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Correlation Between Clinical Features of Type 2 Diabetes Mellitus with CT Findings of Fatty Liver Patients

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ABSTRACT

People with fatty liver disease are at major risk of liver cirrhosis and malignancies. This study aims to evaluate the correlation between fatty liver and diabetes features on computed tomography (CT) using Hounsfield units for the liver and spleen. The research was conducted in Jeddah Hospital's Medical Imaging Department and CT scan department from March 2018 until March 2020. A total of 50 patients with diabetes were chosen randomly, with males (26) and females (24) ranging in age from 31 to 80 years old. Descriptive statistics of body mass index were recorded for the liver and the spleen; the main liver enzymes were Alanine aminotransferase (ALT), Gamma-glutamyltransferase (GGT), albumin, total bilirubin, and direct bilirubin, which were measured and analyzed using the Statistical Package for the Social Sciences program, version 23. We found a significant correlation of ALT and direct bilirubin with liver and spleen HU at p value < 0.017 and < 0.073, respectively; the mean and standard deviation for the other liver enzymes GGT, albumin, and total bilirubin in segment 3 of the left liver were 45.48 ± 7.077 HU, 45.00 ± 7.797 HU, 36.67 ± 5.776 HU, and 37.23 ± 4.885 HU, respectively. We concluded that fatty liver is associated with type 2 diabetes mellitus symptoms such as high ALT and direct bilirubin, with no significant association between GGT, albumin, total bilirubin, and liver and spleen HU.

Keywords: Computed tomography, diabetes mellitus (DM), fatty liver, hounsfield units, liver enzyme

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INTRODUCTION

Type 2 diabetes mellitus (T2DM) is becoming more prevalent worldwide. Globally, 366 million people were diagnosed with diabetes mellitus in 2011, which is anticipated to rise to 552 million by 2030 (Whiting et al., 2011).

Furthermore, there is substantial evidence that patients with T2DM have a high prevalence of fatty liver (Nakahara et al., 2013). As a result, fatty liver disease may pose a significant mortality risk for people with diabetes who also have liver disorders (i.e., cardiovascular disease, cirrhosis, hepatocellular carcinoma, non-liver cancer, and diabetes mellitus). Nonalcoholic fatty liver disease (NAFLD) is when the liver accumulates excessive fat even though the person drinks little or no alcohol. This problem affects at least half of T2DM patients. As a result, assessing fatty liver and related variables in individuals with diabetes mellitus, particularly T2DM, is crucial (Lonardo et al., 2015).

A liver biopsy is a gold standard for diagnosing fatty liver. However, a liver biopsy is not a reliable tool for detecting and assessing fatty liver in a screening assessment because of the procedure's invasiveness, methods, and sampling variability (Ballestri et al., 2012).

The use of abdominal echo examination as a screening and diagnostic test to detect the presence of fatty liver and determine the severity of the condition has long been common; however, researchers have lately reported on the utility and benefits of this test for patients with fatty liver and T2DM, as CT is used to estimate the liver-to-spleen (L/S) Hounsfield unit (HU) ratio (Nagata et al., 2014).

The liver attenuation measured by CT imaging for an average person is around 55 HU, around 10 HU more than that of an average spleen. Because fat has a low attenuation (less than 100 HU), increasing fat accumulation in the liver results in a corresponding decrease in density. To minimize variances across different CT scanner modalities, as reference values, a liver-to-spleen ratio of less than 0.8–1.1 and a liver minus spleen attenuation of less than 9 HU for that spleen are used. However, a simple assessment of liver attenuation using an unenhanced CT image is the best approach for predicting abnormal liver fat content in diabetic-specific T2DM patients. As a result, the spleen's attenuation measurement has no bearing on predicting hepatic fat content. We can avoid invasive biopsy procedures for the liver using these criteria (Osama et al., 2020).

