Research Article
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Comparison of the transient elastography (fibroscan) results among diabetic and non-diabetic patients with non- alcoholic fatty liver disease

Abstract

Background and objective: Diabetes is a risk factor for developing and progressing Non-Alcoholic Fatty Liver Disease (NAFLD) and assessing hepatic fibrosis is necessary to check the prognosis in these patients. Transient Elastography (TE) as a noninvasive, easy to use and reproducible technique could be appropriate in the monitoring of fibrosis among NAFLD patients. This study designed to compare liver stiffness among diabetic and non-diabetic patients by using TE method.

Materials and methods: Overall 67 patients (age range of 20-60 years) with the evidence of fatty liver in sonography and after exclusion of other causes were divided into two groups of diabetics and non-diabetics. Then patients were assessed with TE after lab tests and their lab data and liver stiffness scores were compared between two groups.

Results: Demographic characters of both groups were similar (including mean age, sex, BMI, AST, ALT, Total Cholesterol, LDL and TG) (P>0.05). Mean liver stiffness scores in the diabetic group were significantly higher than non-diabetics (P=0. 025). In diabetic patients group, only mean levels of AST and TG in F3 and F4 stiffness score were significantly higher in comparison with lower stiffness scores (P<0.05).

Conclusion: Significant liver fibrosis is more frequently present in diabetic patients and TE could be appropriate as a monitoring method in diabetic patients with liver fibrosis.

Keywords: nonalcoholic fatty liver disease, diabetes, fibroscan, transient elastography

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Abbreviations: NAFLD, non-alcoholic fatty liver disease; TE, transient elastography; IR, insulin resistance; LSM, liver stiffness measurement

Introduction

Metabolic syndrome is a common clinical condition that involves about 40% of the population over 50 years.[1] Non-alcoholic fatty liver disease (NAFLD) is also one of the most common liver disorders in the adult population, which include a wide range of liver damage from simple steatosis to esteatohepatitis, progressive fibrosis and cirrhosis.[1-3]

Non-alcoholic fatty liver disease is commonly associated with obesity, Diabetes Mellitus type 2, dyslipidemia and insulin resistance (IR) that all are among the features of metabolic syndrome. It is estimated that approximately 70-75% of patients with type 2 diabetes suffering fatty liver disease.[4,5] In addition, type 2 diabetic patients compared with non-diabetic, have a greater risk to involve by non-alcoholic fatty liver disease, and in particular higher risk of fibrosis and its progression to cirrhosis.[2] Recent studies have shown that the existence of fatty liver in diabetics may be associated with an increase in cardiovascular risk and general mortality specially mortality caused by the liver.[3]

For monitoring of prognosis in patients with Non-alcoholic fatty liver disease checking of liver fibrosis is essential especially among high risk patients such as diabetics. Liver biopsy is the gold standard of liver fibrosis evaluation, but it is a painful and invasive procedure, with the possibility of life-threatening complications and it is not done on a routine basis in patients with non-alcoholic fatty liver disease unless there be another indication.[6,7] In the past few years, biochemical or non-invasive method equipment's have been reviewed for this purpose and in many studies accurate and appropriate assessment of liver stiffness, which is associated with liver fibrosis, have been estimated by Fibroscan.[5,8,9] Fibroscan is a non-invasive, easy and repeatable method, which allows fast and accurate assessment of liver stiffness. This method is a reliable marker of hepatic fibrosis that makes possible proper staging of liver disease and can reduce the number of cases refer for biopsy.[7,10-13] According to this fact that most of the studies about Fibroscan are focused on chronic liver disease caused by hepatitis B and C and with regard to the limitation of the studies about the effect of diabetes on liver fibrosis, particularly with the help of a non-invasive and accurate method, in the present study we decided to examine the impact of diabetes on liver fibrosis and to see whether diabetes is a major cause for exacerbating the incidence of esteatohepatitis and liver fibrosis compared with non-diabetic people or not?[14]

