Non-Alcoholic Fatty Liver Disease (NAFLD) — The Hepatic Component of Metabolic Syndrome


Abstract
Aims: To study the prevalence of NAFLD in those patients attending the routine health checkup and to establish a relationship between NAFLD and metabolic syndrome.

Patients and Methods: All patients attending the health check-up had their blood pressure, height and weight, waist circumference measurements, blood sugars, lipid levels and ultrasound abdomen done. The prevalence of NAFLD among these subjects was determined and the presence of risk factors for metabolic disease in each individual was analysed. A relationship between NAFLD and metabolic syndrome was then established.

Results: Of the 1003 people 225 (22.6%) had NAFLD with higher prevalence among males 164/565 (29%) than among females 61/438 (13.9%). In the NAFLD group normal body mass index (BMI) was present in only 49/225 (20%) of the subjects while 119/225 (52.8%) were overweight and 56/225 (24.8%) were obese. Though liver enzymes were normal the mean AST among cases was 37.41 ± 14.50 and 33.93 ± 14.15 among controls and the mean ALT was 38.74 ± 17.96 among cases and 31.62 ± 13.49 among controls. Prevalence of metabolic syndrome was 106/225 (47%) among cases and 179/778 (23%) among controls.

Conclusion: A diagnosis of fatty liver on ultrasound in an asymptomatic person should alert us of metabolic syndrome and its progression to cardiovascular disease. NAFLD may be considered as the hepatic component of metabolic syndrome. ©

Introduction
The presence of non-alcoholic fatty liver disease (NAFLD) is a common benign finding in the ultrasonography reports of apparently healthy individuals. NAFLD refers to a wide spectrum of diseases ranging from simple fatty liver to non-alcoholic steatohepatitis to cirrhosis. All stages have in common accumulation of fat in the liver cells.1 The pathological picture resembles that of alcohol induced liver disease but occurs in those who do not abuse alcohol.2 NAFLD was initially believed to be a benign condition. Recent studies have shown it to be associated with obesity, type II diabetes mellitus, dyslipidemia and hypertension with insulin resistance being a common factor. These conditions cluster to form the metabolic syndrome, which carries a high risk for cardiovascular disease.3

The diagnosis of NAFLD requires a combination of invasive and non-invasive tests. Mild to moderately elevated serum levels of aspartate amino transferase (AST) and alanine aminotransferase (ALT) or both are the most common findings.4 However some studies suggest that use of liver enzymes as a marker of NAFLD underestimates its prevalence.5 Ultrasound has a sensitivity of 89% and a specificity of 93% in detecting steatosis and a sensitivity and specificity of 77% and 89% in detecting increased fibrosis.6 NAFLD can be more accurately diagnosed on computed tomographic scanning and magnetic resonance imaging.7-9 Liver biopsy is considered the gold standard for the definitive diagnosis of NAFLD.10

There are not many Indian studies on prevalence of NAFLD and hardly any studies in the world on its relationship to metabolic syndrome in the normal population. Hence this study was conducted with the aim of determining the prevalence of NAFLD in the apparently healthy population and establishing a relationship between NAFLD and metabolic syndrome.

Patients and Methods
All the patients coming to Wockhardt hospitals aged 18-60 years for routine health check up formed the control group. They had their height, weight and waist circumference measurements, blood pressure, BMI, liver function tests, lipid profile, fasting blood glucose (FBS) post prandial blood sugars (PPBS) and ultrasound abdomen done along with other investigations. NAFLD was defined as fatty liver not resulting from excessive alcohol consumption (>20 grams/day), drugs, toxins, infectious diseases or any other identifiable exogenous causes.11

This was an ultrasound-based study. Sonologically fatty liver was diagnosed as diffuse increase in parenchymal echogenicity with progressive loss of clarity of portal veins and increased attenuation of sound by the liver.12

Those with sonographic evidence of fatty liver along with levels of AST >59 u/dl and ALT> 72 u/dl (normal limits as per our laboratory) had their blood further investigated for thyroid stimulating hormone, hepatitis B virus, hepatitis C virus, serum ceruloplasmin, antinuclear antibody, anti liver kidney mitochondrial antibody, anti smooth muscle antibody, anti
mitochondrial antibody, alpha-1 antitrypsin levels and serum transferrin levels to rule out other causes of liver diseases. The diagnosis of NAFLD was made only after excluding them.

