Correlation between Ultrasound Grading of Diffuse Fatty Liver Changes with Density of Liver Measured by Computed Tomography Scan

Sawsan Mohammed Olfet[1*], Hussain S. Hasan[2], Ali H. Saddam[3]

Abstract

Ultrasound is a good imaging modality for diagnosing and grading fatty liver disease. It is an effective method for quantifying fatty liver alterations since it can be used to estimate mean liver density. Hepatic steatosis is another term for fatty liver. It occurs when the liver becomes clogged with fat. Small levels of fat in the liver are acceptable, but too much might cause health issues. Because considerable alcohol intake causes liver damage, fatty liver is classified as both non-alcoholic fatty liver disease and alcoholic fatty liver disease. The study aims to evaluate the correlation between US grading of fatty liver and computed tomography scan density of the liver, and assessment of the clinical significance of fatty liver changes detected by ultrasound in correlation with patient factors including age, gender, diabetes mellitus, smoking status, alcohol intake, and lipid profile. The collected dataset includes 110 patients that were evaluated by radiologists and diagnosed using Ultrasound and Computed Tomography scan departments at Al-Shaheed General Hospital Baghdad Resafa Health Directorate–Iraq. The experimental results show that the proportion of mates outperformed females by 58.2% and 41.8% respectively. Furthermore, it was noted that 32.7% of patients were diabetics, 66.4% of patients were fat, 25.5% of patients were current smokers, and 6.4% of patients were drinking. Moreover, 40.9% of patients had high s. cholesterol, 57.3% of patients had high s. TG, 14.5% of patients had high LDL, and 41.8% of patients had low HDL. Finally, it was concluded that the mean of liver density of US grades 2 or 3 (27.95) was less than 0 or 1 (35.51). Where, the prevalence of US grades 2 or 3 of fatty liver's patients increased with increasing of BMI, until reaching 47.9% in obese patients.

Key Words: Fatty Liver Disease (FLD), Nonalcoholic Liver Disease (NAFLD), Computed Tomography (CT), Ultrasound (US).

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Introduction

Fatty liver disease (FLD), also known as hepatic steatosis, is a condition where excess fat builds up in the liver. Where, fatty liver disease rarely causes any symptoms but it is an important warning sign that the patient in a critical condition [2]. Furthermore, in these circumstances, it might lead to liver damage. Such that, a healthy liver contains a small amount of fat. It becomes a problem when fat reaches 5% to 10% of your liver's weight [3]. Fatty liver disease is classified into two types; Alcoholic fatty liver disease and Nonalcoholic liver disease. Where, Alcoholic fatty liver disease comes from drinking a large amount of alcohol, even for just a few days, can lead to a build-up of fats in the liver, or may come from insulin resistance and metabolic syndrome. Furthermore, viral hepatitis and the use or abuse of certain medicines represent two main causes of fat buildup in the liver.

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Moreover, dietary and nutritional anomalies, and congenital diseases, may represent the main causes of building-up pf fat in the liver [4].
While, nonalcoholic liver disease (NAFLD) also known as a hepatic steatosis, is a term for a range of conditions caused by a build-up of fat in the liver. It is popular between people who are overweight or obese. Early stages of NAFID do not usually cause any harm, but may be led to the liver damage or to health problems. In a small number of patients, it can progress and eventually lead to fatigue or soreness in the upper right side of the abdomen on occasion [1].

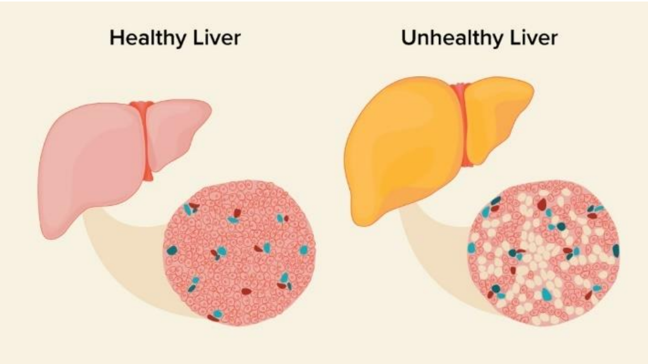

Figure 1. Human healthy and unhealthy fatty liver [1]

