Section: General Medicine

Original Research Article

COMPARISON OF LIPID PROFILE IN DIFFERENT GRADES OF NON-ALCOHOLIC FATTY LIVER DISEASE ON ULTRASONOGRAPHY

Aswin Narendran[1], G . Arul Venkadesh[2], J. Brinda[3], A. Algin Danny[4]

[1]Junior Resident, Department of Cardiology, Government T D Medical College, Alappuzha, Kerala, India.
[2]Assistant Professor, Department of General Medicine, Kanyakumari Govt Medical College, Tamilnadu, India.
[3]Associate Professor, Department of General Medicine, Government Medical College, Dindigul, Tamilnadu, India.
[4]Assistant Professor, Department of General Medicine, Kanyakumari Government Medical College, Tamilnadu, India.

Received : *05/01/2023*
Received in revised form : *29/01/2023*
Accepted : *10/02/2023*

Keywords:
Lipid profile; Non-alcoholic fatty liver disease; Ultrasonography; NAFLD.

Corresponding Author:
Dr. A. Algin Danny
Email: dralgindanny@gmail.com

DOI: 10.47009/jamp.2023.5.2.X

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2023; 5 (2); 378-382

Abstract

Background: Different studies have revealed the association of various lipid profile components with non-alcoholic fatty liver disease (NAFLD). The present study aimed to compare the lipid profile with different grades of NAFLD on ultrasonography. **Materials and Methods:** This analytical cross-sectional study was conducted from April 2020 to April 2021 in the Department of General Medicine, Kanyakumari Government Medical College, Tamil Nadu. A total of 80 patients ageing 18 years or above with NAFLD by Ultrasound abdomen. The written consent and Institutional ethical committee approval were taken before the start of the study. A comparison of lipid abnormalities between different grades of fatty liver diagnosed on ultrasound was made. **Result:** Most patients were female, 51 (63.8%), in the age group of 41 to 50 years (28.8%), with a mean age of 43.36. A total of 23 (28.8%) patients found with overweight, and 6 (7.5%) patients were observed as obese. In our study, the maximum number of patients found with fatty liver in 42 (52.5%), with Grade I in 29 (36.3%) patients. The mean blood parameters RGB, AST, ALT, ALP and GGT were found to be 151.43±73.39, 19.21±7.52, 19.74±8.3, 77.41±25.42 and 21.71±12.11 respectively. The significant effect ($p<0.0001$) of mean TC, TGL, and VLDL values on different fatty liver grades were reported. **Conclusion:** The present study reported a positive correlation between lipid parameters and NAFLD grades. Though liver biopsy is the standard gold method for diagnosing NAFLD, Ultrasonography, a non-invasive, simple tool, can detect NAFLD early in asymptomatic patients.

INTRODUCTION

Ludwig coined the term non-alcoholic steatohepatitis (NASH) in 1980 to describe the biopsy findings in patients with steatohepatitis without significant alcohol consumption.[1] NASH is part of a spectrum of steatosis known as non-alcoholic fatty liver disease (NAFLD), which ranges from simple steatosis (fatty change/deposition) to steatohepatitis with fibrosis or cirrhosis. A NAFLD classification system (grade 1 to grade 3) has been proposed that correlates certain histologic features with the long-term prognosis. In this classification system: Grade I constitute simple steatosis. Grade II is steatosis with lobular inflammation and ballooned hepatocytes. Grade III is steatosis, lobular inflammation, ballooned hepatocytes and Mallory hyaline or fibrosis.[2-3]

NAFLD is now being increasingly recognized as a major health burden.[4] The prevalence of fatty liver in India is as high as 15%-30%, similar to that reported by some western countries.[5] Earlier reports indicated that most cases of NAFLD are relatively mild and have a benign course. However, now it has been documented that a number of these cases can progress to fibrosis, cirrhosis, liver failure and hepatocellular carcinoma and thus contributes to liver-related mortality and morbidity.[6-7]

Most patients with NAFLD have no symptoms or signs of liver disease at the time of diagnosis. However, many patients report fatigue or malaise and a sensation of fullness or discomfort on the right side of the upper abdomen. Hepatomegaly is the only physical finding in most patients.[7] A liver biopsy is a sensitive method for the diagnosis of NAFLD.[8] However, liver biopsy is a painful and invasive procedure with rare but potentially life-threatening

ISSN (O): 2687-5365; ISSN (P): 2753-6556

complications like bleeding and is prone to sampling errors. In addition, given the number of patients with NAFLD, liver biopsy is clinically and financially impractical.[9-10]

The present study aims to evaluate and confirm the usefulness of ultrasonography for diagnosing NAFLD, to diagnose NAFLD non-invasively by ultrasound and to compare ultrasonographically diagnosed NAFLD with serum lipid profile.