Normal weight was defined as BMI from 20 – 25, overweight from 25 – 30 and obesity from 30 – 35. Metabolic syndrome was defined by using the ATP III proposal. Identification of the presence of any three of the five risk factors determines metabolic syndrome. A metabolic syndrome (Table 2) was present in 106/225 (47%) of cases and 179/778 (23%) of controls. Impaired blood glucose levels were seen in 163/225 (72.4%) of cases and 438/778 (56.3%) of controls. Hypertension was prevalent in 64/225 (28.4%) of NAFLD group as against 147/778 (18.9%) of controls. Elevated triglycerides were present in 98/225 (43.6%) of cases and 213/778 (27.4%) of controls and low HDL levels were seen in 66/225 (29.3%) of cases and 247/ 778 (31.7%) of controls. Abdominal obesity was present in 106/225 (47.1%) of cases and 303/778 (38.9%) of controls. Other than HDL, all had significant p value at p<0.05.

### Table 1: Comparison of lipid profile, glucose level and anthropometric values between the two groups

<table>
<thead>
<tr>
<th>Parameters</th>
<th>NAFLD Group (N = 225)</th>
<th>Control Group (N = 778)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HDL</td>
<td>46.61 ± 9.48</td>
<td>49.60 ± 12.74</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>LDL</td>
<td>109.18 ± 29.72</td>
<td>107.08 ± 32.18</td>
<td>—</td>
</tr>
<tr>
<td>FBS</td>
<td>124.62 ± 45.83</td>
<td>109.89 ± 37.80</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>PPBS</td>
<td>156.93 ± 78.83</td>
<td>126.59 ± 63.70</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Total Cholesterol</td>
<td>187.92 ± 36.32</td>
<td>181.81 ± 37.33</td>
<td>—</td>
</tr>
<tr>
<td>TGL</td>
<td>170.02 ± 88.90</td>
<td>132.56 ± 69.77</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>SGOT</td>
<td>37.41 ± 14.50</td>
<td>33.93 ± 14.15</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>SGPT</td>
<td>38.74 ± 17.96</td>
<td>31.62 ± 13.49</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>BMI</td>
<td>28.58 ± 4.25</td>
<td>25.67 ± 5.05</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Waist Circumference</td>
<td>99.96 ± 10.01</td>
<td>93.22 ± 11.04</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

### Table 2: Overall prevalence in study cases

<table>
<thead>
<tr>
<th>NAFLD (n)</th>
<th>Control (n)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total No. of Pts enrolled</td>
<td>225</td>
<td>778</td>
</tr>
<tr>
<td>Prevalence of Metabolic Syndrome</td>
<td>106</td>
<td>179</td>
</tr>
<tr>
<td>Prevalence of impaired blood glucose</td>
<td>163</td>
<td>438</td>
</tr>
<tr>
<td>Prevalence of Hypertension (&gt; 130/85)</td>
<td>64</td>
<td>147</td>
</tr>
<tr>
<td>Prevalence of elevated triglycerides (&gt; 150 mg%)</td>
<td>98</td>
<td>213</td>
</tr>
<tr>
<td>Prevalence of low HDL (&lt; 40mg% in Males &amp; &lt; 50 mg % in Females)</td>
<td>66</td>
<td>247</td>
</tr>
<tr>
<td>Prevalence of increased Waist circumference (&gt; 88 cm in females &amp; &gt; in 102 cm in males)</td>
<td>106</td>
<td>303</td>
</tr>
</tbody>
</table>

Results

The health check up OPD of Wockhardt Hospital was attended by 1026 people from June 2006 to October 2006. Out of the 1026 people 23 had to be excluded due to significant alcohol consumption. Incidentally none of our cases had to be excluded due to causes other than alcohol.