Fatty liver can progress through four stages; first, simple fatty liver occurs when liver cells start to build-up fat with no symptoms, no inflammation or soreness. Second, steatohepatitis (SH) occurs when the build-up of fat in the liver cells is accompanied with inflammation. Third, fibrosis occurs when there is persistent scar tissue in the liver and in the blood vessels around the liver. However, the liver can still function quite well at this stage. Fourth, cirrhosis, the liver stops working properly, and symptoms start to appear, such as yellowing of the skin and whites of the eyes and a dull ache in the lower right side of the ribs. This is the most serious stage and it cannot be reversed [5]. Figure 1 shows the human healthy and unhealthy fatty liver.
With the expanding obesity pandemic and the introduction of new therapies to change metabolism, there is a growing need to measure and monitor liver steatosis imaging approaches for detecting steatosis range from qualitative and simple to complicated and very accurate metrics. Ultrasound can be used as a screening tool to detect aberrant liver morphology in specific clinical situations. However, it lacks the specificity and sensitivity to be used as a diagnostic tool for initiating and monitoring treatment, whereas an unenhanced CT scan may identify and quantify mild to severe steatosis [5]. CT can be defined as one of the non-invasive medical imaging technologies that was selected because it is thought to be a significant approach for an advanced internal porosity detections and characterizations. CT technology is useful in the image-guided interventions, diagnostic medicine, and evaluation of surgical and therapeutic results. Progression of the Computed Tomography applications and technology has resulted in shorter acquisition times, improved image quality, and a dramatic expansion of modern CT's clinical applications [6, 7].
The higher echogenicity of the liver parenchyma compared to the right kidney's cortex was used to diagnose fatty liver. The diaphragm and hepatic veins" interaction was also studied for visibility and sharpness. Steatosis was divided into three classes based on these three factors: Grade 0: no steatosis (echogenicity of liver and renal cortex equal); Grade 1 moderate steatosis: significantly brighter liver compared to renal cortex, obvious viewing of the diaphragm, and crisp outlines at the interface of hepatic veins; Brighter liver with attenuated US beam in deeper portions of the liver, diaphragm, and hepatic veins still visible but with softened contours; Grade 2, mild steatosis: Severe steatosis, grade 3: extremely brilliant liver, severe US beam attenuation [8]. The diagnosis of fatty liver by CT scans the intensity of the attenuated X-ray beam is expressed as a CT number also known as the linear attenuation coefficient, or attenuation value. This number is a measure of attenuation relative to air and water expressed in Hounsfield units (HU) [9]. Liver attenuation of >40 HU represents >30% liver fat content reliably and can also be estimated by comparing the attenuation of the liver to the spleen [10, 11]. The remainder of this study has been organized as: Section 2 examines a few of the latest related works. In Section3, we offer a comprehensive description of how the data was collected in this research study. The detailed experimental consequences are investigated and discussed in Section 4, and lastly, Section 5 indicates the conclusions of the study.

Related Work

As related work including several studies, Trujillo, Chen [12] with his team 2021, demonstrated that The Comparison of multiple techniques (e.g., CT to the US) could not easily be extrapolated because of variations in sample size, population, etc. Several

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investigators, however, have compared multiple techniques in the same patients, yielding better information on relatives. However, various ultrasound and CT-based techniques are improving to the point of comparability. In combination with ultrasound's wide availability and low cost, ultrasound biomarkers have the potential to become first-line diagnostics in the assessment of NAFLD. Trujillo, Chen [12] performed a clinical study on the use of imaging techniques for non-invasive assessment in the diagnosis and staging of non-alcoholic fatty liver disease found US is an acceptable imaging modality for screening patients at risk for NAFLD because it is widely available without risks and shows good diagnostic accuracy to detect moderate and severe hepatic steatosis. The US is used every day, even in primary care, allowing rapid identification of subjects with fatty liver. A CT scan is a reliable tool for detecting advanced fibrosis/cirrhosis. Still, it has low accuracy in discriminating between different fibrosis stages.

