ORIGINAL RESEARCH PAPER

Volume-8 | Issue-4 | April-2019 | PRINT ISSN No 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

PREVALENCE OF NON ALCOHOLIC FATTY LIVER DISEASE IN NEWLY DIAGNOSED TYPE 2 DIABETES MELLITUS PATIENTS IN A TERTIARY CARE HOSPITAL IN BANGLADESH.

Endocrinology

Dr. Md. Shahjamal Khan MBBS, MD, FACE, Associate professor and Head, Department of Endocrinology, Enam Medical College and Hospital, Savar, Dhaka.

Dr. Shakil Shams M.Phil., Assistant Professor, Department Of Anatomy, Dhaka Medical College And Hospital, Dhaka.

ABSTRACT

Nonalcoholic fatty liver disease(NAFLD) and type 2 DM 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 micro and macrovascular complications) as well as augmenting the risk of more severe NAFLD,including cirrhosis, hepatocellularcarcinoma anddeath. 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 newly diagnosed T2DM (type 2 diabetes mellitus) patients and also to study its risk factors. The present study was conducted in a tertiary care hospital, over a period of 6 months. A total of 100 patients with newly diagnosed T2DM underwentultrasonography 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 100 diabetic patients enrolled in this study, 67 (67%) presented with NAFLD. The highest prevalence of NAFLD was recorded in the age group of 41-60 years at 35%. The prevalence rate among males (38%) was higher than for females (29%). The prevalence of NAFLD was positively associated with BMI,waist circumference, LDL cholesterol and Triglyceride. 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 nondiabetic 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 up to 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].Insulin resistance within the liver as well as extra hepatic tissues such as adipose and skeletal muscle is implicated in the pathogenesis of NAFLD[5].In addition bile acids and gut microbiata are now believed to have a crucial role in the pathogenesis of NAFLD[6].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 [7].Obesity and physical inactivity are interlinked risk factors for the development of diabetes and both are clearly implicated in an individual's risk of developing NAFLD.The prevalence of NAFLD varies widely depending on the population studied and the methodology applied. Studies have shown that NAFLD may be present in up to 70% of patients with diabetes[8] whilst the biopsy proven NASH (nonalcoholic steatohepatitis) in asymptomatic type 2 diabetes with normal liver function tests was 20%[9].There is an increase in incidence of DM (diabetes mellitus), obesity and insulin resistance in Bangladesh in the last two decades; hence it is logical to expect increase in incidence of NAFLD in Bangladesh. However, there is limited data on the prevalence of NAFLD in Bangladesh. The prevalence rate of NAFLD in T2DM is estimated to be in the range of 12.5% to 87.5% in India [10].Radiological imaging of liver with ultrasonography, computerized tomography, or magnetic resonance imaging has an adequate threshold for detection of fattyliver. Ultrasound is the most widely available cheap testperformed [11]. The present study was conducted to determine the prevalence of NAFLD in newly diagnosed T2DM patients and also evaluate the risk factors associated with diabetic fatty liver.

MATERIALS AND METHODS:

The study was conducted in the department of Endocrinology, Enam Medical College and Hospital,Savar,Dhaka during the period of January 2016 to June 2016.It was a cross sectional study. The subjects were selected purposively. One hundred subjects with newly diagnosed type 2 diabetes aged 20-70 years were included in this study. Exclusion criteria include history of alcohol consumption, history of diabetes more than one year, presence of endocrine disorders other than Diabetes ,pregnant and lactating mother, patients receiving any medication that may alter blood glucose level, patients currently on treatment (pharmacological or non-pharmacological) for dyslipidemia, patients with known history of liver or renal disease, acute infection, and when type 1 diabetes or secondary causes for diabetes were more likely on clinical grounds than T2DM.. They were selected from outpatient clinic of endocrinology department at Enam Medical College Hospital on the basis of availability.

Selection of the subjects:

Study subjects were selected who were newly diagnosed diabetic patients according to ADA criteria. Diabetic patients labeled as newly diagnosed referred to those with a known duration of up to one year. Those who had history or clinical features of endocrinopathies,renal disease, liver disease, acute infection ,history of taking medication that may alter blood glucose level, history of taking medication for dyslipidemia were excluded from the study. After primary selection, patients were referred to perform following investigation: SGPT, S.creatinine, fasting lipid profile, CBC, USG of whole abdomen to detect fatty liver disease and to exclude renal disease, liver disease and acute infection. Ultrasonography was performed by single experienced radiologist(to prevent interpersonal variation).Fatty liver was defined as the ultrasonographic features consistent with bright liver with ultrasonographic contrast between hepatic and renal parenchymal vessels blurring and narrow of the lumen of hepatic vein in the absence of findings suggestive of chronic liver disease. Study protocol was approved by local Ethical committee and all patients were briefed about the study and informed written consent was obtained. At baseline, demographic data were collected and a detailed physical examination was done. Sitting blood pressure was measured in both arms after at least ten minutes of rest with an appropriate sphygmomanometer.

