

The Triglyceride-glucose (TyG) Index in the Association of Non-alcoholic Fatty Liver Disease, Obesity and Insulin Resistance

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ABSTRACT

Aims: Non-alcoholic fatty liver disease is strongly linked to obesity and insulin resistance. The triglyceride-glucose index (TyG index) has been proposed as a reliable biomarker of insulin resistance. Our aim is to study the contribution of the TyG index as a marker in the association of non-alcoholic fatty liver disease, obesity and insulin resistance. **Material and method:** This was a cross-sectional study of obese women (age > 18 years, BMI ≥ 29.9 Kg/m²). Non-alcoholic hepatitis steatosis was confirmed by abdominal ultrasound. The viral origin of the liver disease was eliminated by microbiological test. A lipid profile was performed. The TyG index was calculated according to the formula $\ln[\text{fasting triglycerides (mg/dL)} \times \text{fasting glucose (mg/dL)}] / 2$. The relations between TyG index, body composition and lipid profile were measured. **Results:** 42 obese women participated in our work. Age = 50.80 ± 10.33 years. BMI = 40.80 ± 5.09 Kg/m²; weight = 98.1 ± 15.99 Kg. Fasting blood sugar was 1.18 ± 0.34 g/L. Triglycerides were 1.37 ± 0.47 g/L. Our study demonstrated that 83% (n = 35) have, in addition to non-alcoholic fatty liver disease, a high TyG index (4.75 ± 0.25) in favour of insulin resistance. The TyG index is strongly linked to fasting glucose ($r_s = 0.83$) and fasting triglycerides ($r_s = 0.78$). A statistically significant link was found between the TyG index and age ($\tau = 0.21$, $p = 0.04$), the TyG index and total cholesterol ($\tau = 0.33$, $p = 0.001$). **Conclusions:** The TyG index is a topical biomarker. This clue is practical. It appears to have a place in the association of obesity, non-alcoholic fatty liver disease and insulin resistance.

Keywords: TyG index, insulin resistance, obesity, non-alcoholic fatty liver disease

INTRODUCTION

Obesity is a global health problem. It is estimated that around 1.5 billion adults worldwide are overweight, of whom around 200 million men and 300 million women are obese [1].

According to the WHO, overweight and obesity are defined as an abnormal or excessive accumulation of fat that is harmful to health. A person is considered overweight when their body mass index (BMI) is greater than 25kg/m² and obese when it is greater than 30kg/m². Obesity leads to the development of a number of co-morbidities, including type 2 diabetes (T2DM), non-alcoholic fatty liver disease (NAFLD), hypertension, hyperlipidaemia, chronic kidney disease, cardiovascular disease (CVD), obstructive sleep apnea, osteoarthritis and malignant tumors, resulting in increased mortality in obese people [2]. The increase in the prevalence and severity of NAFLD is linked to rising levels of obesity [3]. NAFLD has now become one of the leading causes of chronic liver disease. The prevalence of obesity-induced NAFLD and the resulting morbidity may be considered the major health crises of the next decade in the industrialized world [4,5]. Similarly, mortality from NAFLD continues to rise, while mortality from viral hepatitis is declining [6]. Non-alcoholic fatty liver is the most common liver disease in Western countries. The global prevalence of NAFLD is estimated to be around 25% and is expected to increase to 33.5% by 2030 [7]. Non-alcoholic fatty liver disease (NAFLD) is characterized by the diffuse accumulation of triglycerides in hepatocytes. This steatosis is not caused by excessive alcohol consumption or other causes that affect the liver [8]. NAFLD is generally attributed to obesity-induced insulin resistance [8]. NAFLD can be complicated by cirrhosis or even hepatocellular carcinoma [7]. NAFLD is also considered a risk factor for extra-hepatic diseases such as cardiovascular disease (CVD), chronic kidney disease, colorectal cancer, type 2 diabetes mellitus (T2DM) and osteoporosis [7]. There are currently no approved pharmacological treatments for NAFLD, with the exception of lifestyle changes [9]. Early detection of patients at risk of NAFLD using simple and effective diagnostic methods is crucial.

