ORIGINAL ARTICLE

Prevalence of Fatty Liver Disease and Its Risk Factors in Type 2 Diabetic Patients

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ABSTRACT

OBJECTIVE: To determine the prevalence of non-alcoholic fatty liver disease (NAFLD) in type 2 diabetic patients and to assess its possible risk factors.

MATERIALS AND METHODS: Two hundred and seventy two (186 females and 86 males) diabetic patients were studied. Liver ultrasound was performed along with the measurement of such labratoary tests as alanine transaminase, aspartate transaminase, alkaline phospahatase, fasting blood sugar, glycosilated hemoglobin, triglyceride, total cholesterol, low density lipoprotein, high density lipoprotein, thyroid stimulating hormone, thyroxine, blood urea nitrogen and creatinine. Patients with other causes of fatty liver disease such as autoimmune hepatitis or Wilson's disease were excluded.

RESULTS: The mean age of the subjects was 51±10 years. One hundred and eighty nine of them (70%) had fatty liver, of whom 60 (32%) and 129 (68%) subjects were males and females, respectively. One hundred and fifteen (61%) out of 189 patients were in grade 1, 66 (35%) were in grade 2, and the rest, 8 (4%), were in grade 3 of fatty change in liver. In logistic regression analysis, the variables with significant changes were Body Mass Index (BMI) with OR = 1.26 (95% CI = 1.16-1.37) and triglyceride (TG) with OR = 1.46 (95% CI = 1.01-2.11).

CONCLUSION: The prevalence of fatty liver disease was high in the studied patients (70%). In diabetic patients, Body Mass Index (BMI) and triglyceride (TG) had significant relationship with the presence of fatty liver.

KEY WORDS: Fatty liver, Type 2 diabetes mellitus, Steatotic hepatitis, Body Mass Index

INTRODUCTION

Type 2 diabetic patients potentially are at risk of developing non-alcoholic fatty liver disease (NAFLD) (1). NAFLD includes a spectrum of liver disorders from lipid accumulation without inflammation to non-alcoholic steatotic hepatitis (NASH) which leads to advanced parenchymal destruction such as fibrosis and then cirrhosis. Contrary to the previous viewpoint about safety of lipid accumulation in liver, 20-30% of these patients progress to hepatic insufficiency (2, 6). According to a study which was conducted in 76 type 2 diabetic patients in Tehran in 2006, 82.9% showed steatotic hepatitis in ultrasound and only Body Mass Index (BMI) could predict the occurrence of steatosis (3). In another study in Pittsburgh University in 2000, 63% of 83 type 2 diabetic patients showed steatotic hepatitis in ultrasound (4). In a study

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in the govermental hospital Zhejiang in China in 1999-2001, 32% of 166 type 2 diabetic patients showed fatty liver in ultrasound. According to this study, the patients had significantly higher triglyceride (TG) and lower high-density lipoprotein (HDL-C) than non-alcoholic non-diabetic fatty liver cases (5). In another study in Mombai, India in 2004, the overall prevalence of different grades of NASH was reported to be 80% (7). Prashanth and colleagues studied 204 type 2 diabetic patients in Mombai, India in 2009 and reported that 87% of them had NAFLD on histologic findings (8). With recognition and control of risk factors, the progression to fatty liver and irreversible cirrhosis can be prevented (3). According to clinical experiences in Ahvaz, it seems that fatty liver is prevalent among type 2 diabetic patients. The goal of this study was to assess the prevalence of fatty liver and its predictors in diabetic patients referred to diabetes clinic in Ahvaz Golestan Hospital.

MATERIALS AND METHODS

Demographic (ie. age, and sex) and clinical data including such anthropometric measures as height (cm) and weight (kg) were collected through history taking and physical examination. Blood pressure was measured by a mercury sphygmomanometer after 5 minutes sitting on a chair. Laboratory tests including serum level of HDL, total cholesterol (Tch), TG, fasting blood sugar (FBS), glycosylated hemoglobin (HbA_1c), alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP), thyroid stimulaating hormone (TSH), blood-urea nitrogen (BUN), and creatinine (Cr) was measured for each patient. BMI and AST/ALT ratio were calculated for each patient. Low-density lipoprotein (LDL) was calculated using Friedwald formula. All patients were referred to a pre-determined radiology center for liver sonography. In patients with fatty liver in sonography, HBsAg, HCVAb, serum ferritin, serum ceruloplasmin, and 24-hour-collected urine copper were evaluated to rule out other possible causes and if positive, the patient was excluded from the study. In this study, the staging of fatty liver by sonography was as following: Mild (mild increase in echogenicity of liver and normal view of diaphragm and vascular margins in the liver); Moderate (moderate increase in echogenicity of liver and blurring of the vascular margins in the liver); Severe (severe increase in echogenicity of liver and severe blurring of diaphragm and the vascular margins in the liver). The ultrasound instrument used in the study was Hitachi EVB – 525. The probe was Convex EVP – C – 514 with frequency of 2.5 – 3.5 MHZ. For serum or plasma tests, the following materials and methods were used: Plasma glucose by photometry (GOD), Pars Azmun Co. kit, CV inter-assay = 1.19%; Plasma total cholestrol by photometry (CHOD-PAP), Pars Azmun Co. kit, CV inter-assay = 1.14%. Plasma TG by photometry (GPO-PAP), Pars Azmun Co. kit, CV inter-assay = 1.60%; Plasma BUN by photometry (PAP), Pars Azmun Co. kit, CV inter-assay = 2.21%; Serum transaminases including AST and ALT by IFCC method, Pars Azmun Co. kit, CV interassey = 2.51% for AST and 3.17% for ALT; Plasma HDL-C by phosphotungstic acid after deposition of lipoproteins containing Apo-B, LDL-C by Friedwald formula, ALP by DGKC, Pars Azmun Co. kit, CV inter-assay = 1.50%; HbA_1c by chromatographic spectrophotometry, Biosystem Kit, CV inter-assay = 6.2%.

