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Medicine

VARIABILITY OF TG / HDL C RATIO IN NAFLD

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ABSTRACT:
NAFLD IS A LEADING CAUSE OF CHRONIC LIVER DISEASE AS WELL AS A LEADING CAUSE OF LIVER MORBIDITY AND MORTALITY. ELEVATED SERUM TRIGLYCERIDES AND LOW SERUM HDL CHOLESTEROL ARE COMMON IN METABOLIC SYNDROME AND THE TRIGLYCERIDE / HDL CHOLESTEROL (TG / HDL C) RATIO HAS BEEN SHOWN TO BE A PREDICTOR OF INSULIN RESISTANCE, TYPE 2 DIABETES, HYPERTENSION, AND CARDIOVASCULAR DISEASE.
LIMITED CURRENT DATA SUGGEST SIGNIFICANT CORRELATION OF TG / HDL C RATIO WITH NAFLD.
THE OBJECTIVE OF THE PRESENT STUDY IS TO HIGHLIGHT THE CLINICAL SIGNIFICANCE OF THE VARIABILITY OF THE TRIGLYCERIDE / HDL CHOLESTEROL RATIO IN NAFLD.

KEY WORDS: TRYGLICERIDES, HDL CHOLESTEROL, NAFLD, TG / HDL C RATIO

1. INTRODUCTION

Triglycerides (TG), glycerol esters with three fatty acids, constitute a major energy source for the body. Hypertriglyceridemia, common and rising in medical cases, is mostly multifactorial and has been associated with an increased risk of premature cardiovascular diseases (CVD), pancreatitis, neurological disorders, and ophthalmological conditions. Elevated TG often coexists with other conditions on the rise, such as obesity, metabolic syndrome (MS), type 2 diabetes (T2D), and primary hypertension. Several studies have described hypertriglyceridemia in non-alcoholic fatty liver disease (NAFLD), an entity on the rise in medical pathology. [1,2,3].

HDL-cholesterol (HDL C), a group of lipoproteins synthesized and secreted by hepatocytes, is essential in cholesterol metabolism. Elevated HDL C values, considered anti-atherogenic, are associated with increased TG clearance and chronic liver diseases. Various studies detail the association of low or high HDL C levels in NAFLD, correlated with

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associated diseases (obesity, lipid metabolism disorders, T2D, hypertension, CVD, MS) frequently present in individuals with this condition [5, 6].

Recently, studies have emphasized the role of the TG/HDL C ratio (R TG/HDL C) as a risk marker for MS, T2D, hypertension, CVD, cerebrovascular diseases, and peripheral arterial diseases. [7,8,9].

Health experts have suggested R TG/HDL C values: ideal ≤ 2, acceptable 4-6 (without major health risks), and high risk ≥ 6 [11].

R TG/HDL C has proven to be a surrogate marker for insulin resistance, playing a central role in the pathogenesis of NAFLD. However, the relationship between R TG/HDL C and NAFLD has not been well elucidated [12,13].

NAFLD is an emerging cause of chronic liver disease and a major cause of liver morbidity and mortality. Alongside MS, obesity, T2D, hypertension, CVD, NAFLD coexists with other less-studied comorbidities such as colorectal cancer, hypothyroidism, obstructive sleep apnea, polycystic ovarian syndrome, and osteoporosis, signaling a profound impact on health and quality of life. [14,15]. The global prevalence of NAFLD is on the rise. (**Figure nr.1**) [16]. Elevated serum triglycerides and low serum HDL cholesterol are commonly encountered in metabolic syndrome, and the TG/HDL-C ratio has been significantly correlated, as a surrogate marker, with insulin resistance. Additionally, the TG/HDL-C ratio has proven to be a predictor of type 2 diabetes, hypertension, and cardiovascular diseases. Limited current data suggests a significant correlation of the TG/HDL-C ratio with NAFLD [17,18].

The study aims to highlight the clinical significance of TG/HDL C ratio variability in NAFLD.

Material and Method. The retrospective study included adults hospitalized in the Internal Medicine Department of "Nicolae Malaxa" Clinical Hospital in Bucharest from January 2021 to December 2022. Confidentiality agreements and ethical approval were obtained, and medical-social information was gathered from clinical observation sheets of hospitalized individuals diagnosed with non-alcoholic fatty liver disease (NAFLD).