Materials and methods

In this descriptive epidemiological study, all of the patients referred to the Gastroenterology outpatient clinic in Ahvaz Golestan and Imam Hospitals were included. Inclusion criteria included patients between 20 and 60 years old, which had fatty liver on the basis of ultrasonography, negative viral hepatitis and HIV serology, consuming less than 20 grams per day of alcohol during the past year, and exclusion of Wilson disease, hemochromatosis and autoimmune hepatitis. The exclusion criteria were BMI≥30 taking medication containing corticosteroids, estrogen, Tamoxifen, amiodarone, Anti-retroviral medication, cannabis abuse, taking pioglitazone

medication, A history of IV drug abuse, extra hepatic cholestasis (based on associated ultrasound or total bilirubin ≥ 8.2) and evidences in favor of the liver mass in ultrasonography. At first, demographic DATAs of all patients (including age, gender, height, weight, the type of medicines, alcohol consumption and associated diseases, Fasting blood glucose, triglyceride levels and serum cholesterol, a history of associated liver disease such as hepatitis, fatty liver and cirrhosis, the rate of hepatic enzymes and liver biopsy history) were recorded as a questionnaire. Then, Fibroscan performed for all of the patients and LSM (Liver stiffness measurement) numbers were calculated for each patient.

Fibroscan (Transient Elastography) is a non-invasive method, and it acts by ultrasound probes M and a vibrator. Operator of this test is a specialist physician. The patient sleeps in the back and puts his or her right hand in complete abduction; then a probe from the intercostal space on the body surface is placed on the right lobe of the liver. The Target tissue of the liver is specified by ultrasound guide, and vibrating waves are sent to the liver. For each patient, measurement will be done 10 times, non-proportional numbers will be deleted and the liver rigidity is expressed in the form of Kilo Pascal (KPa).

Then, on the basis of the amount of serum concentrations of glucose and HbA1C, patients were divided into two groups: diabetic and non-diabetic. Then the mean number of LSM was compared between two groups on the basis of factors related to the patient and blood biochemistry. Data obtained were analyzed by using SPSS version 19. Chi square test was used to compare demographic data of two groups; the independent t-test was used in order to compare the liver stiffness, liver tests, lipid profile and BMI in the groups. Significant levels in this study were considered as 0.05.

Results

In this study, overall 70 patients referred to Gastroenterology clinics with NAFLD based on ultrasound findings. At final analysis 3 patients excluded: two patients due to taking Tamoxifen for treatment of breast cancer, and one due to Glitazon consumption. The remaining 67 patients were divided into diabetic (n=34) and non-diabetic (n=33) groups. The mean age of diabetic and non-diabetic patients were 39.79±12.86 and 38.78±12.2 respectively (P=0.74) and in terms of gender and BMI, the two groups did not have any significant difference (P>0.05) (Table 1). Biochemical profile of these patients were determined and while the mean AST, ALT, total cholesterol, LDL and TG in diabetic group were higher than non-diabetic group; no statistically significant difference observed between the two groups (P>0.05) (Table 1).

The mean fasting blood glucose in the diabetic group was reported as 128.70 mg/dl and 79.4% of the patients in this group had uncontrolled fasting blood sugar (above 100) (Figure 1).

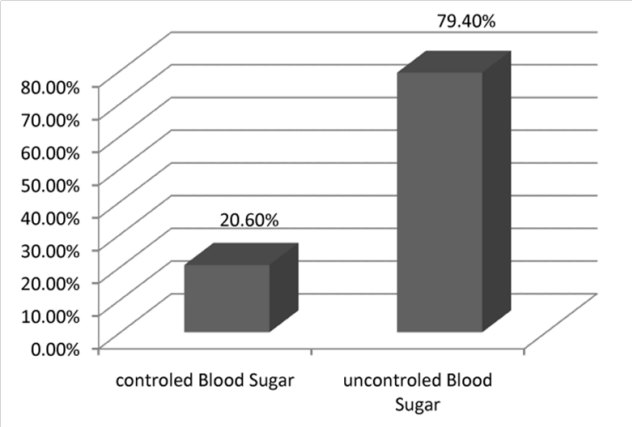

Figure 1 Frequency of controlled and uncontrolled Blood sugar among diabetic patients.

The mean score for the liver stiffness obtained by Fibroscan in the diabetic and non-diabetic groups was 8.32±3.29 and 6.22±4.14, respectively; there was a significant difference between the two groups (P=0.025) (Table 1). There was no significant difference by mean score of liver stiffness among female and male genders as well as two age groups of 20-40 years and 41-60 years (P > 0.05) (Table 2).

