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Computed Tomography Evaluation of the Caudate-to-Right Lobe Ratio in Patients with Liver Cirrhosis and Subjects with Normal Liver in Benin City, Edo State, Nigeria

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Abstract

Background: Liver cirrhosis is the end stage of a range of chronic diffuse liver diseases and is forever progressive leading to hepatic dysfunction, portal hypertension and hepatocellular carcinoma. It is the major cause of morbidity and mortality in developing countries. This study was designed to compare the caudate-to-right hepatic lobe ratio of normal subjects with that of patients with liver cirrhosis with the view of elucidating the value of the ratio in the diagnosis of liver cirrhosis.

Materials and method: A prospective cross-sectional study design was adopted in this study. The participants were examined on a 16-slice Siemens CT machine using standard protocols and techniques in the imaging unit of Union Diagnostics and Clinical Services, Benin City. Ethical approval for this study was obtained from the Human Research and Ethics Committee of Faculty of Health Sciences and Technology, Nnamdi Azikiwe. The procedure was adequately explained to the participants and their consent was properly sought. Information obtained from the participants was treated with high level of confidentiality. Data used for this study were collected using structured data proforma. The obtained data were analyzed SPSS version 21.0 (SPSS Inc., Chicago, IL, USA). Both descriptive and inferential statistics were used for statistical analysis and the level of statistical significance was set at p<0.05.

Results: Of the 214 participants, comprising of 107 liver cirrhosis subjects and 107 healthy adults with normal liver, males were 59.3% (n=63) and 55.3% (n=59) in the studied and control groups respectively. Out of 107 liver cirrhosis subjects, 48% (n=51) were within age group 60 years and above as highest. Of 107 subjects diagnosed with liver cirrhosis, 61.3% (n=92) had history of alcohol consumption. The mean of liver span, right lobe, caudate lobe and C/RL ratio for the liver cirrhosis group are 15.35 \pm 0.80 cm, 7.23 \pm 1.03 cm, 5.25 \pm 0.91 cm and 0.72 \pm 0.06

cm respectively, while the mean of liver span, right lobe, caudate lobe and C/RL ratio in the control group are 15.74 \pm 1.0 cm, 8.51 \pm 0.7 cm, 3.78 \pm 0.5 cm and 0.44 \pm 0.00 cm respectively. There were statistically significant mean differences in the measured liver dimensions across the two groups (p= 0.001, 0.000, 0.000 and 0.000) respectively.

Conclusion: Male preponderance was observed across the two groups. There was a significant difference in the caudate-to-right lobe ratio of subjects when compared with that of the patients with liver cirrhosis, indicating C/RL ratio is a very strong reliable parameter for diagnosing liver cirrhosis even in its early asymptomatic stage.

Keywords: Abdominal computed tomography; Caudateright lobe ratio; Liver cirrhosis

Introduction

Liver cirrhosis is the end stage of a range of chronic diffuse liver diseases and is forever progressive leading to hepatic dysfunction, portal hypertension and hepatocellular carcinoma [1]. Liver disease has a global distribution [2], and a major public health challenge globally [3]. The global prevalence of cirrhosis from autopsy studies ranges from 4.5% to 9.5% of the general population [4-6]. In the United States, cirrhosis is the twelfth leading cause of hospitalization and death [7]. Cirrhosis is a major cause of morbidity and mortality in developing countries. In most of Africa, and indeed Nigeria, there is paucity of reliable statistics regarding liver-related morbidity and mortality. Besides, patients in this part of the world tend to present late to the hospital especially when stunned with the symptoms of liver failure [8].

The most common causes of hepatic cirrhosis are alcoholic fatty liver disease (AFLD), non-alcoholic fatty liver disease (NAFLD) and viral hepatitis [9]. Less frequent causes of cirrhosis include haemochromatosis, alpha1-antitrypsin

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deficiency, Wilson's disease, biliary cirrhosis and cardiac cirrhosis. Chronic inflammation leads to potentially reversible liver fibrosis and ends in irreversible cirrhosis with the cross-linking of collagen fibres and the formation of regenerative nodules.

