Original Article

Ultrasonographic Features Associated with Diffuse Hepatosteatosis among Diabetic Obese and Normal Body Mass Index Patients

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Abstract

Background: The purpose of the study is to evaluate and compare the changes associated with hepatosteatosis in diabetic obese versus diabetic normal-weight patients through ultrasonography. It is estimated that with the prevalence of about 30%–75% of obese individuals accordingto the body mass index (BMI) criteria are at increase risk of developing simple fatty live. Besides obesity, diabetes mellitus is also considered to be one of the important causes of hepatosteatosis. **Methods:** This prospective study was conducted in February 2015–December 2015 on a group of 181 diabetic patients, including 65 males and 116 females with an age range of 40–80 years. The patients were divided into two diabetic groups: those having a BMI ≥30 kg/m^2 were included in the obese group (n = 116) and those with a BMI of 18.5–25 kg/m^2 were included in the normal BMI group (n = 65). Ultrasound machine Esaote MyLab 50 equipped with a 3.5–5 MHz curvilinear multifrequency transducer was used to scan the liver. Independent samples t-test was performed to compare the liver span in the two groups. Chi-square tests were applied to compare the frequencies of fatty changes, border, and surface characteristics. **Results:** The presence of fatty changes among obese groups was statistically significant in the diabetic obese group compared to the normal-weight individuals with $P < 0.0001$. Similarly, hepatic spans were found to be significantly greater in the diabetic obese group than the diabetic normal BMI group on independent samples t-test with $P < 0.0001$. Females were seen to develop hepatosteatosis more frequently compared to males in all diabetic individuals with $P = 0.02$. **Conclusion:** It is concluded that diabetic obese patients are more prone to develop hepatosteatosis as compared to normal BMI diabetic individuals.

Keywords: Diabetes, hepatosteatosis, nonalcoholic fatty liver disease, obesity

Introduction

Hepatosteatosis or fatty infiltration of the liver in itself is characterized by intracellular deposition of excess triglycerides within hepatocytes, which is now exceedingly been termed as nonalcoholic fatty liver disease (NAFLD) when occurs in the absence of excessive alcohol consumption.[1-3] The condition is known to be extremely prevalent in obese and diabetic patients.[2-5] Although fatty liver disease is usually asymptomatic, patient's clinical history including alcohol abuse, chemotherapy, diabetes mellitus (DM), elevated liver function test (alanine aminotransferase, aspartate transaminase, and gamma-glutamyl transferase), pregnancy, and obesity is usually present.[6] Severe fatty infiltration leads to hepatomegaly coupled with inflammation and fibrosis.[7] It is extremely prevalent in obese and diabetic patients.[8-12]

Studies found that body mass index (BMI) is one of the most classical epidemiological indexes assessing obesity and it is associated with the risk of fatty liver.[13-15] As compared with the normal BMI, the risk of fatty liver was approximately 4.1–14-fold

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increase in higher BMI.[16] Although a number of studies reported the association between BMI and fatty liver disease, previous studies were mostly limited to dividing the BMI into categorical variables (underweight, normal, overweight, and obesity).[14-16]

An ultrasound of the liver is an easy way to detect and evaluate fatty liver both qualitatively and quantitatively. On ultrasound, fatty change in the liver caused it to appear bright and echogenic as compare to renal cortex [Figure 1]. The finding is due to increased ultrasound beam reflection from accumulated fatty droplets. Posterior attenuation of the ultrasound beams with impairment of visualization of hepatic and portal veins, bile ducts, gallbladder walls, and diaphragm is an additional ultrasound finding.[17,18] Important quantitative techniques such as sonographic hepatorenal index (SHRI) and controlled attenuation parameter (CAP) have been introduced to assist the evaluation of hepatosteatosis.[17]

The findings of ultrasound have been reported to be highly reliable. A sensitivity of 100% and a specificity of 90% were reported with fatty changes as low as ≥20% found out on histopathological assessment.[19] Ultrasound also has several other advantages of being easy to perform and interpret, widely available, and less costly.[20] Other imaging techniques such as computed tomography or magnetic resonance (MR) imaging with chemical shift imaging, MR elastography, and spectroscopy to provide an estimation of hepatic fat content also show similar diagnostic characteristics, but are more expensive.[1,17,18,21,22] Biopsy, however, is considered as the gold standard for the diagnosis of hepatosteatosis.[23,24] It, however, has its own risks and limitations of being invasive, painful, possibility of bleeding, etc.[1] Various studies showed that raised BMI was an independent risk factor for hepatosteatosis.[13-16] Therefore, the current study plan incorporates both the factors (diabetes and BMI) together to evaluate for hepatosteatosis using ultrasound as an investigating modality.

Materials and Methods

A comparative, analytical study was conducted in February 2015–December 2015 after approval from the ethical review board of the institution (IRB Reference Number = IRB-UOL/150816/0A45; IRB Number = 1046). Written informed consent was taken from all the patients.

