Can Alcoholic Liver Disease and Nonalcoholic Fatty Liver Disease Co-Exist?

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Background: **Nonalcoholic fatty liver disease (NAFLD) by definition would require exclusion of significant alcohol intake. Present study was aimed to assess the prevalence of various components of metabolic syndrome (MS) in patients with alcoholic cirrhosis (AC) and to study the affect of its presence on the severity of liver disease, testing the hypothesis if alcoholic liver disease (ALD) and NAFLD could co-exist.** ***Methods:*** **In a retrospective analysis of 16 months data, 81 patients with AC were analysed for the prevalence of MS. The diagnosis of AC was based on the history of alcohol intake, clinical examination, serum biochemistry, hematological parameters, exclusion of other causes of chronic liver disease, imaging and upper gastrointestinal endoscopy. Severity of liver disease was assessed by Child–Turcott–Pugh (CTP) score. MS was assessed as per the ATP III criteria and the affect of MS on CTP score was evaluated.** ***Results:*** **All 81 patients with AC were male [mean age 50.9 ± 9.5, mean CTP score 8.38 ± 1.66]. But for three patients (3.7%) all other 78 patients (96.3%) with AC had at least one component of MS. Forty-three (53.0%) patients had full blown MS with three or more components of MS. Sixty-one (75.30%) patients were either overweight [22 (27.1%)] or obese [39 (48.1%)], with a mean BMI of 25.35 ± 3.86 kg/m^2. Type II DM was present in 40 (25%) and 28 (34.5%) patients were hypertensive. Twenty-two (27.2%) patients had hypertriglyceridemia and 52 (64.2%) had low HDL. Eleven (13.6%) patients had Child's A cirrhosis, 46 (56.8%) had Child's B and 24 (29.6%) patients had Child's C cirrhosis. Even though not significant statistically, patients with Child's C cirrhosis (17, 70.83%) had higher presence of MS in comparison to Child's A (7, 63.6%) and B (19, 41.3%) cirrhosis.** ***Conclusion:*** **MS is common in patients with AC. Presence of MS may be contributing towards severity of liver disease in these patients indirectly suggesting the co-existence of ALD and NAFLD. (J Clin Exp Hepatol 2017;7:121–126)**

The metabolic syndrome (MS) is a combination of several cardiovascular risk factors including central obesity, elevated blood pressure, fasting glucose and triglyceride levels and low concentration of high density lipoprotein (HDL).[1] It is believed to occur secondary to several factors including sedentary lifestyle, inappropriate diet and genetic predisposition.[2] Though linked closely to nonalcoholic fatty liver disease (NAFLD), individual components of MS may be affected by alcohol consumption. In the present study, we hypothesized that alcohol consumption might increase the risk of developing MS in patients with alcoholic cirrhosis (AC) and its presence might affect the severity of liver disease by causing an additional insult of NAFLD.[3]

Keywords: nonalcoholic steatohepatitis, NASH, fatty liver, metabolic syndrome, cirrhosis

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Abbreviations: AC: alcoholic cirrhosis; BMI: body mass index; CTP: Child–Turcotte–Pugh; DM: diabetes mellitus; HDL: high density lipoprotein; IFG: impaired fasting glucose; MS: metabolic syndrome; NAFLD: nonalcoholic fatty liver disease; TGs: triglycerides

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PATIENTS AND METHODS

Definition of alcoholic cirrhosis

In a retrospective analysis of 16 months data (January 2012 to April 2013), 81 patients with AC, diagnosed on the basis of amount and duration of alcohol intake (≥80 g/day for more than 10 years), clinical examination, serum biochemistry (elevated bilirubin, AST > ALT, low albumin), hematological parameters (low platelets, deranged INR), imaging (heterogenous liver with irregular outline, with or without dilated portal vein, splenomegaly, ascites and collaterals), upper gastrointestinal endoscopy (evidence of oesophagogastric varices and/or portal hypertensive gastropathy) and exclusion of other causes of chronic liver disease were included in the study. Patients with both compensated and decompensated cirrhosis were included and those with acute-on-chronic liver failure (ACLF) and hepatocellular carcinoma were excluded from the study. Patients who were actively consuming alcohol in the 3 months prior to study enrolment were also excluded from the study.

Anthropometry

All patients were subjected to a detailed anthropometric examination and overweight and obesity were defined as per the Asia Pacific criteria.[4] Because of the presence of ascites in patients with decompensated cirrhosis, body mass index (BMI) (modified as per Asia Pacific criteria)

was used as a surrogate marker for central obesity (waist circumference) in all patients. Height in cm using a calibrated scale and body weight in kg using a common bathroom scale were measured to the nearest 0.1 cm and 0.1 kg respectively without shoes. The excessive weight contributed by the presence of ascites was deducted (mild ascites: 2.2 kg, moderate: 6 kg, severe: 14 kg) and BMI (body weight [kg]/height [m]^2) was calculated.[5] Overweight was defined as a BMI $\geq$ 23 but <25 kg/m^2, class I obesity as BMI $\geq$ 25 kg/m^2 but <30 kg/m^2 and class II obesity as BMI $\geq$ 30 kg/m^2.

