Research Article

Prevalence of non-alcoholic fatty liver disease in type 2 diabetes mellitus patients in a rural health care hospital

T.K.V. Sharavanan[1], E. Premalatha[2]
[1]Associate Professor, Department of General Medicine, Tagore Medical College and Hospital, Chennai
[2]Assistant Professor, Department of Microbiology, Tagore Medical College and Hospital, Chennai

***Corresponding author**
T.K.V. Sharavanan
Email: dr.sharavanan@yahoo.com

Abstract: Diffuse accumulation of fat in hepatocytes, occurring in individuals without a significant history of alcohol consumption is termed as Non-Alcoholic Fatty liver disease (NAFLD). It is a common condition, in which diabetic fatty liver accounts for a larger proportion. As a result of epidemic increase in diabetes mellitus, hypertension, obesity and hyperlipidemia, the prevalence of NAFLD is increasing worldwide. The aim of this study was designed to determine the prevalence of NAFLD in T2DM (type 2 diabetes mellitus) patients and also to study its risk factors. The present study was conducted in a rural tertiary care hospital, over a period of 3 months. A total of 249 patients with T2DM underwent ultrasonography to diagnose fatty liver. Patients with NAFLD were compared with those with normal liver ultrasound findings. The risk factors of NAFLD were also evaluated in the study group. Of the 249 diabetic patients enrolled in this study, 76 (30.5%) presented with NAFLD. The highest prevalence of NAFLD was recorded in the age group of 51-60 years at 34.5%. The prevalence rate among females (62.2%) was higher than for males (37.8%). An insight into the predisposing factors of NAFLD, revealed a higher prevalence of obesity, hypertension, hyperglycemia, hyperlipidemia and hyperuricemia in the subjects with NAFLD. T2DM patients with NAFLD are at risk of developing progressive forms of the disease. This liver disorder is another potential complication in T2DM patients that requires intervention in the associated factors and avoids the evolution of NAFLD to chronicity.
Keywords: Type 2 diabetes mellitus, Non-alcoholic fatty liver disease, metabolic syndrome, insulin resistance.

INTRODUCTION

The term NAFLD (non-alcoholic fatty liver disease) is used to describe a wide array of fatty liver changes from simple steatosis to steatohepatitis, cirrhosis and hepatocellular carcinoma in the absence of excessive alcohol intake. NAFLD has emerged as the most common cause of liver disease worldwide [1]. NAFLD is defined by macrovesicular steatosis of more than 5% hepatocytes in the absence of inflammation. T2DM (type 2 diabetes mellitus) patients appear to have an increased risk of developing NAFLD than non-diabetic subjects and certainly have higher risk of developing fibrosis and cirrhosis. Presence of NAFLD in T2DM may also be linked to increased cardiovascular disease risk [2]. T2DM increases the risk of liver related death by upto 22 fold in patients with NAFLD [3]. Diagnosis of NAFLD requires high index of suspicion, especially in obese patient over the age of 45 years with history of diabetes mellitus, because these patients are at increased risk of developing cirrhosis [4]. Numerous studies have shown that NAFLD is the hepatic component of metabolic syndrome. The central features of metabolic syndrome such as the peripheral insulin resistance, obesity, hyperinsulinemia,

hypertriglyceridemia and hypertension are the predisposing factors for NAFLD [5]. The overall prevalence of NAFLD is 15 to 40% in western countries and 9 to 40% in Asian countries. There is an increase in incidence of DM (diabetes mellitus), obesity and insulin resistance in India in the last two decades, hence it is logical to expect increase in incidence of NAFLD in India. However there is limited data on the prevalence of NAFLD in India [6]. Various studies conducted shows the prevalence rate of NAFLD to be around 9-32% in the general Indian population, with a higher incidence among the obese and diabetic individuals. The prevalence rate of NAFLD in T2DM is estimated be in the range of 12.5% to 87.5% in India [7] Radiological imaging of liver with ultrasonography, computerized tomography, or magnetic resonance imaging has an adequate threshold for detection of fatty liver. Ultrasound is the most widely available cheap test performed [8]. The present study was conducted to determine the prevalence of NAFLD in T2DM and also evaluate the risk factors associated with diabetic fatty liver.

