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ANALYSIS OF NON-ALCOHOLIC FATTY LIVER DISEASE IN PATIENTS WITH TYPE 2 DIABETES MELLITUS AND ITS RELATIONSHIP WITH CARDIOVASCULAR RISK

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Abstract

Background and Aim: Compared with nondiabetic subjects, patients with T2DM appear to have an increased risk of developing Non-alcoholic fatty liver disease (NAFLD) and certainly have a heightened risk of developing advanced liver diseases, such as fibrosis, cirrhosis, and hepatocellular carcinoma. This study was primarily done to study the prevalence of NAFLD in patients with T2DM using ultrasound abdomen, NAFLD fibrosis score and transient elastography.

Material and Methods: This hospital based cross-sectional study has been carried out for the duration of 2 years with a sample size of 100 subjects in department of Medicine, Tertiary care institute of India. The patients underwent a detailed history including past, treatment and personal history and a thorough clinical examination. The findings were logged in a specially prepared proforma. NAFLD fibrosis score and FIBROSCAN. ASCVD score was used for correlation between CVD risk and NAFLD.

Results: Out of 100 patients 76 (76%) were having fatty liver based on ultrasound abdomen while 23 (23%) patients were having no fatty liver. As far as steatosis is concerned mean CAP (dB/m) was 246.10±51.05 out of which 44 (44%) were having no or minimal steatosis grade of steatosis respectively. 27 patients out of 100 were of F0 grade (no fibrosis) while 35 (35%), 9 (16%), 13 (13%) and 9 (9%) were of grade F1 (mild fibrosis), F2 (moderate fibrosis), F3 (severe fibrosis) and F4 (cirrhosis) respectively. ASCVD (10 year) risk score was calculated using an

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online calculator to assess the cardiovascular risk of the patients. Mean ASCVD risk score of the study population was 11.45±09.22.

Conclusion: This study showed a high prevalence of non-alcoholic fatty liver disease in patients with type 2 diabetes mellitus. Mean HbA1c of the patients with fatty liver was higher than that of the non-fatty liver group.

Key Words: Cross-Sectional Study, Diabetes Mellitus, Fibrosis, Non-alcoholic fatty liver disease

Introduction

Non-alcoholic fatty liver disease (NAFLD) is a spectrum of liver disease ranging from hepatic steatosis (fatty liver) to non-alcoholic steatohepatitis (NASH) that is associated with inflammation.[1] The major risk factors for NAFLD are obesity and diabetes. The mechanism by which diabetes causes fatty liver is through insulin resistance, oxidative stress and inflammation. The prevalence of NAFLD in an Indian study was found to be 5– 28% in the general population, while it was 44–72% in patients with type 2 diabetes mellitus.[2] NASH (non-alcoholic steatohepatitis) to cirrhosis and rarely HCC in very severe form. It is defined as hepatic steatosis in >5% of hepatocytes according to histological analysis or by proton density fat fraction or >5.6% as assessed by proton magnetic resonance spectroscopy (MRS) or quantitative fat/water selective magnetic resonance imaging (MRI) with no secondary cause for steatosis.[3] NAFLD is the most common cause of abnormal liver function test among western countries and is commonly associated with components of metabolic syndrome supporting the idea of it being a hepatic manifestation of the syndrome.[4] Accumulated evidence has indicated that NAFLD could be regarded as part of or, indeed, a hepatic manifestation of metabolic syndrome associated with metabolic risk factors such as obesity, diabetes mellitus, and dyslipidemia.[5,6]

