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Triglyceride glucose index as a tool to motivate early lifestyle modification in young adults at diabetes risk: The Baependi Heart Study

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A R T I C L E I N F O

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A B S T R A C T

Considering that the incidence of type 2 diabetes mellitus (T2DM) has been increasing especially in developing countries and becoming a global public health problem, this study aims to evaluate the association between triglyceride glucose index (TyG) – which is a mathematical product of the fasting blood glucose and triglyceride levels – and incident T2DM in an adult sample in the Baependi Heart Study (BHS).

The data were from the BHS cohort consisting of two periods: cycle 1 (2005–2006; n = 1712; 119 families) and cycle 2 (2010–2013; n = 3017; 127 families). A total of 1121 individuals (both sexes, 18–100 years) were selected if they were assessed in both cycles and not diagnosed with T2DM at baseline (cycle 1).

Our findings showed that a participant's risk of developing T2DM increased almost 10 times for a one-unit increase in the TyG (odds ratio OR = 10.17, 95% CI, 7.51–13.93). The association when stratified by age was OR = 28.13 [95% CI, 14.03–56.41] for young adults, meaning that the risk of developing T2DM increased more than 28 times for a one-unit increase in the TyG. For the other groups, young middle-aged adults, old middle-aged adults, and seniors, we found OR = 4.84 [95% CI, 2.91–8.06], OR = 28.73 [95% CI, 10.63–77.65, and OR = 9.88 [95% CI, 3.16–30.90], respectively.

A higher TyG implies a significant increase in the risk of developing T2DM, which could be an important screening tool to target early lifestyle intervention in Brazil.

1. Introduction

Type 2 diabetes mellitus (T2DM) is a multifactorial disease associated with various conditions, including genetic predisposition, physical inactivity, unhealthy dietary patterns, and obesity. T2DM is described as a group of metabolic disorders characterized by elevated blood glucose concentration (American Diabetes, 2009). The prevalence of T2DM has increased considerably in recent decades, surpassing previous estimates. In particular, the incidence rates of T2DM are expanding in developing countries (Ogurtsova et al., 2015). Studies on risk factors associated with this non-communicable chronic disease have gained increasing prominence.

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; FPG, fasting plasma glucose; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SBP, systolic blood pressure; T2DM, type 2 diabetes mellitus; TyG, triglyceride-glucose index; WC, waist circumference; CI, confidence interval; OR, odds ratio; SD, standard deviation

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Table 1
Characteristics of subjects in the general sample at Cycle 1 and according to T2DM classification at Cycle 2 in the Baependi Heart Study cohort.

Variables	Cycle 1	Cycle 2		
		Diabetes-free group	Incident Diabetes group	*p-value*
n	1121	1046	75	–
Age, years	42.1 ± 16.0	47.0 ± 16.0	49.3 ± 16.6	0.24
Sex (% men)	44	43	47	*< 0.001*
Hypertension (%)	30	37	75	*< 0.001*
Increased WC (%)	30	42	61	*< 0.001*
Dyslipidaemia treatment (%)	3	7	24	*< 0.001*
SBP, mmHg	125.01 ± 18.7	125.2 ± 16.4	133.4 ± 17.8	*< 0.001*
DBP, mmHg	78.2 ± 11.2	76.7 ± 10.6	76.9 ± 10.3	0.89
BMI, kg/m2	24.3 ± 4.7	25.6 ± 4.9	28.4 ± 6.0	*< 0.001*
WC, cm	86.6 ± 11.8	90.6 ± 11.9	99.1 ± 11.6	*< 0.001*
Fasting glucose, mg/dL	87.5 ± 16.7	89.3 ± 10.2	137.3 ± 49.7	*< 0.001*
Total cholesterol, mg/dL	178.1 ± 47.1	200.6 ± 67.2	206.7 ± 51.9	0.33
HDL-cholesterol, mg/dL	56.4 ± 15.7	47.5 ± 11.8	46.2 ± 11.2	0.33
LDL-cholesterol, mg/dL	96.6 ± 43.1	125.2 ± 34.8	121.6 ± 44.9	0.51
Triglycerides, mg/dL	129.0 ± 68.9	130.2 ± 71.7	186.7 ± 95.3	*< 0.001*
TyG, mg/dL	8.5 ± 0.5	8.6 ± 0.5	9.3 ± 0.7	*< 0.001*

SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; WC, waist circumference; TyG; triglycerides-glucose index. Hypertension: systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥90 mmHg and/or anti-hypertensive drug use. Dyslipidemia treatment: percentage of individuals who used at least one class of lipid-lowering drug. Increased WC: ≥88 cm for women and ≥102 cm for men. Continuous data are expressed as the mean ± standard deviation and categorical data are expressed as percentage.
Baependi Heart Study, Brazil (2005–2013).

Many anthropometric indices have been explored to investigate the causes of T2DM around the world. In this study, we have focused on the triglyceride glucose index (TyG), a mathematical product of the fasting blood glucose and triglyceride levels (Chamroonkiadtikun et al., 2019). Previous studies have suggested this index as a simple and effective measure for metabolic diseases, including T2DM (Er et al., 2016; Low et al., 2018). Although its significance has already been demonstrated in populations of Mexico, China, Korea, and also in an urban Brazilian population, there is evidence that TyG is variable according to ethnicity, adiposity, and lifestyle (Guerrero-Romero et al., 2016; Moon et al., 2017; Vasques et al., 2011; Zhang et al., 2017).

For this investigation, we aimed to explore the role of the TyG in the development of T2DM after 5 years follow-up in a diabetes-free sample of a rural Brazilian cohort, the Baependi Heart Study.

2. Methods

The Baependi Heart Study cohort is a genetic epidemiological cohort study to investigate cardiovascular risk factors (Egan et al., 2016). The data collection process was carried out in a small town – Baependi – where individuals of both genders and ages 18–102 years were randomly considered and have been examined every five years. After recruitment, participants' relatives were invited to participate. Once selected, medical history and physical examination were implemented, and blood samples were collected. At present, the cohort study consists of three periods: cycle 1 (2005–2006; n = 1712; 119 families), cycle 2 (2010–2013; n = 3017; 127 families) and cycle 3 (2015–2018; n = 3423; 245 families). The present study was approved by the ethics committee of the Hospital das Clínicas, University of São Paulo, Brazil (SDC: 3485/10/074). Written informed consent was provided by all participants.

T2DM was defined as fasting blood glucose ≥126 mg/dL or antidiabetic drug use (Padilha et al., 2016). Participants who had T2DM in cycle 1 (baseline) or those that did not have follow-up information in cycle 2 were excluded. Therefore, according to these criteria, only nondiabetic individuals at baseline and those assessed in both cycles were considered (n = 1121).

The participants were divided into two groups at cycle 2: (i) diabetes-free group (those who remained non-diabetic) and (ii) incident diabetes group (diagnosis of T2DM according to the classification).

Blood triglycerides, total cholesterol, HDL-cholesterol, and fasting plasma glucose (FPG) were evaluated by standard techniques in 12-h fasting blood samples (Oliveira et al., 2008) in both cycles. LDL-cholesterol was calculated using the Friedewald formula. Based on triglycerides and FPG, the TyG index was calculated by using the following formula: ln[triglyceride(mg/dl) × FPG (mg/dl)/2] (Chamroonkiadtikun et al., 2019).

Anthropometric parameters such as weight, height, body mass index (BMI), and waist circumference (WC) were measured according to a standard protocol (Oliveira et al., 2008). Increased WC was defined as ≥88 cm for women and ≥102 cm for men (Klein et al., 2007). Using a standard digital sphygmomanometer (OMRON, Brazil), blood pressure was measured on the left arm after 5 min rest in the sitting position. Diastolic and systolic blood pressures (DBP and SBP, respectively) were calculated from three readings (mean value of all measurements), with a minimal interval of 3 min (Oliveira et al., 2008). Hypertension was defined as SBP ≥140 mmHg or DBP ≥90 mmHg or antihypertensive drug use. Dyslipidaemia treatment prevalence was defined as the percentage of individuals who used at least one class of lipid-lowering drugs.