MATERIALS AND METHODS

The present prospective study was conducted in Melmaruvathur Adhiparasakthi Institute of Medical Sciences and Research, for a period of 3 months (August-September) in the year 2013. The study population included a total of 249 patients with T2DM, in the age group of 20-70 years, attending medical outpatient clinic. Informed consent from the patients and approval from the Institutional Ethics Committee were obtained before initiating the study. The patients were interviewed using a structured questionnaire. A complete history taking and physical examination were performed. Anthropometric (waist circumference and body mass index) and metabolic parameters such as fasting and postprandial blood sugar, glycosylated hemoglobin (HbA1c), serum uric acid, blood urea, serum creatinine, fasting lipid profile, serum bilirubin, serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT) and serum alkaline phosphatase (SAP) were measured. Exclusion criteria included patients with history of alcohol consumption, chronic liver disease of any cause and intake of hepatotoxic drugs. All patients enrolled underwent ultrasonography to detect fatty changes in the liver, performed by single experienced radiologist (to prevent interpersonal variation), using a high resolution B-mode ultrasonography system having an electric linear transducer mid frequency of 3-5 MHZ. Fatty liver was defined as the ultrasonographic features consistent with bright liver with ultrasonographic contrast between hepatic and renal parenchymal vessel blurring and narrow of the lumen of hepatic vein in the absence of findings suggestive of chronic liver disease.

NAFLD WAS CLASSIFIED BASED ON THE STANDARD ULTRASONOGRAPHIC CRITERIA:
Grade 1 - (Mild steatosis) slightly increased liver echogenicity with normal vessels and absent posterior attenuation.

Grade 2 - (Moderate steatosis) moderate increase in liver echogenicity with partial dimming of vessels and early posterior attenuation.

Grade 3 - (severe steatosis) diffuse increase in liver echogenicity with absence of visible vessels and heavy posterior attenuation.

Sensitivity of ultrasonogram in detection of hepatic steatosis ranges from 60 to 94% and specificity 84 to 95%. Hepatorenal sonographic index which is the ratio between mean brightness level of liver and right kidney, has also been proposed as a measure of hepatic steatosis with a cutoff value of 1.49, yielding a very high sensitivity (100%) and specificity (91%) for diagnosis of steatosis > 5% [9].

Statistical analysis
Data documented and analysed using Statistical Package for Social Sciences [SPSS], Pearson's Chi Square Analysis test and Fisher exact probability test. Mean and standard deviation were calculated for each variable. The diabetic patients with fatty liver were compared with the diabetic patients without fatty liver.

RESULTS
Among the 249 patients with T2DM, a total of 76 patients were identified to have fatty liver by ultrasonography (Figure 1). Majority of the NAFLD patients showed Grade I fatty liver (22.9%), followed subsequently by Grade II (6.8%) and Grade III (0.8%). The present study observed a higher frequency of NAFLD in the diabetic female population (47/249) compared with the male population (29/249) (Table 1). Statistically, there is no significant difference between male and female subjects. The mean and standard deviation for age was 54.5 and 10.04 respectively. The age distribution of NAFLD patients was given in the Table 2. The frequency of patients with NAFLD was more in the age group of 61-70 years. No significant difference was found between age and disease by statistical analysis.
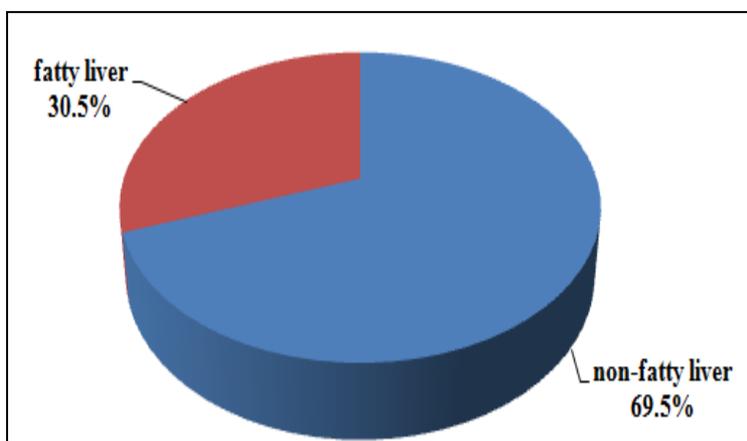

Fig-1. Prevalence of NAFLD in T2DM Patients N=249

Table-1: Showing Gender Distribution of NAFLD in T2DM Patients (N=249)

Gender	T2DM patients	Fatty liver group	Non-fatty liver group
Male	93 (37.3%)	29 (11.6%)	64 (25.7%)
Female	156 (62.7%)	47 (18.9%)	109 (43.8%)
Total	249	76 (30.5%)	173 (69.5%)

