Original Article

Association of Lipid Profile with Non-Alcoholic Fatty Liver Disease diagnosed on Ultrasound

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Abstract

Objectives: To evaluate lipid profile parameters in patients with various grades of non-alcoholic fatty liver disease (NAFLD) diagnosed on sonography.

Material and Method: This descriptive cross-sectional study was conducted at HBS General Hospital, Islamabad over a period of six months from January 2018 to June 2018. Seventy-nine adults of either gender diagnosed with NAFLD on ultrasonography were consecutively included. Fasting blood sample of all the subjects was analyzed for total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C) Comparison of lipid abnormalities between different grades of NAFLD was done by statistical analysis with p-value <0.05 considered statistically significant.

Results: Out of the total 79 patients, grade I, II, and III NAFLD was diagnosed in 56.6%, 45.5%, and 3.9% respectively. Total cholesterol (TC), triglycerides (TG), low density lipoprotein cholesterol (LDL-C) were raised in 28 (35.4%), 43 (54.4%) and 43 (54.4%) patients respectively. Low serum high-density lipoprotein cholesterol (HDL-C) levels were seen in 74 (93.6%) of patients. Statistical analysis showed a significant increase in frequency as well as mean values in all serum lipid profile parameters with the severity of NAFLD grades except total cholesterol (TC).

Conclusion: Increasing grades of NAFLD showed a significant correlation with higher levels of cholesterol, LDL, and decreasing levels of HDL, which are all associated with cardiovascular problems.

Keywords: Non-alcoholic fatty liver disease; Dyslipidemia; Metabolic syndrome.

Introduction

An extensive array of chronic hepatic disorders varying from plain steatosis to steatohepatitis (NASH) with enhanced fibrotic and cirrhotic changes on histology without considerable alcohol use defines non-alcoholic fatty liver disease.^{1,2}

The number of fatty liver patients has risen over the past two decades due to an increase in overweight, obese individuals and their consequent metabolic derangements, possibly due to an unhealthy and sedentary lifestyle.3,4,5 The global prevalence rate of NAFLD is 25.24%. As per the World Gastroenterology Organization Global Guidelines 2014, the NAFLD prevalence rate in the Pakistani population is 18%.67,8 Fatty liver is linked with metabolic risk factors. Observational studies revealed that NAFLD patients exhibit a greater possibility of evolving complications that are extrahepatic, like metabolic syndrome, cardiovascular disease, and diabetes.^{7,8,9} It is postulated that deposition of lipids, primarily triacylglycerol (TAG) in the hepatic cells is the main element of the pathogenesis of NAFLD, however, the exact mechanism is still unclear.^{10,11} NAFLD is linked with raised values of VLDL, TG, and LDL with decreased values of serum HDL which can lead to cardiovascular diseases (CVD) morbidity and mortality.12,13,14

Liver biopsy is the most precise procedure for diagnosing NAFLD, but it is an uncomfortable and invasive method with uncommon potentially serious complications. It is prone to sampling errors.^{15,16,17} Thus, an ultrasonography based classification system is recognized that relates histologic aspects with prognosis.¹⁶

Our study aims at determining the correlation of different lipid profile parameters with the grading of NAFLD as shown on ultrasound. This will aid in the earlier detection of dyslipidemias and effective management in the times to come.

Materials and Methods

This cross-sectional study was conducted at the Department of Radiology and the Department of Medicine, HBS General Hospital, Islamabad from January 2018 to June 2018. The study was approved by

the institution's research ethics committee. The study included 79 patients of either gender aged 18 years or above, diagnosed with non-alcoholic fatty liver disease (NAFLD) on ultrasonography, using non-probability consecutive sampling. Patients with a history of alcohol consumption, viral and autoimmune hepatitis, and those using lipid-lowering medicines were excluded. Pregnant patients were also excluded. The ultrasound examination was done on Toshiba Xario using a 5MHz probe. The hepatic steatosis was graded according to the following criteria,

- Grade I: increased liver echogenicity with normal periportal and diaphragmatic echogenicity.
- Grade II: increased liver echogenicity with imperceptible periportal echogenicity without obscuration of the diaphragm.
- Grade III: increased liver echogenicity with imperceptible periportal echogenicity and obscuration of the diaphragm.

