Prevalence of Non-Alcoholic Fatty Liver among Adults in Khartoum- Sudan: Epidemiological Survey

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Abstract: Non-alcoholic fatty liver disease (NAFLD) is diagnosed increasingly in adults, but the prevalence remains unknown. This study was designed with an aim to determine the prevalence of NAFLD in a population based sample in Khartoum- Sudan by an epidemiological survey. A prospective, cross-sectional study was carried out among 500 Sudanese adults (200; 40% males and 300; 60% females) aged 15 to 80 years, in between March 2011 to March 2013. Participants underwent physical examination, laboratory tests and ultrasonography examination of the liver. Diagnosis of NAFLD in this study was based on sonographic evidence of a NAFLD and testing negative for serum hepatitis B surface antigen (HBsAg) and anti-hepatitis C virus antibody (anti-HCV) antibody. Of the 500 participants negative for HBsAg or anti-HCV antibody, the overall prevalence of NAFLD 15%, 4.4% in males and 6.6% in females. NAFLD prevalence differs by race and ethnicity; location in Sudan (Center: 36.36%; North: 7.27%; South: 21.82%; East: 16.36% and West: 18.18%). The most significant factors associated with the presence of NAFLD were weight category, elevated alanine aminotransferase (ALT) and increase Non high density lipoprotein (Non-HDL) cholesterol level. Obesity is a major risk factor and is associated with high rates of NAFLD. It is recommended that ultrasonography of the liver to be included in the routine health examinations of obese adults. Clinicians must be aware of the limitations in the available methods to diagnose NAFLD.

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1. Introduction

NAFLD is increasing recognized as one of the most important causes of chronic liver disease in Western countries [1]. It encompasses a spectrum of diseases ranging from simple hepatic steatosis to nonalcoholic steatohepatitis (NASH). Hepatic steatosis is a common clinical and histological finding and it is considered a benign condition, whereas NASH is an aggressive liver disease that leads to advanced fibrosis, cirrhosis and even hepatic failure [1-3].

The prevalence of NAFLD in adults is about 20% (range, 15 to 39) and it is the commonest liver disease, accounting for abnormal liver function tests in the majority of asymptomatic subjects [4, 5]. Although generally unprogressive, NAFLD is an important precursor to the development of fibrosis in aetiologically diverse conditions such as hepatitis C, and alcoholic and nonalcoholic liver disease [6]. Furthermore, it has the potential to lead to end stage liver failure via steatohepatitis from lipid peroxidation, even in the non-alcohol drinker, an entity that is being studied with growing interest in the affluent society [7, 8]. Fatty liver is an increasingly common problem worldwide and has been reported in Japan, Australia, America, Europe, and the Middle East, although geographic variations in prevalence are evident [7, 9-15]. Along with the steady improvement of living level and wide use of ultrasonography, the number of patients with a diagnosis of fatty liver is increasing in Sudan recently.

Liver biopsy is considered the gold standard for diagnosis and is the only method for differentiating NASH from steatosis with or without inflammation [16, 17]. Although ultrasound, CT scans, MRI, and proton magnetic spectroscopy have been used to diagnose NAFLD, differences between NASH and steatosis are not apparent with any of the radiologic modalities [17-19]. Although ultrasound has limitations [17, 20-21], the most recent data, as well as cost considerations [22], have made ultrasound the most common imaging modality used for evaluating hepatic steatosis. The primary purpose of this community based study was to determine the prevalence of NAFLD in a specific population; adults in Khartoum- Sudan.

2. Material and Methods

A prospective, cross sectional study was carried out in the Radiology and Ultrasound Departments in Khartoum, Omdurman and Khartoum North Teaching Hospitals, which are the major reference hospitals of Khartoum State, in between March 2011 to March 2013. Study population comprises A total of 500 adults who underwent abdominal ultrasound scanning were enrolled in this prospective study.

For each participant, an extensive medical history was obtained that included alcohol intake, history of chronic liver disease in first-degree relatives; a detailed history of viral hepatitis, gallstone disease and drug abuse; previous diagnosis of diabetes, hypertension and coronary heart disease. Each participant also underwent a detailed physical examination, including measurement of body mass index (BMI), height, waist circumferences. Data regarding the current body height, body weight, together with the waist circumferences of the patients were collected. Weight was measured in light clothing, while height was measured to the nearest 0.1cm with the head held in the Frankfort plane. Waist circumference was taken midway between the inferior margin of the last rib and the crest of the iliac bone in a horizontal plane and measured to the nearest 0.1cm.

After an overnight fast, serum total cholesterol, triglycerides, HDL cholesterol, ALT, fasting plasma sugar, plasma insulin, HBsAg and anti-HCV were measured in all participants. Fasting plasma insulin concentrations, HBsAg and anti-HCV were measured by micro particle enzyme immunoassay (Axsym Insulin Reagent Pack, Abbott Laboratories, and Abbott Park, IL, USA). Total cholesterol, triglyceride, HDL cholesterol and ALT concentration were measured by an enzymatic colorimetric method using a Hitachi 717 automated analyzer (Hitachi Corp, Tokyo, Japan). Non-HDL cholesterol was calculated as total cholesterol minus HDL cholesterol using the Friedewald equation [23]. Homeostasis model assessment- insulin resistance (HOMA-IR) was used to evaluate insulin sensitivity.

