Original Article

Correlating The Diagnostic Accuracy of Radiological Imaging and Histological Findings in the Diagnosis of Non-Alcoholic Fatty Liver Disease(NAFLD) Among Patients in a Tertiary Hospital

***Emanghe U[1], Ekpe Edemekong L[2], Ekpe EL[3], Obiora IC[4], Emin EJ[5], Ogban GI[1], Itam Y[6], Akinmola OO[7]**

[1] *Department of Medical Microbiology and Parasitology University of Calabar, Calabar Nigeria.*
[2] *Department of Mass Communication University Of Calabar, Calabar Nigeria*
[3] *Department of Chemical Pathology and Immunology University Of Calabar, Calabar Nigeria*
[4] *Department of Radiology University Of Calabar Teaching Hospital Calaber, Calabar Nigeria*
[5] *Department. of Chemical Pathology University of Calabar Teaching Hospital, Calabar, Calabar Nigeria*
[6] *Department. Of Biochemistry University Of Calabar Calabar, Calabar Nigeria*
[7] *Department of Clinical Pathology, Lagos University Teaching Hospital Lagos, Calabar Nigeria.*

Article History
Submitted: 27/07/2024; Accepted: 31/07/2024: Published: 22/08/2024

***Correspondence:** Ekpe E.L.
Email: lawsonekpe2002@yahoo.com

ABSTRACT

This study aimed to evaluate the diagnostic accuracy of ultrasound in diagnosing non-alcoholic fatty liver diseases (NAFLD) compared to biopsy. In this study, participants were recruited patients with fatty liver who underwent liver biopsy and baseline ultrasound at the University of Calabar Teaching Hospital between January 2023 and December 2023. Ultrasonographic findings were correlated with the histological findings of liver biopsy which was considered as the gold standard for the diagnosis of NAFLD. A total of 109 subjects were recruited and participated in this study. This comprised 62(56.9%) females and 47(43.1%) males with the highest age bracket presenting at 56-65 years. The mean age of the study participants was 55.5±12.8years (age range was 18-70 years). The female-to-male ratio was 1:1.4. The ultrasonographic findings were correlated with histological data (considered as the gold standard). The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were evaluated. The ultrasonography had a sensitivity of 90.4% (95% confidence interval:83.6-93.6), and specificity of 72.5% (95% confidence interval 68.7-79.8). The PPV and NPV were 74.7% and 65.6% respectively. The area under the curve was 84.5%. The positive likelihood ratio was 1.5(95CI :1.21-1.90), and negative likelihood ratio was 0.30(0.17-0.54).Ultrasound findings are highly significant and useful in detecting advanced steatosis in patients with fatty liver. In the future, as technology advances, it is hoped that the need for liver biopsy may not be necessary as hi-tech radiological involvement may help patients with fatty liver without participation in any invasive procedure.

Keywords: Biopsy, Calabar, Fatty liver, Radiological, Steatosis, Ultrasound.

INTRODUCTION

The most common cause of chronic liver disease is non-alcoholic fatty liver disease (NAFLD), which is considered to have a global prevalence of 25%[1,2]. It is an emerging non-communicable disease (NCD)[3].

The World Health Organization (WHO) statistics have it that the mortality rate accounted for by non-communicable diseases (NCD) is 41 million (74%) of all deaths globally (WHO, 2019)[4]. Seventy-seven percent (77%) of these deaths occur in low-and middle-income countries[4]. To lessen the impact and burden of NCD, early screening, detection, and early intervention are life-saving modalities.

Non-Alcoholic Fatty Liver Disease (NAFLD) is one of the common NCDs known for its terminal sequelae, which could be life-threatening. As the name implies, NAFLD is defined as a condition

