Study of Clinical Profile of Patients of Non Alcoholic Fatty Liver Disease and its Association with Metabolic Syndrome

Rakesh Gaharwar¹, Sushma Trikha², Shubha Laxmi Margekar¹, Om Prakash Jatav³, P Deepak Ganga⁴

Abstract

Background: Non-alcoholic fatty liver disease (NAFLD) is considered to be the commonest liver problem in the western world and is increasingly being recognised as a major cause of liver-related morbidity and mortality. It is known to be associated with various metabolic abnormalities, but not much information regarding association between the metabolic disease and the severity of fatty liver is available.

Aims: To study the clinical profile of patients of NAFLD with varying degrees of severity as diagnosed by ultrasonography and to study the correlation between the non-alcoholic fatty liver disease and metabolic syndrome along with its individual components.

Material and Methods: The study was an observational and analytical study of patients diagnosed as NAFLD, attending OPD and indoor patients of the Department of Medicine, J A Group of hospitals. All patients diagnosed as NAFLD were investigated for metabolic syndrome according to the NCEP ATP 3 Criteria and a relationship between NAFLD and metabolic syndrome was studied.

Results: 51.4% of patients of NAFLD had metabolic syndrome and statistical significance was found in AST, diabetes mellitus and lipid profile.

Conclusions: There is higher prevalence of all the components of metabolic syndrome in cases of NAFLD. Its early detection 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), is now considered to be the commonest liver problem in the western world affecting 15-40% of the general population.¹

Non-alcoholic fatty liver disease is increasingly being recognised as a major cause of liver-related morbidity and mortality.² Because of its potential to progress to cirrhosis and liver failure, interest in this disease is increasing among researchers and clinicians in the relevant basic and clinical science fields.

The pathologic picture of non-alcoholic fatty liver disease, ranging from simple steatosis to steatohepatitis, advanced fibrosis, and cirrhosis, resembles that of alcohol induced liver disease, but it also occurs in patients who do not abuse alcohol.³ Nonalcoholic steatohepatitis that is characterised by hepatic steatosis, liver cell injury, hepatic inflammation, fibrosis and necrosis is believed to be an intermediate stage of non-alcoholic fatty liver disease.²

It has been suggested that fatty liver disease can be considered to be the hepatic consequence of metabolic syndrome or a cluster of metabolic disorders. This disease is often associated with obesity, Type 2 diabetes mellitus, dyslipidaemia and hypertension. Each of these abnormalities carries a cardiovascular disease risk and together they are
often categorised as the insulin resistance syndrome or the metabolic syndrome.5-9

The third report of the national cholesterol education programme expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel III [ATP III]) recommended the use of 5 variables for diagnosing the metabolic syndrome, namely waist circumference, serum triglyceride level, serum high-density lipoprotein (HDL) cholesterol level, blood pressure, and fasting plasma glucose level.10

The frequent association of non alcoholic fatty liver disease with individual components of the metabolic syndrome is now well known. However, it is unknown whether the risk for this disease is increased in patients with the metabolic syndrome. This is important because the metabolic syndrome is an emerging problem worldwide and its prevalence is likely increasing.

This work was designed to study the clinical profile of patients of NAFLD with varying degrees of severity as diagnosed by ultrasonography and evaluate the cross-sectional relationship between the non-alcoholic fatty liver disease and the metabolic syndrome along with its individual components, as defined by the modified NCEP ATP III criteria.

**Material and Methods**

The study was an observational and analytical study of patients suspected as NAFLD, attending OPD and in-patients of the Department of Medicine, JA Group of hospitals.

**Inclusion criteria**

- All patients diagnosed as NAFLD by abdominal ultrasonography.
- Age more than 18 years.

**Exclusion criteria**

- Patients less than 18 years and more than 85 years.
- Patients with history of alcohol intake more than 30 grams/day in males and more than 20 grams/day in females.
- Patients with history of jaundice or HBsAg positive.
- Patients with history of following drug intake - steroids, synthetic oestrogens, heparin, calcium channel blockers, amiodarone, valproic acid, antiviral agents.3

Subjects were included in the study according to the standard criteria accepted by the american gastroenterology association i.e., An increase in hepatic echogenicity as a reference, the presence of enhancement and lack of differentiation in the periportal intensity and the vascular wall due to great hyperechogenicity in the parenchyma.11

Grade 1: Slight diffuse increase in the fine echoes. Liver appears bright as compared to the cortex of the kidney. Normal visualisation of diaphragm and intrahepatic vessel borders.

