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Prevalence of non-alcoholic fatty liver disease and its correlation with coronary risk factors in patients with type 2 diabetes mellitus

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ABSTRACT

Introduction

Non alcoholic fatty liver disease (NAFLD) is commonly associated with obesity, type 2 diabetes, dyslipidemia, and insulin resistance. Presence of NAFLD along with diabetes may also be linked to increased coronary artery disease (CAD) risk[1]. We conducted this study to estimate the prevalence of NAFLD in type 2 diabetes mellitus patients and to assess association of NAFLD with CAD and its risk factors in type 2 diabetes mellitus patients.

Methodology

A Hospital based prospective cross-sectional study was done in 100 consecutive type 2 diabetic patients fulfilling the eligibility criteria, in the Department of Medicine, Sir Takhtsinhji General Hospital, Bhavnagar. NAFLD was diagnosed on the basis of ultrasound assessment of the liver. History, physical examination and results of relevant laboratory investigations were recorded. Patients were grouped in two groups – NAFLD and Non-NAFLD and various parameters were compared. A p value of < 0.5 was considered significant.

Results

The prevalence of NAFLD was 59% in type 2 diabetic patients. CAD was more prevalent in the NAFLD subgroup (49.15%) compared to non-NAFLD subgroups (26.82%). The NAFLD subgroup had significantly higher prevalence of coronary risk factors like family history of diabetes, low HDL, high triglyceride, microalbuminuria and metabolic syndrome. The proportion of patients using insulin, antihypertensive drugs, antiplatelet drugs and lipid lowering agents was higher among patients with NAFLD.

Conclusion

NAFLD is commonly associated with type 2 diabetics. Ultrasonographically detected NAFLD alerts us for metabolic syndrome and increased risk of coronary artery disease. Thus understanding its pathogenesis, biochemical parameters and its management, are vital issues today in clinical practice to identify type 2 diabetics who are at highest risk.

Key words: NAFLD, CAD, type 2 diabetes mellitus, metabolic syndrome

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INTRODUCTION

Nonalcoholic fatty liver disease is rapidly becoming a world-wide public health problem. Over the past couple of decades, it has become increasingly clear that nonalcoholic fatty liver disease (NAFLD) is now the leading cause of liver disease. Prevalence of NAFLD appears to be increasing, in part due to the increasing numbers of adult and pediatric individuals who are obese or overweight, or have metabolic syndrome or type 2 diabetes mellitus, all major risk factors for development of NAFLD[2]. Epidemiological studies suggest prevalence of NAFLD in around 9% to 32% of the general population in India with higher prevalence in those with overweight or obesity and those with diabetes or prediabetes[3].To date, major gaps remain in our understanding of the etiology of NAFLD and why it progresses. It is generally agreed that dysregulation of lipid metabolism is involved. Further, it seems likely that dysregulation of the immune response plays an important role, particularly in progression. Clearly, NAFLD is a complex disease with many interacting metabolic pathways that appear to be regulated by the interplay of genetic predisposition and environmental factors. It seems likely that many of the molecular mechanisms involved in the development and progression of NAFLD will share similarities with those for development of obesity and development and progression of metabolic syndrome, type 2 diabetes mellitus, cardiovascular disease and malignancy[2]. NAFLD, previously considered a benign condition, is now shown to be associated with obesity, diabetes mellitus, dyslipidemia & hypertension. These conditions cluster to form a high-risk factor for cardiovascular diseases.Hence, this study was conducted with the aim of determining the prevalence of NAFLD in diabetic patients of our hospital and also to find association between NAFLD & coronary risk factors.

Materials and method

A cross-sectional study was carried out during year 2012-2013 in the Department of Medicine, Government Medical College and Sir Takhatsinhji General Hospital, Bhavnagar after taking permission from Institutional Review Board (Human Ethics Committee), Government Medical College, Bhavnagar. 100 consecutive type 2 diabetic patients, giving informed consent, fulfilling the eligibility criteria were enrolled in the study. Type 2 diabetes mellitus patients more than 40 years of age were included. Patients with known hepatic disease, HBsAg or Anti HCV positivity, alcoholic and/or use of hepatotoxic drugs were excluded from the study.A detailed history of each patient was noted with emphasis on symptoms and signs of non alcoholic fatty liver disease, presence of coronary artery disease and its risk factors. The presence of coronary artery disease was assessed from history of angina, ECG changes, past history of CAD or treatment taken for coronary artery disease. Detailed physical examination was carried out with emphasis on brachial blood pressure, height, weight, and waist-hip ratio. BMI was calculated. Recommendations for BMI in Indian patients[14]: Normal: 18–22.9 kg/m2, overweight: 23–24.9 kg/m2 and obesity: BMI ≥25 kg/m2. Metabolic syndrome was defined by NCEP-ATP III criteria.Laboratory investigations included fasting and 2-hour postprandial blood glucose, HbA1c, blood urea, serum creatinine, lipid profile, transaminases level and quantitative microalbuminuria estimation. All patients underwent ultrasound (USG) of the abdomen to detect fatty changes in the liver.The study group was divided into two subgroups: a) NAFLD – patients with USG evidence of fatty changes in the liver. b) Non-NAFLD – patients without any USG evidence of fatty changes in the liver. Comparison of various parameters between two groups was done.

