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A Cross-Sectional Study to Evaluate the Association of HbA1c and Triglycerates HDL Ratio as a Non Invasive Marker in Non Alcoholic Fatty Liver Disease in a Tertiary Center

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ABSTRACT

Introduction

Non-alcoholic fatty liver disease (NAFLD) is distinguished by the presence of excess fat deposits within hepatic cells specifically when 5% or more of hepatocytes contain fat, by eliminating secondary causes such as excessive alcohol consumption or medications. It is a globally leading liver disease, affecting adults over 25%, with rising prevalence due to increasing obesity, type 2 diabetes mellitus and metabolic syndrome. This study explores HbA1c levels and the triglyceride-to-HDL ratio as non-invasive diagnostic markers.

Materials and Methods:

This cross-sectional study aims to correlate an association between HbA1c and the triglyceride to HDL ratio in the context of non-invasive NAFLD diagnosis. Conducted at a tertiary care center in Chengalpattu district, the study used a convenient sampling method with 85 participants aged 18–65 years, including those with comorbidities like diabetes, dyslipidemia, and hypertension. Data analysis was calculated with the help of SPSS version 21, and the chi-square test, utilized to assess the relationships between the variables

Results:

Participants mean age in this study was 53.57 ± 14.0. 31 patients were in the grade 1 and 27 patients in Grade 2 and 3 respectively. Most of the patients were having high TGL:HDL and grade III fatty liver (n=21). A significant association was noted among the TGL:HDL cholesterol ratio and grade of liver steatosis (p = 0.038). Higher level of HbA1c was associated with increased grading of fatty liver. 19 patients with HbA1c >6.5 were having grade III fatty liver, 16 patients with HbA1c 6.1-6.4 had grade II fatty liver. No significance was demonstrated between HbA1c and grade of fatty liver (p=0.692).

Conclusion:

The triglyceride to HDL-C ratio and HbA1c are potential non-invasive biomarker for NAFLD, linked to insulin resistance and lipid metabolism. It is accessible, easy to use, and aids early detection. Further more researches are needed to confirm its broader clinical applicability, while it may enhance early diagnosis and management.

Keywords: *NAFLD, HbA1c, diagnosis, Management, MASLD*

INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD), recently updated as Metabolic associated fatty liver disease (MASLD), was described as the appearance of macrovesicular steatosis in hepatocytes of at least 5% without an alternative aetiology, like alcohol or drugs. It is characterized by inflammation, different degrees of fibrosis and cirrhosis, and hepatic lipid build up, particularly triglycerides(1).

It is estimated that 25% of adults worldwide are affected by NAFLD, which is a leading cause of hepatic disease. Its prevalence is increasing, and it is anticipated that the rising rates of type 2 diabetes mellitus (T2DM), obesity, and metabolic syndrome will further escalate NAFLD incidence in both adults and children. Because of the persistent problem of obesity, NAFLD has now became the leading cause of chronic liver disease among the developed nations. Within the next ten years, it is anticipated that the prevalence of NAFLD will surpass 35% worldwide. Men may be roughly twice as likely as women to have non-alcoholic steatohepatitis (NASH), a subtype of NAFLD linked to histological inflammation and cell damage.

An array of genetic, environmental, and metabolic variables contribute to the complicated and multifaceted pathophysiology of NAFLD. Commonly accepted concept for its prognosis is the "multiple-hit" hypothesis, which postulates that hepatic steatosis and subsequent liver damage are caused by an interaction between oxidative stress, insulin

resistance, dyslipidemia, and changes in the gut flora. Furthermore, genetic predisposition is important; certain gene variations, like PNPLA3 and TM6SF2, have been connected to an increased susceptibility to NAFLD and its progression(3,4).

Because NAFLD is quiet in its early stages, it frequently goes undiagnosed despite its high frequency. Many people have no symptoms, and the illness is only discovered by chance through imaging tests or abnormal liver enzyme levels. On the other hand, symptoms of advanced disease stages may include cirrhosis-related problems, weariness, or stomach pain. Because it allows for actions to stop the progression of the disease and its related problems, early diagnosis is essential(5). Liver biopsy, being gold standard for diagnosis, imaging methods like ultrasonography and MRI - magnetic resonance imaging are also used in current diagnostic practices.

One of the main obstacles to the best medical care for NAFLD patients is the underdiagnosis, which also makes it difficult to determine the prevalence and consequences of the condition. NAFLD's initially asymptomatic nature, a lack of standardized diagnostic methods, and patients' and healthcare providers' ignorance of the disorder are all contributing factors. Although liver ultrasonography and serum hepatic aminotransferase levels are frequently used screening methods, still not sensitive enough to diagnose and track NAFLD. The current study was proposed with an objective of using HbA1c levels and TG to HDL cholesterol ratio as a non-invasive marker to diagnose NAFLD in patients.

