Study of Non-Alcoholic Fatty Liver Disease and Its Association with Metabolic Syndrome

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ABSTRACT

BACKGROUND
NAFLD (Non-Alcoholic Fatty Liver Disease) is now one of the commonest causes of abnormal liver function and has a higher incidence among obese and diabetic patients. It is considered to be the hepatic consequence of metabolic syndrome or a cluster of metabolic disorders. The association of NAFLD with each of these individual components is well known. However, it is unknown whether the risk for this disease is increased in patients with the metabolic syndrome.

METHODS
We studied the clinical profile of patients of NAFLD, varying degrees of severity as diagnosed by ultrasonography and evaluated the cross-sectional relationship between NAFLD and the metabolic syndrome along with its individual components.

RESULTS
It was found that most patients with NAFLD were asymptomatic. 55% of the study population which comprised of patients with NAFLD on ultrasonography, had features of metabolic syndrome. In addition, the individual components of metabolic syndrome were highly prevalent. Impaired fasting glucose was seen in half of the study population and elevated systolic BP in more than half (60%). Increased waist circumference, low HDL and high triglyceride levels were seen in majority of the patients (85-87%). There was a greater association of metabolic syndrome with increasing severity of the fatty liver disease.

CONCLUSIONS
Many patients of NAFLD remain undiagnosed as they tend to be asymptomatic, therefore recognizing those at risk is the first step. All patients with metabolic syndrome should be screened for NAFLD for early detection.

KEYWORDS
NAFLD, Non-Alcoholic Fatty Liver Disease, Fatty Liver, NASH, Steatohepatitis, Metabolic Syndrome

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DOI: 10.18410/jebmh/2019/630

Financial or Other Competing Interests: None.

How to Cite This Article:

Submission 06-11-2019,
Peer Review 19-11-2019,
Acceptance 22-11-2019,
Published 26-11-2019.
BACKGROUND

Non-alcoholic fatty liver disease is now considered to be the commonest liver problem affecting 17-33% of the general population worldwide.\(^1\) Prevalence of the disease is estimated to be around 9-32% in the general Indian population, with a higher incidence among obese and diabetic patients.\(^2\) Non-alcoholic fatty liver disease (NAFLD) encompasses a broad spectrum of conditions, ranging from non-progressive bland steatosis to malignant transformation into hepatocellular cancer.

Fatty liver disease is considered to be the hepatic consequence of metabolic syndrome or a cluster of metabolic disorders.\(^3\) The third report of the national cholesterol education program 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.\(^4\) The association of non-alcoholic fatty liver disease with each of these individual components is well known. However, it is unknown whether the risk for this disease is increased in patients with the metabolic syndrome.

Non-alcoholic fatty liver disease is increasingly being recognized as a major cause of liver-related morbidity and mortality and a major health burden. NASH is associated with increased mortality with excess cardiovascular, liver and cancer related deaths.\(^5\)

We studied the clinical profile of patients of NAFLD, varying degrees of severity as diagnosed by ultrasonography and evaluated the cross-sectional relationship between the non-alcoholic fatty liver disease and the metabolic syndrome along with its individual components as such a study was not done previously in south India.

METHODS

Cross-sectional observational study was done in a tertiary care hospital in Telangana over a period of 22 months. The study group included patients, both male and females of age more than 18 years and less than 70 years who were diagnosed as non-alcoholic fatty liver disease by ultrasonography.

Patients with history of alcohol intake more than 21 units per week were excluded from the study. Other exclusion criteria included those with history of HBsAg positive test or jaundice, autoimmune hepatitis, hemochromatosis, Wilson’s disease, HCV positive test, metabolic diseases, storage disorders and patients with history of drug intake (steroids, antivirals, synthetic oestrogen, amiodarone, cytotoxic drugs).

Detailed history was taken, clinical examination done and anthropometric measurements including the waist circumference using a measuring tape, blood pressure recording with sphygmomanometer were carried out after taking informed consent of the patient.

All patients in the study underwent investigations which included complete blood counts, blood sugars, both fasting and postprandial, liver function tests, HBSAg, anti-HCV, lipid profile, HbA1c, serum ferritin, serum copper and ultrasound abdomen.

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 peri-portal intensity and the vascular wall due to great hyper echogenicity in the parenchyma.

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.

Statistical Analysis

After checking for the homogeneity of the data, all the continuous variables were reported as mean and standard deviation. Categorical variables were reported as percentage of the study population or frequency distribution tables. The association between continuous variables were analysed using Pearson’s correlation. The association between various entities of metabolic syndrome with NAFLD either as single variable or in combination were analysed using linear regression analysis to report odds ratio. A p<0.05 was considered significant. All the statistical analysis were done using Statistical Package for Social Sciences (SPSS) version 21.

