

PREVALENCE OF METABOLIC SYNDROME AMONG PATIENTS WITH NON-ALCOHOLIC LIVER DISEASE

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ABSTRACT

Objective: To determine the prevalence of metabolic syndrome among patients with non-alcoholic fatty liver disease (NAFLD).

Study Design: This is a case series of patients with non-alcoholic fatty liver disease diagnosed by ultrasonography at the Metropolitan Medical Center aiming to describe the clinical profile with special emphasis on the prevalence of the metabolic syndrome. Patients who strongly denied significant alcoholic intake, intake of hepatotoxic drugs, with no history of chronic liver disease were included in the study. The study was done through a chart review of 109 patients aged 19 years old and above seen over a one year period between August 2004 to August 2005.

Results: The mean age of the patients in this series was 47.8 ± 15.6 , 70 of whom were males (64.2%) and 39 were females (35.7%). The mean SGPT level was 68.7 ± 56.0 while that of the SGOT was 34.9 ± 15.3 . Elevated SGPT was noted in 71/108 (65.7%) of the patients while elevated SGOT was noted in 14/42 (33.3%). There were 18 (40.9%) patients whose serum cholesterol were above the normal range while 71 (69.6%) patients had elevated serum triglyceride. There were 33 (35.5%) patients whose HDL cholesterol were below the normal range. Insulin assay was done in 19 patients included in the series of which insulin resistance was noted in 16 (84.2%) with a mean insulin assay of 14.8 ± 6.4 . The mean BMI was 28.3 ± 3.2 kg/m². The mean BMI among the male patients was 28.3 ± 3.3 while among females it was 28.4 ± 3.0 , the difference of which was not statistically significant ($p > 0.05$). The classification of the 106 patients included in this series according to the BMI was normal in 6%, overweight in 7% and obese in 87%. Hypertension was present 66.1% while diabetes mellitus was noted in 47.7% of the patients included in this series. The prevalence of the metabolic syndrome among patients with non-alcoholic fatty liver disease diagnosed by ultrasonography was noted to be 51% (56/109) in this series.

Keywords: Non-alcoholic fatty liver disease, Metabolic syndrome.

Introduction

Fatty Liver is a condition of hepatic steatosis caused by many risk factors and may progress to liver fibrosis and cirrhosis.¹ It is due to intrahepatic accumulation of lipids and is the most common liver abnormality associated with abnormal liver function tests among asymptomatic subjects.² It is a common condition encountered on abdominal ultrasound which many clinicians consider as an incidental finding with no clinical significance.³

Only recently did Ludwig et al, identify a syndrome characterized by the association of

fatty liver and lobular hepatitis and chronically elevated alanine aminotransferase plasma levels in patients with negligible alcohol intake. Thus the term non-alcoholic steatohepatitis (NASH) was introduced.⁴ The original syndrome was described mostly among the obese,⁵⁻⁷ diabetics,⁸⁻¹⁰ and those with dyslipidemia.⁸⁻¹²

Fatty liver is an increasingly common problem worldwide and has been reported in Japan,¹³⁻¹⁴ Australia,⁸ America,¹⁵⁻¹⁶ Europe¹⁷ and the Middle East.¹⁸ According to radiologic surveys; post-mortem studies and evidence from the 3rd

National Health and Nutrition Examination Survey (NHANES III), the prevalence of non-alcoholic fatty liver disease (NAFLD) of any type is from 16%-23% and the prevalence of steatohepatitis is from 2%-6% depending on the diagnostic method used, equally affecting men and women.¹⁹

Generally, the diagnosis of fatty liver should be based on the history, physical examination findings, laboratory tests and imaging. Liver biopsy is a useful prognostic indicator but it is an invasive and costly tool that should be done only if necessary.²⁰ However, previous studies in which ultrasound findings were compared to histologic result indicate that the overall sensitivity and specificity of ultrasonographic examination for the diagnosis of fatty liver are approximately 80%-95% and 90%-95% respectively.²¹⁻²³

The study was conducted to determine the prevalence of the metabolic syndrome defined by the NCEP ATP III among patients with non-alcoholic fatty liver disease diagnosed by ultrasonography.

