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Predictive Potential of the Triglycerides-Glucose Index for Type 2 Diabetes in Benin: A Descriptive Cross-Sectional Study

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Abstract This study investigates the Triglycerides-Glucose (TyG) index's predictive potential for type 2 diabetes (T2D) in the Beninese population. Among 850 participants, including 327 with T2D, 25 with prediabetes, and 491 without diabetes, various risk factors were assessed. Anthropometric data, fasting blood glucose, cholesterol levels, and insulin were measured, and indices (HOMA1, HOMA2, TyG) were calculated. Statistical analyses utilized SigmaPlot 14, employing parametric and non-parametric tests based on data distribution. Data were presented as mean ± SD for quantitative, and proportions for qualitative variables. Normality was checked via the Shapiro-Wilk test. Parametric (ANOVA, t-test) and non-parametric (Kruskal-Wallis, Mann-Whitney) tests were employed based on data distribution. Pearson's chi-square test compared proportions, and associations were evaluated with odds ratios (OR). ROC curves assessed diagnostic performance ($p<0.05$). Results revealed a strong association between insulin resistance (IR) and T2D, with significant correlations to body mass index, waist circumference, blood glucose, cholesterol levels, and triglycerides. The TyG index correlated significantly with HOMA1-IR and HOMA2-IR. Elevated TyG index levels were observed in subjects with prediabetes, T2D, visceral obesity, age ≥ 45 years, family history of diabetes, and hypertension. The TyG index demonstrated good diagnostic performance, with an area under the curve of 0.82, outperforming other ratios. The TyG index emerged as a reliable marker for IR, exhibiting strong correlations with established HOMA models. It proved efficient, particularly in subjects with fasting blood glucose levels below 1 g/L, suggesting its potential as a predictive tool for T2D in the Beninese population.

Keywords: *TyG index, insulin resistance, HOMA, diabetes prediction, Benin*

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1. Introduction

The global expansion of type 2 diabetes (T2D) represents a major public health challenge, jeopardizing people's quality of life and placing considerable financial pressure on healthcare systems. In 2021, around 537 million adults aged 20 to 79 were affected by diabetes worldwide, compared to 463 million in 2019 and 108 million in 1980 [1,2]. According to the International Diabetes Federation (IDF) projections, there will probably be 783 million adults with diabetes by 2045 [2]. In Africa, diabetes affected nearly 24 million adults in 2021, resulting in 416,000 deaths, or 12.1% of all deaths from all causes [3]. Diabetes-related healthcare costs in Africa reached US$12.6 billion in 2021 and are expected to rise to $46.7 billion by 2045 if action is not taken to curb this trend [3]. This represents a threat that few African states seem able to contain. Benin, like many other countries, is

not immune to this growing epidemic, as 5.1% of its population with diabetes in 2016 [4]. T2D is associated with serious chronic complications such as cardiovascular disease, neuropathy, retinopathy, and diabetic nephropathy, which have a significant impact on the population's health and quality of life [5,6].

In this context, the prevention of T2D has become an urgent necessity. Predictive biomarkers play an essential role in the primary prevention of T2D, as this disease is generally diagnosed late in patients [7]. The presence of Insulin resistance (IR) (detected 10 to 20 years before the onset of diabetes) represents a real risk for the development of T2D and its complications [7]. At this stage, early detection of islet cell stress preceding loss of function could enable the implementation of therapeutic interventions to delay or even prevent the onset of diabetes and its complications [1]. Given that IR is the central pathophysiological mechanism of T2D and is already present one to two decades before diagnosis, indices of IR could help predict the onset of T2D.

The HOMA-IR model is the validated model for assessing IR [8,9]. However, its determination is limited due to the high cost and lack of integration of an insulin test into laboratory routine in Benin.

Recently, the Triglycerides-Glucose (TyG) index has been suggested as a marker of moderate IR [10,11,12]. It is an indicator that combines fasting blood levels of triglycerides (TG) and glucose, tests commonly performed at low laboratory cost. The TyG index has been correlated with IR assessment according to the HOMA-IR model and with the rate of total glucose metabolism in hyperinsulinemic-euglycemic clamp studies [13,14,15]. Furthermore, among the traditional risk factors for T2D, it is well established that fasting blood levels of glucose and TG are associated with an increased risk of T2D [16]. Indeed, blood glucose and triglyceride levels are linked to IR, a prediabetes state, and a major risk factor for T2D [17].

The TyG index has also been suggested as a marker to classify metabolic health status [18,19,20]. It can serve as a simple, cost-effective tool for identifying individuals at risk [21,22]. Lee et al. have shown that changes in the TyG index over time are associated with the incidence and risk of diabetes [16]. Although numerous studies have been conducted on the TyG index as a predictor of T2D in various populations, such as the Iranian, Korean, White European, and Thai populations [10,11,13,16,23], its use as a specific predictor of T2D in Benin has not yet been sufficiently explored. This study therefore aims to fill this gap by assessing the predictive potential of the Triglyceride-Glucose Index for T2D in Benin. By carrying out an in-depth analysis of cross-sectional data, we aim to determine whether this index can be a valuable tool for identifying individuals at risk of developing this metabolic disease. A better understanding of this association could contribute significantly to T2D prevention efforts in Benin and pave the way for improved population health. The objectives of the present study are to (1) examine the association between risk factors and T2D, (2) describe the association between the TyG index and T2D risk factors, and (3) evaluate the efficiency of the TyG index in predicting T2D risk.

2. Materials and Methods

2.1. Study Population

This study was carried out in Benin from February 2022 to January 2023, employing a random sampling approach. The collected samples were carefully centrifuged, stored, and analyzed at the Research Unit on Non-Communicable Diseases and Cancer (UR-MNTC) within the Applied Biology Research Laboratory (LARBA) at the Polytechnic School of Abomey-Calavi (EPAC), University of Abomey-Calavi (UAC). This was a descriptive cross-sectional study to assess how effectively the TyG index could diagnose IR. The study population was composed of individuals aged 25 years and older. The non-inclusion criteria encompassed non-fasting individuals, individuals below the age of 25, those with type 1 diabetes, pregnant women, or individuals who declined to participate. The sample size was calculated using the Dagnelie formula (1998) [24].

2.2. Ethical Statements

This work is part of a larger study contributing to an ongoing doctoral thesis in our Research Unit (UR-MNTC). The study has received approval from the Local Ethics Committee for Biomedical Research (CLERB-UP) under reference number 0580/CLERB-UP/P/SP/R/SA and was conducted in strict compliance with applicable regulations. Before participating, all individuals received a detailed explanation of the study's objectives and provided written consent.