Thyroid function tests including Thyroxine(T_4) were calculated by competetive immunoluminometric assay, LIAISON Kit, with CV inter-assay < 6.0% and TSH by two-site immunoluminometric assay LIAISON Kit, with CV inter-assay < 5.1%. Data was analyzes by SPSS version 15 using t test, Fisher exact test, tukey and logistic regression used for data analysis.

RESULTS

We studied 272 patients with mean age of 51.2±9.6 years. One hundred and eighty six (68%) subjects were females and 86 (32%) subjects were males. More than 60% of them were between 30 to 60 years old. (Table 1)

Table 1 – Demographic information of studied patients

Variable	Categories	Number	Percent
Age	<10	0	0
	10-19	2	0.7
	20-29	8	2.9
	30-39	27	9.9
	40-49	96	35.3
	50-59	87	32
	60-69	42	15.4
	70-79	10	3.7
Sex	male	86	31.6
	female	186	68.4
BMI kg/m2	< 18.5	0	0
	18.5 – 24.9	80	29.4
	25 - 29.9	98	36
	30 – 34.9	66	24.3
	35 – 39.9	10	3.7
	≥ 40	5	1.8

One hundred and eighty nine (70%) patients suffered from fatty liver: sixty (31.7%) subjects were males and 129 (68.3%) were females. Stage 1, 2 and 3 of fatty liver was observed in 115 (61%), 66 (35%) and 8 (4%) patients, respectively.

None of the patients with BMI≤18.5 kg/m2 had fatty liver. Thirty six (45%) of 80 patients with BMI = 18.5 – 24.9 kg/m2, seventy three (74%) of 98 patients with BMI = 25-29.9 and fifty eight (88%) of 66 patients with BMI >=30 kg/m2 had fatty liver (p<0.001).

Twenty clinical and biochemical characteristics were compared between the patients with and without fatty liver (Table-2).

The differences in ALT, TG, and Tch level, and BMI were statistically significant between two groups.

Mean serum TG was significantly higher in stage 2 fatty liver patients than stage 1 fatty liver and normal ones. (P <0.001 and P = 0.02, respectively)

Mean serum ALT was significantly higher in stage 2 fatty liver patients than stage 1 fatty liver and normal ones. (P <0.001 and P <0.001, respectively)

Mean BMI was significantly lower in normal

Table 2 – Comparing differences of some measured variables in patients with and without NAFLD

Variable	Non-alcoholic fatty liver disease		P value
	No	Yes	
Age (mean±SD in years)	50±12/6	51/2±9/6	0.45
Mean of Time since diagnosis (mean±SD) in months	91/85±81/9	83/52±70/58	0.45
ALT(IU/L)	23/5±13/2	28/03±17/2	0.05
AST(IU/L)	21/7±9/7	24/4±14/6	0.15
ALPh(IU/L)	189/8±75/5	203±94/4	0.35
FBS(mg/dl)	167/4±79/2	169±74/9	0.87
HbA1c(%)	7/9±1/9	7/4±1/5	0.08
Tg(mg/dl)	132/1±56/8	176/5±107/5	0.000
Tch(mg/dl)	168/8±27/4	179/6±48/8	0.02
LDL(mg/dl)	92/3±24/6	96/6±37/9	0.27
HDl(mg/dl)	50±12/7	47/7±13/2	0.18
BMI(kg/m^2)	25±3/8	28/7±4/6	0.000
TSH(μu/dl)	2/1±3/7	3/6±14/5	0.39
T4(μu/dl)	8/8±1/9	8/6±2/8	0.80
BUN(mg/dl)	15/5±5	16/1±7/2	0.52
Cr(mg/dl)	0.92±1	87±0.75	0.68
Bilirubin -total(mg/dl)	0.72±0.27	0.69±0.30	0.63
Bilirubin -directl(mg/dl)	0.23±0.07	0.23±0.11	0.99
AST/ALT	1.01±0.37	0.96±0.49	0.41

group than stage 1, 2, and 3 fatty liver patients. (P <0.001)

No significant relationship was found between fatty liver and such variables as sex, time before diagnosis, age, ALP, FBS, HbA_1c, LDL, HDL, TSH, T4, BUN, Cr, total bilirubin, direct bilirubin, ALT and AST.