METHODOLOGY

The present study is based on a cross sectional study design aimed at identifying the association between HbA1c and Triglyceride(TG) to HDL cholesterol ratio as a non invasive marker to diagnose NAFLD. A tertiary referral hospital in the Chengalpattu district was the site of this research. A convenient sampling method was employed for participant selection and a sample size of 85 was used.

Study included patients in the age between 18 to 65 years with NAFLD including co morbidities like diabetes, dyslipidemia and hypertension, those who were willing to give written consent. Patients with history of alcohol, decompensated liver disease, patients with viral hepatitis, intake of steatogenic medications in the last 3 months were not included. Abdominal ultrasonography, conducted after a 10-hour fast, was utilized for NAFLD diagnosis. Diagnostic confirmation necessitated the identification of at least two of the following sonographic abnormalities: diffuse hepatic hyperechogenicity relative to the renal and splenic parenchyma, attenuation of the ultrasound beam, and compromised visualization of intrahepatic architectural detail. All participants provided informed consent before participating in the study, providing a thorough explanation of the study's objective, procedures, and adverse effects. The study protected the rights of research participants by voluntary participation of all the individuals and all the participants were free to opt out at any point of time during the study period.

The research employed a standardized questionnaire to gather patient demographics, alongside physical measurements including body weight, height, and blood pressure (both systolic and diastolic), which were taken by a certified physician. Body Mass Index (BMI) was calculated from provided body weight and height data. Blood samples, obtained from the cubital vein by a trained nurse, were analysed to determine fasting serum triglyceride (TGL), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), alanine aminotransferase (ALT), aspartate aminotransferase (AST), serum uric acid (SUA), serum creatinine (Scr), and HbA1c (presented as a percentage). The TGL to HDL-Cholesterol ratio, a marker of insulin resistance, was derived by dividing plasma TGL levels (mg/dl) by HDL-C levels (mg/dl). Participants were informed about potential adverse effects related to blood withdrawal, such as pain, swelling, redness, numbness, and thrombophlebitis. They were instructed to report any such occurrences, and were given guidance on general management, including site care, cleaning, treatment, and reassurance.

In the statistical analysis, qualitative factors were expressed as proportions, while quantitative variables were represented by their means and standard deviations. Data analysis was calculated with the help of SPSS version 21, and the chi-square test, utilized to assess the relationships between the variables

RESULTS

The study comprised of 85 patients from a tertiary care centre with diagnosis of NAFLD. Participants ranged in age from 18 to 65 years, with a mean age of 53.57 ± 14.0 years Many of these participants were male 51(60%) and 34(40%) were female. Patients were classified based on presence of Co-morbidities like diabetes, Hypertension, CAD, Dyslipidaemia. Around 64 (75.9%) of them gave history of diabetes. Hypertension patients were 39(45.8%). Nearly half of the patients had CAD (51.7%) and Dyslipidaemia (50.6%). Patients were classified based on Body mass Index (BMI). More than half of them were categorised into overweight/Obese (65.8%) with BMI >/ 25. Participant demographics, including gender and comorbidities, are summarized below

Table 1: Frequency distribution of study population based on gender and co-morbidities:

Variables		No of Patients(n)	Frequency (%)
Gender	Male	51	60
	Female	34	40
Diabetes	Yes	64	75.9
	No	21	24.1
Hypertension	Yes	39	45.8
	No	46	54.2
CAD	Yes	44	51.7
	No	41	48.3
Dyslipidemia	Yes	43	50.6
	No	42	49.4
BMI	Normal <24.99	29	34.2
	Overweight >/25	56	65.8

The participants were categorised based on the grade of fatty liver given in Table 2. 31 patients were in the grade 1 and 27 patients in Grade 2 and 3 respectively.

Table 2: Classification of patients based on grading of Fatty liver:

Fatty liver	No of Patients (n)	Frequency (%)
Grade I	31	36.4
Grade II	27	31.8
Grade III	27	31.8

The patient population was stratified into three groups based on their HbA1c values of <6, 6.1-6.4 and >6.5 and 60% of them were having HbA1c in the range of 6.1-6.4. (Figure 1).