Patients were informed about the aims and design of the study and consent was taken individually. 3ml of blood samples were taken from the study participants after an overnight fast and analyzed for serum TC, TG, HDL, and LDL. Dyslipidemias were defined according to the AACE 2017 guidelines for the management of dyslipidemia and prevention of atherosclerosis as follows: High TC>200 mg/ml; High TG>150 mg/ml; High LDL-C>100 mg/ml; and Low HDL-C<40 mg/ml. The demographic and the clinical data were entered in a pre-designed proforma and analyzed using Statistical Package for Social Sciences (SPSS). Results were reported as mean ± standard deviation (SD) for continuous variables and as frequencies for categorical variables. Frequencies of dyslipidemias and mean values of individual lipids in different grades of NAFLD were statistically compared using chi-square and ANOVA tests respectively.

Results

79 patients of NAFLD were included in the study out of which 7 (8.9%) were males and 72 (91.9%) were females. The mean age was calculated to be 42.2 years. Fatty liver grades in the patients detected by sonography are given in Figure 1 while the laboratory findings of the study participants are given in Table 1.



Figure 1: Grades of NAFLD in the study patients on the basis of ultrasound

| Characteristic | Overall | Male | Female | |
|----------------|--------------|----------|----------|--|
| (mg/dL) | Mean + | (n=7) | (n=72) | |
| | SD | Mean + | Mean + | |
| | | SD | SD | |
| Serum Total | $178.78 \pm$ | 165.43 ± | 180.08 ± | |
| Cholesterol | 37.60 | 45.86 | 36.83 | |
| Serum | 197.53 ± | 176.29 ± | 198.22 ± | |
| Triglycerides | 77.27 | 42.14 | 82.31 | |
| Serum HDL- | 33.81 ± | 31.57 ± | 34.03 ± | |
| Cholesterol | 5.71 | 4.27 | 5.81 | |
| Serum LDL- | 104.63 ± | 93.29 ± | 105.74 ± | |
| Cholesterol | 22.19 | 19.61 | 22.23 | |

 Table 1: Laboratory findings of the study patients

Analysis of the laboratory parameters of the study participants showed abnormally raised serum TG, TC, and LDL-C in 54.4%, 35.4%, and 54.4% of the participants respectively, while low serum HDL-C was observed in 93.7% of the study subjects as shown in Figure 2. The Chi-square test performed showed a significant difference in the various grades of NAFLD for the frequency of dyslipidemia in all lipid profile parameters except serum TC (p-value= 0.183) as evident in Table 2.

Frequency distribuation of dylipidemias



Figure 2: Frequency of dyslipidemias in the patients of NAFLD

| Characteristic (mg/dL) | Overall n (%) | Grade-I n (%) | Grade-II n (%) | Grade-III n (%) | p-value |
|---|------------------|------------------|-------------------|--------------------|---------|
| Serum Total Cholesterol (>200 mg/dL) | 28 (35.4) | 7 (25) | 18 (64) | 3 (10) | 0.183 |
| Serum Triglycerides (>150 mg/dL) | 43 (54.4) | 17 (39.5) | 23 (53.4) | 3 (0.06) | 0.077 |
| Serum HDL-Cholesterol (<40 mg/dL) | 74 (93.6) | 38 (51) | 33 (44.5) | 3 (0.04) | 0.007 |
| Serum LDL-Cholesterol (>100 mg/dL) | 43 (54.4) | 18 (41.8) | 23 (53.4) | 2 (0.04) | 0.037 |

Table 2: Frequency of dyslipidemias in the patients of NAFLD

The ANOVA test performed, revealed a significant association of rising grades of NAFLD with rising mean values of dyslipidemias in all lipid profile parameters except serum TC (p-value= 0.99) as evident in Table 3.