MATERIALS AND METHODS

This analytical cross-sectional study was conducted from April 2020- April 2021 in the Department of General Medicine, Kanyakumari Government Medical College, Tamil Nadu. A total of 80 patients aged 18 years or above with non-alcoholic fatty liver disease by Ultrasound abdomen. The written consent and Institutional ethical committee approval were taken before the start of the study.

Inclusion criteria: Patients of either sex, ageing 18 years or above, diagnosed with non-alcoholic fatty liver disease by ultrasound abdomen were included in the present study.

Exclusion criteria: Patients with Daily alcohol intake > 30gm in men or > 20gm in women. Patients under the use of corticosteroids, tamoxifen, methotrexate or high-dose estrogen. Patients with Jejunoileal bypass or extensive bowel resection. Patients with Liver cirrhosis and other known chronic and acute liver diseases, malignancy, pregnancy and chronic and acute kidney disease were excluded from the study.

Subjects were taken as cases if they have fatty liver according to the standard criteria by the American Gastroenterology Association, i.e., an increase in hepatic echogenicity, the presence of enhancement and lack of differentiation in the periportal intensity and the vascular wall due to great hyperechogenicity in the parenchyma.

The degree of involvement will be standardized with a semi-quantitative scale of the degree of hepatic involvement. Hepatic steatosis was diagnosed based on characteristic sonographic features: increased liver echogenicity; increased liver contrast compared to the kidney; vascular blurring-mainly of portal veins; attenuation of echogenic level in the deep-seated area. The blood samples were collected to estimate the following parameters: serum triglycerides, total serum cholesterol, HDL, LDL and VLDL.

Data are presented as percentages and the number of cases. The correlation between continual variables was analyzed using the Pearson correlation test. ROC curves were used to predict the cut-off value. Significance was defined by P values less than 0.05 using a two-tailed test. Data analysis was performed using IBM-SPSS version 21.0.

RESULTS

In the present study, 80 patients aged 18 years or more having non-alcoholic fatty liver disease by Ultrasound abdomen were enrolled. Most patients were female, 51 (63.8%), in the age group of 41 to 50 years (28.8%), with a mean age of 43.36. Maximum patients 11 (13.8%) were reported with a history of DM. A total of 23 (28.8%) patients found with overweight, and 6 (7.5%) patients were observed as obese. Our study found fatty liver Grade II in 42 (52.5%) and Grade I in 29 (36.3%) patients [Table 1].

Table 1: Observation of demographic, Blood and lipid parameters of patients

Particulars		Observation N (%)
Gender	Female	51(63.8%)
	Male	29 (36.3%)
Age Group	<20	1(1.3%)
	21-30	16 (20%)
	31-40	18(22.5%)
	41-50	23 (28.8%)
	51-60	15 (18.8%)
	>61	7 (8.8%)
Mean Age years ± SD		43.36±13.9
History illness	NIL	61(76.3%)
	DM	11(13.8%)
	DM/SHT	5(6.3%)
	SHT	3(3.8%)
BMI (kg/m2)	Underweight	3(3.8%)
	Normal weight	48(60.0%)
	Overweight	23(28.8%)
	Obese	6(7.5%)
Fatty liver grade	Grade 1	29(36.3%)
	Grade 2	42(52.5%)
	Grade 3	9(11.3%)
Blood parameters	RBG (mg/dL)	151.43 (73.39%)
	AST (U/L)	19.21 (7.52%)
	ALT (U/L)	19.74 (8.30%)
	ALP (U/L)	77.41 (25.42%)
	GGT (U/L)	21.71 (12.11%)
Lipid Profile	TC (mg/dL)	213.59 (40.93%)
	TGL (mg/dL)	255.10 (77.2%)
	HDL-C (mg/dL)	59.48 (10.42%)

ISSN (O): 2687-5365; ISSN (P): 2753-6556

	LDL-C (mg/dL)	114.81 (20.24%)
	VLDL	47.79 (14.09%)

RBG: Random blood glucose; AST: Aspartate Aminotransferase; ALT: Alanine aminotransferase; ALP: Alkaline phosphatase; GGT: Gamma-glutamyl transferase

The mean blood parameters RGB, AST, ALT, ALP and GGT were found to be 151.43±73.39, 19.21±7.52, 19.74±8.3, 77.41±25.42 and 21.71±12.11 respectively. Mean lipid parameters TC, TGL, HDL-C and VLDL were recorded at 213.59±40.93, 255.1±77.2, 59.48±10.42, 114.81±20.24 and47.79±14.09 respectively [Table 1].