Miele, Zocco [13] with his colleagues, University Hospital Southampton NHS Foundation Trust, Southampton, UK, and Human Development and Health In 2019, confirmed Ultrasound is a pragmatic and widely accepted first-line investigation. Ultrasound has the significant advantage of being non-invasive, radiation-free, readily available, and low cost. Ultrasound has good sensitivity (85%) and specificity (95%) compared with histology in identifying moderate and severe steatosis. The main disadvantage is the low sensitivity when less than 20% of hepatocytes is steatosis. Additionally, an accurate quantitative assessment is not performed, and an element of operator dependency. Like ultrasound, CT is widely available, easy to perform, and valid at detecting moderate and severe hepatic steatosis. Unfortunately, this technique is also unreliable at detecting low levels of hepatic steatosis. Additionally, the potential hazard of ionizing radiation makes CT unsuitable for longitudinal monitoring of patients with NAFLD. Zhang, Fowler [5] found Ultrasound is safe, widely available, and low cost, but indirect measurement qualitative, operator and calibration dependent, inaccurate for mild steatosis incorrect steatosis grading, and its confounders are obesity, fibrosis imprecise and localization. But CT scan is Fast acquisition Easy to perform straight forward analysis Quantitative Indirect measurement Variable calibration Inaccurate for mild steatosis Confounders: iron, glycogen Ionizing radiation Requires standard acquisition if contrast-enhanced.

Reddy, Bharath [14] considered ultrasound is the primary modality used for treating FLD, and the quality of diagnosis offered is being affected severely due to the unavailability of skilled sonographers. We proposed deep learning, transfer learning, and fine-tuning for classifying the fatty liver in ultrasound images to address this problem. The performance analysis of the proposed framework shows that the FLD in ultrasound images can be detected with an accuracy of 90.6%.

From the review of the fatty liver diseases, in this paper we will Assess of the clinical significance of fatty liver changes detected by ultrasound in correlation with patient factors including age, gender, diabetes mellitus, smoking status, alcohol intake, and lipid profile between 18- 80 years old. In addition to evaluate the correlation between US grading of fatty liver and CT scan density of the liver.

Materials and Methods

The cross-sectional study performed between March and December 2021, one hundred and eleven patients diagnosed with fatty liver disease, their ages between 18 and 80 years old were registered in this research. Patients were examined by their radiologist and their condition was diagnosed with Ultrasound and Computed Tomography scan departments at Al-Shaheed Al-Sader General Hospital Baghdad Resafa Health Directorate– Iraq). All participants, regardless of gender or age group, gave their agreement to participate in the cross-sectional study and completed the questionnaire, which included questions about age, gender, BMI, diabetes, smoking status, alcohol use, and lipid profile. This study was approved as ethical by the IRB of the College of Medicine at Al- Nahrain University. The patient's characteristics as well as imaging modalities (US and CT scan) were assessed. Age, gender, BMI, DM, Lipid in the blood S. cholesterol, S. triglyceride, HDL, LDL, US grading, CT density were collected as a result at the start of the study. The patients with the following criteria were excluded from our study; patient with a known case of parenchymal liver disease, patient with focal liver mass, pregnant female, and patient has had liver surgery.

Experimental Results

SPSS version 26 was used to analyze the data. The information is displayed as a mean, standard deviation, and range. Frequencies and percentages are used to display categorical data. To compare liver density according to the severity of fatty liver alterations, an independent samples t-test was utilized. When the predicted frequency was less than 5, the Fisher exact test was employed instead of the Chi-square test to analyze the relationship between grades of fatty liver changes percentages and specific information. Figure 2, shows a comparison between age factor and fatty liver disease. The ages of patients were ranges from 14 to 80 (46.1±13.6) years. It is noted that the highest proportion of (50.9%) was achieved among patients aged 40 to 59 years compared with all other age group. Additionally, the proportion of males was higher than females (58.2% versus 41.8%) with a male to female ratio of 1.39: 1, as shown in figure 3.