Grade 2: Moderate diffuse increase in the fine echoes. Slightly impaired visualisation of the intrahepatic vessels and diaphragm.

Grade 3: Marked increase in the fine echoes. Poor or no visualisation of intrahepatic vessel borders, diaphragm and the vessels.

Detailed history, anthropometry and clinical examination was carried out after taking informed consent of the patient. All patients in the study underwent routine investigations including complete blood counts, blood sugar, liver function tests, HBsAg, anti HCV, and lipid profile.

All patients diagnosed as NAFLD were investigated for metabolic syndrome according to the NCEP ATP III CRITERIA10 and a relationship between NAFLD and metabolic syndrome was correlated.

Metabolic syndrome was diagnosed as per NCEP ATP 3 criteria (three or more of the following)
1. Elevated waist circumference (asian indian criteria)12
   a. Men — Equal to or greater than 90 cm
   b. Women — Equal to or greater than 80 cm
2. Elevated triglycerides: Equal to or greater than 150 mg/dL (1.7 mmol/L)
3. Reduced HDL cholesterol:
   a. Men — Less than 40 mg/dL (1.03 mmol/L)
   b. Women — Less than 50 mg/dL (1.29 mmol/L)
4. Elevated blood pressure: Equal to or greater than 130/85 mm Hg or use of medication for hypertension
5. Elevated fasting glucose: Equal to or greater than 100 mg/dL (5.6 mmol/L) or use of medication for hyperglycaemia.

**Results**

Total of 70 cases, ultrasonographically diagnosed as NAFLD were included in the study and showed 47.15%, 42.85% and 10% of cases had grade I, II, and III fatty liver respectively.

Mean age in males was 49.06 years while in females it was 49.20 years. Maximum number of patients were in 4th and 5th decades and Male : Female ratio was 3:4. Twenty four out of 70 patients were asymptomatic while 46 were symptomatic. Abdominal pain and fatigue was present in 55.71% and 52.85% patients respectively. Clinical and biochemical parameters of all the cases of NAFLD are shown in Table 1.
According to BMI, 22(31.42%) patients were overweight, 32 (45.7%) patients were obese, out of which 24 (34.38%) were moderately obese and 8 (11.42%) were severely obese (BMI ≥ 30). 41 (58.57%) patients had increased waist circumference, and 60% patients of NAFLD with metabolic syndrome had grade II fatty liver (Tables 2, 3).

25 (35.72%) of total patients were hypertensive.

### Table 1: Clinical and biochemical profiles of all cases of NAFLD

<table>
<thead>
<tr>
<th>Variable</th>
<th>NAFLD (n=144) Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>41.4±9.65</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>129.0±15.86</td>
</tr>
<tr>
<td>Diastolic blood pressure (mm Hg)</td>
<td>83.17±7.33</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>25.97±7.33</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>86.38±9.44</td>
</tr>
<tr>
<td>Fasting blood sugar (mg/dl)</td>
<td>114.31±44.11</td>
</tr>
<tr>
<td>Total cholesterol (mg/dl)</td>
<td>204.2±47.60</td>
</tr>
<tr>
<td>Serum triglycerides (mg/dl)</td>
<td>198.88±98.88</td>
</tr>
<tr>
<td>High density lipoprotein (mg/dl)</td>
<td>42.94±60.27</td>
</tr>
<tr>
<td>serum LDL (mg/dl)</td>
<td>118.3±33.32</td>
</tr>
<tr>
<td>serum VLDL (mg/dl)</td>
<td>27.48±7.27</td>
</tr>
<tr>
<td>Aspartate amino transferase (u/l)</td>
<td>4.92±6.12</td>
</tr>
<tr>
<td>Alanine amino transferase (u/l)</td>
<td>70.12±5.89</td>
</tr>
</tbody>
</table>

### Table 2: Comparison of prevalence of variables in patients of NAFLD with metabolic syndrome and NAFLD without metabolic syndrome

<table>
<thead>
<tr>
<th>Variables</th>
<th>NAFLD With metabolic syndrome (N=36) N (%)</th>
<th>NAFLD without metabolic syndrome (N=34) N (%)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting Plasma Glucose &gt;100 mg/dl</td>
<td>23 (63.8%)</td>
<td>10 (25.64%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Hypertension &gt;130/85 mmHg</td>
<td>17 (47.2%)</td>
<td>8 (23.5%)</td>
<td>0.034</td>
</tr>
<tr>
<td>Triglycerides &gt;150 mg/dl</td>
<td>31 (86.1%)</td>
<td>16 (47.0%)</td>
<td>0.0005</td>
</tr>
<tr>
<td>HDL M &lt;40mg/dl</td>
<td>34 (94.44%)</td>
<td>16 (47.05%)</td>
<td>0.00019</td>
</tr>
<tr>
<td>F &lt;50mg/dl</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Waist Circumference M &gt;90 cm</td>
<td>28 (77.77%)</td>
<td>13 (38.23%)</td>
<td>0.0009</td>
</tr>
</tbody>
</table>