Liver biopsy is currently the gold standard for the diagnosis of cirrhosis [10]. However, most patients will prefer to have a non-invasive test rather than a biopsy, because of the potential for procedural pain and complications such as bleeding, pneumothorax, biliary puncture and death [11]. Biopsy has a significant sampling error of between 14.5-25% when determining presence or absence of cirrhosis score variability [12]. Biopsy also suffers from poor reproducibility and variability in a sampling scoring by pathologists.

Computed tomography has proven to be a useful noninvasive technique for the diagnosis of liver cirrhosis. Computed tomography has an effective role in the evaluation of the liver and the different disorders of this organ in the setting of chronic liver cirrhosis. It has the ability of assessing adjacent structures that are affected in the course of the illness, including the portal and hepatic vessels, the gall bladder, the spleen, and other intra-abdominal organs [13]. These features make it a preferred method of assessing the liver [14].

The regional morphologic changes that occur in the liver as cirrhosis develops are well known [15,16]. Specifically, the volume loss in Couinaud segments IV-VIII is typically compensated in part by relative hypertrophy of segments I-III. Morphological features of cirrhosis on CT include atrophy of the right lobe and medial left lobe (Couinaud segments IV-VIII) with hypertrophy of the left lateral section and caudate (segments I-III), liver surface nodularity (LSN), hepatic fissure expansion including expansion of the gallbladder fossa and the hilarperiportal space, narrowing of the hepatic veins, and development of a right hepatic posterior notch [17-20]. Many of these characteristics can be subjectively identified on imaging, and some can be measured. One measurement used to capture regional hepatic changes in liver disease is the caudate to right lobe (CRL) ratio [21,22]. Other ratios include left lobe-to-right lobe ratio and portahepatis index [23]. The normal caudate to right lobe (C/RL) ratio is less than 0.6, while 0.6 to 0.65 is considered borderline. This is a globally accepted reference value and any value greater than 0.65 is considered to be a case of liver cirrhosis. Using the C/RL ratio, the imaging scientist may be the first to diagnose cirrhosis, especially in its latent stage (when there is no clinical or laboratory indication of liver disease). Some schools of thought have opined that when a patient presents with abnormal liver function test this ratio may be useful in determining the nature of the hepatic disease [24]. The aim of this study is to determine the significance of C/RL ratio in diagnosing liver cirrhosis and if level of accuracy is confirmed, may serve to eliminate the need for liver biopsy in liver cirrhosis.

Materials and Methods

This is a prospective cross-sectional study, which involve the evaluation of the transverse caudate lobe-to-right lobe ratio in patients diagnosed with liver cirrhosis and patients with apparently normal liver who were referred by their physicians for abdominal CT imaging at Union Diagnostics and Clinical Services, Benin City, Nigeria. All the abdominal computed tomography (CT) examinations were performed using a 16slice Siemens® CT scanner manufactured in Germany. The participants were placed in the supine position in the CT gantry and scanned from the level of about 2 cm above the diaphragm to the iliac region with standard protocols and techniques (slice thickness: 5mm, slice interval: 5 mm, helical scan mode, matrix: 1024*1024, 120 KV, 200 mAs, rotation time: 0.6 seconds, 60 ml of contrapaque ® was injected intravenously for the contrast-enhanced series while the scan was going on using a power injector). The images acquired were analyzed by the researchers and two consultant radiologists. An ethical approval for this study was obtained from the Human Research and Ethics Committee of Faculty of Health Sciences, NnamdiAzikiwe University, Anambra State, Nigeria and management permission to use their facility was also obtained from the study center. The procedure for this study was explained to the participants and their consent was properly sought. All information related to the patients' identity were treated with high level of confidentiality and used for the purpose of this study only.