| Table 3: Com | parison of Serun | n Lipid Profile a | mong different s | zrades of NAFLD |
|--------------|------------------|-------------------|------------------|-----------------|
| | r | | | |

| 1 | | 0 |) | | |
|-------------------------|--------------------|---------------------|------------------|-----------------|-------|
| Characteristic | Overall | Grade-I | Grade-II | Grade-III | Anova |
| (mg/dL) | Mean ± SD | Mean ± SD | Mean ± SD | Mean ± SD | |
| Serum Total Cholesterol | 178.78 ± 37.60 | 167.55 ± 31.267 | 189.1 ± 41.5 | 205 ± 21.93 | 0.099 |
| Serum Triglycerides | 196.28 ± 79.65 | 190 ± 85 | 199 ± 63 | 278 ±107 | 0.047 |
| Serum HDL-Cholesterol | 33.81 ± 5.71 | 33 ± 5 | 35 ± 7 | 32 ± 4 | 0.040 |
| Serum LDL-Cholesterol | 104.63 ± 22.19 | 100 ± 8 | 109 ± 24 | 111 ± 43 | 0.047 |

Discussion

Common metabolic aberrations like obesity, hyperglycemia, dyslipidemia, and hypertension are known as major health risk factors worldwide leading to an increase in hepatic steatosis regardless of age and gender.⁷

Being the major focus of this study, the association of dyslipidemias with various grades of NAFLD was evaluated.

The age of patients varied from 23 to 65 years, the mean being 42.2 in our study. Many studies have stated 41-45 years as the mean age of fatty liver disease. Thus, the above forty years age group is at a significantly higher risk of developing NAFLD as they may be more prone to metabolic abnormalities including dyslipidemias due to deposition of fats. A study by Goh et al on the Asian population in Malaysia also reported this.¹⁹

In our study 54.4% (43) of all NAFLD patients had hypertriglyceridemia. Increased levels of serum TC, LDL-C, and decreased levels of serum HDL were present in 35.4% (28), 54.4% (43), and 93.7% (74) respectively of all NAFLD subjects.

Dyslipidemia among NAFLD patients has been studied and compared with healthy subjects in various studies.²⁰ Mahaling et al. (2013) and Bano et al. (2008) showed hypertriglyceridemia as the commonest dyslipidemia, and the next common dyslipidemia was low HDL-C. Nevertheless, in our study, the most significant dyslipidemia was low HDL-C (93.7%).

The pathogenesis of NAFLD is poorly understood but variation in oxidant systems or body fat distribution, most likely due to a genetic predilection may be amongst the explanation.

A total accumulation of fats within hepatocytes commonly TG leads to the development of the fatty liver. Lipid accumulation and the preceding principal metabolic defects are not fully comprehended. A possible explanation is derangements in hepatic triglyceride metabolism pathways due to insulin resistance. The most reproducible factor for fatty liver disease occurrence in diabetics is insulin resistance.^{22,23} NASH and NAFLD are commonly identified parenthetically or in concurrence with different comorbidities like obesity. As the prevalence of the fatty liver disease is rising,^{7,8} and corresponds with the metabolic syndrome, clinical practice guidelines now propose that all obese or diabetic patients should be scrutinized for NAFLD.

Our study showed that 32.9% (26) patients with NAFLD were diabetic, 27.8% (22) were overweight,

55.7% (44) were obese, 5.1% (4) were morbidly obese and 11.4% (9) had normal BMI.

Biopsy (liver) is the most sensitive test in identifying hepatic steatosis, but as it is an invasive procedure causing pain with associated complications and sampling errors, it is not appropriate for asymptomatic subjects.

Thus keeping this view, ultrasonography offers a favorable alternative to diagnose fatty liver disease. This is proven by statistically significantly deranged lipid profile parameters in this study.

The specificity and sensitivity of sonographic detection are high (83.9% and 84.6% respectively) in higher grades of steatosis. Sonography is a cheaper safe modality for early detection of NAFLD thus minimizing invasive investigations in these patients.

There were a few limitations to our study. Ultrasonography based detection of NAFLD and its grading cannot detect cases of mild steatosis for which liver biopsy is the gold standard. The study cohort may not be representative of all the major ethnic groups of Pakistan, so a bigger multi-racial, casecontrol study design using liver biopsy to identify and grade fatty liver disease may be required.

Conclusion

Results in our study lead to the conclusion of a significant correlation between increasing grades of NAFLD and increased frequency of dyslipidemias. The most frequent dyslipidemia being low HDL-C followed by raised LDL-C and hypertriglyceridemia.

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