2.3. Anthropometric Measurements

Sociodemographic information, family and clinical history, lifestyle habits, occupation, age, sex, alcohol consumption, smoking habits, and medication use were collected through a survey questionnaire using the KoboCollect application. Alcohol consumption was assessed based on weekly and weekend consumption of different alcoholic beverages. The weight of the participants was measured while standing, lightly dressed, and without shoes, using a mechanical scale. Height was also measured while standing, feet together, arms by the sides, without shoes or belt, using a stadiometer. Waist circumference was measured with a tape measure at the midpoint between the last palpable rib and the iliac crest at the end of expiration. Body mass index (BMI) was calculated by dividing weight by the square of height. Systolic and diastolic blood pressure was measured twice on the right arm of seated participants after at least 15 minutes of rest by an experienced nurse. The average of the two measurements was used for the analyses.

2.4. Laboratory Assay

Blood was collected from fasting participants using both dry tubes and tubes containing sodium fluoride. In the event of potential delays in analysis, the serum was

subdivided into 1.5 ml Eppendorf tubes and stored at -20°C until needed for the determination of specific parameters. The panel of parameters for testing included fasting glucose, TG, total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), aspartate aminotransferase (AST), alanine aminotransferase (ALT), serum total proteins, and creatinine. These parameters were chosen because, collectively, they offer a comprehensive perspective on metabolic health, IR, and diabetes risk factors. This facilitates the assessment of their interconnectedness and their impact on the development and progression of diabetes within the Beninese population. All of these parameters were analyzed in a standard laboratory using an automated biochemical analyzer with kits from ELITech (ELITech Group, France). Additionally, fasting serum insulin levels were quantified using the quantitative sandwich enzyme immunoassay technique, employing the Human/Canine/Porcine Insulin Quantikine ELISA Kit, Catalog Number DINS00 (R&D Systems, Minneapolis, MN, USA). The study also estimated the Glomerular Filtration Rate (GFR) using the Cockcroft-Gault equation and calculated the Homeostatic Model Assessment (HOMA) indices (HOMA1 and HOMA2) to evaluate IR and beta-cell function, respectively, through specific equations and software tools [25]. Moreover, the TyG index, a complementary marker for IR, was computed based on fasting TG and glucose levels.

HOMA1-IR = [Fasting Insulin (mUI/L) x Fasting Glucose (mmol/L)]/22,5 [26]

HOMA1-β = 20 x Fasting Insulin (mUI/L)/[Fasting Glucose (mmol/L)-3,5] [26]

TyG index = ln[Fasting Triglycerides (mg/dl) x Fasting Glucose (mg/dl)/2] [27]

2.5. Case Definition

The case definition encompasses prediabetes, hypertension, and metabolic syndrome, as per the specific criteria outlined by the International Diabetes Federation (IDF) in 2021 [28]. IR was determined using the 75th percentile of HOMA1-IR.

2.6. Statistical Analysis

Statistical analyses and graphs were performed using SigmaPlot software version 14 (year 2017). The results are presented as mean ± Standard Deviation (SD) for quantitative variables and as proportions for qualitative variables. The normality was examined by the Shapiro-Wilk test. For comparing quantitative data following a normal distribution and with equal variances between groups, the classical ANOVA test was used. If significant, Turkey's method was employed to compare means. Regarding parameters that did not meet all the required conditions, the Kruskal-Wallis ANOVA test, a non-parametric method, was used. If significant, Dunn's method was used to compare means. Comparison of means between two groups was performed using Student's t-test for normally distributed data and Mann-Whitney test for non-parametric data. Pearson's chi-square test was used for comparing proportions. We calculated measures of association using the odds ratio (OR) along with its corresponding 95% confidence interval. To evaluate the diagnostic efficiency of various markers, we generated a Receiver Operating Characteristic (ROC) curve, using the HOMA1-IR with its 75th percentile as the reference threshold. The threshold values were determined based on the ROC curve. A p-value <0.05 was considered statistically significant.

3. Results

3.1. Features of the Study Population

This study involved a total of 850 participants, comprising 327 (38.47%) individuals with confirmed T2D and 523 (61.53%) individuals without diabetes, aged between 25 and 84 years (Table 1). Among those without diabetes, 491 (93.88%) exhibited fasting blood glucose levels of ≤1.10 g/L, 25 (4.78%) fell within the range of 1.10 g/L to 1.26 g/L, and 7 (1.34%) had fasting blood glucose levels ≥1.26 g/L. The average age of all participants was 49.65 ± 11.72 years, with 465 participants (54.71%) identified as females and 385 (45.29%) as males.

Patients with known T2D demonstrated a significant increase in age, BMI, waist circumference, systolic blood pressure, and pulse rate compared to individuals without T2D (Table 1). Notably, women were more affected by T2D ($p<0.001$) (refer to Table 1). Additionally, factors such as fasting hyperglycemia, arterial hypertension, metabolic syndrome, sedentary behavior, a family history of diabetes, and lower educational levels were statistically more prevalent among T2D patients than those without diabetes (Table 1). Conversely, individuals with prediabetes exhibited significantly higher levels of fasting blood glucose, serum insulin, and HOMA1-IR and HOMA2-IR indices compared to those with normal glucose levels (Table 2). Conversely, individuals with prediabetes displayed lower indices of pancreatic beta-cell function (HOMA1-%β and HOMA2-%β) and insulin sensitivity (Table 2).

Individuals with T2D had elevated levels of fasting blood glucose, HDL-C, TG, and total proteins, as well as HOMA1-IR and HOMA2-IR indices (Table 2). Similar to individuals with prediabetes, individuals with T2D also exhibited lower indices of pancreatic beta-cell function (HOMA1-%β and HOMA2-%β) and insulin sensitivity (Table 2).

3.2. Risk Factors in type 2 Diabetes

There is a positive association between T2D and risk factors such as age (from 45 years onwards), metabolic syndrome, sedentary lifestyle, family history of diabetes, low level of education, overweight, visceral obesity, arterial hypertension, and insulin IR (Table 3). In the population, the odds of developing T2D are increased approximately twelve times by IR, eight times by metabolic syndrome, six times by family history of diabetes, five times by age 45 or older, four times by visceral obesity, three times by education level below or equal to secondary level, and twice by sedentary lifestyle and overweight (Table 3).