Only BMI (OR = 1.26 CI: 1.16-1.37) and TG (OR = 1.46 CI: 1.01-2.11) remained in final logistic regression model for prediction of the presence of fatty liver.

The probability of occurrence of liver steatosis was non-linearly correlated with BMI (Figure 1).

DISCUSSION

In this study hepatic steatosis was detected by sonography which had a sensitivity and specificity of 83% and 100%, respectively, as compared with histologic finding as the gold standard method (10, 11).

The results declare that BMI and TG are the best predictors of the presence of hepatic steatosis in type 2 diabetic patients.

Non-alcoholic steatohepatitis (NASH) is a kind of chronic hepatitis with a histologic pattern similar to alcoholic hepatic disease, this it is recently known as non-alcoholic fatty liver disease (NAFLD)(2). NAFLD is a clinical status which includes an expanded spectrum from simple steatosis to steatohepatitis, advanced fibrosis and cirrhosis (2, 12).

In various studies, the prevalence of NAFLD in type 2 diabetic patients has been estimated to be from 25% to 75% (13). Considering the prevalence of 70% in our study, we assume that NAFLD is a highly prevalent disease in our population.

Insulin resistance is responsible for disturbance in lipid storage and lipolysis in insulin sensitive tissues which increases the flow of fatty acids from adipose tissue to liver and leads to steatosis.

In addition, insulin resistance induces lipid peroxidation which activates inflammatory cytokines and facilitates the progression of simple steatosis to non-alcoholic steatohepatitis and hepatic fibrosis (6).

Various retrospective studies have indicated that female sex, obesity, hyperglycemia and hyperlipidemia are risk factors for this disease. Other known risk factors are total parenteral nutrition (TPN), protein-calorie malnutrition, jejunoileal bypass and some drugs (6, 9).

In 1994 Bacon and colleagues showed that the disease can develop in many persons without any definite risk factors. But any way, NAFLD has two strong risk factors: obesity and insulin resistance (14). According to a study in Tehran in 2006 on 76 type 2 diabetic patients, 82.9% were affected by hepatosteatosis on ultrasound. Only BMI significantly predicted the occurrence of steatosis (3).

In another study in 2003 in a state hospital in Saudi Arabia, 66% of 116 type 2 diabetic patients showed fatty liver on ultrasound. According to that study obesity had the strongest relationship with non-alcoholic fatty liver.

In this study, no relationship was found between time before diagnosis and control of blood sugar with fatty liver (15).

Kim and colleagues studied 1898 type 2 diabetic patients in South Korea in 2008 and reported visceral adiposity as a predictor of fatty liver disease (16).

In a study on 352 patients in Israel in 2006, the prevalence of fatty liver on ultrasound was 30%. NAFLD was more prevalent in men than women (38% vs. 21%; P=0.001) (17).

In our study, 20 known risk factors for hepatosteatosis (sex, age, time before diagnosis of diabetes, ALT, AST, ALP, FBS, HbA_1C, TG, Tch, LDL, HDL, BMI, TSH, T4, BUN, Cr, total and direct bilirubin, and

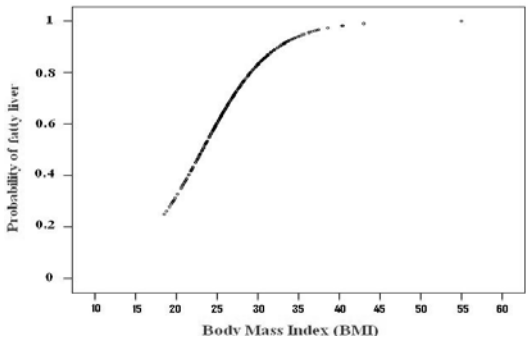

Figure 1 – Nonlinear correlation between BMI and fatty liver disease

AST/ALT) were assessed using logistic regression analysis. Despite statistically significant difference of plasma values of TG, ALT, Tch, and BMI between diabetic patients with and without fatty liver, only BMI and TG had significant relationship with steatosis.

The results of this study revealed that BMI and serum triglyceride level can predict the occurrence of steatosis. The prevalnec of fatty liver increases 26% and 46% for 1 unit increase in BMI, and 100 mg/dl increase in TG, respectively.

CONCLUSION

The results indicate the high prevalence of fatty liver (70%) in type 2 diabetic patients in our population and therefore it is necessary to follow them for the incidence of fatty liver. BMI and TG are two predictors of fatty liver in type 2 diabetic mellitus

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