Anthropometric measurements including height and weight were obtained and recorded. The weight of the patient was measured using a weighing scale while the height was obtained using a measuring rod with a scale. The BMI was derived from the measured weight and height of the patients using the equation: BMI=Weight $(kg)/Height (M)^2$. The measurement of the liver was done on the CT monitor using the method described by Harbin et al[21]. and illustrated in Figure 1. Three different measurements of the liver were obtained and the average calculated. Serial and recorded tomographs were examined until the main portal vein was identified. A line was drawn parallel to the midsagittal plane through the right lateral wall of the bifurcation of the main portal vein (Figure 1). A second line (line 2) was drawn parallel to line 1 through the most medial margin of the caudate lobe. A third line (line 3) was drawn perpendicular to lines 1 and 2 midway between the main portal vein and the inferior vena cava and extended to the right lateral margin of the liver. The distances (along line 3) between lines 1 and 2(A) was the transverse diameter of caudate lobe and the distance along line 3 between the right margin and line 1(X) was the transverse diameter of the right lobe. The ratio of A to X was calculated as the caudate-to- right lobe ratio. All the data used in this study were collected using structured data proforma and questionnaire. The obtained data were processed and analyzed using Statistical Package for Social Sciences (SPSS) version 21.0 (SPSS Inc. Chicago IL, USA). Data analysis was carried out using Pearson and Spearman Correlation analysis, the chi-square test for categorical data and the student t-test and ANOVA where applicable. At 95%

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interval, two-tailed p-values less than or equal to 0.05 was considered statistically significant.





Figure 1 An illustration of the method for liver measurement on CT image.

Results

Out of 214 subjects included in this study, those diagnosed with liver cirrhosis with various liver diseases as retrieved from their clinical records were 50% (n=107), while the remaining 50% (n=107) were those with apparently normal liver, which served as the control group. The mean age of the liver cirrhosis patients was) while those of the controls was 46.97 ± 19.36 years (range 19-80 years). There was a statistically significant mean difference between the two study groups (p=0.000). The mean of body mass index (BMI) for liver cirrhosis and the control group subjects was 24.93 ± 4.03kg/m² and 24.18 ± 2.11 kg/m² respectively (Table 1). Out of 107 subjects diagnosed with liver cirrhosis, 59.3% (n=63) were males while 40.7% (n=44) were females. In the controls group, males accounted for 54% (n=59) as against 46% (n=48) females. There was no significant difference in the sex distribution of the study subjects (X^2 =0.564; p=0.484). In the liver diseased group, out of 107 subjects, civic servants were highest 80.7% (n=80) and none were student, while in the control group, both civil servants and self-employed subjects were highest, which is 41.3% (n=44) each respectively. There was statistically significant relationship between the occupations of the two groups (X²=55.986, p=0.000) (Table 2). Among the liver cirrhosis subjects, 59.3% (n=89) had a history of yellowness of eyes while 61.3% (n=92) had history of alcohol use. Out of 61.3% (n=92) identified with history of alcohol consumption, 22% (n=33) had history of alcohol intake for twenty years as

highest, followed by those that history of alcohol use for thirty years 19.3% (n=29) and the least were those that had history of alcohol use for fifty years, which is 4% (n=6) **(Table 3)**.

 Table 1 Mean of age, weight, height and BMI of study subjects.

Anthropometic	Liver cirrho Group	osis	Control gro	P-value	
Measurement	Mean ± Std	Range	Mean ± Std	Range	
Age (years)	60.14 ± 13.00	39.00- 85.00	46.97 ± 19.36	19.00- 80.00	0.000*
Weight (Kg)	60.33 ± 5.48	50.00- 75.00	61.98 ± 4.73	50.00- 75.00	0.006*
Height (M)	1.55 ± 0.06	1.40-1.70	1.59 ± 0.05	1.40-1.70	0.000*
BMI (Kg/M ²)	24.93 ± 4.03	13.46- 39.38	24.18 ± 2.11	18.75- 33.33	0.045*

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Ohennetteristiss	Liver cirrhosis frequency	Control frequency
Characteristics	(%)	(%)
Sex		
Male	63 (59.3)	59 (55.3)
Female	44 (40.7)	48 (44.7)
Total	107 (100)	107 (100)
Age (years)		
< 40 Years	5 (4.0)	46 (43.3)
40-49 Years	22 (20.7)	20 (18.7)
50-59 Years	29 (27.3)	9 (8.0)
60 And Above Years	51 (48.0)	31 (29.3)
Total	107 (100)	107 (100)
Occupation		
Civil Servant	86 (80.7)	44 (41.3%)
Self Employed	21 (19.3)	44 (41.3)
Student	0 (0)	19 (17.4)
Total	107 (100)	107 (100)

 Table 3 Medical and social history of study subjects.

