

## The prevalence of fatty liver disease among diabetics in Mosul

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### ABSTRACT

**Objectives:** To examine the occurrence of fatty liver disease in diabetic patients type 1 and 2 disease and to focus the attention in our locality about this serious condition.

**Method:** This prospective study of one hundred ten diabetic patients and one hundred patients as control was conducted in Ibn-Sena Teaching Hospital. Patients and control were referred from Al-Wafa Diabetic Center in Mosul, the outpatient department, and from the Medical Center of Mosul Medical College University of Mosul. All were referred for clinical assessment and for ultrasound examination of their abdomen.

**Results:** The patients include 34 patients with type 1 and 76 patients with type 2 diabetes. Of the 110 patients examined, 52.7% proved to have fatty infiltration in the liver by ultrasonography with no statistically significant difference between male and female.

Patients with type 2 diabetes mellitus were more vulnerable to develop fatty infiltration of the liver than type 1 diabetes mellitus, with statistically significant difference between them. Eighty six percent of patients with NAFLD were type 2 diabetes and 13.7% were type 1 diabetic disease. The control group have NAFLD in 8% only.

The age of the patients shows positive correlation and fatty infiltration in the liver increased with age. The longer the duration of diabetes mellitus makes the patients more likely to develop fatty infiltration in the liver.

The postprandial blood sugar level correlates significantly with the presence of fatty infiltration in the liver while the fasting blood sugar level does not.

**Conclusion:** Nonalcoholic fatty liver disease is common in our diabetic patients, occurs in both type 1 and type 2 diabetes. Ultrasound may be used for epidemiological studies for detection of NAFLD in diabetics.

**Keywords:** Diabetes mellitus; fatty infiltration; Ultrasound.

### الخلاصة

تم اجراء دراسة للتحري عن وجود ترسبات الشحوم في الكبد من عدمه في المرضى المصابين بداء السكر. أجريت الدراسة في مستشفى ابن سينا التعليمي بالموصل على 110 مريض مصاب بداء السكر، 34 منهم مصاب بداء السكر المعتمد على الأنسولين و76 مريض مصاب بداء السكر المعتمد على المعالجة بالحبوب المخفضة للسكر في الدم. وتم كذلك فحص مجموعة ضابطة من 100 شخص لا يعانون من داء السكر. أخذت عينة من دم مرضى السكر لفحص نسبة السكر في الدم وهم صائمون وكذلك بعد الأكل. تم اجراء فحص الأمواج فوق الصوتية للمرضى وللعينة الضابطة للتحري عن وجود ترسبات الشحوم في الكبد.

**النتائج:** تبين ان 52.7% من العينة المفحوصة من مرضى السكر يعانون من وجود ترسبات الشحوم في الكبد، وتبين ان ٨٦% منهم مصابين بداء السكر المعتمد على المعالجة بالحبوب المنخفضة للسكر و13.7% منهم مصاب بداء السكر المعتمد على الانسولين. كذلك تبين ان عمر المريض ومدة الاصابة بالسكر تتناسب طرديا مع درجة الاصابة بترسبات الشحوم في الكبد. نسبة الاصابة بترسبات الشحوم في الكبد في العينة الضابطة كانت ٨% فقط.

**N**onalcoholic fatty liver disease (NAFLD) was described first by Ludwig in 1980<sup>(1)</sup>. Most patients with nonalcoholic fatty liver disease are asymptomatic, but some may complain of fatigue and right upper quadrant abdominal fullness or pain with or without hepatomegaly<sup>(2)</sup>. The prevalence of NAFLD in the general population is estimated to be 20%<sup>(3)</sup>. Nonalcoholic fatty liver disease now refers to a spectrum of diseases of the liver ranging from steatosis (i.e., fatty infiltration of the liver) to nonalcoholic steatohepatitis (NASH) (i.e., steatosis with inflammation and hepatocyte necrosis) to cirrhosis. The prevalence of nonalcoholic steatohepatitis (NASH) in the United States is 2-3% , which makes NASH the potentially most common hepatic disease<sup>(4)</sup>.

