ROLE OF ULTRASOUND IN NON-ALCOHOLIC FATTY LIVER DISEASE IN SUDANESE ADULT WOMEN

*Bahaaedin A. Elkhader

Sudan University of Science and Technology, College of Medical Radiological Science, P. O. Box: 1908, Khartoum- Sudan * Author for Correspondence

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 role of ultrasound in diagnosing NAFLD in women in Khartoum- Sudan by an epidemiological survey. A prospective, cross-sectional study was carried out among 300 Sudanese adults' women, aged 15 to 80 years, in between March 2011 to March 2013. Participants underwent ultrasonography examination of the liver. Diagnosis of NAFLD in this study was based on sonographic evidence of a NAFLD. The overall prevalence of NAFLD 11%. NAFLD prevalence differs by race and ethnicity; location in Sudan. The most significant factors associated with the presence of NAFLD were weight category. 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.

Key Words: Non-alcoholic Fatty Liver Disease NAFLD), Liver, Ultrasound

INTRODUCTION

NAFLD is increasing recognized as one of the most important causes of chronic liver disease in Western countries (Mulhall *et al.*, 2002). 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 (Mulhall *et al.*, 2002; Farrell, 2003; Younossi *et al.*, 2002).

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 (Farrell, 2006; Lonardo, 1999). Although generally unprogressive, NAFLD is an important precursor to the development of fibrosis in etiologically diverse conditions such as hepatitis C, and alcoholic and nonalcoholic liver disease (McCullough *et al.*, 1999). 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 (Matteoni, 1999; James and Day, 1999). 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 (Matteoni, 1999; Tominaga *et al.*, 1995; Yano *et al.*, 2001; Powell *et al.*, 1990; Araujo *et al.*, 1988; Bellentani *et al.*, 2000; Mathiesen *et al.*, 1999; El-Hassan *et al.*, 1992). 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 (Bianchi, 2001; Saadeh *et al.*, 2002). 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 (Saadeh *et al.*, 2002; Szezepaniak *et al.*, 1999; Siegelman and Rosen, 2001). Although ultrasound has limitations (Saadeh *et al.*, 2002; Zweiman *et al.*, 2000; Graif *et al.*, 2000), the most recent data, as well as cost considerations (Clark and Diehl ,2003), have made ultrasound the most common imaging modality used

Research Article

for evaluating hepatic steatosis. The primary purpose of this community based study was to determine the role of ultrasound in diagnosing NAFLD in a specific population; adults women in Khartoum- Sudan.

MATERIALS 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 300 adults women 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.

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 (Joseph *et al.*, 1991; Lonardo *et al.*, 1997). 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 (Needleman *et al.*, 1986). The diagnosis of NAFLD in this study was based on sonographic evidence of a fatty liver. None of the participants had a history of alcohol consumption and liver disease, hypertension or diabetes.

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 \pm 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.

RESULTS AND DISCUSSION

Results

NAFLD was detected by ultrasound examination in (33; 11%) participants, while (267; 89%) show normal liver parenchymal echo texture. In this study, the mean age of female participants $(43.4\pm23.5\text{years})$, aged 15 to 80 years (Table 1).

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

Research Article

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).

		No. of Non fatty	
Characteristic	All subjects (n=300)	liver	No. of NAFLD
Mean age±SD	43.4±23.5		
		267,89%	33, 11%
Race/ethnicity			
(Sudanese)			
Center	150, 50%	138, 51.7%	12, 36.4%
North	60, 20%	58, 21.7%	2,6%
South	15, 5%	8, 3%	7, 21.2%
East	15, 5%	9, 3.4%	6, 18.2%
West	60, 20%	54, 20.2%	6, 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

Table 1: Characteristics of the study population

In this survey (33, 11%) patients with NAFLD were detected by ultrasonography. The age, BMI, waist circumference in patients with NAFLD liver was significantly higher than participants without NAFLD (267, 89%) persons. Typically, NAFLD patients present with fatigue, malaise, and vague right upper quadrant abdominal discomfort (RUQ abdominal discomfort) and hepatomegaly (Table 2).