Article Access
Website: www.wjmbs.org
10.5281/zenodo.13381751

How to cite this article
**Emanghe U, Ekpe Edemekong L, Ekpe EL, Obiora IC, Emin EJ, Ogban GI, Itam Y, Akinmola OO. Correlating The Diagnostic Accuracy of Radiological Imaging and Histological Findings in the Diagnosis of Non-Alcoholic Fatty Liver Disease(NAFLD) Among Patients in a Tertiary Hospital. West J Med & Biomed Sci. 2024;5(3):122-128. DOI:10.5281/zenodo.13381751.*

characterized by the presence of hepatic steatosis, not caused by alcohol intake (Bhatt and Smith, 2015)[5]. It is one of the most common causes of chronic liver diseases and may progress to liver cirrhosis and other associated complications if prompt attention is not given to patients on time.[6,7] When examined histologically e.g., in a liver biopsy, excess accumulation of lipids (predominantly triglycerides) is usually evident within the hepatocytes.[7] In some cases, NAFLD may progress from steatosis to steatohepatitis (with evidence of inflammation and cell injury), cirrhosis (hepatic fibrosis), and ultimately, liver failure. The diagnosis of NAFLD is mainly derived from excluding alcohol-related hepato-pathology.[6]

Liver biopsy remains the gold standard for the accurate diagnosis of hepatic steatosis, however, this has its drawbacks.[9] Liver biopsy has two advantages of accurate diagnosis and its further ability to differentiate non-alcoholic steatohepatitis (NASH) from simple hepatic steatosis. Usually, liver biopsy liver for histological diagnosis of fatty liver is graded into different types. However, liver biopsy is observer-dependent and invasive, conveying a non-negligible risk of significant morbidity and mortality among other serious medical complications. The relatively small core size of the biopsy also introduces sampling errors, especially as steatosis is known to be heterogeneous. These limitations make liver biopsy a suboptimal tool for screening, monitoring, and research. For this reason, imaging can be seen as an alternative to liver biopsy in the diagnosis and optimal management of patients with NAFLD. Basic and available conventional techniques for evaluating steatosis include ultrasound, computed tomography (CT) magnetic resonance (MR) spectroscopy, and magnetic resonance imaging (MRI). This present research aims to assess and outline the performance and clinical utility of ultrasound scans with histological findings of patients with NAFLD presenting at the University of Calabar Teaching Hospital. Imaging and related non-imaging techniques can also be used to accurately assess the important disease markers of liver steatosis and advanced liver fibrosis which are being studied globally to assess their usefulness in the diagnosis and management of these disease conditions. The primary objective of this study is to explore adults with biopsy-proven NAFLD, the diagnostic performance, and reliability in comparison with abdominal USS for predicting histology-determined NAFLD using histologic grade as the reference standard. This study is relevant as there is limited data available on the comparative assessment of NAFLD using histology and radiological approaches in our environment. Furthermore, studies done in this regard have been on Caucasians with little or no emphasis on blacks. Based on these, there is a need for clinicians to formulate measures to help curb the impact of NAFLD among persons at risk by initiating a local study in this regard.

This research assesses the correlation between NAFLD patients diagnosed by ultrasound at the University of Calabar Teaching Hospital (UCTH) and compared with those diagnosed by histology.

MATERIALS AND METHODS

This study was cross-sectional, with an analytical component. The study was done in the Radiology and Pathology departments of the University of Calabar Teaching Hospital from January 2023 to December 2023. Every recruited subject who presented for this study had a liver biopsy done for histology, to assess those that had accurate diagnosis of fatty liver. Histological diagnosis of the fatty liver following liver biopsy is considered the gold standard for diagnosis of fatty liver. Patients with absent liver biopsy results were excluded. Furthermore, patients with jaundice, ascites, and altered blood profiles were also excluded or if the biopsy was performed for focal lesions or autoimmune liver disease. All patients sent to the radiology department of UCTH for ultrasound-guided liver biopsy were included. The nature and purpose of the study, in simple terms, were first explained to each recruited patient by the researcher or her assistant and informed consent was given. Then, relevant socio-demographic data and relevant clinical information from a semi-structured questionnaire were filled in by the researcher or research assistants to get relevant information. The participants then had a complete physical

examination. Data was collected using an administered questionnaire distributed to participants in this study to obtain demographic data, duration of illness (diabetes mellitus /NAFLD), treatment details, and other information to be analyzed. Patients' confidentiality was maintained and held in high esteem.

Sample Size

A total of 109 willing participants were recruited for this study.

