

Research Article

Comparison of Computed Tomographic Hounsfield Numbers with Ultrasonographic Categorization of the Fatty Liver Disease

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Abstract

Objective: To compare CT Hounsfield Numbers with Ultrasonographic categorization of the FLD.

Material and Methods: It was a Cross sectional analytical study. By Purposive sampling 227 Patients of FLD were sampled from Radiology Department AL Razi Healthcare MM Alam Road Lahore and Radiology Department Shalamar Hospital Shalamar Road Lahore. The data was collected for 9 months. Patients of both gender of age between 20-80 years, who underwent both CT and USG scans of abdomen and with Ultrasonographic diagnosis of diffuse FLD was included. The USG categories of FLD were compared with mean Liver CTHFN. Statistical analysis was done by ANOVA; p value of CTHFN was found significant for each Ultrasonographic category of FLD.

Results: In this study 227 patients of FLD was taken. The mean age of population was 49.88 ± 14.52 years. The frequency of male population was 141(62.11%) and female was 86 (37.89%). The mild, moderate and severe FLD was found in 159 (70.04%), 50(22.03%) and 18(7.93%) patients respectively. The mean values of Liver CTHFN in mild, moderate and sever FLD categories by USG were 42.08 ± 5.07 HU, 24.41 ± 4.19 HU and 3.09 ± 6.64 HU respectively. These values along with P values and 95% Confidence Interval (CI). In multiple comparison the Least Significant Difference (LSD) of USG categories of FLD with mean Liver CTHFN, p value was significant when mild FLD was compared with moderate and severe FLD, Moderate FLD was compared with mild and severe FLD and severe FLD was compared with mild and moderate FLD.

Conclusion: In best of our knowledge to date this is third study comparing USG grades of FLD with CTHFN to

determine CTHFN for each Ultrasonographic category of FLD. We found significant p values of CTHFN for all grades of FLD by USG. CTHFN decreased with severity of FLD. Hence we can conclude that USG is a reliable and sensitive modality for the grading of FLD.

Keywords: Fatty Liver Disease (FLD); Computed Tomography Hounsfield Numbers (CTHFN)

1. Introduction

Fatty Liver Disease (FLD) also known as Hepatic Steatosis (HS) is identified by the abnormal build-up of lipids particularly triglyceride in the cytoplasm of hepatocytes [1]. In Asia, the prevalence of FLD ranges from 12–24% with most estimates within the range of 6–14% in the general population [2]. The prevalence of FLD has been increasing worldwide most likely due to eating habits, lifestyle changes and improvements in diagnostic techniques [3]. When energy intake exceeds the required amount, the excess energy is stored in the adipose tissues in the form of fat leading to obesity. Insulin resistance associated with obesity is considered as the key factor to develop metabolic syndrome and FLD [4]. FLD is the most common reason for elevated liver enzymes throughout the world [5]. Although up to 70% of FLD patients are normal on laboratory findings [6]. Most of the patients of FLD are asymptomatic or have nonspecific findings that do not correlate with the severity of disease. The most common clinical symptoms of FLD are right upper quadrant pain, feeling of fullness and lethargy or malaise. In addition hepatomegaly can also be found on physical examination [7]. Other findings are related to metabolic syndrome, obesity or overweight [8].

From pathogenic interpretation FLD can be viewed as a single disease with multiple etiologies. Clinically FLD can be divided into Non-Alcoholic Fatty Liver Disease

(NAFLD) and Alcoholic Fatty Liver Disease (AFLD) [9]. NAFLD is defined as FLD in the absence of hepatic damaging factors including alcohol use, hepatitis viruses and metabolic disorders [10]. In Pakistan the prevalence of NAFLD in general population is 18% [11, 12]. In western countries the prevalence of NAFLD in adults ranges from 20 to 33% [13]. AFLD is induced by consumption of excessive alcohol. It has been reported that 30 gram of alcohol intake per day can induce liver damage [14]. AFLD and NAFLD passes through similar pattern of changes consisting of fatty infiltration to Steatohepatitis that leads to cirrhosis and hepatocellular carcinoma. Despite different etiologies AFLD is difficult to distinguish from NAFLD because of similar pathological features of alcoholic steatohepatitis (ASH) and non-alcoholic steatohepatitis (NASH) [15].