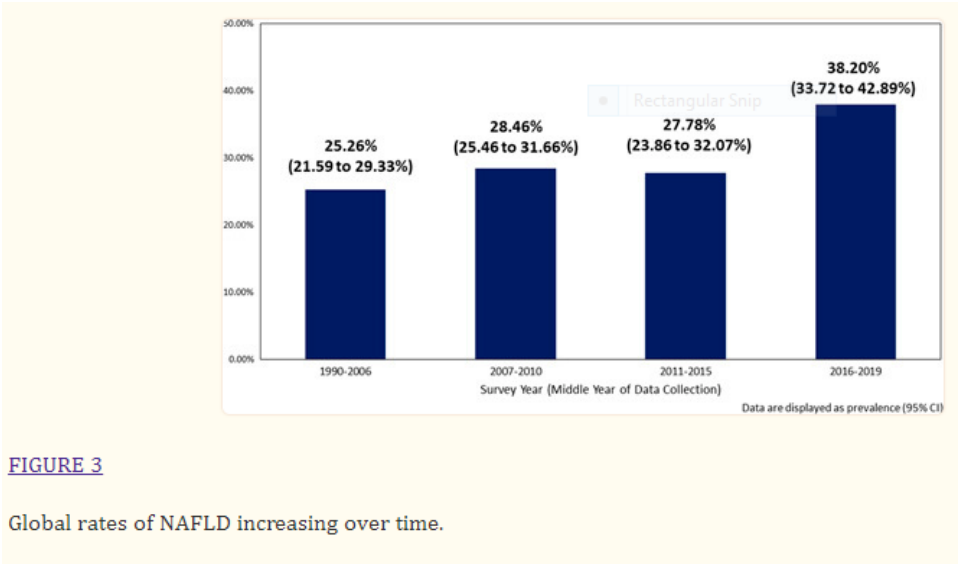

Figure no.1 - The global prevalence of NAFLD
(Younossi ZM, Golabi P, Paik JM, Henry A, Van Dongen C, Henry L. *The global epidemiology of nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH): a systematic review.* Hepatology. 2023 Apr 1;77(4):1335-1347)

The data from FO includes the medical history, clinical laboratory tests, imaging investigations, and disease therapy of the hospitalized person. Biochemical serum indicators, including TG and HDL C, were measured using venous blood obtained from participants, collected in the morning before meals. Biochemical parameter testing was performed through the spectrophotometric method with the ILAB 600 Clinical Chemistry Analyzer (Chema Diagnostica). The reference ranges for TG were 1-200 mg/dl, and for HDL C, they were 40-60 mg/dl.

Results. The study included 145 hospitalized individuals with NAFLD and comorbidities such as CVD, T2D, and obesity. Of these, 72 were men (26-84 years old) and 73 were women (34-78 years old). (**Figure no.2**).

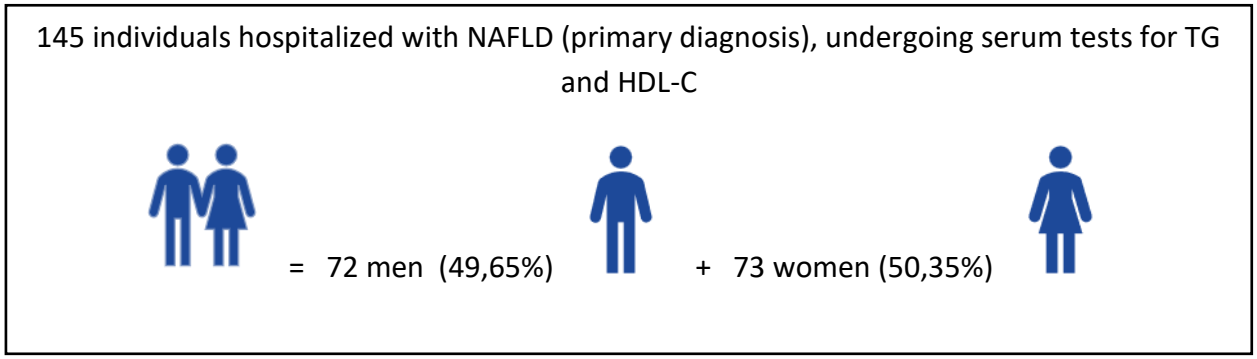

Figure no.2 - The distribution of cases in the study group

The reference range of the TG/HDL-C ratio in the present study was calculated based on the reference intervals for TG and HDL-C (values specified in the prospectus of the reagent kit used).