Table 2: Showing Age Distribution of NAFLD in T2D Patients (N=249)

Age in years	T2DM patients	Fatty liver group	Non-fatty liver group
<40 yrs	27 (10.8%)	10 (4.0%)	17 (6.8%)
41-50 yrs	59 (23.7%)	15 (6.0%)	44 (17.7%)
51-60 yrs	86 (34.5%)	34 (13.7%)	52 (20.9%)
61-70 yrs	77 (30.9%)	17 (6.8%)	60 (24.1%)
TOTAL	249	76 (30.5%)	173 (69.5%)

Table 3: Showing Comparison of the Demographic and Laboratory variables in diabetic patients with and without fatty liver

S.No	Characteristics	Fatty Liver group (n = 76) (Mean $\pm$ SD)	Non-Fatty Liver group (Normal) (n=173) (Mean $\pm$ SD)	t/Z value	P valve
1.	BMI (kg/m 2)	29.54 $\pm$ 2.67	28.71 $\pm$ 2.65	2.263	0.025
2.	WC (cm)	101.63 $\pm$ 8.36	98.02 $\pm$ 7.89	3.266	0.001
3.	FBS (mg/dl)	161.92 $\pm$ 55.43	133.18 $\pm$ 43.54	4.399	0.000
4.	Postprandial (mg/dl)	280.21 $\pm$ 86.32	236.68 $\pm$ 69.59	4.214	0.000
5.	HbA1c (mg/dl)	10.10 $\pm$ 2.46	8.43 $\pm$ 1.963	5.700	0.000
6.	DM (duration in yrs)	3.88 $\pm$ 2.32	2.95 $\pm$ 1.76	3.473	0.001
7.	HT (duration in yrs)	3.45 $\pm$ 2.28	2.66 $\pm$ 1.75	2.945	0.004
8.	Uric acid (mg/dl)	7.26 $\pm$ 1.85	4.67 $\pm$ 1.18	13.259	0.000
9.	Cholesterol (mg/dl)	203.74 $\pm$ 27.18	183.49 $\pm$ 25.9	5.594	0.000
10.	TGL (mg/dl)	205.82 $\pm$ 50.29	159.95 $\pm$ 51.21	6.543	0.000
11.	LDL (mg/dl)	125.43 $\pm$ 26.57	107.69 $\pm$ 25.79	4.952	0.000
12.	VLDL (mg/dl)	36.26 $\pm$ 9.15	32.31 $\pm$ 10.06	2.934	0.004
13.	HDL (mg/dl)	41.57 $\pm$ 5.03	43.61 $\pm$ 3.85	3.494	0.004

Comparison of the different characteristics observed in the present study was done in the diabetic patients with and without fatty liver. The significant characteristics of the diabetic patients with fatty liver was given in the Table 3. The above shown variable shows a higher prevalence and significant association of fatty liver disease in patients with diabetes mellitus, hypertension, obesity, hyperuricemia and dyslipidemia.

DISCUSSION

NAFLD is characterized by fatty infiltration of the liver, mostly in the form of triglycerides, which exceeds 5% of the liver weight, without a history of significant of alcohol intake and not due to other identifiable causes of liver[10]. Fatty liver is a common finding among T2DM individuals. NAFLD and T2DM together have poorer prognosis in terms of higher frequency of cirrhosis and mortality[11]. In this study, the overall prevalence of T2DM patients, screened for the evidence of fatty liver by ultrasonography was 30.5%. Geographic variations existed in the prevalence of NAFLD worldwide. Studies done earlier have reported that around 10-75% of NAFLD patients have

T2DM and 21-72% of patients with diabetes are reported to have NAFLD[12]. The prevalence rate of NAFLD was highest in the 51 to 60 years age group (34/249), subsequently followed by 61-70 years (17/249), 41-50 years (15/249) and less than 40 years age groups (10/249). The study also revealed a higher prevalence of NAFLD in female patients (47/249) with T2DM compared with the male community (29/249). The larger number of female subjects included in the study population may account for the female predilection seen in this study. This similar trend was also reported by Sanjay Kalra et al, in which the frequency of the disease was more in female patients. Previous studies have shown that the prevalence of NAFLD increases with age[1]. In many published series, NAFLD has been reported to be most common in women, aged 40-60 years[13]. Obesity has been commonly reported in female patients, concurrently showing a increase in frequency of fatty liver disease. Hypertension, obesity and dyslipidemia are the elements in metabolic syndrome, and also serves as predisposing factors of NAFLD along with diabetes mellitus. [14,15] Several studies have suggested the