CT imaging determines the L/S ratio, which has recently been found to be beneficial for diabetes mellitus patients (Osama et al., 2020). For example, serum adiponectin 1209 levels have been associated with the L/S ratio (Yoneda et al., 2007). In liver illnesses, CT scans of visceral adipose tissue (VAT) are considered a useful measure of precancerous lesions such as hepatocellular carcinoma. However, the relationship between the L/S ratio and diabetes mellitus clinical markers such as VAT, subcutaneous adipose tissue (SAT), body mass index (BMI), alcohol intake, and various liver enzymes is yet unknown (Yoneda et al., 2007).

For assessing and analyzing fatty liver, CT imaging is regarded as a valid approach. The L/S ratio, the ratio of the liver parenchyma and splenic texture intensities, can be calculated using CT (Matteoni et al., 1999; Osawa & Mori, 1996).

For those at risk of developing metabolic disorders, such as T2DM, CT is a good modality for fat measures in the liver. Thus, the purpose of this research is to determine whether there is a correlation between fatty liver and diabetes features according to CT using HU for the liver and spleen by assessing and characterizing the most common liver enzymes (Alanine aminotransferase [ALT], Gamma-glutamyltransferase [GGT], albumin, total bilirubin, and direct bilirubin) using L/S HU.

MATERIALS AND METHODS

The research was carried out at Jeddah hospital's Medical Imaging Department and CT scan department. Sudan University of Science and Technology in Khartoum and the Department of Radiological Sciences are conducting research and have been accepted by the ethical approval board in Sudan.

Cases were analyzed retrospectively from a database of patients who underwent abdomen CT scans between March 2018 and March 2020. A straightforward sampling procedure was used to choose 50 patients at random. Liver function tests were performed to analyze the morphology and function of the liver, spleen, and pancreas for all patients with T2DM. All individuals studied had non-enhanced CT scans of the liver.

Inclusion Criteria

Patients with diabetes mellitus, either confirmed or newly diagnosed, who had a fasting plasma venous glucose level less than 7 mmol/l (126 mg/dl) or a random or two-hour postprandial plasma venous glucose level less than 11.1 mmol/l (200 mg/dl) according to the World Health Organization's (1999) criteria were included.

Exclusion Criteria

Patients with normal results were non-diabetic, and patients aged < 18 years were excluded.

CT Liver Protocol and Attenuation Measurements

However, the best method for predicting the pathological fat content of the liver for a person with T2DM using CT is the simple measurement of liver attenuation on unenhanced CT scans. The abdominal CT scans were performed on a (TOSHIBA) CT machine at 120 kV, 50-100 mA (AP&LAT), and a 5 mm slice thickness (1 mm for the Axial plane, −1 mm for the Coronal plane) automatically. With a pitch of 0.8 mm, collimation was 0.5 × 80 mm. Every patient was scanned from above the diaphragm to the level of the iliac crests supine,

usually feet first on the scanner. The patients were instructed to hold their breath at the end of inspiration. We measured five regions of interest within the liver on the CT scans of each patient: the left liver lobe (segment 3), right liver lobe (segments 5 and 6), middle of the spleen, and body of the pancreas. Attenuation measurements were obtained for each region of interest, including larger liver and spleen areas. Regions excluded were of non-uniform parenchymal attenuation, including apparent hepatic vessels. Additionally, two-dimensional axial and coronal measurements of the liver and spleen sizes were obtained.

When using computed tomography (CT) imaging to measure liver attenuation, an average liver CT density (attenuation) measures approximately 55 HU, about 10 HU higher than the average spleen. Fat has low attenuation (−100 HU), so a proportionate decrease in density is seen with increasing fat accumulation in the liver. A liver-to-spleen ratio less than 0.8–1.1 and a liver minus spleen attenuation less than −9 HU for that spleen is used as a reference value to minimize variations across different CT scanner modalities.

Blood Sample for Liver Function Test

A disposable plastic syringe drew 5 mL of venous blood from each patient. The pathology department used an automatic 550 Express Plus Chemistry Analyzer to test serum bilirubin, ALT, aspartate aminotransferase (AST), alkaline phosphatase (ALP), GGT, albumin, total bilirubin, direct bilirubin, and prothrombin time (PT). ALT (10–45) U/L, GGT (8–61) U/L, albumin (32–48) g/L, total bilirubin (0–26) umol/L, and direct bilirubin (0-5) umol/L were all within the average range.