Tuble 2. Onlicut presentation of 1 (11 12 Sumples			
Clinical presentation of NAFLD	Number of patients (n)	Percentage (%)	
Asymptomatic	135	45%	
A symptomatic	165	55%	
Fatigue	14	8.00%	
Malaise	8	5.00%	
RUQ abdominal pain	20	12%	
Hepatomegaly	123	75.00%	

Table 2: Clinical presentation of NAFLD samples

In the scanned sample, diagnosed NAFLD cases were graded as mild, moderate and severe degree sonographically, where the percentage of NAFLD grades incidence was 57.6% for mild grade and 33.3%, 9.1% for moderate and severe grades respectively (Table 3).

Table 5. WATED sonographic grades				
NAFLD sonographic grades	Number of NAFLD patients (n)	Percentage (%)		
Mild	19	57.60%		
Moderate	11	33.30%		
Severe	3	9.10%		
Total	33	100%		

Table 3: NAFLD sonographic grades

Research Article

Discussion

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 (Brunt, 2001). NAFLD is a common disease of liver without specific clinical features and lack of confirmatory laboratory tests (Skelly *et al.*, 2001; Skelly *et al.*, 2001). This wide range in the prevalence of NAFLD is probably related to differences in the study design. Therefore, current best estimates make the prevalence of NAFLD approximately 20% in the general population (Falck *et al.*, 2001).

In the present study, the prevalence of NAFLD was 11% 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 (Joseph *et al.*, 1991; Layer *et al.*, 1999; Mendler *et al.*, 1998).

In addition, the severity of NAFLD is positively associated with how overweight the subject is, in this study as well as others (Hsiao *et al.*, 2004; Chan *et al.*, 2004). This indicates that an increased severity of obesity causes more fat to be accumulated in the liver, resulting in more severe NAFLD. 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. 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 women.

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.

REFERENCES

Araujo LM, De Oliveira DA and Nunes DS (1998). Liver and biliary ultrasonography in diabetic and non-diabetic obese women. *Diabetes & Metabolism* 24 458-462.

Bellentani S, Saccoccio G, Masutti F, Croce LS, Brandi G, Sasso F, Cristanini G and Tiribelli C (2000). Prevalence of and risk factors for hepatic steatosis in Northern Italy. *Annals of Internal Medicine* 132 112-117.

Bianchi L (2001). Liver biopsy in elevated liver function tests? An old question revisited. *Journal of Hepatology* 35 290-294.

Brunt EM (2001). Nonalcoholic steatohepatitis: definition and pathology. *Seminars in Liver Disease* 21 3-16.

Chan DF, Li AM, Chu WC, Chan MH, Wong EM and Liu EK (2004). Hepatic steatosis in obese Chinese children. *International Journal of Obesity and Related Metabolic Disorders* 28 1257-1263.

Clark JM and Diehl AM (2003). Defining nonalcoholic fatty liver disease: implications for epidemiologic studies. *Gastroenterology* 24 248-250.

El-Hassan AY, Ibrahim EM, al-Mulhim FA, Nabhan AA and Chammas MY (1992). Fatty infiltration of the liver: analysis of prevalence, radiological and clinical features and influence on patient management. *British Journal of Radiology* **65** 774-778.

Falck-Ytter Y, Younossi ZM, Marchesini G and McCullough AJ (2001). Clinical features and natural history of nonalcoholic steatosis syndromes. *Seminars in Liver Disease* 21 17-26.

Research Article

Farrell GC and Larter CZ (2006). Nonalcoholic fatty liver disease: from steatosis to cirrhosis. *Hepatology* 43 S99-S112.

Farrell GC (2003). Non-alcoholic steatohepatitis: what is it, and why is it important in the Asia-Pacific region? *Journal of Gastroenterology and Hepatology* **18** 124-138.

Graif M, Yanuka M and Baraz M (2000). Quantitative estimation of attenuation in ultrasound video disease. *Investigative Radiology* **35** 319-324.

Havel RJ (1994). Postprandial hyperlipidemia and remnant lipoproteins. *Current Opinion in Lipidology* 5 102-109.

Hsiao TJ, Chen JC and Wang JD (2004). Insulin resistance and ferritin as major determinants of nonalcoholic fatty liver disease in apparently healthy obese patients. *International Journal of Obesity and Related Metabolic Disorders* 28 167-172.

James O and Day C (1999). Non-alcoholic steatohepatitis: another disease of affluence. *Lancet* 353 1634-1636.

