

Non-alcoholic Fatty Liver Disease in a Jamaican Patient Population

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ABSTRACT

Objectives: This study determined the prevalence and clinical features of non-alcoholic fatty liver disease over a six year period in a patient population.

Methods: Patients diagnosed with fatty liver disease by ultrasound and/or liver biopsy between June 2006 and June 2012 at the University Hospital of the West Indies, Jamaica, were reviewed.

Results: There were 384 cases of fatty liver disease identified and 230 patients were included in the study. The overall prevalence was 2.4%. The patient population consisted of 54% females and 41% males with a mean age of 53 years for females and 51 years for males. Increased body mass index (BMI) was present in 85.5% with a preponderance in females (63%). The risk factors for fatty liver disease identified were increasing age, obesity, diabetes mellitus (39%) and dyslipidaemia (21%). Hypertension was present in 51% of patients. Hepatomegaly was found in 10.7% of patients. Elevated serum aspartate aminotransferase (AST) was present in 21.2% of patients tested and elevated alanine aminotransferase (ALT) in 3.7%. Liver biopsy in ten patients revealed macrovesicular fatty changes in 40% of cases, 10% had steatohepatitis and 10% had evidence of advanced fibrosis. An underlying malignancy was present in 12.8% of patients.

Conclusion: The prevalence of fatty liver disease is low with ultrasound detection in this Jamaican patient population. Obesity, male gender, advancing age, diabetes and dyslipidaemia were significant associated factors. Further studies are required to ascertain the full extent and outcome of this disease in Jamaica.

Keywords: Fatty liver, liver, obesity

Enfermedad del Hígado Graso no Alcohólico en una Población de Pacientes Jamaicanos

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RESUMEN

Objetivos: Este estudio determinó la prevalencia y características clínicas del hígado graso no alcohólico en un periodo de seis años en una población de pacientes.

Métodos: Se revisaron pacientes diagnosticados con hígado graso mediante r ultrasonido o biopsia del hígado entre junio de 2006 y junio de 2012 en el Hospital Universitario de West Indies, Jamaica, fueron repasados.

Resultados: Se identificaron 384 casos de hígado graso y se incluyeron 230 pacientes en el estudio. La prevalencia global fue del 2.4%. La población de pacientes consistió en 54% mujeres y 41% varones con una edad promedio de 53 años en el caso de las hembras y 51 años en los hombres. El índice de masa corporal (IMC) estuvo presente en 85.5% con predominio en las mujeres (63%). Los factores de riesgo de la enfermedad del hígado graso identificados fueron: aumento de edad, obesidad, diabetes mellitus (39%) y dislipidemia (21%). La hipertensión estuvo presente en el 51% de los pacientes. Se encontró hepatomegalia en 10.7% de los pacientes. Una cantidad elevada de aspartato amino-transferasa (AST) en suero estuvo presente en 21.2% de los pacientes probados y una cantidad elevada de alanina amino-transferasa (ALT) en 3.7%. La biopsia del hígado en diez pacientes reveló cambios grasos macrovesiculares en el 40% de los casos, 10% tuvieron esteatohepatitis, y 10% tenían evidencia de fibrosis avanzada. Una malignidad subyacente estuvo presente en 12.8% de los pacientes.

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Conclusión: La prevalencia de hígado graso es baja según la detección de ultrasonido en esta población de pacientes jamaicana. La obesidad, el sexo masculino, el avance en la edad, la diabetes y la dislipidemia fueron factores asociados significativos. Se requieren otros estudios a fin de determinar la magnitud y el resultado de esta enfermedad en Jamaica.

Palabras claves: Obesidad, hígado, hígado graso

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INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is the clinical entity in which there is hepatic steatosis, diagnosed on imaging or histology with no other cause for accumulation of secondary hepatic fat (1). Heavy alcohol use, medications (amiodarone, methotrexate) that are steatogenic or hereditary disorders (haemochromatosis) may be associated with fatty liver (1). Non-alcoholic fatty liver disease may be further divided histologically into non-alcoholic fatty liver (NAFL) and non-alcoholic steatohepatitis (NASH). Non-alcoholic fatty liver disease is the existence of hepatic steatosis without damage to hepatic cells as evidenced by ballooning of the hepatocytes, while NASH is the existence of steatosis of the hepatocytes, inflammation and hepatocyte injury with or without fibrosis (1).

Obesity, hyperlipidaemia, insulin resistance and Type 2 diabetes mellitus (DM) are components of the metabolic syndrome which is associated with NAFLD (2, 3). Based on several assessment methods, including imaging, liver enzymes and liver biopsy, the prevalence of NAFLD worldwide in different countries is estimated to range from 6.3 to 33%, with an average of 20% in the general population (1, 4).

Non-alcoholic fatty liver disease is amongst the most common causes of deranged liver function tests in the United States of America (3–5). As age increases, not only does the prevalence of NAFLD increase, but also the potential for progression to cirrhosis or death (6, 7). Male gender and Hispanic ethnic group seem to be other risk factors for NAFLD (3).

