ORIGINAL ARTICLE

Incidence of Non-alcoholic Fatty Liver Disease among Referral Outpatients to the Internal Medicine Clinic

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Abstract

Objective: Non-alcoholic fatty liver disease (NAFLD) is as silent comorbidity in many different settings including; diabetes mellitus (DM), obesity, and hyperlipidemia. In this study, we aimed to determine the incidence of NAFLD in referral outpatients to the internal medicine clinic to evaluate correlations between NAFLD in the other clinical backgrounds. **Materials and Methods:** We performed a cross-sectional study on 88 consecutive referral patients to the internal medicine clinic. Patients with a history of liver disease and alcohol consumption were excluded. Liver ultrasound was performed for diagnosing of NAFLD to be mild to moderate (Grade 1), or moderate to a severe degree of involvement (Grade 2). Clinical backgrounds of the patients, including history and laboratory exam tests such as age, exercise, and DM as well as lipid profile, and liver enzyme test results investigated in our study. **Results:** The incidence of NAFLD was 62% (40% Grade 2; 60% Grade 1). Patients with NAFLD had a higher body mass index, (30 ± 5 vs. 27 ± 4; P = 0.04). They were younger than patients who had not NAFLD (46 ± 15 vs. 58 ± 10 years; P = 0.0001). Total cholesterol level was higher in patients with NAFLD (198 ± 46 vs. 175 ± 46 mg/Dl; P = 0.03). Patients with NAFLD had higher serum alanine aminotransferase (ALT) level (50 ± 14 vs. 46 ± 15 IU/l; P = 0.0001). The aspartate aminotransferase/ALT ratio was lower in patients with NAFLD (0.8 ± 0.3 vs. 1 ± 0.2; P = 0.0001). Patients with NAFLD had sedentary lifestyle compared to those with normal liver (P = 0.001). **Conclusion:** More than half of the referral outpatients to the internal medicine clinic have NAFLD. It occurs in the young age population of patients and has a strong correlation with high-cholesterol level and sedentary lifestyle.

Key words: Body mass index, high cholesterol level, hyperlipidemia, non-alcoholic fatty liver disease

INTRODUCTION

Fatty liver disease (FLD) results from the accumulation of triglyceride (TG) and the other lipids in the liver cells. It may be accompanied by hepatic inflammation and cell death. Potential pathophysiologic mechanisms for FLD include; increased fatty acid synthesis or delivery to liver, defect in exporting TG as very low-density lipoprotein, and/or decreased mitochondrial fatty acid beta-oxidation.[1] Alcohol is the main cause of FLD with the prevalence of 94.5% in obese heavy drinkers of the western country.[2] It's usually asymptomatic, but in severe forms can result in symptoms of malaise, weakness, anorexia, nausea, and abdominal discomfort.[3]

Non-alcoholic FLD (NAFLD) is the most common liver disease among different groups of people. It is the third cause of chronic liver disease in adults in the United States (after hepatitis C and alcohol) which may be the leading cause of mild elevations of transaminase. [4-6]

We undertook a study to determine the incidence and common risk factors of NAFLD in asymptomatic population without

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Received: 18-03-2018
Revised: 26-03-2018
Accepted: 31-03-2018

liver disease in their background, who enrolled as outpatients in the internal medicine clinic.

MATERIALS AND METHODS

Study population

All patients over 18-year-old attending the internal medicine outpatient clinic were considered eligible. Exclusion criteria were alcohol consumption and use of over the counter medications associated with fatty liver changes. Furthermore, we excluded patients with a history of liver disease, advanced kidney disease requiring dialysis, patients who were newly undertaken surgery, and patients with malignancy. Ethical approval was provided by Shahid Beheshti University of Medical Sciences. All study participants provided informed consent.

We defined NAFLD as the presence of hepatic steatosis in the absence of alcohol consumption.[7-9] Experienced radiologists that were blinded to the clinical presentation and laboratory findings obtained ultrasounds (US). NAFLD (hepatic steatosis) was defined as a diffuse increase of fine echoes in the liver parenchyma.[10] The ultrasonography was used to classify the patients as normal (Grade 0); and/or mild to moderate (Grade 1), and moderate to severe (Grade 2) NAFLD.

Blood samples were collected after an overnight fast of at least 12 h. We measured blood glucose (fasting blood glucose), triglycerides (TG), high-density lipoprotein cholesterol and low-density lipoprotein cholesterol (HDL-C and LDL-C), urea, creatinine, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and hepatitis viral antigen/antibody.

