Comparison of lipid profile and de-ritis ratio in ultrasound diagnosed non-alcoholic and alcoholic fatty liver disease

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Abstract
Introduction: Non-alcoholic fatty liver disease (NAFLD) is a major cause of chronic liver disease. NAFLD can progress to fibrosis, cirrhosis, liver failure and hepatocellular carcinoma, like alcoholic fatty liver disease (AFLD). However there are only few studies regarding lipid profile in NAFLD and AFLD that have been undertaken. Recently AST/ALT Ratio (also known as De-ritis Ratio), has been used as a marker of alcoholic liver disease. Hence this study was conducted to study the biochemical markers in NAFLD and AFLD.

Objectives: 1. To compare lipid profile and De-ritis ratio in ultrasound diagnosed NAFLD and AFLD 2. To assess the usefulness of these parameters to differentiate NAFLD from AFLD and also to monitor their prognosis.

Materials and Methods: 30 cases of USG diagnosed NAFLD and 30 cases of USG diagnosed alcoholic liver disease aged between 25 to 60 years, from MCH, VIMS, Ballari were studied and compared with 30 healthy age and sex matched healthy controls. After obtaining informed consent from all the patients, 5ml of fasting blood was collected and lipid profile, AST, ALT levels were estimated and De-ritis ratio was calculated.

Results: There was significant increase in the total cholesterol, LDL and Triglycerides levels in NAFLD patients (p=0.0001) when compared to AFLD patients. De-ritis ratio was significantly increased in AFLD patients (p=0.0001).

Conclusion: Hence it was concluded from our study that, NAFLD patients showed atherogenic dyslipidemia when compared to AFLD. De-ritis ratio can be used as parameter to differentiate between NAFLD from AFLD.

Keywords: Non-alcohol fatty liver, Alcoholic fatty liver, De-ritis ratio, Lipid profile, Fatty liver.

Introduction
Non-alcoholic fatty liver disease (NAFLD) is now being considered as a major health burden[1]. It has been documented that majority cases of NAFLD can progress to fibrosis, cirrhosis, liver failure and hepatocellular carcinoma, thus contributing to liver related mortality and morbidity like alcoholic liver disease (ALD)[2]. Prevalence of fatty liver in India has been shown to be as high as 15-30%[1]. Dyslipidemia in patients with NAFLD is atherogenic in nature and accumulation of lipids, mainly triglycerides in hepatocytes is the characteristic feature of the pathogenesis of NAFLD[3]. Also, it has been reported that the circulating non-esterified fatty acid pool contributed to the majority of the lipids that flow to the liver and constituted the bulk of the fasting liver triglyceride pool[4].

Fatty liver is the most common form of ALD which develops in more than 90% of heavy drinkers, but only about 30% of heavy drinkers develop a more severe form of ALD, such as fibrosis and cirrhosis[5]. Molecular pathogenesis of ALD involves alcohol metabolism such as oxidative stress, endotoxin, cytokines and immune regulators[6]. Liver plays a key role in the metabolism of plasma lipids and lipoproteins[7]. A majority of endogenous cholesterol is synthesized in the hepatic microsomes. The synthesis and metabolism of cholesterol is impaired resulting in worsening of the serum lipoprotein pattern[8].

DeRitis Ratio is the ratio between aspartate amino transferase (AST) and alanine amino transferase (ALT)[9]. The ratio of serum activities of AST and ALT was described by Fernado De Ritis in 1957 and since then it is known as De Ritis ratio. De Ritis is useful indicator of hepatitis and his work was confirmed and further investigated by Wroblewski This ratio was originally used to distinguish aminotransferase elevations of the inflammation type (De Ritis ratio <0.7) from the necrosis type (De Ritis ratio >0.7). Several studies have shown that this ratio is useful in differential diagnosis and classification of hepatic disorders[10]. This ratio is non-invasive cost effective test to diagnose and differentiate liver disorders[11].

It is known that long term ingestion of alcohol causes lipid profile abnormalities. The excess alcohol leads to increased oxidative stress, cell membrane permeability, cell necrosis and leakage of mitochondrial AST in to blood[9]. This has raised the interest, so the present study was undertaken with following aims and objectives.