Several imaging techniques can detect FLD with their own advantages and disadvantages. Ultrasound is still in the first line for determining FLD because of its safety, easy availability, cost effective and radiation-free nature. However, the grading of fatty liver by ultrasound is subjective and there is inter observer variability [16]. The reported sensitivity and specificity of ultrasound for diagnosing mild FLD ranges from 55.3% to 66.6% and 77.6% to 93.1% respectively while for moderate-severe FLD is about 90% and 95% respectively [17].

Computed Tomography (CT) can represent Liver fat content quantitatively by measuring Liver attenuation/Computed Tomographic Hounsfield numbers (CTHFN) expressed in Hounsfield Units (HU). Liver attenuation of <40 HU represents >30% liver fat content reliably [18]. FLD can also be estimated by comparing attenuation of liver with spleen [19]. It is 100% specific for diagnosis of moderate to severe FLD when liver-to-spleen attenuation ratio is <0.8. From evaluation of transplant

donors, it has been concluded that unenhanced CT is excellent for detecting hepatic fat of $\geq 30\%$ with specificity and sensitivity of 100% and 82% respectively. Radiation exposure can be reduced by using low dose protocols [20]. MR spectroscopy is the most accurate and fast method of detecting fat but it is expensive and software is not available on all MR units. MR elastography a new technique to detect liver stiffness has not been demonstrated to detect NAFLD and is still undergoing research for patients of hepatitis and cirrhosis [21]. At present percutaneous biopsy of liver is considered as the gold standard for diagnosis of FLD. However, it is not indicated in healthy individuals because it is an invasive procedure and more importantly it has many serious complications [22].

Current imaging methods including USG, CT, and MRI have shown their values to serve as noninvasive imaging methods to evaluate FLD progression, but they are still relatively limited in the detection of inflammation (NASH), which is more important than FLD in terms of its high risk for fibrosis, cirrhosis, and HCC. Detection of NASH by imaging remains the future direction in FLD [23].

FLD is subjectively categorized into mild, moderate or severe grade depending upon sonographic appearance. But there is no arithmetically defined demarcation for this grading. On the other hand, CT scan has the facility to numerically categorize different tissues on the basis of density. In this study the CT Hounsfield numbers will be compared with the sonographic grading of the fatty liver disease to define it more precisely. A good association will avoid unwanted radiation to the patient.

2. Aim

Determination of the range of CTHFN in different categories of FLD by USG.

3. Objective

To compare CT Hounsfield Numbers with Ultrasonographic categorization of the FLD.

4. Material and Methods

The rules and regulations set by the ethical committee of the University of Lahore was followed while conducting the research and the rights of the research participants were respected. It was a Cross sectional analytical study. By Purposive sampling 227 Patients of FLD were sampled from Radiology Department AL Razi Healthcare MM Alam Road Lahore and Radiology Department Shalamar Hospital Shalamar Road Lahore. The data was collected for 9 months.

Patients of both gender of age between 20-80 years, who underwent both CT and USG scans of abdomen and with Ultrasonographic diagnosis of diffuse FLD was included. Patients with Liver abnormalities including acute hepatitis and cirrhosis, right renal malformations including agenesis, right nephrectomy, right pelvic kidney and right kidney with cortical abnormalities and with congenital or acquired abnormalities of spleen were excluded.