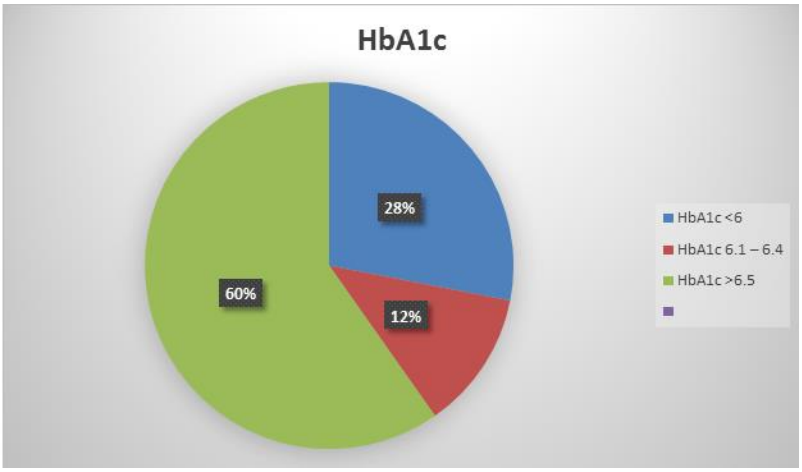

Figure 1: Classification of patients based on HbA1c levels:

Analysis was done with chi square test to demonstrate association of HbA1c and TGL/HDL ratio with grading of fatty liver. TGL and HDL ratio was categorized into 2 groups as borderline <3.0 and high >3.1 (Table 3). Most of the patients were having high TGL:HDL and grade III fatty liver(n=21). Significant association was related between TGL:HDL ratio and grade of fatty liver (p = 0.038). Triglyceride levels among patients were classified as <150, 150-200 and more than 200 (Table 4). The statistical analysis did not demonstrate a proving significance between HbA1c and TGL levels among the patients studied (p=0.198).

Table 3: Association between TGL to HDL ratio and grade of fatty liver:

TGL : HDL	Grade I	Grade II	Grade III	p-value
Borderline <3.0	16	8	6	***0.038****
High >3.1	15	19	21	

Table 4: Association between HbA1c and Triglyceride levels among patients:

Variables	TGL <150	TGL 150-200 (Borderline)	TGL >200 (high risk)	p-value
HbA1c <6	15	4	4	0.198
HbA1c 6.1 – 6.4	3	4	5	
HbA1c >6.5	20	18	12	

Figure 2 shows the association between HbA1c level and Fatty liver among the participants. Higher level of HbA1c was associated with increased grading of fatty liver. 19 patients with HbA1c >6.5 were having grade III fatty liver, 16 patients with HbA1c 6.1-6.4 had grade II fatty liver. No significance was demonstrated between HbA1c and grade of fatty liver (p=0.692).

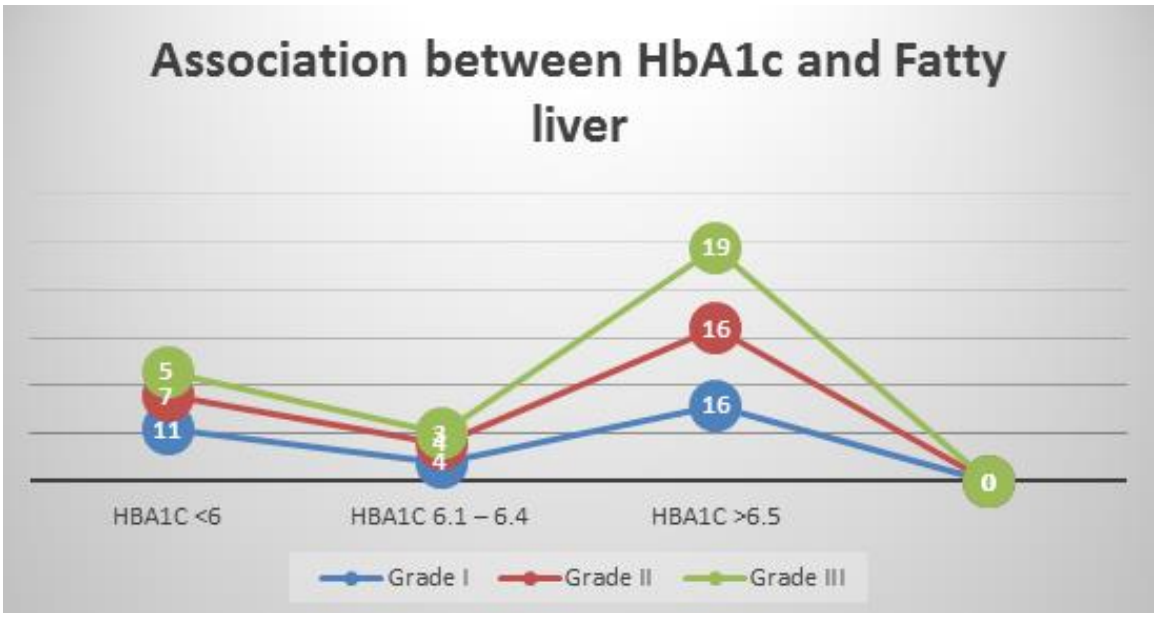

Figure 2: Association between HbA1c level and grade of Fatty liver among patients:

DISCUSSION

In recent periods of time, have seen a major increase in interest in the non-invasive measurement of triglycerides to HDL cholesterol (TG/HDL-C) in NAFLD patients.

