A STUDY OF NON ALCOHOLIC FATTY LIVER DISEASE IN PATIENTS WITH METABOLIC SYNDROME

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DOI: http://dx.doi.org/10.24327/ijrsr.2019.1003.3223

ABSTRACT

Background: Non-alcoholic fatty liver disease (NAFLD) has been rising in incidence in the past two decades in developing nations like India as well as in many western nations and is being taking over the position of most common liver disease in the world.

Aims & objectives: To study ultrasonographically diagnosed NAFLD with various grades and its association with metabolic syndrome and its components.

Material and Methods: The study was cross sectional descriptive study of patients with NAFLD, attending OPD and in patients of the Department of General Medicine, tertiary care hospital. All patients with as NAFLD were investigated for metabolic syndrome according to the NCEP ATP 3 Criteria and association between NAFLD and metabolic syndrome was studied.

Results: There was a significance association between fasting blood sugar level and USG grading of NAFLD. Age, HDL, VLDL & SBP were close to the statistical significant level.

Conclusions: NAFLD found to be in higher degree in all the components of metabolic syndrome. Its early screening will help in modifying the disease course, delaying complications and will also play a major role in preventive cardiology.

INTRODUCTION

Non Alcoholic Fatty Liver Disease (NAFLD) has been rising in incidence in the past two decades in developing nations like India as well as in many Western nations and is being taking over the position of most common liver disease in the world. The autopsy studies and other non-randomised studies have shown about 21 to 31 % of the individuals in the western nations having NAFLD. Two types of NAFLD have been recognised, namely simple fatty liver and non alcoholic steatohepatitis (NASH).

Simple fatty liver means you have fat in liver, but you may not have any inflammation in your liver or damage to your liver cells. It usually doesn’t get worse or cause problems with your liver. Most people with NAFLD have simple fatty liver. Non alcoholic steatohepatitis is more serious than simple fatty liver. NASH means you have inflammation in your liver. You may also have damage to liver cells. NASH which may ultimately improve on to cirrhosis, hepato cellular carcinoma, cardiovascular disease and death.

Many studies regarding the study of risk factors associated with NAFLD have shown it to be related with increasing age, diabetes mellitus Type 2, obesity and hyperlipidaemia. (1,2) Even visceral obesity and female gender are related with this disease. Further NAFLD patients are at greater risk of severe hepatic disease (non-alcoholic steato hepatitis [NASH]) which may ultimately improve on to cirrhosis, hepato cellular carcinoma, cardiovascular disease and death. (3-5)

The Metabolic syndrome (MS) is a combination of risk factors that vastly affects a person’s chance for emerging atherosclerotic heart disease (ASCVD), diabetes mellitus type 2 and chronic kidney disease. The common underlying risk factors seems to be obese abdomen, dyslipidaemia, hypertension, abnormal glucose, a pro-thrombotic state, and a pro-inflammatory state. (6,7)
The MS is diagnosed by the occurrence of more than three findings: “waist circumference more than 102 cm in Men, more than 88 cm in Women, high Triglycerides (more than 150 mg/dl), Reduced HDL-C level (less than 40 mg/dl in men, less than 50 mg/dl in women), Increased blood pressure (systolic blood pressure more than 130 mmHg or diastolic blood pressure more than 85 mm Hg) and plasma glucose value 100 - 125 mg/dl or on anti diabetic drug treatment”.(9,10)

**METHODOLOGY**

**Study Subjects**

Patients with non alcoholic fatty liver both OP & IP attending General Medicine department

**Study Design**

This is a cross-sectional descriptive study which was carried out in the Medicine department

**Ethical Approval**

Ethical approval was obtained from Institutional Ethical committee With no : 2017/292

**Inclusion Criteria**

i. All patients who were diagnosed as fatty liver by abdominal ultrasonography.
ii. Age more than 18 years
iii. Patients with metabolic syndrome criteria.