5. Equipment

5.1 Ultrasound

Toshiba Xario with 3.5MHZ probe at both centers was used to scan patients in supine and left lateral decubitus position. Images of sagittal view of liver and right kidney were obtained; also scans were performed in multiple planes for better comparison of echogenicity. The severity of FLD was diagnosed in the presence of one of the following standards laid down by the American Gastroenterology Association: Grade 0- normal echogenicity. Liver appears equal to or slightly echogenic than right renal parenchyma. Grade I – Mild diffuse increase in echogenicity. Liver appears bright compared to the cortex of the kidney and normal picturing of diaphragm and intrahepatic vessel borders as shown in Figure 1A. Grade II - Moderate diffuse increase in echogenicity. Slightly diminished visualization of the intrahepatic vessels and diaphragm as shown in Figure 1B. Grade III - Noticeable increase in echogenicity. Poor or no visualization of intrahepatic vessels and diaphragm and poor penetration of the posterior segment of the right lobe of the liver as shown in Figure 1C [24].



Figure 1A: Grade I FLD.

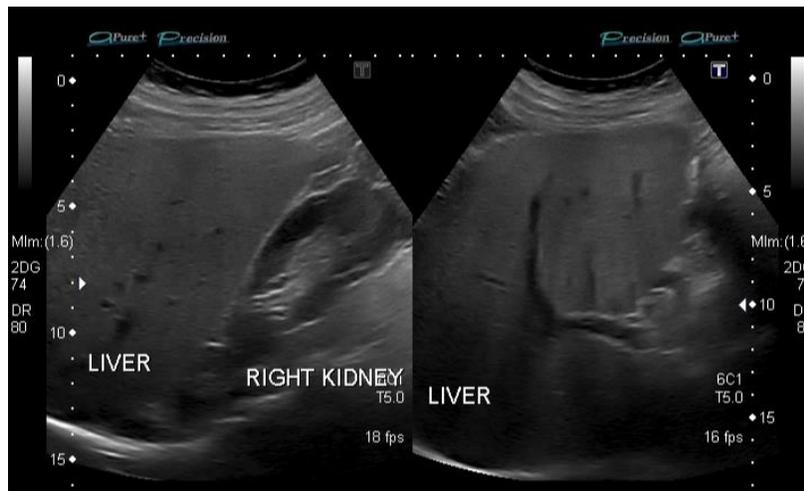


Figure 1B: Grade II FLD.

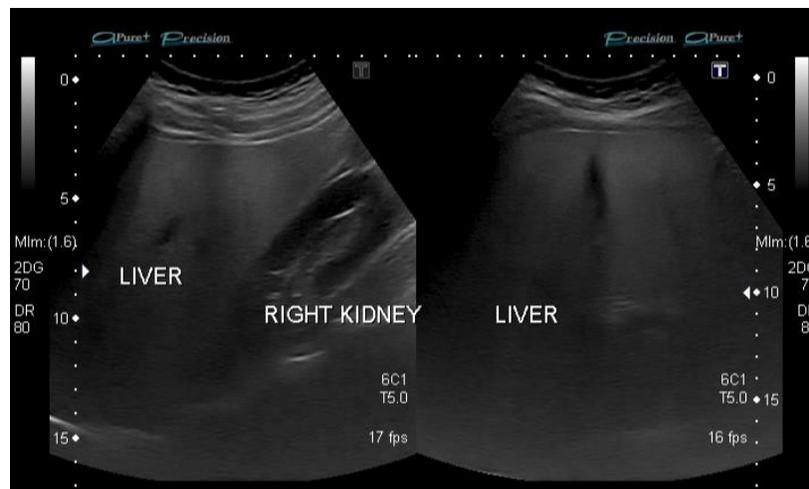


Figure 1C: Grade III FLD.

