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Original Article

Triglycerides and glucose index as an insulin resistance marker in a sample of healthy adults

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ABSTRACT

Aim: To assess the association between elevated triglycerides/glucose index (TGI) and insulin resistance (IR) or hyperinsulinemia after oral glucose tolerance test (OGTT) in a sample of healthy adults.
Methods: We conducted an analytical cross-sectional study in euthyroid non-diabetic adults, who attended the outpatient service of a private clinic in Lima-Peru during the 2012–2016 period. Participants were categorized in two groups according to the presence or absence of elevated TGI, IR or hyperinsulinemia after OGTT. A TGI value ≥ 8.65 was considered as elevated. We defined IR as a Homeostasis Model Assessment (HOMA-IR) value ≥ 2.28 and hyperinsulinemia after OGTT as a serum insulin value $\geq 80\mu U/mL$ after 120 min of 75-g glucose intake. We elaborated crude and adjusted Poisson regression models to assess the association between elevated TGI and IR or hyperinsulinemia after OGTT. The reported association measure was the prevalence ratio (PR) with their respective 95% confidence intervals (95%CI).
Results: We analyzed 118 individuals, the average age was 37.5 ± 11.3 years, 21 (17.8%) were males and the median BMI was $22.7 \pm 1.6\ kg/m^2$. The prevalence of elevated TGI was 25.4% (n=30) while the prevalence of IR and hyperinsulinemia after OGTT was 24.6% (n=29) and 17.0% (n=20) respectively. In the adjusted model, elevated TGI was associated with both IR (aPR=6.36; 95%CI: 3.41–11.86) and hyperinsulinemia after OGTT (aPR=4.19; 95%CI: 1.81–9.70).
Conclusions: We found that elevated TGI was associated with both IR markers in a sample of euthyroid adults without T2DM and with a normal BMI. The simplicity of the TGI calculation makes it the first-choice alternative when the hyperinsulinemic-euglycemic clamp or HOMA-IR are not available.

1. Introduction

Insulin resistance (IR) is defined as a metabolic condition in which there is an impaired sensitivity to insulin-mediated glucose disposal [1]. This condition has been previously linked with obesity, type 2 diabetes mellitus (T2DM) and metabolic syndrome [2–5]. However, recent studies have also found that IR plays a key role in the development of other non-communicable diseases. Thus, IR has been closely associated with hypertension [6], cancer [7,8], polycystic ovary syndrome [9], chronic kidney disease [10] and even brain disorders [11,12].

Given its clinical relevance, accurate measurements of IR are essential and the hyperinsulinemic-euglycemic clamp is currently considered the gold standard [13,14]. However, this technique is considered very expensive, labour-intensive and time-consuming [14]. Therefore, it is important to develop easier and less expensive methods that we can use as surrogate markers. In this sense,

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the Homeostatic Model Assessment (HOMA-IR) has been the mathematical model most widely used in studies, since first described in 1985 [15,16]. However, since this method requires insulin determination, an important limitation is the lack of accessibility to people with low incomes [17].

The triglycerides/glucose index (TGI) was first proposed and validated by Simental-Mendía LE et al. (2008) in a sample of Mexican adults [18]. This index has proven to be an accurate diagnostic tool for IR, in some cases even better than HOMA-IR [19]. In recent years, different studies have compared the TGI with the hyperinsulinemic-euglycemic clamp [20] and other surrogate markers [19,21–24]. In Latin America, validation studies have been conducted in Mexico [17,25], Brazil [19], Argentina [22] and Venezuela [26]. However, to date there are no studies conducted in Peru, which is a country with high rates of overweight, obesity and metabolic syndrome [27,28].

For the above mentioned, the objective of the present study was to assess the association between elevated TGI and IR or hyperinsulinemia after oral glucose tolerance test in a sample of healthy adults.

2. Methods

2.1. Study design and population

We carried out an analytical cross-sectional study in euthyroid adults of both sexes with a normal body mass index (BMI) and no medical history of T2DM, who attended the outpatient service of a private clinic in Lima-Peru through 2012–2016.

2.2. Sample type and analysis unit

We performed a non-probabilistic sampling. The sample consisted of all patients who attended the outpatient service of the private clinic between January 2012 and December 2016 and met the eligibility criteria of the study.