**Exclusion Criteria**

i. Subjects < 18 years and who were more than 85 years.
ii. Patients with previous history of harmful alcohol intake.
iii. Patients with previous jaundice or Hepatitis B positive, HCV positive.
iv. Patients with previous history of drug use for chronic ailments -steroids, synthetic oestrogens, heparin, Ca channel blockers, amiodarone, valproate, antiviral agents.

**Sample Size**

Hundred subjects with NAFLD

**Study Duration**

18MONTHS (DEC /2016 TO MAY /2018)

**Study Procedure**

Subjects were recruited in the study based on the standard American Gastroenterology Association criteria. (8) As per the criteria patients were graded:

**Grade 1**

a. Slight diffuse increase in the fine echoes.
b. Liver appears bright as compare to that of the cortex of the kidney.
c. Normal visualisation of diaphragm and intra hepatic vessel borders.

**Grade 2**

a. Moderate diffuse in the fine echoes.
b. Slightly impaired visualisation of the intra hepatic vessels and diaphragm.

**Grade 3**

a. Marked increase in the fine echoes
b. Poor or no visualisation of intra hepatic vessels borders, diaphragm and the blood vessels.

In depth history, height, weight examination and medical assessment were carried out only after explaining the procedure and then obtaining informed consent of the patient. All subjects in the study underwent the following investigations:

i. Complete blood counts,
ii. Blood sugar,
iii. Liver function tests,
iv. HBsAg, anti HCV,
v. Lipid profile

**Statistical Methods**

Data was entered using MS-excel data sheet. The Data was analysed using the statistical package for social sciences (SPSS) version 23.0. Descriptive statistics such as frequency and percentage were calculated. Continuous variables were expressed in Mean and Standard Deviation. Association between the groups of USG grades and various study variables predominantly continuous variables will be done by Analysis of Variance test (ANOVA). When the categorical variables were associated with another categorical variable, chi-square test was used. A p-value of 0.05 or less was taken to indicate a statistically significant difference.

**RESULTS**

In our study, there was a significant association between Fasting blood sugar level and USG grading with p-value of 0.003. Age was close to significance level. VLDL is just insignificant with p value of 0.07. None of the other variables were significantly correlated with the USG. However Age, LDL, VLDL and Systolic blood pressure were close to the statistical significant level. Majority 59(59%) of the study subjects belonged to the age group of 46-60 years. 94(94%) of the study subjects were females. 86(86%) of the study subjects belonged to overweight category. 61(61%) and 29(29%) of subjects belonged to grade II and grade III USG classification. 63(63%) of the study subjects were diagnosed with hypertension. 90(90%) of the study subjects were diagnosed with Diabetes Mellitus. None of the variables were significantly correlated with the USG. However Age, LDL, VLDL and Systolic blood pressure were close to the statistical significant level.

![Figure 1 USG Grading among the study population](image-url)
The table shows that 13 (13%), 61 (61%) and 26 (26%) of subjects belonged to grade I, grade II and grade III USG classification among the study population.

Table 1 Association between USG categories and FBS among the study population

<table>
<thead>
<tr>
<th>N</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>Minimum</th>
<th>Maximum</th>
<th>p-Value (ANOVA test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>10</td>
<td>176.50</td>
<td>47.240</td>
<td>128</td>
<td>270</td>
</tr>
<tr>
<td>II</td>
<td>61</td>
<td>146.23</td>
<td>20.101</td>
<td>120</td>
<td>224</td>
</tr>
<tr>
<td>III</td>
<td>29</td>
<td>158.03</td>
<td>30.293</td>
<td>120</td>
<td>235</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>152.68</td>
<td>28.260</td>
<td>120</td>
<td>270</td>
</tr>
</tbody>
</table>

The table shows the association between USG categories and FBS. Fasting blood sugar level an important predictor for impending metabolic syndrome was proved in our study.