Statistical Analysis

Statistical Package for the Social Sciences, version 23, a statistical software package, was used to analyze the data (SPSS Inc, Chicago, IL). Both frequency and percentage are used. The descriptive analysis results are presented as the standard deviation of the mean to describe the qualitative data. Different populations were sampled to compare the means of two continuous, normally distributed variables; the student's t-test was utilized. All patients' CT attenuation values of the liver, spleen, and pancreas were compared using an independent sample t-test. The duration of T2DM and the CT mean attenuation values for the liver, spleen, and pancreas were correlated using the Pearson correlation coefficient. If the *P* value was less than 0.05, it was considered significant.

RESULTS

A total of 50 people with T2DM were included in this study. Table 1 presents the gender distribution of the participants, with 48% female and 52% male.

Table 2 shows the descriptive statistics of age, BMI, duration, and liver spleen HU (min, max, mean ± standard deviation). The mean and standard deviation for age was 57.52 ± 11.755, while BMI was 31.21±6.800, the duration of T2DM was 13.56 ± 6.80, liver HU (left liver lobe, segment 3) was 44.62±7.340, and spleen HU was 52.48 ± 8.057. Table 3 compares the mean ALT and the mean HU for the liver and the spleen.

Segment 3 of the left liver lobe had a mean and standard deviation of 51.00 ± 2.608; the mean HU for the spleen was slightly higher than that of the liver and measured 59.20 ± 1.059 compared with normal ALT levels for liver HU. The mean and standard deviation for segment 3 of the left liver lobe was 43.20 ± 6.888, and average spleen HU ALT levels were 51.10 ± 7.715. The *P* value was 0.017 indicating a significant correlation of ALT for the liver HU, and the *P* value for the spleen HU was 0.044.

Table 4 compares the mean GGT levels for the liver and the spleen. GGT levels were high for segment 3 of the left liver lobe with a mean and standard deviation of 45.48 ± 7.077. The spleen HU mean was slightly higher than the liver's, measuring 54.92 ± 6.097; the average GGT levels for segment 3 of the left liver lobe were 44.14 ± 7.446 HU, and the average levels of GGT for the spleen were 51.47±8.654 HU. There was a *P* value of 0.724 for the HU of the left liver lobe, segment 3, and a *P* value of 0.368 for the spleen HU.

Table 5 compares the mean albumin levels for the liver and the spleen. Albumin levels were low for segment 3 of the left liver lobe, with a mean and standard deviation of 45.00 ± 7.797. The mean HU for the spleen was slightly higher than that of the liver, measuring 53.67 ± 8.335; the average albumin levels for segment 3 of the left liver lobe were 44.57 ± 7.369 HU, and the average levels of albumin for the spleen were 52.32 ± 8.103 HU. There was a *p* value of 0.894 for the HU of the left liver lobe, segment 3, and a *p* value of 0.705 for the spleen HU.

Table 6 compares the mean total bilirubin levels for the liver and the spleen. Total bilirubin levels were high for segment 3 of the left liver lobe, with a mean and standard deviation of 46.67 ± 5.776. The mean HU for the spleen was slightly higher than that of the liver, measuring 54.33 ± 8.145; the average total bilirubin levels for segment 3 of the left liver lobe were 44.49 ± 7.460 HU, and the average levels of total bilirubin for the spleen were 52.36 ± 8.125 HU. There was a *P* value of 0.623 for the HU of the left liver lobe, segment 3, and a *p* value of 0.685 for the spleen HU.

Table 7 compares the mean direct bilirubin levels for the liver and the spleen. Direct bilirubin levels were high for segment 3 of the left liver lobe, with a mean and standard deviation of 47.23 ± 4.885. The mean HU for the spleen was slightly higher than that of the liver, measuring 55.92 ± 6.304; the average direct bilirubin levels for segment 3 of the left liver lobe were 43.70 ± 7.877 HU, and the average levels of direct bilirubin for the spleen were 51.27 ± 8.325 HU. There was a *p* value of 0.138 for the HU of the left liver lobe, segment 3, and a significant correlation with a *p* value of 0.073 for the spleen HU.