In both cycles, clinical characteristics were assessed using descriptive statistics. Continuous variables were expressed as the mean ± SD and categorical variables were expressed as percentages. The normality of all data was tested with the Kolmogorov–Smirnov test, and characteristics of participants' diabetes-free group and incident diabetes group were compared using *t*-test (continuous variables) or Pearson's chi-squared test (discrete variables). Mixed-effects logistic regression was used to test the association between TyG and the incidence of T2DM, and to evaluate the risk it represents for developing T2DM as well. The regression model was carried out having TyG as the main parameter, and sex, age, WC, and LDL-cholesterol as control variables. Taking into account the kinship relations among individuals, we also considered family as a random effect. All statistical analyses were carried out using the R (version 3.5.1) statistical software (R Core Team, 2019), with the level of significance set at 5%.

3. Results

Clinical and laboratorial characteristics were summarized in Table 1 for the overall sample in both cycles. After 5-year follow-up,

Table 2
Variables associated with diabetes mellitus in a logistic regression analysis in the Baependi Heart Study cohort – Overall population.

Variables	Beta	OR	95% CI	*p-value*
Sex	−0.14	0.87	0.48–1.51	0.61
Age	0.01	1.01	0.76–1.33	0.32
WC	0.03	1.03	0.77–1.37	**0.02**
TyG	2.32	10.17	7.51–13.93	**< 0.001**
LDL-cholesterol	−0.01	0.99	0.74–1.32	**0.03**

WC, waist circumference; TyG, triglycerides-glucose index. Statistically significant p values are in bold ($p < 0.05$).
Diabetes mellitus: diagnosis was established in patients with fasting glucose equal to or greater than 126 mg/dL, or in patients who were under the use of anti-diabetic drugs.
Predictive variable: TyG.
Control variables: sex, age, WC, and LDL-cholesterol.
Baependi Heart Study, Brazil (2005–2013).

Table 3
Variables associated with diabetes mellitus in a logistic regression analysis in the Baependi Heart Study cohort.

	Variables	Beta	OR	95% CI	*p-value*
18–30	Sex	0.17	1.18	0.36–3.86	0.78
	WC	0.00	1.00	0.52–1.94	0.89
	TyG	3.34	28.13	14.03–56.41	**< 0.001**
	LDL-cholesterol	0.01	1.01	0.58–1.76	0.21
31–45	Sex	−0.76	0.47	0.15–1.47	0.19
	WC	0.04	1.04	0.64–1.70	0.07
	TyG	1.58	4.84	2.91–8.06	**0.002**
	LDL-cholesterol	−0.03	0.98	0.52–1.84	**0.01**
46–60	Sex	0.62	1.86	0.36–9.64	0.45
	WC	0.08	1.09	0.38–3.09	0.05
	TyG	3.36	28.73	10.63–77.65	**0.001**
	LDL-cholesterol	−0.02	0.98	0.42–2.28	0.06
> 60	Sex	−0.61	0.54	0.11–2.69	0.45
	WC	0.04	1.04	0.47–2.29	0.26
	TyG	2.29	9.88	3.16–30.90	**0.03**
	LDL-cholesterol	0.00	1.00	0.51–1.95	0.85

WC, waist circumference; TyG, triglycerides-glucose index. Statistically significant p values are in bold ($p < 0.05$).
Diabetes mellitus: diagnosis was established in patients with fasting glucose equal to or greater than 126 mg/dL, or in patients who were under the use of anti-diabetic drugs.
Predictive variable: TyG.
Control variables: sex, WC, and LDL-cholesterol.
Baependi Heart Study, Brazil (2005–2013).

approximately 6.7% developed T2DM (mean age 49-y), and men tend to develop diabetes more than women. When comparing groups according to T2DM classification (diabetes-free group and incident diabetes group) after 5-year (cycle 2), we noted that DBP and cholesterol (total, HDL, and LDL) did not increase significantly. On the other hand, hypertension diagnosis increased, and WC and dyslipidemia treatment, SBP, BMI, WC, glycemia, triglycerides, and TyG were higher in the incident diabetes group.

