Original Article

Association of Nonalcoholic Fatty Liver Disease with Coronary Artery Disease in Type 2 Diabetes Mellitus: A Cross-Sectional Study from a Tertiary Care Medical College Hospital

Neelakandan Ramya, Golepu Karthikeya[1], Sethu Prabhu Shankar

Department of General Medicine, Trichy SRM Medical College Hospital and Research Centre, Tiruchirapalli, Tamil Nadu, [1]Department of General Medicine, Trident Hospitals, Hyderabad, Telangana, India

Abstract

Introduction: Nonalcoholic fatty liver disease (NAFLD) is a risk factor for increased morbidity, mortality, and cardiovascular disease. This study was done to assess the association of NAFLD with coronary artery disease (CAD) in type 2 diabetes mellitus. **Materials and Methods:** The study was done as a cross-sectional study in a tertiary care medical college hospital for 2 years among 218 adults patients of both sexes with type 2 diabetes mellitus. The study protocol was approved by the institutional ethics committee of the hospital. Age, sex, lifestyle, hypertension, personal history for smoking, and details of any previous CAD were recorded. Electrocardiogram (ECG) and ultrasonography of the abdomen were done. The association of NAFLD in type 2 diabetes mellitus patients with symptoms of angina according to modified rose and ECG changes using Minnesota codes was studied. Data collected were analyzed with Statistical Package for the Social Sciences (SPSS) version 20. **Results:** Of the total 218 diabetic patients, there were 92 (42.2%) were in the age group of 65–74 years. One hundred and forty-two (65.1%) had NAFLD and 76 (34.9%) had normal liver. Eighty-eight males and 54 female diabetic patients had NAFLD. Of the NAFLD patients 88 (58%) were smokers, 77 (54%) were obese, and 72 (51%) had hypertension. Low-density lipoprotein was increased in 132 (93%) patients with NAFLD. Angina symptoms according to modified rose questionnaire was present in 26 (18%) of NAFLD patients. Probable ST/T and Q/QS ECG changes according to Minnesota coding was present in 32 (22.53%) and in 26 (18.3%) of diabetic patients with NAFLD. **Conclusion:** There is significant association of coronary artery disease and cardiovascular risk factors with NAFLD in type 2 diabetes.

Keywords: Cardiovascular risk factors, coronary artery disease, diabetes, nonalcoholic fatty liver disease

Introduction

The most significant risk factors for nonalcoholic fatty liver disease (NAFLD) include the components of metabolic syndrome namely obesity, glucose intolerance or diabetes, hypertension, and dyslipidemia, particularly elevated triglycerides and low levels of high-density lipoprotein (HDL) cholesterol.[1] NAFLD is becoming a major public health problem due to increasing prevalence of obesity and type 2 diabetes.[2] The overall prevalence of NAFLD is 15%–40% in Western countries while 9%–40% in Asian countries.[3] NAFLD in type 2 diabetes may be linked to increased coronary artery disease (CAD) risk, independent of the risk correlated by the other components of the metabolic syndrome.[4] In type 2 diabetic mellitus patients, up to 70% may have NAFLD.[5] Ultrasonographic findings of bright liver, with increased echogenicity in comparison with the kidneys, vascular blurring, and deep attenuation, are suggestive of liver steatosis.[6] Previous studies has shown strong association between NAFLD and cardiovascular diseases.[7] Our study was conducted to estimate the magnitude of NAFLD as

Address for correspondence: Dr. Sethu Prabhu Shankar, Department of General Medicine, Trichy SRM Medical College Hospital and Research Centre, Irungalur, Tiruchirapalli - 621 105, Tamil Nadu, India.
E-mail: drprabhumd@gmail.com

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diagnosed by ultrasound examination of the liver and to assess the association between NAFLD and CAD in type 2 diabetes. Magnitude of CAD was assessed using Modified Rose Questionnaire[8] and electrocardiogram (ECG) changes by Minnesota codes.[9]

Materials and Methods

Study design

The study was done as a comparative cross-sectional study.