Statistical analysis

Significant differences between groups were evaluated using the Student t-test, chi-square test wherever appropriate. Data was analyzed using SPSS statistical software and p value of less than 0.05 was considered significant.

Results

Out of a total of 100 enrolled type 2 diabetic patients, 59 had NAFLD based on ultrasonographic evidence of fatty liver. Comparison of various parameters in between both groups is as in **Table 1.**

Table 1: Comparison of baseline parameters between patients with and without NAFLD

Variable (Mean ± S.D.)	Group I NAFLD (N=59)	Group II Non-NAFLD (N=41)	p value
Age (years)	55.08 ± 9.13	56.44 ± 8.55	0.45
Weight (Kg)	71.73 ± 7.57	69.34 ± 6.62	0.10
Waist circumference (cm)	96.49 ± 6.15	93.35 ± 5.53	**0.009**
BMI (kg/m²)	26.09 ± 2.48	25.72 ± 2.32	0.45
WHR	0.89 ± 0.04	0.88 ± 0.04	0.21
SBP (mm of Hg)	141.93 ± 17.92	134.78 ± 18.61	0.05
DBP (mm of Hg)	87.08 ± 7.91	83.75 ± 8.86	**0.047**
FBS (mg/dl)	186.25 ± 55.33	173.65 ± 62.06	0.28
PPBS (mg/dl)	268.72 ± 82.54	279.39 ± 83.37	0.52
B. Urea (mg/dl)	30.93 ± 10.97	34.46 ± 13.83	0.15
S. Creatinine (mg/dl)	1.15 ± 0.39	1.16 ± 0.45	0.90
HbA_1c (%)	8.06 ± 1.94	7.74± 1.12	0.35
T. Cholesterol	204.83 ± 56.84	210.34 ± 52.34	0.62
LDL (mg/dl)	103.88 ± 30.61	104.02 ± 24.47	0.98
HDL (mg/dl)	44.88 ± 9.90	47.90 ± 6.26	0.08
Triglycerides (mg/dl)	212.49 ± 92.90	150.43 ± 53.98	**0.0001**
AST (U/L)	49.06 ± 54.43	36.83 ± 16.86	0.16
ALT (U/L)	49.38 ± 73.39	33.53 ± 14.25	0.17
AST/ALT	1.162 ± 0.47	1.164 ± 0.57	0.98
Microalbuminuria	26.20 ± 11.72	22.26 ± 9.23	0.07
Prevalence of MS	47 (79.66%)	23 (56.09%)	**0.015**
Prevalence of CAD	29 (49.15%)	11 (26.82%)	**0.03**

The prevalence of NAFLD among men was 61.82% and among women was 55.56% which was not statistically different (p=0.52). The frequency of NAFLD among different age groups was compared which did not show any significant differences (p=0.36). The individuals with NAFLD (8.7 years) had longer diabetes duration than those without NAFLD (5.85 years). The prevalence of obesity (calculated from BMI) in patients with NAFLD was 57.62%, as compared to 53.06% in Non-NAFLD patients.CAD and metabolic syndrome were more prevalent in the NAFLD subgroup compared to the non-NAFLD subgroup. The difference was highly significant, thereby relating NAFLD to CAD and metabolic syndrome. Among other parameters, only the mean triglyceride level and diastolic blood pressure showed significant correlation with the presence of NAFLD. The proportion of patients using insulin, antihypertensive drugs, antiplatelet drugs and lipid lowering agents was higher among patients with NAFLD, whereas the proportion using oral hypoglycemic agents was similar in both groups.Comparison of risk factors for CAD among two groups as shown in **Table 2** revealed that the NAFLD subgroup had significantly higher prevalence of family history of diabetes, low HDL, high triglyceride, metabolic syndrome and microalbuminuria.