Investigations

Fasting blood samples (after 10–12 h of overnight fast) were collected from the antecubital vein to measure serum concentration of glucose, total cholesterol, triglyceride (TG), HDL, low density lipoprotein (LDL). A fasting blood sugar (FBS) of $\geq$110 and <126 mg/dL was taken as impaired fasting glucose (IFG) whereas an FBS $\geq$ 126 mg/dL was defined as diabetes mellitus (DM). Liver function tests (serum bilirubin, alanine aminotransferase (ALT) and aspartate aminotransferase (AST), total protein and albumin) were also done in all patients using the fasting sample at the random access autoanalyser (Modular-P, Roche Diagnostics, Germany). All patients were also subjected to a complete hemogram (Hb, TLC, DLC, platelets) and coagulogram (PT, PTI, INR and APTT) using an autoanalyser and all patients were screened for HBsAg and anti-HCV (SD HBsAg and Anti-HCV ELISA, Bio standard diagnostics, Gurgaon, India). Other etiological work up like anti-HBc (total), autoimmune markers, iron profile, serum ceruloplasmin and celiac serology were done if clinically indicated. All patients were also subjected to an abdominal ultrasound and an upper gastrointestinal endoscopy was done in all patients at the baseline.

Metabolic Syndrome

MS was defined as presence of 3 or more of the following 5 risk factors as per the National cholesterol Education Program (NCEP) Adult Treatment Panel (ATP)-III criteria.[6] As mentioned earlier, because of the presence of ascites in patients with decompensated cirrhosis, BMI was used as a surrogate marker for central obesity in all patients.

(1) Class I obesity as BMI $\geq$ 25 kg/m^2 but <30 kg/m^2 and class II obesity as BMI $\geq$ 30 kg/m^2.

(2) Serum triglyceride >150 mg/dL.

(3) Serum HDL cholesterol <40 mg/dL for men and <50 mg/dL for women.

(4) Systolic/diastolic blood pressure >130/85 mmHg or known hypertensive.

(5) Fasting plasma glucose >110 mg/dL or known diabetic.

Statistical Analysis

All statistical analysis was performed using SPSS software (version 22, SPSS Inc., Chicago, IL, USA) Mean and standard deviation was used for continuous variables whereas frequency and percentages was used for discrete data. For comparison of frequencies, Chi-Square Test was used. For comparison of continuous variables, ANOVA (analysis of variance) was used and post hoc analysis by least square difference (LSD) method was employed to compare the means of individual groups. *P* value was set at a significance of 0.05.

RESULTS

All 81 patients with AC included in the study were male (mean age of 50.92 $\pm$ 9.5 years) (Table 1). Sixty-one (75.30%) patients were either overweight [22 (27.2%)] or obese [class I obesity *n* (14.8%), class II obesity 39 (48.1%)], with a mean BMI of 25.35 $\pm$ 3.86 kg/m^2. Fifteen (18.5%) patients had IFG whereas twenty-five (30.8%) had type II DM and twenty-eight (34.5%) patients were hypertensive. Dyslipidemia in the form of low HDL was seen in fifty-two (64.2%) and twenty-two (27.2%) patients had elevated TG (Table 2).

But for three patients (3.7%) all other 78 patients (96.3%) with AC had at least one component of MS. The prevalence of full blown MS with $\geq$3 components of ATP III criteria was present in 43 (53.0%) patients with two components present in 18 (22.2%), 3 components in 25 (30.8%), 4 components in 15 (18.5%) and all five components in 3 (3.7%) patients (Table 2).

Table 1 Showing the Baseline Characteristics of Patients with Alcoholic Cirrhosis.

Parameters	*N* = 81
Age	50.92 $\pm$ 9.5
Sex (M:F)	81:0
AST (IU/ml)	75.40 $\pm$ 69.39
ALT (IU/ml)	51.17 $\pm$ 57.62
Bilirubin	3.8 $\pm$ 7.6
AST	75.40 $\pm$ 69.39
ALT	51.17 $\pm$ 57.62
Albumin	3.3 $\pm$ 1.02
CTP A	11 (13.58%)
CTP B	46 (56.79%)
CTP C	24 (29.62%)
Mean CTP Score	8.38 $\pm$ 1.66

CTP: Child–Turcotte–Pugh.
AST: aspartate aminotransferase.
ALT: alanine aminotransferase.