<0.001). We found the TyG Index cut-off value to predict IR in people living with HIV (PLWH) to be 8.25.

Conclusion: Our study identified correlation between the TyG index and HOMA IR index in PLWH. The TyG index may serve as an effective alternative to HOMA-IR for evaluating insulin resistance in PLWH.".

Keywords: HIV, Insulin resistance, triglyceride glucose index.

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Advances in the treatment of HIV infection over the last 20 years have extended the life expectancy of people living with human immunodeficiency virus (HIV) (PLWH).[1,2] Today, PLWH are living longer, chronic diseases are occurring at an earlier age than the general population, and the rate of non-acquired immunodeficiency syndrome causes of death has increased.[2,3] This may be due to weight gain and insulin resistance.[2-4] All these dysmetabolic conditions increase atherogenic cardiovascular risk insulin resistance (IR) is a condition that supports the development of these

pathologies, especially metabolic syndrome, diabetes, atherosclerosis, etc.[4-6] Even in patients without diabetes mellitus, IR alone has been found to be a distinct risk factor for cardiovascular events.[7] Therefore, it is important to use a simple and practical method for early detection of individuals with IR in PLWH.

Given the increasing burden of metabolic complications among PLWH and the necessity for accessible diagnostic tools, our study aims to evaluate the concordance between the triglyceride glucose (TyG) index and homeostatic model assessment of insulin resistance (HOMA-IR) in assessing IR in HIV-infected patients. Additionally, we seek to establish a cut-off value for the TyG index that can accurately identify IR in this population.

Methods. This is a retrospective, observational study. The records of patients diagnosed with HIV who were followed up in the infectious diseases outpatient clinic of Sakarya Training and Research Hospital between January 2019 and January 2024 were scanned from the hospital data processing system and patient files. The study protocol was approved by the institutional review board of Sakarya University.

Insulin resistance was defined using the HOMA-IR threshold specific to the Turkish population (>2.5).[8] This study is to investigate the optimum cut-off values for HOMA-IR in the Middle Black Sea Region of Turkey and was selected due to its geographical proximity. Additionally, shared dietary habits and cultural similarities supported the use of this threshold in our study. Patients were divided into 2 groups based on their HOMA-IR levels: Group A (patients without IR) and Group B (patients with IR). We used consecutive sampling in our study. Adult patients diagnosed as HIV-1 positive via Western blot or polymerase chain reaction analysis with complete clinical data were included. Exclusion criteria included age below 18 years, diagnosed diabetes or dyslipidemia, use of lipid-lowering medications, and missing or questionable data.

Homeostatic model assessment of insulin resistance was calculated using the formula: fasting plasma insulin (μU/mL)×fasting plasma glucose (mmol/L)/22.5. The TyG index was computed as the logarithm of the product of fasting triglycerides (mg/dL) and fasting glucose (mg/dL) divided by 2 (in standard international units).

Statistical analysis. As descriptive statistics, mean±standard deviation for numerical data, number (n) and percentage (%) for categorical data were given. The use of TyG value above Homa IR 2.5 as a diagnostic test was tested with receiver operating characteristic (ROC) analysis. Area under curve (AUC), 95% confidence intervals, cut-off value determined according to Youden Index are given together with sensitivity and selectivity percentages. The data were valuated with the independent sample t-test for numerical variables and Pearson Chi-Square test for categorical data. Whether there is a significant difference between the groups in terms of the variables examined, in the evaluation of the relationship between HOMA and TyG index. Pearson correlation coefficient was given and significance test was performed. The analysis of the study was performed with IBM SPSS version 25 program and $p<0.05$ was considered statistically significant.

Results. In this study, insulin resistance was investigated in 147 PLWH between the ages of 18-68. According to HOMA-IR, group A consists of 72 patients without insulin resistance, group B consists of 75 patients with insulin resistance. Baseline characteristics of all participants are summarized in Table 1.

Risk factor analysis of insulin resistance among PLWH are presented in Table 2. When evaluating individual risk factors influencing IR, men were found to exhibit a 2.9-fold higher risk compared to women. Additionally, elevated TyG index, triglyceride levels, and glucose levels were identified as individual risk factors affecting IR. In the multivariate analysis, male gender and high body mass index (BMI) emerged as significant risk factors.