Table 1. Socio-anthropometric and clinical characteristics of the population

	Non-T2D n=523	T2D n=327	p-value
Age (year)	45.74 ± 10.40	55.45 ± 11.17	<0.001
Female gender (%)	260 (49.71)	205 (62.69)	<0.001
BMI (Kg/m²)	26.41 ± 6.02	27.34 ± 5.58	<0.01
Waist size (cm)	90.81 ± 14.11	97.62 ± 13.53	<0.001
SBP (mmHg)	131.70 ± 20.58	137.06 ± 22.08	<0.001
DBP (mmHg)	82.96 ± 14.70	81.94 ± 12.77	0.58
Fasting hyperglycemia (%)	32 (6.12)	227 (69.42)	<0.001
Arterial hypertension (%)	152 (29.06)	199 (60.86)	<0.001
Metabolic syndrome (%)	69 (13.19)	195 (59.63)	<0.001
Sedentary lifestyle (%)	173 (33.07)	203 (62.08)	<0.001
Family history of diabetes (%)	66 (12.61)	146 (44.65)	<0.001
Low education level (%)	404 (77.24)	300 (91.74)	<0.001

T2D: Type 2 Diabetes, n: number of subjects, BMI: Body Mass Index, SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure, Hypertension is defined as blood pressure values ≥140/90 mmHg and/or the use of antihypertensive medications. Fasting hyperglycemia is defined as a fasting blood glucose level ≥1.10 g/L. Low educational level refers to secondary education or lower. Metabolic syndrome is identified according to the criteria established by the International Diabetes Federation (IDF). Sedentary behavior is defined as engaging in physical activity for less than 150 minutes per week, and a family history of diabetes is present when at least one first-degree relative has diabetes.

Table 2. Clinical and Metabolic Characteristics of the Population

	Non-T2D n=491	Prediabetes n = 25	T2D n = 327	p-value
Fasting blood glucose (g/L)	0.81 ± 0.13	1.15 ± 0.04***	1.66 ± 0.87***	<0.001
TC (g/L)	1.61 ± 0.47	1.64 ± 0.32	1.70 ± 0.74	0.574
HDL-C (g/L)	0.45 ± 0.19	0.42 ± 0.18	0.57 ± 0.29***	<0.001
LDL-C (g/L)	0.97 ± 0.44	1.03 ± 0.23	0.96 ± 0.60	0.271
TG (g/L)	1.13 ± 0.44	1.14 ± 0.34	1.20 ± 0.37*	0.001
AST (UI/L)	30.60 ± 23.19	25.67 ± 8.58	30.23 ± 21.02	0.725
ALT (UI/L)	23.49 ± 17.79	17.00 ± 4.58	16.5 ± 11.59**	0.002
Total proteins (g/L)	68.61 ± 8.29	70.03 ± 3.84	74.05 ± 4.14**	<0.001
Serum creatinine (mg/L)	9.00 ± 1.84	7.30 ± 1.90	9.79 ± 2.30	0.201
eGFR	96.87 ± 29.91	126.28 ± 27.63	94.12 ± 31.07	0.173
TG/HDL-C	3.08 ± 1.98	2.92 ± 1.10	2.68 ± 2.26***	<0.001
TC/HDL-C	4.20 ± 2.29	4.38 ± 1.61	3.73 ± 2.48***	<0.001
Fasting serum insulin (mUI/L)	7.24 ± 7.97	13.33 ± 21.22*	7.87 ± 8.04	0.043
HOMA1-IR	1.49 ± 1.49	3.86 ± 6.39*	3.21 ± 3.94***	<0.001
HOMA2-IR	0.83 ± 0.80	1.55 ± 2.32*	1.08 ± 1.11***	<0.01
HOMA1-%β	324.46 ± 823.50	89.20 ± 130.13*	68.82 ± 156.83***	<0.001
HOMA2-%β	102.48 ± 81.37	67.86 ± 62.00*	44.45 ± 42.63***	<0.001
HOMA1-%S	120.91 ± 188.27	54.94 ± 23.03*	70.16 ± 87.35***	<0.001
HOMA2-%S	203.75 ± 283.78	128.68 ± 54.13*	190.05 ± 319.60***	0.001

*: p<0.05; **: p<0.01; ***: p<0.001. T2D: Type 2 Diabetes, n: number of subjects, TC: Total Cholesterol, HDL-C: high-density lipoprotein cholesterol, LDL-C: low-density lipoprotein cholesterol, TG: triglycerides, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, eGFR: Estimated Glomerular Filtration Rate, HOMA-IR: homeostatic model assessment of insulin resistance, HOMA-%□ : homeostatic model assessment of □ cells functions, HOMA-%S: homeostatic model assessment of insulin sensitivity.

Table 3. Type 2 diabetes risk factors

Factor	T2D		
	Odds Ratio	95% CI	p-value
Age ≥ 45 years	5.22	3.66 – 7.44	<0.001
Metabolic syndrome	8.08	5.72 – 11.41	<0.001
Sedentary lifestyle	1.95	1.43 – 2.66	<0.001
Family history of diabetes	5.83	4.03 – 8.43	<0.001
Low education level	3.29	2.06 – 5.24	<0.001
Overweight	1.73	1.26 – 2.36	<0.001
Visceral overload	3.77	2.67 – 5.32	<0.001
Arterial hypertension	2.51	1.84 – 3.42	<0.001
IR	11.93	6.23 – 22.93	<0.001

T2D: Type 2 Diabetes, IR: Insulin Resistance, CI: Confidence Interval. IR is defined as having a HOMA1-IR index greater than the 75th percentile (2.408).