When different lipid parameters were evaluated with all fatty liver grades, it was found there was a significant effect ($p<0.0001$) of mean TC, TGL and VLDL on different fatty liver grades [Table 2].

Table 2: Observation of different lipid variables in correlation with Fatty liver grade

Lipid parameters		Mean	Std Deviation	P-value
TC (mg/dL)	Grade 1	181.21	23.92	
	Grade 2	218.83	22.64	<0.0001
	Grade 3	293.44	28.21	
TGL (mg/dL)	Grade 1	190.28	32.64	
	Grade 2	265.60	35.02	<0.0001
	Grade 3	415.00	65.23	
HDL-C (mg/dL)	Grade 1	57.55	8.77	0.003
	Grade 2	58.50	10.79	
	Grade 3	70.22	7.64	
LDL-C (mg/dL)	Grade 1	113.48	19.86	
	Grade 2	118.21	20.79	0.296
	Grade 3	124.78	18.03	
VLDL (mg/dL)	Grade 1	37.90	6.66	
	Grade 2	48.17	7.16	<0.0001
	Grade 3	77.89	12.97	

TC: Total cholesterol; TGL: Triglycerides; HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol; VLDL: Very low-density lipoprotein.

DISCUSSION

Non-alcoholic fatty liver disease (NAFLD) occurs in patients with little or no history of alcohol intake and has histological characteristics similar to alcohol-induced liver injury. It includes hepatic steatosis with a necro-inflammatory component that may or may not is linked with fibrosis.[11] NAFLD is a histopathological spectrum ranging from steatosis and steatohepatitis to cirrhosis. A diagnosis of non-alcoholic steatohepatitis requires steatosis, lobular inflammation, inflated hepatocytes, and fibrosis. Based on the degree of hepatic steatosis, ballooning and disarray, and inflammation, Brunt et al. defined the necro-inflammatory grades of NASH as grade 1 (mild), grade 2 (moderate), and grade 3 (severe) (intralobular and portal).[12] NAFLD are now regarded as a major health hazard. NAFLD is diagnosed through liver biopsy. Although rare, problems like haemorrhage and sample errors can occur during the liver biopsy.[13] Furthermore, considering the prevalence of NAFLD, liver biopsy is not clinically nor economically feasible. The current study seeks to identify NAFLD non-invasively by ultrasound and compare ultrasonographically diagnosed NAFLD with serum lipid profile.

Patients from different age groups were included in the study, with the age group 41-50 years recording the highest prevalence frequency. In a parallel study by Mahaling et al., the predominant age group of maximum NAFLD prevalence was 48-57.[14]

Similar to our study, patients of the age group <20 and >60 appeared in low numbers. In a likely analysis performed by Rafat et al., the predominant age group that recorded the presence of NAFLD was 40-49 years, with a very low NAFLD incidence within the age group <29 and >60 years.[15] Most NAFLD patients were females (63.8%) compared to males, with an incidence rate of 36.3%. In a previous study by Mahaling et al., females with NAFLD were recorded in larger numbers than males.14 However, in an analysis by Bhusal et al., the number of males (n=67) was recorded in larger numbers.[16]

NAFLD is both a cause and a consequence of metabolic syndrome (MetS). Worldwide, a considerable proportion of the general population is expected to have the condition, with metabolic co-morbidities being the most common.[17] The current study indicated the presence of DM alone in 13.8% of patients and both DM and SHT in 6.3% of them. SHT was recorded in 3.8% of NAFLD patients. 76.3% of NAFLD patients did not record the presence of any co-morbidity. Age, gender, and diabetes are all metabolic risk factors for disease progression. Indeed, NAFLD is both a cause and a consequence of MetS. Musso et al. also proposed that NAFLD is linked to an increased risk of liver and cardiovascular disease, as well as a 2-fold greater risk of type 2 diabetes.[18]

Obesity is defined as a body mass index (BMI) > 30 kg/m2, and severe obesity is defined as a BMI > 40 kg/m2. NAFLD is strongly associated with obesity, with a prevalence of up to 80% in obese patients and

ISSN (O): 2687-5365; ISSN (P): 2753-6556

just 16% in healthy persons. Hepatic steatosis was often found to the associated with BMI levels.[19] The BMI of the study patients were noted and grouped into four groups. With most of them grouped under normal weight, 28.8% were recorded as overweight. While 7.5% of them were obese, 3.8% of them were underweight. In a previous study conducted by Bhusal et al. on a correlation between BMI and NAFLD, the study data displays that most patients are overweight.16 This disparity may be because visceral adipose tissue volume and truncal obesity may better predict Metabolic syndrome and NAFLD than BMI.