Study setting

A study was done for 2 years from in a tertiary care medical college hospital.

Sample size

A total of 218 the adult patients of both sexes with type 2 diabetes mellitus, who gave informed written consent were taken up for the study. Patients with a history of type 1 diabetes mellitus, gestational diabetes mellitus, known case of liver disease, and chronic alcohol consumption were excluded from the study.

Ethical approval

The study protocol was approved by the Institutional Ethics Committee of the hospital (IECH/AVMCH/PG/SI No 19/2014).

Data collection and analysis

A detailed history including age, sex, lifestyle, symptoms of angina using modified rose questionnaire, hypertension, personal history for smoking, and details of any previous treatment were recorded. Detailed physical examination including anthropometric measurements and vital signs was done. All the necessary investigations such as HbA1c, fasting lipid profile, ECG, and ultrasound of the abdomen were done. The study group was divided into two subgroups based on ultrasonography finding of the liver, one group with NAFLD and the other with normal liver. The presence of CAD was assessed using the Modified Rose questionnaire and by ECG changes using Minnesota codes. Risk factors for CAD were also compared between diabetic patients with and without NAFLD. Data collected were analyzed with Statistical Package for the Social Sciences (International Business Machines Corporation. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp).

Modified Rose Questionnaire for angina

A. Have you ever had pain or discomfort in your chest?
   1. Yes
   2. No

B. Do you get this pain or discomfort when you walk up hill or hurry?
   1. Yes
   2. No

C. Do you get it when you walk at an ordinary pace on the level?
   1. Yes
   2. No

D. When you get any pain or discomfort in your chest, what do you do?
   1. Stop
   2. Slow down
   3. Continue at the same pace

E. Does it go away if you stand still?
   1. Yes
   2. No

If yes

F. How soon?
   1. 10 min or less
   2. More than 10 min

G. Where do you get this pain or discomfort
   Mark the place with an X on the diagram

H. Have you ever had a severe pain across the front of your chest lasting for half an hour or more?
   1. Yes
   2. No

Resting 12-lead ECG was Minnesota coded

Probable CHD was defined as Minnesota coding

- 1.1–1.2 (large Q and QS waves) in all leads

Possible CHD as Minnesota coding

- 1.3 (small Q and QS) in all leads
- 4.1–4.4 (ST-T depression) in all leads
- 5.1–5.3 (flattened or inverted T waves) in all leads
- 7.1.1 (complete left bundle branch block) in all leads

Results

Of the total 218 diabetic patients, there were 92 (42.2%) were in the age group of 65–74 years [Table 1]. One hundred and forty-two (65.1%) diabetic patients had NAFLD and 76 (34.9%) had normal liver [Table 2]. Male patients were 130 (59.6%) and females were 88 (40.4%). Of the total 142 NAFLD patients, 88 (62%) were males and 54 (38%) were female diabetic patients [Table 3]. Of the 142 NAFLD patients, 78 (55%) had grade 1 fatty liver [Table 4]. Of the NAFLD patients, 88 (58%) were smokers, 77 (54%) were obese and 72 (51%) had hypertension [Tables 5-7]. Low-density lipoprotein (LDL) was increased in 132 (93%) and HDL was decreased in 130 (92%) patients with NAFLD [Table 8]. Angina symptoms according to the modified rose questionnaire were present in 26 (18%) of NAFLD patients and were absent

Table 1: Distribution of age

Age group	*n* (%)
35-44	16 (7.3)
45-54	76 (34.9)
55-64	30 (13.8)
65-74	92 (42.2)
≥75	4 (1.8)
Total	218 (100)

Table 2: Age distribution in type 2 diabetes mellitus with nonalcoholic fatty liver disease

Age group	NAFLD (%)	Normal liver (%)
35-44	12	4
45-54	46	30
55-64	20	10
65-74	62	30
75-85	2	2
Total, *n* (%)	142 (65.1)	76 (34.9)