Liver Biopsy and Histological examination

Each patient for this study had a liver biopsy done to make a diagnosis of fatty liver based on histology. The liver biopsy was performed under ultrasound guidance by an experienced consultant radiologist, and the findings were interpreted by a hepato-pathologist who was oblivious to the clinical history and presentation of the patient. Non-targeted percutaneous biopsies of the right liver lobe were performed for clinical care using a 16- or 18-gauge needle by hepatologists. Although biopsies were performed for clinical care, histology slides subsequently were reviewed by an expert hepato-pathologist for this research. A consultant pathologist carried out the histological examination of all liver biopsies suspected to have fatty liver. Blinded to clinical and radiologic data, this hepato-pathologist scored steatosis at low-to-medium power using a 4-point ordinal score, as defined by the Nonalcoholic Steatohepatitis Clinical Research Network scoring system our study included only patients with biopsy-proven NAFLD, only three steatosis grades (1, 2, and 3) were observed in the study cohort.

Imaging

Patients were asked to fast for a minimum of 4 hours before imaging. Ultrasound examinations were performed on the same day if possible. The same patients who had liver biopsies were made to have an abdominal ultrasound to assess for the presence of fatty liver based on imagining. The essence was to correlate the imaging findings and diagnoses with the histological diagnoses. Though liver biopsy is the gold standard for making a diagnosis of fatty liver, however, because of its associated complications and high cost, it is a lot easier and cheaper to consider radio-imaging for the same diagnostic purpose. An ultrasound scan was performed by an experienced radiologist, using a 3.5MHz probe Siemens G60S scanning machine, who looked for radiological evidence of hepatic steatosis in each recruited participant. This was further confirmed by yet another consultant radiologist to ensure certainty of diagnosis. with a curved vector array transducer. This transducer has a nominal frequency range of 1–4.5 MHz(in this case 3.5Hz). Scanning was done with the patient in the dorsal decubitus position with the right arm at maximum abduction. The transducer was placed at 90° to the liver capsule through the right inter-costal approach. The ultrasound beam scattering by fat droplets in steatosis caused more echo signals to return to the transducer, creating the appearance of a “bright” or hyperechoic liver. Furthermore, fat also attenuates the beam which decreases beam penetration into tissue. This attenuation leads to poor visualization of structures within the steatotic liver parenchyma—such as intrahepatic vessels, bile ducts, and in some cases liver lesions and of structures deep to the liver, such as the diaphragm. Thus, the presence of steatosis can be inferred if the liver is too bright and/or if liver structures are blurry or poorly visualized radiologically.

Ethical Approval

Ethical approval was obtained from the Health Research Ethics Committee (HREC) of the University of Calabar Teaching Hospital (with NHREC/07/10/2012 as UCTH HREC Registration number and UCTH/HREC/33/Vol.111/123 as the HREC protocol assigned number) before carrying out the study. The study was carried out without coercion of participants and a signed informed consent was obtained from caregivers including adults aged 18-70 years after duly explaining the purpose of the study in simple and clearly understood language and obtaining consent.

Sample Analysis

Data was entered and analyzed using SPSS version 20(Chicago, USA). Quantitative variables like age, height, and BMI had mean and standard deviation

calculated. Also, sensitivity specificity, PPV, and NPV were noted in the ability of the abdominal USS to pick fatty liver whose diagnosis was already made on histology, which is considered the gold standard.

RESULTS

A total of 109 participants were recruited and participated in this study. This was made of 62(56.9%) females and 47(43.1%) males with the highest age bracket presenting at 56-65 years. The mean age of the study participants was 55.5±12.8 years (age range was 18-70 years). The female-to-male ratio was 1:1.4. The ultrasonographic findings were correlated with histological data (considered as the gold standard). The sensitivity, specificity, positive predictive value, and negative predictive value were evaluated. The ultrasonography had a sensitivity of 85.4%((95% confidence interval:83.6-93.6), specificity of 72.5% (95% confidence interval 68.7-79.8).The PPV and NPV were 74.7% and 65.6% respectively (see Figure 1). The area under the curve was 85.4%. The positive likelihood ratio was 1.5(95CI :1.21-1.90), and negative likelihood ratio was 0.30(0.17-0.54).

