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Novel Formulas Derived from Triglyceride–Glucose Index for Assessment of Insulin Resistance in Patients with Type 2 Diabetes

Introduction

The homeostasis model assessment of insulin resistance (HOMA-IR) can be used to diagnose IR. The HOMA-IR cut-off value varied according to population and related disorders, with a value of > 2.9 indicating IR [1]. Low-grade chronic inflammation is a common pathogenic condition linked to type 2 diabetes (T2D) and insulin resistance (IR) [2]. The triglyceride–glucose index (TYGI) is a valuable biomarker for measuring insulin resistance, and some research suggests that it is superior to the HOMA-IR [3].

Objective

The goal of this study is to develop a new index for assessing insulin resistance in T2D patients by replacing the glucose molecule with liver enzymes and inflammatory markers in the TYGI.

Materials and methods

This observational study was conducted at the College of Medicine, University of Diyala, between January 1, 2022, and December 31, 2022. The information was gathered from diabetes clinics and centers. The laboratory blood chemistry (lipid profiles, glycemic

indices, liver enzymes, and inflammatory biomarkers) was obtained from patients' records.

HOMA-IR was calculated using the following equation:

$$\frac{\text{Fasting insulin} \left(\frac{\mu\text{U}}{\text{mL}} \right) \times \text{fasting glucose} \left(\frac{\text{mg}}{\text{dL}} \right)}{405}$$

TyGI was calculated using the following equation:

$$\text{LN} \frac{\text{Fasting triglyceride} \left(\frac{\text{mg}}{\text{dL}} \right) \times \text{fasting glucose} \left(\frac{\text{mg}}{\text{dL}} \right)}{2}$$

The triglyceride–high sensitivity C-reactive protein (TyCRPI), triglyceride–interleukin-6 (TyIL6 I), and triglyceride–alanine aminotransferase (ALT) or aspartate-to-aminotransferase (AST) were calculated using the abovementioned equation, but instead of fasting glucose, the hs-CRP, IL-6, ALT, and AST were substituted, respectively.

The ALT-to-TG (ALTyR) and AST-to-TG (ASTyR) ratios were calculated by using the following equation:

$$\frac{\text{ALT} \left(\frac{\text{U}}{\text{L}} \right) \text{ or } \text{AST} \left(\frac{\text{U}}{\text{L}} \right)}{\text{Ln fasting triglyceride} \left(\frac{\text{mg}}{\text{dL}} \right)}$$

Data were analyzed using the statistical package SPSS version 24 (SPSS Inc., Chicago, Illinois, USA).

Results

Of 112 T2D patients, 94 had a HOMA-IR of ≥ 3.0 (n = 94) and 18 had a HOMA-IR of < 3.0. Table 1 shows that the mean values of TyIL6I, TYASI, and IL-6 were significantly higher in patients with HOMA-IR ≥ 3.0 compared with HOMA-IR < 3.0. Table 2 shows that TyIL6I at a cutoff value of 9.2 is a significant marker

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Table 1. Comparison between the Triglycerides Derived Indexes and Ratios at a Cut-Off Value of Homeostasis Model Assessment of Insulin Resistance at 3.0

Variables	HOMA-IR	HOMA-IR < 3.0 (n = 18)	P1-value ≥ 3.0 (n = 94)	P2-value
Glucose	209.4 ± 69.0	217.5 ± 68.3	0.645	0.915
Triglycerides	137.9 ± 39.7	161.4 ± 82.2	0.239	0.552
C-reactive protein	3.6 ± 1.8	2.8 ± 1.6	0.059	0.111
Interleukin-6	154.0 ± 46.1	206.1 ± 96.0	0.027	0.001
ALT	13.0 ± 5.8	15.4 ± 7.1	0.174	0.224
AST	15.2 ± 4.5	18.0 ± 7.2	0.104	0.156
TyGI	9.48 ± 0.44	9.62 ± 0.63	0.390	0.524
TyCRPI	5.25 ± 0.67	5.07 ± 0.8	0.381	0.375
TyIL6I	9.19 ± 0.45	9.54 ± 0.55	0.013	0.012
TyALI	6.66 ± 0.71	6.92 ± 0.58	0.092	0.211
TyASI	6.88 ± 0.42	7.09 ± 0.45	0.66	0.044
ALTyR	2.61 ± 1.08	3.15 ± 1.55	0.163	0.197
ASTyR	3.10 ± 0.87	3.72 ± 1.66	0.123	0.249