5.2 Computed tomography

Siemens 64 slice dual source at both centers was used to scan patients. Patients were scanned in supine position. Unenhanced CT (80-140 kV, 100-300 mAs, 5mm section thickness) was performed. To calculate CTHFN of liver attenuation values were measured using random selection of regions of interest (ROIs) ranging from 50 to 100 mm². ROIs of greater than 100mm² were measured where

possible while taking care to exclude regions of non-uniform parenchymal attenuation, including hepatic vessels and biliary structures. The ROIs circles were placed when maximum part of both lobes of liver were visible in a slice. There were two ROIs placed in the right liver lobe anterioposteriorly, one ROI in the left lobe of liver as shown in Figure 2. The ROIs values were averaged to get mean liver attenuation in Hounsfield Unit (HU) [25].

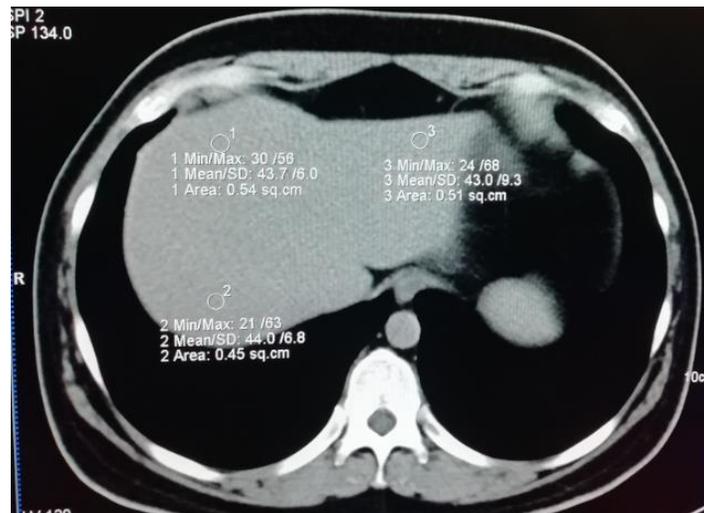


Figure 2: CTHFN of liver and Spleen measured by 2 ROI in right lobe of liver 1 ROI in left lobe of liver and 1 ROI in Spleen

6. Results

In this study 227 patients of FLD was taken. The mean age of population was 49.88 ± 14.52 years and range was 20-80 years as shown in Table 1 and Figure 3. The mean Values of CTHFN of liver was 36.16 ± 12.84 HU and range was -11.83-53.20 HU with significant p value as shown in Table 2 and Figure 4A. The frequency of male population was 141(62.11%) and female was 86 (37.89%) as shown in

Figure 4B. The mild, moderate and severe FLD was found in 159 (70.04%), 50(22.03%) and 18(7.93%) patients respectively as shown in Figure 4C. The mean values of Liver CTHFN in mild, moderate and sever FLD categories by USG were 42.08 ± 5.07 HU, 24.41 ± 4.19 HU and 3.09 ± 6.64 HU respectively. These values along with P values and 95% Confidence Interval (CI) are as presented in Table 3 and Figure 5.

Mean	Std. Deviation	Minimum	Maximum	Range
49.88	14.58	20.00	80.00	60.00

Table 1: Mean Age of Population.

Mean	Std. Deviation	Minimum	Maximum	P Value
35.16	12.84	-11.83	53.20	0.000

Table 2: Liver Mean CTHFN.

FLD Category on USG	N	Liver CTHFN Mean HU	Std. Deviation	95% Confidence Interval for Mean		P Values
				Lower Bound	Upper Bound	
Mild	159	42.0822	5.07276	41.2876	42.8768	0.000
Moderate	50	24.7167	4.19824	23.5235	25.9098	
Severe	18	3.0926	6.64668	-.2127	6.3979	
Total	227	35.1655	12.84042	33.4861	36.8449	

Table 3: Mean values of Liver CTHFM in USG categories of FLD.