NAFLD: Nonalcoholic fatty liver disease

Table 3: Sex distribution in type 2 diabetes mellitus patients with nonalcoholic fatty liver disease

Gender	NAFLD, *n* (%)	Normal liver, *n* (%)
Male	88 (62)	42 (55)
Female	54 (38)	34 (45)
Total	142	76

NAFLD: Nonalcoholic fatty liver disease

Table 4: Distribution of grade of nonalcoholic fatty liver disease (*n*=142)

Grade	*n* (%)
Grade 1	78 (55)
Grade 2	52 (36.6)
Grade 3	12 (8.4)

in 72 (95%) of diabetic patients with normal liver [Table 9]. Probable ST/T and Q/QS ECG changes according to Minnesota coding were present in 32 (22.53%) and in 26 (18.3%) diabetic patients with NAFLD [Table 10]. Eighty-eight (62%) diabetic patients with NAFLD had CAD [Table 11].

Discussion

NAFLD is defined as hepatic steatosis either by imaging or by histology in the absence of secondary hepatic steatosis such as alcohol consumption, use of steatogenic drugs, or hereditary disorder.[1-3] The prevalence of NAFLD is increasing due to increasing prevalence of obesity and type 2 diabetes.[1-3] NAFLD usually diagnosed with the help of ultrasonography of the liver is found to be linked to cardiovascular diseases including CAD and stroke.[4-7] Our study was conducted on type 2 diabetes mellitus patients to find the association of NAFLD with CAD using the modified rose questionnaire[8] and ECG changes by Minnesota codes.[9] Among the 218 type 2 diabetes mellitus patients in our study, 59.6% were male. In our study, out of 218 type 2 diabetes mellitus patients, 65.1% of patients had NAFLD. The proportion of NAFLD in diabetes in our study was similar to the previous studies.[5,10] NAFLD was seen more in males (62%) than females (38%). This indicates male gender as a risk factor for NAFLD.[10,11] Of the NAFLD patients 55% had grade 1 fatty liver, 36.5% had grade 2, and 8.5% had 3 fatty liver. In our study, 88 patients were smokers in

Table 5: Association of nonalcoholic fatty liver disease in smokers with type 2 diabetes mellitus

Liver	Smokers (88), *n* (%)	Nonsmokers (130), *n* (%)
NAFLD (*n*=142)	82 (58)	60 (42)
Normal liver (*n*=76)	6 (8)	70 (92)

NAFLD: Nonalcoholic fatty liver disease

Table 6: Association nonalcoholic fatty liver disease with body mass index

Liver	Increased (≥30), *n* (%)	Normal <30, *n* (%)
NAFLD (*n*=142)	77 (54)	65 (46)
Normal liver (*n*=76)	22 (29)	54 (71)

NAFLD: Nonalcoholic fatty liver disease

Table 7: Association of nonalcoholic fatty liver disease in type 2 diabetes mellitus with hypertension

Liver	Hypertensive, *n* (%)	Normotensive, *n* (%)
NAFLD (*n*=142)	72 (51)	70 (49)
Normal liver (*n*=76)	44 (58)	32 (42)