Diabetes is an important independent predictor of severe hepatic fibrosis in NASH<sup>(5)</sup>. Up to one third of patients with NAFLD have diabetes or fasting hyperglycemia at the time of diagnosis with NASH<sup>(6-7)</sup>. Nonalcoholic fatty liver disease if untreated, will progress to NASH and end up by cirrhosis, because of that some of them will die in few years time<sup>(8)</sup>. The fibrosis of the liver may progress to cirrhosis, hepatocellular cancer and liver-related death<sup>(9,10)</sup>. The most frequent association of NASH is type 2 diabetes, although difficult-to-control insulin-dependent diabetes may also be affected<sup>(11)</sup>.

In type 2 diabetes mellitus and in obesity, insulin resistance plays a fundamental role and is the most predisposing and reproducible factor in NASH<sup>(12)</sup>.

Ultrasonography of the liver has a sensitivity of 82 to 89 percent and a specificity of 93 percent for identifying fatty liver infiltrate<sup>(13,14)</sup>.

As it is known that nonalcoholic fatty liver (NAFL) is a medical condition that may progress to end-stage liver disease with the consequent development of portal hypertens-

ion and liver failure<sup>(8)</sup>, this study aimed to examine the occurrence of fatty liver disease in diabetes mellitus type 1 and 2 disease and to focus the attention in our locality about this serious condition.

## Methods

This was a prospective study for one hundred ten (110) diabetic patients and one hundred (100) patients as control group referred mainly from Al-Wafa Center in Mosul, the outpatient department, and from the Medical Center of Mosul Medical College University of Mosul, for clinical assessment and for ultrasound examination. The patients' agreements were taken by their verbal consent. The control group was selected randomly from patients consulting the radiology department for ultrasound of the abdomen.

The inclusion criteria and the clinical assessments of the patients and the control group were mainly to exclude the presence of obesity (Body Mass Index (BMI) more than of  $\geq 30$  Kg/m<sup>2</sup>) and to exclude any history of alcohol intake. There must be no evidence of chronic liver diseases, this specifically for history of hepatitis B (HBsAg) and hepatitis C. Furthermore there must be no history of chronic renal diseases.

All the ultrasound examinations were done in Ibn-Sena Teaching Hospital.

The age of the patients ranged from 11 to 73 years, 47 male and 67 female, the duration of diabetes was from 8 to 32 years. While the age of the control group patients ranged from 13 to 75 years, 52 males and 48 female with their age group distribution .

The patients include 34 patients with type 1 and 76 patients with type 2 diabetes mellitus, 43 patients on insulin therapy and 67 on oral hypoglycemic drugs. All the patients had their fasting and postprandial blood sugar done, HbA1c done only for 69 patients who agree to do the test in a private laboratory.

The statistical calculations were done for all parameters and the different variables by using the means, SD, cross-tabulation, the chi-Square test (Fishers exact test).

## Results

Of the 110 patients examined 58 (52.7%) proved to have fatty infiltration in the liver by

ultrasonography and 52 (47.2%) patients had no fatty infiltration in the liver. There was no statistically significant difference between male and female with p-value  $>0.05$  (NS) when tested by the cross-tabulation and the chi-Square test as in table (1):

Table (1): Fatty liver changes in correlation with the sex of the patients

Sex	Non-fatty liver		Fatty liver		p-value
	No.	%	No.	%	
Male	24	51.1	23	48.9	>0.05 (NS)
Female	28	44.4	35	55.6	
Total	52		58		

As it was expected, our study indicates that the type of diabetes mellitus correlates very well with the frequency of fatty infiltration in the liver and was found to have positive correlation

with p-value  $< 0.001$  by using the cross-tabulation and the chi-Square test (Fishers exact test) as in table (2):

Table (2): Fatty liver changes in correlation with the type of diabetes mellitus

DM	Non-fatty liver		Fatty liver		p-value
	No.	%	No.	%	
Type 1	26	76.5	8	23.5	<0.001
Type 2	26	34.2	50	65.8	
Total	52		58		

Patients on oral hypoglycemic treatment as in type 2 diabetes mellitus were more vulnerable to develop fatty infiltration in the liver than those with insulin dependent type 1 diabetes

mellitus with statistically significant difference between them with p-value of  $<0.001$ , although (23.5%) of our patients with type 1 diabetes found to have NAFLD as shown in table (3):