Hence our study group comprised of 1003 people who had 438 females and 565 males. Of the 1003 people 225 people had USG evidence of fatty liver. Thus the prevalence of NAFLD was 225/1003 (22.6%). It was present among 61/438 (13.9%) females and 164/565 (29%) males. Of the 225 people with NAFLD only 1 person (0.4%) was underweight with a BMI less than 20.

Normal BMI was present in 49(21.7%). Overweight was present in 119(52.8%), while 56(24.8%) of them had frank obesity. Among those with sonographic evidence of fatty liver only 12 subjects had elevated transaminases yet none had values corresponding to the definition of NASH which meant elevation of liver enzymes by 1.5 to 5 times. They were made to undergo additional blood investigations as mentioned earlier. Fatty liver due to any of these causes were then excluded. Liver biopsy was not a part of our protocol as it is not practical to do an invasive test in a healthy asymptomatic population limiting our study to be an ultrasound based study.

Although most of our cases (Table 1) had liver enzymes within the normal range yet the mean values were higher with AST being 37.41±14.50 in cases and 33.93±14.15 in controls and ALT with 38.74±17.96 and 31.62±13.49 among cases and controls respectively. Hypertriglyceridemia was present in the NAFLD group with mean of 170.02±88.90 and among controls it was 132.56±69.77. Levels of low density lipoprotein (LDL) were 109.18±29.72 and 107.08±32.18 respectively for cases and controls. The total cholesterol levels were 187.92±36.32 for cases and 181.81±37.33 for controls. The HDL level was low for cases with mean being 46.61±9.48 and 49.60±12.74 for controls. The FBS was elevated with cases having 124.62±45.83 and controls with 109.89±37.80. Post prandial sugars were higher in cases 156.93=78.83 and among controls it was129.59=63.70. The BMI was higher in NAFLD group, mean of 28.58±4.25 and among controls it was 25.67±5.05.

All the observation and data were analysed in the statistical package social sciences (SPSS). The level of significance was set at p<0.05.
Not even a single risk factor of metabolic syndrome (Table 3) was present in 10/225 (0.4%) of cases and 124/778 (15.9%) of controls, while one risk factor was prevalent in 37/225 (16.4%) of cases and 258/778 (33.2%) of controls. The presence of two risk factors were similar in both groups at 63/225 (28%) among cases and 206/778 (26.5%) among controls. Three risk factors were present in 66/225 (29.3%) of NAFLD group and 129/778 (16.6%) of controls. Four risk factors were noted in 37/225 (16.4%) and 46/778 (5.9%) of cases and controls respectively. All the components of metabolic syndrome were present in 9/225(4%) of cases and 6/778 (0.8%) of controls.

### Discussion

NAFLD is present in 10% to 24% of the general population in various countries.14 An USG based study conducted in India had showed a prevalence of 24.5%.15 The present study showed a prevalence of 22.6% with a higher prevalence among males than among females. The results of the present study were almost similar to that study. Marchesani et al showed that 80% of patients with NAFLD were obese.16 Our study had only 21% of the population with normal BMI while the remaining 79% were either overweight or obese. There are many conditions to be excluded before coming to a diagnosis of NAFLD but our study population had no exclusion criteria other than alcohol. Although majority of the cases had normal liver enzymes the mean values of the enzymes were higher in the NAFLD group as compared to the controls.