NAFLD: Nonalcoholic fatty liver disease

total and among NAFLD patients smokers were 58% patients and 8% of smokers had normal liver. This was significant as a study done by Zein *et al*. showed the significant bivariate associations between advanced liver fibrosis and age, diabetes, and smoking history.[12] In our study, 116 patients were hypertensive in total, among them, 72 patients had NAFLD and 44 patients had normal liver.[13] In our study, 99 patients were obese (body mass index ≥30) in total, among them, 77 (54%) had NAFLD and 22 had normal liver. This was similar to the study done by Bhatia *et al*., which showed the prevalence parallels that of increasing rates of obesity and type 2 diabetes worldwide, with up to 95% of obese persons and 75% of diabetics likely to have NAFLD, which carries a higher risk of cardiovascular disease and mortality.[13] The prevalence of NAFLD in subjects with metabolic syndrome is increased four-fold compared with those without the disease and 30% of NAFLD subjects have metabolic syndrome.[14] In our study, 160 (73.4%) patients had elevated LDL levels in total, among them, 132 (82.5%) patients had NAFLD and 28 (17.5%) had normal liver. Serum triglycerides level was elevated in 150 (68.8%) patients in total, among them 124 (82.7%) patients had NAFLD and 26 (17.4%) had normal liver. In our study, 142 (65.1%) patients had decreased HDL levels, among them, 130 (91.5%) patients had NAFLD and 12 (8.5%) had normal liver. In a study done by Gaggini *et al*. dyslipidemia, hypercholesterolemia, hypertriglyceridemia, or both was been reported in 20% to 80% of cases associated with NAFLD.[15] In another study done by Mellinger *et al*., NAFLD was significantly associated with dyslipidemia and dysglycemia.[16] The association of increased LDL, decreased HDL, elevated triglyceride with NAFLD was statistically

Table 8: Dyslipidemia and nonalcoholic fatty liver disease in type 2 diabetes mellitus

	LDL		Triglycerides		HDL	
	Increased, *n* (%)	Normal, *n* (%)	Increased, *n* (%)	Normal, *n* (%)	Decreased, *n* (%)	Normal, *n* (%)
NAFLD	132 (93)	10 (7)	124 (87)	18 (13)	131 (92)	11 (8)
Normal liver	28 (37)	48 (63)	26 (34)	50 (66)	13 (17)	63 (83)
P	<0.0001		0.0003		0.002	

NAFLD: Nonalcoholic fatty liver disease, LDL: Low density lipoprotein, HDL: High density lipoprotein

Table 9: Symptoms of angina according to Modified Rose Questionnaire in type 2 diabetes mellitus patients

Liver	Symptoms present, *n* (%)	No symptoms, *n* (%)
NAFLD (*n*=142)	26 (18)	116 (82)
Normal liver (*n*=76)	4 (5)	72 (95)

NAFLD: Nonalcoholic fatty liver disease

Table 10: Electrocardiogram changes according to minnesota coding

ECG	Minnesota codes			
	ST/T changes		Q/QS changes	
	Probable	Possible	Probable	Possible
NAFLD (*n*=142)	32	16	26	14
Normal liver (*n*=76)	6	0	4	0

ECG: Electrocardiogram, NAFLD: Nonalcoholic fatty liver disease

Table 11: Association of nonalcoholic fatty liver disease with coronary artery disease in type 2 diabetes mellitus

Liver	CAD present, *n* (%)	No CAD, *n* (%)	*P*
NAFLD (*n*=142)	88 (62)	54 (38)	0.0001
Normal liver (*n*=76)	10 (14)	66 (86)	

CAD: Coronary artery disease, NAFLD: Nonalcoholic fatty liver disease

significant in our study similar to the previous studies.[15-17] In our study, symptoms of angina according to modified rose questionnaire were present in 26 (18%) of the NAFLD patients.[17] In our study, of the 142 patients who had NAFLD, 88 (62%) patients had CAD as identified by ECG changes according to Minnesota coding, which is found to be statically significant. Taking both the modified rose questionnaire and Minnesota coding, 114 (80%) had CAD in NAFLD diabetic patients when compared to 14 (18%) in diabetic patients with normal liver. Previous studies also showed a significant association of CAD in type 2 diabetes mellitus patients with NAFLD.[17-20]

Conclusion

Our study showed a significant association of NAFLD in type 2 diabetes mellitus patients. There is also a significant association of CAD with NAFLD in type 2 diabetes mellitus patients. NAFLD is also significantly associated with cardiovascular risk factors. The presence of NAFLD in type 2 diabetes mellitus should be considered as a strong coronary risk factor and all patients with type 2 diabetes mellitus should be screened for NAFLD, so that appropriate primary prevention for CAD may be initiated.

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Conflicts of interest

There are no conflicts of interest.

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