Table (3): Fatty liver changes in correlation with type of treatment

Type of treatment	Non-fatty liver		Fatty liver		p-value
	No.	%	No.	%	
Insulin	29	67.4	14	32.6	0.001
Oral	23	34.3	44	65.7	
Total	52		58		

The age of the patients according to the age groups shows statistically significant correlation, the frequency of the development of fatty infiltration in the liver increases with the

age of the patients as tested by using the cross-tabulation and the chi-Square test as in table (4):

Table (4): Fatty liver changes according to age distributions

Age groups (year)	Non-fatty liver		Fatty liver		p-value
	No.	%	No.	%	
11-20	9	81.8	2	18.2	<0.01
21-30	8	66.7	4	33.3	
31-40	8	81.8	3	18.2	
41-50	11	52.4	10	47.6	
51-60	11	29.7	26	70.7	
>60	5	27.8	13	72.2	
Total	52		58		

As it was expected, the duration of diabetes mellitus makes the patients more likely to develop fatty infiltration in the liver with nearly 74% of the patients with fatty infiltration in the

liver had their duration of diabetes for more than 10 years as indicated by the cross-tabulation and the chi-Square test as in table (5):

Table (5): Fatty liver changes in correlation with the duration of diabetes mellitus

Duration of DM (year)	Non-fatty liver		Fatty liver		p-value
	No.	%	No.	%	
6-9	27	64.3	15	35.7	<0.05
10-14	11	42.3	15	57.7	
≥15	14	33.3	28	66.7	
Total	52		58		

Diabetic patients with fatty liver had higher mean postprandial blood sugar (PPBS) than those with no fatty liver, with a positive correlation between PPBS and NAFLD. Fasting blood sugar (FBS) level and the

HbA1c value showed no significant correlation with the development of NAFLD, from the calculation of the means, SD and the grouping variable between FBS and PPBS as shown in table (6):

Table (6): Fatty liver changes in correlation with FBS, PPBS and Hb1AC

Parameters	Mean ± SD		p-value
	Fatty liver	Non-fatty liver	
PPBS (mmol/L)	21.10 ± 5.65	18.45 ± 5.38	0.01
FBS (mmol/L)	13.68 ± 7.33	12.75 ± 7.80	>0.05 (NS)
HbA1c (%)	9.51 ± 1.59	9.25 ± 1.52	>0.05 (NS)

Of the 100 patients of the control group examined only 8 (8%) proved to have fatty infiltration in the liver by ultrasonography, 5 female and 3 male patients as in table (7):

Table (7): Age distributions of the control group and the NAFLD among them.

Age groups (year)	Number of patients	Fatty liver	Female positive	Male positive
11-20	8	0	5	3
21-30	11	0		
31-40	22	0		
41-50	27	2		
51-60	16	3		
>60	16	3		
Total	100	8 (8%)		

## Discussion

Typical patient with NAFLD as had been described by Powell EE and coauthors, is a middle-aged woman<sup>(15)</sup>. In our studied sample 58 patients were labeled to have NAFLD by ultrasound, 23 male and 35 female patients with no statistically significant difference between male and female.

Males generally have greater abdominal visceral fat mass, which has a lipolytic nature and is in close proximity with the portal system. Furthermore, visceral fat and therefore free fatty acids, exposing the liver to large amounts of oxidizing substances or triglycerides which may either get stored (steatosis) or secreted into the circulation<sup>(16)</sup>. This phenomenon may explain our finding. Furthermore, epidemiologic studies of NAFLD suggest that men are at least as likely as women to have NAFLD or even higher<sup>(6,17,18,24)</sup>. All these findings are similar and support our results.

Fatty liver disease was found in (52.7%) of our patients with diabetes, this result is the same as in other studies, where they found that NAFLD occurs in about 50 percent (range, 21 to 78 percent) of patients with diabetes<sup>(6,7,19)</sup>.

Fifty out of the fifty eight diabetic patients with fatty liver disease, were type 2 diabetes mellitus (86%) of all patients with NAFLD and form (65.789%) of patients with type 2 diabetes mellitus. Furthermore, 44 patients on oral hypoglycemic therapy have NAFLD which makes 75.9% of the patients with NAFLD, this difference in the number is because some of our patients on insulin therapy were originally type 2 diabetes, these findings were similar to others<sup>(6,7,20)</sup>.