The association between NAFLD and type 2 diabetes mellitus (T2DM) has been well established, which could be explained by the insulin-resistance and compensatory hyperinsulinemia progressing to defective lipid metabolism and hepatic triglyceride (TG) accumulation in NAFLD or to b-cell dysfunction in T2DM.[7] Compared with nondiabetic subjects, patients with T2DM appear to have an increased risk of developing NAFLD and certainly have a heightened risk of developing advanced liver diseases, such as fibrosis, cirrhosis, and hepatocellular carcinoma.[8-10] There is a 5-fold risk of developing T2DM in a patient of NAFLD.[11] A great deal of evidence suggests that the metabolic syndrome predicts incident cardiovascular disease (CVD), so it is possible to hypothesize that NAFLD patients might portend a greater CVD risk and that NAFLD itself might confer a CVD risk above that associated with individual metabolic syndrome risk factors.[12] If these data holds true, the identification of NAFLD in type 2 diabetes may help in CVD risk prediction with important management implications.[3] Also this would help us manage actively this subgroup of diabetic patients with NAFLD and reduce CVD related complications.

Radiologic imaging studies like ultrasonography (USG), computed tomography (CT) and magnetic resonance imaging (MRI) are used for identifying fatty liver in patients. NAFLD is

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postulated to be an independent risk factor for cardiovascular disease in patients with type 2 diabetes mellitus (DM).

This study was primarily done to study the prevalence of NAFLD in patients with T2DM using ultrasound abdomen, NAFLD fibrosis score and transient elastography.

Material and Methods

This hospital based cross-sectional study has been carried out for the duration of 2 years with a sample size of 100 subjects in department of Medicine, Tertiary care institute of India.

The study group consisted of patients with T2DM with age greater than 18 years and excluding other causes of chronic liver disease like viral infection (hepatitis B and hepatitis C), history of intake of hepatotoxic drugs (e.g. ATT, valproate), patients with significant alcohol intake and patients of congestive heart failure. The patients underwent a detailed history including past, treatment and personal history and a thorough clinical examination. The findings were logged in a specially prepared proforma. The cases were subjected to following investigations: ECG, Hb, TLC, DLC, ESR, urine routine and microscopy, HbA1c, random blood sugar, SGPT/SGOT, serum bilirubin total and differential, kidney function test,serum total protein, albumin and globulin, USG whole abdomen, transient elastography. The patients were then graded in grades of fatty liver (grade I, grade II and grade III) based on USG abdomen and hepatic steatosis based of CAP value of transient elastography. Patients were categorized for liver fibrosis using E value of transient elastography. Cardiovascular risk was assessed using 10-year ASCVD risk.

Statistical analysis

The recorded data was compiled and entered in a spreadsheet computer program (Microsoft Excel 2007) and then exported to data editor page of SPSS version 15 (SPSS Inc., Chicago, Illinois, USA). For all tests, confidence level and level of significance were set at 95% and 5% respectively.

Results

Out of the 100 cases 47 (47%) were male and 53 (53%) were female. 9% of the participants had age: 31-40 years. 29% of the participants had age: 41-50 years. 33% of the participants had age: 51-60 years. 25% of the participants had age: 61-70 years. 4% of the participants had age: 71-80 years.

Out of 100 patients 76 (76%) were having fatty liver based on ultrasound abdomen while 23 (23%) patients were having no fatty liver. As far as steatosis is concerned mean CAP (dB/m) was 246.10±51.05 out of which 44 (44%) were having no or minimal steatosis grade of steatosis respectively. The mean E (kpa) of the study population was 9.25±6.14. Patients were graded for liver fibrosis using E (kpa) value obtained from transient elastography into F0 (E 16 kpa). 27 patients out of 100 were of F0 grade (no fibrosis) while 35 (35%), 9 (16%), 13 (13%) and 9 (9%) were of grade F1 (mild fibrosis), F2 (moderate fibrosis), F3 (severe fibrosis) and F4 (cirrhosis) respectively. ASCVD (10 year) risk score was calculated using an online calculator to assess the cardiovascular risk of the patients. Mean ASCVD risk score of the study population was 11.45±09.22.

