STUDY TO IDENTIFY VARIOUS STAGES OF HEPATIC CHANGES IN METABOLIC SYNDROME

General Medicine

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ABSTRACT

Background: A spectrum of liver damage ranging from simple steatosis to Non Alcoholic Fatty Liver Disease (NAFLD), Nonalcoholic Steatohepatitis (NASH), advanced fibrosis, and rarely, Hepatocellular Carcinoma has been associated with Metabolic Syndrome. Various studies in past have tried to establish association between serological markers and these liver disorder, but have not been proven to be effective in determining the further prognosis of disease.

Aims and Objective: To determine the prevalence of NAFLD & other grades of Liver disorder in MS and establish a correlation between various serological parameters grades of Liver disorder in USG and to calculate BMI in NAFLD patients to determine the presence of Lean NASH.

Materials and methods: Detailed history, sociodemographic profile and serum markers including Hb, Lipid profile, ALT, AST, FBS, hsCRP, Fasting insulin level were estimated in 200 patients of Metabolic Syndrome (NCEP ATP III) at the Department of Medicine, NRS Medical College & Hospital, Kolkata from August 2019 to August 2020. Diagnosis of NAFLD was made using USG and patients were Grouped in to Grade 1 (mild steatosis), Grade 2 (moderate steatosis) and Grade 3 (severe steatosis). Waist circumference, Serologic Markers & BMI was evaluated amongst all group to identify the presence of NAFLD & NASH.

Results: In our study liver, Liver steatosis of any grade was 66% and significantly higher in patients with age group >52 years. Steatosis was significantly higher in patients with smokers, T2DM, FBS >110 mg/dL, increasing SGPT, Total Chol >200 mg/dL, S Triglycerides >150 mg/dL, WC ≥90 cm ,SBP of ≥130 mmHg, DBP ≥80 mmHg, LDL >130 mg/dL, HDL <30 mg/dL, fasting insulin >25 units, WHR between 0.9-1.1. Some of those with WC <90 cm ,TG >150 mg/dL, LDL >130 mg/dL, HDL level <40 ,Fast Insulin >25 units also had NASH which was Comparable to Overweight & Obese suggesting the importance of NASH even in Otherwise Lean patients.

Conclusion: Any grade of Steatosis was higher amongst MS patients. Most of them had direct association with WC, TG, LDL, TC, ALT, serum uric acid, hSCRP and fasting insulin abdominal obesity, WHR, fasting blood sugar, and inverse correlation with HDL. We also found significant NAFLD amongst the patients of MS and Normal BMI.

KEYWORDS

fatty liver disease, serological markers, metabolic syndrome,

INTRODUCTION

Metabolic syndrome (MS) is becoming highly prevalent amongst Urban and Rural area particularly with adaptation of modernized lifestyle. NAFLD ranges from Fatty liver to steatohepatitis and may progress to end stage liver disease Cirrhosis and Hepatocellular Carcinoma.

Various studies have shown Fatty liver as an accompaniment of MS and prevalence of fatty liver is found high (up to 70%) in Diabetic and dyslipidemic person. Invasive Procedure like Liver Biopsy compels us to look for less invasive, readily available and easy to perform serum markers like Lipid profile, ALT, AST, FBS, hs CRP, fasting insulin level that help in correlating and understanding the severity and prognosis and also lead to early intervention. 2,5 We also tried to compare this amongst groups of lean (BMI<23kg/m2), overweight (BMI 23-25kg/m2) and obese (>25 kg/m2) patients having NAFLD in terms of various biochemical and physical parameters.

MATERIAL AND METHODS

200 patients of MS at the Department of Medicine, NRS MC, Kolkata from Aug 2019 to August 2020 were included in study.

Patients fulfilling the criteria for MS as per AHA and AHA/NHLBI which update the NCEP ATP III guidelines for MS were included. Those with history of known liver disease, ultrasonographic proven liver disease other than fatty liver, consumption of alcohol, with other co morbid conditions like hypothyroidism and patients taking estrogen, amiodarone, methotrexate, pyrazinamide which are known to produce fatty liver were excluded from the present study.

The diagnosis of NAFLD was made on the basis of characteristics real time USG.Serum markers such as Hb, Lipid profile, ALT, AST, FBS, hsCRP, fasting insulin were estimated using B500 Automated Biochemistry Analyzer. Sonographic Grade 1 (mild steatosis); slightly increased liver echogenicity with normal vessel and absent posterior attenuation; Grade 2 (mod steatosis) moderately increase liver echogenicity with partial dimming of vessel and early posterior attenuation; Grade 3 (severe steatosis) diffused increased liver echogenicity with absence of visible vessels and heavy posterior attenuations.

