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Original Article

Diagnostic Accuracy of Non-Invasive Hepatic Ultrasound Score for Non-Alcoholic Fatty Liver Disease Keeping Computed Tomography as a Gold Standard

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ABSTRACT

Objective: To determine the diagnostic accuracy of non-invasive hepatic ultrasound score for the diagnosis of non-alcoholic fatty liver disease (NAFLD) by keeping computed tomography. (CT) as the gold standard.

Study Design: Cross-sectional study.

Place and Duration of Study: Armed Forces Institute of Radiology and Imaging Rawalpindi from Dec 2017 to May 2018.

Methodology: All patients from any ethnicity and gender with more than 18 and less than 60 years of age were considered for the study. Hepatic ultrasound score based on the anteroposterior diameter of the right lobe of the liver, deep beam attenuation was calculated, and results were compared with CT scan findings.

Results: A total of 101 patients were included. A total of 69 patients had a total Ultrasound score of 2 or more, fulfilling the study's criteria to be labelled as Non-Alcoholic Fatty Liver Disease. On a CT scan, 71 patients fulfilled the criteria to be labelled as having Non-Alcoholic Fatty Liver Disease. Keeping the Computed Tomography scan gold standard, 59 patients were true positive, and 10 were false positive. The sensitivity and specificity of this score were 83.09 % and 66.67%, respectively. The hepatic ultrasound score had a Positive Predictive Value of 85.50% and a Negative Predictive Value of 62.5%.

Conclusion: Ultrasound score based on hepatic attenuation and the anteroposterior diameter of the right hepatic lobe is a reliable, reproducible and accurate tool for diagnosing Non-Alcoholic Fatty Liver Disease.

Keywords: Hepatic attenuation index, Hepatic steatosis, Non-alcoholic fatty liver disease, Ultrasound liver.

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INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is defined by the presence of 10% fat in the liver parenchyma. This condition incorporates a spectrum of diseases ranging from mild fatty infiltration of liver parenchyma to decompensated liver cirrhosis. The pathological features resemble alcohol-induced liver injury, but it is a disease of patients who do not abuse alcohol. NAFLD is the most common type of chronic liver disease. Its prevalence varies between 20% and 50% in the developed world. Risk factors for developing NAFLD include obesity, diabetes, hypertension and dyslipidemia. NAFLD is now regarded as the hepatic manifestation of metabolic syndrome.[1] In Pakistan, NAFLD affects around 15% of the general population, and its prevalence is increasing in Pakistan and worldwide.[2] NAFLD is an increasingly recognized cause of liver cirrhosis and even hepatocellular carcinoma in Pakistani.[3] Liver biopsy is the gold standard test for diagnosing and staging NAFLD. However, this diagnostic modality is limited by its invasive nature, associated adverse events, cost and sampling error. It is also pertinent to mention that liver biopsy is not always readily available at all hospitals. An increase in the anteroposterior diameter of the right hepatic lobe is associated with hepatic steatosis. Non-invasive methods for diagnosis of NAFLD include ultrasonography, Computed Tomography (CT) scan and Magnetic Resonance Imaging (MRI).

Conventional B-mode ultrasonography is the most common non-invasive method for screening asymptomatic patients with suspected NAFLD. The most common method of detecting and grading fatty infiltration of the liver is by comparing the echogenicity of the liver with the surrounding structures and normal or impaired visualization of the diaphragm or intrahepatic vessels. Abdominal ultrasonography is a relatively inexpensive, easily available, reproducible and moderately sensitive imaging modality to diagnose fatty liver. Nevertheless, it has low specificity and sensitivity if the liver parenchyma contains 30% or less fat. It is also associated with operator bias. The degree of hepatic steatosis is determined by Unenhanced

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abdominal CT using liver Hounsfield Units (HU) and spleen HU. Generally, it is considered that liver HU ≤40 HU or liver minus spleen density difference less than-10 HU are characteristic of hepatic steatosis. Radiation exposure and variable results by conditions like oedema or copper accumulation in the liver are some limitations of CT scan, but CT scan is excellent for the qualitative diagnosis of macrovesicular steatosis of 30% or greater. Its results are operator-independent and reproducible.