Aims and Objectives
1. To compare lipid profile and De-ritis ratio in ultrasound diagnosed non-alcoholic and alcoholic fatty liver disease.
2. To assess the usefulness of these parameters to differentiate between NAFLD from AFLD.
Materials and Methods

30 cases of USG diagnosed NAFLD and 30 cases of USG diagnosed AFLD aged between 25-60 years from MCH, VIMS, Ballari were included in the study and compared with 30 healthy age and sex matched controls.

Inclusion criteria for the study:
- For AFLD, cases with history of alcoholism with clinical evidence and USG evidence of fatty liver were included. Detail history of alcohol intake was taken in every patient.
- For NAFLD, cases with USG evidence of fatty liver were included in the study.

Exclusion criteria for the study:
For NAFLD, cases with history of alcohol intake were excluded from study.
Patients with diabetes mellitus, nephrosis, thyroid dysfunction, HIV patients, chronic smokers and those taking the drugs which might affect the serum lipid profile were excluded from the study.

Institutional Ethical committee approval was obtained. After obtaining informed consent from all the patients, 5 ml of fasting blood sample was collected and centrifuged at 3000 rpm for 5 min to separate the serum. Following parameters were estimated.

All parameters were estimated by using automated Erba Manheim XL 640 analyzer. Total cholesterol (TC) was estimated by CHOD-PAP method and triglycerides (TG) by GPO-POD method, HDL direct by Detergent solubilizing method, LDL was determined by Freidelwald’s formula. AST and ALT were estimated by IFCC Kinetic method. Statistical analysis of data was done online by using Graph Pad Prism.

Results

Comparison of lipid profile, AST, ALT and De-ritis ratio in NAFLD and AFLD

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Controls Mean±SD (n=30)</th>
<th>NAFLD Mean±SD (n=30)</th>
<th>AFLD Mean±SD (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TC (mg/dl)</td>
<td>179.87±12.05</td>
<td>226.57±43.32***</td>
<td>146.4±15.47***</td>
</tr>
<tr>
<td>Triglycerides (mg/dl)</td>
<td>124.37±29.48</td>
<td>290.6±118.38***</td>
<td>226.77±68.45***</td>
</tr>
<tr>
<td>LDL (mg/dl)</td>
<td>102.9±13.49</td>
<td>144.43±113.29*</td>
<td>56.23±24.31***</td>
</tr>
<tr>
<td>HDL (mg/dl)</td>
<td>52.1±6.86</td>
<td>42.2±113.29*</td>
<td>38.97±4.94***</td>
</tr>
<tr>
<td>AST (IU/L)</td>
<td>24.7±7.89</td>
<td>28.27±10.36</td>
<td>76.13±37.94***</td>
</tr>
<tr>
<td>ALT (IU/L)</td>
<td>28.57±8.99</td>
<td>32.3±10.87</td>
<td>65.7±32.50***</td>
</tr>
<tr>
<td>De-ritis Ratio</td>
<td>0.869±0.10</td>
<td>0.867±0.1</td>
<td>1.22±0.3***</td>
</tr>
</tbody>
</table>

n = number of samples, SD = standard deviation, p = test of significance,
*p < 0.05 = statistically significant, ***p < 0.0001 = very high statistically significant

1. The levels of total cholesterol were significantly increased in NAFLD and significantly decreased in AFLD patients when compared to controls (p = 0.0001).
2. The levels of triglycerides were significantly increased in both NAFLD and AFLD patients when compared to controls (p = 0.0001).
3. The levels of LDL were significantly increased in NAFLD (p = 0.05) but the increase of LDL levels in AFLD patients were highly significant when compared to controls (p = 0.0001).
4. AST and ALT levels were increased in NAFLD cases when compared to controls but these increased levels were not statistically significant. However the increase of AST and ALT levels in AFLD cases were very highly significant when compared to controls (p = 0.0001).
5. There was no difference in De-ritis Ratio in NAFLD when compared to controls, but there was a statistically significant increased in De-ritis Ratio in AFLD when compared to control (p = 0.0001)

Discussion

Patients with NAFLD and ALD have increased liver related mortality and morbidity throughout world. NAFLD occurs in approximately 20% of obese and 5% over weight subject. A 2.6 fold increase in prevalence of NAFLD was found when it occurs in association with Type-2 diabetes\[12\].