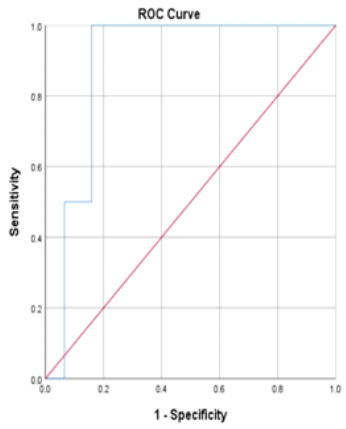

Figure. 1:Receiver operatingcharacteristic (ROC) curve for ultrasonography

DISCUSSION

This study highlights the high sensitivity of ultrasonography in the diagnosis of nonalcoholic fatty liver diseases when compared with histology. Nonalcoholic fatty liver disease (NAFLD) is the most common cause of chronic liver disease in Western countries[5]. Many studies have proven that it has a high prevalence ranging from 20% to 40%[2,10,11]. It encompasses a histological spectrum that ranges from simple steatosis to steatohepatitis, which can progress to cirrhosis in up to 20% of patients. The diagnosis of fatty liver is usually a diagnosis of exclusion.NAFLD is diagnosed by the presence of steatosis in ≥5% of the hepatocytes in the absence of other liver diseases. Other causes of hepatic steatosis, systemic diseases, pancreatic diseases, effects of drugs, congenital abnormalities, and iatrogenic causes have to be ruled out[12,13,14]. The diagnosis of NAFLD is confirmed by the presence of hepatic steatosis seen on abdominal ultrasound assessment and the exclusion of significant alcohol (defined as alcohol intake less than 30g/day in men and less than 20g/day in women ingestion in susceptible patients and the presence of hepatic steatosis on ultrasound evaluation[15]. Liver biopsy is also the hallmark for assessing the severity of the NAFLD. Grades of fatty liver severity can be assessed by liver biopsy under histological examination. However, radiological findings are unable to express features that suggest similar diagnosis with high sensitivity as evidenced in this and other resraches[16]

Sadly, accurate non-invasive modalities for diagnosing non-alcoholic steatohepatitis (NASH) and monitoring disease progression or regression are rare to come by. This has placed liver biopsy to remain the gold standard in diagnosing NAFLD. This procedure is not without associated risks and sampling errors. Since liver biopsy cannot be performed as a screening method to detect NAFLD in the general population, abdominal ultrasonography as a noninvasive modality has been widely used. Abdominal ultrasonography has been shown to have a sensitivity of 60%-94% and specificity of 84%-95% for detecting fatty liver. This study obtained a high sensitivity of 85.4%. This tallies with the works of other researchers who had a sensitivity value of 92% and 100% specificity[17,18,19]. High diagnostic accuracy in correlating ultrasonography with histology has been obtained from various other studies[20,21,22]. The inability of ultrasonography to distinguish different forms of NAFLD and staging hepatic fibrosis limits the use of ultrasonography as a stand-alone investigation for detecting NAFLD.[23,24]

Although liver biopsy remains the gold standard for diagnosis, its limitations have already been stressed necessitating the use of imaging modalities. However, a major limitation of radiological diagnosis is the inability to distinguish between simple steatosis and steatohepatitis. In the future, serum markers together with advancements in imaging modalities may potentially diminish or obviate the need for liver biopsy. It is hoped that the best diagnostic approach for patients with NAFLD may be abdominal USS and potentially replace the necessity for liver biopsy in most patients.

Currently, methods of nonalcoholic fatty liver diagnosis include well-established techniques, such as conventional ultrasonography, computed tomography, and magnetic resonance imaging. Findings in NAFLD patients with these techniques are based on the accumulation of lipids in hepatic cells. Newer imaging technologies, such as ultrasound elastography, quantitative ultrasound techniques, magnetic resonance elastography, and magnetic resonance-based fat quantitation techniques are being explored as they have higher sensitivity[25,26]

Imaging studies of the liver has several advantages over liver biopsy in the evaluation of NAFLD. Apart from being a non-invasive, imaging has the dual advantage of evaluating of a greater volume of liver parenchyma than biopsy, which reduces sampling error in heterogeneously distributed diffuse liver disease processes; and less variability and more quantitative than histopathologic liver biopsy specimen evaluation.[27]

However, despite the several advantages of ultrasonography, certain limitations of conventional ultrasonography, for fatty liver evaluation include the fact that it is qualitative and therefore subjective to individual opinion. The value of conventional US to evaluate fatty liver is limited by the subjective nature of the criteria used to differentiate fatty from normal liver and a lack of sonographic criteria for different degrees of steatosis. The sensitivity is limited when there are few steatotic hepatocytes[28].Furthermore, the sensitivity and specificity of B mode sonography decreases as body mass index (BMI) increases, varying between 49%-100% and 75%-95%[29]; and finally, conventional sonography cannot differentiate steatosis and steatohepatitis or stage fibrosis[30,31]

We are therefore of the opinion that ultrasonography is an important non-invasive tool in the assessment of NAFLD. Normal or grade 1 hepatic echogenicity can soundly exclude histological NAFLD and obviate the need for liver biopsy.