Table 1 Demographic and biochemical comparison of diabetic and non-diabetic groups

	Diabetic (%) Number	Non-diabetic (%) Number	P value
Gender			
Male	21 (31.34%)	19 (28.36%)	0.8
Female	13 (19.4%)	14 (20.9%)	
BMI	24.32±2.83	24.14±2.41	0.77
AST	45.61±25.45	39.54±15.65	0.24
ALT	57.2± 33.68	45.6±14.61	0.07
Total cholesterol	203.08±41.53	197.45±33.73	0.54
LDL	121.5±26.54	108.9±25.42	0.52
TG	220.94±49.76	199.84±47.13	0.08
Liver stiffness score (KPS)	8.32±3.29	6.22±4.14	0.025
Fasting glucose	128.70±26.65	90.84±9.44	0

Three patients in the non-diabetic group and two patients in the diabetic group had been previously biopsied (P >0.05) and all of the five patients were cirrhotic; based on the findings of Fibroscan, these patients had also liver stiffness above 8 KPS and equivalent to ≥ F3 (scores of 16, 14.5, and 18.5 in the diabetic group; 16.5 and 25 in the non-diabetic group respectively). Based on liver stiffness score in concordance with biopsy results and based on references 10 and 14, Patients were divided into five categories; for these five categories, both diabetic and non-diabetic groups had a significant difference together (P=0.000.0) (Table 3).

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Table 2 Comparison between mean score of the liver stiffness in both genders and age groups

	The mean score of liver stiffness	P-Value
Gender	Mean±(SD)	
Male	4.09±7.49	0.6
Female	3.53±6.98	
The age groups		
20-40 Years	3.11±6.51	0.052
41-60 Years	4.54±8.37	

Table 3 Comparison of liver stiffness among diabetic and non-diabetic groups

	Diabetic	Non-diabetic	P value
	Number (%)	Number (%)	
F0 (0-5.56)	9 (13.43%)	21 (31.34%)	
F1 (5.57-6.65)	2 (2.99%)	7 (10.45%)	
F2 (6.66-8)	5 (7.46%)	2 (2.99%)	<0.001
F3 (8.1-17)	17 (25.37%)	2 (2.99%)	
F4(≤17.1)	1 (1.48%)	1 (1.48%)	

Based on this division, there was a significant difference in the mean level of AST and TG between the groups of liver stiffness in the diabetic patient group, so these tests in the F3 and F4 groups compared to groups with lower fibrosis, were significantly higher but the difference could not be seen among these groups in terms of age, BMI, ALT level, LDL, and fasting blood sugar (Table 4). Also in the non-diabetic group based on this division, there was no significant difference in terms of age, BMI, AST, ALT, LDL, TG and fasting blood glucose (Table 5).

Table 4 Comparison between liver stiffness groups in terms of age, BMI, AST, ALT, LDL, TG and fasting blood sugar in diabetic patients

	F0	F1	F2	F3	F4	P value
	Mean±(SD)	Mean±(SD)	Mean±(SD)	Mean±(SD)	Mean±(SD)	
Age	32.66±13.91	41.51±6.36	37.2±7.36	12.7±44.23	38	0.29
BMI	23.2±2.53	22.25±1.06	2.46±24.16	3.1±25.2	24	0.4
AST	31.44±10.4	33.5±3.35	5.11±38.8	18.26±50	157	0
ALT	40.22±14.39	37.5±3.35	16.78±63.4	42.9±65.41	79	0.34
LDL	114.44±31.02	180.5±14.84	53.19±201	42.4±253.7	200	0.25
TG	181.44±20.43	180.5±14.84	53.19±201	253.7±42.47	200	0.001
Fasting blood sugar	130.77±22.9	119.5±20.5	111.2±24.22	138.52±30.96	149	0.35

Table 5 Comparison between liver stiffness groups in terms of age, BMI, AST, ALT, LDL, TG and fasting blood sugar in non-diabetic patients

	F0	F1	F2	F3	F4	P value
	Mean±(SD)	Mean±(SD)	Mean±(SD)	Mean±(SD)	Mean±(SD)	
Age	37.23±11.87	24.14±2.96	26±1.41	20.25±1.76	44	0.36
BMI	23.73±2.32	36.14±12.48	48.5±16.26	52±9.89	27	0.48
AST	36.85±14.67	44.14±19.92	35.5±14.43	44.5±9.19	62	0.48
ALT	45.42 ±16.98	48.71±12.02	44±2.28	39±5.65	44	0.95
LDL	107.95±92.99	108.85±16.25	110±70.71	107.5±10.6	130	0.95
TG	196.9±48.8	202.14±54.14	192.5±38.89	78.5±6.36	230	0.95
Fasting blood sugar	9.3±90.57	93.28±10.19	93±4.24	215±50.91	100	0.3