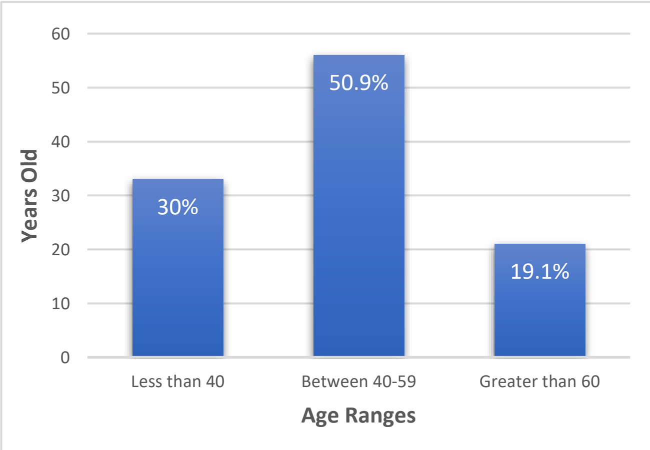

Figure 2. Distribution of studied patients by age

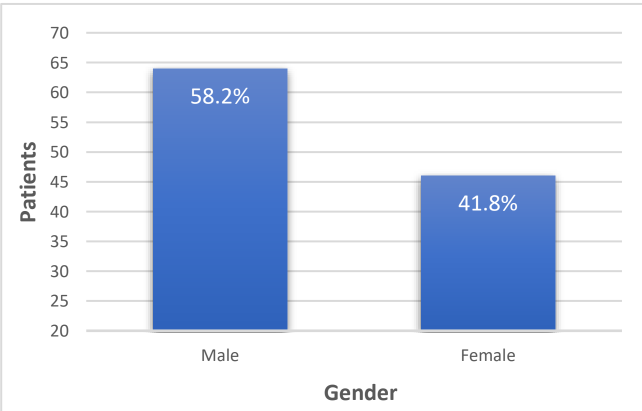

Figure 3. Distribution of study patients by gender

Table 1, illustrate the distribution of patients by general characteristics. Where, it is noted that 32.7% of patients were diabetics, 66.4% of patients were obese, 25.5% of patients were current smokers, and 6.4% of patients drank alcohol.

Table 1. Distribution of patients by clinical information

Variable	No. (n= 110)	Percentage (%)
Diabetes Mellitus		
Yes	36	32.7
No	74	67.3
BMI level		
Normal	5	4.5
Overweight	32	29.1
Obese	73	66.4
Smoking status		
Current smoker	28	25.5
Non-smoker	82	74.5
Alcohol Drinking		
Yes	7	6.4
No	103	93.6

Table 2, shows that Prevalence of grade 2 or 3 fatty liver was increased considerably with the increasing in BMI level to 47.9% in obese patients. The achieved p-value when measuring the significance between BMI level and grades of fatty liver was 0.012. while, there was no significance associations (p-value was ≥ 0.05) was detected between the grades of fatty liver changes by US and all other general characteristics.

Table 3, shows the distribution of patients by lipid profile. Where, 40.9% of overall patients had a high level of s. cholesterol, 57.3% of overall patients had a high level of s. TG, 14.5% of overall patients had high LDL level, and 41.8% of overall patients had low HDL level. The highest proportion of grades 2 and 3 of fatty liver changes was seen in patients who had high S. TG levels (49.2%) with a significant association (p-value= 0.006) between grade of fatty liver changes by US and S. TG level. No statistically significant associations were detected (p-value≥ 0.05) between the grade of fatty liver changes by US and all other lipid profile parameters. Figure 4, shows that 60% and 34.5% of patients were graded 1 and 2 respectively of fatty liver by US examination. Table 4 compares the density of the liver by CT scan to the degree of fatty liver alterations by US. Patients with grade 2 or 3 US had substantially lower mean liver density determined by CT scan than patients with grade 0 or 1 (27.95 versus 35.51, P= 0.029).