Despite being the gold standard for diagnosing NAFLD, invasive treatments like liver biopsies are not appropriate for widespread screening because of their expense, possible side effects, and discomfort to patients. Researchers have looked for non-invasive biomarkers that can assist in diagnosing and evaluating the severity of NAFLD in response to these restrictions. The TG/HDL-C ratio and HbA1c are among the many suggested markers that have showed promise(6).

A prevalent characteristic of metabolic syndrome is dyslipidaemia, which can be identified by low HDL cholesterol and high triglyceride levels.(TG) The build up of fat in the liver, a defining feature of NAFLD, is closely associated to these lipid abnormalities. While low HDL-C hinders the liver's capacity to export fat, elevated triglycerides can directly deposit in the liver, aggravating steatosis.

In this study, the participants were categorised based on the grading of fatty liver, 31 patients were in the grade 1 and 27 patients in Grade 2 and 3 respectively (Table 2). Also most of the patients were having high TGL:HDL and grade III fatty liver (n=21). Significant association was also observed between TGL:HDL ratio and grade of fatty liver (p = 0.038). Triglyceride to HDL Cholesterol ratio has been assessed in a number of studies in relation to NAFLD, and associations with it have been noted in a variety of groups. For example, a study by Ren et al(7), elaborated that, NAFLD patients had a considerably greater TG/HDL-C ratio than the participants with no illness, indicating that the ratio may be an early predictor of the formation of liver fat. This is in line with research by Ting et al(8). Fan et al., which identified a proving correlation between the occurrence of steatotic hepatic disease and TG/HDL-C ratio in a Japanese population. According to these studies, the TG to HDL-C ratio could be helpful as a non-invasive screening method.

Furthermore, the TG to HDL cholesterol ratio has been used to predict the severity of NAFLD, according to recent studies. A higher TG to HDL cholesterol ratio, for instance, was linked to a higher risk of advanced liver fibrosis and NASH in a group of individuals with NAFLD(4,9). These diseases have a higher propensity to develop into cirrhosis and liver failure. In our study also 21 participants with higher TGL and HDL ratio were found to have grade III fatty liver. This implies that

in addition to aiding in the diagnosis of NAFLD, the TG/HDL-C ratio may also be used as a predictive tool to gauge the severity of the illness, enabling improved risk stratification.

Type 2 diabetes, obesity, metabolic syndrome, and insulin resistance (IR) are all closely connected to NAFLD. HbA1c, as a good measure of glycemic control and chronic hyperglycemia since it measures the mean blood glucose level over the period of last two to three months. The pathophysiology of NAFLD is significantly influenced by insulin resistance and lipotoxicity, both of which are exacerbated by chronic hyperglycemia. Our study results also showed that more patients with NAFLD had HbA1c levels of more than 6.5 but however significant association was not established. Similar observations where seen in study by Masroor et al(10)., and Chen et al(11)., where higher HbA1c levels were associated with more advanced fibrosis among the patients with biopsy-confirmed NAFLD.

However the study has certain limitations. TG to HDL-C ratio's predictive value can change depending on the population. For instance, baseline triglyceride and HDL-C levels may vary among ethnic groups, which may impact the sensitivity and specificity of the ratio in certain populations. Larger multicentre trials are required to confirm the TG to HDL-C ratio's diagnostic and prognostic utility in a variety of clinical scenarios, despite the fact that it has demonstrated promise in numerous studies.

CONCLUSION

One promising non-invasive biomarker for identifying and evaluating the severity of NAFLD is the TG to HDL-C ratio. Its usefulness in early detecting those at risk for NAFLD has biological validity as it has high relation with both insulin resistance and problems in lipid metabolism. It has benefits over other markers in terms of ease of use, accessibility, and early detection. To overcome its drawbacks and confirm its applicability in various clinical settings and demographics, more research is necessary. The TG to HDL-C ratio, in conjunction with other pertinent clinical and laboratory parameters, may serve as a critical tool for the timely recognition and therapeutic intervention of NAFLD, thereby optimizing patient outcomes in this increasingly prevalent condition.

Conflicts of Interest: Nil

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