Discussion

Non-alcoholic fatty liver disease is a common and increasing cause of chronic liver disease around the world that are intimately associated with diabetes; so that not only non-alcoholic fatty liver disease prevalence in diabetic patients is more but also diabetes is a major risk factor for induction and progression of non- alcoholic fatty liver disease towards fibrosis, cirrhosis, and hepatocellular carcinoma; and the probability of diabetes in patients with non- alcoholic fatty liver disease would be much more in the future.[1,8] Our findings indicated that among diabetic patients with sonographic evidences of non-alcoholic fatty liver disease, the liver stiffness score is more than non-diabetic patients with non-alcoholic fatty liver disease in Fibroscan and no differences were found between diabetic and non-diabetic groups with non-alcoholic fatty liver disease in terms of age, BMI, fat profile and liver enzymes.

Contrary to these findings, in a study conducted by Younossi et al.,[15] in 2004, evaluation of 132 patients with evidences of non-alcoholic fatty liver disease have cleared that ages of diabetic patients with non-alcoholic fatty liver disease were significantly higher, and their average TG level were more than non-diabetic individuals; however, the level of AST and ALT did not show significant differences between the two groups. In addition, in that study based on biopsy results, diabetic patients were suffering from a more severe stage of disease compared to non-diabetic patients and the percentage of cirrhosis in diabetic patients was significantly more than non-diabetic patients.

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Our study showed that the average level of AST and TG in the higher degrees fibrosis (≥ 6.66 KPS equal to ≥ F2) among diabetic patients group was more than the people without fibrosis (< F2) and their amount increasing with progresion of fibrosis; however, it was not factual in the case of ALT, LDL cholesterol, and fasting blood glucose and also average of all of these parameters were not different between various stages of liver stiffness in non-diabetic patients. The higher AST level in higher stages fibrosis could be explained by reduction of its clearance with progression of sinusoidal fibrosis.[2]

Unlike our study, in an Australian research conducted by Casey et al.,[16] in 2012 on 74 diabetic patients without known liver disease, it has been found that patients with a liver stiffness score above 7.65 KPS compared with lower degrees of stiffness score, had a higher level of ALT (P=0.02) and the difference was not seen for other parameters. In a study conducted by Amarapukar et al.,[17] in 2006 on diabetic patients with non-alcoholic fatty liver disease, it was determined that among patients with fibrosis in liver biopsy in comparison with the group without fibrosis, there is a significant correlation between stage of fibrosis and levels of ALT and AST. The presence of fibrosis in NAFLD indicates a more severe and advanced damage to the liver and with concordance of diabetes Mellitus, the possibility of more sever fibrosis raising.[3] Diabetes is associated with the inflammation, oxidative stress and the excessive production of hepatotoxic cytokines that all are involved in the pathophysiology of non-alcoholic fatty liver disease and diabetic patients with non-alcoholic fatty liver disease would experience a higher probability of advanced fibrosis and cirrhosis and as a resultant, their complications and mortality will be raise.[6,15,18]

Due to importance of detection and assessment of fatty liver among diabetics, the detection of early stages of fibrosis can be potentially preventive of bad prognosis by more frequent monitoring and more strict therapeutic interventions, but the majority of studies has indicated that Fibrosis in diabetic patients is less than the actual detectable threshold by ultrasound and NASH can only be diagnosed definitely by liver biopsy.[16,18] In most studies, the proper functioning of the Fibroscan in evaluating liver stiffness and accurate staging of liver disease has been proved and it have been shown that Fibroscan as a non-invasive, quick and repeatable method can reduce the number of liver biopsies. Therefore this method could be a proper way for screening of fibrosis in the early stages of non-alcoholic fatty liver disease before developing NASH among high risk patients.[6,7,11,19]

In our study, 79.4% of patients in diabetic group had uncontrolled fasting blood sugar (above 100); and it seems that deteriorating insulin resistance as a key factor in pathogenesis of non-alcoholic fatty liver disease, can aggravate the pathological changes of this disease in diabetics. Although our findings showed that mean fasting blood glucose has no significant difference in the various stages of fibrosis among diabetics; the study of Petta et al.,[6] in 2011 cleared not only higher degrees of NAFLD associated fibrosis on Fibroscan and liver biopsy among diabetics than non-diabetics, but also a meaningful relation between liver fibrosis and higher values of mean fasting blood sugar. So it seems that in diabetic patients with non-alcoholic fatty liver disease, the progression of the disease towards the advanced stages of fibrosis and cirrhosis can be prevented by better control of blood sugar particularly by using insulin-sensitizing agents.