When grouping was carried out according to the determined cut-off, a significant cut-off value was found for the TyG index. Having a TyG index of 8.25 indicates the presence of insulin resistance. The sensitivity value was 77.3%, the specificity value was 69.4%.

Pearson correlation significance test was performed to evaluate the relationship between HOMA-IR and TyG index (Figure 1). There was a significant 62.8% positive linear relationship between HOMA-IR and TyG index ($p<0.001$; r=0.628) (Figure 2).

Discussion. Currently, with appropriate follow-up and treatment, the life expectancy of PLWH is comparable to that of the general population.[1-3] Hence, there is a critical need to detect and manage insulin resistance, which is linked to chronic diseases in this demographic.[3-6] Due to the complexity and

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Table 1 - Characteristics of the subjects (N=147).

Parameters	Group A	Group B	*P*-value
Female / Male	8(11.1)/64(88.9)	20(26.7)/55(73.3)	0.016[a]
CD4 <250 / >250cell/mm^3	18(25.0)/54(75.0)	27(36.0)/48(64.0)	0.148[a]
RNA <5000 / >5000copy/ml	28(38.9)/44(61.1)	18(24.0)/57(76.0)	0.052[a]
BMI <25/>25	56(77.8)/16(22.2)	62(82.7)/13(17.3)	0.457[a]
Age	30 (19-67)	35(18-68)	0.153[c]
Triglycerid	120 (50-280)	162(100-310)	<0.001[c]
TyG index	8.112±0.257	8.43±0.231	<0.001[b]
Glucose	69.47±14.911	80.64±14.965	<0.001[b]

[a]Pearson Chi-Square test; n (%), [b]Independent sample t test; mean±standard deviation, [c]Mann-Whitney U test; median (min-max)

Table 2 - Risk factors of insulin resistance through binary logistic regression analysis.

Parameters	Univariate		Multiple	
	OR (%95 CI)	*P*-value*	OR (%95 CI)	*P*-value*
Gender (male)	2.9 (1.2-7.1)	0.019	4.8 (1.5-16.1)	0.019
Age	1.0 (0.99-1.04)	0.221	-	
CD4 (>250 cell-mm^3)	1.7 (0.8-3.4)	0.150	-	
RNA (>5000 copy-ml)	0.5 (0.2-1.01)	0.053	-	
BMI (>25)	1.4 (0.6-3.1)	0.457	10.8 (2.8-41.9)	<0.001
Triglyceride glucose-index	235 (34.5-1599)	<0.001	-	
Triglyceride	1.03 (1.02-1.04)	<0.001	-	
Glucose	1.05 (1.02-1.08)	<0.001	-	

