[1]Ricardo Salas-Flores,
[2]Brian González-Pérez,
[3]Alonso Echegollen-Guzmán

Hepatic steatosis and type 2 diabetes mellitus

in health workers

[1]Hospital General Regional 6, Instituto Mexicano del Seguro Social. Departamento de Investigación, Universidad del Noreste
[2]Unidad de Medicina Familiar 38, Instituto Mexicano del Seguro Social
[3]Coordinación Delegacional de Investigación en Salud, Instituto Mexicano del Seguro Social

Tampico, Tamaulipas, México

Comunicación con: Ricardo Salas-Flores
Fax: (833) 241 2800. Correo electrónico: risafl@yahoo.com; ricardo.salas.flores@hotmail.com

Resumen

Objetivo: determinar la prevalencia de hígado graso no alcohólico en trabajadores de la salud con diabetes mellitus tipo 2 mediante ultrasonido hepático.

Métodos: del 1 de junio de 2009 al 1 de junio de 2010 se incluyeron trabajadores de la salud portadores de diabetes mellitus 2 adscritos a la Unidad de Medicina Familiar 77, Ciudad Madero, Tamaulipas. Se evaluaron factores de riesgo, índice de masa corporal, porcentaje de grasa corporal, masa grasa, perímetro de cintura, presión arterial, hemoglobina glucosilada y perfil lipídico. Los pacientes fueron categorizados con y sin hígado graso no alcohólico. Las diferencias fueron evaluadas con *t* de Student para muestras independientes y χ^2.

Resultados: la prevalencia de esteatosis hepática en mujeres fue de 40 % y en hombres de 17.1 %. Los pacientes con hígado graso no alcohólico fueron significativamente más obesos ($p < 0.001$) y con valores más altos de porcentaje de grasa corporal ($p < 0.001$), masa grasa ($p < 0.01$), perímetro de cintura ($p < 0.01$), hemoglobina glucosilada ($p < 0.04$) y triglicéridos ($p < 0.03$).

Conclusiones: se debe desarrollar iniciativas para prevenir la progresión del hígado graso no alcohólico entre trabajadores de la salud con diabetes mellitus tipo 2.

Palabras clave

diabetes mellitus tipo 2
hígado graso no alcohólico
hígado graso
obesidad

Summary

Background: patients with type 2 diabetes mellitus (T2DM) appear to have an increased risk of developing nonalcoholic fatty liver disease (NAFLD) and have higher risk to develop hepatic fibrosis and cirrhosis. The aim was to determine the prevalence of NAFLD in health workers with T2DM by liver ultrasound.

Methods: health workers with T2DM attended at the Family Medicine Unit No. 77, Madero City, Tamaulipas, Mexico, were screened. Risk factors, BMI, % of body fat (% BF), fat mass, waist circumference (WC), blood pressure, HbA_{1C} and lipid profile, were evaluated. The patients were categorized into two groups according to NAFLD status. Differences between groups were assessed by independent *t* test and χ^2 test.

Results: the NAFLD prevalence found in females on ultrasound examination was 40 % and 17.1 % in males. NAFLD patients were more obese ($p < 0.001$) and they had significantly higher values of % BF ($p < 0.001$), fat mass ($p < 0.01$) and WC ($p < 0.01$). They also had significantly higher values of HbA_{1C} ($p < 0.04$) and triglycerides ($p < 0.03$) than patients without NAFLD.

Conclusions: NAFLD is common among health workers with T2DM. It is important to prevent NAFLD progression.