CONCLUSION

Using ultrasonography of the liver to assess for NAFLD has high diagnostic accuracy as a valuable diagnostic tool in resource-poor environments. It can make a correct diagnosis easier for patients to have earlier attention from managing physicians thereby cutting off the anticipated delay usually occasioned by tissue processing demands from biopsy for histology.

Recommendations

Ultrasound performs best at qualifying liver steatosis when there are no other associated liver diseases; however, it remains relatively insensitive to the detection of fatty liver at the early stage of fatty liver. Despite its many limitations, it may be reasonable to use ultrasound in the appropriate clinical setting as an initial screen for steatosis, though it is not suitable for clinical trials.

REFERENCES

1. Browning, J. D., Szczepaniak, L. S., Dobbins, R., Nuremberg, P., Horton, J. D. Prevalence of hepatic steatosis in an urban population in the United States-impact of ethnicity. Hepatology 2004; 40:1387-1395.
2. Younossi, M., Koenig, A. B., Abdelalif, D., Fazel, Y., Henry, L. & Wymer, M. Global epidemiology of non-alcoholic fatty liver disease-a meta-analytic assessment of prevalence, incidence, and outcome. Hepatology 2016; 64:73-84.
3. Pouwel, S., Sakran, N., Graham, Y., Leal, A., Pinter, T., Kassir, R. Non-alcohol Fatty Liver Disease (NAFLD): A review of Pathophysiology, Clinical Management and Effects of Weight Loss. BMC Endocrine Disorders2022;22:63.

4. WHO STEPS Surveillance Manual, Part 3, Data Collection, Section 5: Collecting Step 2 Data: Physical measurements (online) Available: http://www.cdn.who.int/media/docs/default-source/ncd-surveillance/steps/part3-section5.pdf?sfvn=a46653c72.[Accessed28April2023]

5. Bhatt, H. B., Smith, R. J. Fatty Liver Disease in Diabetes. Hepatobiliary Surgery and Nutrition 2015;4(2):101 – 108.

6. Takashi Y., Fukusato T. Histopathology of non-alcoholic Fatty Liver Disease Steatohepatitis. World Journal of Gastroenterology 2014;120(42):15539 – 15548.

7. Marusic, M., Paic, M., Knobloch, M., Ana-Marija, L. P. NAFLD, Insulin Resistance, and type 2 diabetes mellitus. Canadian Journal of Gastroenterology and Hepatology 2021: e6613827.

8. Zhang, J. Z., Cai, J. J., Tu, Y., She, Z. G., Li, H. Non-Alcoholic Fatty Liver Disease: An update on the diagnosis. Gene 2019;19(3):187– 198.

9. Sumida Y, Nakajima A, Itoh Y. Limitations of liver biopsy and non-invasive diagnostic tests for the diagnosis of nonalcoholic fatty liver disease/nonalcoholic steatohepatitis.World J Gastroenterol. 2014;20(2):475-85.

10. Goyal A, Arora H, Arora S. Prevalence of fatty liver in metabolic syndrome. J Family Med Prim Care. 2020;9(7):3246-3250.

11. Teng ML, Ng CH, Huang DQ, Chan KE, Tan DJ, Lim WH. Global incidence and prevalence of nonalcoholic fatty liver disease. Clin Mol Hepatol.2023;29(Suppl): S32-S42.

12. Vernon, G., Baranova, A., Younossi, Z. M. Systematic review: the epidemiology and natural history of non-alcoholic fatty liver disease and non-alcoholic steatohepatitis. Alimentary and Pharmacological Therapy 2011; 34:274-285.