### Table 3: Distribution of grades of NAFLD with and without metabolic syndrome

<table>
<thead>
<tr>
<th>Variable</th>
<th>Grade I n=145</th>
<th>Grade II n=145</th>
<th>Grade III n=145</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptomatic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALT ≥ 41U</td>
<td>15 (50%)</td>
<td>5 (15.4%)</td>
<td>5 (16.67%)</td>
</tr>
<tr>
<td>AST ≥ 38IU</td>
<td>18 (60%)</td>
<td>6 (20.64%)</td>
<td>4 (13.33%)</td>
</tr>
<tr>
<td>Central Obesity (WC ≥ 90 cm)</td>
<td>6 (18.18%)</td>
<td>4 (13.33%)</td>
<td>5 (16.67%)</td>
</tr>
<tr>
<td>Impaired fasting glucose (&gt;100 mg/dl)</td>
<td>4 (12.12%)</td>
<td>7 (21.21%)</td>
<td>3 (10%)</td>
</tr>
<tr>
<td>Hypertension (130/85 mmHg)</td>
<td>5 (15.15%)</td>
<td>5 (15.15%)</td>
<td>3 (10%)</td>
</tr>
<tr>
<td>Low HDL (≥ 50 mg/dl,F &lt;40 mg/dl-M)</td>
<td>7 (21.21%)</td>
<td>11 (33.33%)</td>
<td>4 (13.33%)</td>
</tr>
<tr>
<td>Hypertriglyceridaemia (≥150 mg/dl)</td>
<td>6 (18.18%)</td>
<td>6 (20%)</td>
<td>1 (14.28%)</td>
</tr>
</tbody>
</table>

Percentage of hypertensive patients increased as grade of NAFLD increased in patients with metabolic syndrome i.e. 15.15%, 23.34% and 71.42% in grade I, II and III respectively (Table 3).

23(32.86%) of total patients were diabetics, majority of grade III fatty liver patients had diabetes i.e. 4(57.14%) while 12 (40%) of grade II and 7(21.21%) of grade I patients were diabetics. Impaired fasting glucose was found in 45.71% of patients. 71.42% patient of grade III fatty liver had impaired fasting glucose (Table 3). ALT and AST levels were elevated in 80% and 61.42% of patients and ALT/AST ratio was > 1.0 in all the patients.

Hypercholesterolaemia was seen in 45.71% patients., Hypertriglyceridaemia was seen in 67.14% patients. 86.1% patients of fatty liver with metabolic syndrome had hypertriglyceridaemia (Table 2) and 85.71% patients of grade III fatty liver with metabolic syndrome had hypertriglyceridaemia (Table 3). Low serum HDL level were seen in 94.44% patients (Table 2). Increased serum LDL levels were seen in 34.28% patients. Increased serum VLDL levels were seen in 25.71% patients.

When comparing the mean of variables in different grades of fatty liver, statistical significance was found in AST, diabetes and lipid profile. On statistical analysis there was positive correlation with waist circumference, blood sugar, AST, ALT, Triglycerides, total cholesterol, LDL, and VLDL and negative correlation was seen with HDL (Tables 2, 4). 51.4% of patients of NAFLD had metabolic syndrome as per NCEP ATP III criteria using asian indian criteria for waist circumference. 61.1% of patients of NAFLD with metabolic syndrome had grade II fatty liver ultrasonographically where as in those without metabolic syndrome 73.5% had grade I fatty liver.

### Discussion

NAFLD is known to be associated with various metabolic abnormalities including central obesity, type 2 diabetes mellitus, dyslipidaemia, and hypertension which are all well established cardiovascular risk factors. Liver ultrasonography is frequently used to...
assess fatty infiltration of the liver, but there is little information on the association between the metabolic disease and the severity of fatty liver (as detected by ultrasound).

51.4% (36) of NAFLD cases had metabolic syndrome according to the NCEP ATP III modified criteria using asian indian standards for waist circumference. Ajay Duseja et al (50%) and Deepa Uchil et al (47.1%) have had similar findings.13,14

Majority of patients (61.1%) having metabolic syndrome had grade II NAFLD whereas in those without metabolic syndrome majority (73.5%) had grade I fatty liver. 6 cases out of 7 having grade III fatty liver had metabolic syndrome.