Table 4. Characteristics of insulin resistance in the population

	Non-IR (n=432)	IR (n=143)	p-value
Age (year)	50.38 ± 11.54	53.29 ± 12.54	0.031
BMI (Kg/m²)	26.55 ± 5.73	28.12 ± 6.16	0.006
Waist circumference (Cm)	94.07 ± 13.60	98.96 ± 14.16	0.001
Fasting blood glucose (g/L)	1.04 ± 0.44	1.94 ± 1.04	<0.001
TC (g/L)	1.53 ± 0.48	1.98 ± 0.94	<0.001
HDL-C (g/L)	0.46 ± 0.22	0.55 ± 0.33	<0.001
LDL-C (g/L)	0.88 ± 0.44	1.02 ± 0.73	0.043
TG (g/L)	1.01 ± 0.42	1.17 ± 0.43	<0.001
TG/HDL-C	2.81 ± 2.02	2.82 ± 2.41	0.589
TC/HDL-C	4.12 ± 2.34	4.05 ± 2.60	0.328
Fasting serum insulin (mIU/L)	5.38 ± 2.24	14.49 ± 14.01	<0.001
HOMA1-IR	1.28 ± 0.54	5.66 ± 4.99	<0.001
HOMA2-IR	0.71 ± 0.41	1.80 ± 1.65	<0.001
HOMA1-%β	108,58 ± 133.04	86.98 ± 129.86	<0.001
HOMA2-%β	73.83 ± 47.64	74.86 ± 111.84	<0.001
HOMA1-%S	105.77 ± 100.45	24.94 ± 10.29	<0.001
HOMA2-%S	196.48 ± 190.36	123.07 ± 307.21	<0.001

*: p<0.05; **: p<0.01; ***: p<0.001. IR: Insulin Resistance, n: number of subjects, TC: Total Cholesterol, HDL-C: high-density lipoprotein cholesterol, LDL-C: low-density lipoprotein cholesterol, TG: triglycerides, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, eGFR: Estimated Glomerular Filtration Rate, HOMA-IR: homeostatic model assessment of insulin resistance, HOMA-%□ : homeostatic model assessment of □ cells functions, HOMA-%S: homeostatic model assessment of insulin sensitivity. Insulin resistance is defined as having a HOMA1-IR higher than the 75th percentile here equal to 2.408.

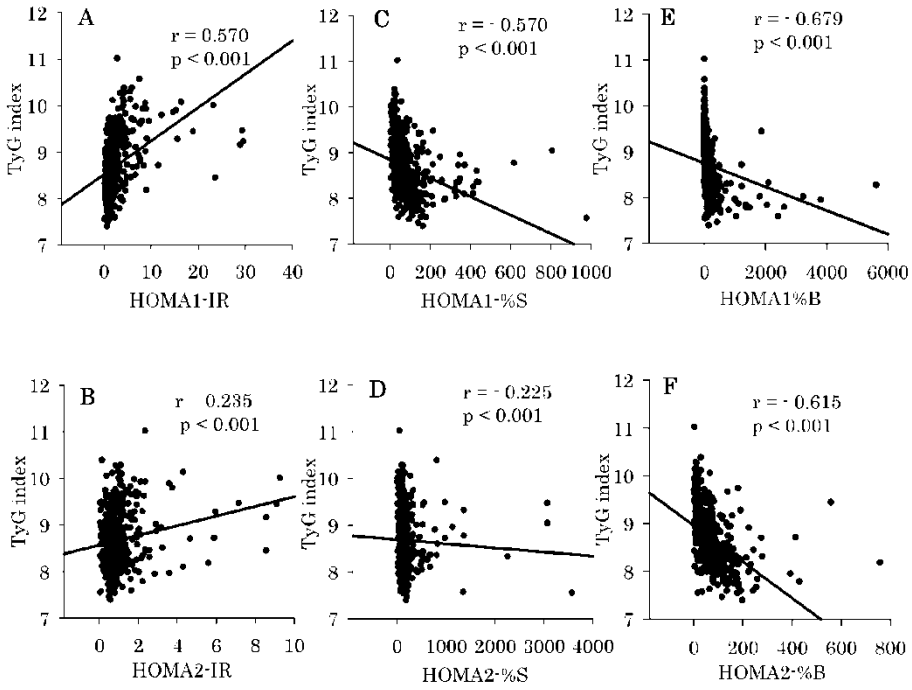

Figure 1. TyG index profile in the HOMA model

3.3. Insulin Resistance Profile

IR is associated with significantly elevated levels of BMI (p<0.01), waist circumference (p<0.01), blood glucose (p<0.001), TC (p<0.001), HDL-C (p<0.001), LDL-C (p<0.05), TG (p<0.001), and serum insulin (Table 4)

3.4. Association between TyG Index and Type 2 Diabetes Risk Factors

The TyG index displayed a positive correlation with HOMA1-IR (Figure 1A, r = 0.570, p<0.001) and HOMA2-IR (Figure 1B, r = 0.235, p<0.001), indicating a simultaneous increase in the TyG index with the level of insulin resistance according to the HOMA models. Moreover, significant associations were found between the TyG index and HOMA1-%S (Figure 1C, r = -0.570, p<0.001), HOMA2-%S (Figure 1D, r = -0.225, p<0.001), HOMA1-%β (Fig. 1E, r = -0.679, p<0.001), and HOMA2-%β (Figure 1F, r = -0.615, p<0.001), all serving as indicators of beta cell function and insulin sensitivity (Figure 1). Furthermore, a significant elevation in the TyG index was observed in subjects with prediabetes (p<0.01), type T2D (p<0.001), and risk factors for T2D, including visceral obesity (p<0.001), age above 45 years (p<0.001), family history of diabetes (p<0.001), and hypertension (p<0.01) (Figure 2).

The figure illustrates the TyG index profile within the HOMA model, showcasing the correlation between TyG

and various components. The correlation coefficient (r) is depicted, with TyG referring to the triglycerides-glucose index, HOMA-IR representing the homeostatic model assessment of insulin resistance, HOMA-%B denoting homeostatic model assessment of beta cell functions, and HOMA-%S indicating homeostatic model assessment of insulin sensitivity. The TyG index exhibits correlations with HOMA1-IR (A), HOMA2-IR (B), HOMA1-%S (C), HOMA2-%S (D), HOMA1-%β (E), and HOMA2-%β (F), as visually represented in the corresponding subfigures.