Early identification of people at high risk of NAFLD enables preventive strategies to be put in place and slows down the morbidity and mortality of liver-related diseases. Traditionally, the diagnosis of NAFLD has required various techniques such as liver ultrasound, magnetic resonance imaging and biopsy [10]; however, some of these techniques are either invasive or expensive and have limited applicability in clinical practice. The most widely used diagnostic tool is liver ultrasound. NAFLD is often associated with multiple metabolic disorders that may be partly explained by insulin resistance. The triglyceride-glucose index (TyG) is derived from the formula:

$$\ln(\text{fasting triglycerides (mg/dL)} * \text{fasting blood glucose$$

$$\text{(mg/dL)/2}) \text{ [11], is increasingly used because of its better performance in estimating insulin resistance. In practice, insulin resistance is measured by the homeostasis model assessment (HOMA) [12-14]. It is derived from the formula } \text{[Fasting blood glucose (mmol/L)} * \text{Fasting blood insulin (}\mu\text{mol/L)/22.5]. It is used to assess insulin resistance (IR). The HOMA-IR index requires a delicate biochemical technique [15]. Given its ease of acquisition and calculation, the TyG index is widely accepted and used in clinical practice to assess IR [14,16]. It uses two serum parameters, triglycerides and glucose, which are strongly linked to the regulation of insulin secretion. Insulin sensitivity can be subtly affected by the metabolism of these two parameters.}$$

Insulin resistance, which increases lipolysis [17] and stimulates de novo lipogenesis favouring the production and storage of triglycerides in the liver [18] as well as fat reserves. These reserves are directly associated with liver inflammation [19] and play an important role in the pathogenesis of NAFLD. Triglyceride accumulation in hepatocytes is due to an imbalance between lipid accumulation and elimination [17]. Several causes can lead to this excessive accumulation of triglycerides, such as increased fat intake due to a high-fat diet, reduced metabolism of fats in the form of very low density lipoproteins (VLDL) and triglycerides, reduced beta oxidation of free fatty acids and de novo lipogenesis [18]. This excess of triglycerides leads to the development of NAFLD (Non Alcoholic Fatty Liver Disease) through liver dysfunction [17,18]. Furthermore, the accumulation of fatty liver is linked to insulin resistance [19]. Excess fatty acids from lipogenesis and fatty acid synthesis accumulate in peripheral tissues, the liver and adipose tissue, leading to peripheral insulin resistance [20]. All these mechanisms contribute to the metabolic disorders that may characterise NAFLD, which is an inflammatory component of NAFLD [21]. Non-alcoholic fatty liver disease (NAFLD) is strongly linked to obesity, and insulin resistance is the key pathogenic factor in the development of NAFLD. The TyG index is dependent on disorders affecting glucose and triglyceride metabolism. It is possible that it could provide information on insulin resistance in obese people with non-alcoholic fatty liver disease.

OBJECTIVE

The aim of this study was to investigate the contribution of the TyG index as a metabolic marker in obese women with hepatic steatosis in favor of non-alcoholic fatty liver disease.

METHOD AND MATERIALS

This is a descriptive cross-sectional study carried out between January and December 2022 in the metabolic physiology and nutrition department of Batna University Hospital. The inclusion criteria were met by 42 women (aged 18 years and over, female, obese BMI≥29.9 kg/m² and having undergone a liver ultrasound scan which revealed steatosis). Children, men, people without abdominal ultrasound results, pregnant women and those with cancer or viral hepatitis were excluded from this study. Also we excluded people with diabetes and those presenting heart disease. Weight and height were measured in patients wearing light clothing and no shoes.

Body composition was analysed using 8-electrode impedancemetry of the Tanita® BC 418 MA type. A fasting blood glucose level and a lipid profile were determined. Patients were classified according to their degree of obesity on the basis of their BMI. The cardiometabolic profile was

identified on the basis of fasting blood glucose and lipid profiles. The TyG index was calculated using the formula $TyG\ index = \ln[\text{fasting triglycerides (mg/dl)} \times \text{fasting blood glucose (mg/dl)}] / 2$ [22].

Statistical values are expressed as percentages, mean plus or minus standard deviation. Spearman’s and Kendall’s tests were used to look for associations between the TyG index, body composition and lipid balance. Statistical analysis was performed using the biosta TGV website [23]. A p value of <0.05 was considered statistically significant.

RESULTS

42 obese women took part in our study (Table 1). The mean age was 50.80±10.33 years. The mean weight was 98.1±15.99 kg and the mean BMI was 40.80±5.09 kg/m². Half (n=21) of our patients were morbidly obese with a BMI ≥ 40 Kg/m² (Figure 1).