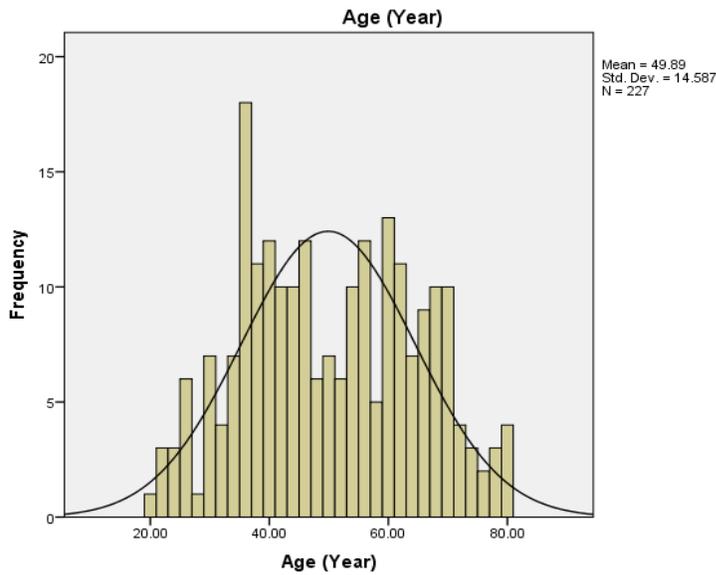


Figure 3: Mean Age of Population.

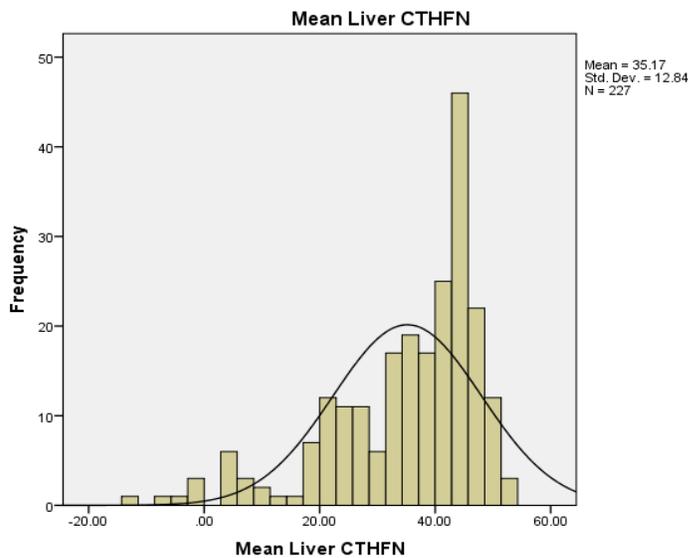


Figure 4A: Mean Liver CTHFN.

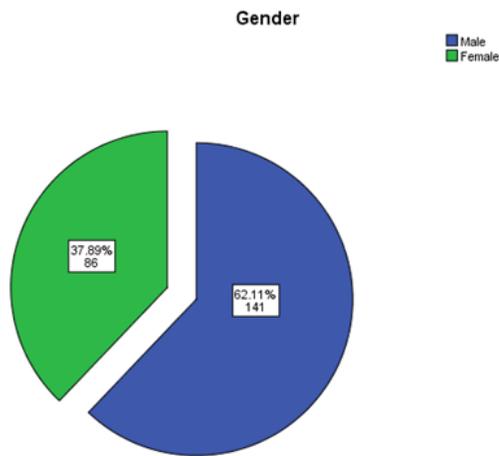


Figure 4B: Gender Frequency and Percentage.

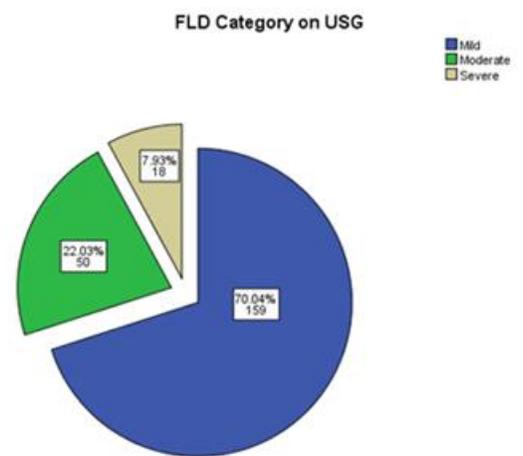


Figure 4C: Percentage of FLD Grades.

