Study of Prevalence of Nonalcoholic Fatty Liver Disease in Type II Diabetes Mellitus Patients and Variations in Liver Enzymes and Lipid Profile in Diabetic Patients with Fatty Liver in Comparison With Patients Without Fatty Liver

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Abstract

Background: Type 2 diabetes mellitus (T2DM) patients potentially are at risk of developing non-alcoholic fatty liver disease (NAFLD), Non-alcoholic fatty liver disease (NAFLD) is the most prevalent chronic liver disease in developing and developed countries, Global prevalence of NAFLD is 25.24% with highest prevalence in the Middle East and South America and lowest in Africa.

Aim of Study: This study aimed to determine the prevalence of NAFLD among T2DM patients, diagnosed by ultrasonography of liver, to study the age, sex in NAFLD and to compare liver enzymes and lipid profile between individuals with NAFLD and without NAFLD.

Patients and Methods: A prospective study was conducted of 100 type 2 diabetic Patients visited a private clinic in Aden republic of Yemen, in the period from October 2017 to June 2018.

Results: Total of (100 patients) type 2 diabetes mellitus ambulatory patients were selected for the study. 62 patients (62%) had NAFLD and 38 patients (38%) had normal liver on ultrasonography, the prevalence of NAFLD in the present study was 62%, Majority of the study population observed with type 2 diabetes mellitus and NAFLD were females (n=40, 65%), and 22 were males (35%), the age range of diabetic patients with NAFLD was 40-65 years, mean age 53.16 SD ±7.64, Subjects with diabetes mellitus and NAFLD had significant elevation in Alanine transaminase (ALT), cholesterol, LDL, and triglyceride than diabetic subjects without NAFLD.

Conclusions: Early detection and optimum control of diabetes mellitus is important to minimize the effect of diabetes on liver. Hence, assay of serum levels of hepatic enzymes, and abdominal ultrasound to detect NAFLD should be done in all patients with T2DM as preliminary diagnostic tests.

Key Words: *Nonalcoholic fatty liver disease– Liver enzymes– Liver function – Type 2 diabetes mellitus.*

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Introduction

NAFLD is a type of chronic liver disorder, which is gaining significance worldwide. Most of the patients with NAFLD are asymptomatic, although some may experience fatigue, malaise or pain in the right hypochondriac region of abdomen. Hepatomegaly is the common finding in majority of patients. The definitive diagnosis of NAFLD is based on the histological examination of liver biopsy, but it is an invasive and costly procedure and is associated with many complications. Hence, NAFLD is generally diagnosed by most widely available ultrasonography examination that has a sensitivity of 90% and specificity of 95% in detection of moderate and severe cases [1].

Nonalcoholic fatty liver disease (NAFLD) is the most common cause of liver disease worldwide with prevalence estimates ranging from 25% to 45% in most studies, increasing in parallel with that of obesity and diabetes, Nonalcoholic fatty liver disease was first described in 1980 and is divided into the histological categories of:

Nonalcoholic fatty liver, which includes patients with isolated hepatic steatosis and patients with steatosis and mild nonspecific inflammation, and nonalcoholic steatohepatitis, which is distinguished from the former by the additional presence of features of hepatocellular injury with or without fibrosis, the presence of hepatic fibrosis is the most important determinant of outcome [2].

Non-alcoholic fatty liver disease (NAFLD) and type 2 diabetes (T2DM) are common conditions that regularly co-exist and can act synergistically to drive adverse outcomes. The presence of both NAFLD and T2DM increases the likelihood of the

development of complications of diabetes (including both macro- and micro-vascular complications) as well as augmenting the risk of more severe NAFLD, including cirrhosis, hepatocellular carcinoma and death [3].

NAFLD occurs in up to 20% of the general population and possibly up to 90% in obese patients 5. NAFLD presents a wide spectrum of lesions that include steatosis, hepatitis and fibrosis. These three types of lesions can occur in different grades in the same patient. In the presence of fibrosis, progression to cirrhosis and hepatocellular carcinoma may occur in 20% and 10% of cases, respectively1 [4].

The highest prevalence of NAFL is in the Middle East and South America and lowest in Africa. Metabolic comorbidities associated with NAFLD included obesity (51.34%; 95% CI: 41.38-61.20), type 2 diabetes (22.51%; 95% CI: 17.92-27.89), hyperlipidemia (69.16%; 95% CI: 49.91-83.46%), hypertension (39.34%; 95% CI: 33.15-45.88) and metabolic syndrome (42.54%; 95% CI: 30.06-56.05) [5].

The criteria for definition of NAFLD requires that (a) there is evidence of hepatic steatosis, either by imaging or by histology and (b) there are no causes for secondary hepatic fat accumulation such as significant alcohol consumption, use of steatogenic medication or hereditary disorders [6].

Abdominal ultrasound scans are the most frequently used imaging tool for diagnosing NAFLD. Five point ultrasonography criteria of diagnosis of fatty liver disease recommended by Dasharty's was used to diagnose NAFLD: (1) Increased hepatic brightness" or hyper echogenicity (He), (2) Posterior attenuation of the right lobe (RLpA), (3) Increased contrast between the right kidney and liver (HRC), (4) Loss of visualization of right diaphragm and (5) Diminished visibility of the intrahepatic vessels [7].