Table 1

Frequency distribution of gender

Gender	Frequency	Percent
Female	24	48.0
Male	26	52.0
Total	50	100.0

Table 2

Descriptive statistical analysis of age, BMI, duration, liver spleen, and pancreas HU (min, max, mean ± Std. Deviation)

	N	Minimum	Maximum	Mean	Std. Deviation
Age	50	31	80	57.52	11.755
Body mass index	50	20	48	31.21	6.800
Duration of diabetes/years	50	4	35	13.56	6.923
Liver CT number HU (LT segment 3)	50	28	60	44.62	7.340
Liver CT number (RT Segment 5)	50	31	56	43.30	7.183
Liver CT number (RT Segment 6)	50	28	54	41.14	6.993
Spleen CT number (middle only)	50	30	71	52.48	8.057
Valid N (listwise)	50				

HU: Hounsfield unit, CT: computed tomography, RT: Right, LT: Left, N: Number

Table 3

Comparison means ALT and means HU for liver and spleen

ALT (10–45) U/L		Report			
		Liver CT number HU (LT segment 3)	Liver CT number (RT Segment 5)	Liver CT number (RT Segment 6)	Spleen CT number (middle only)
High	Mean	51.60	49.80	49.20	59.20
	Std. Deviation	2.608	3.033	3.633	1.095
Low	Mean	49.00	45.80	44.00	56.80
	Std. Deviation	9.247	9.418	9.165	10.710
Normal	Mean	43.20	42.18	39.78	51.10
	Std. Deviation	6.888	6.876	6.339	7.715
Total	Mean	44.62	43.30	41.14	52.48
	Std. Deviation	7.340	7.183	6.993	8.057
P value		0.017	0.055	0.008	0.044

Table 4

Correlation of the means GGT and means HU for liver and spleen

GGT (8–61) U/L		Liver CT number HU (LT segment 3)	Liver CT number (RT Segment 5)	Liver CT number (RT Segment 6)	Spleen CT number (middle only)
High	Mean	45.58	43.58	42.50	54.92
	Std. Deviation	7.077	8.096	6.626	6.097
Low	Mean	47.50	47.50	45.00	56.00
	Std. Deviation	10.607	7.778	8.485	4.243
Normal	Mean	44.14	42.97	40.47	51.47
	Std. Deviation	7.446	6.984	7.117	8.654
Total	Mean	44.62	43.30	41.14	52.48
	Std. Deviation	7.340	7.183	6.993	8.057
P value		0.724	0.687	0.508	0.368

Table 5

Compare mean Albumin and means HU for liver and spleen

Albumin (32– 48) g/L	Liver CT number HU (LT segment 3)	Liver CT number (RT Segment 5)	Liver CT number (RT Segment 6)	Spleen CT number (middle only)
Mean	45.00	43.67	41.17	53.67
Std. Deviation	7.797	8.524	8.377	8.335
Mean	44.57	43.25	41.14	52.32
Std. Deviation	7.369	7.094	6.897	8.103
Mean	44.62	43.30	41.14	52.48
Std. Deviation	7.340	7.183	6.993	8.057
P value	0.894	0.896	0.992	0.705

Table 6

Correlation of the mean Bilirubin total and mean HU for liver and spleen

Bilirubin TOTAL (0–26) umol/l		Liver CT number HU (LT segment 3)	Liver CT number (RT Segment 5)	Liver CT number (RT Segment 6)	Spleen CT number (middle only)
High	Mean	46.67	44.33	42.33	54.33
	Std. Deviation	5.774	6.351	6.351	8.145
Normal	Mean	44.49	43.23	41.06	52.36
	Std. Deviation	7.460	7.290	7.088	8.125
Total	Mean	44.62	43.30	41.14	52.48
	Std. Deviation	7.340	7.183	6.993	8.057
P value		0.623	0.800	0.764	0.685