The results are expressed as mean ± SD. P1-value was calculated using two-tailed independent two sample t-test (assuming equal variance) and P2-value was calculated by independent samples Mann Whitney U test

ALT — alanine aminotransferase; ALTyR — alanine aminotransferase-to-triglyceride ratio; AST — aspartate aminotransferase; ASTyR — aspartate aminotransferase-to-triglyceride ratio; TYALI — triglyceride–alanine aminotransferase index; TYASI — triglyceride–aspartate aminotransferase index; TyCRP — triglyceride–high sensitivity C-reactive protein; TyGI — triglyceride–glucose index; TyIL6I — triglyceride–interleukin 6 index

Table 2. Statistical Analysis of the Variables at a Cut-Off Value of HOMA-IR of ≥ 3.0

	Cutoff value	Odds ratio	Sensitivity	Specificity	Positive predictive Value	Negative predictive Value	Youden's index	Area under curve
TyGI	9.25	0.610 (0.185–2.009)	82.1 (71.7–89.8)	11.8 (3.3–27.5)	68.1 (64.5–71.5)	22.2 (9.2–44.6)	–0.06	0.548 (0.423–0.672)
TyCRPI	4.5	0.993 (0.295–3.339)	83.9 (74.5–90.9)	16.0 (4.5–36.1)	77.7 (74.1–80.9)	22.2 (9.4–44.2)	–0.01	0.434 (0.298–0.570)
TyIL6I	9.2	8.98* (2.975–27.104)	85.1 (76.3–91.6)	61.1 (35.8–82.7)	83.9 (75.8–90.2)	92.0 (86.4–95.4)	0.462	0.687 (0.565–0.808)†
TyALI	6.5	1.179 (0.402–3.454)	70.2 (59.9–79.2)	33.3 (13.3–59.0)	84.6 (79.5–88.7)	64.3 (54.7–73.1)	0.035	0.593 (0.434–0.753)
TyASI	7.1	2.372 (0.821–6.852)	54.3 (43.7–64.6)	66.7 (41.0–86.7)	89.5 (81.2–94.4)	21.8 (15.8–29.3)	0.21	0.650 (0.521–0.780)††
ALTyR	2.0	3.378** (1.168–9.771)	80.9 (71.4–88.2)	44.4 (21.5–69.2)	88.4 (83.3–92.1)	30.8 (18.6–46.3)	0.25	0.596 (0.438–0.755)
ASTyR	2.6	3.273*** (1.157–9.260)	76.6 (66.7–84.7)	50.0 (26.0–74.0)	88.9 (83.3–92.8)	29.0 (18.5–40.4)	0.27	0.586 (0.463–0.709)

The results were presents as absolute numbers (95% confidence interval); *p < 0.001; **p = 0.025; *** p = 0.026; †p = 0.012; †† p = 0.044

ALTyR — alanine aminotransferase-to-triglyceride ratio; ASTyR — aspartate aminotransferase-to-triglyceride ratio; TYALI — triglyceride–alanine aminotransferase index; TYASI — triglyceride–aspartate aminotransferase index; TyCRP — triglyceride–high sensitivity C-reactive protein; TyGI — triglyceride–glucose index; TyIL6I — triglyceride–interleukin 6 index

of IR with a sensitivity of 85.1%, a specificity of 61.1%, and a J-statistic of 0.462. The area under the curve (AUC) and 95% confidence interval (C.I.) of TyIL6I were significantly different (p = 0.012) accounting for 0.687 (0.565–0.808).

Discussion

The results showed that the formulation of an equation of inflammatory biomarkers, liver enzymes, and triglycerides could be applicable for the assessment of IR. Previous studies showed a non-significant

correlation between TYGI and inflammatory indices or liver enzymes, e.g., CRP, IL-6 [4, 5]. The odd ratios of the formulated equations in this study (which included TG, IL-6, AST, and ALT) were significantly higher in diabetic patients with HOMA-IR > 3 compared with those with HOMA-IR <3.0, and the best results were observed with TyIL6I compared with other indices and ratios. It concludes that using the natural logarithm (Ln) of triglyceride value with inflammatory markers and liver enzymes could provide new indices in the assessment of insulin resistance. The Ln TG-to-IL-6 index is a significant associated biomarker with a HOMA-IR value of more than three.

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Conflict of interests

None declared.

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