Clinical features	Liver cirrhosis frequency (%)	Control frequency (%)	X ²	P-value	
Yellowness of Eyes	89 (59.3)	0 (0)			
How long					
Between one month to one year	76 (50.7)	0 (0)			
Between one to two years	13 (8.7)	0 (0)	104.942	0.000*	
Above two years	3 (2.0)	0 (0)			

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Diagnosed of Liver disease before	3 (2.0)	0 (0)				
Do you drink alcohol?	92 (61.3)	0 (0)				
How long have you been drinking? (years)						
0-10	9 (6.0)	0 (0)				
Nov-20	33 (22.0)	0 (0)				
21-30	29 (19.3)	0 (0)	5.552	0.981		
31-40	15 (10.0)	0 (0)				
41-50	6 (4.0)	0 (0)				
NB: The emboldened asterisked numbers are statistically significant						

The mean of liver span, right lobe, caudate lobe and C/RL ratio for the liver cirrhosis group are 15.35 ± 0.80 cm, 7.23 ± 1.03 cm, 5.25 ± 0.91 cm and 0.72 ± 0.06 cm respectively, while the mean of liver span, right lobe, caudate lobe and C/RL ratio in the control group are 15.74 ± 1.0 cm, 8.51 ± 0.7 cm, 3.78 ± 0.5 cm and 0.44 ± 0.00 cm respectively. There were statistically significant mean differences in the measured liver dimensions across the two groups (p=0.001, 0.000, 0.000 and 0.000) respectively (Table 4). Comparison of the hepatic

dimensions based on sex is shown in **Tables 5 and 6**. The liver span was significantly higher in normal males and females than in the corresponding cirrhotic subjects (p=0.001, 0.007 respectively). The caudate lobe was significantly higher in cirrhotic male and female subjects compared to the controls (p=0.001), the right lobe of the males and females were significantly smaller in the cirrhotic subjects than in the corresponding normal subjects (p=0.018, 0.001 respectively) (**Table 5**).

Table 4 Measured liver dimensions in the study subjects.

	Liver cirrhosis Group		Control group	P-value			
CT measurement of the Liver	Mean ± Std	Range of liver	Mean ± Std	Range of liver			
Liver Span (cm)	15.35 ± 0.80	13.44-17.41	15.74 ± 1.05	12.77-19.10	0.001*		
Right Lobe (cm)	7.23 ± 1.03	5.12-11.12	8.51 ± 0.72	7.18-10.71	0.000*		
Caudate Lobe (cm)	5.25 ± 0.91	3.52-8.03	3.78 ± 0.56	3.06-5.29	0.000*		
C/RL Ratio	0.72 ± 0.06	0.66-0.89	0.44 ± 0.05	0.36-0.61	0.000*		
NB: The emboldened asterisked numbers are statistically significant							

Table 5 Comparison of liver dimensions between subjects of the same sex in each study group.

Males				Females			
	Liver cirrhosis	Control	P-value	Liver cirrhosis	Control		
CT. measurement of the liver	Mean ± Std	Mean ± Std	-	Mean ± Std	Mean ± Std	P-value	
Liver span (cm)	15.51 ± 0.69	15.70 ± 1.08	0.189	15.14 ± 0.90	15.80 ± 1.02	0.000*	
Right lobe (cm)	7.25 ± 0.81	8.51 ± 0.77	0.000*	7.23 ± 1.30	8.53 ± 0.66	0.000*	
Caudate lobe (cm)	5.25 ± 0.80	3.79 ± 0.57	0.000*	5.23 ± 1.05	3.76 ± 0.56	0.000*	
C/RL-ratio	0.72 ± 0.06	0.40 ± 0.06	0.000*	0.72 ± 0.06	0.44 ± 0.05	0.000*	
NB: The emboldened asterisked numbers are statistically significant							

Table 6 compares the liver indices in males and females in each study group. The averages of the liver span, right lobe, caudate lobe and CRL ratio did not differ significantly between male and female cirrhotic subjects (p=0.600, 0.971, 0.809 and 0.682 respectively). Similarly, in the controls, the liver span, caudate lobe, right lobe and CRL ratio did not differ significantly between males and females (p=0.191, 0.358,

0.314 and 0.899 respectively). significantly between males and females (p=0.191, 0.358, 0.314 and 0.899 respectively). significantly between males and females (p=0.191, 0.358, 0.314 and 0.899 respectively). significantly between males and females (p=0.191, 0.358, 0.314 and 0.899 respectively). significantly between males and females (p=0.191, 0.358, 0.314 and 0.899 respectively).

