Section: General Medicine

Original Research Article

A STUDY OF ASSESSMENT AND CORRELATION OF LIPID PROFILE AND LIVER ENZYMES IN NON-ALCOHOLIC FATTY LIVER DISEASE PATIENTS IN TERTIARY CARE CENTRE

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Abstract

Background: Non-alcoholic fatty liver disease (NAFLD) is characterized by excess lipid accumulation in hepatocytes (>5% liver weight) without alcohol or hepatitis infection, ranging from simple steatosis to cirrhosis, with type 2 diabetes and metabolic syndrome as key risk factors. This study aimed to investigate the lipid profile and liver enzymes in patients with NAFLD. **Materials and Methods:** The study assessed ninety-five participants through BMI calculations, detailed histories, clinical examinations, and laboratory tests, including liver enzymes and fasting lipid profiles. Abdominal ultrasound diagnosed and staged fatty liver into three grades: grade 1 (mild), grade 2 (moderate), and grade 3 (severe), based on liver echogenicity and visibility of portal structures and the diaphragm. **Result:** Among the 95 patients, 39.4% were aged 40-50, 30.8% were 50-60, and 29.8% were 35-40, with 51 females and 44 males. Among them, 37 had diabetes, 20 had hypertension, 7 had coronary artery disease, 57 had dyslipidaemia, and 2 had cerebrovascular accidents. Significant positive correlations were observed between fatty liver grade and FBS, AST, ALT, GGT, total cholesterol, triglycerides, LDL, and VLDL ($p<0.05$). HDL levels showed a significant negative correlation ($p=0.184$, $r=-0.137$) with fatty liver severity. The median values for FBS, AST, GGT, total cholesterol, TGL, LDL, and VLDL increased with fatty liver grade. **Conclusion:** This study suggests that significant biochemical changes in patients may be indicative of NAFLD. Thus, abdominal ultrasonography is recommended for early detection to prevent or delay complications.

INTRODUCTION

The accumulation in the hepatocytes of lipids more than 5% of liver weight without consumption of alcohol and hepatitis B or C virus infections is called Non-alcoholic Fatty Liver Disease (NAFLD).[1] The NAFLD spectrum includes Non-alcoholic Fatty Liver (NAFL), Non-alcoholic Steato Hepatitis (NASH), fibrosis and cirrhosis.[2] Hepatic Steatosis is the initially recognized state. Hepatic inflammation leads to non-alcoholic steatohepatitis (NASH), a condition with a greater risk of progression to fibrosis, cirrhosis, and hepatocellular carcinoma. Worldwide NAFLD is becoming a global problem, with a prevalence of approximately 24% among the general population.[3] The actual burden of NAFLD is the tip of the iceberg, as there is a prolonged natural history, lack of awareness among people, and the cause of death is not related to the liver.[4]

Central Obesity is an important risk factor for the development of NAFLD and a key determinant in the pathogenesis of NAFLD.[5] Central Obesity is one of the components of metabolic syndrome, which is associated with the development of diabetes mellitus. The hepatic component of metabolic syndrome is now considered to be NASH.[6] The Liver enzymes, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and gamma glutamyl transferase (GGT), are usually elevated in NAFLD, and these are found to act as markers of hepatocellular injury.[7] Especially, ALT is elevated two to three times normal in patients with NAFLD. NAFLD is associated with dyslipidaemia in nearly three-fourths of the patients.[8] There is an imbalance

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between fatty acid synthesis and the delivery of fatty acids by VLDL, which results in the development of steatosis.

Impaired fasting glucose or impaired glucose tolerance are risk factors for the development and progression of NAFLD, leading to fibrosis. Type 2 Diabetes Mellitus is an independent risk factor for NAFLD.[9] The risk of development of nephropathy and retinopathy, which are microvascular complications of diabetes, is known to be increased in patients with NAFLD.[10] Glycated haemoglobin (HbA1c) level also increases as fibrosis progresses.[11] The vice-versa can also occur, that is, the presence of NAFLD can increase the risk of development of Diabetes Mellitus. NAFLD can be diagnosed by obtaining the patient's detailed history, clinical examination, and performing proper laboratory investigations and ultrasound abdomen.[12] Liver biopsy is considered the gold standard for NAFLD grading. Transient Elastography (Fibroscan) is a non-invasive method that can also be used to assess the stages of hepatic fibrosis.[13] It has been proposed to include NAFLD in the National Programme for Control of Non-communicable Diseases (NPCDCS). There are a very small number of studies on NAFLD in our population. Understanding the correlation of different biochemical parameters in NAFLD helps in understanding disease severity and progression and early intervention.