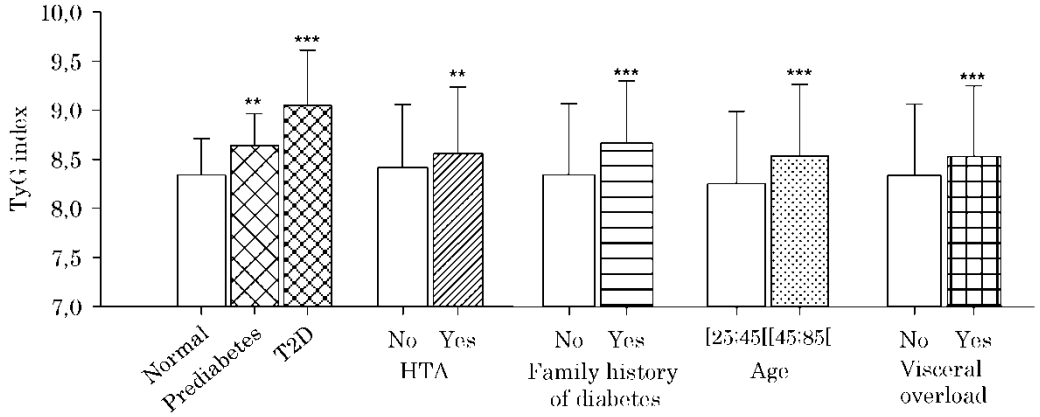

Figure 2. TyG index profile in the HOMA model

The TyG index levels were analyzed according to T2D risk factors. **: p<0.01; ***: p<0.001, T2D: Type 2 Diabetes, HTA: Arterial hypertension, TyG: triglycerides-glucose index

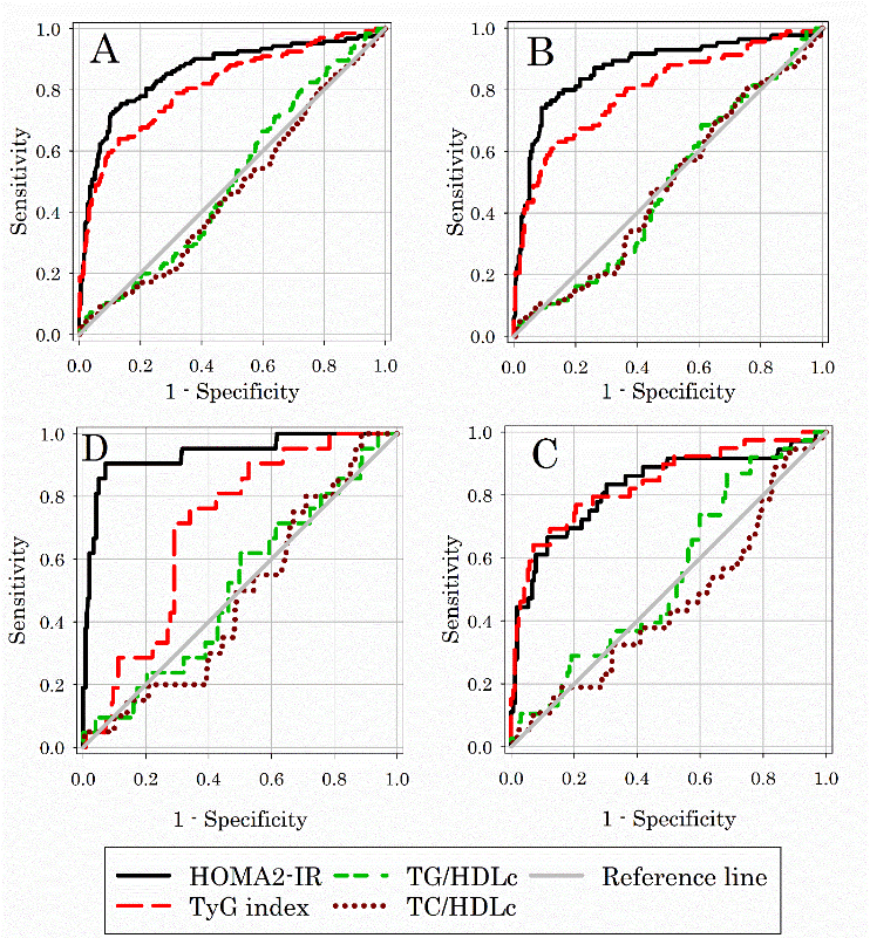

Figure 3. ROC curve of markers for insulin resistance in the Beninese population

ROC curve analysis of insulin resistance markers in the Beninese population is presented. The markers include TyG (triglycerides-glucose index), TC (Total Cholesterol), HDL-C (high-density lipoprotein cholesterol), and TG (triglycerides). The performance of TyG index, HOMA2-IR, TG/HDL-C ratio, and TC/HDL-C ratio as insulin resistance markers were assessed across the general population (A), women (B), men (C), and subjects with fasting blood glucose levels below 1g/L (D).

Table 5. TyG index profile in the HOMA model

	AUC (95% CI)	Cutoff value	Sensitivity % (95% CI)	Specificity % (95% CI)	p-value
General population					
TyG	0.82 (0.77 – 0.86)	8.67	81.20 (73.52 - 87.45)	62.07 (56.96 - 66.99)	<0.001
HOMA2-IR	0.86 (0.82 – 0.90)	0.81	81.15 (73.07 - 87.66)	76.50 (71.82 - 80.75)	<0.001
TG/HDL-C	0.51 (0.45 – 0.56)	2.04	53.60 (44.46 - 62.56)	48.46 (43.17 - 53.78)	0.83
TC/HDL-C	0.47 (0.41 – 0.53)	3.29	50.00 (40.81 - 59.19)	46.80 (41.43 - 52.23)	0.38
Female					
TyG	0.80 (0.74 – 0.86)	8.67	81.52 (72.07 - 88.85)	60.19 (53.16 - 66.93)	<0.001
HOMA2-IR	0.87 (0.82 – 0.92)	0.83	83.53 (73.91 - 90.69)	78.50 (72.15 - 83.98)	<0.001
TG/HDL-C	0.49 (0.41 – 0.56)	2.04	55.81 (44.70 - 66.52)	47.42 (40.23 - 54.70)	0.72
TC/HDL-C	0.48 (0.41 – 0.56)	3.29	53.57 (42.35 - 64.53)	48.13 (40.78 - 55.54)	0.69
Male					
TyG	0.84 (0.76 – 0.92)	8.65	82.05 (66.47 - 92.46)	62.35 (54.61 - 69.66)	<0.001
HOMA2-IR	0.82 (0.74 – 0.91)	0.73	80.56 (63.98 - 91.81)	70.91 (63.34 - 77.71)	<0.001
TG/HDL-C	0.54 (0.45 – 0.64)	1.94	52.63 (35.82 - 69.02)	47.53 (39.64 - 55.51	0.40
TC/HDL-C	0.45 (0.35 – 0.56)	3.19	48.65 (31.92 - 65.60)	40.38 (32.61 - 48.53)	0.39
Subject with blood glucose < 1					
TyG	0.70 (0.77 – 0.86)	8.44	81.01 (58.09 - 94.55	58.02 (51.17 - 63.99)	0.001
HOMA2-IR	0.94 (0.82 – 0.90)	1.02	90.48 (69.62 - 98.83	87.39 (82.50 - 91.33)	<0.001
TG/HDL-C	0.51 (0.45 – 0.56)	2.23	57.14 (34.02 - 78.18	50.22 (43.59 - 56.84	0.88
TC/HDL-C	0.48 (0.41 – 0.53)	3.43	50.00 (27.20 - 72.80)	45.70 (39.00 - 52.52)	0.76

AUC: Area Under the Curve,CI: Confidence Interval, TyG: Triglycerides-Glucose index, HOMA-IR: homeostatic model assessment of insulin resistance, TC: Total Cholesterol, HDL-C: high-density lipoprotein cholesterol, TG: triglycerides.