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Table 1: Descriptive data of the study population

USG	Number	Percentage (%)
USG grade		
Normal	23	23
Grade 1	45	45
Grade 2	27	27
Grade 3	3	3
Fatty liver	76	76
Fibroscan: CAP (mean±SD)	246.10±51.05	
Steatosis grade N (%)		
S0	44	44
S1	20	20
S2	16	16
S3	20	20
Fibroscan: E (KPa) (mean±SD)	9.25±6.14	
Fibrosis grade N (%)		
F0	27	27
F1	35	35
F2	16	16
F3	13	13
F4	9	9
ASCVD (10 year) risk score (mean±SD)	11.45±09.22	

Discussion

Several shared pathophysiological pathways link NAFLD and T2DM to increased cardiovascular risk including proatherogenic lipid alteration, increase in thrombosis factors, insulin resistance, low-grade inflammation and microbiome alteration.[13] A study by Jayarama et al reported the prevalence of NAFLD to be 60% in type 2 diabetic patients that was comparable to the prevalence in the present study.[14]

Kalra et al conducted a study to determine frequency and risk factors in type 2DM patients. Out of 924 patients (335 females/569 males) in an age group of 15-85 years were identified as having NAFLD. In our study as well the prevalence of fatty liver was quite high than in general population. 76 (76%) participants had fatty liver (grade 1, 2 and 3) on USG while 23 (23%) had no fatty liver. Also the average HBa1c of the fatty liver group was higher than that of the non-fatty liver group although this difference wasn't significant statistically.

Subgroup analyses indicated that the prevalence of NAFLD was significantly higher in male T2DM patients than female T2DM patients. This finding is consistent with many previous studies.[10-12]

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There was no significant difference in terms of ASCVD score in both these groups (fatty liver and non fatty liver) with ASCVD risk score of the fatty liver and non-fatty liver group as 10.55 (SD-10.12) and 13.80 (SD-12.10) respectively. Toung et al conducted a cross-sectional design in T2DM adults who attended Dai Phuoc Ho Chi Minh Polyclinic and Polyclinic of Pham Ngoc Thach University of Medicine and found in their study that the prevalence of NAFLD in T2DM patients based on FibroScan was 73.3%. The prevalence of steatosis in our study population was 56% (56/100) based on transient elastography. 20 (20%), 16 (16%) and 20 (20%) out of 100 study subjects had steatosis of grade S1, S2 and S3 respectively based on CAP. There was no difference in the prevalence of cardiovascular disease in the NAFLD and non-NAFLD groups in this study. However, Targher et al in their study found a significant association of CVD in patients with NAFLD [15]. Similarly, Agarwal et al in their study reported a significant association of coronary artery disease (CAD) in diabetics with NAFLD as compared to those without NAFLD.[16] Brea et al did a study in 40 subjects with primary NAFLD (diagnosed by ultrasonography) and showed that the mean CIMT values were significantly higher in patients with NAFLD as compared to the control subjects. The presence of NAFLD and old age were found to be independent predictors of high CIMT values in their study.[17] The results of this study are comparable with the results of a meta-analysis done by Sookoian et al. in patients with NAFLD. Analysis of 3497 subjects from seven studies was done by them and a significant association was found between CIMT and NAFLD.[18]

There was a moderate positive correlation between ASCVD risk score (%) and fibroscan: E (KPa) and this correlation was statistically significant. For every 1 unit increase in ASCVD risk score (%), the fibroscan: E (KPa) increases by 0.19 units. Conversely, for every 1 unit increase in fibroscan: E (KPa), the ASCVD risk score (%) increases by 0.48 units.

The limitation of the present study was a relatively small sample size. Future studies have to be directed with larger sample size. Also since the study was conducted at a tertiary centre which may not be a representative of the general population.

Conclusion

This study showed a high prevalence of non-alcoholic fatty liver disease in patients with type 2 diabetes mellitus. Mean HbA1c of the patients with fatty liver was higher than that of the non-fatty liver group. The prevalence of steatosis (56.4%) and fibrosis (65.5%) as measured by transient elastography was also higher in our study population showing the facts that patients with T2DM are at increased risk of developing NALFD.

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