Aim

This study aimed to investigate the lipid profile and liver enzymes in patients with non-alcoholic fatty liver disease in a tertiary care centre, GVMCH, Vellore.

MATERIALS AND METHODS

This hospital-based cross-sectional study was conducted on 95 patients at the Government Vellore Medical College from January 2022 to December 2022. This study was approved by the Institutional Ethics Committee before initiation, and informed consent was obtained from all patients.

Inclusion criteria

Patients aged 35-60 years, of both sexes, who were willing to voluntarily participate in this study after obtaining informed consent were included.

Exclusion criteria

Patients with acute and chronic liver disease including Hepatitis B and C, acute or chronic kidney disease, alcoholics of any duration and time, history of intake of drugs such as methotrexate, amiodarone, glucocorticoids, synthetic oestrogens, non-nucleoside analogues, pregnancy, proven hemochromatosis, Wilson's disease, or known liver disease were excluded.

Methods

Each participant was asked predetermined questions based on a standardised protocol, and their body mass index (BMI) was calculated. Blood samples were collected for laboratory investigations. The study included a total of ninety-five participants, assessed through a detailed medical history, clinical examination, and various laboratory tests. Fasting blood samples were analysed for biochemical markers including alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, and gamma-glutamyl transferase. The fasting lipid profile included total cholesterol, triglycerides, high-density lipoprotein, low-density lipoprotein, very low-density lipoprotein, FBS, PPBS, HBsAg, and anti-HCV. Abdominal ultrasonography was performed to diagnose and stage the fatty liver.

Fatty liver was categorised into three grades based on ultrasonographic findings as follows: Grade 1 (mild), elevated echogenicity of the liver parenchyma with visible normal echogenicity of the periportal region and the diaphragm. Grade 2 (moderate): elevated echogenicity of the liver parenchyma with obscured portal vein branches, but the diaphragm remained unaffected. Grade 3 (severe): elevated echogenicity of the liver parenchyma with undetectable echogenicity of the periportal area and obstruction of the diaphragm.

Statistical analysis: Data were entered into Microsoft Excel and analysed using the Software Package for Statistical Study (SPSS), trial version 23. The distribution of the general characteristics of the study population, such as age, gender, hypertension, diabetes, and dyslipidaemia, was presented as proportions with a 95% Confidence Interval. The correlation of various liver enzymes and lipid profiles with the grade of fatty liver was analysed using Spearman's correlation. The mean values of different biochemical parameters across the various NAFLD grades were compared using Box and Whisker plots.

RESULTS

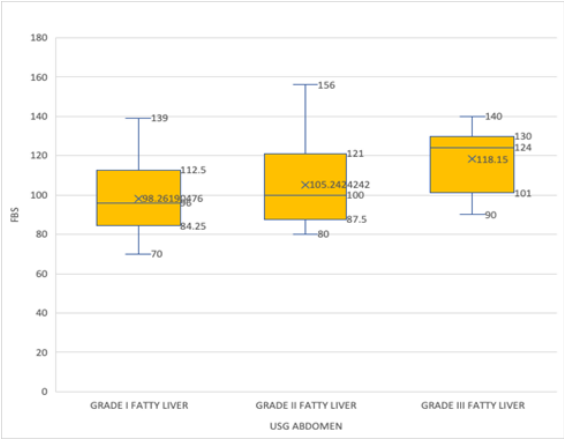

Figure 1: FBS values vs. grade of fatty liver

Among the study population of 95 participants, 37 (39.4%) were aged 40-50 years, 29 (30.8%) were aged 50-60 years, and 29 (29.8%) were aged 35-40 years, with a gender distribution of 51 females and 44 males. Diabetes was present in 37 patients, while 58 were non-diabetic. Hypertension was observed in 20 patients, whereas 75 had no history of hypertension.

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CAD was present in only 7 patients, and dyslipidaemia affected the majority of 57 (60%) patients. CVA was rare, with only 2 affected patients [Table 1].

There was a significant positive correlation with FBS (r=0.283), AST (r=0.547), ALT (r = 0.611), GGT (r=0.237), total cholesterol (r=0.217), TGL (r=0.469), LDL (r=0.517), and VLDL (r=0.722) between the grades of fatty liver ($p<0.05$). There was a significant negative correlation between serum HDL levels and fatty liver grades (r=-0.137) (p=0.184) [Table 2].

[Figure 1] shows a comparison of the mean, median, minimum, maximum values, and interquartile range of fasting blood sugar across different grades of fatty liver disease, with a median value of 98.26 in Grade I and 118.15 in Grade III. These values increased as the fatty liver grade increased.

