NON-ALCOHOLIC FATTY LIVER DISEASE IN PREDIABETIC PATIENTS: A CROSS SECTIONAL STUDY

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There is no conflict of interest and the study was performed in a manner to confirm with the Helsinki Declaration of 1975, as revised in 2000 and 2008 concerning Human and Animal Rights.

ABSTRACT
The simultaneous occurrence of NAFLD and type 2 diabetes is common and the role of insulin resistance in this area has been studied but few studies have been conducted on the relationship between NAFLD and prediabetes. The present study aimed at determining the prevalence of NAFLD, by sonographic detection in prediabetic patients. Methods: In this Cross sectional study, 191 consecutive prediabetic patients, referred to internal clinic in Razi referral hospital of Rasht, Iran, from May 2012 to November 2013, compared with 191 healthy controls of hospital staff. Diagnosis of prediabetes was based on abnormal oral glucose tolerance test or fasting plasma glucose test. Both groups underwent ultrasonography for assessing fatty liver. The collected data were statistically analyzed using Chi Square and T-Test. Subjects in patient group, 71(37.1%) male and 120(62.8%) female, and in the control group, 84(43.9%) male and 107(56.0%) female, were 20-70 years old and the mean age was 41.04 ± 12.66 years. Among the 382, 142 (37.2%) had evidence of NAFLD on ultrasound exam from whom 93 (65.4%) were prediaibetic patients. This results showed a significant difference between NAFLD and prediabetes (P=0.001, OR=2.75). Conclusion: Our study indicates that the prevalence of NAFLD in prediabetic patients is higher than healthy persons. Since NAFLD increases the risk of liver and cardiovascular diseases, we suggest that prediabetic patients be screened by sonography during the early stages of the disease.

KEYWORDS: Non-alcoholic Fatty Liver Disease; Ultrasonography; Prediabetes; Glucose

INTRODUCTION

Prediabetes is a situation in which the body produces more insulin than the normal level to regulate blood sugar resulting from glucose intolerance. This condition usually has no symptoms and can cause serious resistance to insulin.(Garber et al, 2008). Insulin resistance can lead to the formation of type 2 diabetes mellitus and has a key role in formation of hepatic steatosis so that it can increase peripheral lipolysis and production of triglycerides and uptake of fatty acids from the liver (Ferrannini, 1983; Sanyal, 2001; Sheth, 1997). Hepatic steatosis, in the absence of secondary causes of fat accumulation in the liver, is called non-alcoholic fatty liver disease (NAFLD). (Caldwell, S.H. and D.M. Crespo, 2004; Caldwell, 1999). NAFLD is the most common liver disease in the world and its prevalence in different communities has been reported from 2.8 to 24 percent. (Bellentani S, S.G., Masutti F, Crocè LS, Brandi G, Sasso F 2000; Neuschwander-Tetri BA, C.S. 2003). Pathogenesis of NAFLD is not well understood but it seems that impaired fatty acid metabolism in the liver causes the formation of this disease. Day, C.P. and O.F. James, 1998. NAFLD can progress to liver fibrosis and subsequently cirrhosis (Caldwell, S.H. and D.M. Crespo, 2004; Caldwell, S.H., et al , 1999; Day, C.P. and O.F. James, 1998).

Investigations have shown that patients with NAFLD, are in the serious risk of increased prevalence of carotid atherosclerotic plaques and cardiovascular diseases.(Lu H, Z.L., Liang B, Shu X, Xie D , 2009; Stepanova M, Y.Z. 2012). The simultaneous occurrence of NAFLD and type 2 diabetes is common and the role of insulin resistance in this area has been studied but few studies about the relationship between NAFLD and prediabetes have been conducted. Therefore, this study aimed to determine the prevalence of non-alcoholic fatty liver disease using sonographic detection in prediabetic patients.

MATERIALS AND METHODS

This cross-sectional study was conducted from May 2012 to November 2013 in Razi referral hospital of Rasht, Iran. In this study, 191 consecutive patients, diagnosed with prediabetes, referred to internal clinic of the hospital, compared with 191 healthy controls of hospital staff (including: doctors, nurses and medical residents) Demographic and clinical data such as sex, age, stature, weight, history of diabetes mellitus and known liver diseases were recorded.

Patients aged less than 18 and more than 70 years, history of diabetes mellitus and known liver disease (viral hepatitis, autoimmune hepatitis) and hemochromatosis were excluded from the study. Then, Aspartate aminotransferase (AST, SGOT), Alanine aminotransferase (ALT, SGPT), Alkaline phosphatase, HAV Antibody, HCV Antibody, HBs Ag, Antinuclear antibody, Serum Iron, Serum Ferritin, GAMMA-GT, fasting blood glucose and oral glucose tolerance tests for all subjects were performed. Diagnosis of prediabetes was based on abnormal oral glucose tolerance test or fasting plasma glucose test. Both tests were done with Pars Azmoon KIT (GOD-PAP method). The normal ranges of these kits for oral glucose tolerance test and fasting plasma glucose test were 75-139 and 75-100mg/dl, respectively. The oral glucose tolerance test from 140 to 199 mg/dl and/or fasting plasma glucose test from 100 to 125 mg/dl were regarded as pre-diabetes. In addition, both groups underwent ultrasonography for assessing about the fatty liver. This study was approved by the Ethical Committee of Guilan University of medical Sciences and informed consent for participation in the study was obtained from subjects.