Goland et al proved patients with NAFLD had a significantly higher BMI of 31.4 vs 26.4, higher blood glucose levels of 100.6 vs. 83.3 and triglyceride values of 200 vs. 126 respectively.18 There was no significant difference in the nutritional intake among both the groups. Lee et al showed higher anthropometrics values among NAFLD patients than among controls. The ALT and AST levels were higher with an increase in total cholesterol, triglycerides, atherogenic index, FBG, systolic and diastolic blood pressures and a decrease in HDL cholesterol in the USG diagnosed patients as against controls. There was no significant difference in the LDL cholesterol values among both the groups.19

The present study too showed similar results with genetic predisposition towards raised anthropometric values, elevated blood glucose values, lipid levels and blood pressure values. Hypertriglycerideremia rather than hypercholesterolemia can be considered to be a significant risk factor. There is a strong association between NAFLD and metabolic syndrome with its prevalence being double in the NAFLD group as compared to the controls. The liver histology is closely associated with the number of risk factors.20 Our study showed the increased presence of the number of risk factors of metabolic syndrome in those with ultrasonic evidence of fatty liver as compared to the controls. NAFLD can rightly be called the hepatic component of metabolic syndrome. This was a fact finding study.

Dixon JR study et al quotes NAFLD to be the hepatic component of metabolic syndrome.17 However these studies were done on symptomatic patients who were diagnosed as NAFLD based on USG, liver function tests, liver histology and the prevalence of many components of metabolic syndrome was noted in them. There are hardly any studies to compare the risk factors of metabolic syndrome in the healthy asymptomatic patients with NAFLD and in those without fatty liver, making this study one of the few in this direction. Most of the studies are based on the curative aspects of NAFLD but the present one studies the presence of risk factors of metabolic syndrome in the asymptomatic population. The International Diabetic Federation states that once the diagnosis of metabolic syndrome is made the future management of the condition should be aggressive and uncompromising and the aim is to reduce the risk of type II diabetes mellitus and coronary vascular disease.

In summary USG evidence of fatty liver should be taken seriously as a predictor of metabolic syndrome. It is atherogenic and predisposes to diabetes, hypertension, dyslipidemia and has a strong potential for coronary vascular disease. Prevention is better than cure. Hence a diagnosis of NAFLD on ultrasound in an asymptomatic patient should alert us of the preventable metabolic syndrome and its progression to coronary vascular disease making it necessary to take the same precautions we would take for any other predictors of metabolic syndrome.

### Table 3: Comparison of the number of risk factors between two groups

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>NAFLD Group (N = 225)</th>
<th>Control Group (N = 778)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Risk Factors</td>
<td>10</td>
<td>124</td>
<td>0.04%</td>
</tr>
<tr>
<td>I</td>
<td>37</td>
<td>258</td>
<td>16.4%</td>
</tr>
<tr>
<td>II</td>
<td>63</td>
<td>206</td>
<td>28.0%</td>
</tr>
<tr>
<td>III</td>
<td>66</td>
<td>129</td>
<td>29.3%</td>
</tr>
<tr>
<td>IV</td>
<td>37</td>
<td>46</td>
<td>16.4%</td>
</tr>
<tr>
<td>V</td>
<td>09</td>
<td>06</td>
<td>04.0%</td>
</tr>
</tbody>
</table>

### References


**Announcement**

Newly elected Office Bearers of API, Tirupati Chapter, for the year 2009.

**Chairperson** : Dr. B. Vengamma

**Vice Chairman** : Dr. G. Lepakshi

**Hon. Secretary** : Dr. S. Guru Prasad

**Treasurer** : Dr. B. Siddhartha Kumar

**Joint Secretary** : Dr. C. Chandra Sekhar Reddy
Dr. I. Chiranjeevi Manohar

**Announcement**

43rd Annual Conference of
The Indian College of Allergy, Asthma & Applied Immunology
(ICAICON 2009)
1st - 4th October, 2009.

Early Bird Registration closes on 28th February, 2009.

For registration and other details, please contact: Prof. A.K. Janmeja, Organizing Secretary ICAICON 2009, Pulmonary Medicine, Govt. Medical College & Hospital, Chandigarh.

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