RESULT

Table: NAFLD and NASH prevalence in various grades of MS and other co-morbid conditions.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Absent</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Total</th>
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<tbody>
<tr>
<td>FBS</td>
<td>≤110</td>
<td>6</td>
<td>12</td>
<td>8</td>
<td>34</td>
</tr>
<tr>
<td></td>
<td>&gt;110</td>
<td>64</td>
<td>32</td>
<td>54</td>
<td>166</td>
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<tr>
<td>Bilirubin</td>
<td>≤1.1</td>
<td>48</td>
<td>18</td>
<td>24</td>
<td>108</td>
</tr>
<tr>
<td></td>
<td>&gt;1.1</td>
<td>20</td>
<td>24</td>
<td>32</td>
<td>66</td>
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<tr>
<td>TC</td>
<td>&lt;200</td>
<td>22</td>
<td>14</td>
<td>34</td>
<td>83</td>
</tr>
<tr>
<td></td>
<td>≥200</td>
<td>40</td>
<td>38</td>
<td>24</td>
<td>102</td>
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<tr>
<td>SGOT/SGPT</td>
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<td>0</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>≥40</td>
<td>70</td>
<td>36</td>
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<td>160</td>
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<tr>
<td>TG</td>
<td>&lt;150</td>
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<td>16</td>
<td>36</td>
<td>116</td>
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<td>≥150</td>
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<td>LDL</td>
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<td>54</td>
</tr>
<tr>
<td></td>
<td>≤130</td>
<td>28</td>
<td>20</td>
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<td>66</td>
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<tr>
<td>HDL</td>
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<td>6</td>
<td>2</td>
<td>48</td>
<td>24</td>
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<tr>
<td></td>
<td>≥30</td>
<td>30</td>
<td>32</td>
<td>14</td>
<td>78</td>
</tr>
<tr>
<td></td>
<td>&gt;40</td>
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<td>8</td>
<td>2</td>
<td>42</td>
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<td>hsCRP</td>
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<td>32</td>
<td>2</td>
<td>8</td>
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<td></td>
<td>&gt;3</td>
<td>14</td>
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<tr>
<td>Fasting insulin</td>
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<td>34</td>
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<td></td>
<td>≤25</td>
<td>0</td>
<td>12</td>
<td>30</td>
<td>66</td>
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<td>BMI (kg/m2)</td>
<td>Obese (25-30)</td>
<td>22</td>
<td>12</td>
<td>16</td>
<td>64</td>
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<td>Leans (23-25)</td>
<td>16</td>
<td>10</td>
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<td>56</td>
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<td>Lean NASH (&lt;23)</td>
<td>28</td>
<td>22</td>
<td>30</td>
<td>84</td>
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<td>WHR</td>
<td>0.9-1.1</td>
<td>72</td>
<td>24</td>
<td>38</td>
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<td>&lt;0.9</td>
<td>32</td>
<td>18</td>
<td>26</td>
<td>78</td>
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<tr>
<td>WC (cm)</td>
<td>&lt;90</td>
<td>10</td>
<td>10</td>
<td>12</td>
<td>44</td>
</tr>
</tbody>
</table>

DISCUSSION

Presence of various grades of NAFLD (65.8%) in MS which is consistent with the previous studies where the prevalence of NAFLD ranges from 57% to 83%. In another study in which NAFLD was
detected in 54.1% subjects, of whom 28% had mild steatosis and 16.8% had moderate-to-severe steatosis in is in agreement with the present study. Many cross-sectional studies have demonstrated that NAFLD is strongly associated with MS. Our study is consistence with these previous findings.

NAFLD was found to be significantly higher in group >55 yrs. (47%) compared to lower age groups which means prevalence of NAFLD increases with increasing age. In a previous study, highest prevalence was recorded in 61–70-year age group, at 63%.

In present study, 61% patients of WC (>90 cm) have NAFLD. Soler et al did the abdominal ultrasound examinations on 69 patients and reported that WC was significantly higher in patients with NAFLD, which is in agreement with the present study.