Key words

diabetes mellitus, type 2
non alcoholic fatty liver disease
fatty liver
obesity

Introduction

For a long time, hepatic steatosis was believed to be a benign condition. Recently, liver steatosis, also termed nonalcoholic fatty liver disease (NAFLD), has gained much interest. The spectrum of liver damage in NAFLD ranges from simple steatosis to nonalcoholic steatohepatitis (NASH), which can progress to end-stage liver disease.[1-3] The etiology is unknown, but the disease is often associated with type 2 diabetes mellitus (T2DM), insulin resistance, dyslipidemia, (visceral) obesity and hypertension,[4-6] all of them are components of the metabolic syndrome, strongly supporting the notion that NAFLD is the hepatic manifestation of the syndrome.[7-9]

Most patients with NAFLD are asymptomatic. Although some may experience malaise on right upper-quadrant in abdominal region.[10] NAFLD is generally diagnosed by ultrasonographic that has a sensitivity of 90 % and specificity 95 % in detection moderate and severe hepatic steatosis.[11]

The prevalence of NAFLD in T2DM is unknown. However it has been estimated that 70-75 % of T2DM patients may have NAFLD.[12] In Mexico the prevalence is unknown maybe because is underestimated for his association with T2DM and obesity which are very common in Mexican population.

All patients who have T2DM or are severely obese appear to have an increased risk of developing NAFLD and certainly have a higher risk of developing hepatic fibrosis and cirrhosis. Currently, NAFLD has gained interest because of its asymptomatic evolution, in the identification of a clinical pattern and to prevent progression to liver failure, cirrhosis and to hepatocellular carcinoma.[13] Considering that these complications constitute a substantial decrease in quality of life and life expectancy and accounts it high cost in health care budget, one of the mayor problems to resolve is the prevalence of NAFLD which is unknown in our health worker community, the purpose was to determine the prevalence of NAFLD among health workers with T2DM diagnosed by liver ultrasound, which is the most widely used imaging test for detecting hepatic steatosis.

Methods

All health workers with T2DM attended at the Family Medicine Unit No. 77, Madero City, Tamaulipas, Mexico, from June 1st 2009 to June 1st 2010 were screened. Patients with history of hepatitis infection, liver cirrhosis, pregnant women and those who have not laboratory tests and liver ultrasound image were excluded. An informed consent was obtained. A questionnaire was applied to patients who accepted to participate. They were referred to an endocrinologist in the General Regional Hospital No.6, Mexican Institute of Social Security for medical evaluation and hepatic ultrasound. The local ethics committee 2801 approved the study.

In the standing position, weight and height were measured with the subjects in light clothing and without shoes. Body weight was measured recorded to the nearest 0.1 kg using a digital scale (Tanita Corporation, Japan). Height was obtained by using a portable stadiometer 225 cm (SECA, Hamburg, Germany) to nearest 0.1 cm. Adiposity was measured by bioelectrical impedance analysis using a TANITA TBF310 model with a frequency of 50 kHz. Height, sex and age were entered manually, while weight was recorded automatically using 0.5 kg as an adjustment for clothing weight in all subjects.

Body mass index (BMI) was calculated by dividing weight in kilograms by the square of height in meters. Waist circumference (WC) was measured in a standing position at the level of the umbilicus. Blood pressure was measured with a standard mercury manometer. Venous blood was drawn in the morning after an overnight fast. Plasma glucose concentrations were measured using the glucose oxidase method, total cholesterol, HDL cholesterol and LDL cholesterol by enzymatic reaction, triglycerides by a colorimetric method and HbA_{1C} by chromatography (Syncron CX 4; Beckman Instruments, Fullerton, CA).

The hepatic steatosis evaluation was made by ultrasound. The apparatus used (TOSHIBA) was equipped with a convex 3.5 MHz probe. Longitudinal, sub-costal, ascending, and oblique scans were performed always by the same experienced radiologist, who was unaware of the clinical course and laboratory details of the patients.