Joseph AE, Saverymuttu SH, al-Sam S, Cook MG and Maxwell JD (1991). Comparison of liver histology with ultrasonography in assessing diffuse parenchymal liver disease. *Clinical Radiology* **43** 26-31.

Layer G, Zuna I, Lorenz A, Zerban H, Haberkorn U, Bannasch P, van Kaick G and Rath U (1999). Computerized ultrasound B-scan texture analysis of experimental diffuse parenchymal liver disease: Correlation with histopathology and tissue composition. *Journal of Clinical Ultrasound* **19** 193-201.

Lonardo A, Bellini M, Tartoni P and Tondelli E (1997). The bright liver syndrome. Prevalence and determinants of a "bright" liver echopattern. *Italian Journal of Gastroenterology and Hepatology* 29 351-356.

Lonardo A (1999). Fatty liver and nonalcoholic steatohepatitis. Where do we stand and where are we going? *Digestive Diseases and Sciences* 17 80-89.

Mathiesen UL, Franzen LE, Fryden A, Foberg U and Bodemar G (1999). The clinical significance of slightly to moderately increased liver transaminase values in asymptomatic patients. *Scandinavian Journal of Gastroenterology* **34** 85-91.

Matteoni CA, Younossi ZM, Gramlich T, Boparai N, Liu YC and McCullough AJ (1999). Nonalcoholic fatty liver disease: a spectrum of clinical and pathological severity. *Gastroenterology* **116** 1413-1419.

McCullough AJ and Falck-Ytter Y (1999). Body composition and hepatic steatosis as precursors for fibrotic liver disease. *Hepatology* **29** 1328-1330.

Mendler MH, Bouillet P, LeSidaner A, Lavoine E, Labrousse F, Sautereau D and Pillegand B (1998). Dual-energy CT in the diagnosis and quantification of fatty liver: Limited clinical value in comparison to ultrasound scan and single-energy CT, with special reference to iron overload. *Journal of Hepatology* 28 785-794.

Mulhall BP, Ong JP and Younossi ZM (2002). Non-alcoholic fatty liver disease: an overview. *Journal of Gastroenterology and Hepatology* 17 1136-1143.

Needleman L, Kurtz AB, Rifkin MD, Cooper HS, Pasto ME and Goldberg BB (1986). Sonography of diffuse benign liver disease: accuracy of pattern recognition and grading. *AJR American Journal of Roentgenology* **146** 1011-1015.

Powell EE, Cooksley WG, Hanson R, Searle J, Halliday JW and Powell LW (1990). The natural history of nonalcoholic steatohepatitis: a follow-up study of forty-two patients for up to 21 years. *Hepatology* **11** 74-80.

Reid AE (2001). Nonalcoholic steatohepatitis. Gastroenterology 121 710-723.

Saadeh S, Younossi ZM, Remer EM, Gramlich T, Ong JP and Hurley M (2002). The utility of radiological imaging in nonalcoholic fatty liver disease. *Gastroenterology* **123** 745-750.

Siegelman ES and Rosen MA (2001). Imaging of hepatic steatosis. Seminars in Liver Disease 21 71-80.

Research Article

Skelly MM, James PD and Ryder SD (2001). Findings on liver biopsy to investigate abnormal liver function tests in the absence of diagnostic serology. *Journal of Hepatology* **35** 195-199.

Szezepaniak LS, Babcock EE, Schick F, Dobbins RL, Garg A and Burns DK (1999). Measurement of intracellular triglyceride stores by 1h spectroscopy: validation in vivo. *American Journal of Physiology* **276** E977- E989.

Tominaga K, Kurata JH, Chen YK, Fujimoto E, Miyagawa S, Abe I and Kusano Y (1995). Prevalence of fatty obesity. An epidemiological ultrasonographic survey, *Digestive Diseases and Sciences* **40** 2002-2009.

Yano E, Tagawa K, Yamaoka K and Mori M (2001). Test validity of periodic liver function tests in a population of Japanese male bank employees. *Journal of Clinical Epidemiology* **54** 945-951.

Younossi ZM, Diehl AM and Ong JP (2002). Nonalcoholic fatty liver diseases: an agenda for clinical research. *Hepatology* 35 746-752.

Zweiman B, Parrott CM, Graif Y, David M and Lessin SR (2000). Quantitative estimation of attenuation in ultrasound video images: correlation with histology in diffuse liver disease. *Investigative Radiology* **319** 24-35.