The severity of ALD not only depends on the amount of alcohol consumption but also depends on genetic and environmental factors\[13\].

Infact the majority of long term heavy drinkers develop fatty liver, but only 10-35% develop hepatitis and only 8-20% will progress to cirrhosis\[14\].

Aminotransferases are sensitive indicator of hepatocytes injury. The pattern of aminotransferases elevation, i.e. Deritis ratio can be helpful diagnostically\[15\].

In the present study of NAFLD, increased serum total cholesterol, TG, LDL and decreased HDL were seen when compared to controls. The result obtained in present study was in agreement with Roli Agarwal et al\[16\], and Dhumal Ualtareshvar et al\[17\], who reported hyper triglyceridemia (63.7%), hypercholesterolemia (50.80%), increased VLDL, LDL and decreased HDL levels.

For NAFLD, difference in the body fat distribution or antioxidant system, possible in the context of a genetic predisposition may be among the explanations. A net retention of lipids within hepatocytes, mostly in the form of triglycerides, is a pre-requisite for the development of NAFLD. The primary metabolic abnormalities leading to lipid accumulation is not well understood, but there could consist of alteration in the
pathway of uptake, synthesis, degradation, or secretion in hepatic metabolism resulting from insulin resistance. Insulin resistance is the most reproducible factor in the development of NAFLD[18].

In the present study of AFLD total cholesterol, LDL and HDL levels were decreased and TG levels were increased when compared to controls. The result obtained in the present study was in agreement with Jyoti Prakash Phukan et al[19] and Sanjay Kumar Mandal et al[20] who reported decreased levels of total cholesterol, HDL, LDL and increased levels of TG in alcoholic cirrhotic and alcoholic liver disease patients. However, in contrast to this some other studies revealed that serum TG levels decreased in alcoholic liver disease[21]. Hypolipidemia is expected in alcoholic liver disease due to liver biosynthesis is reduced[19].

In the present study, AST and ALT levels were increased in NAFLD cases when compared to controls but these increased levels were statistically non-significant and AST/ALT ratio was also non-significant in NAFLD when compared to controls. According to Quazi Najeeb et al.,[22] who reported significant elevated levels of ALT as well as AST among NAFLD patients, when compared to controls but ratio of AST/ALT was not significant.

The liver enzymes are poor measures of NAFLD. Although elevation of serum transaminases is common in NAFLD, normal values can be found in up to 78% of patients even in the presence of histologic findings. The whole spectrum of clinicopathologic features of NAFLD may exist without elevation of transaminases[23].

In this present study, AST, ALT levels and Deritis ratio were increased in AFLD when compared to controls and NAFLD. The result obtained in the present study was in agreement with Majhi et al.[24] who showed mean levels of AST and ALT to be 124.8 IU/L and 54.21 IU/L respectively. Study on ALD by Cochen et al[25] showed that a Deritis ratio was > 1 in 92% and > 2 in 70% of ALD patients. This was also in agreement with Mittal A et al[26] showed, mean levels of AST and ALT to be 131.5, 85.12 and Deritis ratio > 1.

An increase in serum concentration of aminotransferases are potential sensitive indicator of liver cell injury and are helpful in recognising hepatocellular diseases such as hepatitis, alcoholic liver disease and cirrhosis[27]. The increased ratio reflects the low serum activity of alanine aminotransferase in patients with alcoholic liver disease. This decrease was due to an alcoholic related deficiency of pyridoxal 5 – phosphate. It could also be due to the damage of mitochondria, cell necrosis and increased in cell membrane permeability, leading to an increase in serum AST especially in patients with high alcohol intake[28].

Conclusion

In conclusion there is a significant dyslipidemia seen in NAFLD and AFLD. NAFLD patient showed atherogenic dyslipidemia when compared to AFLD. Deritis Ratio appears to be a useful index and has potential value for distinguishing NAFLD from AFLD. Therefore in routine practice, the magnitude and rate of changes of aminotransferases alteration may provide initial insight into differential diagnosis. Deritis ratio is increased in AFLD, hence can be used as a marker to differentiate between NAFLD from AFLD.

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