STATISTICAL ANALYSIS

To estimate the adjusted odds ratios, logistic regression analysis was used. Analysis was performed using student T test and Chi square test. All statistical analyses were conducted using SPSS software Ver 19 for Windows. P values less than 0.05 were considered significant.

RESULTS

In this study, subjects in patient group, 71(37.1%) male and 120(62.8%) female, and in the control group, 84(43.9%) male and 107(56.0%) female, were 20-70 years old and the mean age was 41.04±12.66 years. Demographic and laboratory characteristics of the subjects were listed and summarized separately in Table 1. Among the 382, 142 (37.2%) had evidence of NAFLD on ultrasound exam 93 (65.4%) being prediaibetic patients. This results showed a significant difference between NAFLD and prediabetes (P=0.001, OR=2.75). Serological markers for viral hepatitis were negative in all cases and levels of serum ferritin, serum iron and antinuclear antibody was in normal range in both groups. Elevated AST & ALT up to 3 fold in prediabetic group & control group were %52.3 and %23.5 respectively (p<0.05). We observed that the lowest prevalence of NAFLD in prediabetic patients was in 20-30 years old and the highest prevalence was in 60-70 that was statistically significant (P=0.0001). BMI has a significant relation with NAFLD in prediabetic patients (P=0.003) because the lowest prevalence of NAFLD in prediabetic patients was found in BMI<20 and the highest prevalence was in BMI>30. In addition, there was a significant correlation between sex and NAFLD in prediabetic patients (P=0.049); of 71 prediabetic men, 28(39.4%) and of 120 prediabetic female, 65(54.2%) ones had NAFLD. Using Binary Logistic Regression, it was found that sex did not affect the incidence of NAFLD (P=0.095), but age and BMI affected its incidence (P = 0.0001).

DISCUSSION

Insulin resistance can cause formation of metabolic syndrom and even before the onset of overt diabetes can have adverse effects on liver cells. Patients with NAFLD at least have one of the components of metabolic syndrome including: hypertension, hyperlipidemia, obesity and diabetes (Marchesini, G., et al., 2003). Gender distribution of NAFLD is highly variable in studies from different countries (Bacon, B.R., et al. , 1994; Browning, J.D., et al. 2004; Lee, R.G.1989; Ludwig, J., et al. 1980; Williams CD, S.J., Asike MI, Torres DM, Shaw J, Contreras M. 2011). In our study 39.4% prediabetic men, and 54.2% prediabetic female, had NAFLD; the prevalence of NAFLD statistically in prediabetic female was more than prediabetic men. Several studies reported that most patients with a diagnosis of NAFLD are in the 4 and 5 decades of their life and the prevalence of NAFLD increases with age (Bahcecioglu, I.H., et al. 2006; Falck-Ytter, Y., et al. 2001; Schwimmer JB, M.N., Deutsch R, Finegold MJ, Lavine JE. 2005); In the present study, we also observed that the prevalence of NAFLD in prediabetic patients significantly increases with age. Obesity is one of the most important diseases associated with fatty live disease. Obese subjects with a higher probability have insulin resistannce which increases the fatty acids in the liver. (Marchesini, G., et al. 2003). The relation between NAFLD and obesity has been documented in several studies (Lankarani, K.B., et al., 2013; Ruhl, C.E. and J.E.

Everhart, 2003). In the present study the most prevalence of NAFLD in prediabetic patients was seen in BMI>30 so it can be concluded that the prevalence of NAFLD increased with increasing body mass index. FBS, GTT, AST, ALT, GTT and alkaline phosphatase had significant differences between prediabetic and healthy groups in our study while in past similar studies these parameters were compared between NAFLD and non NAFLD subjects. (Mohan, V., et al. , 2009). The overall prevalence of NAFLD in our subjects, both prediabetic and healthy persons, was 37.2% which was higher than the prevalence reported in Jimba, Mohan and Lankarani and lower than the Bedogni and Ruckert studies. (Lankarani, K.B., et al. 2013; Mohan, V., et al.2009; Jimba, S., et al. 2005). In the present study, the prevalence of NAFLD in prediabetic patients and non-prediabetes was 48.7% and 25.7%, respectively. This was similar with the results obtained from Jimba and Mohan studies. (Mohan, V., et al. 2009; Jimba, S., et al. 2005). In this study, we observed a significant relation between NAFLD and prediabetes and chi-square test showed that the risk of NAFLD in prediabetic patients is 2.75 vs. control group. In recent studies, it was demonstrated that prediabetes was closely associated with NAFLD. These studies have shown that prediabetic patients with NAFLD have significant insulin resistance in comparison with prediabetic persons without NAFLD and that mentionedthat insulin resistance plays a key role in hepatic steatosis and NAFLD. (Sanyal, A.J., et al., 2001; Williams CD, S.J., Asike MI, Torres DM, Shaw J, Contreras M. 2011; Pagano, G., et al. 2002).

CONCLUSION

This study indicates that the prevalence of NAFLD in prediabetic patients is higher than healthy persons. Since NAFLD increases the risk of liver and cardiovascular diseases, it is suggested that prediabetic patients be screened by sonography in early stages of disease. Also, to prevent disease progression, weight loss and exercise are recommended.

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