

Diagnostic Performance of the TG/HDL-C Ratio in the Prediction of Insulin Resistance in Brazzaville, Republic of Congo

Reine Freudlendrich Eboka-Loumingou Sakou¹, Benjamin Longo-Mbenza^{2,5,6},
Guenole Guie¹, Albert Mûnka Nkalla-Lambi³, Etienne Mokondjimobe⁴,
José Simo Louokdom¹, Henry Germain Monabeka⁴, Herve Alex Tukadila⁵,
Alexis Dockekias Elira¹, Ange Antoine Abena¹, Aliocha Nkodila Natuhoyila⁵,
Donatien Moukassa⁴

¹National Laboratory of Public Health, Brazzaville, Republic of Congo, Faculty of Health Sciences, Marien Ngouabi University. Brazzaville, Republic of Congo,

²Department of Internal Medicine, University of Kinshasa, Democratic Republic of Congo,

³Leyono Municipal Clinic, Brazzaville, Republic of Congo

⁴Faculty of Health Sciences, Marien Ngouabi University. Brazzaville, Republic of Congo, Hospital and University Center. Brazzaville, Republic of Congo,

⁵Lomo University of research, Kinshasa, Democratic republic of Congo,

⁶Faculty of Health Sciences, Walter Sisulu University. Mthatha, South Africa,

Corresponding Author: Benjamin Longo-Mbenza

ABSTRACT

Insulin resistance (IR) is an excellent predictor of type 2 diabetes mellitus, its measure is a key approach to prevent the development of cardiometabolic diseases. Recent studies suggest that the triglyceride-to-high-density lipoprotein ratio is a biomarker for predicting insulin resistance.

The objective of this study was to assess the diagnostic performance of the TG/HDL-C ratio compared to the HOMA-IR score in insulin resistance in Brazzaville, Republic of Congo. A cross-sectional study was conducted with 500 participants at least 18 years of age apparently healthy in a population of Brussels, Republic of Congo. Insulin resistance was defined by the evaluation of the insulin resistance homeostasis model (HOMA-IR - 2.5). Univariate/ROC and multivariate/logistical regression analyses were used respectively to obtain diagnostic performance of insulin resistance.

The prevalence of insulin resistance was 28% (n=140). There was a positive and significant correlation (p<0.0001) between HOMA-IR and the TG/HDL-C ratio. The optimal threshold value of the TG/HDL-C ratio was 2.5 with a sensitivity of 0.85 [95% CI- 0.81-0.89] and a specificity of 0.73 [95% CI-0.65-0.80]. The area under the curve (AUC) was 0.79 [95% CI- 0.74-0.83] (Model 1). After multiple logistic regression and adjustment for sex, age, waist circumference, hip circumference alone the TG/HDL-C ratio - 2.5 and BMI - 30 Kg/m² were the independent determinants of insulin resistance (HOMA-IR - 2.5). The TG/HDL-C ratio of 2.5 can be considered a simple and accurate substitute biomarker in the diagnosis of insulin resistance in Congolese adults.

Keywords: prediction, insulin resistance, HOMA-IR, TG/HDL-C, Brazzaville.

INTRODUCTION

The diabetes mellitus (DM) epidemic is a growing economic and social challenge that therapeutic, pharmacological, nutritional, biological and patient management strategies are trying to curb. [1]

More than six million diabetics are discovered each in the world. [1] According to estimates by the International Diabetes Federation (IDF), nearly half a billion (or 451 million) adults aged 18 to 99 worldwide suffer from DM and low- and middle-

income countries bear almost 80% of the burden. [2] With cardiovascular disease, cancer and chronic respiratory disease, DM accounts for more than 80% of all premature deaths from non communicable diseases (NCDs). [3]

Diabetes has been considered a major public health problem in recent years and the term epidemic is increasingly being applied to type 2 diabetes (T2D), which accounts for about 90% of all diabetes mellitus. [4,5] The pathogenesis of T2D involves an abnormality of insulin secretion, an increase in liver glucose production and insulin resistance of peripheral muscle and adipose tissues. [5] The exact mechanism of insulin resistance (IR) is multifactorial and has not been established accurately, but factors such as metabolic syndrome (Smet), obesity, dyslipidemia and hyperinsulinemia have been implicated. [6,7] IR is a key risk factor for the development of DM2 and metabolic syndrome (Smet) in adults and even children. [8-12] Therefore its measure is crucial for early intervention and primary prevention of the development of cardiometabolic diseases.