Overweight was defined as a BMI > 25 < 29.9 kg/m^2 and obesity if BMI > 30 kg/m^2.[14] A WC > 90 cm in men and > 84 cm in women was considered as abdominal obesity.[15] Blood pressure was considered high if the systolic was > 130 mm Hg or diastolic was > 80 mm Hg according to our guides for institutional clinical practice.[16] The diabetic control was considered good with HbA_{1C} values < 7 %, total cholesterol < 200 mg/dL, LDL cholesterol < 100 mg/dL, HDL cholesterol > 40 mg/dL in men and > 50 mg/dL in women, triglycerides < 150 mg/Dl.[17,18] The criteria for determining the presence of steatosis was the hyperechogenicity of the liver tissue with tightly packed fine echoes and hepatomegaly.[19]

The patients were categorized into two groups according to NAFLD status. Descriptive data were expressed as mean values ± SD for continuous variables and number of subjects (percentage) for categorical variables. Differences between groups were assessed by independent *t* test and χ^2 test using SPSS statistical software (version 12; SPSS Inc, Chicago IL, USA). All reported with *p* values < 0.05 were considered statistically significant.

Results

Fifty eight health workers were identified, four were not contacted and 19 patients declined to participate in the study or not complete the liver ultrasound examination or laboratory test. A total of 35 health workers aged 31-58 years were included in the analysis. The baseline characteristics of the study participants grouped according to NAFLD status were in table I, the prevalence of ultrasonography hepatic steatosis was found in 57.1 % (*n* = 20) of patients. Individuals with hepatic steatosis were younger, more frequent females (*n* = 14) and the proportion using oral hypoglycemic agents was higher among patients with NAFLD (*n* = 20). They also had significantly higher values of BMI, % BF, fat mass and WC. They were significantly more obese and present high values of blood pressure. Accordingly, patients

Table I Characteristics of the study participants, grouped according to nonalcoholic fatty liver disease status*

Variables	Without NAFLD	With NAFLD	*p***
n	15	20	–
Sex (% F/M)	22.8/20	40/17.1	ns
Age (years)*	49.73 ± 7.3	44.40 ± 6.5	0.03
Oral hypoglycemic users (%)	37.1	57.1	ns
Insulin users (%)	5.7	0	
BMI*	28.81 ± 3	34.56 ± 7.07	
Overweight (%)	31.4	14.2	0.005
Obesity (%)	11.4	42.8	
% Body fat*	28.94 ± 7.2	38.79 ± 8.2	0.001
Fat mass (kg)*	25.04 ± 8	35.1 ± 13.4	0.01
Waist circumference (cm)*	96 ± 10.2	107 ± 14.2	0.01
Systolic blood pressure (mm Hg)*	128.67 ± 15.5	133.35 ± 14.03	ns
Diastolic blood pressure (mm Hg)*	82.3 ± 7.7	85 ± 9.1	ns
HbA_{1C} (%)*	6.68 ± 1.5	7.92 ± 2.02	0.04
Triglycerides (mg/dL)*	153 ± 60.1	221.1 ± 105.5	0.03
Total cholesterol (mg/dL)*	195.26 ± 34.8	201.1 ± 31.07	ns
HDL cholesterol (mg/dL)*	43.2 ± 10.3	39.15 ± 7.1	ns
LDL cholesterol (mg/dL)*	119.44 ± 43.6	139.3 ± 22.1	ns
Good diabetic control (%)	20	0	0.001
Bad diabetic control (%)	22.8	57.1	

* *Data are mean ± SD or proportions.*

** *Statically significant $p < 0.05$ (independent test for continuous variables and χ^2 test for categorical variables).*

HDL = high-density lipoprotein, LDL = low-density lipoprotein, HbA_{1C} = glycated hemoglobin

with NAFLD had significantly higher values of HbA_{1C} and triglycerides. Plasma HDL cholesterol, LDL cholesterol and total cholesterol concentrations were not significantly different between the groups. Bad diabetic control occurred more frequently among patients with NAFLD.