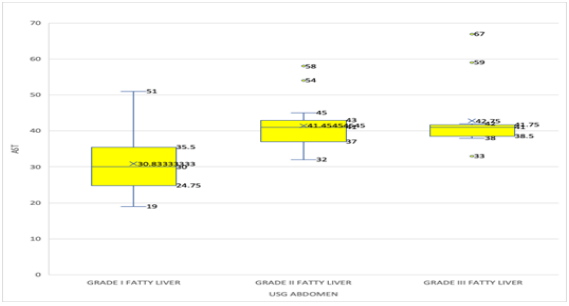

Figure 2: AST values vs. grade of fatty liver

[Figure 2] shows a comparison of serum AST levels across different grades of NAFLD, with a median value of 30.83 in Grade I and 41 in Grade III.

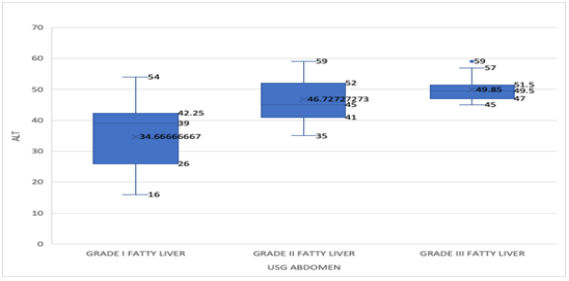

Figure 3: ALT values vs. grade of fatty liver

[Figure 3] shows a comparison of serum AST values across different grades of NAFLD, with a median value of 34.6 in Grade I and 49.85 in Grade III.

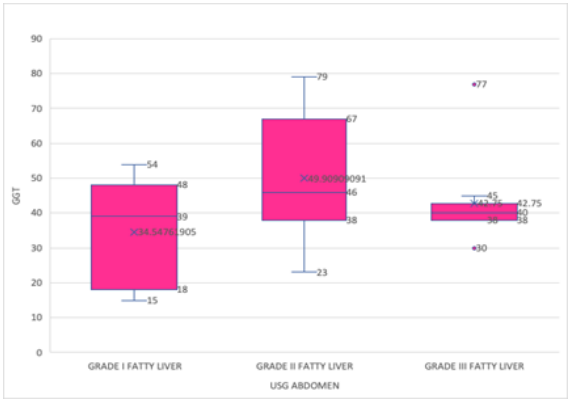

Figure 4: GGT values vs. grade of fatty liver

[Figure 4] shows a comparison of Serum GGT levels across different grades of NAFLD. The median GGT levels were 34 and 4 for grades I and III, respectively.

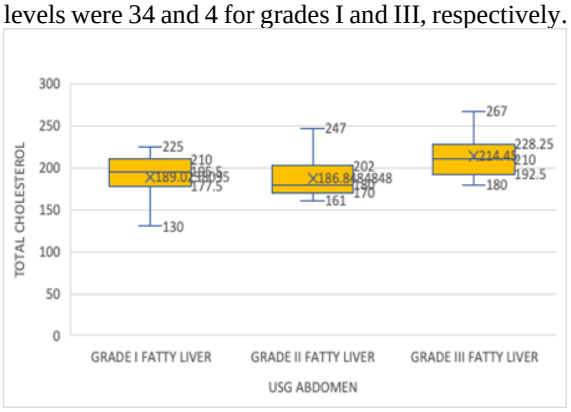

Figure 5: Total cholesterol values vs grade of fatty liver

[Figure 5] shows a comparison of serum total cholesterol values across different grades of NAFLD. The median values of total cholesterol in grades I and III were 189 and 210, respectively.

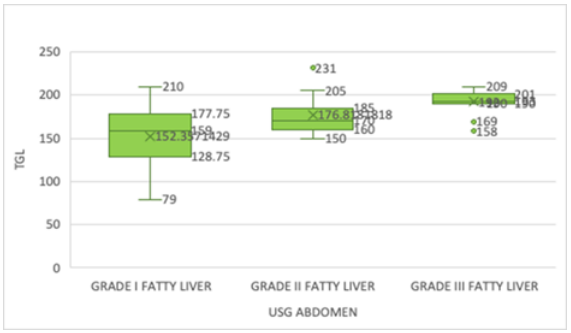

Figure 6: TGL values vs grade of fatty liver

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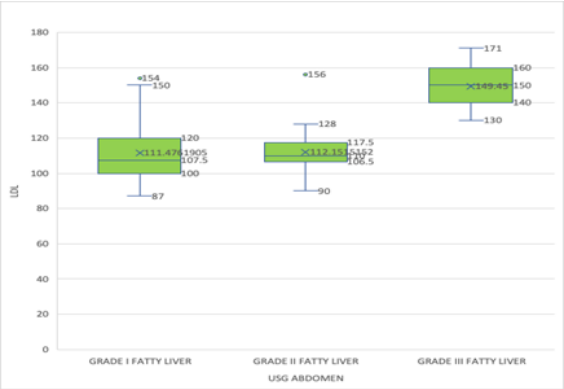