The mean age group of those having metabolic syndrome was 49.67 ± 9.30 which is higher by a decade to that reported by Bajaj et al (40.11 ± 1.1).15

Out of the 36 patients, 22(61.1%) were females and 14(38.9%) were males but was not statistically significant when compared to NAFLD cases not having metabolic syndrome. 67% were females in a study conducted by Ajay Duseja et al.13

50% of grade II and 57.14% of grade III fatty liver who were symptomatic belonged to those have metabolic syndrome as compared to only 16.67% and 14.28% of grade II and grade III respectively who were in the group not having metabolic syndrome suggesting that patients with metabolic syndrome were more likely to be symptomatic.

Similarly deranged ALT and AST was observed in greater percentages in patients of NAFLD with metabolic syndrome than those without metabolic syndrome. 85.71% of grade III who had deranged ALT and AST had metabolic syndrome. 70% and 60 % (ALT and AST) who had grade II fatty liver had metabolic syndrome (Table 3).

28(77.77%) of those having metabolic syndrome had increased waist circumference (male > 90cms, female > 80 cms) with a mean of 90.27 ± 8.13 cms and this observation was statistically significant (Table 2). 58.7% and 47.1% of cases had increased waist circumference as reported by Bajaj et al and Ajay Duseja et al respectively.13,15

Type 2 diabetes mellitus is a major component of metabolic syndrome and is associated with both obesity and NAFLD. Diabetes is not only associated with NAFLD but may also be a risk factor for development of progressive fibrosis. Mean fasting plasma glucose (mg/dl) of patients with NAFLD and metabolic syndrome was 127.89 ± 53.57 mg/dl (Table 4). 17(47.2%) were having diabetes (≥126 mg/dl) as compared to 9% described by Kaushal et al in those having metabolic syndrome.16 23(63.8%) cases had impaired fasting glucose (≥100 mg/dl) and was found to be statistically significant when compared to NAFLD without metabolic syndrome. 72.4% and 28% patients had impaired fasting glucose as reported by Ajay Duseja et al and Bajaj et al respectively.13,15

Impaired fasting glucose found in 46.67% and 71.42% of grade II and III fatty liver respectively had metabolic syndrome which was higher than that found in cases without metabolic syndrome.

17(47.2%) patients had blood pressure ≥130/85 mm Hg with a mean of 131.33 ± 14.30/84.89 ± 7.50 mm Hg which was similar to that reported by Bajaj et al (48.72%).15 Comparison of the mean values between the groups with and without NAFLD was insignificant. Hypertension found in 23.34% and 71.42% of grade II and III fatty liver respectively had metabolic syndrome.

In patients of NAFLD with metabolic syndrome 31(86.1%) had hypertriglyceridaemia (>150 mg/dl) with a mean of 225.47 ± 112.07 which is significantly higher than those reported by Bajaj et al (48.72%).15 Hypertriglyceridaemia found in 63.34% and 85.71% cases of grade II and III fatty liver respectively had metabolic syndrome.

34(94.4%) patients had low HDL levels (<40 mg/dl in males and <50 mg/dl in females) with a mean of 39.81 ± 5.19 mg/dl as compared to 66.7% described by Bajaj et al.18 Low HDL levels found in 63.34% and 85.71% of grade II and III fatty liver respectively had metabolic syndrome.

Dyslipidaemia between the two groups i.e., NAFLD with and without metabolic syndrome was significant both for prevalence as well as the respective means. The incidence of impairment of various parameters in grade II and III fatty liver is consistently higher in cases of NAFLD with metabolic syndrome when compared with those without metabolic syndrome (Table 3). Therefore a conclusion can be drawn that there is a greater association of metabolic syndrome with increasing severity of fatty liver disease.
Conclusion

From the above observations it can be inferred that a clinician should have a high index of suspicion in order to detect NAFLD early in the course of the disease as symptoms and signs of NAFLD are non specific and occur later in the course of the disease.

Our study also reveals that there is higher prevalence of all the components of metabolic syndrome in cases of NAFLD. Therefore whenever these parameters are encountered in the clinical setting, patients must be evaluated for the presence of NAFLD by abdominal ultrasonography.

Early detection would help not only in modifying the disease course and delaying its complications but would also play a major role in preventive cardiology as its association with metabolic syndrome is frequent and its components are well documented cardiovascular risk factors.

Acknowledgements and Disclosures

None

Statement of Interests

None

References