3.5. Assessment of the TyG Index in Type 2 Diabetes Risk Prediction

The Area Under the Curve (AUC) for both HOMA2-IR and the TyG index was statistically significant ($p<0.001$). These indices demonstrated comparable efficiency ($p>0.05$) in excellently discriminating the state of IR according to the HOMA1 model across the entire participant population (Figure 3A), among women (Figure 3B), and among men (Figure 3C), as evidenced by their overlapping 95% confidence intervals (Table 5)On subjects with fasting blood glucose levels below 1g/L, HOMA2-IR appeared to be more effective than TyG index in discriminating IR (Figure 3D). However, TyG index still displayed good discrimination ability in these individuals (Table 5). Conversely, the TG/HDL-C and TC/HDL-C ratios exhibited poor efficiency in detecting IR in the aforementioned cases (Figure 3D). The optimal threshold values for IR identified on the ROC curve are presented in Table 5.

As a marker of IR (TyG index > 8.67), the TyG index displayed a robust positive association with T2D (Table 6). A TyG index exceeding 8.67 increased the odds of T2D by approximately twelve times. This relationship resembled that observed between T2D and IR according to the HOMA1-IR model, as indicated by their overlapping 95% confidence intervals (6.23 – 22.93 for HOMA1-IR and 7.98 – 16.92 for TyG index). Similarly, a TyG index > 8.67 raised the odds of prediabetes by over three times within the study population (Table 6).

Table 6. Type 2 diabetes risk factors

	IR (TyG > 8.67)		
	OR	95% CI	p-value
T2D	11.62	7.98 – 16.92	<0.001
Prediabetes	3.13	1.71 – 5.75	<0.001

IR: insulin resistance, OR: Odd ratio, CI: Confidence Interval, TyG: Triglycerides-glucose index, T2D: Type 2 Diabetes. This table illustrates the association between IR detected with the TyG index and T2D as well as prediabetes.

4. Discussion

The present study examined the predictive potential of the TyG index for T2D within the Beninese population to identify individuals at high risk of developing T2D at an early stage. It demonstrated a positive association between T2D and risk factors such as age (from 45 years onwards), metabolic syndrome, sedentary lifestyle, family history of diabetes, low educational level, overweight, visceral obesity, hypertension, and IR. Age is a determining factor in the onset of IR, which is caused by progressive impairment of insulin secretion, action, and glucose clearance, and is associated with worsening glucose tolerance with advancing age [29].

This study revealed that IR is characterized by elevated levels of BMI, waist circumference, fasting blood glucose, TC, HDL-C, LDL-C, TG, and serum insulin levels. These findings corroborate the results reported by Sossa et al. in 2015 [30]. Our results show that in apparently healthy subjects, fasting blood glucose levels within the overlapping range (1.10 – 1.25 g/L), as well as elevated levels of HOMA-IR (homeostatic model assessment of IR) and low indices of beta cell function and insulin sensitivity, are associated with prediabetes. This profile indicates a reduction in metabolic responses to the insulin signal, with impaired fatty acid oxidation, further emphasizing the role of IR in the development and progression of T2D [29]. TG levels in the liver and muscle cells are major determinants of IR, confirming the importance of TG in IR and progression to T2D [16,31].

The biochemical markers characteristic of T2D that emerge from our study are elevated levels of HDL-C, TG, total proteins, and HOMA-IR indices, as well as low HOMA-%β and HOMA-%S indices. Analyzing these markers according to the stratification of diabetes status into subjects without diabetes, subjects with prediabetes, and subjects with T2D confirms the progressive nature of diabetes, which often passes through a prediabetic stage.

The HOMA1-IR model was the first to be validated for assessing IR [8]. Subsequently, the HOMA2-IR model was developed, offering a more precise representation of the metabolic process by modeling the feedback relationship between insulin and glucose in various organs of the body [9]. However, the determination of these IR indices, whether the older model (HOMA1-IR) or the newer model (HOMA2-IR), relies on blood glucose and insulin levels. Therefore, the use of a serum insulin test is limited due to its high cost and the need for it to be conducted in primary healthcare centers, which also limits accessibility to the HOMA model.

In recent years, the TyG index has garnered significant attention. However, the precise mechanisms underlying its association with diabetes are not yet fully elucidated. The TyG index has been recognized as a dependable marker of IR, a pivotal factor in the development of glucose intolerance and diabetes mellitus. IR occurs when the body's cells become less responsive to insulin, resulting in elevated levels of glucose and lipids in the bloodstream. Its calculation relies solely on fasting levels of TG and glucose, both of which reflect IR and are routine tests conducted in primary healthcare center laboratories in Benin. Consequently, the TyG index can serve as a valuable tool for assessing IR in healthcare facilities in developing countries [31]. In contemporary times, the TyG index is widely employed for detecting IR and related conditions in numerous countries.

This study demonstrates a significant correlation between the TyG index and HOMA models in the Beninese population. A similar result was reported in the Indonesian population by Aman et al. in 2021, in subjects with T2D in the Indian population by Selvi et al., 2021, and in the Korean population by Yoon et al. in 2022 [23,32,33]. The positive correlation between the TyG index and fasting glucose aligns with the findings reported by Yoon et al. in 2022, who also demonstrated a positive correlation with glycated hemoglobin levels [23]

The TyG index shows similar efficiency to the HOMA2-IR model in discriminating IR compared to the HOMA1-IR model in the Beninese population, with overlapping 95% confidence intervals. The area under the curve presented by the TyG index for detecting IR in this study population is satisfactory and similar to that reported by Aman et al. in 2021, with overlapping 95% confidence intervals. Moreover, it is slightly higher than that reported for predicting T2D by Chamroonkiadtikun et al. in 2020 in a prospective cohort study. Yoon et al. reported in 2022 a better efficiency of the TyG index compared to HOMA-IR in identifying subjects with T2D.

