



Metabolic Syndrome in Adults with Nonalcoholic Fatty Liver Disease

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Abstract

Nonalcoholic fatty liver disease (NAFLD) is associated with insulin resistance, obesity, and other features of metabolic syndrome. It is identified as the most common cause of liver enzyme derangement. Lately, NAFLD has generated interest in exploring treatment options, including weight loss and dietary interventions. An association of NAFLD with metabolic syndrome has been suggested in contemporary literature. In this study, we attempted to look into the association of NAFLD with metabolic syndrome. In this study, 80 adult NAFLD patients were recruited from a tertiary care hospital. Among these, 42 were males and 38 females with a mean age of 44.46 ± 13.146 years (range 18–82 years). Grades of fatty liver and presence or absence of metabolic syndrome were studied in this patient population. Patients who did not qualify for the criteria of metabolic syndrome were placed in Group 1 and those who fulfilled the stated criteria were considered in Group 2. There were 29 (36.25%) patients in Group 1 and 51 (63.75%) in Group 2. All the patients in Group 1 were having Grade I fatty liver whereas patients in Group 2 were found to having varying grades of fatty liver, with six patients having Grade III fatty liver. We found statistically significant difference in various parameters of study (liver enzymes, high-density lipoprotein (HDL), triglycerides, and blood pressure) between Group 1 and Group 2. Ultrasound evidence of a fatty liver should be considered as a predictor of metabolic syndrome, and these patients must be investigated for the different components of metabolic syndrome so as to have early diagnosis and intervention to alter development of long-term metabolic disorders and their inherent complications.

Keywords: fatty liver; metabolic syndrome; NAFLD

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Introduction

Metabolic syndrome is a cluster of metabolic abnormalities. It helps detect people at risk of diabetes and cardiovascular disease. Nonalcoholic fatty liver disease (NAFLD) is defined as a disorder with excess fat in the liver due to nonalcoholic reasons. Glucose and triglycerides, which happen to be the two important components of metabolic syndrome, are over-produced by fatty liver. Therefore, liver plays an important

role in metabolic disorders. Prevalence of both metabolic syndrome and NAFLD increases with obesity. Other acquired causes for these disorders include excessive consumption of simple sugar and physical inactivity. NAFLD and metabolic syndrome contribute to development of type 2 diabetes, cardiovascular disease, and hepatocellular carcinoma. Metabolic syndrome has been defined in different ways and its association with NAFLD is increasingly studied world

over. It appears that NAFLD might turn out to be a predictor of development of these metabolic disorders (1). The early detection of NAFLD helps clinicians take measures to avoid or delay the development of these metabolic disorders by utilizing non-pharmacologic and pharmacologic measures. The National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III, 2001) guidelines for the diagnosis of metabolic syndrome require at least three of the following to label a patient with metabolic syndrome (2):

1. Central obesity: Waist circumference ≥ 102 cm or 40 inches (males) and ≥ 88 cm or 36 inches (females).
2. Increase triglycerides ≥ 150 mg/dL. Reduce high-density lipoprotein (HDL) cholesterol (HDL-C), < 40 mg/dL (males) and < 50 mg/dL (females).
3. Blood pressure $\geq 130/85$ mmHg.
4. Fasting plasma glucose ≥ 110 mg/dL.

There are hardly any studies which have investigated the concomitant occurrence of metabolic syndrome in asymptomatic patients with NAFLD (3,4). In a recent detailed review, various aspects of steatohepatitis and the factors contributing to it, including gene and environment interactions, have been elaborated (5).

Material and Methods

After having approval from Ethical Committee, we recruited 80 adult patients who had been detected to have NAFLD (varying grades) based on ultrasonography (USG). These patients had no previous evidence of liver dysfunction. Patients who had a history of alcohol consumption of more than 20 g/day or who had a deranged liver functions in the past were not included in our study. Patients with hepatitis B surface antigen (HBsAg) and/or anti-hepatitis C virus (HCV) positive status, history of intake of drugs causing NAFLD, intake of lipid-lowering drugs, known patients of previous liver disease, and exposure to toxins or alternate medications were also excluded from our study. All participants were explained the purpose of this study and they provided informed consent. They were subjected to thorough check-up through history-taking, physical examination, blood pressure, and body mass index (BMI) assessment. Liver function tests, lipid profile, fasting blood glucose, and postprandial blood glucose were carried out in all the included patients. Echogenicity of the liver was evaluated using Logiq 500 PRO series GE Doppler ultrasound machine with multifrequency curvilinear transducer having frequency of 3.5–5 MHz. Fatty liver was graded as follows:

- Mild (Grade I): Minimal diffused increase in hepatic echogenicity; normal visualization of intrahepatic vessel borders and diaphragm.
- Moderate (Grade II): Moderate diffused increase in hepatic echogenicity; slightly impaired visualization of intrahepatic vessels and diaphragm.
- Severe (Grade III): Marked increase in echogenicity; poor penetration of the posterior segment of right lobe of the liver and poor or non-visualization of hepatic vessels and diaphragm.

Patients with sonographic evidence of fatty liver along with levels of AST > 37 U/dL and ALT > 40 U/dL had their blood further investigated for serology for hepatitis B and hepatitis C virus. Waist circumference was measured as per NCEP ATP III guidelines (2). It was measured immediately above the iliac crest. BMI in the range of 18.5–24.9 kg/m² was considered normal. BMI in the range of 25–29.9 kg/m² was considered as overweight and BMI = 30 kg/m² and above was considered as obese. Metabolic syndrome was defined by using the ATP III proposal (2).

All the selected patients of this study were divided into the following two groups:

- **Group 1:** Patients with USG-documented fatty liver not fulfilling the criteria of metabolic syndrome.
- **Group 2:** Patients with USG-documented fatty liver and fulfilling the criteria of metabolic syndrome.

Results and Observations

This study included 80 patients: 42 males and 38 females with a mean age of 44.46 ± 13.14 years (range 18–82 years). Clinical and biochemical parameters of the patients are shown in Table 1. Group 1 had 29 and Group 2 had 51 patients. There was statistically significant difference in all the studied parameters between the study groups, with patients in group 2 having higher BMI, liver enzyme levels, systolic and diastolic blood pressures. As can be seen in Table 2, higher the grade of fatty liver, more likely the patient had metabolic syndrome. Comparison of different BMI ranges between the two groups is shown in Table 3, indicating that more patients in Group 2 were overweight or obese.

Discussion

The histopathologic profile of NAFLD ranges from simple steatosis to nonalcoholic steatohepatitis (NASH). Initially, it was considered as benign, but that is not the case now as more and more aspects of NAFLD are studied and information is accumulated. It contributes significantly to hepatic morbidity and mortality. Overtime, NAFLD may progress to cirrhosis, liver failure, and can lead to development of hepatocellular carcinoma. Newer evidences suggest its association with metabolic syndrome. NAFLD and metabolic syndrome share a common pathologic link called

Table 1: Mean values of variables used in the study.

Parameters	Group	N	Mean	Std. Deviation	P-value
Age	1	29	35.31	10.146	<0.05
	2	51	49.67	11.798	
	Total	80	44.46	13.146	
AST	1	29	40.90	12.402	<0.05
	2	51	60.88	18.265	
	Total	80	53.64	18.951	
ALT	1	29	46.62	18.829	<0.05
	2	51	69.67	17.303	
	Total	80	61.31	20.963	
Body mass index (BMI)	1	29	24.88	1.967	<0.05
	2	51	29.75	2.597	
	Total	80	27.99	3.346	
Waist	1	29	89.90	6.635	<0.05
	2	51	99.51	6.676	
	Total	80	96.03	8.090	
Sr. TG	1	29	107.28	19.346	<0.05
	2	51	160.22	36.532	
	Total	80	141.03	40.413	
Sr. HDL	1	29	49.97	6.062	<0.05
	2	51	40.45	6.564	
	Total	80	43.90	7.841	
Blood glucose	1	29	82.21	7.575	<0.05
	2	51	109.37	24.414	
	Total	80	99.53	23.880	
BP (systolic)	1	29	128.97	8.082	<0.05
	2	51	146.90	8.857	
	Total	80	140.40	12.169	
BP (diastolic)	1	29	83.52	6.063	<0.05
	2	51	90.98	4.027	
	Total	80	88.28	6.027	

AST: Aspartate aminotransferase; ALT :Alanine aminotransferase; TG: Triglyceride; BP: Blood Pressure; HDL: High density lipid; BMI: Body Mass Index

Table 2: Comparison of grades of fatty liver between the two groups.