Patients and Methods

This was a prospective study carried out in a private clinic in Aden-Yemen, over a period of nine months, from October 2017 to June 2018.

100 subjects of type 2 DM were recruited into study, Descriptive data like name, age, sex, were obtained by interviewing the patients. All patients were subjected for the estimation of liver enzymes as aspartate transaminase (AST), alanine aminotransferase (ALT), fasting lipid profile, which includes total cholesterol, triglycerides, high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C), at the time of inclusion into the study. NAFLD was diagnosed on ultrasonography.

Inclusion criteria which were opted for this study: (1) Type 2 diabetics mellitus, (2) Age ≥40 years, (3) Bright liver on ultrasound imaging.

Subjects with history of qat chewing, alcohol intake, history of systemic illnesses known to cause fatty liver disease, and those who were receiving or had recently received drugs (including herbal medicines) known to raise liver enzymes or cause fatty liver disease were excluded from this study.

After diagnosing Non-Alcoholic Fatty Liver Disease (NAFLD) by ultrasound, patients were grouped into two groups, Group I with DM type 2 with NAFLD and Group II with DM type 2 without NAFLD.

Subjects did not have a liver biopsy and histological examination. Performance of this invasive procedure was not feasible; we used ultrasound to detect fatty liver in our study.

The parameters adopted for abnormal values were, cholesterol ≥200mg/dl, triglycerides ≥150mg /dl, LDL ≥150mg/dl, HDL <40mg/dl for men and <50mg/dl for women [4]. Serum liver enzymes ALT, AST, were estimated by modified IFCC method, and normal kit ranges were ALT: 10-40 international units per liter (IU/L), AST: 10-35 IU/L, [8].

The size of the liver was measured in midclaviclar line longitudinally and <14cm was taken as controls and >14 was considered as hepatomegaly [1].

All the subjects underwent abdominal ultrasonography by the radiologist for evidence of fatty liver through the standard criteria. The standard criteria accepted by the American gastroenterology association is an increase in hepatic echogenicity as a reference, the presence of enhancement and lack of differentiation in the periportal intensity and the vascular wall due to great hyper echogenicity in the parenchyma [9].

Data were expressed as mean ± SD. *p*-value <0.05 is considered as statistically significant. Statistical analysis was performed using SPSS 21.0s.

Ethical consideration: Verbal informed consent was obtained from all participating subjects. The

research and ethics committee in the faculty of medicine university of Aden approved the study design.

Results

The present study was conducted in a private clinic, from October 2017 to June 2018, 100 subjects of type 2 DM were recruited into study.

Table (1) showed 62 patients (62%) had NAFLD and 38 patients (38%) had normal liver on ultrasonography, the prevalence of NAFLD in the present study was 62%.

Table (2) showed a prominence of female gender (n=40,65%) versus (n=22,35%) being male.

Table (3) showed the age range of diabetic patients with NAFLD, Their age ranged from 40-65 years, mean age 53.16 SD ±7.64.

Age group (50-59) constitute (n=26,41.93%).

Table (4) revealed Subjects with NAFLD had higher ALT, AST, than subjects without NAFLD.

In group 1 patients with DM type 2 and NAFL, ALT was significantly increased when compared to group 2 patients, while AST was also increased but not significant.

Table (5) revealed group 1 patients with type 2 DM and NAFL, Cholesterol, Triglycerides, LDL cholesterol were significantly increased when compared to group 2 patients.

Table (1): Prevalence of NAFL among Type 2 DM.

	No. of patients	%
Type 2 DM with NAFL	62	62
Type 2 DM without NAFL	38	38
Total	100	100

Table (2): The sex distribution among Type 2 DM with NAFL.

Sex	No. of patients	%
Female	40	65
Male	22	35
Total	62	100

Table (3): Age distribution among diabetic patients with NAFL.

Age group	No.	%
40-49	19	30
50-59	26	41.9
>60	17	27

Table (4): Liver enzymes variants among diabetic patients with NAFL and without NAFL.

	DM with NAFL		DM without NAFL		p-value
	Mean	± SD	Mean	± SD	
ALT	35.0	14.5	27.2	11	0.03
AST	70.0	22.0	32.3	17.4	0.06

Table (5): Lipid profile variants among diabetic patients with NAFL and without NAFL.

	DM with NAFL		DM without NAFL		p-value
	Mean	± SD	Mean	± SD	
Cholesterol	223.6	44.1	182.9	17.1	0.0001
LDL	148	39.8	107	25.7	0.03
Triglyceride	197	38.8	162.9	13.8	0.0001
HDL	35.3	6.7	37.9	6.8	0.06

Discussion

The prevalence of Nonalcoholic fatty liver disease in type 2 Diabetes Mellitus was found to be 62% in our study. Close to the result of Raminderpal Singh Sibia and his colleges in a study published in the National Journal of Laboratory Medicine demonstrated that, NAFLD was prevailed in (61%) among 100 patients of type 2 diabetes mellitus [10].