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0.314 and 0.899 respectively). significantly between males and females (p=0.191, 0.358, 0.314 and 0.899 respectively).

Table 6 Comparison of liver dimensions between subjects ofopposite sex in each study group.

	Liver cir	rhosis		Control		
CT measurem ent of the	Males	Females		Males	Females	
liver	Mean ± Std	Mean ± Std	P-value	Mean ± Std	Mean ± Std	P-value
Liver Span (cm)	15.51 ± 0.68	15.12 ± 0.89	0.005 *	15.69 ± 1.08	15.80 ± 1.01	0.51
Right Lobe (cm)	7.25 ± 0.81	7.21 ± 1.30	0.837	8.50 ± 0.77	8.54 ± 0.65	0.701
Caudate Lobe (cm)	5.25 ± 0.80	5.25 ± 1.05	0.988	3.78 ± 0.57	3.76 ± 0.55	0.794
C/RL ratio	0.72 ± 0.06	0.72 ± 0.05	0.619	0.44 ± 0.06	0.44 ± 0.05	0.474

Discussion

Liver cirrhosis which is among the chronic liver diseases usually occurs from the repeated trauma or insults to the hepatic parenchyma, which normally results to fibrosis and cirrhosis, which is irreversible and the end stage of chronic damage to the liver [25]. It is often a torpid disease; in which majority of the patients remain asymptomatic until the occurrence of decompensation characterized by ascites, hydronephrosis, liver pleural effusion, spontaneous bacterial peritonitis, hepatic encephalopathy or variceal bleeding from portal hypertension [26].

In this study, majority of the patients diagnosed with liver cirrhosis were those within the fifth decade and above with overall mean age of 60.14 ± 13.00 , which accounted for over 60% of the total patients with liver cirrhosis while in the control group, younger adults were highest with an overall mean age of 46.97 ± 19.36 years. These findings are not in keeping with the findings of related studies conducted by Lesi et al. [27] in Lagos State, Nigeria, Ndubula et al. [25] and Balla et al. [28] in Sudan. In Lesi et al. [27] study, they reported an average age of 44.1 \pm 14 years for the study subjects and 43 \pm 11.2 years for the controls. In Ndububa et al. [25] study, which evaluated 145 patients with chronic liver disease, had a mean age 46.8 \pm 15.7 years, which was also comparable to the index study. Balla et al. [28] study conducted in Sudan reported an average age of 43.9 years and 38 years respectively for the patients and controls. The differences in our findings could be attributed to the differences in the sample size used for the various studies and the geographical variations of the studies. The mean age of presentation of the patients with liver cirrhosis from the aforementioned studies is usually in the fourth decade. This has been ascribed to the fact that liver cirrhosis and chronic liver disease are treacherous progressive disease, which may not be clinically evident till about seventy five percent of the hepatic cells are affected [29]. Even though,

the hepatic insult occurred quite early, the slow progression of the disease may make clinical manifestations show later in life.

In this study, greater numbers of those diagnosed with liver cirrhosis were males when compared with their female counters. This finding is in agreement with findings of similar studies conducted by Balla et al. [28], Giorgio et al. [30], Lesi et al. [27], Ndububa et al. [25] and Adrian et al. In Balla et al. [28] study, males were 62% and females 38%. Giorgio et al, reported males to be 64.9% and females 35.1%. In Lesi et al study, they reported 67% males against 33% females. Ndububa et al. [25] documented 70.3% males and 29.6% females and Adrian et al. study conducted in Switzerland, reported 73.7% males and 26.3% females. This could be attributed to the fact that males are more predisposed to the factors responsible for the development of liver cirrhosis, which include heavy alcohol consumption when compared with their female counterparts [31]. In addition, a study carried by Schimizu et al. [32] in Japan, showed that estradiol is a potent endogenous antioxidant, which suppresses hepatic fibrosis and the greater progression of hepatic fibrosis and hepatocellular carcinoma in men may be due, at least in part, to the lower production of estradiol. Furthermore, it has been reported that after alcohol consumption, estrogen stimulation of Kupffer cells increases their sensitivity to endotoxins and may lead to higher levels of chemical mediators [33]. These findings suggest that chronic alcohol may induce more rapid and more severe liver injury in females than in males, [34]. Although, females are more susceptible to damages associated with alcohol, because they have a smaller volume of distribution and lower gastric alcohol dehydrogenase activity [35].