Figure 4, shows samples of four patients from the collected dataset that were used in this study. Where, the first row includes transverse images of the liver, and the second row includes axial unenhanced CT images of the liver at the level of the spleen. Steatosis grade was determined at liver fat vacuoles as the following percentages; none (0%), mild (0–33%), moderate (33–66%), and severe

(>66%). Where, steatosis grades increase from left to right in each row. From the ultrasound images, the liver parenchyma echogenicity was increased and definition of intrahepatic structures such as vessel walls was decreased. While, steatosis can be detected with unenhanced computed tomography (CT) when absolute attenuation of the liver is ≤ 40 Hounsfield units (HU), especially when hepatic fat is > 30%.

Table 2. Association between grade of fatty liver changes by US and general characteristic

Characteristics	Grades of fatty liver changes by U/S		Total (%) n= 110	P-Value
	0 & 1 (%) n= 68	2 & 3 (%) n= 42		
Age (Years)				
< 40	18 (54.5)	15 (45.5)	33 (33.0)	0.225
40 - 59	39 (69.6)	17 (30.4)	56 (50.9)	
≥ 60	11 (52.4)	10 (47.6)	21 (19.1)	
Gender				
Male	40 (62.5)	24 (37.5)	64 (58.2)	0.862
Female	28 (60.9)	18 (39.1)	46 (41.8)	
Diabetes Mellitus				
Yes	19 (52.8)	17 (47.2)	36 (32.7)	0.173
No	49 (66.2)	25 (33.8)	74 (67.3)	
BMI level				
Normal	4 (80.0)	1 (20.0)	5 (4.5)	0.012
Overweight	26 (81.3)	6 (18.7)	32 (29.1)	
Obese	38 (52.1)	35 (47.9)	73 (66.4)	
Smoking status				
Current smoker	18 (64.3)	10 (35.7)	28 (25.5)	0.756
Non-smoker	50 (61.0)	32 (39.0)	82 (74.5)	
Alcohol drinking				
Yes	4 (57.1)	3 (42.9)	7 (6.4)	0.792
No	64 (62.1)	39 (37.	103 (93.6)	

Table 3. Distribution of patients by lipid profile

Lipid Profile	Grade of fatty liver changes by US		Total (%) n= 110	P-Value
	0 & 1 (%) n= 68	2 & 3 (%) n= 42		
S. Cholesterol Level				
High	30 (66.7)	15 (33.3)	45 (40.9)	0.384
Normal	38 (58.5)	27 (41.5)	65 (59.1)	
S. Triglyceride Level				
High	32 (50.8)	31 (49.2)	63 (57.3)	0.006
Normal	36 (76.6)	11 (23.4)	47 (42.7)	
LDL Level				
High	11 (68.8)	5 (31.2)	16 (14.5)	0.537
Normal	57 (60.6)	37 (39.4)	84 (85.5)	
HDL Level				
Low	31 (67.4)	15 (32.6)	46 (41.8)	0.308
Normal	37 (57.8)	27 (42.2)	64 (58.2)	

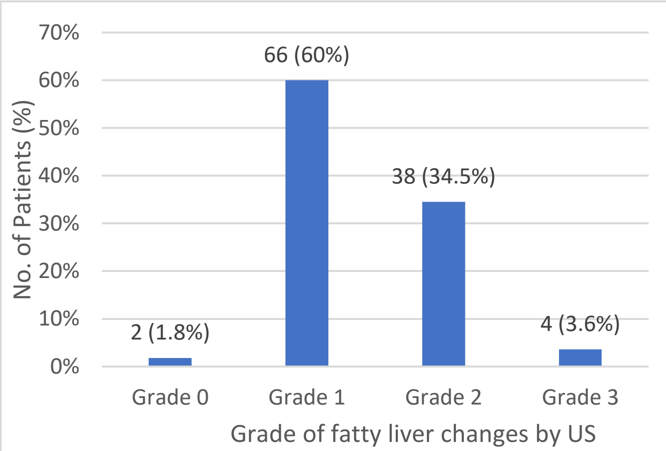

Figure 4. Distribution of study patients by grades of fatty liver changes by US

Table 4. Comparison in the density of liver measured by CT-scan according to the grade of fatty liver changes by the US