The TG/HDL-C ratio in the study group, the reference range, variability intervals, and critical values for both genders are presented in **Tables No. 1 and No. 2.**

Table no.1 - Details regarding the TG/HDL-C ratio in the study group (I)

Study Group: 145 individuals with the primary diagnosis of NAFLD	R TG / HDL C		
	Reference range (biochemistry reagents ILAB 600)	Range of variability	Critical values reported
72 men	0,02 - 3,33	0,46 - 15,04	15,04
73 women		0,50 - 17	17

Table no.2 - Details regarding the TG/HDL-C ratio in the study group (II)

R TG / HDL C	
≥ 3,33	≥ 6
men: 25 / 17,24%	men: 8 / 5,51%
women: 16 / 11,03%	women: 6 / 4,13%

The variability of the TG/HDL-C ratio in cases with NAFLD + comorbidities (HTN, T2DM, obesity - most frequently encountered), detailed by gender, is presented in **Table No. 3.**

Table no.3 - The variability of the TG/HDL-C ratio in cases with NAFLD + comorbidities

NAFLD + Comorbidities in the study group		R TG / HDL C
NAFLD + HTA: 114 cases / 78,61%	men: 53 cases / 36,55%	men: 0,47 - 9,57
	women: 61 cases / 42,06%	women: 0,69 - 17
NAFLD + DZ2: 63 cases / 43,44%	men: 37 cases / 25,51%	men: 0,65 - 9,57
	women: 26 cases / 17,93%	women: 0,9 - 12,02
NAFLD + Obesity: 62 cases / 42,75%	men: 36 cases / 24,82%	men: 0,47 -15,04
	women: 26 cases / 17,93%	women: 0,98 - 4,27

Discussion: The study group encompassed a wide age range (26 - 84 years), including information about their basic characteristics such as gender, marital status, the primary diagnosis of non-alcoholic fatty liver disease (NAFLD), and secondary diagnoses like cardiovascular diseases (CVD), type 2 diabetes (T2DM), and obesity (most frequently noted). This retrospective study, based on chart notes, does not reflect the causal relationship between the TG/HDL-C ratio and NAFLD, possibly due to the medication for associated comorbidities, especially those administered for TG and HDL-C regulation. The diagnosis of NAFLD was confirmed through abdominal ultrasound according to the diagnostic criteria for non-alcoholic fatty liver disease, with hepatic steatosis defined by increased liver lobe dimensions, diffuse hyperechogenicity of the liver, and poor visualization of intrahepatic architectural details. Alcohol consumption, viral or autoimmune hepatitis were excluded before diagnosing NAFLD. Additionally, the influence of diet, exercise, and statins was not evaluated.

In recent years, an increasing body of medical evidence has shown an association between the TG/HDL-C ratio and more unfavorable metabolic profiles, including dyslipidemia, obesity, and type 2 diabetes [19,20,21].

Establishing an optimal critical value (the value at which the risk of developing conditions such as metabolic syndrome, hypertension, cardiovascular diseases, type 2 diabetes, dyslipidemia, and cerebrovascular diseases begins) is suggested to be ≥ 6 (according to medical experts). However, this requires multiple studies involving various factors such as diet, physical activity, other associated diseases (autoimmune diseases, neoplasms, kidney diseases, lung diseases), current medication, compliance with medication, genetic status, as well as the performance of medical laboratories [22,23,24].

Conclusions: The obtained data revealed a clinically significant correlation between the TG/HDL-C ratio and NAFLD. In the sample of this study, it was observed that a TG/HDL-C ratio ≥ 3.33 would be an optimal critical value, crucial for the early identification and management of NAFLD, especially among hospitalized individuals with comorbidities such as hypertension (HTN). Men were more frequently noted with values ≥ 3.33 and even ≥ 6 (optimal critical value suggested by medical experts).

The variability range of the TG/HDL-C ratio = 0.50 - 17 was higher in women, with the critical value reported for women and in the study group being 17.

Hospitalized individuals with an elevated TG/HDL-C ratio present a high risk of NAFLD, especially if they also have comorbidities such as HTN, type 2 diabetes (T2DM), and obesity.

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The TG/HDL-C ratio can be considered a surrogate marker that would assist clinicians in identifying medical cases susceptible to NAFLD, requiring targeted management.

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