Reference methods designed to measure insulin resistance, such as hyperinsulinemic-euglycemia clamp and intravenous glucose tolerance (FSTGT) test, can only be performed in specialized centres. [13,14] Nevertheless, there are simple methods such as the Whole Body Insulin Sensitivity Index (WBISI), the evaluation of the insulin resistance homeostasis model (HOMA-IR) and several other indexes proposed to date present limitations related to their low reproducibility and reliability. [12-15] It is therefore necessary to have other standard, clinically easy-to-implement standard diagnostic measures that provide good accuracy and are inexpensive to predict IR. Because triglycerides (TG) and high-density protein cholesterol (HDL-C) are directly involved in IR, [16-19] the TG/HD-C ratio is closely related to IR, as first reported by McLaughlin et al. [20] Subsequently, several studies have recommended the use of the TG/HD-C ratio

as a simple and efficient biomarker of IR. [7,12,19,21-28] Although the ratio was assessed as a predictor of IR, some studies have found ethno-racial differences. [11,21,23,24,29-33]

To our knowledge, no studies have reported the prediction of IR using the TG/HDL-C ratio in Congolese adults living in Brazzaville. It is with this in mind that we proposed to carry out this study, the objective of which was to evaluate the diagnostic performance of the TG/HDL-C ratio in IR with and without Smet in apparently healthy Congolese adults.

PARTICIPANTS AND METHODS

Type and Study Period

This was an analytical cross-sectional study that ran from February 14 to May 22, 2019.

Study Framework

This study was conducted in the city of BZ/RC. The city of Brazzaville has a multi-ethnic population estimated at 1,838,348 at present. [34] It is divided into 9 boroughs (Makélékélé, Bacongo, Poto-poto, Mougali, Ouenze, Talangai, Mfilou, Ndjiri and Madibou). The biological examinations were carried out at the National Reference Centre of the Drepanocytosis Antoinette SASSOU N'GUESSO in Brazzaville, Republic of Congo.

Study Population

The study population was a probabilistic sample from the general and eligible population of the city of Brazzaville according to the logigram (Figure1). Participants were recruited from Catholic churches in the city of Brazzaville.

The selection criteria required for inclusion (anyone at least 18 years old who have lived in Brazzaville for at least 10 years, with informed consent) and for exclusion (all participants under the age of 20, a known DM, pregnancy, HIV/AIDS, kidney failure, stroke, ischemic heart disease, heart failure, hemoglobinopathy and all participants on hypolipidemic therapy, thyroid hormones, oral contraceptives).

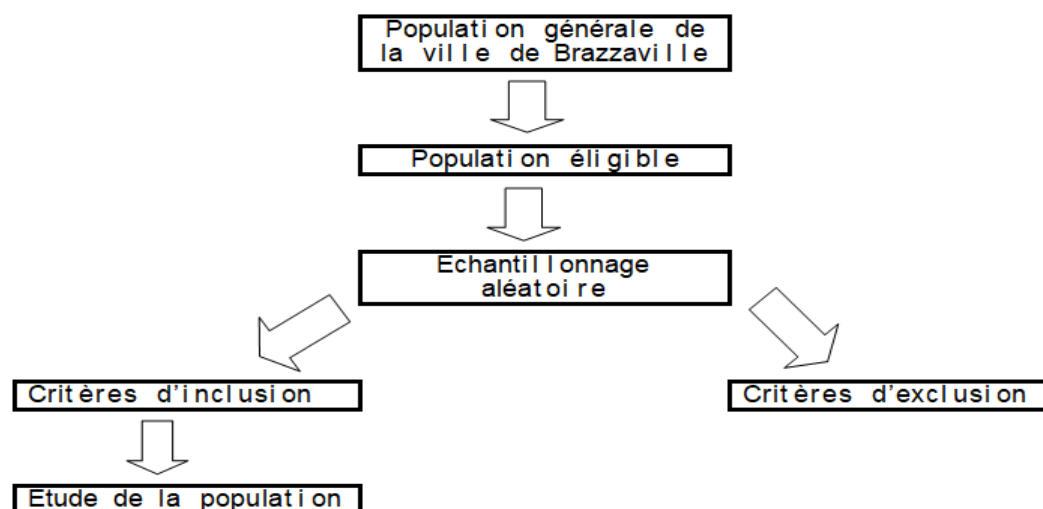


Figure 1: study logigram

Sample size

Random sample size was calculated using the following formula:

$$n_i = \frac{(z)^2 \times p(q)}{(d)^2}$$

Z-parameter related to statistical risk of admitted error-1.96 for a 0.05% error risk
 q- assumed proportion of the target population not having the problem (q-1-p)
 p Expected prevalence for IR from a recent known prevalence of absolute accuracy-0.05
 Given that the prevalence of IR in the city of Brazzaville has never been studied, it is considered that p-0.50 and q-0.50.

$$n_i = \frac{(1,96)^2 \times (0,50)(0,50)}{(0,05)^2} = 384 \approx 4$$

We add 25% possible loss which makes a total of 500 participants included. Thus 50 participants randomly drawn from lists from the 9 boroughs and the administrative center of the city of Brazzaville.

Methods

Variable Methods of Interest

Demographic characteristics including gender, age, height, weight, waist circumference and hip circumference were collected. Participants' measurements were obtained according to STEP criteria. [35] The size (cm) was measured using a vertical toise (type SECA 220) to the nearest half centimeter. Weight was measured using an electronic scale (type SECA 762), with an

accuracy of 0.1 kg. The hip circumference and waist circumference were measured at about 0.1 cm at the end of minimal breathing using a flexible tape meter graded to the millimetre at the top of the iliac crest. The body mass index (BMI) was calculated by dividing an individual's weight by the square of his height (kg/m²). [36] Participants were divided according to BMI into underweight, normal weight, overweight and obese. [36] Blood pressure values were obtained using an electronic type blood pressure monitor (OMRON M3 Comfort) after participants rested for at least 15 minutes in a sitting position. Systolic and diastolic pressure values have been replicated three times in a row to have blood pressure values.

Blood samples and treatment of blood samples

Blood samples were taken after at least 8 hours of fasting by antecubital venous puncture in Vacutainer tubes. All samples were taken between 7 a.m. and 10 a.m. The samples were sent to the biochemistry laboratory. Plasma and serum were collected after low-speed centrifugation at 3000 laps at 4°C for 15 minutes and analyzed on the day of the samples. Insulin was analyzed using a COBAS e411 (Roche Diagnostics, Mannheim, Germany) [37] using the immunochemistry method with a detection interval of between 0.200-1000 U/mL. Glucose, total cholesterol (CT),

triacylglycerols (TG), high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) were measured enzymatically by the color method using Cypress kits, Spain using a KE-type spectrophotometer. To ensure the accuracy of the calibration, three reference pools were analyzed on both the Cobas e411 and the spectrophotometer. These tests were calibrated according to the surgical procedures. The quality control procedures recommended by manufacturers for all biochemical tests were followed throughout the study. Total cholesterol levels greater than 5.2 mmol/l, LDL greater than 2.6 mmol/l and triglycerides above 1.7 mmol/l were considered high, while HDL concentrations below 1.04 mmol/l were considered low. Blood glucose and insulin were used to calculate HOMA-IR according to the following formula $[\text{Insulin (M)/L} - \text{Glycemia (mmol/L)} / 22.5]$.^[14] The reference method used in this study was HOMA-IR - 2.5.^[20] The standards of the other parameters were those proposed by.^[38]

Statistical analyses

Quantitative variables were expressed on average deviation - type, these averages were compared with student's t test. For qualitative variables, frequencies (n) and proportions (%) have been calculated. These frequencies were compared with Pearson's Chi square test. Univariate and multivariate logistic regression analyses were used to obtain the probability of insulin resistance (HOMA-IR - 2.5). Following the multivariate logistic regression, a step-by-step selection procedure in accordance with Akaike's (AIC) information criteria was used to select the optimal model (Model 2). The area below the curve of this model was compared to that consisting solely of the TG/HDL-C ratio (Model 1) using the DeLong test. Subsequently, the analysis of the function characteristics of the receptor (ROC) was carried out to assess the area under the curve (ASC) thus the ability of the

TG/HDL-C ratio to properly discriminate against false and real insulin-resistant subjects and the tG/HDL-C ratio threshold in the diagnosis of insulin resistance. The diagnostic characteristics of this threshold (sensitivity, specificity, positive predictive value, negative predictive value) were assessed in the general population. The statistical analysis was carried out using the R software (Core Team) version 3.5.3. All of these tests were done at the threshold of 0.05.