The study was conducted on patients having diabetes for at least 5 years duration, confirmed from their previous clinical record. These patients came to the ultrasound clinic for abdominal ultrasound with complaints other than involving hepatic pathologies. The patients were categorized into two groups: first having normal BMI, comprised those individuals who were having a BMI in the range of 18.5–25 kg/m^2, and those having a BMI ≥30 kg/m^2 were included in the obese group. BMI was calculated using the formula of weight in kilograms (kg) divided by height in meters squared (m^2).[12] Nondiabetic individuals, cirrhotic patients, patients with disrupt corticomedullary ratio of kidneys, cystic liver disease, and liver fibrosis were excluded from the study.

A total of 181 diabetic patients including 65 males and 116 females with an age range of 40–80 years (mean: 51.7 years) were included in the study. Ultrasound examinations were done blindly about the patient condition using Esoate MyLab 50 ultrasound machine equipped with a 3.5–5MHz curvilinear multifrequency transducer by a radiologist having 10 years of experience.

The right and left lobes of the liver were imaged using intercostal/subcostal approach and anterior subxiphoid approach with the patient in the left posterior oblique position or left lateral decubitus position for the left lobe, so that the liver moves slightly medial and inferior. The assessment was made in both sagittal and transverse planes with deep inspiration. Liver length, parenchymal echogenicity, and surface and border characteristics were assessed in all cases. The hepatosteatosis was diagnosed in the liver having increased parenchymal echogenicity compared to the cortex of the kidney.

Independent samples *t*-test was performed to compare the liver span in the two groups. Chi-square tests were applied to compare the frequencies of fatty changes, border, and surface characteristics. A two-sided *P* value of 0.05 was considered statistically significant. An area under the curve was also calculated for the hepatic span between the two groups which showed sensitivity and specificity.

Results

The distribution of diabetic normal BMI and diabetic obese patients in male and female is given in Table 1. The average liver span was found to be 14.2 ± 1.81 cm in diabetic normal-weight and 15.3 ± 1.43 cm in diabetic obese patients. It was significantly greater in the diabetic obese group than the normal BMI group on independent samples *t*-test with $P < 0.0001$ [Table 2 and Figure 2]. An area under the curve was also calculated for the hepatic span between the two groups, which showed a sensitivity and specificity of 68% and 69% with a hepatic span of 14 cm as a cutoff value. It also showed $P < 0.0001$ [Figure 3]. Out of 181 diabetic patients,

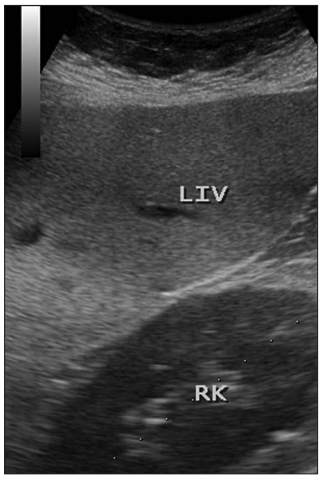

Figure 1: Ultrasound scans show hepatosteatosis in diagram. Echogenicity of the liver parenchyma is hyperechoic in comparison with echogenicity of renal parenchyma

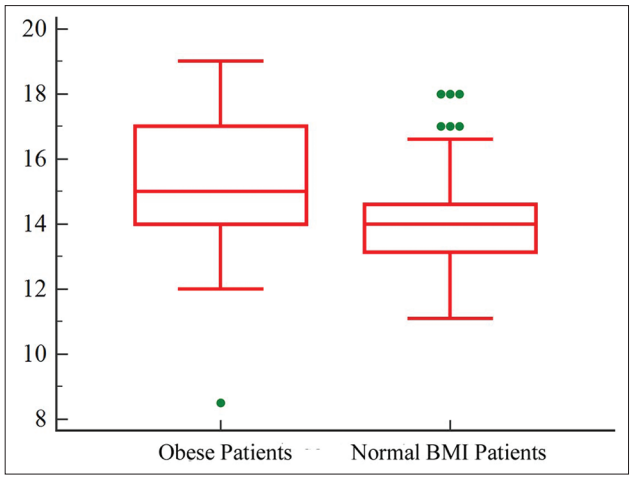

Figure 2: Box and whisker plot represents the hepatic length (cm) of diabetic normal-weight (body mass index: 18.5–25 kg/m^2) and diabetic obese (body mass index: ≥30 kg/m^2) patients. Boxes represent the lines at lower, median, and upper quartile values, while the whiskere show the extent of remaining data, excluding only the outliers

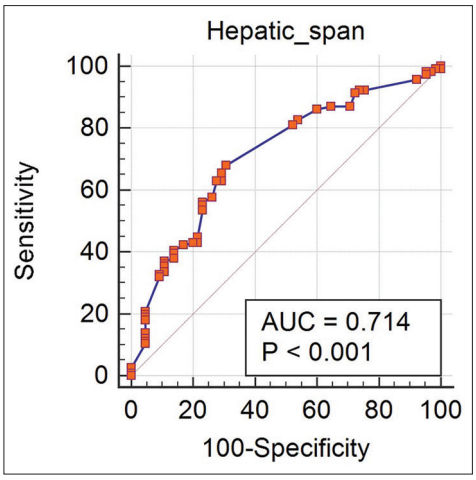

Figure 3: Receiver operating characteristic curve analysis shows the sensitivity of 68.10% and specificity of 69.23% for hepatic length of 14 cm with *P* value of < 0.0001