A study performed by Goulart *et al*. showed that the non-invasive hepatic ultrasound score is reproducible and accurate for NAFLD screening having a sensitivity of 85.1% and specificity of 73.4%, keeping the CT scan abdomen as a gold standard.[4] This score is based on the cumulative score of hepatic attenuation and the anteroposterior diameter of the right hepatic lobe. The rationale of this study was that the non-invasive hepatic ultrasound score for detection of NAFLD, if proven to be a more sensitive and specific method of diagnosing NAFLD, can replace the conventional B-mode Ultrasound for screening and diagnosing fatty liver disease.

METHODOLOGY

This Cross-sectional study was performed at the Armed Forces Institute of Radiology and Imaging Rawalpindi from December 2017 to May 2018. Non-probability consecutive sampling technique was used to recruit the study participants. Using the OpenEpi sample size calculator, keeping a Confidence Interval of 95%, anticipated population proportion of 30%,[5] absolute precision of 9%, and a sample size of 101 patients were used for this study. The study was started after obtaining permission from the Hospital Ethical Committee (IERB Approval Certificate No. 0015 dated 30 July 2020). Written informed consent was taken from every patient.

Inclusion Criteria: All patients more than 18 and less than 60 years of age and belonging to any ethnicity or gender were included in the study.

Exclusion Criteria: All the patients referred to the ultrasound department of the hospital with a suspected diagnosis of fatty liver, or those patients who had abdominal Ultrasound for any reason but were found to have fatty liver, were considered for the study.

A detailed history was taken from the patient or the family. Demographic characteristics (name, age, gender, residence, and contact number) were documented for each patient. Clinical parameters, symptoms, history of hypertension or diabetes mellitus and clinical examination findings like hepatomegaly and obesity of all the patients were recorded as well. Patients with a history of alcohol intake, those who were hepatitis B or C positive, patients having space-occupying lesions or heterogenous liver on Ultrasound and those who had already developed liver cirrhosis were excluded from the study. Ultrasound abdomen of those patients already diagnosed with NAFLD was performed, and hepatic ultrasound score was calculated. Imaging was performed using the 64-MDCT scanner to evaluate the hepatic attenuation in Hounsfield units (HU).

Statistical Package for Social Sciences (SPSS) version 20.0 was used for the data analysis. Mean and standard deviation were determined for quantitative variables like age. Two by two table was drawn, and the likelihood ratio was calculated for true positive (TP), true negative (TN), false positive (FP) and false negative (FN).

RESULTS

A total of 101 patients were studied. The mean age of the studied population was 41±15.603 years (range: 19-71 years). Forty (39%) were males, and sixty-one (60.4%) of the patients were females. Among the study population, twenty (19.8%) were symptomatic (mostly pain right hypochondrium or on and off dyspepsia symptoms), while eighty-one (80.2%) were asymptomatic. Almost fifty percent had a history of Diabetes Mellitus, more than sixty percent were found to have hepatomegaly on clinical examination, and almost the same number were obese.

The hepatic Ultrasound score was calculated by adding the hepatic attenuation score (Normal liver parenchyma:0 points, Grade:1 point, Grade II: 2 points and Grade III was given 3 points). Antero-posterior diameter of the right hepatic lobe of more than 119.5 mm in men or more than 102.5 mm in women was given 1 point, and less than this diameter was given zero point. Ten, fifty-one and forty patients had hepatic attenuation index of 0, 1 and 2, respectively. Fifty-nine patients had an AP diameter more than the cut-off. A total of 69 patients had a USG score of 2 or more, fulfilling the study's criteria to be labelled as NAFLD (Figures-1,2,3). By using CT scan as the gold standard modality, 71 patients fulfilled the criteria to be labelled as NAFLD (Hepatic attenuation index <48 and hepatic, splenic attenuation difference between -5 to 10). Keeping the CT scan gold standard, 59 patients were true positive, and 10 were false positive. The

sensitivity of using the USG score to Diagnose NAFLD was 83.09 %, and the specificity was 66.67%.