2.3. Procedures

We reviewed all the medical records of the patients treated during the study length and collected all the data of interest. The laboratory values were only collected if the patient laboratory tests were performed with a maximum of 30 days after they were attended in the outpatient service of the private clinic. All participants had a minimum fasting period of 8 h for laboratory tests, according to the protocols established by the medical centre.

2.4. Eligibility criteria

We included participants aged ≥18 with a BMI between 18.50 and 24.99 kg/m^2 and no medical background of T2DM, hypothyroidism, subclinical hypothyroidism, hyperthyroidism, polycystic ovary syndrome or metabolic syndrome. Besides, we excluded patients aged ≥60, with fasting glucose values ≥ 126 mg/dL, oral glucose tolerance test (OGTT) ≥200 mg/dL, thyroid hormones values outside the following ranges: free triiodothyronine (FT3): 2.3–4.2 pg/mL, free thyroxine (FT4): 0.89–1.76 ng/dL, thyroid stimulating hormone (TSH): 0.40–5.0 μU/mL [29]; and pregnant women.

2.5. Variables definition

2.5.1. Exposure: TGI

We defined the TGI using the following calculation: ln[triglycerides (mg/dL) x fasting glucose (mg/dL)/2]. Then, participants were categorized in two groups according to the 75-percentile value of the TGI: normal TGI group (TGI values < 8.65) and elevated TGI group (TGI values ≥ 8.65). In addition, this cut-off point was similar to the 75-percentile value described in a previous article [30].

2.5.2. Outcomes: IR and hyperinsulinemia after OGTT

IR was defined as a HOMA-IR value ≥ 2.28, that correlates with the 75-percentile. We used this cut-off point based in a previous study [31]. Mathews et al. (1985) proposed HOMA-IR in a mathematical model to assess hyperinsulinemia. The gold standard to assess IR is the hyperinsulinemic euglycemic clamp, however, HOMA-IR is well correlated with it. HOMA-IR was calculated using the formula: fasting glucose (mg/dL) x fasting insulin (μU/mL)/405 [32].

Hyperinsulinemia after OGTT was defined as a serum insulin value ≥ 80 μU/mL after 120 min of 75-g glucose intake [33]. Participants were divided in two groups according to these criteria.

2.5.3. Other variables

The following variables were also included in the analysis: age (years), sex, body mass index (BMI), fasting glucose, postprandial blood glucose, glycated haemoglobin A1c, fasting insulin, triglycerides, FT3, FT4 and TSH.

2.6. Statistical analysis

We used STATA v14.0 (StataCorp, TX, USA) for our analysis. Descriptive results for numeric variables were presented as means with standard deviation (SD) or medians with interquartile range (IQR), depending on their distributions; otherwise, we expressed the qualitative variables as numbers with percentages. The study population characteristics according to the TGI groups, IR or hyperinsulinemia after OGTT were compared using the student T-test or the Wilcoxon rank sum test as appropriate for continuous variables and using the Chi-square test for categorical variables.

Two generalized linear models (1 crude and 1 adjusted) from Poisson family with robust standard errors were constructed to evaluate the association between elevated TGI and IR or hyperinsulinemia after OGTT. The reported association measure was the prevalence ratio (PR) with their respective 95% confidence intervals (95%CI). The adjusted model included the following confounding variables: age, sex, FT3 (pg/mL) and TSH (μU/mL) [29,30]; and the reported association measure was the adjusted prevalence ratio (aPR) with their respective 95%CI.

2.7. Ethical considerations

The data was collected by two researchers from the private clinic to study epidemiological surveillance. For this study, participant information was delivered in a Microsoft Excel 2010 file without biological identifiers, maintaining the confidentiality of the information.

3. Results

In total, we enrolled 1817 patients during the study period; we excluded 222 participants because they were 60 or older. Besides, 625 patients were withdrawn due to hyperthyroidism, hypothyroidism, subclinical hypothyroidism or T2DM, 695 because their BMI was not between 18.50 and 24.99 kg/m^2 and 157 because they did not have the variables of interest. Finally, 118 participants were analyzed.