The density of the liver by CT-scan	Grade of fatty liver changes by U/S		P-Value
	Grade 0 & 1 Mean ± SD	Grade 2 & 3 Mean ± SD	
	35.51 ± 14.7	27.95 ± 18.7	0.029

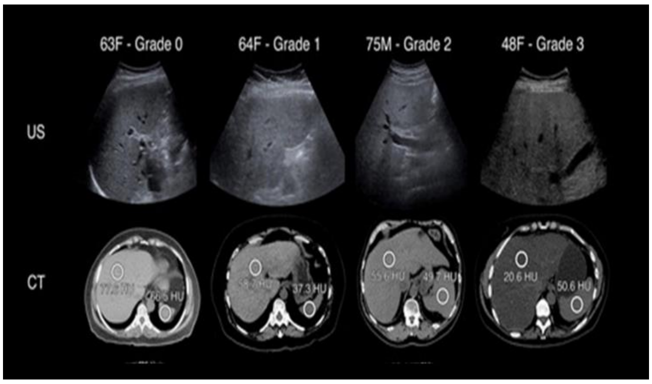

Figure 5. Samples of ultrasound and CT liver images from obtained data.

The experimental results show that the obtained proportion of males outperformed females. Where, males and females made up 58.2% and 41.8% respectively [15, 16]. Moreover, the distribution of patients by clinical information as demonstrated in Figures 2 and 3 and Table 1, showed that 32.7% of overall patients were diabetics as reported in [17, 18]. As, the Prevalence of grade 2 or 3 fatty liver increased directly with the increasing of BMI level to reach 47.9% in obese patients, with a significant difference between BMI level and grades of fatty liver (p-value= 0.012). While, statistically there was no difference between the grades of fatty liver changes by US and all other general characteristics as demonstrated in Table 2 (p-value> 0.05). As reported in [19], the prevalence of NAFLD increased with almost linearly with BMI. The mean density of liver measured by CT scan by US procedure was significantly lower in patients with grades 2 or 3, than those with grades 0 or 1 (27.95 versus 35.51, P= 0.029). These results match the results obtained by Pirmoazen, Khurana [20] and Sung, Wild [21]. This study was also proved that 40.9% of patients had a high level of s. cholesterol, 57.3% of patients had a high level of s. TG, 14.5% of patients had high LDL level, and 41.8% of patients had low HDL level, similar to obtained results by Fabbrini, Sullivan [22]. Finally, it was noted that there was the highest proportion of grades 2 and 3 of fatty liver changes was associated immediately with patients who had high S. TG levels. Where, statistically proved that there no difference between grades of fatty liver changes by US and S. TG level (p-value=0.006), as proved by Alves-Bezerra and Cohen [23].

Conclusion

In this study, we have provided a comparative study to evaluate the correlation between US grading of fatty liver and CT scan density of the liver, as well as assess of the clinical significance of fatty liver changes detected by ultrasound in correlation with several factors such as age, gender, diabetes mellitus, smoking status, alcohol intake, and lipid profile. It was concluded that ultrasound is an excellent and effective imaging tool for diagnosis and grading of fatty liver disease, though still showing decreased sensitivity in mild steatosis. Furthermore, CT imaging technique is an alternative method for quantifying fatty liver changes with the ability to measure the mean liver density. Nevertheless, it still not always applicable due to radiation exposure. Additionally, it was concluded that the patient's factors that are mentioned above contribute immediately in developing of steatotic changes.

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