Original Article

Correlation of Sonographic Grading of Fatty Changes of Liver with Lipid Profile

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Abstract

Background: Ultrasound Imaging can be used as a painless, non-invasive modality for the detection of nonalcoholic fatty liver disease (NAFLD) Aims: To determine the association of abnormal lipid profiles in persons identified with NAFLD using ultrasound. Settings and Design: Retrospective observational study design at a single Centre. **Subjects and Methods:** The study included subjects aged 20 to 70 years, identified with NAFLD based on ultrasound findings, with biochemical test results of lipid profile and with NAFLD graded based on ultrasound findings. Statistical Analysis used: A one way Analysis of Variation test (ANOVA) was used to compare the lipid profiles by grades of NAFLD. The lipid profiles were also categorized as optimal or normal and abnormal values and compared by grades of NAFLD. A p value of <0.05 was considered as statistically significant. **Results:** The study included 100 subjects (males=87) with a mean age of 46.1 ± 11.2 years. Eighty nine subjects were categorized as grade I NAFLD, 9 as grade 2 NAFLD and 2 subjects as Grade III NAFLD. The mean ± SD total cholesterol was 195.55 ± 43.78, serum triglycerides was 190.09±122.03, HDL was 42.14±10.75, and LDL was 120.47±36.58 md/dL, cholesterol HDL ratio was 4.90±1.52 and LDL HDL ratio was 2.92±1.07 (range 0.56 to 5) in the study subjects. Thirty three (33.0%) of subjects had borderline high total cholesterol and 15 (15.0%) subjects had high total cholesterol. Twenty two (22.0%) subjects had borderline high serum triglycerides and 33 (33.0%) subjects had high serum triglycerides. **Conclusion:** An increasing dyslipidaemia was noticed with increasing severity of NAFLD graded using ultrasound imaging.

Keywords: Ultrasound, Nonalcoholic fatty liver, dyslipidemia, cholesterol, triglycerides.

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Introduction

Non-alcoholic fatty liver disease (NAFLD) is a common cause for chronic liver disease with an increasing incidence worldwide.[1-3] NAFLD is associated with metabolic syndrome, obesity, type 2 diabetes and dyslipidemia.[4-8] NAFLD is also associated with an atherogenic dyslipidemia that is characterised by increased levels of serum triglycerides, decreased levels of high density lipoproteins (HDL) and increased levels of oxidised low density lipoproteins (LDL).[9-13] The alterations in lipid and lipoprotein profiles in NAFLD are not well understood but have been attributed to dysregulated clearance of various lipoproteins and hepatic over production of very low density lipoproteins (VLDL).[14]

Ultrasound is a simple, non-invasive, easily available imaging modality with a sensitivity of 60-94% and specificity of 66-97% in NAFLD.[15] Ultrasound for fatty liver is operator dependent as the assessment of fatty liver depends on a subjective assessment of the hepatic echogenicity and posterior attenuation of the ultrasound beam.[16,17] In this manuscript, we describe the lipid profiles in persons with various grades of NAFLD identified through ultrasound.

Subjects and Methods

An observational study design was used to retrospectively retrieve information of persons with NAFLD graded by ultrasound at the department of Radiodiagnosis of A.J.Institute of Medical Sciences & Research Centre, Mangalore, Karnataka, India from June 2017 to December 2017. The study protocol was approved by the institutional ethics committee and informed consent was waived due to the retrospective nature of data collection. The study included subjects aged 20 to 70 years, identified with NAFLD based on ultrasound findings and excluded subjects who were discharged to long term care facilities, pregnant women and persons with a weekly alcohol intake more than 20 gram/week.