Methodology

This is a case series of patients with non-alcoholic fatty liver disease diagnosed by ultrasonography at the Metropolitan Medical Center aiming to describe the clinical profile with special emphasis on the prevalence of the metabolic syndrome. The study was done through a chart review of 256 selected patients aged 19 years old and above with a diagnosis of fatty liver seen over a one year period between August 2004 to August 2005 at the Metropolitan Medical Center. Patients seen as in-patient or out-patient who strongly denied significant alcoholic intake, intake of hepatotoxic drugs, with no history of chronic liver disease were included in the study. Fatty liver was diagnosed by ultrasonography using a Hitachi EUB-525 abdominal probe at 3.5 MHz. Longitudinal, subcostal, ascending and oblique views were taken. The ultrasonographic criteria used to diagnose fatty liver included liver and kidney echo discrepancy and the presence of an increased liver echogenicity or "bright liver",

echo penetration into deep portions of the liver and clarity of the liver's blood vessel structures.

Most of the patients included in the study underwent determination of the serum transaminases, total cholesterol, triglyceride, HDL, LDL, albumin, fasting blood sugar, insulin assay and hepatitis profile. The Body Mass Index (BMI) was calculated as body weight in kg per height in meter squared. An overweight individual was defined as having a BMI of ≥ 23 while an obese individual was defined as having a BMI of ≥ 25 . Insulin resistance was computed using the Homeostatic Model Assessment index (HOMA)²⁵. $IR = \text{Insulin assay (microunits/ml)} \times \text{FBS (mmol/ml)} / 22.5$. The HOMA has been used extensively as a reliable marker to determine insulin resistance among normal and diabetic patients. This has been proven by studies made by Lansang²⁶ and Bonora²⁷ both of whom compared HOMA with the more complex glucose clamp technique and concluded that HOMA can be used reliably as a less expensive alternative for determining insulin resistance. A HOMA-IR value of 2.77 was chosen as the threshold for insulin resistance based on the Bruneck Study.

Exclusion criteria included primary liver disorders other than fatty liver disease that could account for steatosis including hepatitis B and C, alcohol intake of ≥ 20 grams/day, history of jaundice for the past six months, previous intake of steatogenic drugs such as amiodarone, estrogen, chemotherapeutic drugs and anti-koch's medications. Also excluded were patients who were pregnant, with CHF (NYHA class III), with COPD, and those with a history of sepsis or administration of parenteral nutrition.

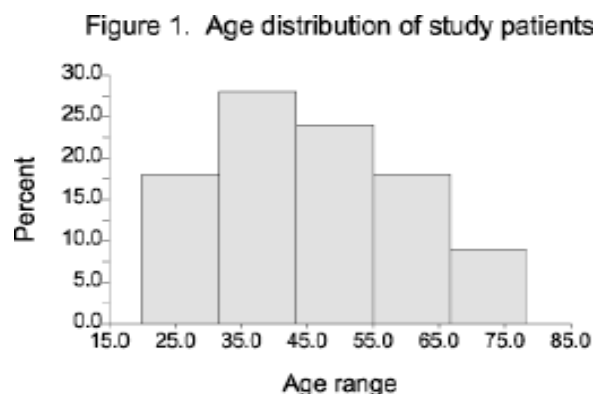
Metabolic syndrome also known as Syndrome X was diagnosed according to the new National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) report which is defined as having 3 or more of the following; hypertension (BP $\geq 130/\geq 85$ mmHg), fasting blood glucose ≥ 110 mg/dl, hypertriglyceridemia (≥ 150 mg/dl), HDL-cholesterol < 40 mg/dl for men and < 50 mg/dl for women, abdominal obesity (waist circumference of ≥ 102 cm for men and ≥ 88 cm for women).²⁸

Data were expressed as prevalence and as mean \pm SD. All data were encoded and presented using the Statistical Package for Social Sciences (SPSS) version 10.

Results

A total of 256 patients with findings of fatty liver on ultrasound were selected for the study, of which only 180 charts were available for review. Out of the 180 subjects 71 were excluded including 52 who were alcoholic. Only a total of 109 patients were then included in this case series.

The mean age of the entire subject population was 47.8 ± 15.6 , 70 of whom were males (64.2%) and 39 were females (35.7%) with a male to female ratio of 1.8:1 (Table 1). The age distribution of the patients in the series is shown in Figure 1. Only 106 patients were included in the computation of the BMI.



The mean SGPT level was 68.7 ± 56.0 while that of the SGOT was 34.9 ± 15.3 . Elevated SGPT was noted in 71/108 (65.7%) of the patients while elevated SGOT was noted in 14/42 (33.3%). There were 18 (40.9%) patients whose serum cholesterol were above the normal range while 71 (69.6%) patients had elevated serum triglyceride. There were 33 (35.5%) patients whose HDL cholesterol were below the normal range (Table 2). Insulin assay was done in 19 patients included in the series of which insulin resistance was noted in 16 (84.2%) with a mean insulin assay of 14.8 ± 6.4 .