Targher et al., [11] and Agarwal et al., [12] also found high prevalence of NAFLD among diabetics as 69.5%, 87% respectively.

In our present study, prevalence of NAFLD was higher than the result mentioned in Nagaraj et al., 2016 [1] and Prashanth M et al., [13]. Where prevalence of nonalcoholic fatty liver was 52% and 57.2% respectively.

It was observed, out of 62 cases of NAFLD, 40 (65%) were females, and 22 (35%) were males, Thus the prevalence was higher in females. With p-value was 0.5, which was not significant similar to the result conducted in western India by Shailaja v Rao and Kusum K Sikariya in among 77 patients with type 2 diabetes mellitus and NAFLD, The prevalence of NAFLD was more in females 64.9% (50/77) which was statistically not significant Shailaja v Rao and Kusum K Sikariya 2016 [14], Similar study conducted by merat et al showed the prevalence of NAFLD was higher among women (60.1%) than men (44.8%) which was also not statistically significant p=0.069 [15].

The range of age among diabetic patients with NAFLD was 40-65 years, mean age 53. 16 SD ±

7.64, p-value significant (0.0001), similar result was found in the study made by Raminderpal Singh Sibia et al., Mean age of type 2 diabetes mellitus and NAFLD was 55.64±11.653 and p-value was also statistically significant (0.002) [10].

In our present study, ALT was significantly increased (p-value .003) in type 2 diabetes mellitus patients with NAFLD When compared to type 2 diabetes mellitus patients without NAFL. While AST was not significantly increased (p-value 0.06)

Elmahi and Abdrabo reported in their study that, raised ALT levels are the most common abnormality Email HM and Abdrabo AA [16] while in Nagaraj S et al., [1] and Prabhudeva N et al., [17].

AST, ALT, were both significantly increased in type 2 diabetes mellitus patients with NAFLD.

In the study reported from western India by Shailaja v Rao and Kusum K Sikariya, patients had liver enzymes almost within normal range but the mean values were higher making it statistically significant [14].

Cholesterol, Triglycerides and LDL cholesterol were statistically significantly increased in group 1 patients when compared to group 2 patients (p-value <0.0001), (p-value<0.0001), (p-value <0.03) respectively, while HDL p-value was not significant (0.06).

In the study made by Shailaja and Kusum in a Tertiary Care Centre In Western India, the difference in triglyceride in NAFLD and in non-NAFLD diabetic patients was found statistically significant (p-value 0.011) like our present study, while cholesterol in NAFLD was statistically not significant (p-value 0.162). The difference was very highly significant between Mean HDL in NAFLD group and in non-NAFLD group p-value 0.000 [14], while in the present study, HDL p-value was not significant 0.06.

Nagaraj et al., study revealed that Cholesterol and Triglycerides In group 1 patients were significantly increased when compared to group 2 patients [1].

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دراسة حول إنتشار الكبد الدهنى الغير كحولى وسط مرضى السكر النوع الثانى والأختلافات فى نسبة أنزيمات الكبد ودهون الدم بين مرضى السكرى المصابين والغير مصابين بدهون الكبد الغير كحولى

يعانى مرضى السكرى النوع الثانى من خطورة الإصابة بالكبد الدهنى غير الكحولى أكثر أمراض الكبد الدهنى غير الكحولى أكثر أمراض الكبد المزمنة أنتشاراً فى الدول النامية والدول المتطورة، يشكل أنتشاره على مستوى العالم ٢٥.٢٤٪ يمثل الشرق الأوسط وجنوب أمريكا الأعلى أنشاراً وتمثل أفريقيا الأقل أنتشاراً.

الأهداف: هدفت الدراسة لتحديد مدى أنتشار دهون الكبد غير الكحولى وسط مرضى السكرى النوع الثانى مستخدماً جهاز الموجات الصوتية فى التشخيص، وعمل مقارنة فى نسبة أنزيمات الكبد ونسبة دهون الدم بين مرضى السكرى المصابين والغير مصابين بدهون الكبد غير الكحولى.

الأساليب: شملت الدراسة ١٠٠ مريض من مرضى السكرى النوع الثانى الزائرون إحدى العيادات الخاصة فى عدن من أكتوبر ٢٠١٧ إلى مايو ٢٠١٨.

النتائج: ٦٢٪ من مرضى السكرى النوع الثانى كانوا مصابين بدهون الكبد غير الكحولى شكلت الإناث ٦٥٪ من هذه النسبة والذكور ٣٥٪، متوسط العمر ٥٣.١٦ هناك إرتفاع فى أنزيمات الكبد، الكوليسترول، الدهون منخفضة الكثافة والدهون الثلاثية عند مرضى دهون الكبد غير الكحولى.

الأستنتاج: يعتبر التشخيص البكر وتنظيم السكر من أهم العوامل لتخفيف أثر السكر على الكبد، لهذا كل مرضى السكرى النوع الثانى عليهم أن يخضعوا لقياس نسبة أنزيمات الكبد وعمل جهاز الموجات الصوتية للبطن.