Ultrasound exams for NAFLD were performed PHILIPS EPIC 5G and PHILIPS AFINITY 30 Ultrasonography machine using 1-5 MHz convex transducer. NAFLD was graded based on a visual analysis of the intensity of echogenicity with an optimal gain setting. A minimally

increased echogenicity was categorized as Grade I [Figure 2], an obscuration of the echogenic walls of portal vein branches by the echogenic liver as grade II [Figure 3] and an obscuration of the diaphragmatic outline by the echogenic liver was categorized as grade III [Figure 4] NAFLD.18 Results of the biochemical tests for serum triglycerides and cholesterol done for persons identified with NAFLD were retrieved from the medical case records. A level of total cholesterol from 200 to 239 mg/dL was considered as borderline high and values > 240 mg/dL as high, values of HDL < 40 mg/dL was considered as low and values between 41 and 59 mg/dL as borderline low, values of non-HDL cholesterol < 130 mg/dL was considered as optimal, values of LDL from 130 to 159 mg/dL was considered as borderline high and values >160 mg/dL as high, values of VLDL ≤ 30mg/dL were considered as normal, and serum triglyceride values of 150-199 mg/dL were considered as borderline high and >200 as high.

The retrieved data were initially entered into a MS Excel spreadsheet and then exported to STATA version 10.0 (College Station, TX, US) for statistical analysis. The frequency distribution, mean and standard deviations were estimated for continuous variables. A one way Analysis of Variation test (ANOVA) was used to compare the lipid profiles by grades of NAFLD. The lipid profiles were also categorized as optimal or normal and abnormal values and compared by grades of NAFLD. A p value of <0.05 was considered as statistically significant.

Results

The study included 100 subjects with a mean age of 46.1 ± 11.2 years (range 20 to 67 years, median 47.0 years). The majority of subjects in the study were males (n=87, 87.0%). Eighty nine subjects were categorized as grade I NAFLD, 9 as grade 2 NAFLD and 2 subjects as Grade III NAFLD. [Table 1] presents the distribution of NAFLD by age and sex.

Table 1: Distribution of non-alcoholic fatty liver disease (NAFLD) by age and sex in the study population.

Demographics	Grade I NAFLD (n=89)	Grade II NAFLD (n=9)	Grade III NAFLD (n=2)
Age <40 years	21 (23.60%)	4 (44.44%)	2 (100.00%)
Age 40-49 years	33 (37.08%)	2 (22.22%)	0 (0.00%)
Age 50-59 years	28 (31.46%)	0 (0.00%)	0 (0.00%)
Age ≥ 60 years	7 (7.87%)	3 (33.33%)	0 (0.00%)
Male	76 (85.39%)	9 (100.00%)	2 (100.00%)
Female	13 (14.61%)	0 (0.00%)	0 (0.00%)

Thirty three (33.0%) of subjects had borderline high total cholesterol and 15 (15.0%) subjects had high total cholesterol. Twenty two (22.0%) subjects had borderline high serum triglycerides and 33 (33.0%) subjects had high serum triglycerides. HDL was borderline low in 45 subjects and low in 48 subjects and non HDL was abnormal in 71 subjects. LDL was borderline high in 25 subjects and high in 13 subjects and VLDL was abnormal in 54 subjects. The mean ± SD total cholesterol was 195.55 ± 43.78, serum triglycerides was 190.09±122.03, HDL was 42.14±10.75,

and LDL was 120.47±36.58 md/dL. The mean cholesterol HDL ratio was 4.90±1.52 (range 1.81, 10.72) and the mean LDL HDL ratio was 2.92±1.07 (range 0.56 to 5) in the study subjects. [Table 2] presents the distribution of lipid profiles by grades of NAFLD. The mean total cholesterol, serum triglycerides and HDL and LDL values were significantly different by grade of NAFLD (all p values <0.05) with increasing grade of NAFLD associated with increasing dyslipidaemia.

Table 2: Distribution of non-alcoholic fatty liver disease (NAFLD) by Lipid Profile in the study population.