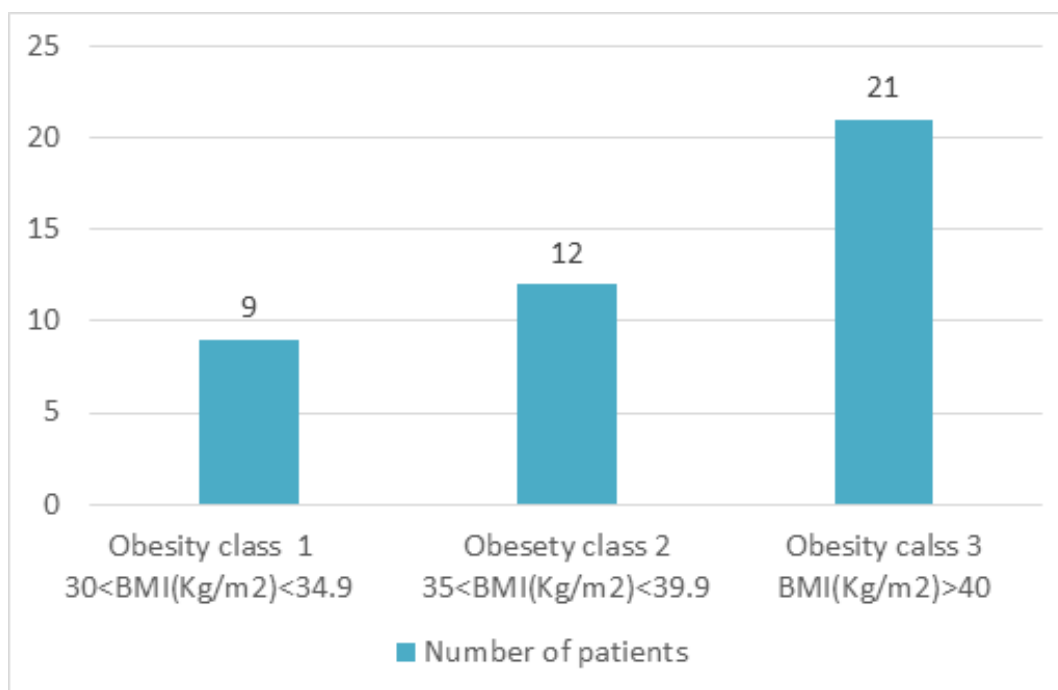


Figure 1: Distribution according to stages of obesity.

Table 1: General data of the study population.

	Means	Standard deviation (+/-)
Age (years)	50.80	10.33
Weight (Kg)	98.1	15.99
BMI (kg/m ²)	40.80	5.09
Fasting blood glucose (g/L)	1.18	0.34
TG (g/L)	1.37	0.47

In addition to hepatic steatosis, 80% (n=32) of our patients had a TyG index > 4.49 in favour of insulin resistance. 71% (n=30) had a cholesterol level > and almost (1/3) had either a triglyceridaemia > 1.5 g/L or a low HDLc (Figure 2).

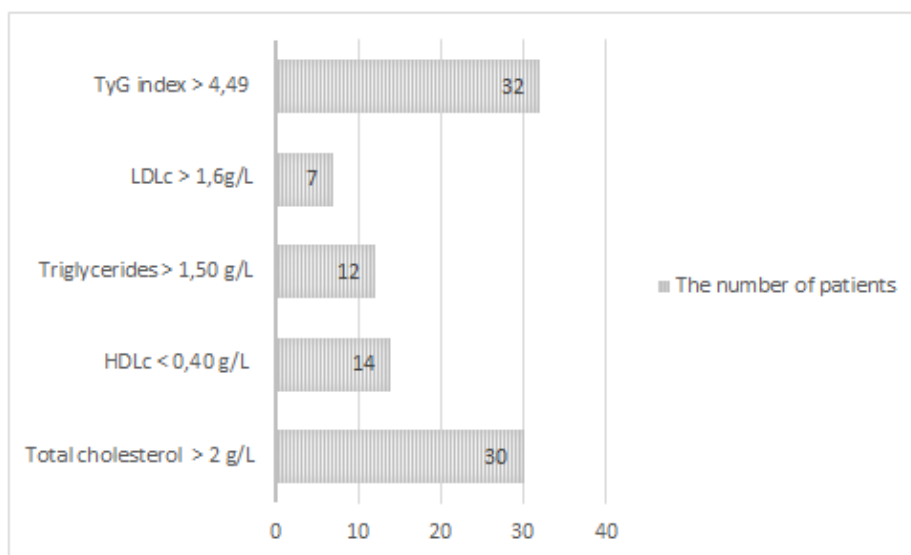


Figure 2: The number of patients with metabolic disorders.