Figure 7: LDL values vs grade of fatty liver

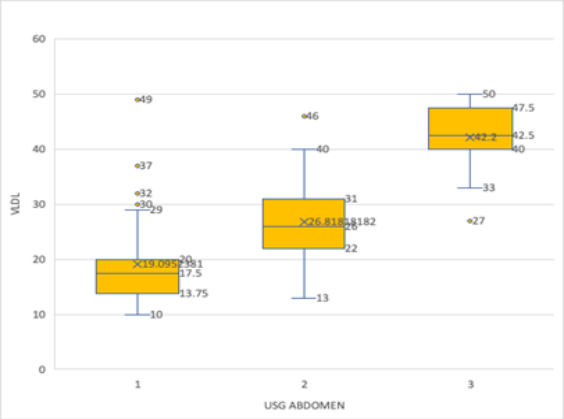

Figure 8: VLDL values vs grade of fatty liver

[Figure 6] shows a comparison of serum TGL levels across different grades of NAFLD. The median TGL values were 152 and 190 for Grades I and III, respectively.

[Figure 7] shows a comparison of LDL levels across different grades of NAFLD. Median LDL levels in grades I and III were 111 and 149, respectively.

[Figure 8] shows a comparison of VLDL levels across different grades of NAFLD. The median value of VLDL in Grade I was 19.09 and in Grade III it was 42.2.

[Figure 9] shows a comparison of serum HDL levels across the different grades of NAFLD. The median value of HDL in Grade I was 49.7 and in Grade III, it was 46.

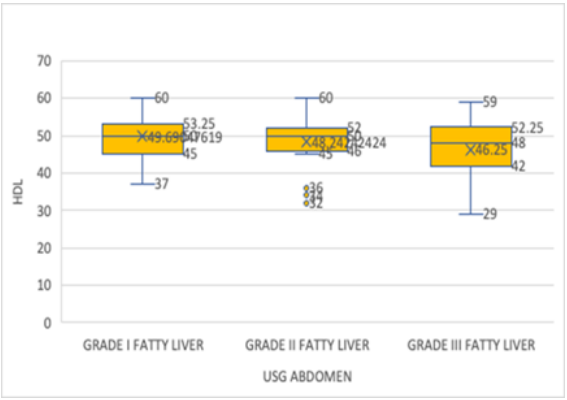

Figure 9: HDL values vs grade of fatty liver

Table 1: Demographic details and prevalence of comorbidities.

		Frequency (%)	95% Confidence Interval	
			Lower	Upper
Age in years	35-40	29 (29.8%)	20.2	39.4
	40-50	37 (39.4%)	29.8	48.9
	50-60	29 (30.8%)	21.3	40.4
Gender	Male	44 (46.3%)	36.8	56.8
	Female	51 (53.7%)	43.2	63.2
Diabetes	Yes	37 (38.9%)	29.5	48.4
	No	58 (61.1%)	51.6	70.5
Hypertension	Yes	20 (21.1%)	12.6	29.5
	No	75 (78.9%)	70.5	87.4
CAD	Yes	7 (7.4%)	2.1	12.6
	No	88 (92.6%)	87.4	97.9
Dyslipidaemia	Yes	57 (60%)	49.5	69.5
	No	38 (40%)	30.5	50.5
CVA	Yes	2 (2.1%)	0	5.3
	No	93 (97.9%)	94.7	100

Table 2: Correlation of the biochemical parameters with the grade of fatty liver

	Mean	Grade of fatty liver	r value	p value
FBS	104.87±20.623	1.77±0.778	0.283	<0.05
AST	37.03±9.371	1.77±0.778	0.547	<0.05
ALT	42.05±10.44	1.77±0.778	0.611	<0.05
GGT	41.61±15.843	1.77±0.778	0.237	0.021
T. Cholesterol	193.62±26.182	1.77±0.778	0.217	<0.05
TGL	169.2±32.943	1.77±0.778	0.469	<0.05
LDL	119.71±21.901	1.77±0.778	0.517	<0.05
VLDL	-	26.64±11.541	0.722	<0.05
HDL	48.46±7.199	1.77±0.778	-0.137	0.184