Ethical Consideration

All patients gave their consent after receiving explanations of the purpose of the work. The study protocol was approved by the Health Sciences Research Ethics Committee (CERSSA). Confidentiality of the information collected was respected and the results were provided individually to participants.

RESULTS

The descriptive study (demographic, clinical and biological characteristics of participants), the determinants of IR, the optimal threshold value of the TG/HDL-C ratio to predict insulin resistance were classified by HOMA-IR using a threshold value of 2.5.

Demographic and clinical characteristics of participants according to HOMA-IR

A total of 500 participants constituted this study, of which 45% (n=225) men and 55% (n=275) women: sex ratio of 0.82 close to 1 man: 1 woman. The average age of the study population was normally distributed from 47.4-13.7 years, with a median at 47 years, and from the extremes of 18 and 80 years, the interquartile was 37-57 years. There were no significant differences (P-0.05) between sex, age, blood pressure and HOMA-IR (Table 1).

Participants' anthropometric characteristics by HOMA-IR

Body mass index, waist circumference, hip circumference and waist-to-hip ratio were significantly higher in the high HOMA-IR group (p-0.05) (Table 2).

Biological characteristics of participants according to HOMA-IR

In this study averages of blood glucose, triglycerides, insulin, LDL-C and TG/HDL-C ratio were significantly higher (p<0.001) in the high HOMA-IR group. The odds ratios and confidence intervals associated with these variables as a result of a univariate logistic regression were represented in Table 3. In contrast to the HDL-C average which was significantly low (Table 3).

Correlations between HOMA-IR and study variables

A correlation analysis of anthropometric, biological and HOMA-IR variables. There is a negative and significant correlation between HOMA-IR and HDL Cholesterol. On the other hand, positive and significant correlations were observed between HOMA-IR and other variables (P -0.0001), but the strongest correlation was homA-IR with the TG/HDL-C ratio (Figure 2).

Table 1. Participant Characteristics

Variables		[HOMA-IR <2,5] N=360	[HOMA-IR ≥2,5] N=140	Odds ratio [IC 95%]	P.value
Sexe	F	275 (55.0%)	200 (55.6%)	75 (53.6%)	0,764
	M	225 (45.0%)	160 (44.4%)	65 (46.4%)	
Age (year)		47.2 ±13.6	46.7 ±14.1	48.3 ±12.4	0,237
	[18-34]	107 (21.4%)	85 (23.6%)	22 (15.7%)	
	[35-54]	242 (48.4%)	166 (46.1%)	76 (54.3%)	
	[55-80]	151 (30.2%)	109 (30.3%)	42 (30.0%)	
BP	SBD	[100-129]	147 (40.8%)	44 (31.7%)	0,066
		[130-231]	213 (59.2%)	95 (68.3%)	
	DBP	[56-84]	155 (43.1%)	45 (32.4%)	
		[85,150]	205 (56.9%)	94 (67.6%)	