The frequency of NAFLD in the general population along with the risk of developing cirrhosis are factors that make this disease clinically relevant and important. Non-alcoholic fatty liver disease is associated with higher overall and liver-related mortality (7). Matched control studies show that these patients have a greater risk of death and the most common cause of mortality was cardiovascular disease (8). There is also an increased likelihood for hepatocellular carcinoma, particularly in the patients with advanced fibrosis and cirrhosis (9).

To date, there have been no studies in Jamaica on NAFLD. This study reports on the characteristics of patients who have this disease as diagnosed by abdominal ultrasound. This will aid in determining the burden of the disease and guide appropriate risk factor identification and modification.

SUBJECTS AND METHODS

All patients having abdominal ultrasound performed at the Radiology Department, University Hospital of the West Indies (UHWI), Jamaica, were eligible for study. These patients were inpatients and outpatients of the hospital and the information was obtained from computer files at the Radiology Department. Patients who had abdominal ultrasound from June 2006 to June 2012 were analysed. The patients diagnosed with fatty liver, radiologically, had their charts reviewed to ascertain relevant information regarding age, gender, history, co-morbidities, body mass index (BMI), medications and biochemical investigations including: aspartate aminotransferase (AST) and alanine aminotransferase (ALT), bilirubin, albumin, gamma-glutamyl transferase (GGT), alkaline phosphatase, platelets, prothrombin time and glucose.

The medical records of the subset of patients who underwent liver biopsy were obtained and the histology reports from the Department of Pathology were reviewed to determine the degree of histological inflammation and fibrosis represented on the biopsy specimens.

The information obtained was extracted from the study patients' medical records and each individual was identified by a unique identification number. Information obtained was recorded on an SPSS spread sheet and was kept in strictest confidence. Univariate summaries (frequencies, means, *etc*) and bivariate tests (Chi-squared) were used to analyse the data.

The study protocol was reviewed and approved by the ethics committee of The University of the West Indies/University Hospital of the West Indies/the Faculty of Medical Sciences.

RESULTS

There were 384 patients with fatty liver disease diagnosed by ultrasound during the study period June 2006 to June 2012. Abdominal ultrasound was performed on 15 999 patients during this time span, resulting in a prevalence of 2.4% for fatty liver disease in this patient population. Data were available on 230 of these patients, diagnosed from June 2009 to June 2012. All patients were Jamaicans; however, the ethnicity was not documented in most cases. There was a predominance of females, 124 (54%) as compared to 95 (41%) males (gender was not documented for 11 patients). The mean age was 53 years for females and 51 years for males.

Subjective assessments of body habitus revealed that nine patients (3.9%) were of normal weight, eight (3.5%) were overweight, 48 (20.9%) obese and one (0.4%) morbidly obese.

Of those with documented BMI, 85.5% of them were overweight or obese. There were 63% of females over the normal BMI compared to 37% males. Of the other risk factors studied, diabetes mellitus was the most prevalent, 39.2% and 21% had dyslipidaemia and both were more common in females (Table). The frequency of diabetes, hypertension and dyslipidaemia increased with age. Hypertension was present in 51% of patients.

Table: Associated disorders

Diabetes (DM)				
	Male	Female	Total	Percentages
Non-DM	53	68	121	60.80%
DM	34	44	78	39.20%
Total	87	112	199	100%
Dyslipidaemia				
	Male	Female	Total	Percentages
Normal lipid	73	73	146	79.35%
Dyslipidaemia	11	27	38	20.65%
Total	84	100	184	100%
Hypertension				
	Male	Female	Total	Percentages
Normotensive	52	47	99	49.25%
HTN	38	64	102	50.75%
Total	90	111	201	100%

DM; diabetes mellitus; HTN; high blood pressure

Hepatomegaly was present in 10.7% of patients. Of 108 patients (47%) who had documented AST levels, 21.2% had elevated levels. Elevated AST values ranged from 34–665 IU/L fourteen (6%) patients had documented ALT levels of which 3.7% had elevated levels.

Liver biopsy was performed in 10 (4.3%) patients. Biopsies primarily revealed macrovesicular fatty changes in 40% of cases, 10% had steatohepatitis and 10% had evidence of advanced fibrosis.

In this series, 12.8% of patients with fatty liver disease had cancer and 92.6% of these patients were over 45 years old ($p = 0.014$). The types of malignancies included breast, prostate, renal cell, multiple myeloma and melanoma.

DISCUSSION

Non-alcoholic fatty liver disease is one of the most common chronic liver conditions in the western world and which affects a large proportion of the world's population (2, 3). The incidence of NAFLD is under-reported and increasing, as the prevalence of its risk factors increase (4). Additionally, there is increased awareness that NAFLD is not as benign as was previously thought, as it may lead to advanced fibrosis and cirrhosis (2). The prevalence of fatty liver disease was found to be low in this study by ultrasound, 2.4%, in comparison to other studies (4). This may be due to the fact that the condition is under-reported as most physicians consider it to be a

benign condition. Additionally, most people at high-risk of NAFLD may not be sent for the necessary evaluation partly due to lack of awareness of the condition. Also, most patients with NAFLD have no symptoms or signs of liver disease (2). Insulin resistance and metabolic syndrome are often associated with NAFLD. This was borne out in this study where a significant percentage of patients were found to be overweight/obese, hypertensive, diabetic and dyslipidaemic. The prevalence of NAFLD was 69% in one study using ultrasound in patients with diabetes mellitus (DM) which was associated with obesity, mainly abdominal, hypertriglyceridaemia and high-normal ALT levels (10). Another study showed, 127 of 204 patients with DM had ultrasonographic evidence of fatty infiltration; and of those who had biopsy, 87% had evidence on histology of NAFLD (11). A previous report found fatty infiltration of the liver was evident in approximately 50% of patients with hyperlipidaemia, which was the most commonly associated condition (12).