DISCUSSION

Non-alcoholic fatty liver disease (NAFLD) has emerged as a serious health problem in recent years. Its prevalence has been increasing in both developing and developed countries due to urbanization and changes in lifestyle patterns, including unbalanced diets and sedentary lifestyles. It is emerging as a great

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challenge to healthcare because predisposing factors are linked to the social and cultural environment. This study attempted to determine the correlation between biochemical parameters and disease severity and, in turn, can help in early diagnosis and management. Abdominal ultrasound can be used for the preliminary diagnosis of NAFLD. It can be stated that Ultrasonography with a low cost and minimal complications is the cost-effective method for identifying the changes associated with NAFLD.

In the present study, the majority of the study participants with non-alcoholic fatty liver disease belonged to the age group of 40-50 years and were female. This is in contrast to the findings of a study conducted in North India by Singh et al., where 63 were males and 30 females and the majority of the cases were found in the age group of 30–40 years.[14] In our study, nearly 38% of the patients with NAFLD were diabetic. This may be because common insulin resistance of different degrees causes cellular abnormalities that may lead to the development of both NAFLD and Type 2 diabetes. More than half of the patients with NAFLD had dyslipidaemia. Patients with non-alcoholic fatty liver disease (NAFLD) frequently have associated dyslipidaemia together with other components of metabolic syndrome including diabetes mellitus, obesity and hypertension. Although the pathogenesis of dyslipidaemia in NAFLD is not clear, it may be related to the hepatic overproduction of VLDL and decreased clearance of lipoproteins from the circulation. Adequate treatment of dyslipidaemia is crucial for the management of NAFLD. Similar results were also found in studies done by Novakovic et al., which had a significantly higher incidence of hypertension, diabetes, and hypercholesteremia ($p<0.001$), compared with patients without NAFLD.[15]

A study by Pardhe et al. found that ALP and ALT levels were significantly different between NAFLD grades, while no significant change in AST was observed. The changes in TGL and HDL-C were also statistically significant in different grades of NAFLD, where TGL was found to increase, while HDL-C decreased with steatosis. There was no significant change in TC and LDL-C between different grades of NAFLD.[16] In another study by Jain et al., NAFLD was significantly higher in patients with increasing SGPT ($p=0.026$), total cholesterol ≥ 200 mg/dL ($p=0.042$), triglycerides ≥ 150 mg/dL ($p=0.040$), LDL > 130 mg/dL ($p=0.027$), HDL < 30 mg/dL ($p=0.023$).[17]

In our study, there was a positive correlation between elevated FBS levels and the NAFLD grade. Similar findings were also reported by Novakovic et al., where fasting glucose and insulin levels were significantly higher in study patients ($p=0.001$) than in patients without NAFLD.[15] Pardhe et al. study shows that fasting glucose and insulin levels were significantly greater in study patients ($p<0.001$).[16] Jain et al. found that NAFLD was significantly higher in patients with FBG > 110 mg/dL ($p=0.042$).[17]

In our study, there was a significant correlation between the hepatic enzymes AST, ALT, and GGT ($p<0.05$) and NAFLD severity. The reports of a study in the Philippines by Cuenza et al. showed that ALT($p=0.001$) and AST($p=0.000$) had a significant relationship with grading NAFLD by ultrasound.[18]

In our study, there was a significant positive correlation between the grading of NAFLD and lipid profile parameters, including total cholesterol, LDL, VLDL, Triglycerides, and an inverse relationship with HDL. Similarly, Mahaling et al. showed a positive correlation of total cholesterol ($p=0.001$), LDL ($p=0.001$) and VLDL ($p=0.003$) and a negative correlation of HDL ($p=0.000$) with grades of NAFLD, but in contrast, in their study there was no significant correlation with triglyceride level. ($p=0.05$).[19] Further, a study in Nepal by Pardhe et al. showed a significant correlation between hepatic enzymes (ALT, ALP) and across different grades of NAFLD.[16]

Limitations

Our study has the limitation that ultrasound was used to detect NAFLD while Liver Biopsy is considered the gold standard for diagnosing fatty liver. Because it is invasive, expensive, and associated with the risk of complications, biopsy is not routinely recommended for the general population, whereas abdominal USG, in contrast, is non-invasive and cost-effective.

CONCLUSION

This study indicated that there was a considerable change in biochemical parameters in patients with Non-alcoholic Fatty Liver Disease. Therefore, in patients with changes in biochemical values and lipid profiles, ultrasound examination should be performed to screen for NAFLD, as early diagnosis can prevent and delay complications.

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