Table 2. Participants' Anthropometric Characteristics

Variables	[HOMA-IR <2,5] N=360	[HOMA-IR ≥2,5] N=140	Odds Ratio[IC 95%]	P.value
BMC	25.6 ±4.62	28.5 ±5.53	1.12 [1.08-1.17]	
<18,5]	12 (3.33%)	1 (0.71%)	Ref.	<0,001
[18.5-24.49]	159 (44.2%)	44 (31.4%)	3.32 [0.42-26.2]	
[25-29.99]	146 (40.6%)	38 (27.1%)	3.12 [0.39-24.8]	
[≥30]	43 (11.9%)	57 (40.7%)	15.9 [1.99-127]	
WAIST CIRC	91.5 ±13.4	97 ±13.5	1.03 [1.02-1.05]	
[48-84]	88 (24.4%)	17 (12.1%)	Ref..	<0.001
[85-133]	272 (75.6%)	123 (87.9%)	2.34 [1.34;4.10]	
HIP CIRC	103 ±14.1	107 ±14.5	1.02 [1.00-1.03]	
[54-96]	116 (32.2%)	36 (25.7%)	Ref.	0.011
[97-137]	244 (67.8%)	104 (74.3%)	1.37 [0.89;2.13]	
RTH	0.89 ±0.09	0.91 ±0.09	11.8 [1.45-94.9]	
RTH-	183 (50.8%)	70 (50.0%)	Ref.	0,017
RTH+	177 (49.2%)	70 (50.0%)	1.03 [0.70-1.53]	

Table 3. Participants' Biological Characteristics

Variables	[HOMA-IR <2,5] N=360	[HOMA-IR ≥2,5] N=140	Odds Ratio [IC 95%]	P.value
CT	1.66 ±0.33	1.69 ±0.30	1.44 [0.78-2.64]	0,226
<2]	301 (83.6%)	110 (78.6%)	Ref.	
[2-2.81]	59 (16.4%)	30 (21.4%)	1.39 [0.85-2.27]	
TG	1.43 ±0.40	1.69 ±0.38	6.45 [3.57-11.7]	<0,001
<1.50]	193 (53.6%)	41 (29.3%)	Ref.	
[1.50-2.71]	167 (46.4%)	99 (70.7%)	2.79 [1.84-4.24]	
HDL-C	0.74 ±0.21	0.62 ±0.18	0.03 [0.01-0.10]	<0,001
[0.30-0.45]	19 (5.28%)	22 (15.7%)	Ref.	
[≥0.45]	341 (94.7%)	118 (84.3%)	030 [0.16-0.57]	
LDL-C	0.63 ±0.26	0.74 ±0.24	5.36 [2.40-11.9]	<0,001
<1.15]	353 (98.1%)	136 (97.1%)	Ref.	
[1.15-1.66]	7 (1.94%)	4 (2.86%)	1.48 [0.43-5.15]	
TG/HDL	2.01 ±0.63	2.90 ±0.87	5.40 [3.76-7.75]	<0,001
<2.5]	307 (85.3%)	38 (27.1%)	Ref.	
[2.5-5.41]	53 (14.7%)	102 (72.9%)	15.5 [9.69-25.0]	

Table 4. Multivariate Logistic regression model

Variables explicatives	[HOMA-IR <2.5]	[HOMA-IR ≥2.5]	Odds Ratio [IC 95%]
BMC			
[15.9-18.5]	37 (10.3)	6 (4.3)	Réf.
[18.5-24.99]	134 (37.2)	39 (27.9)	1.55 (0.56-4.81, p=0.422)
[25-29.99]	146 (40.6)	38 (27.1)	1.69 (0.61-5.27, p=0.333)
[30-48.6]	43 (11.9)	57 (40.7)	6.41 (2.26-20.55, p=0.001)
Ratio TG/HDL-C			
[0.577-2.49]	307 (85.3)	38 (27.1)	Réf.
[2.5-5.41]	53 (14.7)	102 (72.9)	14.26 (8.80-23.61, p<0.001)