Table 1: Demographic and Clinical Characteristics of Patients with Nonalcoholic Fatty Liver

Characteristics	n	Percent	Mean \pm SD
Age	109		47.8 ± 15.6
BMI	106		28.3 ± 3.2
Gender	109		
Male		70 (64.2%)	
Female		39 (35.7%)	
Diabetics	109	52 (47.7%)	
Hypertensive	109	72 (66.1%)	

Table 2: Laboratory Data of Patients with Nonalcoholic Fatty Liver

Laboratory Test	n	Mean \pm SD	Median	Range
SGPT	108	68.7 ± 56.0	50.6	17-363.9
SGOT	42	34.9 ± 15.3	32.9	12.5-78
Cholesterol	45	190.5 ± 35.0	190.3	121.7-265
Triglycerides	102	180.6 ± 62.5	185.2	49.4-361
HDL	93	49.5 ± 11.0	48	28.18-81.3
FBS	106	129.8 ± 49.7	114.9	77.9-373
Insulin assay	19	14.8 ± 6.4	13.5	3.7-33.

The mean BMI was 28.3 ± 3.2 kg/m². The mean BMI among the male patients was 28.3 ± 3.3 while among females it was 28.4 ± 3.0 the difference of which was not statistically significant ($p > 0.05$). The classification of the 106 patients included in this series according to the BMI was normal in 6%, overweight in 7% and obese in 87%. Hypertension was present 66.1% while diabetes mellitus was noted in 47.7% of the patients included in this series (Table 1).

The prevalence of the metabolic syndrome among patients with non-alcoholic fatty liver disease diagnosed by ultrasonography was noted to be 51% (56/109) in this series.

Discussion

Obesity has been noted to be associated with fatty liver²⁹ and is a common observation in developed countries. Sixty to 100% of patients with non-alcoholic steatohepatitis (NASH) were noted to be associated with obesity.³⁰ NAFLD has also been noted to be associated with hypertension and was shown in a study by Donati et al³¹ to have a high prevalence among non-obese hypertensive patients. Insulin resistance accompany type 2 diabetes mellitus.^{32,33} and both peripheral and hepatic insulin resistance are present in almost all patients with non-alcoholic fatty liver disease, irrespective of the coexistence of other related factors.³² Diabetes mellitus together with hyperlipidemia, obesity and hypertension are considered manifestations of the metabolic syndrome that is associated with insulin resistance.³³ Recent studies have pointed to hyperinsulinemia and insulin resistance as pathogenic factors in NAFLD. Marchesini et al³⁴ showed that insulin resistance was the laboratory finding most closely associated with the presence of NAFLD in a large series of patients, irrespective of BMI, fat distribution or glucose tolerance.

Accordingly NAFLD represent another feature of the metabolic syndrome.³⁵ Since patients with this syndrome have a 30% increased risk of cardiovascular death in the absence of type 2 DM and a 40-70% increased risk of cardiovascular death in the presence of type 2 DM³⁶, patients with the metabolic syndrome require treatment regardless of the severity of any associated non-alcoholic fatty liver disease. Non-alcoholic fatty liver disease can be an isolated abnormality but more likely be part of a systemic illness that can progress from mild steatohepatitis to severe fibrosis and cirrhosis.¹⁰ Although the etiology of non-alcoholic steatohepatitis has been explained extensively, the complicated and multifactorial pathogenesis of this condition had remained poorly understood. Several of the recognized associated conditions such as intestinal by-pass surgery, steroid treatment and total parenteral nutrition, can cause a metabolic shift favoring lipogenesis rather than lipolysis and lead to steatosis.³⁰

Recently, a 'two-hit' hypothesis for the

development of non-alcoholic steatohepatitis has been proposed. The first hit is insulin resistance which produces steatosis, the second is any source of oxidative stress that increase the lipid peroxidation and subsequently leads to increased liver damage.³⁷

At present there is no established therapy for NAFLD based on evidence from large randomized controlled trials. Treatment of all patients whatever the severity of their disease, should therefore be directed at the associated metabolic syndrome risk factors: obesity, type 2 DM, dyslipidemia and hypertension. This strategy may reduce the resultant morbidity and mortality and may in addition be beneficial to the liver.³⁸

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