The optimal threshold identified for detecting IR in the Beninese population with the TyG index differs from that identified in the Indonesian population. It is important to note that the detection thresholds for IR vary across studies, limiting their comparability. The highest sensitivity obtained was 96% with the HIEC model, while the highest specificity was 99% with the HOMA-IR model. However, a TyG index value above the threshold identified on the ROC curve for this population is more associated with T2D than in the study conducted by Aman et al. in 2021. Nevertheless, our study shows that the relationship between IR and T2D does not vary depending on the marker used to detect IR (HOMA1-IR or TyG index).

Due to its strong association with IR, beta cell function decline, and diabetes risk factors, the TyG index proves to be effective in identifying individuals potentially at risk of developing T2D. Currently, it is reported that the TyG index can detect IR-related diseases even more effectively than HOMA-IR [22,23]. In adults, the TyG index has been found useful in detecting T2D development and evaluating glycemic control in T2D patients. In Korea, it has been established that a TyG index above the threshold of 8.31 increases the risk of T2D nearly sevenfold in subjects with fasting blood glucose below 1 g/L [23]. In the same population, a TyG index above 8.80 in individuals with obesity is associated with the onset of T2D [23]. These findings align with the association between the tyG index, prediabetes, and T2D observed in our population.

Our study also shows that the TG/HDL-C and TC/HDL-C ratios do not discriminate IR in the Beninese population. These results are consistent with the work of Sossa et al. in 2015 on the inability of the TG/HDL-C ratio to detect IR, while they diverge from the results reported by Sossa et al. in 2015 on the ability of the TC/HDL-C ratio to detect IR [30].

In studies on the diagnostic efficiency of the TyG index for detecting IR, HOMA1-IR has served as the reference. However, HOMA2-IR has the disadvantage of having only one acceptable value range for calculation. Additionally, there are no stable reference values for HOMA-IR in IR detection in the literature. In this study, we adopted the 75th percentile as the threshold value for HOMA1-IR. This threshold is lower than the one obtained by Sossa et al. in 2015 when evaluating the prediction of IR by lipoprotein ratios in adults [30]. We also identified a threshold value of 0.81 for detecting IR with HOMA2-IR. This diagnostic threshold is lower than the value reported by the Brazilian study on the metabolic syndrome (BRAMS), which suggested a value of 1.8 for detecting IR [34]. These differences highlight the need to standardize diagnostic thresholds for more precision and comparability in studies on IR and T2D.

5. Study Limitations

While this study provides valuable insights into the predictive potential of the TyG index for T2D in the Beninese population, the sample size might be limited. A larger sample could provide more robust statistical power and enhance the generalizability of the findings to a broader population. This study primarily relies on cross-sectional data, which can capture associations and correlations but does not establish causality. Longitudinal studies tracking individuals over time would provide a clearer understanding of how the TyG index evolves and its role in predicting T2D development. We acknowledge variations in the detection thresholds for IR and T2D across different research studies. This lack of standardization makes it challenging to directly compare findings between studies and underscores the need for consistent diagnostic thresholds. Our study primarily focuses on assessing the diagnostic efficiency of the TyG index and its association with IR and T2D. Interventional studies exploring whether the TyG index can be used to guide preventive measures or interventions for T2D are not covered. Also, cross-sectional studies like this one are susceptible to selection bias, as participants may not be representative of the entire population. Efforts to minimize bias and enhance the representativeness of the sample should be considered in future research. In summary, while this study contributes significantly to our understanding of the TyG index's predictive potential for T2D in the Beninese population, it is essential to recognize these limitations for a comprehensive assessment of its findings and implications.

6. Conclusion

This study focused on evaluating the diagnostic potential of the TyG index in predicting T2D and assessing IR within the Beninese population. The findings provide valuable insights into the early identification of individuals at high risk of developing T2D and understanding the intricate relationships between metabolic health, IR, and diabetes risk factors. These findings underscore the importance of considering these factors in diabetes prevention and management strategies in the Beninese population. These results contribute to the growing body of evidence supporting the TyG index's utility as a practical and cost-effective tool for assessing IR and identifying individuals at risk of T2D.

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References

[1] Organisation Mondiale de la Santé. *Rapport sur le diabète.* Genève; 2016. 88 p.

[2] International Diabetes Federation. *The global picture. In: IDF Diabetes Atlas*. 10th ed. Brussels: IDF; 2021. p. 30–63.

[3] International Diabetes Federation. *Diabetes by region. In: IDF Diabetes Atlas 10th edition*. 10th ed. Brussels: IDF; 2021. p. 72–101.

[4] Organisation Mondiale de la Santé. *Profils des pays pour le diabète*. 1st ed. 2016; Available from: http://www.who.int/diabetes/country-profiles/ben_fr.pdf

[5] International Diabetes Federation. *What is diabetes? In: IDF Diabetes Atlas*. 10th ed. Brussels: IDF; 2021. p. 10–9.

[6] Wu Y, Ding Y, Tanaka Y, Zhang W. Risk Factors Contributing to Type 2 Diabetes and Recent Advances in the Treatment and Prevention. *Int J Med Sci*. 2014;11[11]: 1185–200.

[7] Punthakee Z, Goldenberg R, Katz P. Definition, Classification and Diagnosis of Diabetes, Prediabetes and Metabolic Syndrome. *Canadian Journal of Diabetes*. 2018; 42:S10–5.

[8] Levy JC, Matthews DR, Hermans MP. Correct homeostasis model assessment (HOMA) evaluation uses the computer program. *Diabetes Care*. 1998;21[12]: 2191–2.

[9] Wallace TM, Levy JC, Matthews DR. Use and abuse of HOMA modeling. *Diabetes Care*. 2004;27[6]: 1487–95.

[10] Chamroonkiadtikun P, Ananchaisarp T, Wanichanon W. The triglyceride-glucose index, a predictor of type 2 diabetes development: A retrospective cohort study. *Primary Care Diabetes*. 2020;14[2]: 161–7.

[11] Simental-Mendía LE, Rodríguez-Morán M, Guerrero-Romero F. The Product of Fasting Glucose and Triglycerides As Surrogate for Identifying Insulin Resistance in Apparently Healthy Subjects. *Metabolic Syndrome and Related Disorders*. 2008;6[4]: 299–304.