Table 2 Association between Age groups and USG categories

<table>
<thead>
<tr>
<th>N</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>Minimum</th>
<th>Maximum</th>
<th>p-Value (ANOVA test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGE</td>
<td>I</td>
<td>10</td>
<td>47.80</td>
<td>10.390</td>
<td>27</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>61</td>
<td>48.84</td>
<td>9.329</td>
<td>24</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>29</td>
<td>53.14</td>
<td>11.357</td>
<td>33</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>49.98</td>
<td>10.161</td>
<td>24</td>
<td>75</td>
</tr>
</tbody>
</table>

The table shows the association between USG categories and age groups.

Table 3 Association between presence of HTN and USG categories

<table>
<thead>
<tr>
<th>N</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>Minimum</th>
<th>Maximum</th>
<th>p-Value (ANOVA test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HTN</td>
<td>I</td>
<td>10</td>
<td>144.00</td>
<td>16.303</td>
<td>134</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>61</td>
<td>143.41</td>
<td>8.753</td>
<td>130</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>29</td>
<td>142.28</td>
<td>27.840</td>
<td>10</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>143.14</td>
<td>17.033</td>
<td>10</td>
<td>190</td>
</tr>
</tbody>
</table>

The table shows the association between USG categories and SBP.

Table 4 Association between USG categories and VLDL among the study population

<table>
<thead>
<tr>
<th>N</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>Minimum</th>
<th>Maximum</th>
<th>p-Value (ANOVA test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>VLDL</td>
<td>I</td>
<td>10</td>
<td>34.20</td>
<td>8.135</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>61</td>
<td>30.54</td>
<td>5.784</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>29</td>
<td>29.24</td>
<td>5.054</td>
<td>22</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>30.33</td>
<td>5.947</td>
<td>20</td>
<td>44</td>
</tr>
</tbody>
</table>

The table shows the association between USG categories and VLDL.

Table 5 Association between USG categories and LDL among the study population

<table>
<thead>
<tr>
<th>N</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>Minimum</th>
<th>Maximum</th>
<th>p-Value (ANOVA test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDL</td>
<td>I</td>
<td>10</td>
<td>105.80</td>
<td>12.200</td>
<td>86</td>
</tr>
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<td></td>
<td>II</td>
<td>61</td>
<td>100.75</td>
<td>11.621</td>
<td>82</td>
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<tr>
<td></td>
<td>III</td>
<td>29</td>
<td>99.28</td>
<td>10.498</td>
<td>82</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100.83</td>
<td>11.391</td>
<td>82</td>
<td>128</td>
</tr>
</tbody>
</table>

The table shows the association between USG categories and LDL.

Table 6 Association between USG categories and WC among the study population

<table>
<thead>
<tr>
<th>N</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>Minimum</th>
<th>Maximum</th>
<th>p-Value (ANOVA test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>WC</td>
<td>I</td>
<td>10</td>
<td>103.00</td>
<td>12.410</td>
<td>85</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>61</td>
<td>106.10</td>
<td>10.018</td>
<td>84</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>29</td>
<td>103.10</td>
<td>8.139</td>
<td>88</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>104.92</td>
<td>9.785</td>
<td>84</td>
<td>126</td>
</tr>
</tbody>
</table>

The table shows the association between USG categories and WC.

Table 7 Association between USG categories and Triglycerides among the study population

<table>
<thead>
<tr>
<th>N</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>Minimum</th>
<th>Maximum</th>
<th>p-Value (ANOVA test)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>I</td>
<td>10</td>
<td>184.30</td>
<td>21.792</td>
<td>162</td>
</tr>
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<td></td>
<td>II</td>
<td>61</td>
<td>179.20</td>
<td>18.863</td>
<td>109</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>29</td>
<td>184.93</td>
<td>15.531</td>
<td>138</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>181.37</td>
<td>18.290</td>
<td>109</td>
<td>236</td>
</tr>
</tbody>
</table>

The table shows the association between USG categories and Triglyceride.