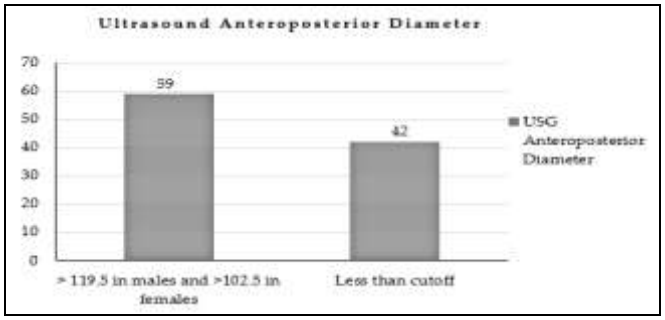

Figure-1: Antero-posterior(AP) Diameter of the Right Hepatic Lobe(≥ 119.5 mm (men) or ≥ 102.5 mm (women) was given 1 point and Less than this Diameter was given zero point) (n=101)

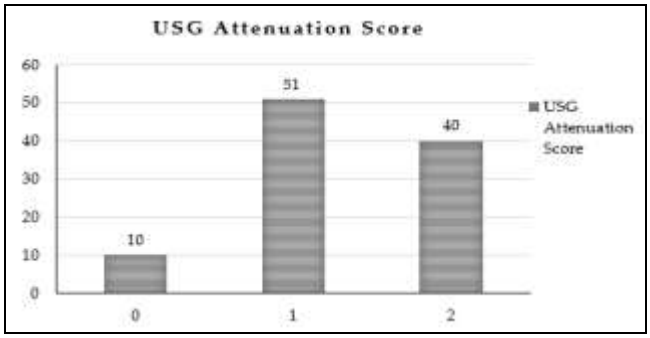

Figure-2: Ultrasound Hepatic Attenuation Score (Normal:0 point,Grade I:1 point, Grade II: 2 points,Grade III:3 points) (n=101)

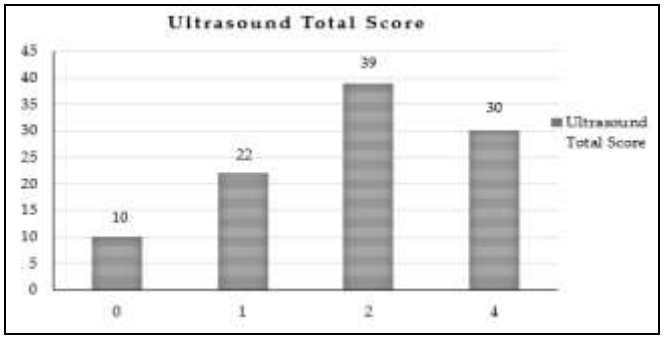

Figure-3: Non Invasive Ultrasound Score Categories among the study population. A score of two or more was considered diagnostic of Non-Aalcoholic Fatty Liver Disease on Ultrasound (n=101)

The positive predictive value of the hepatic ultrasound score was 85.50%, and the negative predictive value was 62.5% (Table).