Anthropometric measurement:

Standing height and weight was measured using appropriate

scales.BMI was calculated using standard formula, BMI=weight (kg)/height (m2).Waist circumference was measured at the plane between anterior superior iliac spine and lower costal margin at the narrowest part of the waist line on the midaxillary line while the patient was standing and at the end of normal expiration. It was measured with a soft non elastic measuring tape.

Blood sample collection:

Subjects were requested to fast at least eight hours and fasting venous blood sample was collected between 7am to 8 am. Serum fasting glucose was measured at the day of sample collection. Serum fasting lipid profile, SGPT, creatinine, CBC, HbA1c were measured within three days of sample collection .

NAFLD WAS CLASSIFIED BASED ON THE STANDARD ULTRASONOGRAPHIC CRITERIA:

Grade 1 - (Mild steatosis) slightly increased liverechogenicity with normal vessels and absent posterioratten uation.

Grade 2 - (Moderate steatosis) moderate increase inliver echogenicity with partial dimming of vessels andearly posterior attenuation.

Grade 3 - (severe steatosis) diffuse increase in liverechogenicity with absence of visible vessels and heavyposterior attenuation. Sensitivity of ultra-sonogram in detection ofhepatic steatosis ranges from 60 to 94% and specificity84 to 95%. Hepatorenal sonographic index which is theratio between mean brightness level of liver and rightkidney, has also been proposed as a measure of hepaticsteatosis with a cutoff value of 1.49, yielding a veryhigh sensitivity (100%) and specificity (91%) for diagnosis of steatosis>5%.

Statistical analysis

Data documented and analyzed 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 100 patients with T2DM, a total of 67 patients were identified to have fatty liver by ultrasonography . Majority of the NAFLD patients showed Grade I fatty liver (18.9%), followed subsequently by Grade II (5.5%) and Grade III (0.6%).The present study observed a higher frequency of NAFLD in the diabetic male population (38/100)compared with the female population (29/100) (Table 1).Statistically, there is no significant difference between male and female subjects. 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 41-60 years. No significant difference was found between age and disease by statistical analysis.

Table -1: Showing Gender distribution of NAFLD in newly diagnosed T2DM patients (n=100)

Gender	T2DM patients	Fatty liver group	Non fatty liver group
Male	58(58%)	38(38%)	20(20%)
Female	42(42%)	29(29%)	13(13%)
Total	100(100%)	67(67%)	33(33%)

Table-2: Showing Age distribution of NAFLD in newly diagnosed T2DM patients (n=100)

Age in years	T2DM patients	Fatty liver group	Non fatty liver group
40 years	46(46%)	30(30%)	16(16%)
41-60 years	48(48%)	35(35%)	13(13%)
60 years	06(6%)	02(2%)	04(4%)
Total	100(100%)	67(67%)	33(33%)

Table 3: Showing comparison of the demographic and laboratory variables in newly diagnosed diabetic patients with and without fatty liver

Sl. No.	Characteristics	Fatty liver group(n=67) (Mean±SD)	Non fatty liver group(n=33) (Mean±SD)	t value	P value
1	BMI(kg/m2)	26.77±3.78	23.44±3.92	-4.09	.000
2	WC(cm)	85.95±5.19	81.97±5.4	-3.53	.001
3	FBS(mmol/L)	11.34±4.21	15.36±12.73	2.34	.021
4	2 hours after breakfast (mmol/l)	18.06±5.99	20.39±8.93	1.51	.133
5	HbA1c (%)	10.20±2.29	10.55±2.60	.69	.492
6	SGPT(U/L)	44.49±23.97	39.30±26.97	-.976	.331
7	Total cholesterol (mg/dl)	211±42	208±43.68	-.298	.767
8	HDL(mg/dl)	38.12±8.50	37.04±7.69	-.616	.540
9	LDL(mg/dl)	136.77±33.56	127.06±32.52	-1.37	.172
10	Triglyceride (mg/dl)	226.01±127.99	194.21±104.11	-1.239	.218

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 liverwas given in the Table 3. The above shown variable shows a higher prevalence and significant association of fatty liver disease with BMI, andWC inpatients with diabetes mellitus.