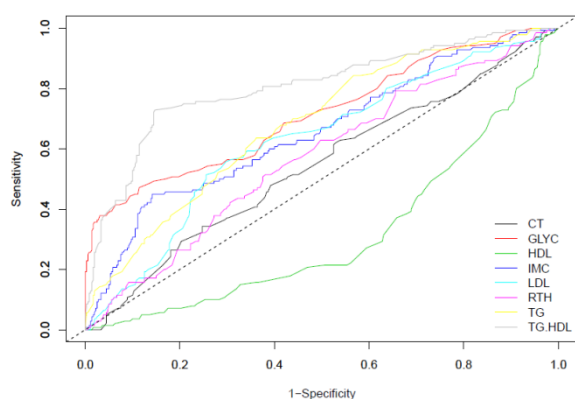


Figure 2. Correlations between HOMA-IR and different variables

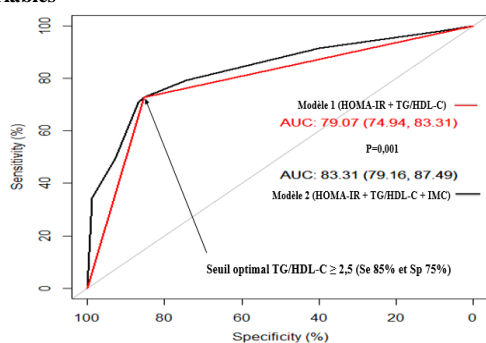


Figure 3. ASC ROC Curves

Independent Determinants of Insulin Resistance

In multivariate analysis by logistic regression after adjustment of BMI - 30 kg/m² and the TG/HDL-C ratio were identified as the independent and significant determinants of insulin resistance. Compared to BMI - 30 kg/m², BMI - 30 kg/m² conferred a 6-times greater risk of insulin resistance. Similarly, compared to the TG/HDL-C ratio of 2.5, the TG/HDL-C ratio of 2.5 conferred a 14-times greater risk of insulin resistance. Two models were established, Model 1 contained only TG/HDL-C as a predictor, and Model 2 contained BMI in addition to the TG/HDL-C ratio that were achieved by multi-step logistic regression (Table 4).

Predictive value of insulin resistance by the TG/HDL-C ratio

The optimal threshold value of the predictive TG/HDL-C ratio of insulin resistance was 2.5. The evaluation of the diagnostic characteristics of insulin resistance by the TG/HDL-C ratio at the specified threshold resulted in a sensitivity of 0.85 [0.81-0.89] and a specificity of 0.73 [0.65-0.80]. The positive predictive value was 0.66 [0.58-0.73] and the negative predictive value was 0.89 [0.85-0.92]. This optimal threshold value of the TG/HDL-C ratio was determined from the study of the ROC curve, whose area below the curve (ASC) was 0.79 [IC to 95%- 0.74-0.83] (Model 1). The CSA of the Model 2 obtained after multivariate logistic regression was 0.83 [95% CI- 0.79-0.87]. The value of P between the different models was 0.0004, Sp 0.91 [0.78-0.97]; VPP 0.92 [0.81-0.98]; VPN 0.81 [0.67-0.91] (Figure 3)

DISCUSSION

Overall the results of this are consistent with those of the literature. [18,19,29,33,39,40-42] This study assessed the accuracy of insulin resistance prediction using the TG/HDL-C ratio with or without metabolic syndrome in Congolese adults. These results showed that more than half of the insulin-resistant participants were overweight or obese. In addition, 50% of these participants had android obesity. This confirms a possible association between overeating, overweight or obesity and insulin resistance as demonstrated in various studies. [15,39-44] Excess intake of saturated fatty acids promotes insulin resistance and increases the risk of type 2 diabetes. [45]

Insulin resistance in humans is correlated with the amount of visceral fat and the alteration of the distribution of free fatty acids between fat cells, liver and muscles. Visceral obesity would result in increased release of fatty acids into the portal vein and liver insulin resistance. [43]

Previous studies have shown that insulin resistance, DT2 and CVD are generally associated with hypertriglyceridemia and low HDL-C. [44,46] However, blacks with these conditions generally have normal triglycerides (TG) levels. [46,47] Therefore, the individual use of high Levels of TG as a diagnostic criterion for insulin resistance needs to be reassessed. The results of this study are consistent with those of others, 70% of insulin-resistant participants had TG levels of 1.50 g/L. Unlike these studies, the present study found that 84.3% of insulin-resistant participants had above-normal HDL-C levels and 97.1% of LDL-C levels below 1.15/Lg. Several studies have reported that the TG/HDL-C ratio among African Americans for an optimal threshold of 2.5 is a more important marker than the traditional profiles used to predict cardiometabolic diseases. [20,33,42] These authors believe that measuring the TG/HDL-C ratio could help identify insulin resistance and therefore cardiometabolic diseases, whereas sometimes LDL levels are normal. This study showed that it had a strong positive and significant correlation between the TG/HDL-C ratio and HOMA-IR. These results are consistent with those of the other authors [18,32,33,39-42] showing that the TG/C-HDL ratio appears to reflect significantly better the effect of insulin resistance on lipid metabolism and overcomes the limits of individual use of TG and C-HDL as indicators of cardiometabolic risk.