Table 2:Prevalence of risk factors for CAD between NAFLD and Non-NAFLD group

Variable	Group I NAFLD	Group II Non-NAFLD	p Value
Hypertension	52 (88.13%)	31(75.60%)	0.11
Smokers	16 (27.12%)	09 (21.95%)	0.6
F/H of DM	15 (25.42%)	03 (7.31%)	**0.03**
BMI ≥ 25/m²	34 (57.62%)	26 (63.41%)	0.67
WHR (≥ 0.90 males; ≥0.85 females)	38 (64.40%)	25 (60.97%)	0.83
HbA1c > 7%	37 (62.71%)	31 (75.60%)	0.19
T. Cholesterol ≥200 mg%	33 (55.93%)	20 (48.78%)	0.54
S. LDL≥130 mg%	08 (13.55%)	02 (4.87%)	0.19
S. HDL <40 mg% Male; <50 Female	31 (52.54%)	10 (24.39%)	**0.007**
S. Triglyceride ≥150mg%	44 (74.57%)	16 (39.02%)	**0.0004**
Microalbuminuria	20 (33.89%)	06 (14.63%)	**0.037**
Prevalence of Metabolic syndrome	47 (79.66%)	23 (56.09%)	**0.015**

Among the CAD patients, the prevalence of NAFLD was 72.5%. Only high triglyceride levels showed significant higher prevalence in these patients as compared to patients with CAD without NAFLD as shown in **Table 3.**

Table 3: Comparison of risk factors in patients with CAD

Variable	Group I NAFLD Pts.	Group II Non-NAFLD	p Value
Hypertension	26	10	1.0
Smokers	12	3	0.48
BMI ≥ 25/m²	18	7	1.0
HbA1c > 7%	19	10	0.23
S. LDL≥130 mg%	3	0	0.54
S. HDL <40 mg% Male; <50 Female	19	4	0.15
S. Triglyceride ≥150mg%	24	5	**0.042**
Microalbuminuria	12	2	0.26
Prevalence of Metabolic syndrome	27	8	0.11

Discussion

There is a growing need to determine the prevalence of NAFLD in the type 2 diabetic population and to evaluate its association with CAD. A major finding of this study was that the prevalence of NAFLD, as diagnosed by characteristic ultrasonographic features, in the type 2 diabetic population was very high (59%) of type 2 diabetic patients, which was comparable with the prevalence found in other studies. The prevalence of NAFLD in study by AK Agrawal et al[1] was 57.20%, 62.25% in Study by M Prashanth et al[4], 54.5% in Study by Mohan et al[5] and 55.8% in Study by Merat et al[6].There were no significant gender differences between the two groups (p=0.52), however the prevalence of NAFLD among men and women varied in different clinical studies. In some studies, NAFLD was considered to be more common among women,[7,8] whereas it was reported to be more prevalent among men in others.[9] However, in more recent studies, it has been suggested that both gender might be afflicted equally.[7]The mean age of patients in both the groups was not statistically significant (p=0.45). The frequency of NAFLD among different age groups was compared which again did not show significant differences (p=0.36). In the Diabetes Care work study from Targer[10], it was found that the prevalence of NAFLD increased with age in patients with type 2 diabetes; (65.4% in aged 40 – 59 years and 74.6% among those ≥ 60 years; p < 0.001). In a similar study by S Merat[6], there was no significant statistical difference in the occurrence of NAFLD among different age groups.Another major finding of this study was that NAFLD was associated with a higher

prevalence of CAD. Targher et al[12] found that NAFLD was associated with increased risk of future CAD events among type 2 diabetics. Arslan et al[13] found that the presence of NAFLD increased the risk for CAD.Interestingly, this study provided further evidence that a normal serum ALT level provides little diagnostic or prognostic value when assessing patients for NAFLD, because most of the patients with NAFLD had normal ALT levels. Therefore, serum ALT levels appear to be insensitive markers for NAFLD. Indeed, it is known that the full histological spectrum of NAFLD may be present among patients with normal liver enzymes, which therefore cannot be reliably used to exclude the presence of more advanced stages of NAFLD. In many other similar studies it was seen that, although mild to moderate elevations of serum aminotransferase were common in NAFLD, normal values can be found in many of the patients at any time, even when complete histological findings were present. Hence, there is a poor correlation between transaminase levels and disease severity[6,10].Study results significantly correlate NAFLD to metabolic syndrome. Mishra et al[11] found the prevalence of metabolic syndrome and NAFLD to be 24% and 14.8% respectively, in non-alcoholic North Indian men. Study also reveals higher prevalence of risk factors for CAD in patients with NAFLD.

Conclusion

Our results suggest that NAFLD is common in people with type 2 diabetes mellitus and it is more commonly seen with increasing diabetes duration. Ultrasonography is a simple and non-invasive method to diagnose NAFLD. Surprisingly, it can also occur without any abnormalities in transaminase levels. NAFLD is associated with a higher prevalence of coronary risk factors, CAD and metabolic syndrome. The association between NAFLD and CAD appears to be irrespective of classical risk factors like smoking, glycaemic control, hypertension, and total cholesterol and LDL levels. Thus, these results further indicate that the identification of NAFLD in type 2 diabetes patients may help in CVD risk prediction. Follow-up studies are needed to determine whether NAFLD predicts the development and progression of CVD.

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