Table 8 Association between USG categories and HDL among the study population

<table>
<thead>
<tr>
<th>N</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>Minimum</th>
<th>Maximum</th>
<th>p-Value (ANOVA test)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>I</td>
<td>10</td>
<td>36.80</td>
<td>3.425</td>
<td>32</td>
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<tr>
<td></td>
<td>II</td>
<td>61</td>
<td>37.36</td>
<td>8.410</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>29</td>
<td>35.31</td>
<td>5.008</td>
<td>26</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>36.71</td>
<td>7.202</td>
<td>26</td>
<td>92</td>
</tr>
</tbody>
</table>

The table shows the association between USG categories and HDL.

DISCUSSION

The presence of non alcoholic fatty liver disease as a strong predictor for impending metabolic syndrome was proved in our study.

Metabolic Syndrome criteria According to NCEP ATP iii(10)

Out of this, if three factors are found to be contributing to the study subjects it as considered as positive

i. Abdominal obesity indicated by waist circumference measuring more than 102 cm (Men), more than 88cm (women)
ii. Hypertriglyceridaemia: Triglycerides more than or equal to 1.7 mmol/L
iii. Low HDL cholesterol: Less than 1.0 mmol/L (Men), less than 1.3 mmol/L (women)
iv. Hypertension: Blood pressure more than or equal to 135/85 mm Hg or on drug
v. Fasting plasma glucose more than or equal to 100mg/dl

In our study, there was a significant association between Fasting blood sugar level and USG grading with p-value of 0.003. Age was close to significance level. VLDL is just insignificant with p-value of 0.07. None of the other variables were significantly correlated with the USG. However Age, LDL, VLDL and Systolic blood pressure were close to the statistical significant level. Majority 59(59%) of the study subjects belonged to the age group of 46-60 years. 94(94%) of the study subjects were females. 86(86%) of the study subjects belonged to overweight category. 61(61%) and 26(26%) of subjects belonged to grade II and grade III USG classification. 63(63%) of the study subjects were diagnosed with hypertension. 90(90%) of the study subjects were diagnosed with Diabetes Mellitus. None of the variables were significantly correlated with the USG. However Age, LDL, VLDL and Systolic blood pressure were close to the statistical significant level.

Present statistics on epidemiology, pathophysiology and diagnostic supports the relationship of non-alcoholic fatty liver disease as a likely component in the cluster of metabolic syndrome. Clinical, experimental and epidemiological studies...
maintain that NAFLD may be the hepatic expression of metabolic syndrome.(11) Because metabolic syndrome can be defined in many different ways, NAFLD might be a more direct predictor of these diseases.(12)

Treatment of NAFLD includes weight management, drugs aiming at Insulin resistance and Lipid lowering drugs.

The robust indication provisions lifestyle modifications with weight loss, but there is some proof to support bariatric surgery, medical therapy with insulin-sensitizing agents, and/or pharmacotherapy to encourage weight loss. Cardiovascular disease is the major reason of mortality in patients with NAFLD, so management must include adjustment of cardiovascular risk factors. (13,14)

In a study by Banerjee S et al aimed at studying the association of clinicopathological profile of hepatic involvement in type-2 diabetes mellitus and its significance found that USG detected, defect correlated poorly with HPE. (15)

Bedogni G, et al. conducted a cross-sectional study among 3,345 subjects from Italy. They found that NAFLD was occurring more normal subjects and connected with many findings of the MS. (16)

CONCLUSION

There was a significant association between Fasting blood sugar level and USG grading with p-value of 0.003. Age was close to significance level. VLDL is just insignificant with p value of 0.07. None of the other variables were significantly correlated with the USG. However Age, LDL, VLDL and Systolic blood pressure were close to the statistical significant level. Liver function tests were not significantly associated with parameters related to metabolic syndrome in this study.

Limitations

1. This is a cross sectional study hence incidence and cause effect relationship cannot be studied.
2. The study involves less sample size of about 100 study subjects. Hence studies with larger sample size will give more accurate conclusions.

References