DISCUSSION

Ultrasound is the first-line diagnostic test in patients with abnormal liver enzymes.[6] Characteristic ultrasonographic features identifying NAFLD have been validated over a while. When added to ultrasound features, clinical risk factors like obesity and Diabetes Mellitus have high utility and accuracy in diagnosing NAFLD patients.[7]

Table: Comparison of CT Scan and Non Invasive Hepatic Ultrasound Score for the Diagnosis of Non-Aalcoholic Fatty Liver Disease (n=101)

		CT Scan (Non-Aalcoholic Fatty Liver Disease)	
		Yes n (%)	No n (%)
Non Invasive Ultrasound Score (Non-Aalcoholic Fatty Liver Disease)	Yes n (%)	59 (85.5)	10 (14.5)
	No n (%)	12 (37.5)	20(62.5)

Ultrasound is non-invasive, easy to perform, and an inexpensive diagnostic modality with no ionizing radiation. Additionally, the upper abdomen can be easily screened at the same time. However, operator and equipment bias is a shortcoming of this modality and assessment of steatosis is subjective due to the lack of a standardized measure of liver echogenicity. Some factors causing suboptimal ultra-sonographic study include obese patients and excessive intestinal gas. Ultrasound was 84.8% sensitive and 93.6% specific for the diagnosis of NAFLD in a study, but these parameters dropped to 53.3–65 and 77–81.2%, respectively, in the case of mild steatosis.[8] The presence of inflammation or fibrosis further adversely affects the specificity.[9,10] Liver steatosis can be classified into various grades depending on characteristic ultrasound features; mild (increased echogenicity but vessels and diaphragm appear normal), moderate (poor visualization of the intrahepatic vessels) and severe (diaphragm and deep parenchyma are not visualized).[11]

Liver biopsy is considered the gold standard for quantifying and diagnosing fatty liver. With the wide availability and usage of Ultrasound-guided liver biopsies, it is generally a very safe procedure. However, like any other invasive procedure, complications like pain, bleeding, and viscus perforation might occur.[12] Other limitations include poor patient compliance and sampling errors. Other radiological diagnostic modalities for NAFLD include Computed Tomography (CT) scan, and Magnetic Resonance Imaging (MRI) based Spectroscopy. However, the limitations of MRI include cost, limited availability, and the need for expertise in spectral analysis. CT scan is a very sensitive and speci-

fic tool for diagnosing NAFLD, but some of its limitations are high cost, less wide availability and the potential hazard of ionizing radiation.

Ultrasonography is still considered the initial screening and diagnostic test for NAFLD, and the addition of a hepatic ultrasound score augments the diagnostic accuracy of this tool, making it comparable to CT scan but at the same time lacking the pitfalls associated with CT scans like availability, cost and radiation exposure to name a few. The risk of developing Diabetes Mellitus is twofold among patients with NAFLD. In a large population-based study from Sri Lanka, more patients with ultrasonographically diagnosed NAFLD developed diabetes than those without NAFLD.[13] Our results are comparable with regional and global studies. A meta-analysis by Banerjee *et al.* in which forty-nine studies were included showed comparable sensitivity and specificity of Ultrasound for diagnosing NAFLD.[14] Ozturk *et al*. have shown high sensitivity (89%) and specificity (93%) for the imaging quantification of liver parenchymal fat using ultrasound.[15] A study by Lee *et al.* showed that Ultra-sound had a sensitivity of 92.3% in diagnosing NAFLD when hepatic fat content was greater than 30%.[16] Another study by Khov *et al*. concluded that bedside ultrasound is an accurate and reliable method in detecting NAFLD that can even be an alternative for liver biopsy in the appropriate patients.[17] Many inter-national publications support the use of non-invasive scoring systems to diagnose NAFLD.[18,19]

LIMITATIONS OF STUDY

CT scan has been used as a gold standard which was 80-90 % sensitive, and the data has not been stratified further to ascertain the impact of the presence of Diabetes Mellitus or obesity on the diagnostic sensitivity of Ultrasound.

CONCLUSION

The non-invasive hepatic ultrasound score is a reliable and accurate diagnostic tool for screening NAFLD.

Conflict of Interest: None.

Author's Contribution

SW:, AURS: Concept of study, ST:, DA: Data collection, UN: Manuscript the results, WR: Concept of writing.

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