The prevalence of NAFLD increases with age (1, 6), and the results of the present study is in keeping with this finding. In a previous report, older patients had significantly more risk factors and had significantly greater fibrosis on biopsy (6). In contrast to other reports (13), in which male gender was a risk factor for NAFLD, this study revealed a preponderance of females (53.9% versus 41.3%). In this study, obesity was more common in females and this may account for the difference in gender. Several studies have clearly depicted the prevalence of NAFLD to be associated with race and ethnicity. The highest prevalence of NAFLD, elevated aminotransferase levels and hepatic steatosis is in Hispanics and non-Hispanic Whites, while African-Americans have the lowest rate (3, 13). The majority of the Jamaican population (90%) is of African descent. Increased liver transaminases, AST and ALT, have been used as non-invasive markers of NAFLD (4). In this study, 21.2% of patients who were tested had elevated AST values and for ALT, 3.7% had elevated levels. Although increased ALT is usually associated with histological NASH, patients may have NAFLD or advanced fibrosis with normal ALT levels. As a result, ALT levels cannot be used solely to negate hepatic impairment in patients thought to have NAFLD, especially those with hepatomegaly or Type 2 diabetes (13).

Non-alcoholic fatty liver disease has been divided histologically into non-alcoholic steatohepatitis (NASH) and non-NASH (2, 4, 13). The non-NASH subtype refers to patients with simple steatosis with or without non-specific changes. The non-NASH subtype may progress slower than NASH. Histologic findings include, (1) steatosis, mainly macrovesicular but may be microvesicular or mixed; (2) inflammatory infiltrates consisting of mixed neutrophilic and mononuclear cells (3) ballooning degeneration and (4) fibrosis. In this study, 10% had evidence of NASH, however, a small percentage of patients actually had this procedure done, thus, firm conclusions about histological findings cannot be drawn from this study. The low frequency of liver biopsy for fatty liver disease is consistent with international trends. For patients with

NAFLD, liver biopsy is the most definitive method to detect steatohepatitis and fibrosis, however, this is invasive and has associated morbidity and rarely mortality.

Interest has been focussed on non-invasive means of detecting significant fibrosis in patients with suspected NAFLD. The NAFLD fibrosis score which incorporates: age, hyperglycaemia, BMI, platelet count, serum albumin and AST/ALT ratio is one such non-invasive method (2). A NAFLD fibrosis score > 0.675 or a BARDS score > 2 suggests a high probability of fibrosis (14, 15). Applying these models may result in avoiding liver biopsy in the majority of patients (14). Elevated cytokeratin-18 levels have been found in several studies to be elevated in patients with steatohepatitis, but this is not yet recommended for routine use (16).

Ultrasonography has a sensitivity of 89 per cent and a specificity of 93 per cent in detecting steatosis (2). An incidental finding of fatty liver on ultrasound with or without signs or symptoms of hepatic disease and normal biochemistries warrant evaluation for metabolic risk factors and alternate causes of fatty liver such as alcohol use and medications. Patients with fatty liver on ultrasound, an elevated NAFLD fibrosis score with the metabolic syndrome are at greater risk of steatohepatitis and cirrhosis and would benefit from liver biopsy (1).

Once the diagnosis of NAFLD is made management involves a gradual weight loss of 3–5%, as this has been proven to improve steatosis and the degree of fatty infiltration usually decreases with weight loss in most patients. In addition, associated metabolic conditions should be treated. In patients with diabetes mellitus or hyperlipidaemia, good metabolic control is recommended (2). Patients should also be encouraged to avoid consuming alcohol. The use of metformin, ursodeoxycholic acid, pioglitazone, Vitamin E and bariatric surgery have been looked at but has not been beneficial in treating NAFLD (13). Statins are advocated for the management of dyslipidaemia but randomized control trials are needed to determine its benefit in steatohepatitis (1).

An interesting aspect of this study is that 12.8% of patients with NAFLD were diagnosed with cancer, and the incidence of this increased with age ($p = 0.014$). This is in accordance with previous data from the USA, where 91% of cancers from all sites are diagnosed in patients over age 45 years (17).

There were limitations in the present study. Some patients diagnosed with NAFLD on ultrasound were not analysed due to missing data. In addition, some information was not available in all the patients included.

This is the first study on NAFLD in Jamaica, and although the prevalence was found to be low in this report, in light of its growing incidence worldwide, this should propel further study into this very important and under-reported disease.

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