RESULTS

Table 1. Sex Distribution

<table>
<thead>
<tr>
<th>Sex</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>85</td>
<td>42.5</td>
</tr>
<tr>
<td>Male</td>
<td>115</td>
<td>57.5</td>
</tr>
<tr>
<td>Total</td>
<td>200</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Table 2. Frequency Distribution of Symptomatic and Asymptomatic Patients

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic</td>
<td>89</td>
<td>44.5</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>40</td>
<td>20.0</td>
</tr>
<tr>
<td>Fatigue</td>
<td>35</td>
<td>17.5</td>
</tr>
<tr>
<td>Pain abdomen</td>
<td>36</td>
<td>18.0</td>
</tr>
<tr>
<td>Total</td>
<td>200</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Table 3. Frequency Table of Abnormal Waist Circumference

<table>
<thead>
<tr>
<th>WC</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal</td>
<td>129</td>
<td>64.5</td>
</tr>
<tr>
<td>Normal</td>
<td>71</td>
<td>35.5</td>
</tr>
<tr>
<td>Total</td>
<td>200</td>
<td>100.0</td>
</tr>
</tbody>
</table>
In this study, Male to female sex ratio 2:3. In this study, 89 out of 200 were asymptomatic. Of the symptomatic cases, majority (43.4%) had dyspepsia and pain abdomen (39.3%) as presenting complaint. Abnormal waist circumference >88 cm in females and >90 cm in males as per NCEP criteria Asian standards is seen in 64.5% of cases.

In this study done on 200 patients who were diagnosed as NAFLD on ultrasonography, 48%, 41%, 11% cases were of Grade 1, Grade 2 and Grade 3 respectively. Out of all the cases, 109 (54.5%) had metabolic syndrome as per NCEP criteria.

**DISCUSSION**

In this study 200 subjects with NAFLD were included out of which 109 (54.5%) of NAFLD cases had metabolic syndrome according to NCEP ATP III Criteria using Asian Indian standards for waist circumference, which was similar to studies of Ajay Duseja et al (50%) and P Asati et al (51%). Mean age of those with metabolic syndrome was 50.67 and 45.13% were females and 64 (58.7%) were males.

Majority of the cases with metabolic syndrome had grade 1 fatty liver (50%). 18 of 22 with grade 3 fatty liver had metabolic syndrome. 51.2% and 61% of cases with
grade 2 and grade 3 fatty liver with metabolic syndrome were symptomatic when compared to 36% an 50% in those without metabolic syndrome suggesting that patients with metabolic syndrome are more likely to be symptomatic. 75 (37.5%) patients had blood pressure >130/85 with a mean of 128.7 ± 10.6/82.8 ± 5.6 mmHg. Comparison of the mean values between the groups with and without NAFLD was significant. Hypertension was found in 41.5% and 44.4% of grade II and III fatty liver respectively who had metabolic syndrome.

Mean fasting plasma glucose (mg/dl) of patients with NAFLD and metabolic syndrome was 114.41 ± 17.51 mg/dl. 51(46.7%) were having diabetes (>126 mg/dl). 65(59.6%) cases had impaired fasting glucose (>100 mg/dl) and was found to be statistically significant when compared to NAFLD without metabolic syndrome. Impaired fasting glucose which was found in 65.9% and 66.7% of grade II and III fatty liver respectively had metabolic syndrome which was far higher than that found in cases without metabolic syndrome. AST, ALT elevations were high in cases with grade 3 fatty liver than in grades 1 and 2.

93 (85.3%) of patients with metabolic syndrome had increased waist circumference (>90cm in males and >80 cm in females) with a mean of 91.312 ± 6.2859 and it was statistically significant. 77.77% and 58.7% had increased waist circumference in Rakesh Gaharwar et al7 and Bajaj et al11 respectively.

In patients of NAFLD with metabolic syndrome, 93(85.3%) had hypertriglyceridemia with a mean of 185.72 ± 26.052.78% and 88.9% of grade 2 and grade 3 fatty liver had metabolic syndrome. 95 (87.2%) of those with metabolic syndrome had low HDL levels with a mean of 37.018 ± 4.89% of those with grade 2 and grade 3 had low HDL levels which was significant when compared to those without metabolic syndrome.

In summary, there was a high association of metabolic syndrome with NAFLD and dyslipidemia 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 2 and 3 fatty liver is consistently higher in cases of NAFLD with metabolic syndrome when compared with those without metabolic syndrome. Therefore, a conclusion can be drawn that there is a greater association of metabolic syndrome with increasing severity of the fatty liver disease.

CONCLUSIONS

NAFLD is a rapidly growing cause of chronic liver disease, along with the rising incidence of obesity and the metabolic syndrome. From the observations in the present study, the prevalence of NAFLD is more in males when compared to females. It is evident from our study that NAFLD is asymptomatic in a majority of the patients in the early course of the disease and the symptoms are nonspecific. There was a greater association of metabolic syndrome with increasing severity of the fatty liver disease.

55% of the study population had features of metabolic syndrome. The prevalence of all components of metabolic syndrome was found to be very high in patients of NAFLD. Impaired fasting glucose was seen in half of the study population and elevated systolic BP in more than half (60%). Increased waist circumference, low HDL and high triglyceride levels were seen in majority of the patients (85-87%). Hence, all the patients with metabolic syndrome are to be screened for the presence of NAFLD for early detection.

Liver biopsy is the gold standard investigation for diagnosing NAFLD, but a non-invasive test like USG abdomen can be used to stratify the severity of the disease. 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. Future studies would ideally be of a larger sample size and include study of Insulin Resistance ("HOMA IR") and use newer imaging modalities like Transient Elastography (Fibroscan) to detect liver fibrosis. Early diagnosis would help in modifying the disease course and delaying complications. As of now, there is no specific treatment for NAFLD approved. So, preventive programs should be launched to encourage people to adopt healthy lifestyle i.e., regular exercise, low calorie & high fiber diet.

REFERENCES