Discussion

NAFLD is the most common cause of chronic liver disease in adults and is frecuently associated with obesity, metabolic syndrome and T2DM.[20] The prevalence of NAFLD among T2DM patients has been estimated 34-74 % and it is an almost universal finding in obese patients with T2DM.[21] In Mexico, there are few studies on the frequency of NAFLD in population with diabetes, which is estimated at 10.3 cases per 100 inhabitants in general population and 18.5 cases in population with diabetes.[22] In the present study, we found a high prevalence of NAFLD as diagnosed by means of characteristic sonographic features in health workers with T2DM compared with reported by Bernal *et al.* and Roesch *et al.*[22,23] and similar presence of NAFLD in females. Contrary to reported in others studies we found that patients with NAFLD were younger.[24] We consider this finding of concern because early presentation of NAFLD represents an important burden of disease for health workers.

Another finding was the increased % BF and abdominal obesity, which suggest the presence of NAFLD. In most studies, liver fat is closely and positively correlated with measures of total adiposity such as BMI or percentage body fat. Furthermore, the correlation of liver fat with visceral adiposity, measured as waist circumference, is particularly strong.[25-27]

The liver fat content in T2DM patients could contribute to diabetic dyslipidemia. Serum triglycerides and/or LDL cholesterol levels might be elevated in patients with NAFLD. In our study, serum triglyceride levels were found significantly higher in patients with NAFLD. In other studies, hyperlipemia prevalence was detected as varying between 21-44 % in the patients with NAFLD.[28]

Fatty liver results from accumulation of fatty acids in various forms, predominantly triglycerides. This accumulation occurs when there is a shift in fatty acid metabolism to favor net lipogenesis rather than lipolysis. This can occur when the amount of fatty acid supplied to the liver from the gut or adipose tissue exceeds the amount needed for mitochondrial oxidation, phospholipids and cholesterol ester synthesis. This is the presumed mechanism for steatosis in the setting of diabetes mellitus, obesity, malnutrition, parenteral nutrition, steroid treatment and excessive dietary intake of fat. Hyperinsulinism and insulin resistance is an important component in the development of steatosis in these diseases. It has been demonstrated that a fatty liver is insulin resistant, resulting in elevated HbA_{1C} values and therefore a bad control of diabetes.[29]

This study is the first to describe the NAFLD prevalence in health workers with T2DM in Tamaulipas State. Overall, our results suggest that NAFLD is very common among T2DM health workers with a poor diabetic control. These findings might have possible clinical and public health implications. We suggested that a consideration should be given to referring our health workers with priority to endocrino-logist and gastroenterologist for further evaluation. This will be particularly important once an effective treatment for NASH has been established, and better noninvasive methods for assessing disease severity are validated. It is important to develop innovative and interventionist initiatives in liver disease management approaches to prevent progression to NAFLD. The Family Medicine Units have an important work in health promotion, prevention, early detection and control, and also in the early treatment of diabetes and its complications. The activities developed to preventing the complications of diabetes and improving the health outcomes for our health workers would be (when diabetes is under effective management), to be more productive, positively contribute to their family life, to their place of employment and their community. They would also favored a better quality of life to patients.

The study has some limitations that should be noted. The diagnosis of NAFLD was based on ultrasound imaging and the exclusion of other causes of chronic liver disease was based on self-report by the patients such a viral hepatitis or liver cirrhosis but were not confirmed by liver biopsy. It is known that none of the radiological features can distinguish between NASH and other forms of NAFLD and that only liver biopsy can assess the severity of damage and the prognosis. However, liver biopsy would be impossible to perform routinely in a large epidemiological study. Conversely, ultrasonographic is by far the most common way of diagnosing NAFLD in clinical practice and has good sensitivity and specificity in detecting moderate and severe steatosis. Indeed, it has been reported that the presence of more than 30 % fat on liver biopsy is optimal for ultrasound detection of steatosis, whereas ultrasonographic is not totally sensitive, particularly when hepatic fat infiltration is < 30 %.[30] Thus; it is likely that we misclassified patients with NAFLD based only on ultrasonographic. On the other hand we did not know the type of insulin and antidiabetic agents and how this may have affected our results, mainly because it has been proposed that metformin has shown beneficial effects in lowering hepatic steatosis.

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