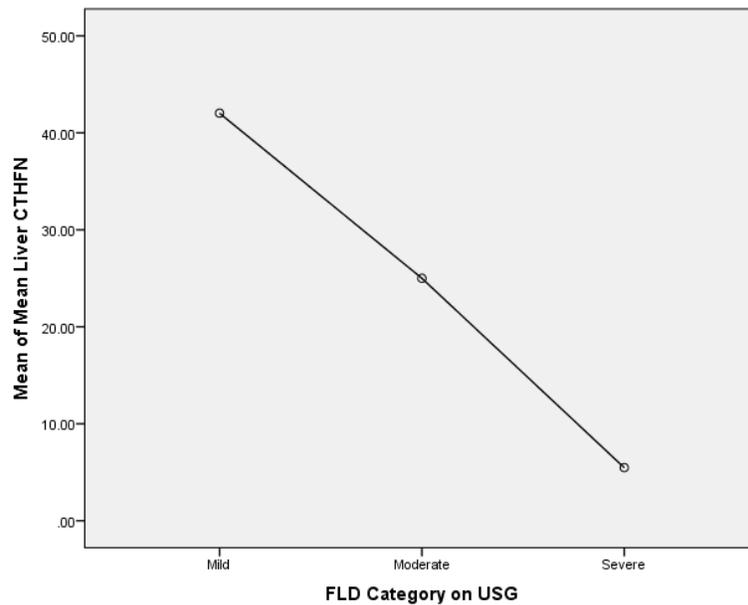


Figure 5: Mean values of Liver CTHFN in USG categories of FLD.

In multiple comparison the Least Significant Difference (LSD) of USG categories of FLD with mean Liver CTHFN, p value was significant when mild FLD was compared with

moderate and severe FLD, Moderate FLD was compared with mild and severe FLD and severe FLD was compared with mild and moderate FLD as shown in Table 4.

Mean Liver CTHFN			
Mild	Moderate	17.36551*	0.000
	Severe	38.98959*	0.000
Moderate	Mild	-17.36551*	0.000
	Severe	21.62407*	0.000
Severe	Mild	-38.98959*	0.000
	Moderate	-21.62407*	0.000

Table 4: Least Significant Difference (LSD) of USG categories of FLD with mean Liver CTHFN.

7. Discussion

The incidence of FLD is gradually increasing in our country and especially in developed world. The definitive diagnosis of FLD is histological examination but unfortunately this is an invasive technique. Most of the patients are not willing to perform this invasive procedure therefore majority of reversible FLD becomes complicated due to non-availability of definitive diagnostic technique. Ultrasound is the first line modality used for characterization of FLD but sonographic grading of the FLD is more subjective. There is no universal consensus on the USG classification of FLD. But CT Hounsfield numbers are a quantitative measurement of fat. This research was therefore intended to compare the sonographic grading of FLD with CT Hounsfield numbers.

FLD occurs worldwide in obese and excessive alcohol consumers [26]. FLD also occurs in metabolic disorder and several conditions that effect fatty acid metabolism [27]. The diagnosis of FLD is made when lipid content in the liver exceeds 5–10% by weight [15]. . If the cause persist, FLD invariably progresses to steatohepatitis, cirrhosis and liver cancer [28]. In 2016 Wolff L et.al. reported severe FLD is associated with excessive pericardial fat and suggested it as a marker for vascular disease [29]. FLD is a precursor or it may signal the development of hypertension,

cardiovascular diseases and type II diabetes mellitus which is associated with high rates of mortality [30].