In this study, the major clinical features at presentation of liver cirrhosis subjects to the clinics included ascites (34.0%), jaundice (59.3%), Renal Mass (24.0%),Gall Bladder Stone (22.7%) and shrunken liver (50.7%). These findings are similar to the findings documented in a related conducted by Lesi et al. [27]. In their study, ascites (66%), hepatomegaly (51%) and jaundice (47%) of the patients respectively. The relatively high number of patients with hepatomegaly in their study may have been due to the fact that the study was inclusive of patients with hepatocellular carcinoma which presents with enlarged macronodular liver. These categories of patients were excluded from our study.

This study, there is a hypertrophy of the caudate lobe in liver cirrhosis. This is in keeping with finding of the study conducted by Lelio et al. [36] in Italy. In their study, which recruited 75 patients with suspected liver cirrhosis or chronic liver disease and 50 normal subjects in Italy, found caudate lobe hypertrophy to be a highly specific sign for liver cirrhosis or others chronic liver disease, noting that it was absent in all the normal subjects examined.

In the index study, the mean value of the caudate lobe in the liver cirrhosis subjects was significantly higher than that of the normal subjects $(5.25 \pm 0.91 \text{ vs } 3.78 \pm 0.56 \text{ cm})$. This could be attributed to the fact that the venous drainage of the caudate lobe is sustained by emissary veins that pass directly from the caudate lobe to the vena cava, thus fibrosis and subsequent narrowing resulting in obstruction of the hepatic

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veins in cirrhosis causes greater blood flow through the caudate lobe, thereby resulting in hypertrophy [15].

Previous studies have shown different sensitivities and specificities of the caudate to right lobe ratio in diagnosing liver cirrhosis [28,37]. In a study conducted by Balla et al. [28] in Sudan on 50 patients with liver cirrhosis and other chronic liver disease from schistosomiasis and 20 controls revealed that the caudate-to-right lobe ratio was notably higher in patients with these liver diseases with ratios as high as 0.70 in patients with decompensation. Likewise, Harbin et al. [21] study conducted in United States, reported a sensitivity of 84% and a specificity of 100% in diagnosis of cirrhosis based on the criterion of a caudate-to-right lobe ratio greater than or equal to 0.65 (borderline, 0.60-0.65), while Giorgio et al[30]in Italy, reported a sensitivity of 43% and specificity of 100%. Awaya et al. [11] in Japan, examined 121 patients with pathologically proven chronic liver disease and 115 controls using MRI, reported a sensitivity and specificity of 71.7% and 77.4% respectively.

Report has shown that Computed tomography scan have been reported to be more valuable when compared with ultrasound scans for the evaluation of deep soft tissue structures, and it is the imaging modality employed in this study to position beam attenuation on cirrhotic liver [38]. It is however important to note that in this study 91 (84.7%) of the liver cirrhosis cases had caudate to right lobe ratio greater than 0.66. while 102 (95.3%) of the controls had a caudate to right lobe ratio less than 0.55. Findings from this study have shown that the caudate to right lobe ratio is an objective and reproducible non-invasive assessment of the liver in patients with suspected or clinical features of liver cirrhosis and other related chronic liver disease.

Conclusion

Liver cirrhosis was commonly seen in older adults and also male preponderance was noted in this study. The caudate lobe size as well as caudate-to-right lobe ratio is significantly increased in liver cirrhosis subjects as compared with the controls. Thus, fulfilling the aim of this study, and determining the significance of caudate-to-the right lobe ratio in the diagnosis of liver cirrhosis in a Nigerian population. Therefore, from this study, caudate-to-right lobe ratio shows a very strong reliable parameter with a high reliability for diagnosing liver cirrhosis and other chronic liver diseases, even in its early asymptomatic stage. From all these findings we concluded that; the caudate-to-right lobe ratio in subjects with established liver cirrhosis was significantly higher when compared with that of normal subjects and there was a significant difference in the caudate-to-right lobe ratio of subjects with suspected/ established liver cirrhosis when compared with subjects with apparently normal liver.

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