13. Liebe R, Esposito I, Boak H, Dahl S, Stindt J. Diagnosis and management of secondary causes of steatohepatitis. Journal of Hepatology 2021;74(6):1455-1471

14. Patel V, Sanyal AJ. Drug-induced steato-hepatititis. *Clin.Liver Diseases* 2013;17(4):533-7

15. Nassir F, Rector RS,Hammoud GM, Ibdam JA.Pathogenesis and prevention of hepatic steatosis.Gastroenterol Hepatol 2015;11(3):167-175

16. Obika M, Noguchi H. Diagnosis and evaluation of nonalcoholic fatty liver disease. Exp Diabetes Res. 2012; 1:145754.

17. Yen-Ying Chen, Matthew M. Yeh.Non-alcoholic fatty liver disease: A review with clinical and pathological correlation. J. of the Formosan Medical Association 2021;120(1):68-77.

18. Jang JK, Choi SH, Lee JS, Kim SY, Lee SS, Kim KW. Accuracy of the ultrasoundattenuation coefficient for the evaluationof hepatic steatosis: a systematic reviewand meta-analysis of prospective studies. Ultrasonography. 2022;41(1):83-92.

19. Noninvasive biomarkers in non-alcoholic fatty liver disease: current status and a glimpse of the future. World J Gastroenterol. 20:10851–10863.

20. Jang JK, Choi SH, Lee JS, Kim SY, Lee SS, Kim KW. Accuracy of the ultrasoundattenuation coefficient for the evaluationof hepatic steatosis: a systematic reviewand meta-analysis of prospective studies. Ultrasonography. 2022;41(1):83-92.

22. Hernaez R, Lazo M, Bonekamp S, Kamel I, Brancati FL, Guallar E, Clark JM. Diagnostic accuracy and reliability of ultrasonography for detecting fatty liver: a meta-analysis. Hepatology.2011;54(3):1082-1090.

23. Paul, J. Recent advances in non-invasive diagnosis and medical management of non-alcoholic fatty liver disease in adults. *Egypt* Liver Journal 2020;10: 37

24. Baisakh P, Baisakh MR, Kumari BS, Mohanty BB, Panda DK, Pradhan S. Diagnostic accuracy of ultrasonography-guided fine needle aspiration cytology in abdominopelvic masses:

a prospective study. Cureus. 2023;15(6):e41228.

25. Ahmed M, Diggory T. The correlation between ultrasonography and histology in the gallstone search. *Ann R Coll Surg Engl.* 2011;93(1):81-3.

26. Petzold G. Role of Ultrasound Methods for the Assessment of NAFLD. J Clin Med.2022;11(15):4581.

27. Gomercić M, Duvnjak M, Barsić N. Ultrasonography in the diagnosis of nonalcoholic fatty liver disease. Acta Med Croatica. 2009;63 (Suppl 3):1-3.

28. Li Q, Dhyani M, Grajo JR, Sirlin C, Samir AE. Current status of imaging in nonalcoholic fatty liver disease. World J Hepatol. 2018;10(8):530-542.

29. Fargion S, Porzio M, Fracanzani AL. Nonalcoholic fatty liver disease and vascular disease: state-of-the-art. World J Gastroenterol. 014; 20:13306–13324.

30. Marzuillo P, Grandone A, Perrone L, Miraglia Del Giudice E. Controversy in the diagnosis of pediatric non-alcoholic fatty liver disease. World J Gastroenterol.2015*;*21:6444–6450.

31. Shannon A, Alkhouri N, Carter-Kent C, Monti L, Devito R, Lopez R. Ultrasonographic quantitative estimation of hepatic steatosis in children With NAFLD. J Pediatr Gastroenterol Nutr. 2015;53:190–195.

32. Fitzpatrick E, Dhawan A. Noninvasive biomarkers in non-alcoholic fatty liver disease: current status and a glimpse of the future. *World J Gastroenterol.* 2014;20:10851–10863

33. Charatcharoenwitthaya P, Lindor KD. Role of radiologic modalities in the management of non-alcoholic steatohepatitis. Clin Liver Dis. 2007;11:37–54

34. Barr RG, Ferraioli G, Palmeri ML, Goodman ZD, Garcia-Tsao G, Rubin J. Elastography Assessment of Liver Fibrosis: Society of Radiologists in Ultrasound Consensus Conference Statement. Ultrasound Q. 2016;32:94–107.