Ultrasonography is suggested as a first choice for the diagnosis of FLD, considering its wide availability, low cost and absence of side effects or risks to the patient, furthermore liver enzymes are not a good parameter for detection of FLD [31]. The prevalence of FLD in routine Sonography is much higher as compared to laboratory findings [32]. Utilizing USG the prevalence of FLD ranges from 20-40% in industrialized countries [33]. The most common criteria for grading of FLD by USG takes into account the echogenicity of liver and its comparison with echogenicity of right kidney. The grading is defined as: G 0- normal echogenicity, Liver appears slightly echogenic or isoechoic to right kidney cortex). G I- mild increase in echogenicity, Liver appears bright than right renal cortex with normal appearance of intrahepatic vessels and diaphragm; G II-Moderate increase in echogenicity with slightly blurred visualization of intrahepatic vessels and diaphragm; G III- Severe increase in echogenicity with poor or no visualization of intrahepatic vessels and diaphragm [34].

In 2011 Hernaez R et.al. [35] conducted a met-analysis on 49 studies and reported sensitivity and specificity of USG

for detection of moderate-severe FLD as compared to histology (gold standard) 84.8% and 93.6% respectively. Latest studies comparing USG with histopathology have confirmed that it is a pertinent non-invasive tool for evaluation of FLD and intends Grade 0 or 1 do not require biopsy [36].

Cruz JF et.al found high prevalence of FLD in males as compared to females. They found prevalence of FLD in grade I, II and III in 51.5%, 40.4% and 8.6% patients respectively. In current study we also found high frequency of FLD in males as compared to females. We found frequency of FLD in grade I, II and III in 70.0%, 22.0 and 7.9% patients respectively.

CT can measure degree of FLD quantitatively. It employs attenuation values to estimate liver fat content. There is a reduction in Liver attenuation with an increase in intrahepatic fat content [23]. There are many studies which have shown a decrease in CTHFN with increase in severity of FLD [37]. Unenhanced normal Liver parenchyma has CTHFN (attenuation) values in the range of 50 to 65HU, typically 8-10HU greater than liver [38]. Unenhanced CT has sensitivity of 43-95% and specificity of 90-100% for detection of Liver Steatosis [39]. CT has been proved to be a sensitive modality for quantitative measurement of moderate to severe FLD but its performance for mild FLD is limited [40]. The most common diagnostic criteria for diagnosis of FLD on CT is liver CTHFN less than 40 HU or liver CTHFN less than 10HU as compared to Spleen CTHFN which correlates with pathologic fat content of 30% or more [41]. However this diagnostic criteria excludes mild FLD decreasing overall prevalence as much as 40% as compared to other CT criteria [42].

CT provides fast, objective and reproducible assessment of liver fat having a good correlation with pathologic findings

obviating the need of biopsy in most of the cases [43]. But to date there has been no standard criteria for grading of FLD on CT. The first study correlating USG grading of FLD with CT was published in 1985 by John CS et al. [44] to evaluate accuracy of USG for diagnosis of FLD. They reported the overall accuracy of USG for detection of FLD 85%, with 100% sensitivity and 56% specificity. The USG/CT correlation was found particularly well for the diagnosis of grade I and II FLD.

The second study correlating USG grading of FLD with CT was done in 2015 by Jumana R³⁷ and associates for the estimation of CT HU for different grades of FLD by USG. They reported the significant HU p values between different grades of FLD. The mean age of the patients in their study was 45years whereas in current study mean age of patients was 47 years. In their study percentage of male patients was 55% and female was 47%, in our study percentage of male patients was 62% and 37% females. They found mean values of CTHFN in grade I, II and III of FLD 37.74, 24.16 and 0.75 HU respectively. In present study we found mean values of CTHFN in grade I, II and III of FLD 42.08, 24.71 and 3.09 HU respectively.

8. Conclusion

In best of our knowledge to date this is third study comparing USG grades of FLD with CTHFN to determine CTHFN for each Ultrasonographic category of FLD. We found significant p values of CTHFN for all grades of FLD by USG. CTHFN decreased with severity of FLD. Hence we can conclude that USG is a reliable and sensitive modality for the grading of FLD.

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