Demographics	Grade I NAFLD (n=89)	Grade II NAFLD (n=9)	Grade III NAFLD (n=2)
Borderline High Total Cholesterol	31 (34.83%)	2 (22.2%)	0 (0.0%)
High Total Cholesterol	14 (15.73%)	0 (0.0%)	1 (50.0%)
Borderline High serum triglycerides	20 (22.47%)	2 (22.2%)	0 (0.0%)
High Total serum triglycerides	31 (34.83%)	2 (22.2%)	0 (0.0%)
Borderline low HDL	41 (46.07%)	3 (33.3%)	1 (50.0%)
Low HDL	42 (47.19%)	5 (55.56%)	1 (50.0%)
Abnormal non HDL	64 (71.91%)	6 (66.67%)	1 (50.0%)
Borderline High LDL	25 (28.09%)	0 (0.0%)	0 (0.0%)
High LDL	11 (12.36%)	1 (12.50%)	1 (50.0%)
Abnormal VLDL	50 (56.18%)	4 (44.44%)	0 (0.0%)

Figure 1: (Grade 0: Normal echogenicity of liver with echogenic margin of portal veins)

Figure 2: (Grade I: Mild increased echogenicity of liver with echogenic margin of portal veins)

Figure 3: (Grade II: Increased echogenicity of liver with obscuration of the echogenic walls of portal veins)
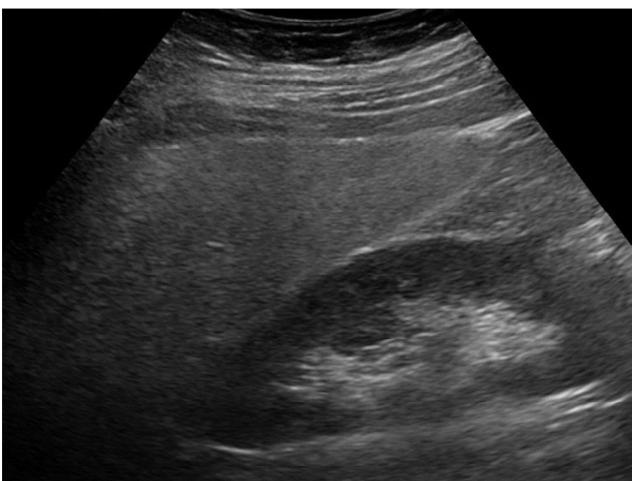

Figure 4: (Grade III: Increased echogenicity of liver with obscuration of the echogenic walls of portal veins & diaphragmatic outline)

Discussion

The prevalence of NAFLD is estimated as varying from 9% to 32% of the general population in India.[19] Liver biopsy has been the gold standard for the diagnosis of NAFLD, however, the procedure is invasive and has its own limitations. Imaging modalities including ultrasound are painless, non-invasive reliable alternates to identify and quantify NAFLD.

The pathogenesis of NAFLD is based on an initial triglyceride accumulation within hepatocytes that results in steatosis and is associated with insulin resistance and obesity and followed by primary lipotoxicity caused by oxidative stress from lipid peroxidation, reactive oxygen species production within hepatocytes, mitochondrial dysfunction, and inflammation.[20-23] NAFLD is leads to an increased risk of cardiovascular disease and is associated with atherosclerotic signs including carotid plaques and coronary arterial calcium.[24-28]

NAFLD was more common among those aged 40 to 60 years in this study and was more prevalent in males compared to females. The association of NAFLD with metabolic syndrome may explain the increased prevalence in the middle ages. An increasing dyslipidaemia was noticed with increasing severity of NAFLD. These findings are consistent with previous reports in the global literature.

The association of abnormal lipid profiles with NAFLD is important in India as there is an increasing prevalence of metabolic syndrome, cardiovascular diseases and other non-communicable lifestyle diseases in India. Our study shows that ultrasound imaging may be used as a non-invasive, painless diagnostic modality for the detection of NAFLD.

Conclusion

An increasing dyslipidaemia was noticed with increasing severity of NAFLD graded using ultrasound imaging.

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