Conclusion

According to more prevalence and less detection of advanced liver fibrosis among diabetics, Fibroscan can be a proper method for screening and detection of early hepatic fibrosis in diabetics; and by early detection of fibrosis, aggressive treatment options and tight control of blood sugar, the progress ofthis disease toward advanced stages could be prevented.

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Conflicts of interest

Authors declare that there is no conflict of interest.

References

1. Angelico F, Del Ben M, Conti R, et al. Insulin Resistance, the Metabolic Syndrome, and Nonalcoholic Fatty Liver Disease. *J Clin Endocrinol Metab*. 2005;90(3):1578–1582.
2. Tan HH, Pik-Eu Chang J. Non-alcoholic Fatty Liver Disease. *Proceedings of Singapore Healthcare*. 2010;19(1):36–50.
3. Oh MK, Winn J, Poordad F. Review article: diagnosis and treatment of non-alcoholic fatty liver disease. *Aliment Pharmacol Ther*. 2008;28(5):503–522.
4. Targher G, Bertolini L, Padovani R, et al. Prevalence of nonalcoholic fatty liver disease and its association with cardiovascular disease among Type 2 diabetic patients. *Diabetes Care*. 2007;30:1212–1218.
5. Prashanth M, Ganesh HK, Vima MV, et al. Prevalence of Nonalcoholic Fatty Liver Disease in Patients with Type 2 Diabetes Mellitus. *J Assoc Physicians India*. 2009;57:205–210.
6. Petta S1, Di Marco V, Cammà C, et al. Reliability of liver stiffness measurement in non-alcoholic fatty liver disease. *Aliment Pharmacol Ther*. 2011;33(12):1350–1360.
7. Mayers RP. Noninvasive diagnosis of Non-alcoholic Fatty Liver Disease. *Ann Hepatol*. 2009;8(Suppl 1):S25–33.
8. Dowman JK, Tomlinson JW, Newsome PN. Systematic review: the diagnosis and staging of non-alcoholic fatty liver disease and non-alcoholic steatohepatitis. *Aliment Pharmacol Ther*. 2011;33(5):525–540.
9. Foucher J, Chanteloup E, Vergniol J, et al. Diagnosis of cirrhosis by transient elastography (FibroScan): a prospective study. *Gut*. 2006;5599(3):403–408.
10. Fung JY, Lai CL, Yuen MF. Clinical Application of Transient Elastography (Fibroscan) in Liver Diseases. *Hong Kong Medical Diary*. 2009;14(11):22–25.
11. Coco B, Oliveri F, Maina AM, et al. Transient elastography: a new surrogate marker of liver fibrosis influenced by major changes of transaminases. *J Viral Hepat*. 2007;14(5):360–369.
12. Malekzadeh R, Poustchi H. Fibroscan for assessing liver fibrosis: An acceptable alternative for liver biopsy. *Hepat Mon*. 2011;11(3):157–158.
13. Murtagh J, Foerster V. Fibroscan for noninvasive assessment of liver fibrosis. J Canadian agency for drugs and technologies in health 90; 2006.
14. Costina Dina R, Moţa M, Vladu I, et al. Hepatic fibrosis, measured by Fibroscan in a group of patients with obesity. *Rom J Diabetes Nutr Metab Dis*. 2012;19(2):123–129.

15. Younossi ZM, Gramlich T, Matteoni CA, et al. Nonalcoholic fatty liver disease in patients with type 2 diabetes. *Clin Gastroenterol Hepatol*. 2004;2(3):262–265.

16. Casey SP, Kemp WW, McLean CA, et al. A prospective evaluation of the role of transient elastography for the detection of hepatic fibrosis in type 2 diabetes without overt liver disease. *Scand J Gasteroenterol*. 2012;47(7):836–841.

17. Amarapukar DN, Amarapukar AD, Patel ND, et al. Nonalcoholic Steatohepatitis (NASH) with diabetes: predictor of liver fibrosis. *Ann Hepatol*. 2006;5(1):30–33.

18. Obika M, Noguchi H. Diagnosis and Evaluation of Nonalcoholic Fatty Liver Disease. *Exp Diabetes Res*. 2012;2012:145754.

19. Hajiani E, Hashemi SJ, Masjedizadeh AR, et al. Comparison of Liver Biopsy with Transient Elastography as a Non-invasive Method for Assessment of Liver Fibrosis. *Journal of GHR*. 2014;3(3):1013–1016.

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