Ultrasonographic examination of the liver was performed by two experienced Ultrasonologists, using Aloka SSD 500, Hitachi, Siemens, Philips HDI 1000, Shimadzu SDU 350, Toshiba just vision and Honda electronics HS 2000 units with 3.5 MHz convex probe. Printing facility issued through the ultrasound digital graphic printer, 100 V; 1.5 A; and 50/60 Hz, with the serial number of 3-619-GBI-01 and made by Sony Corporation- Japan. The time to gain control (TGC) was set at a constant level, with a gain of 60 dB. The probe was positioned in a right intercostal scan in each patient so that stable parenchymal echo images of the liver and the right kidney were obtained simultaneously with no vessels in the images.

NAFLD was defined as the presence of an ultrasonographic pattern consistent with “bright liver,” with evident ultrasonographic contrast between hepatic and renal parenchyma, vessels blurring, and narrowing of the lumen of the hepatic veins in the absence of findings suggestive of chronic liver disease [24, 25]. Although NAFLD was diagnosed based on the ultrasonographic pattern and graded as mild, moderate and severe according to the criteria described by Needleman et al. in the sonography of diffuse benign liver disease: accuracy of pattern recognition and grading [26]. The diagnosis of NAFLD in this study was based on sonographic evidence of a fatty liver (Figure 1) and a negative test result for HBsAg and anti-HCV antibody. None of the participants had a history of alcohol consumption and liver disease, hypertension or diabetes.

Figure 1. Demonstrate NAFLD consistent with “bright liver” and evident ultrasonographic contrast between hepatic and renal parenchyma

Formal approval was obtained by the Ethics and Scientific Committee of the Radiological and Ultrasound Departments in the major reference hospitals of Khartoum State. The details of the study were explained fully and carefully to participants and their parents, and written informed consent was obtained from the consecutively enrolled participants.

Data were initially summarized into means, standard deviations (SD); mean±SD and percentages in a form of comparison tables and graphs. Statistical analysis was performed using Microsoft Excel Software and the standard Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL, USA) version 15 for windows and P-value was used for significance.

3. Results

NAFLD was detected by ultrasound examination in (55; 15%) participants, while (445; 89%) show normal liver parenchymal echo texture. In this study, the mean age of male participants (47.3±14.7 years) was older than the female participants (43.4±23.5 years), P<0.01. Despite of the studied participants, there were 200; 40% males and 300; 60% females; percentage of 2:3 among cases and aged 15 to 80 years (Table 1). Chronic liver disease other than NAFLD was detected in only a small number of subjects: chronic hepatitis (n=5), sclerosing cholangitis (n=2), adenoma (n=1), granuloma (n=1), and hemangioma (n=2).

Table 1. Characteristics of the study population

Characteristic	All subjects (n=500)	No. of Non fatty liver	No. of NAFLD
Mean age±SD	45.35±19.1	445,89%	55,15%
Gender, n (%)			
Male	200,40%	178,40%	22,40%
Female	300,60%	267,60%	33,60%
Race/ethnicity (Sudanese)			
Center	250,50%	230,51.7%	20,36.4%
North	100,20%	96,21.6%	4,7.3%
South	25,5%	13,2.9%	12,21.8%
East	25,5%	16,3.6%	9,16.4%
West	100,20%	90,20.2%	10,18.2%
BMI (kg/m2), Mean±SD	22.9±2.8	22.2±2.4	26.0±2.4
Waist circumference (cm)	80.15±11.7	74.7±10.3	85.6±13.2

The mean BMI was 22.93±2.82kg/m2. Among them 31.6% had BMI>24 kg/m2, which were considered as overweight, 53.3% had a BMI between 20 to 24 kg/m2; and 15.1% had BMI<20 kg/m2 (Table 1). The mean value of waist circumference was 80.15±11.7cm; 74.7±10.3cm in non fatty liver and 85.6±13.2cm in NAFLD (Table 1).

Table 2. Obesity indices and lipid parameters in males and females

Parameters	Mean value in all cases (n=500)	Mean value in Non NAFLD cases (n=445)	Mean value in NAFLD cases (n=55)
Triglyceride (mg/dL)	88±44	74±36	102±52
Total cholesterol (mg/dL)	157.5±28.8	151.5±26	163.5±31.5
HDL cholesterol (mg/dL)	57.8±11.5	60.5±13.5	55±9.5
Non-HDL cholesterol (mg/dL)	99.5±26.5	91±22	108.5±31
HOMA-IR	1.5±1.4	1.1±0.9	1.9±1.9
ALT (IU/L)	22.5±19.1	15.5±8.1	29.4±30.1

The mean triglyceride was 88±44mg/dL, mean cholesterol 157.5±28.8mg/Dl, HDL cholesterol was 57.8±11.5mg/dL, non-HDL cholesterol was 99.5±26.5mg/dL and HOMA-IR was 1.5±1.4. Among the 55 adults with NAFLD, only (20, 23.3%) showed an abnormality for ALT. However, there was an increasing trend of ALT (29.4±30.1IU/L) abnormality as the severity of NAFLD liver increased (Table 2).