Type1 diabetes is less likely to cause NAFLD but in our patients 13.7% of those with NAFLD were type 1 diabetes, which form nearly (23.5%) of our patients with type 1 diabetes. These findings are different from our control group where NAFLD are found in 8% only. Although our control group is not big enough to represent the Iraqi population, our control group had a lower figure of NAFLD if we compare it with other studies<sup>(3)</sup>. The prevalence of NAFLD in type 1 diabetes in our

study is in agreement with other studies where they found even children with type 1 diabetes mellitus may develop NAFLD, although our figure is somewhat higher probably due to the older age group among our adult patients and even among the children in our patients<sup>(11,21,22)</sup>. The established risk factors for NAFLD in children include obesity, insulin resistance, and diabetes<sup>(23)</sup>. Although the evidence of insulin resistance is common among type 2 diabetic in youth, it is also seen in 30% of youth with type 1 diabetes<sup>(35)</sup>. These findings may explain the prevalence of fatty liver in our studied patients with type 1 diabetic disease .

The postprandial blood sugar (PPBS) level correlates significantly with the presence of NAFLD, while the fasting blood sugar (FBS) level and the HbA1c value showed no significant correlation with the development of NAFLD. The PPG is a marker of glycemic burden and is as predictive or more predictive of the risk for complications of diabetes when compared with FPG<sup>(36)</sup>. The positive correlation between fatty liver and the level of postprandial blood sugar may indicate the presence of insulin resistance in this group of patients. Insulin resistance is a major feature of NAFLD that, in some patients, can progress to steatohepatitis<sup>(37)</sup>. The HbA1c level was done only in about 62% of our patients, therefore its value may be not truly representative of the its real correlation with the NAFLD.

Ultrasonography as a diagnostic test had been found to have a sensitivity of 89 percent and a specificity of 93 percent in detecting NAFLD<sup>(13,25)</sup>.

Nonalcoholic fatty liver disease is usually diffusely distributed or occasionally focal. Consequently, CT scans may be misinterpreted as malignant liver masses<sup>(26)</sup>. Few studies compare ultrasound and CT scans for diagnostic accuracy in NAFLD and they were nearly the same with a sensitivity of 75%, 80% respectively<sup>(27)</sup>.

The histopathological diagnosis by liver biopsy is logically the golden standard method for detection of NAFLD, but this requires the equipments, laboratory investigations,

preparation of the patients by doing blood group and cross match , the expertise in doing liver biopsy and the patient's consent because of the expected complication of this rather invasive and sometimes harmful procedure. Furthermore, recent studies have questioned its reliability because it may frequently miss the diagnosis. More than 24% of proven NAFLD may be missed if only one biopsy sample had been taken <sup>(28)</sup>.

For all the above reasons we decided that our radiologist should examine our patients by using the new version of ultrasound (MEDISON 8000 LIVE KOREA) which is available in Ibn-Sena Teaching Hospital, as this procedure is available and affordable free off charge to all our patients.

Hepatic magnetic resonance spectroscopy imaging is more sensitive than ultrasound for detecting minor degrees of steatosis and allows a quantitative assessment of fatty infiltration of the liver <sup>(29,30)</sup>.

This rather small study indicates that NAFLD is present in our diabetic patients involving more than 50% of them. These findings should raise the alarm for the problem of NAFLD in our diabetic patients and to look for all the available means to prevent and/or to treat the high risk group patients. Furthermore, increased prevalence of liver disease occurs in both type 1 and type 2 diabetic patients, resulting in an increased prevalence of cirrhosis, portal hypertension, liver failure, steatosis, iron overload, and even hepatoma <sup>(31)</sup>. Nonalcoholic fatty liver disease some times follows a relatively benign course and remains stable <sup>(32)</sup>. However NAFLD is the most common cause of elevated liver enzymes in adults in the United States and the most common cause of cryptogenic cirrhosis <sup>(33,34)</sup>.

## Conclusion

Nonalcoholic fatty liver disease is common in our diabetic patients, occurs in both sexes and in type 1 and type 2 diabetes mellitus. Ultrasound may be used for epidemiological studies for detection of NAFLD in diabetics, general population and obese people.

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