Table 1: Descriptive statistics of patient's variables in diabetic normal-weight and diabetic obese group

	Number of patients (*n*)	Age range (mean), years	Gender male:female
Normal-weight group	65	40-78 (53.5)	33:32
Obese group	116	40-80 (50.7)	32:84
Total	181	40-80 (51.7)	65:116

Table 2: Comparison of hepatic spans in the two diabetic groups (normal weight and obese)

	Normal-BMI group (65)	Obese group (116)	Total (181)
Minimum	11.1	8.5	8.5
Maximum	18	19	19
Mean	14.2±1.8147	15.35±1.4311	15±1.8
Two-tailed probability (*t*-test)		*P*<0.0001	

BMI: Body mass index

Table 3: Comparison of liver parenchymal changes in male and female patients

	Parenchymal changes		Total
	Fatty	Nonfatty	
Males	30	35	65
Females	74	42	116
Total	104	77	181
χ^2		5.273	
Degrees of freedom		1	
Significance level (*P*)		0.0217	

104 (57.5%) showed fatty liver associated with hyperechoic hepatic parenchyma on ultrasound. Females were seen to develop hepatosteatosis more frequently compared to males in all diabetic individuals with *P* value of 0.02 using Chi-square test [Tables 1 and 3]. The presence of fatty changes among diabetic obese group was statistically significant compared to normal-weight individuals with $P \leq 0.0001$ compared using Chi-square test. The presence of bumpy hepatic surface and irregular borders was seen only in four and three patients, respectively, with fatty changes in the liver without any significant statistical difference in the two groups.

Discussion

Our results clearly indicated a higher degree of risk, associated with obesity, of developing hepatosteatosis in diabetic individuals. In our understanding, the reason for this accentuated risk might be increased insulin resistance known to occur in obesity. Progressive obesity and ectopic fat deposits in the body cause disturbance in the lipid metabolism and result in insulin resistance. Elevated availability of circulating free fatty acid levels occurs which is partly related to diminished suppression of adipose tissue lipolysis by insulin and consequently liver synthesizes triglycerides.[24,25] The liver damage eventually results from a combination of oxidative stress and aberrant inflammatory response of the hepatocytes, which initiates apoptosis.[26]

It has also been suggested by Bhatt and Smith that insulin resistance in the context of obesity occurs in a state of continuous intake of excessive amount of calories. They recommended that maintaining a healthy lifestyle with weight reduction and balanced calorie-restricted diet in combination with exercise can reverse the usual course of NAFLD.[3]

De Moura Almeida *et al*.[26] reported that the reliability of ultrasound decreases as obesity becomes more and more severe. The reason suggested was the deposition of more and more layers of fat in the abdominal wall affecting the image quality and causing technical difficulties in the performance of the sonographic examination. We did not account for these effects in our study, as we did not further subgroup our obese

population into moderately obese and severely obese groups. This pitfall of ultrasound imaging, however, exists but may vary according to the operator and ultrasound equipment used.

In this study, females were seen to have fatty liver significantly more than males, which when compared using Chi-square test yielded the *P* value of 0.0217. This result differed slightly from the report of Suzuki and Abdelmalek.[27] who suggested that men are more prone to develop fatty liver disease compared to women, but they also mentioned that the underlying mechanisms for gender differences are very complex and multifactorial. The women who are described to be hormonally protected premenopausally lose this protection after menopause and get more prone to deposit fat in subcutaneous as well as in viscera. In our study, the fact that all patients were above 40 years of age explains the cause of women having more fatty liver than men.

Although there have been few reported instances with increase risk of hepatosteatosis in diabetic individuals with presence of obesity.[3] Our study is unique in a sense that it incorporated both the factors together in a single study population using ultrasound as an investigating modality. In our opinion, however, the study had some limitations such as the sample size for this study should have been bigger. In addition, a normal nondiabetic group should have been added to have a better insight of the risk of development of NAFLD in normal-weight diabetics and obese diabetics.

Conclusion

Diabetic obese individuals are more prone to develop hepatosteatosis as confirmed by the ultrasound in our study.

Limitation

Patients with BMI 25–30 kg/m^2 were not included in our study because most of the liver's size overlaps in two groups and also DM duration, timing (onset age), severity (high HBA1C >7), and sequence of obesity and DM were in the limitation of our study.

Recommendation

Further researches should made to check DM duration, timing (onset age), and severity (high HBA1C > 7) to know that all of these have a proportional relationship with hepatosteatosis and also to find the sequence of obesity and DM. More researches should be done with large sample size having variables: SHRI and CAP scoring/grading to get the significantly higher results in DM/obese group in comparison with DM/normal BMI group.

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Conflicts of interest

There are no conflicts of interest.

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