OR: odds ratio; CI: confidence interval, BMI: body mass index

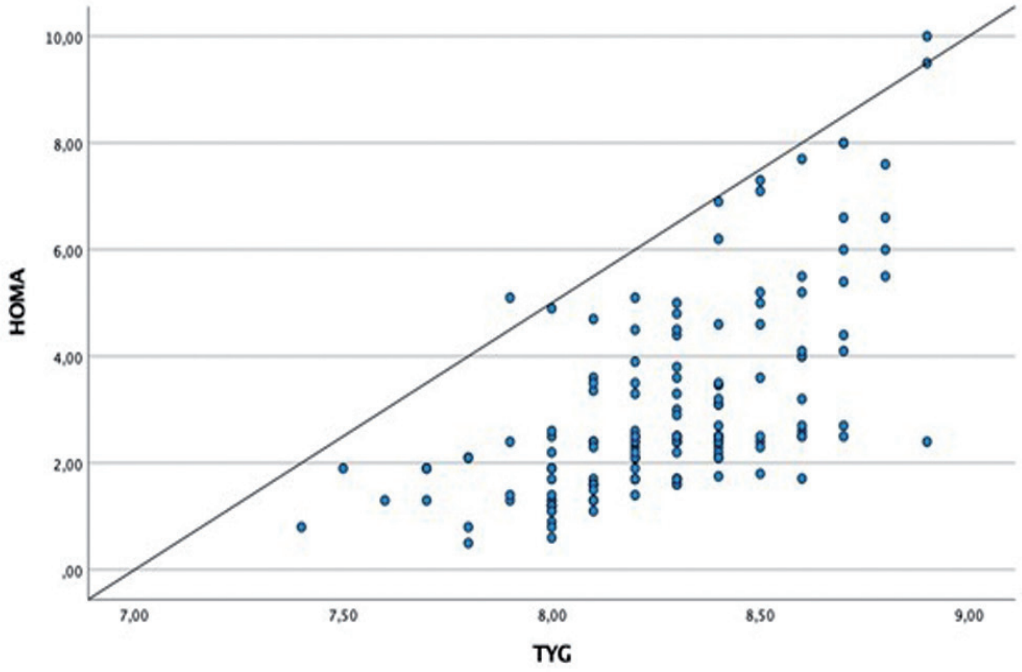

Figure 1 - The positive correlation between TyG (triglyceride glucose) index TyG and HOMA-IR. HOMA-IR: homeostatic model assessment of insulin resistance

Table 3 - TyG Index value for predicting IR.

Parameters	Group A	Group B	*P*-value
TyG <8.25	50 (69.4)	17 (22.7)	<0.001
TyG> 8.25	22 (30.6)	58 (77.3)	

IR: insulin resistance, TyG: triglyceride glucose

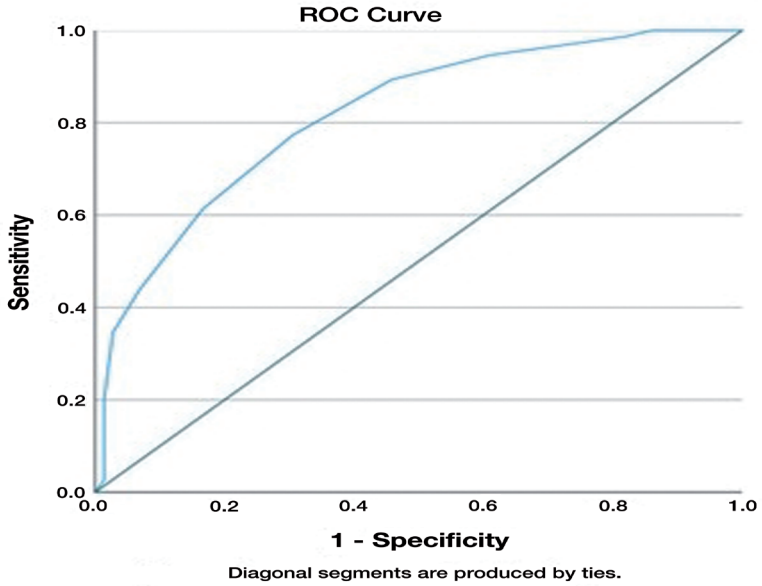

Figure 2 - Receiver operating characteristic (ROC) curve of triglyceride glucose index for predicting insulin resistance.

cost associated with the hyperinsulinemic euglycemic clamp (HIEC), which serves as the gold standard for evaluating insulin resistance, alternative methods such as HOMA-IR and the TyG index have been proposed as more accessible and cost-effective alternatives.[9-12] In our study involving individuals living with HIV, we utilized the HOMA-IR index to assess insulin resistance and explored the predictive role of the TyG index.

Homeostatic model assessment of insulin resistance is the most common method used for IR measurement.[13] For the assessment of IR, the HOMA-IR has shown itself to be a reliable instrument.[9,10,13] Several population-based studies have been conducted to establish the HOMA-IR cut-off values for IR diagnosis in different geographic areas. Nonetheless, the threshold HOMA-IR levels used to define IR vary widely.[14,15] There are some challenges when using this method to calculate IR using the HOMA-IR index. Serum insulin level measurements used to calculate the HOMA-IR index are not yet sufficiently standardized.[16] Additionally, the insulin measurement method is expensive for everyday practical use, and in cases where insulin measurement is not feasible, alternative tests are required to identify insulin resistance.[17] Many populations around the world have validated the TyG index for use as an IR screen.[9-13,17] The TyG index's sensitivity and specificity ranges in different studies are 73%–90% and 45%–99%, respectively.[9]