Table 7

Compares mean Bilirubin direct and means HU for liver and spleen

Bilirubin direct (0–5) mol/l		Liver CT number HU (LT segment 3)	Liver CT number (RT Segment 5)	Liver CT number (RT Segment 6)	Spleen CT number (middle only)
High	Mean	47.23	44.46	41.62	55.92
	Std. Deviation	4.885	5.190	5.440	6.304
Normal	Mean	43.70	42.89	40.97	51.27
	Std. Deviation	7.877	7.785	7.522	8.325
Total	Mean	44.62	43.30	41.14	52.48
	Std. Deviation	7.340	7.183	6.993	8.057
P value		0.138	0.504	0.779	0.073

DISCUSSION

Fatty liver may pose a significant mortality risk due to liver damage for people with diabetes. Worldwide, hepatocellular carcinoma is associated with obesity, and type 2 diabetes mellitus (T2DM) is rising. As a result, assessing and diagnosing fatty liver and related variables in diabetic patients is crucial (Manaviat et al., 2008).

Our research aims to determine whether there was a correlation between fatty liver detected by CT and the clinical features of T2DM. We studied 50 patients with abdominal CT scans (for clinical indications such as abdominal discomfort and abnormal ultrasonography results) from March 2018 to March 2020. Patients who met the following criteria were not eligible to participate in the study: (1) patients with normal liver tests but no T2DM, (2) children, and (3) patients with a splenectomy history.

T2DM was found to be substantially linked with fatty liver in the current investigation. Fatty liver is more common in those with metabolic problems, including obesity and T2DM. Osama et al. observed in their research on T2DM patients that fatty liver is highly linked with T2DM features, especially at younger ages (Osama et al., 2020).

This study included 50 T2DM patients. Table 1 presents the sample's distribution of gender: 48% were female, and 52% were male.

Table 2 presents the descriptive statistics (min, max, mean ± standard deviation) of age, BMI, duration, L/S, and pancreas HU: age was 57.52 ± 11.755, and BMI was 31.21 ± 6.800. The probability of increased ALT levels was considerably lower for longer durations of diabetes (Manaviat et al., 2008). Males were more likely than females to have increased ALT levels.

Table 1 presents the mean and standard deviation of HU for segment 3 of the left liver lobe. The mean and standard deviation for the left liver lobe, segment 3, was 44.62 ± 7.340, while the mean and standard deviation for the right liver lobe, segment 5, was

43.30 ± 7.183; these measurements are less than that of the HU for the spleen, which was 52.48 ± 8.057. The HU of the pancreas was lower than that of the liver and the spleen for people with diabetes, with values of 36.08 ± 9.041. These statistical measurements agree with the findings reported by Osama et al. (2020), who evaluated the HU attenuation of the liver and spleen for people with and without diabetes and found that the liver attenuation for people with diabetes was significantly lower than for people without diabetes. People with T2DM had considerably lower CT attenuation for segment 3 of the left liver lobe than those without diabetes (56.2 ± 10.69 HU vs. 44.62 ± 9.93 HU, $p<0.01$). For people with T2DM and people without diabetes, the CT attenuation of the right lower lobe (segment 5) was 43.46 ± 9.77 HU and 56.02 ± 10.65 HU, respectively ($p<0.01$) and 44.62 ± 9.93 HU and 56.2 ± 10.69 HU, respectively ($p<0.01$), for segment 6.

Table 3 presents the relation between the mean ALT levels and the mean HU for the liver, spleen, and pancreas at a p value < 0.01. This study found a correlation between ALT levels and liver HU for the left liver lobe, segment 3, with a p value of 0.01. There was also a significant correlation for the right liver lobe, segment 6, with a p value < 0.008, and there was a significant correlation between the ALT levels and the HU of the spleen, with a p value < 0.044. ALT levels were elevated for people with T2DM, with high levels in segment 3 of the left liver lobe, with a mean and standard deviation of 51.00 ± 2.608. The mean spleen HU was slightly higher than the liver and measured 59.20 ± 1.059. Typical ALT levels for the left liver lobe, segment 3, were 43.20 ± 6.888 HU, and typical ALT levels for the spleen were 51.10 ± 7.715.