In the 35 obese women with non-alcoholic fatty liver disease, the TyG index was (4.75+/-0.25) in favour of insulin resistance. The TyG index was strongly associated with glycaemia (rs=0.83) and triglycerides (rs=0.78), but this association was not statistically significant (table 2). However, a statistically significant link was found between TyG index and age ($\tau=0.21$, $p=0.04$), TyG index and total cholesterol ($\tau=0.33$, $p=0.001$).

	rs	P value*	τ	P value*
Weight (KG)	-0,08	0,57	-0,06	0,52
BMI (Kg/m²)	-0,01	0,93	-0,04	0,96
Age(Years)	0,29	0,05	0,21	0,04
Triglycerides (g/L)	0,83	NS	0,69	NS
Fasting blood glucose (g/L)	0,78	NS	0,59	NS
Total cholesterol (g/L)	0,48	0,001	0,33	0,001
Total body fat (g/L)	-0,10	0,51	-0,07	0,51
Visceral fat	-0,40	0,77	-0,03	0,77

Table 2: The different correlations of the TyG index with the different study parameters.

(rs) Spearman correlation, (τ) Kendall correlation, (NS) not significant.

* p value statistically significant for a value > 0.05.

In 35 obese women with non-alcoholic fatty liver disease, the TyG index was (4.75±0.25) in favour of insulin resistance. The TyG index was strongly associated with glycaemia ($r_s=0.83$) and triglycerides ($r_s=0.78$), but this association was not statistically significant. However, a statistically significant link was found between TyG index and age ($\tau=0.21$, $p=0.04$), TyG index and total cholesterol ($\tau=0.33$, $p=0.001$).

DISCUSSION

Non-alcoholic fatty liver (NAFLD) is characterised by the diffuse accumulation of triglycerides in the hepatocytes. This accumulation is not caused by excessive alcohol consumption or other causes of liver disease [8]. NAFLD is generally attributed to obesity-induced insulin resistance [8]. It is considered a risk factor for extra-hepatic diseases such as cardiovascular disease (CVD), chronic kidney disease (CKD), colorectal cancer, type 2 diabetes mellitus (T2DM) and osteoporosis [7]. The aim of this study was to investigate the contribution of the TyG index as a cardiometabolic biomarker in obese women with non-alcoholic fatty liver disease confirmed by ultrasound imaging. We found a TyG index > 4.49 in 32 people (N = 42). Sonia Hossain's study in 2020 [20] showed that the onset of hepatic steatosis increased significantly with increasing levels of TyG index. Our results are consistent with the cohort conducted by Kitae et al [24]. In this study the authors showed that the TyG index is significantly associated with the incidence of NAFLD based on ultrasound in the general adult population. NAFLD is becoming a silent global epidemic with a significant health and economic burden [25]. NAFLD is largely ignored by patients because there are no obvious clinical signs. However, if left untreated, NAFLD can lead to serious complications such as cirrhosis and even hepatocellular carcinoma [26]. Therefore, early detection and intervention for NAFLD patients is essential to prevent further complications of NAFLD and other associated chronic diseases such as diabetes. IR is the major contributor to the pathogenesis of NAFLD via increased supply of free fatty acids to the liver, inadequate fatty acid oxidation and increased de novo lipogenesis [26]. IR is evidenced by the HOMA-IR (Homeostasis Model Assessment - Insulin Resistance) test, which should measure serum insulin levels; however, widespread screening in primary care settings using HOMA-IR does not appear to be evident [27]. Similar to our findings, a cohort study by Rivière et al [25], used liver biopsy to detect NAFLD in obese patients. This study showed a strong association between the TyG index and NAFLD. The TyG index is a convenient new surrogate marker for IR that has recently gained ground due to its simplicity of calculation. In addition,