In this survey (55, 15%) patients with NAFLD were detected by ultrasonography. The age, BMI, waist circumference, levels of serum triglyceride and total cholesterol in patients with NAFLD liver were significantly higher than participants without NAFLD (445, 89%) persons. A large proportion of patients with NAFLD (25, 45.5%) are asymptomatic. Typically, NAFLD patients present with fatigue, malaise, and vague right upper quadrant abdominal discomfort (RUQ abdominal discomfort) and hepatomegaly (Table 3).

Table 3. Clinical presentation of NAFLD samples

Clinical presentation of NAFLD	Number of patients (n)	Percentage (%)
Asymptomatic	225	45%
Asymptomatic	275	55%
Fatigue	23	8.4%
Malaise	13	4.7%
RUQ abdominal pain	33	12%
Hepatomegaly	206	74.9%

In the scanned sample, diagnosed NAFLD cases were graded as mild, moderate and severe degree sonographically, where the percentage of NAFLD grades incidence was 56.4% for mild grade and 32.7%, 10.9% for moderate and severe grades respectively (Table 4).

Table 4. NAFLD sonographic grades

NAFLD sonographic grades*	Number of NAFLD patients (n)	Percentage (%)
Mild	31	56.4%
Moderate	18	32.7%
Severe	6	10.9%
Total	55	100%

*Mild NAFLD= Diffuse increase in fine echoes in the hepatic parenchyma with normal visualization of the diaphragm and intra-hepatic vessel borders. Moderate NAFLD= Increase in fine echoes with slightly impaired visualization of the intra-hepatic vessels and diaphragm. Severe NAFLD= Enlarge liver with a marked increase in fine echoes with poor or no visualization of the intra-hepatic vessel borders, diaphragm, and posterior portion of the right lobe of the liver [26].

4. Discussions

The natural history of NAFLD ranges from asymptomatic indolent to end stage liver disease. Diagnosis of NAFLD may involve ultrasonography,

liver biopsy and recognition of the related condition [27]. NAFLD is a common disease of liver without specific clinical features and lack of confirmatory laboratory tests [28, 29]. In patients undergoing liver biopsy, the prevalence of NAFLD ranges between 15% and 39% [30]. This wide range in the prevalence of NAFLD is probably related to differences in the study design. Because patients undergoing liver biopsy were highly selected, these data might not reflect the true prevalence of NAFLD in the general population. Therefore, current best estimates make the prevalence of NAFLD approximately 20% in the general population [30].

In the present study, the prevalence of NAFLD was 4.4% in males and 6.6% in females according to ultrasonic criteria for diagnosis of fatty liver. While it could be argued that in the absence of histology this figure may not reflect the true prevalence of fatty infiltration, previous studies in which ultrasound findings were compared to histological results indicate that the overall sensitivity and specificity of ultrasound examinations for the diagnosis of fatty liver are approximately 80-95% and 90-95% respectively [24, 31, 32].

Of note, the higher ALT, HOMA-IR, cholesterol, triglyceride, and non-HDL cholesterol levels and lower HDL cholesterol as the severity of fatty liver increased indicates that a higher ALT and degree of abnormal lipid levels are predictive of severe NAFLD graded by ultrasound. In addition, the severity of NAFLD is positively associated with how overweight the subject is, in this study as well as others [33, 34]. This indicates that an increased severity of obesity causes more fat to be accumulated in the liver, resulting in more severe NAFLD.

The findings in this study were mostly consistent with other researchers in that elevated ALT is a predictor of NAFLD [13, 34]. In addition, it was found that there was an increasing trend of ALT abnormality as the severity of NAFLD increased. Thus, sonographic examination of the liver would seem to be a good approach to the examination of liver, because it is safe, noninvasive and an easily accessible procedure. Therefore, it is suggested that ultrasonographic examination of the liver be included in the routine health checkups of adults to allow the detection of NAFLD at an early stage. Some limitations of the present study should be mentioned. Firstly, although it is a community based study, the number of females was much higher than males. Therefore, caution needs to be exercised in applying our results to other communities in Sudan. Secondly, this study was of a cross sectional design, which precludes a cause and effect relationship between the associated factors and the development of NAFLD. Therefore additional longitudinal studies comprising of a larger sample with varying degrees of obesity are needed to explore the cause and progression of NAFLD in an adult Sudanese population.

In conclusion, NAFLD is the most common form of adults' hepatic disease. Obesity is a major risk factor and is associated with high rates of NAFLD. It is recommended that ultrasonography of the liver should be included in the routine health examinations of obese adults. The prevalence of NAFLD will continue to increase in concert with the rapidly growing prevalence of obesity and diabetes. Clinicians must be aware of the limitations in the available methods to diagnose NAFLD.

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