In our study, 71% of patients of WHR >0.9 have NAFLD. In a previous study 75% patients of NAFLD have a WHR >0.9 whereas only 17.9% patients were having WHR >0.9 amongst Non NAFLD group. In another study high WHR was found in 84.6% patients of NAFLD. Agrawal et al found that mean WHR was 0.97 and 0.93 in NAFLD and Non NAFLD population with T2DM respectively.

Amongst the patients having DM2, 88% had NAFLD and 19% were suffering from Grade 3 NAFLD. Suez et al found prevalence of NAFLD as 57.2% in T2DM patients. Mohan et al found prevalence of NAFLD (54.5%) was significantly higher in patients with T2DM compared to those with Pre-Diabetes (IGT or IGF) (33%), isolated IGT (32.4%), isolated IGF (27.3%) and normal glucose tolerance. Our findings are consistent with this.

We found 63 % patients of SBP > 130 and 62 % patients of DBP >80 mmHg were having NAFLD. In a previous study the incidence rate of hypertension increased according to the degree of NAFLD (normal: 14.4%, mild: 21.8%, moderate to severe: 30.1%).

Generally, hypertriglyceridemia and low HDL are the lipid fraction disorders most often associated with the presence of steatosis. Boza et al observed significantly lower mean HDL levels in class III obese individuals with NAFLD, when compared with the group without the disease, which is the only lipid fraction which evaluated lipid fraction with more advanced stages of the disease.

Contrary to present study Uchil et al reported that SGPT level was significantly higher in NAFLD group (38.74 ± 17.96) compared to control (31.62 ± 13.49) (p=0.05). Manopriya et al also found contrary results. This was in consistence with our finding that SGPT was found to be raised in only certain patients & cant be regarded as good marker of NAFLD.

We found a significant association amongst patients having hscrP >3 to be having NAFLD grade 3. The risk for NAFLD increased as the hscrP level increased (p=0.011). Lee et al reported same.

Total 66 patients out of 100 MS patients had fasting insulin >25, amongst them 48% patients have NAFLD. This signifies hyperinsulinemia is significantly correlated with the presence of NAFLD. Singh et al studied 68 NAFLD patients and reported that patients with NAFLD had higher HOMA-IR than those with MS alone. Presence of NAFLD can detect insulin resistance with a patients with NAFLD had higher HOMA-IR than those with MS.

Regarding the presence of NAFLD. Singh et al studied 68 NAFLD patients and reported that patients with NAFLD had higher HOMA-IR than those with MS. These studies were similar to previous studies like where Lean NASH was in the range between 13% to 52 %.[3,10] The lower preponderance of lean NAFLD (13.2%) in our hospital-based cohort suggests that many of lean NAFLD patients do not seek medical advice. Thus, although obesity is clearly a risk factor for NAFLD but gets modified strongly by ethnicity, genetic predisposition, or environmental factors, which may explain risk of NAFLD in lean subjects.

Waist circumference was significantly higher and comparable in lean NASH (p=0.0012) subjects suggesting the possibility of importance of abdominal obesity even in an otherwise lean individual. Previous studies proved that the accumulation of body fat in the abdominal region, regardless of the individual's total body fat content, is an independent predictive factor for fat accumulation in hepatocytes and, therefore, crucial in the pathogenesis of NAFLD.

Few limitations of our study; small sample size and control group was not taken. These combinations of serologic markers cannot be of help in determining the severity nor could they be helpful in determining which of the patients of Fatty Liver will progress to NASH or Cirrhosis. We would like to include Healthy (Control group) people without MS for comparing them with Lean NASH in patients of MS. A large randomized clinical trial is required to strengthen the present study findings.

CONCLUSION

A high prevalence of fatty liver disease was seen in persons having MS. Majority of them were having a direct association with waist circumference, abdominal obesity, WHR, FBS, serum triglyceride levels, LDL, total cholesterol, ALT, hscrP and fasting Insulin and inverse correlation with HDL. These serologic biomarkers can be helpful in early identification of fatty liver and early intervention so as to prevent their further progression to end stage liver disease but cannot be of help in determining the severity nor could they be helpful in determining which of the patients of fatty liver will progress to cirrhosis. We also found significant F amongst the patients of MS and Normal BMI (Lean NASH). Presence of NAFLD was comparable amongst those with BMI < 23 (lean NASH) and BMI 23-25(Overweight) and BMI ≥25(Obese). That means BMI cannot be the criteria to determine development of complications of MS like fatty liver or cardiovascular risk.

REFERENCES

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