We obtained a patient history including history of liver disease or alcohol usage, metabolic syndromes (hyperlipidemia and diabetes), heart disease, renal complaints, hypertension, and smoking (duration and frequency). Patients were considered sedentary if they undertook an aerobic exercise for <20 min/day, 6 days a week. We determined body mass index (BMI) from weight (kg) divided by the square of the height (meter).

Statistical analysis

Variables are expressed as a mean ± standard deviation. Data were analyzed using one-way analysis of variance (ANOVA) and paired *t*-test. Categorical variables were presented as total number and percentages, and they were analyzed using Chi-squared test.

RESULTS

A total of 88 patients were included; 49 male and 39 female in the study. Mean ages of patients were 50 ± 14 years old. Based on US findings, 55 patients had NAFLD. Among patients with NAFLD; 33 had Grade 1, and 22 had Grade 2 NAFLD. The incidence rate of NAFLD in this study was 62.5% [Table 1].

In our study, patients in younger ages had NAFLD in comparison with the older ones; 46 ± 15 versus 58 ± 10 years ($P = 0.001$). Moreover, among the patients who had NAFLD, the younger ones had high stages of liver involvement (Grade 2 vs. Grade 1; $P = 0.0001$).

Patients with higher BMI had a more chance to get NAFLD ($P = 0.04$), and obese patients with BMI over 30 had more Grade 2 involvement ($P = 0.01$).

In our study, 27% of patients with normal liver had regular exercise training in comparison to 9% of patients with NAFLD ($P = 0.02$). The likelihood ratio of fatty liver occurrence in sedentary life was 4.7, and the odds ratio was 2.72 (95% confidence interval; 2.08–2.90).

Patients with NAFLD had a higher total cholesterol level than patients with normal liver ($P = 0.03$). Furthermore, more patients with NAFLD had abnormal liver function tests than patients without fatty liver changes [Table1].

Patients with a higher stage of liver involvement had more increased serum alkaline phosphatase (ALP) level and AST/ALT ratio ($P = 0.0001$).

DISCUSSION

FLD occurs in all age groups, and it may affect 20–30% of the adult population[11] and reaches 80% of obese people with alcohol drinking history.[12] Although the highest prevalence of FLD is in the 40–49-year-old age group, it is the most common liver abnormality in children aged 2–19.[13] The exact mechanism of NAFLD pathology is unknown. Several hypotheses suggest that the liver damage is multifactorial.[14] NAFLD is responsible for the third most common cause of chronic liver disease in adults and leading reason for transaminases elevation which can be recurred after liver transplantation.[4-6] This problem involves all races with a different vulnerability, and it may be related to hemochromatosis gene mutation that may happen more in some races.[15,16] There are studies indicating simple changes in people lifestyles, who can recover FLD.[17,18] It seems that prevalence and progression of these disorders are not the same in different areas. In northern Italy, it may happen in 46.6% and reaches up to 94.5% in heavy drinkers.[2,19] In Asia AFLD have different functions and forms that show its complex pathophysiology because it occurs in lower BMI groups.[20-22] Histology is the gold standard for diagnosis and staging of FLD, but abdominal US can also detect FLD.[23,24]

Our study was done in selected patients who entered to be visited other than nutritional or gastroenterology clinics,

although they possibly ignored their risk factors predisposing them to FLD. In fact, it evaluates the importance of effective screening for NAFLD in patients involved with diseases other than the ones who had renal diseases. As our study showed 55 out of 88 cases (62.5%) had NAFLD including Grade 1 60%, and other 40% of cases had Grade 2. NAFLD occurred in 44% of diabetics, although in this selective group, the existence of diabetes was not related to the severity of fatty liver. This rate is similar to the other studies that reported the prevalence of NAFLD in patients with Type 2 DM ranges from 42.1% to 75.2% in China.[24,25] They found that fatty liver is a complex matter and its management need to correct many factors such as blood pressure, dyslipidemia, and glycemic control.[26]

Lifestyle plays an important role in establishing fatty liver in our patients because fatty liver was seen less in cases who exercised regularly. Sedentary life increases likelihood ratio of NAFLD 4.7 more common than those who exercise regularly.

The importance of exercise as a standard therapy was focused on by other studies. They believe exercise provides a valid, low-cost therapy for NAFLD. This benefit is apparent with minimal or no weight loss. Even exercising below current exercise recommended level is an effective remedy for obesity management.[27] Other factors such as gender and smoking have not played any role in the occurrence of NAFLD or its severity in our study.