[12] Zhang Y, Ding X, Hua B, Liu Q, Gao H, Chen H, et al. Predictive effect of triglyceride‐glucose index on clinical events in patients with type 2 diabetes mellitus and acute myocardial infarction: results from an observational cohort study in China. *Cardiovascular Diabetology*. 2021 Feb 11; 20[1]: 43.

[13] Guerrero-Romero F, Simental-Mendía LE, González-Ortiz M, Martínez-Abundis E, Ramos-Zavala MG, Hernández-González SO, et al. The Product of Triglycerides and Glucose, a Simple Measure of Insulin Sensitivity. Comparison with the Euglycemic-Hyperinsulinemic Clamp. *The Journal of Clinical Endocrinology & Metabolism*. 2010; 95[7]: 3347–51.

[14] Warram JH, Martin BC, Krolewski AS, Soeldner JS, Kahn CR. Slow glucose removal rate and hyperinsulinemia precede the development of type II diabetes in the offspring of diabetic parents. *Ann Intern Med*. 1990; 113[12]: 909–15.

[15] DeFronzo RA. From the Triumvirate to the Ominous Octet: A New Paradigm for the Treatment of Type 2 Diabetes Mellitus. *Diabetes*. 2009; 58[4]: 773–95.

[16] Lee DY, Lee ES, Kim JH, Park SE, Park CY, Oh KW, et al. Predictive Value of Triglyceride Glucose Index for the Risk of Incident Diabetes: A 4-Year Retrospective Longitudinal Study. *PLoS One*. 2016; 11[9]: e0163465.

[17] Ormazabal V, Nair S, Elfeky O, Aguayo C, Salomon C, Zuñiga FA. Association between insulin resistance and the development of cardiovascular disease. *Cardiovasc Diabetol*. 2018; 17: 122.

[18] Campos Muñiz C, León-García PE, Serrato Diaz A, Hernández-Pérez E. Diabetes mellitus prediction based on the triglyceride and glucose index. *Med Clin (Barc)*. 2023; 160[6]: 231–6.

[19] Navarro-González D, Sánchez-Íñigo L, Pastrana-Delgado J, Fernández-Montero A, Martinez JA. Triglyceride–glucose index (TyG index) in comparison with fasting plasma glucose improved diabetes prediction in patients with normal fasting glucose: The Vascular-Metabolic CUN cohort. *Preventive Medicine*. 2016; 86: 99–105.

[20] Zheng S, Shi S, Ren X, Han T, Li Y, Chen Y, et al. Triglyceride glucose-waist circumference, a novel and effective predictor of diabetes in first-degree relatives of type 2 diabetes patients: cross-sectional and prospective cohort study. *Journal of Translational Medicine*. 2016; 14[1]: 260.

[21] da Silva A, Caldas APS, Rocha DMUP, Bressan J. Triglyceride-glucose index predicts independently type 2 diabetes mellitus risk: A systematic review and meta-analysis of cohort studies. *Primary Care Diabetes*. 2020; 14[6]: 584–93.

[22] Park HM, Lee HS, Lee YJ, Lee JH. The triglyceride–glucose index is a more powerful surrogate marker for predicting the prevalence and incidence of type 2 diabetes mellitus than the homeostatic model assessment of insulin resistance. *Diabetes Research and Clinical Practice*. 2021; 180: 109042.

[23] Yoon JS, Lee HJ, Jeong HR, Shim YS, Kang MJ, Hwang IT. Triglyceride glucose index is superior biomarker for predicting type 2 diabetes mellitus in children and adolescents. *Endocr J.* 2022; 69[5]: 559–65.

[24] Dagnelie P. *Statistique théorique et appliquée. Statistique descriptive et bases de l'inférence statistique*, tome 1. Paris: De Boeck; 1998. 508 p.

[25] The oxford Center for Diabetes, *Endocrinology, and Metabolism DTU. HOMA2 Calculator* [Internet]. [cited 2023 Jan 20]. Available from: https://www.dtu.ox.ac.uk/homacalculator/

[26] Placzkowska S, Pawlik−Sobecka L, Kokot I, Piwowar A. Indirect insulin resistance detection: Current clinical trends and laboratory limitations. *Biomed Pap Med*. 2019; 163: 187−199.

[27] Simental−Mendía LE, Rodríguez−Morán M, Guerrero−Romero F. The Product of Fasting Glucose and Triglycerides As Surrogate for Identifying Insulin Resistance in Apparently Healthy Subjects. *Relat Disord.* 2008; 6: 299−304.

[28] International Diabetes Federation. *IDF Diabetes Atlas*. 10th ed. Brussels: IDF; 2021. 141 p. Available from: www.diabetesatlas.org.

[29] Basu R, Breda E, Oberg AL, Powell CC, Dalla Man C, Basu A, et al. Mechanisms of the Age-Associated Deterioration in Glucose Tolerance: Contribution of Alterations in Insulin Secretion, Action, and Clearance. *Diabetes*. 2003; 52[7]: 1738–48.

[30] Sossa C, Agueh V, Saizonou J, Moussiliou PN, Kpozehouen A, Makoutode M, et al. Prédiction de l'insulino-résistance par les ratios de lipoprotéines chez les adultes béninois. *International Journal of Biological and Chemical Sciences*. 2015; 9[3]: 1319–29.

[31] Lee SH, Park SY, Choi CS. Insulin Resistance: From Mechanisms to Therapeutic Strategies. *Diabetes Metab J*. 2022; 46[1]: 15–37.

[32] Aman M, Resnawita D, Rasyid H, Kasim H, Bakri S, Umar H, et al. The concordance of triglyceride glucose index (TyG index) and homeostatic model assessment for insulin resistance (Homa-IR) in non-diabetic subjects of adult Indonesian males. *Clinical Epidemiology and Global Health*. 2021; 9: 227–30.

[33] Selvi NMK, Nandhini S, Sakthivadivel V, Lokesh S, Srinivasan AR, Sumathi S. Association of Triglyceride-Glucose Index (TyG index) with HbA1c and Insulin Resistance in Type 2 Diabetes Mellitus. *Maedica (Bucur)*. 2021; 16[3]: 375–81.

[34] Geloneze B, Vasques ACJ, Stabe CFC, Pareja JC, Rosado LEFP de L, Queiroz EC de, et al. HOMA1-IR and HOMA2-IR indexes in identifying insulin resistance and metabolic syndrome: Brazilian Metabolic Syndrome Study (BRAMS). *Arq Bras Endocrinol Metab*. 2009 Mar; 53: 281–7.