	Grades of Fatty Liver			Total
	I	II	III	
Group 1	29 (55.8%)	0 (0%)	0 (0%)	29 (36.3%)
Group 2	23 (44.2%)	22 (100%)	6 (100%)	51 (63.8%)
Total	52 (100%)	22 (100%)	6 (100%)	80 (100%)

Table 3: Comparison of body mass index (BMI) values between the patients of two groups.

BMI (kg/m ²)	Group 1	Group 2	Total
Normal (18.5–24.9)	19 (65.5%)	0 (0%)	19 (23.8%)
Overweight (25–29.9)	10 (34.5%)	32 (62.7%)	42 (52.5%)
Obese (>30)	0 (0%)	19 (37.3%)	19 (23.8%)
Total	29 (100%)	51 (100%)	80 (100%)

insulin resistance. Kotronen et al. in their study observed that content of liver fat was significantly increased in patients with metabolic syndrome as compared to those without syndrome, and this association was found to be independent of age, gender, and BMI (6). In the study conducted by Völzke et al., an association was established between hepatic steatosis, carotid atherosclerotic plaques, and endothelial dysfunction (7). India with a huge population base with changing lifestyles is encountering a marked rise in metabolic disorders such as diabetes, metabolic syndrome, etc. There is a need of robust clinical studies so as to devise strategies to prevent the development of these disorders by addressing the risk factors and using largely non-pharmacologic measures to control the rise of these diseases. The relationship between NAFLD and metabolic syndrome has seldom been studied in the Indian context. The results of the study conducted by Marchesini et al. summarize the contemporary information on the observations that strongly suggest the association of NAFLD as a possible component of metabolic syndrome. It is observed that NAFLD is characterized by clinical and laboratory data similar to those found in diabetes and obesity. NAFLD may be considered an additional feature of metabolic syndrome, with specific hepatic insulin resistance (8). Younossi et al. in their study observed an association between NASH and metabolic disorders such as diabetes mellitus and obesity (9). The prevalence of NAFLD in the general population was 24.5% according to the results of a study conducted in India (10). Hanley et al. studied 633 subjects from the Insulin Resistance Atherosclerosis Study (IRAS) who did not have metabolic syndrome (11). The authors followed the subjects for 5.2 years. Assessment of aspartate aminotransferase (AST), alanine aminotransferase (ALT),

and C-reactive protein was done to find out whether liver enzymes could predict the development of metabolic syndrome (11). It was determined after 5.2 years of follow-up that 127 patients developed metabolic syndrome and patients in the upper quartiles of ALT, AST, and C-reactive protein were at increased risk of having metabolic syndrome (11). According to Wai-Sun et al., NAFLD has become a global epidemic, affecting 20–40% of the general adult population (12). In some patients, it leads a progressive course, resulting in cirrhosis, hepatocellular carcinoma, and liver-related mortality (12). NAFLD is observed in 10–24% of the general population in various countries (10,13). Marchesini et al. observed in their study that 80% of NAFLD patients were obese (8). In our study, only 23.8% of the patients had normal BMI, while 52.5% were overweight, 23.8% were obese, and 83.3% of the patients with Grade III fatty liver had low HDL levels. Marchesini et al. reported in their study that type 2 diabetes mellitus was found in 33% of NAFLD patients (8). Another study conducted by Cortez et al. in Japanese population demonstrated that prevalence of NAFLD was 43% in individuals with impaired fasting glucose (14). Shannon et al. stated that the proportion of cases with hypertension was 21.2% greater in individuals having NAFLD than those without NAFLD (15). According to Yang et al., NAFLD was proposed to be an early predictor of metabolic dysfunction in healthy populations (16). Our study also established that blood pressure was higher in the group with metabolic syndrome compared to the group without metabolic syndrome ($P < 0.05$). In a study conducted in the Indian context, 73% patients of metabolic syndrome according to NCEP ATP III criteria were having fatty liver compared to 38% in the control group (17).

Conclusion

We directly compared NAFLD and metabolic syndrome according to NCEP ATP III criteria in normotensive and nondiabetic subjects, and found that metabolic syndrome was present in 63.7% of the study subjects. Therefore, we suggest that fatty liver, as analyzed by USG, could fairly predict the presence of metabolic syndrome.

Conflict of Interest

The authors declare no potential conflicts of interest with respect to research, authorship and/or publication of this article.

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