Most of the NAFLD cases diagnosed belonged to grade 2 (52.5%), followed by grades 1 (36.3%) and 3 (11.3%), respectively. This implies that most patients belonged to moderate NAFLD conditions followed by mild and severe conditions. In Buhsal et al. study, most NAFLD patients were mild, with few intermediates.16 They couldn't identify severe NAFLD. In Khanal et al. study, most NAFLD patients belonged to Grade I followed by grades II and III. This variance is presumably related to sample selection. There were few samples of Grade 3 fatty liver in this investigation.[20]

One of the main components of metabolic syndrome is insulin resistance and, consequently, high blood sugar and also the association between metabolic syndrome and NAFLD is well documented. Liver enzymes are hepatocellular damage markers that can be utilized to diagnose NAFLD. As a result, the Random Blood Glucose (RBG) and the levels of AST, ALT, ALP, and GGT were measured. With a mean patient age of 43.36, the mean RBG level was 151.43mg/dL followed by 19.21, 19.74, 77.41 and 21.71 U/L of AST, ALT, ALP as well as GGT, respectively. In a likely study by Pradhan et al., it was observed that the levels of liver enzymes elevated at higher rates in NAFLD patients compared with that of healthy people.[21] They also propose in their study that in type-2 diabetes, mildly elevated liver enzymes and fatty liver alterations could be employed as an indirect biomarkers of insulin resistance.

Lipid profile analysis in NAFLD patients included the measurements of TC, TGL, HDL-C, LDL-C (mg/dL) and VLDL that yielded values of 213.59, 255.10, 59.48, 114.81 and 47.79, respectively. The NAFLD patients were detected with higher levels of TC, TGL and VLDL. HDL values were slightly abnormal, and LDL values were also in a range that indicated early prognosis of NAFLD to the grade II stage. HDL and LDL levels were still insignificant across all age groups among all grades of NAFLD. In a similar study by Mahaling et al., it was reported that elevated blood triglycerides, total cholesterol, LDL, and VLDL were seen in NAFLD cases.[14] Hypertriglyceridemia was found in most patients, hypercholesterolemia in a significant number of NAFLD patients raised LDL in a smaller number of patients, and elevated VLDL in more than half of patients.

A correlation between fatty liver grades and TC and TGL levels was statistically different ($p<0.0001$). HDL and LDL levels negatively correlated with the prevalence of NAFLD (p-0.003 and 0.296). VLDL levels positively correlated with NAFLD grades ($p<.0001$). Mean TC levels associated with moderate and severe NAFLD, similar to our study, were comparable to those proposed by Sen et al. Parallel to our investigation, both TCL and TGL levels were higher in Grade III patients than those in Grades II and I.[22] Similar to our study Mahaling et al. also reported a statistically significant association of TC and VLDL with increasing grades of NAFLD.[14] However, they reported insignificant levels of rise in TGL with higher grades of NAFLD. A likely decrease in HDL levels similar to our study was also reported by Bhusal et al.[16]

CONCLUSION

This study found a definite association between NAFLD and high blood levels of Total cholesterol, Triglycerides and VLDL. Higher blood levels of Total cholesterol, Triglycerides and VLDL were found in higher grades of NAFLD diagnosed on ultrasonography. A liver biopsy is the most accurate in diagnosing NAFLD. Still, it is clinically impractical because of the large number of patients with NAFLD and the high cost of liver biopsy and sampling errors. Early detection of NAFLD by ultrasonography supported by serum lipid profile provides us with a valuable window of opportunity to initiate interventions to prevent the progression of the disease to irreversible fibrosis and eventual morbidity and mortality.