The relationship between the TG/HDL-C ratio and insulin resistance was first reported in the US in 2003, [20] as a result of numerous studies that have shown that the TG/HDL-C ratio predicts insulin resistance in both adults and children. [15,18,26,29,33,39,48] A recent study conducted in

Mexico by Behiry et al [26] showed that a ratio of 1.36 is a significant and early predictor of insulin resistance in children instead of HOMA-IR. Studies by other authors have shown that the TG/HDL-C ratios - 1.67; ASCROC 0.79, [33] TG/HDL-C - 2; ASCROC 0.66, [15] TG/HDL-C - 3.52, [39] the authors conclude that the ratio is significantly associated with insulin resistance. This study documented a clear association between the TG/HDL-C ratio and insulin resistance. The predictive threshold value for insulin resistance by the TG/HDL-C ratio was 2.5 and corresponds to a ROC ASC of 0.79 according to the TG/HDL-C model alone.

After multivariate logistic regression the Model 2, which included in addition to the TG/HDL-C ratio, BMI significantly increased the predictive probability of insulin resistance, the area under the ROC curve increased from 0.79 to 0.83. In a study of an East African population, the TG/HDL-C ratio was significantly associated with insulin resistance measured by HOMA-IR. [49] In contrast, other studies have shown no association between the TG/HDL-C ratio and insulin resistance in black adults [50] and adolescents. [51] The difference between the Brazzaville series and those elsewhere can be explained by the difference in the threshold values used.

Implication of Medical biology and perceptual scans of public health and research

The diagnostic accuracy of the TG/HDL-C ratio for an optimal threshold value of 2.5 established by this study will improve primary prevention of DM and cardiovascular disease in the Republic of Congo. The ratio threshold will be organized for the detection and diagnosis of insulin resistance at all secondary and tertiary primary levels in the Republic of Congo and other sub-Saharan countries. Indeed, this study constitutes from the perspective of medicine with 5P (predictive, personalized, accurate, participatory with evidence). [52]

Like other blood biomarkers, the optimal TG/HDL-C ratio threshold in this study will improve the management of overweight or obese people with an early and scientific diagnosis if not accurate, early prophylactic and pharmacological treatment, and rational cost-effectiveness therapeutic follow-up in continuing education, public health and research perspectives at BZ/RC and sub-Saharan Africa. The integrated and holistic global approach bringing understanding of pathophysiological mechanisms with psychological, behavioral and sustainable development dimensions will ensure the success of controlling projected cardiometabolic syndrome more than an epidemic in the year 2045. This optimal tG/HDL-C ratio threshold will be taught and validated in health centres and universities focused on clinical biology, early treatment and therapeutic follow-up of insulin resistance and DM.

The optimal TG/HDL-C ratio of 2.5 specific for the BZ/RC Bantou population avoided inaccuracy, underestimation and overestimation of insulin resistance. Thus, intermediate/prediabetes-sweet endosm and DM according to HbA1c respectively between 5.5 and 5.9% and 6% are proposed for subsequent validation on a much larger sample in both the Republic of Congo and other African countries.

Forces and Limits

For the first time, the performance of the TG/HDL-C ratio to identify apparently healthy individuals who are insulin-resistant and have an increased cardiometabolic risk was evaluated in Brazzaville, Republic of Congo. But there is a potential limitation on the interpretation of these results since previous research has shown that ethnicity has an impact on the association between the TG/HDL-C ratio and insulin resistance and therefore the diagnostic accuracy obtained in this study will require additional evaluation to be applied to other ethnic groups.

CONCLUSION

This study showed that the diagnostic accuracy of insulin resistance defined by the TG/HDL-C ratio for an optimal threshold value of 2.5 can be used as an appropriate biomarker for insulin resistance detection. The results of this study also suggest that the TG/HDL-C-2.5 ratio may be a simple and clinically useful approach to identifying apparently healthy insulin-resistant Congolese who have an increased cardiometabolic risk.

Conflict of interest statement

The authors do not declare any conflict of interest.

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