Non-Alcoholic Fatty Liver Disease and Prediabetes

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ABSTRACT

BACKGROUND: Non-alcoholic fatty liver disease (NAFLD) is the most common liver disease in the world. The simultaneous occurrence of NAFLD and type 2 diabetes is common, however, few studies on the prevalence of NAFLD in prediabetic patients have been performed. Therefore, the aim of this study was to determine the prevalence of NAFLD by sonography in prediabetic patients and to compare the prevalence of NAFLD between prediabetic patients and normal population.

METHODS: In this cross-sectional study, 191 consecutive prediabetic patients who were referred to the internal medicine clinic in the Razi Referral Hospital of Rasht, Iran, were compared with 191 healthy controls. Diagnosis of prediabetes was based on abnormal oral glucose tolerance test or fasting plasma glucose. Both groups underwent ultrasonography for the assessment of NAFLD and data was analyzed by Student's t test and Chi-square test.

RESULTS: Patient population was between 20 and 70 years old and the mean age of participants was 41.04±12.66 years. Prediabetic group had 71(37.1%) males while healthy group had 84(43.9%) males. Of the 382 subjects, 142 (37.2%) had evidence of NAFLD on ultrasound examination of which 93(65.4%) were prediaibetics (P=0.001).

CONCLUSION: We show that the prevalence of NAFLD in prediabetic patients is higher than healthy individual.

Keywords: Non-alcoholic Fatty Liver Disease; Prediabetes; Ultrasonography

INTRODUCTION

Prediabetes is a condition in which body produces more insulin than normal to regulate blood glucose. Prediabetes is due to insulin resistance and patients are usually asymptomatic [1]. Insulin resistance can lead to the development of type 2 diabetes mellitus and may play a key role in the development of hepatic steatosis [2-4]. Hepatic steatosis, in the absence of secondary causes of fat accumulation in the liver, is called non-alcoholic fatty liver disease (NAFLD) [5, 6]. NAFLD is one of the most common liver diseases in the world and its prevalence has been reported between 2.8 and 24 percent in different studies [7]. Pathogenesis of NAFLD is not well understood but it seems that impaired fatty acid metabolism in the liver can lead to the development of this disease [8-10]
Investigations have shown that insulin resistance can increase the peripheral lipolysis and triglyceride synthesis and hepatic uptake of fatty acids; free fatty acids may lead to production of oxygen free radicals and consequently liver cell injury and fibrosis [11]. On the other hand, investigators found that insulin sensitizing agents such as rosiglitazone and pioglitazone reduce insulin resistance and improve steatosis in patients with fatty liver disease [12]. Previous studies have evaluated the prevalence of NAFLD in patients with diabetes [13-15]. Few studies on the prevalence of NAFLD in prediabetic patients have been performed. Therefore, the aim of this study was to determine the prevalence of NAFLD by sonography in prediabetic patients and to compare the prevalence of NAFLD between prediabetic patients and normal population.

METHODS

This cross-sectional study was performed from May 2012 to November 2013 in the Razi Referral Hospital of Rasht, Iran. We compared

191 consecutive prediabetic patients with 191 healthy hospital staff (including doctors, nurses and medical residents) that acted as controls. Demographic and clinical data such as sex, age, stature, weight, history of diabetes mellitus and known liver diseases were recorded. Patients younger than 18 or older than 70 years and those with a history of diabetes mellitus, alcohol consumption, known liver disease (viral hepatitis or autoimmune hepatitis) or hemochromatosis were excluded.

Aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), hepatitis A virus antibody, hepatitis C virus antibody, hepatitis B surface antigen, antinuclear antibody, serum iron, serum ferritin, gamma-glutamyl transpeptidase (GGT), fasting blood sugar (FBS) and oral glucose tolerance test (GTT) were performed on all subjects. Diagnosis of prediabetes was based on abnormal fasting plasma glucose test or abnormal oral glucose tolerance test. Both tests were done by GOD-PAP method with Pars Azmoon kits; the normal ranges of these kits for fasting plasma glucose test and oral glucose tolerance test were 75-100 mg/dL and 75-139 mg/dL, respectively. The fasting plasma glucose test from 100 to 125 mg/dL and/or oral glucose tolerance test from 140 to 199 mg/dL were regarded as prediabetes.

In addition, both groups underwent ultrasonography to determine the presence or absence of fatty liver. The sensitivity of ultrasonography in detecting fatty liver ranges from 60 to 94% and the specificity ranges from 84 to 95%. NAFLD on ultrasonography is characterized by shiny or echogenic liver tissue because of diffuse infiltration of fat. Radiographic evaluations are enough for the diagnosis of NAFLD in patients without symptoms of liver cirrhosis, high risk factor for liver cirrhosis and fibrosis or other liver diseases [16]. This study was approved by the local ethical committee and informed consent for participation in the study was obtained from subjects.