There is a controversy about the relation of aging to the prevalence of NAFLD. Some studies showed that the prevalence rates of NAFLD significantly decreased as age increased[24,26] that was inconsistent with Targher study that estimated fatty liver in the diabetic group could reach up to 74% at age over 60, which was performed in the USA.[28] In another study of white and Hispanic races, the prevalence of NAFLD was lower among people aged 20–39 compared to those aged ≥40 years.[17]

As our study suggests, the NAFLD occurs at lower age compared to the group without this disorder diagnosed by US the mean age was 46 ± 15 years, while in those without NAFLD, it was 58 ± 10 years. This shows the lower age of involvement with NAFLD. Our result confirms the age of 40–49 as the highest prevalence for NAFLD like other reports.[12]

BMI can play a role in histological changes of liver steatosis and hepatic fibrosis in Singaporean Chinese non-diabetic patients.[20] Obesity is another term for increased BMI associated with NAFLD in different races of Indian and Korean.[21]

Our study shows NAFLD is more common in cases with higher BMI compared to lower ones. Our study shows near half of the patients with fatty liver had BMI over 30, while 80% of cases without fatty liver had BMI fewer than 30.

Mild to moderate elevation of serum aminotransferases (ALT and AST) is the most common and often as the only laboratory abnormality in patients with NAFLD.[29] There is no significant correlation between the degree of serum aminotransferase elevation and the histologic severity of hepatic inflammation or fibrosis.[30-32] Patients with

Table 1: Comorbidities in patients with and without non-alcoholic fatty liver diseases

Characteristics	Normal liver *n*=33		Fatty liver *n*=55	*P*
Gender male/ female	20/13		29/26	0.3
Exercise	Yes 9 (27%)		Yes 5 (9%)	0.02
Smoking	Yes 5		Yes 4	0.2
Diabetes	Yes 10 (30%)		Yes 8 (15%)	0.08
BMI (kg/m^2)	27±4	28±4	31±5	0.01
Age (years)	57±10	48±15	42±13	0.0001
Laboratory data				
Cholesterol (mg/dl)	175±46		198±46	0.03
TG (mg/dl)	170±98		185±105	0.5
HDL (mg/dl)	43±11		46±11	0.2
LDL (mg/dl)	100±38		116±38	0.06
VLDL (mg/dl)	30±18		38±17	0.1
AST (IU/L)	23±6		33±24	0.007
ALT (IU/L)	22±6		50±41	0.0001
ALP (IU/L)	180±73		213±76	0.06

BMI: Body mass index, TG: Triglyceride, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, VLDL: Very low-density lipoprotein, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, ALP: Alkaline phosphatase

NAFLD usually have an AST/ALT ratio <1.[30,33,34] As our study shows, levels of all liver enzymes such as AST, ALP, and ALT increased mildly in NAFLD, but this increment was significant for AST and ALT, in addition, ALT level also can be related to grades of liver involvement. This was also true for the AST/ALT ratio levels that significantly decreased not only in affected patients but also the grades of NAFLD. ALT higher than 31 IU/ml was observed in 50% of patients with NAFLD, while it occurred in 10% without NAFLD.

Dyslipidemia is another risk factor for liver steatosis.[26] High TG were independent predictors for fatty liver.[26,35] HDL-C was another lipid that had a role in NAFLD.[26]

Our study showed that although both TG and cholesterol are higher in the fatty liver group, the increment of cholesterol was significantly higher in fatty liver compared to non- affected ones. These changes for TG were not significant, and these values were evaluated in different grades of NAFLD that showed both cholesterol and TG levels were not related to NAFLD grades.

Other components of lipid profile including HDL, very LDL, and LDL were not differentiated between two groups of normal and NAFLD and these lipid measures also did not differ significantly in different grades of NAFLD and those without NAFLD.

CONCLUSION

NAFLD is a complex matter that can reflect the healthy background and the future of a society and sounds like it differs based on patients lifestyle as it is varied geographically. It is a common finding in asymptomatic visited patients in a clinic other than gastroenterology, and it can reach up to 62% in a nephrology clinic as in our study. Exercising is the most important factor against it and increased BMI is a risk factor for NAFLD. Age of the affected is lower than the non-affected and the most observed laboratory tests are hypercholesterolemia, increased ALT, and decreased AST/ALT ratio.

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Source of Support: Nil. **Conflict of Interest:** None declared.