DISCUSSION

NAFLD is characterized by fatty infiltrationof the liver, mostly in the form of triglycerides, whichexceeds 5% of the liver weight, without a history ofsignificant alcohol intake and not due to other identifiable causes of liver [12]. Fatty liver is a common finding among T2DM individuals. NAFLD and T2DMtogether have poorer prognosis in terms of higherfrequency of cirrhosis and mortality[13].There is emerging evidence demonstrating an additive detrimental liver outcome for people with co-existing diabetes and NAFLD.A diagnosis of diabetes makes an individual more likely to have more severe NAFLD with the associated complications of cirrhosis and mortality. In this study, the overall prevalence of fatty liver by ultrasonography in newly diagnosed T2DM patients was67%. Geographic variations existed in the prevalenceof NAFLD worldwide. Studies done earlier havereported that around 10-75% of NAFLD patients haveT2DM and 21-72% of patients with diabetes arereported to have NAFLD[14]. The prevalence rate ofNAFLD was highest in the 41 to 60 years age group (35/100), subsequently followed by 40years (30/100), and 60(2/100)years age groups. This study also revealed a higherprevalence of NAFLD in male patients (38/100) withT2DM compared with the female community (29/100).The larger number of male subjects included in thestudy population may account for the malepredilection seen in this study. This similar trend wasnot reported by Sanjay Kalra et al, in which thefrequency of the disease was more in female patients. Previous studies have shown that the prevalence ofNAFLD increases with age [15]. In many publishedseries, NAFLD has been reported to be most commonin women, aged 40-60 years [16]. Obesity has beencommonly reported in male and female patients, concurrentlyshowing an increase in frequency of fatty liver disease. Hypertension, obesity and dyslipidemia are theelements in metabolic syndrome, and also serves aspredisposing factors of NAFLD along with diabetesmellitus[17].Several studies have suggested thewell-established relationship of the disease with thesecomorbid conditions. In this present study, difference inserum transaminases level between the fatty liver andnon-fatty liver group of patients were not statisticallysignificant. The liver enzymes are a poor measure ofNAFLD. Although elevations of serum transaminases are common in NAFLD, normal values can be found inupto 78% of patients in the presence of histologic findings. The whole spectrum of clinic-pathologicfeature of NAFLD may exist without elevation oftransaminases. Thediagnosis of NAFLD in our study was based on standard ultrasonography, which is by for thecommonest way of diagnosing this increasinglyrecognized liver disorder in clinical practice. Radiologicimaging such as sonography has an adequate thresholdfor diagnosing fatty liver[18]. This study substantiatesthe necessity of early diagnosis and intervention ofNAFLD in patients with T2DM.

CONCLUSION

Diabetes and NAFLD are reciprocal risk factors and when they are occur together, diabetes is more difficult to manage and that NAFLD is more likely to progress. The pathogenesis of NAFLD is complex although the accumulation of intrahepatic lipid is central.NAFLD is a common chronic hepatic disorder globally. T2DM and NAFLD are rapidly increasing, reaching levels of a pandemic in countries like Bangladesh. 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.

ACKNOWLEDGEMENT

The author would like to thanks all doctors and non-teaching staff

ofDepartments of Endocrinology and Radiology, Enam Medical College, for guiding me for each & everystep of this research work by giving useful suggestions and made me complete this work successfully.

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 withnonalcoholic 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 type2 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. Kantartzis K, Peter A, Machicao F, Machann J, Wagner S, Königsrainer I, et al. Dissociation between fatty liver and insulin resistance in humans carrying a variant of the patatin-like phospholipase 3 gene. Diabetes 2009;58:2616–23.
6. Abdul-Hai A, Abdallah A, Malnick SD. Influence of gut bacteria on development and progression of non-alcoholic fatty liver disease. World J Hepatol 2015;7:1679–84
7. Bayard M, Holt J, Boroughs E; Nonalcoholic fatty liver disease. Am Fam Physician, 2006; 73(11):1961-8.
8. Williamson RM, Price JF, Glancy S, Perry E, Nee LD, Hayes PC, et al.Prevalence of and risk factors for hepatic steatosis and nonalcoholic fatty liver disease in people with type 2 diabetes: the Edinburgh Type 2 Diabetes Study.Diabetes Care 2011;34:1139–44.
9. Sanchez PP, Bril F, Maximos M, Lomonaco R, BiernackiD,Orsak B, et al. High prevalence of nonalcoholic fatty liver disease in patients with type 2 diabetes mellitus and normal plasma aminotransferase levels. J Clin Endocrinol Metab2015:jc20151966.
10. 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.
11. 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. BMCGastroenterology, 2007; 7: 41.
12. Angulo P; Obesity and nonalcoholic fatty liver disease. Nutrition Reviews, 2007; 65:S57–63.
13. Merat S, Yarahmadi S, Tahaghoghi S, AlizadehZ;Prevalence of Fatty Liver Disease among Type 2Diabetes Mellitus Patients and its Relation toInsulinResistance., Middle East Journal ofDigestive Diseases, 2009;1:74-79.
14. Angulo P; Nonalcoholic fatty liver disease. N Engl J Med; 2002; 346(16):1221-31.
15. Kalra S, Vithalani, M, Gulati G, KulkarniCM,Kadam Y, Pallivathukkal J, Modi K.D; Study ofprevalence of nonalcoholic fatty liver disease(NAFLD) in type 2 diabetes patients in India(SPRINT). J Assoc Physicians India, 2013; 61(7),448-453.
16. Russo MW, Jacobson IM; Nonalcoholic Fatty Liver Disease. Hospital Physician, 2002; 67: 36-41.
17. Marchesini G, Brizi M, Bianchi G; Nonalcoholic fatty liver disease: a feature of the metabolic syndrome. Diabetes, 2001; 50:1844–50.
18. Luxmi S, Sattar RA, Ara J; Association of Non Alcoholic Fatty Liver with type 2 Diabetes Mellitus. JLUMHS, 2008; 188-193.