As a preliminary stage, we used a mixed-effects logistic regression model in the overall sample where T2DM was the response variable, and sex, age, WC, LDL-cholesterol, and TyG as explanatory covariates. We identified a one-unit increase on TyG to be associated with 10 times the risk of developing T2DM, approximately (odds ratio OR = 10.17, 95% CI, 7.51–13.93).

We have also stratified the sample according to age-group (following the structure presented in Table 2). The mixed-effects logistic regression model was used again for the sample stratified keeping the previous structure (T2DM as a response variable, and sex, WC, LDL-cholesterol, and TyG as explanatory covariates). Although in the case of the pooled sample (preliminary stage), age was not a significant covariate in the association between the TyG and the development of T2DM, it could be a significant effect modifier when stratified. Considering such a possible effect, we analyzed such association in each one of the age groups, and we observed a strong association between TyG and the development of T2DM for age groups, Table 3. The highest OR was found for old middle-aged adults, the risk of developing T2DM increased more than 28 times for a one-unit increase in the TyG (OR = 28.73 [95% CI, 10.63–77.65]). For the other groups, young adults, young middle-aged adults, and seniors, we found the following effect sizes: OR = 28.13 [95% CI, 14.03–56.41], OR = 4.84 [95% CI, 2.91–8.06], and OR = 9.88 [95% CI, 3.16–30.90], respectively.

4. Discussion

Our findings showed that the TyG is significantly associated with the risk of developing type 2 diabetes mellitus in a rural sample of a Brazilian population. Considering that effects may be different depending on the individual age, we decided to stratify participants by age. We found that TyG is highly associated with T2DM for the four age strata considered, being the highest OR found for old middle-aged adult (46–60 years old).

Vasques et al. (Guerrero-Romero et al., 2016) already explored the relevance of the TyG in a smaller Brazilian sample (n = 82). They found this index represents a useful tool for assessment of insulin resistance, besides being an accessible measure. Corroborating Vasques et al. (Guerrero-Romero et al., 2016) findings, we support the good performance of the TyG in studies with Brazilian adults, regardless of age. Such a biomarker is an easily accessible measure and it discriminates the groups very efficiently. Besides, TyG could also be useful in both prepubertal and pubertal children studies, as demonstrated in children from the Mexican population (Rodríguez-Morán et al., 2017).

Overall, it is important to highlight that T2DM is an important public health problem in Brazil as well as in other developing countries. The use of TyG for selecting people at early risk of future diabetes may be a powerful tool in disease prevention, as pointed by Navarro-González et al. (2016). According to Simental-Mendía et al. (2008), such indicator could also be useful as a surrogate to identify insulin resistance in apparently healthy subjects.

However, it is important to take into account that TyG is not the only indicator associated with T2DM. Other adiposity indexes are also proven to be associated with T2DM (Alvim et al., 2014), as well as family effects and even social contacts (Raghavan et al., 2016). Related to the Baependi Heart Study cohort, De Oliveira et al. (2019) have focused on the relationship between body adiposity index and T2DM, and a strong association between them was demonstrated.

Finally, as an additional strength of this work, we highlight that hypertriglyceridemia has epidemiological importance that goes beyond dyslipidemia and cardiovascular disease since the product of the fasting blood glucose and triglyceride levels may have predictive value in the diabetology field and should be seriously investigated. Based on our findings, we suggest that participants with high triglyceride glucose levels should be motivated to early lifestyle modification. We also encourage preventive efforts target to this group and groups traditionally considered at risk.

Author contributions

C.M.O, J.P, M.B., A.C.P., and R.O.A performed the statistical analysis design and drafted the manuscript. C.A.M.J contributed to the acquisition and interpretation of the data. J.E.K, A.C.P., and C.M.O. contributed to the conception and design of the study. All authors read and approved the manuscript.

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Competing interests

The authors declare that they have no competing interests.

Availability of supporting data

The data sets used and analyzed during the current study are available from the corresponding author on reasonable request.

Consent for publication

Not applicable.

Ethics approval and consent to participate

The study protocol was approved by the ethics committee of the Hospital das Clínicas (SDC: 3485/10/074), University of São Paulo, Brazil, and each subject provided informed written consent before participation.

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