Average GGT levels in the liver and spleen were (8–61)U/L, and GGT levels were high in segment 3 of the left liver lobe with a mean and standard deviation of 45.48 ± 7.077. The mean spleen HU was slightly higher than that of the liver and measured 54.92 ± 6.097, and GGT levels were low in segment 3 of the left liver lobe with a mean and standard deviation of 47.50 ± 10.607. The spleen HU had low GGT levels measuring 56.00 ± 4.243; average GGT levels for segment 3 of the left liver lobe HU were 44.14 ± 7.446, and typical GGT levels for the spleen HU were 51.47 ± 8.654. There was a p value of 0.724 for the HU of segment 3 of the left liver lobe and a p value of 0.368 for the HU of the spleen. These findings show no correlation between GGT levels and HU attenuation in the liver and the spleen (Table 4).

Compare Tables 3 and 4 with the results reported by Sakitani et al. (2017), who discuss elevated levels of liver enzymes with HU L/S and the clinical characteristics of T2DM. Their findings indicate that male fatty liver patients had significantly higher albumin, bilirubin, GGT, ALT, and triglyceride levels than female patients with fatty liver ($p<0.0001$).

Typical albumin levels in the liver and spleen were 32–48 g/L, and albumin levels were low for the left liver lobe, segment 3, with a mean and standard deviation of 45.00 ± 7.797. The mean spleen HU was slightly higher than that of the liver and measured 53.67 ±

8.335, while typical albumin levels for segment 3 of the left liver lobe were 44.57 ± 7.369 and typical levels of albumin for the spleen HU were 52.32 ± 8.103. There was a *P* value of 0.894 for the left liver lobe, segment 3, and a *p* value of 0.705 for the spleen HU with no significant correlation between albumin levels and L/S HU attenuation in CT (Table 5).

The average limit for total bilirubin levels in the liver and the spleen was 0–26 mol/l; in our study, total bilirubin levels were high for segment 3 of the left liver lobe with a mean and standard deviation of 46.67 ± 5.776. The mean spleen HU was slightly higher than the liver's and measured 54.33 ± 8.145 compared with typical total bilirubin levels for segment 3 of the left liver lobe 44.49 ± 7.460 while typical levels of total bilirubin for the spleen HU were 52.36±8.125. There was a *p* value of 0.623 for the HU of the left liver lobe, segment 3, and a *p* value of 0.685 for the spleen HU (Table 6).

Comparing Tables 6 and 7, which indicate that the average direct bilirubin level is 0–5 mol\l, there was a high direct bilirubin level in the liver and spleen for people with T2DM. The direct bilirubin level was high in segment 3 of the left liver lobe, with a mean and standard deviation of 47.23 ± 4.885. The mean spleen HU was slightly higher than that of the liver and measured 55.92 ± 6.304 compared with typical levels of direct bilirubin for the left liver lobe, segment 3, which was 43.70 ± 7.877, while typical levels of direct bilirubin for the spleen HU were 51.27 ± 8.325. There was a *P* value of 0.138 for the HU of the left liver lobe, segment 3, and a significant correlation with a *P* value of 0.073 for the spleen HU. Thus, we found no significant relationship between high levels of direct bilirubin for the HU of the left liver lobe, segment 3, and a slight correlation of spleen HU with direct bilirubin enzyme levels with a *P* value ≥ 0.073.

There are limitations to our study. First, the sample size of patients was small, and a large sample of random patients is recommended to give more accurate results. Second, these results should be compared against people without diabetes, or another control group, using CT scans and laboratory testing. Third, the same patients should be investigated using another imaging modality to eliminate radiation hazards for patients that would otherwise result from CT scans. Our study is beneficial because although computerized tomography is an invasive technique, it gives accurate and reliable measurements to assess and characterize the liver and spleen to study fatty liver for people with T2DM.

CONCLUSION

This study found that fatty liver was associated with clinical characteristics of T2DM. Individuals with T2DM had higher incidences of abnormalities for the liver enzymes evaluated. Fatty liver was associated with features of T2DM, including elevated ALT and direct bilirubin levels with a significant correlation with L/S HU and no significant correlation of GGT, albumin, and total bilirubin with L/S HU.

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