well-established relationship of the disease with these comorbid conditions. In this present study, difference in serum transaminases level between the fatty liver and non-fatty liver group of patients were not statistically significant. The liver enzymes are a poor measure of NAFLD. Although elevation of serum transaminases are common in NAFLD, normal values can be found in upto 78% of patients in the presence of histologic findings.The whole spectrum of clinic-pathologic feature of NAFLD may exist without elevation of transaminases. This result is in broad agreement with the study conducted in Shobha Luxmi et al. The diagnosis of NAFLD in our study was based on standard ultrasonography, which is by for the commonest way of diagnosing this increasingly recognized liver disorder in clinical practice. Radiologic imaging such as sonography has an adequate threshold for diagnosing fatty liver[16]. This study substantiates the necessity of early diagnosis and intervention of NAFLD in patients with T2DM.

CONCLUSION

NAFLD is a common chronic hepatic disorder globally. T2DM and NAFLD are rapidly increasing, reaching levels of a pandemic in countries like India. Prevalence of NAFLD has increased along with the multiple components of metabolic syndrome. The results from this study have established a prevalence pattern of NAFLD in T2DM patients, emphasizing the need to formulate preventive strategies.

REFERENCES
1. Kalra S, Vithalani, M, Gulati G, Kulkarni CM, Kadam Y, Pallivathukkal J, Modi K.D; Study of prevalence of nonalcoholic fatty liver disease (NAFLD) in type 2 diabetes patients in India (SPRINT). J Assoc Physicians India, 2013; 61(7), 448-453.
2. Targher G, Day CP, Bonora E; Risk of cardiovascular disease in patients with nonalcoholic fatty liver disease. New England Journal of Medicine, 2010; 363(14), 1341-1350.
3. Younossi ZM, Granlich T, Matteoni CA, Boparai N, McCullough AJ; Non-alcoholic fatty liver disease in patients with type 2 diabetes. Clinical Gastroenterology and Hepatology, 2004; 2: 262-265.
4. Day C P; Non-alcoholic liver disease: Current concepts and management strategies. Clin J Med, 2006; 6; 19-25.
5. Bayard M, Holt J, Boroughs E; Nonalcoholic fatty liver disease. Am Fam Physician, 2006; 73(11): 1961-8.
6. Farrell GC, Larter CZ; Nonalcoholic Fatty Liver Disease: from Steatosis to cirrhosis. Hepatolog,y 2006; 43: S00-S112.
7. Prashanth M, Ganesh HK, Vima MV, John M, Bandgar T, Joshi SR, et al.; Prevalence of nonalcoholic fatty liver disease in patients with type 2 diabetes mellitus. J Assoc Physicians India, 2009; 57: 205-10.
8. Caballeria Ll, Auladell AM, Toran P, Miranda D, Aznar J, Pera G, et al.; Prevalence and factors associated with the presence of non alcoholic fatty liver disease in an apparently healthy adult population in primary care units. BMC Gastroenterology, 2007; **7:** 41.
9. Saadesh S,Younossi ZM, Remer EM, Gramlich T, Ong JP, Hurley M *et al*.; The Utility of Radiological imaging in NAFLD. Gastro Enterology, 2004; 99:1316-20.
10. Angulo P; Obesity and nonalcoholic fatty liver disease. Nutrition Reviews, 2007; 65:S57–63.
11. Merat S, Yarahmadi S, Tahaghoghi S, Alizadeh Z; Prevalence of Fatty Liver Disease among Type 2 Diabetes Mellitus Patients and its Relation to Insulin Resistance., Middle East Journal of Digestive Diseases, 2009;1:74-79.
12. Angulo P; Nonalcoholic fatty liver disease. N Engl J Med; 2002; 346(16):1221-31.
13. Russo MW, Jacobson IM; Nonalcoholic Fatty Liver Disease. Hospital Physician, 2002; 67: 36-41.
14. Marchesini G, Brizi M, Bianchi G; Nonalcoholic fatty liver disease: a feature of the metabolic syndrome. Diabetes, 2001; 50:1844–50.
15. Angelico F, Del Ben M, Conti R; Non-alcoholic fatty liver syndrome: a hepatic consequence of common metabolic diseases. J Gastroenterology Hepatol, 2003; 18: 588–94.
16. Luxmi S, Sattar RA, Ara J; Association of Non Alcoholic Fatty Liver with type 2 Diabetes Mellitus. JLUMHS, 2008; 188-193.