Statistical analysis: Chi squared test was used to examine the differences in the distribution of categorical variables between prediabetic and control groups. To compare the means of normally distributed variables between groups, the Student's t test was performed. All statistical analyses were done by means of the program SPSS software Version 19 for Windows. P values less than 0.05 were considered significant.

RESULTS

The mean ± SD age of participants was 41.04 ± 12.66 years. Prediabetic group had 71(37.1%) males while healthy group had 84(43.9%) males (Table 1). Of the 382 subjects, 142 (37.2%) had evidence of NAFLD on ultrasound examination of which 93(65.4%) were prediabetics (P=0.001). Serological markers for viral hepatitis were negative in all subjects as were the levels of serum ferritin, serum iron and antinuclear antibody.

Significant elevations in serum ALT and AST levels were present in 52.3% of prediabetic patients and 23.5% of control subjects (P value < 0.05). We found a significant relation between gender and NAFLD in prediabetic patients (P value = 0.049); of 71 prediabetic men, 28(39.4%) and among 120 prediabetic women, 65(54.2%) subjects had NAFLD. Older pre-diabetic individuals were more likely to have NAFLD than younger individuals (P =0.0001 between 20-30 years group versus 60-70 years group). Similarly, patients with BMI>30 kg/m2 were more likely to have NAFLD than individuals with BMI<20 kg/m2 (P = 0.003).

DISCUSSION

We have found a high prevalence of NAFLD in patients with prediabetes. We also found that the prevalence of NAFLD increases in prediabetic patients with increasing age and BMI. Thus we show that insulin resistance can lead to adverse effects on liver cells even before the onset of diabetes. Studies have shown an association between NAFLD and metabolic syndrome. It seems that NAFLD and metabolic syndrome have common pathophysiological mechanisms and insulin resistance is a key factor in both [17]. Studies have shown that the prevalence of NAFLD increases with age [18, 19]. Similarly, in our study, we observed that the prevalence of NAFLD in prediabetic patients significantly increased with age. Obesity is often associated with fatty live disease and obese subjects are at a higher risk to develop insulin resistance, which increases fatty acids within the liver [20]. The relationship between obesity and NAFLD has been shown in several studies; in Zelber-Sagi et al study, the mean BMI of the patients with NAFLD was reported 29.6±3.8 [15, 21]. In the present study, the highest prevalence of NAFLD in prediabetic patients was observed in BMI > 30 kg/m^2.

Table1: Demographic and laboratory characteristics of the subjects

Variables	Prediabetic group (n=191)	Healthy group (n=191)	P value
Age, mean ± SD (years)	40 ± 10	41 ± 11	(NS)
Body mass index, mean ± SD (kg/m^2)	25 ± 5	24 ± 4	(NS)
Sex (% males)	37.1	43.9	(NS)
Fast blood sugar, mean ± SD (mg/dl)	111 ± 5	78 ± 6	< 0.001*
Glucose tolerance test, mean ± SD (mg/dl)	154 ± 10	123 ± 8	< 0.001*
Aspartate aminotransferase, mean ± SD (IU/L)	115 ± 32.5	92 ± 39.4	< 0.001*
Alanine aminotransferase, mean ± SD (IU/L)	120 ± 28.3	84 ± 24.2	< 0.001*
Gamma-glutamyl transpeptidase, mean ± SD (IU/L)	43.2 ± 20.4	23.8 ± 8.5	< 0.001*
Alkaline phosphatase, mean ± SD (IU/L)	180 ± 44.5	145 ± 30.3	< 0.001*

* P values less than 0.05 were considered significant - NS= not significant

FBS, GTT, AST, ALT, GTT and ALP were significantly different between prediabetic group and the healthy one in our study. Ortiz-Lopez et al found significant difference between FBS, AST, ALT between NAFLD and non-NAFLD groups [13]. Singh et al studied 515 NAFLD patients and 100 healthy controls and compared some of the above parameters in patients with NAFLD with type 2 diabetes mellitus and NAFLD without type 2 diabetes mellitus groups. They found significant difference between the two groups in terms of FBS while AST and ALT were not significantly different [14].

CONCLUSION

This study shows that the prevalence of NAFLD in prediabetic patients is higher than healthy individual. Weight loss and exercise should be encouraged for the prevention of NAFLD and diabetes.

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