the TyG index shows some predictive superiority of IR over HOMA-IR [28]. In addition, the TyG index has been shown to be the best test for detecting simple steatosis compared with other NAFLD indices, such as SteatoTest, NashTest and the hepatic steatosis index [29]. These indices are not widely used in clinical practice, due to their complexity and difficulty of calculation, as well as their high cost [29]. The TyG index is easy to calculate and can therefore be a practical tool for screening for NAFLD. This index even surpasses the HOMA-IR in the prediction of NAFLD [30]. Previous studies have demonstrated a strong dose-response association between TyG index and NAFLD when categorizing TyG into quartiles [31- 34]. Guo et al [33] showed that the prevalence of NAFLD increased from 30.9% to 53.3%, to 71.7%, to 86.4% in increasing TyG quartiles (Q1, Q2, Q3 and Q4, respectively; p -value for trend < 0.001). Huanan et al [32] further demonstrated that the higher the level of the TyG index, the higher the incidence of NAFLD, whether the TyG index was analysed as a continuous or categorical variable. However, Khamseh et al suggest that the TyG index combined with other indices such as obesity stage and waist circumference may be more accurate than the TyG index alone [35]. In our work, we found no link between BMI and TyG index. This was a single-centre study with a relatively small sample size. Evidence of liver damage was based on ultrasound findings, which reported radiological lesions in favour of hepatic steatosis. Several aspects need to be clarified. The definition of steatotic liver disease was re-examined by a group of international experts in 2020 [36,37]. The group reached a consensus in favour of changing the nomenclature. A distinction has already been made between non-alcoholic fatty liver disease (NAFLD) and metabolic dysfunction-associated fatty liver disease (MAFLD) [36]. According to these authors, MAFLD is defined by the presence of hepatic steatosis, in addition to one of the following three criteria: overweight or obesity, the presence of T2DM or the presence of metabolic dysfunction. We believe that our population precisely meets the definition of MAFLD (metabolic dysfunction-associated fatty liver disease) rather than NAFLD. These are obese women with fatty liver disease, half of whom ($n=21$) are morbidly obese. Histologically, NAFLD is a common term that encompasses a broad spectrum of diseases ranging from isolated steatosis known as simple hepatic steatosis or Non Alcoholic Fatty Liver (NAFL) to NAFLD, the latter potentially leading to hepatic fibrosis, cirrhosis or hepatocellular carcinoma [38,39]. At the cellular level, in addition to hepatic steatosis, NAFLD is defined by lobular inflammation and signs of hepatocyte damage (distinguished by ballooning of the hepatocytes) with varyin

degrees of fibrosis [40]. The cohort study conducted by Rivière et al [25] used liver biopsy in obese patients to detect NASH. A strong association was demonstrated between the TyG index and NASH. NASH is a silent global epidemic with a significant health and economic burden [24]. It is a silent disease that may be underpinned by several pathophysiological mechanisms. Fat accumulation in the visceral liver is linked to insulin resistance [18]. Excess fatty acids from lipogenesis and triglyceride synthesis from excess glucose accumulate in peripheral tissues, adipose tissue and the liver, promoting peripheral insulin resistance [19]. Our work focuses on the MAFLD entity [41] where multiple metabolic disorders have been identified, hypercholesterolemia, hypertriglyceridemia, a glycaemic disorder favouring pre-diabetes and an increased risk of cardiovascular disease (low HDLc and/or high LDLc). These results suggest that the syndromic grouping of metabolic disorders in an obese person with radiological signs of hepatic steatosis exposes them to major risks of cardio-metabolic damage. Similarly, the presence of obesity and hyperlipidaemia is also associated with an increased risk of progressive liver disease [42]. Visceral fat appears to be the predominant factor in the genesis of insulin resistance. We found a negative correlation between visceral fat and the TyG index, which seems contradictory. Metabolic syndrome is based on the combination of at least two or three criteria, including the location of abdominal fat. Measurement of waist circumference confirms this location and assesses its extent [43]. According to the guidelines of certain learned societies [39], all people with incidental steatosis should be screened for metabolic syndrome, independently of functional liver tests. Although an increase in waist circumference was associated with a higher risk of NAFLD, independently of abdominal obesity status [44], we support the hypothesis that waist circumference, which is a simple and practical anthropometric tool, is not in itself sufficient to judge the metabolic severity of visceral fat. Physiopathological mechanisms, involving the nature of the fatty tissue and above all the secretion of mediators by the latter, may explain the appearance (or not) of a metabolic disorder such as insulin resistance.

As demonstrated in this study, the TyG index can consolidate the existence of a Mets-MAFLD syndromic cluster. However, it cannot, on its own, be a predictor of this disorder. Parameters such as TyG-BMI or TyG-WC appear to be more relevant [8]. They should therefore be promoted.

CONCLUSION

Obesity aggravates non-alcoholic liver diseases, NAFL, MAFLD, NAFLD and NASH. Early diagnosis of these diseases enables complications to be prevented more effectively. Diagnosis is based on radiological and biological techniques, including HOMA-IR. The TyG index is a topical biomarker and appears to be a simple, practical and affordable tool for screening for insulin resistance.

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