Our findings revealed a significant concordance between the TyG index and HOMA-IR index in identifying insulin resistance within the HIV-infected population. While not considered the gold standard for estimating insulin resistance (IR), the TyG index has been recognized as a readily applicable and cost-effective marker.[9,10] Early detection and effective management of insulin resistance in PLWH are therefore vital to improving overall health outcomes, potentially mitigating early cardiovascular disease risks. A primary advantage of the TyG index is its independence from serum insulin measurements in its calculation. Moreover, it can be easily computed during out patient clinic visits using routine measurements of glucose and triglycerides. We observed that the TyG index

demonstrated a sensitivity of 77.3% and specificity of 69.4% in predicting IR.

Due to variations in threshold values across studies, accurately determining the prevalence and incidence rates of insulin resistance has been challenging.[11,12] These findings highlight the potential of the TyG index as a viable tool for assessing insulin resistance. Its accessibility and effectiveness make it a promising alternative to more complex and costly methods, providing clinicians with a practical means to evaluate metabolic health and potentially intervene earlier in at-risk populations. Demir et al[8] reported a prevalence of insulin resistance among adult participants in our country at 33.2%. Conversely, in our study, we observed a notably higher prevalence of 51% for insulin resistance. This elevated risk among PLWH stems from alterations in glucose and lipid metabolism, necessitating the use of different thresholds compared to the general population when assessing insulin resistance prevalence in this group.[18-20] A significant finding of our research was the identification of a TyG index cut-off value of 8.25 for predicting insulin resistance in our study population.

Compared to the general population, individuals living with HIV experience cardio vascular disease (CVD) at a younger ages and exhibit higher mortality rates related to CVD.[21,22] The aging demographic of PLWH is characterized by a heightened prevalence of metabolic disorders, including increased adiposity, insulin resistance, diabetes, and dyslipidemias, which contribute to elevated risks of CVD, metabolic complications, and multimorbidity.[23] Hence, there is a pressing need for more accurate cardiovascular risk assessment among PLWH. The triglyceride glucose index (TyG) has been identified as a marker associated with increased risk of atherosclerotic cardiovascular disease.[24] By identifying a reliable and practical method for early detection of IR, we hope to improve the management of metabolic health and reduce the associated cardiovascular risks in this vulnerable population.

Our study observed a positive association between increased body mass index (BMI) and IR, consistent with existing literature findings.[25] However, contrary to expectations, no significant relationship was detected between age and IR in our study cohort. Clinical markers indicating HIV treatment efficacy, such as high CD4 counts and low HIV-RNA levels, did not correlate with IR. These findings suggest that achieving viral suppression alone may not suffice for managing metabolic health in PLWH, emphasizing the necessity for a comprehensive, multidisciplinary approach to their care.

Our results differ from the general population, which we attribute to HIV infection status and treatment diversity. The HIV infection and HIV treatment are independently associated with glucose and lipid metabolism.[26] The HIV infection disrupts multiple factors that affect glucose metabolism, adipose tissue, and inflammatory pathways.[27] The HIV infection may negatively impact T-cell and mitochondrial function, whereas HIV treatment may positively impact metabolic dysfunction through viral suppression and preservation of CD4 cells.[28,29] Taking into account these various metabolic interactions, specific cut-off values for HIV patients should be determined. The HIV patients should be examined in new studies with larger samples and different subgroups.

Study limitations. This study include the reliance on single measurement values for analysis, as well as the inability to capture data on dietary habits and physical activity that may influence the TyG index. One of the limitations of this article is that antiretroviral treatment modalities were not analyzed. Awareness of these limitations is crucial when interpreting our findings.

In conclusion, our study emphasizes that there is a significant correlation between the TyG index and the HOMA-IR index for evaluating insulin resistance in HIV-infected patients. Calculated using routine laboratory tests for glucose and triglycerides, the TyG index may serve as an effective alternative to HOMA-IR in PLWH. Increasing early diagnosis of insulin resistance in HIV patients will help prevent metabolic diseases that are increasingly common in PLWH. Our research will provide valuable insights into the applicability of the TyG index in clinical practice for HIV-infected individuals.

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