REFERENCES

1. Ludwig J, Viggiano TR, McGill DB, Oh BJ. Non-alcoholic steatohepatitis Mayo Clinic experiences with a hitherto unnamed disease. Mayo Clin Proc 1980; 55: 434-8.
2. Pierre Bedossa. Current histological classification of non-alcoholic fatty liver disease: strength and limitations. Hepatol Int 2013; 7(suppl. 2): 1-6.
3. David AS, Chang P, Chopra K. Non-alcoholic fatty liver disease: a clinical review. Digest Dis Sci 2005; 50: 171-80
4. Agarwal AK, Jain V, Singla S, Baruah BP, Arya V, Yadav R, et al. prevalence of non-alcoholic fatty liver disease and its correlation with coronary risk factors in patients with Type 2 diabetes. J Assoc Physician India 2011; 59: 1-4.
5. Bellentani S, Scaglioni F, Marino M, Bedogni G. Epidemiology of non-alcoholic fatty disease. Dig Dis 2010; 28(1): 155-61.
6. Baffy G, Brunt EM, Caldwell SH. Hepatocellular carcinoma in non-alcoholic fatty liver disease: an emerging menace. J Hepatol 2012; 56: 1384-91.
7. De Minicis S, Marzioni M, Saccomanno S, Rychlicki C, Agostinelli L, Trozzi L, et al. Cellular and molecular mechanisms of hepatic fibrogenesis leading to liver cancer. Transl Gastrointest Cancer 2012; 1: 88-94.
8. Obika M, Noguchi H. Diagnosis and evaluation of non-alcoholic fatty liver disease. Exp Diabetes Res 2012; 2012: 1-12.
9. Chalasani N, Younossi Z, Lavine JE, Diehl AM, Brunt EM, Cusi K, et al. The diagnosis and management of non-alcoholic fatty liver disease: practice Guideline by the American Association for the Study of Liver Diseases, American College

ISSN (O): 2687-5365; ISSN (P): 2753-6556

of Gastroenterology, and the American Gastroenterological Association. Hepatology 2012; 55: 2005-2023.
10. Shahin M, Rasoul S, Mehdi N, Masoumeh PH, Sadaf GS, Reza M, et al. Sampling error in histopathology findings of non-alcoholic fatty liver disease: a post mortem liver histology study. Arch Iran Med 2012; 15: 418-21
11. Brunt EM. Pathology of fatty liver disease. Modern Pathology. 2007; 20: S40-8.
12. Brunt EM, Janney CG, Di Bisceglie AM, Neuschwander-Tetri BA, Bacon BR. Non-alcoholic steatohepatitis: a proposal for grading and staging the histological lesions. Am. J. Gastroenterol. 1999; 94:2467-74.
13. Tanwani BM, Jamali AA, Jamali GM, Jamali AA, Sohail MA. Non-Alcoholic Fatty Liver Disease: Assessment of Lipid Profile Estimation in Different Grades of Fatty Liver on Ultrasound. Open J. Prev. Med. 2018; 8:70.
14. Mahaling DU, Basavaraj MM, Bika AJ. Comparison of lipid profile in different grades of a non-alcoholic fatty liver disease diagnosed on ultrasound. Asian Pac. J. Trop. Biomed. 2013; 3:907-12.
15. Rafat FK, Nabil M, Salah M, Mohamed MA, Ibrahim W. Study of Lipid Profile in Different grades of Non-Alcoholic Fatty Liver Disease. Egypt. J. Hosp. Med. 2018; 73:7388-93.
16. Bhusal KR, Simkhada R, Nepal P. Lipid profile in different grades of ultrasonic non-alcoholic fatty liver disease. J. Coll. Med. Sci. Nepal. 2017; 13:258-61.
17. Pardhe BD, Shakya S, Bhetwal A, Mathias J, Khanal PR, Pandit R, et al. Metabolic syndrome and biochemical changes among non-alcoholic fatty liver disease patients attending a tertiary care hospital of Nepal. BMC Gastroenterology. 2018; 18:1-8.
18. Musso G, Gambino R, Cassader M, Pagano G. Meta-analysis: a natural history of non-alcoholic fatty liver disease (NAFLD) and diagnostic accuracy of non-invasive tests for liver disease severity. Annals of medicine. 2011; 43:617-49
19. Milić S, Lulić D, Štimac D. Non-alcoholic fatty liver disease and obesity: biochemical, metabolic and clinical presentations. World J. Gastroenterol: WJG. 2014; 20:9330.
20. Khanal UP, Paudel B, Gurung G, Hu YS, Kuo CW. A correlational study of a non-alcoholic fatty liver disease diagnosed by ultrasonography with lipid profile and body mass index in adult Nepalese population. J. Med. Ultrasound. 2019; 27:19.
21. Pradhan B, Patel J. Hepatic Dysfunction in Type-2 Diabetes Mellitus. J. Med. Sci. Clin. Res; 2020; 8:631-37.
22. Sen A, Kumar J, Misra RP, Uddin M, Shukla PC. Lipid profile of patients having the non-alcoholic fatty liver disease as per ultrasound findings in north Indian population: A retrospective observational study. J Med Allied Sci. 2013; 3:59-62.

ISSN (O): 2687-5365; ISSN (P): 2753-6556