FREQUENCY OF NON-ALCOHOLIC FATTY LIVER DISEASE IN TYPE 2 DIABETES MELLITUS

Amanullah, Nazir Shah, Mohammad Hussian, Sheraz Jamal and Mumtaz Ali

ABSTRACT

Objective: To determine the frequency of non-alcoholic fatty liver disease (NAFLD) in patients with type 2 diabetes mellitus and compare its features with the non fatty liver disease in the same patients.

Material and methods: This descriptive and comparative study was performed on 145 consecutive type 2 diabetic patients collected from OPD and wards in Hayatabad medical complex peshawar. The bio data, duration of diabetes, and ultrasound findings of fatty liver from the same sonologist for all patients were noted in a proforma. Patients having pregnancy, chronic liver disease due to viral or non viral causes or those using alcohol, were excluded from the study. Patients who were using certain drugs like steroids, oral contraceptive pills in female, amiodarone, statins and pioglitazones were also excluded from the study because of their association with producing similar findings on ultrasound.

Results: One hundred & forty five type-2 diabetic patients, 51 %(n=74) females and 49 %(n=71) males with age range of 40 to 50 years were collected from the OPD and wards of Hayatabad Medical Complex Peshawar. The overall frequency of NAFLD was 51 % n=74. We further divided these patients in multiple groups according to their presentation, co morbid conditions and some biochemical parameters and compared them with the patients with no fatty liver disease (FLD). The comparison showed no significant differences in symptoms/signs between the two groups apart from obesity which was more common in patients with NAFLD (Table-1). It was found to be more prevalent in the urban than the rural population (fig-1). There were some differences in the triglyceride and total cholesterol level between the two groups (Table-2). NAFLD tends to be more common in the age range of 40 to 49 as shown in table 3.

Conclusion: Obesity control may decrease the frequency of non alcoholic fatty liver disease and its consequences in type 2 diabetic patients. As blood cholesterol and triglyceride levels were found to be higher in the NAFLD patients as compared to those with no fatty liver disease, therefore controlling these levels may also prove beneficial in controlling NAFLD.

Key words: Type 2 diabetes mellitus, Non alcoholic fatty liver disease, Obesity.

INTRODUCTION:

Type 2 diabetes mellitus (T2DM) and cardiovascular diseases represent a serious threat to the health of the population worldwide. Although overall adiposity and particularly visceral adiposity are established risk factors for these diseases, but recently fatty liver emerged as an additional and independent risk factor.[1]

Diabetes by most estimates is now one of the common causes of liver disease. Cryptogenic cirrhosis of which diabetes is by far the most common cause, has become the third leading indication for liver transplantation in the U.S.[2]

Nonalcoholic fatty liver disease(NAFLD) is a chronic liver condition characterized by insulin resistance and hepatic fat accumulation in the absence of other identifiable causes of fat accumulation such as alcohol abuse, viral hepatitis, autoimmune hepatitis, alpha-l antitrypsin deficiency, medication like corticosteroids and estrogens.[3] Hepatic steatosis may range from a 'benign' indolent deposition of fat to severe lipotoxicity-induced steatohepatitis i.e. Non-alcoholic steatohepatitis(NASH).NASH is frequently associated with fibrosis and approximately 10% of the patients develop cirrhosis. There is also increase risk of hepatocellular carcinoma.[4] Diabetes, dyslipidemia, and hypertension and cardiovascular diseases occur more frequently in individuals with NAFLD.[5] NAFLD may also be associated with a greater risk of renal disease in patients with T2DM.[6]

However, recent work has broadened our understanding of the disease and offered new treatments modalities. Therefore it may become important in future to screen for NAFLD in diabetic patients just like we routinely evaluate for other chronic complications of diabetes mellitus.[7]

Non-alcoholic fatty liver disease has high prevalence of (60.8%) in a local study.[8] Much work has been done on NAFLD and NASH in the western world but its presentation and etiology has not been well studied in Asian population because of its asymptomatic presentation.[8]

The Rationale of this study is to determine the frequency of Non-alcoholic fatty liver disease in type

2 diabetes on the basis of Ultrasound. NAFLD is usually asymptomatic and it is not routinely screened like diabetic retinopathy, nephropathy and neuropathy. Having known that NAFLD may range in severity from simple fatty liver to NASH, followed by cirrhosis and ultimately hepatocellular carcinoma, so it is important to know the frequency of this serious but ignored aspect of T2DM. Unfortunately very little work has been done locally on this problem as many clinicians think NAFLD is a benign condition of no clinical significance. The benefit of this study will be that it will give us the frequency of NAFLD in our local population and by timely diagnosing NAFLD using the easily available, cheap and non-invasive method i.e. ultrasound abdomen. If the frequency of NAFLD in T2DM is found to be significant compared to international and other local studies then clinicians will be suggested to intervene early thereby preventing its progression to cirrhosis and hepatocellular carcinoma. Moreover this study will provide basis for further studies regarding preventive and treatment strategies for this important issue.

MATERIAL AND METHODS:

This descriptive and cross sectional study was performed in Medical B unit Hayatabad Medical Complex Peshawar from Feb to Nov 2011. Patients age 40 years or above, were collected from the OPD and medical units of the hospital. Patients were either known type 2 diabetic or newly diagnosed. Diagnosis was made on the basis of fasting glucose of e"7mmol/L (126mg/dl), random glucose e"11.1mmol/L (200mg/dl) detected by venous blood in the laboratory of Hayatabad Medical Complex Peshawar.

NAFLD was confirmed through expert Sonologist by looking to the abdominal ultrasound, which will show "bright liver" (in which the echogenicity of the liver was similar to that of the central echo-complex of the kidney).

All non alcoholic patients having Type 2 diabetes mellitus above 30 years of age were included. Patients with positive viral markers (Detected by HCV antibody and HBs Ag in blood), already diagnosed cases of hemochromatosis, Wilsons diseases, autoimmune hepatitis (By clinical record), pregnancy and patients using certain drugs like steroids, oral contraceptive pills, amiodarone, statins and pioglitazones (clinical record and history) were excluded from the study. The patients related DATA was collected in a pro forma and interpreted for results.

RESULTS:

A total of one hundred and forty five patients of either sex having type 2 diabetes mellitus attending out-patient department or admitted in medical unit of Hayatabad Medical Complex Peshawar were included in the study. Out of these, 74(51%) were female and 71 (49%) were male. Age varied from 40-70 years and mean age of the patients was 45.93 ± 8.57 years. Seventy four (51%) of these patients had fatty liver. Age wise distribution was intense in age group 40-50 for diabetics; while fatty liver presentation was also intense in this group almost 78(54%).

It is interesting to note that as the area wise distribution of the patients showed, the frequency of NALFD was highest in the patients belonging to Peshawar city indicating the role of relative physical inactivity of the patients.

Table 1: Showing the frequencies of different clinical features

Symptoms/signs	Fatty liver patients	Non fatty liver patients
Fatigue	53	47
Generalized weakness	46	47
Haviness right upper abdomen	32	35
Pain right uppr abdomen	42	41
Itching	22	32
Nausea	43	40
Anorexia	53	46
Obesity		

Table-2: Showing different biochemical parameters

Investigation	Fatty liver patients	Non fatty liver patients	P values
Triglycerides(more than 150 mg/dl	47(32.4%)	39(26.8%)	.65
Serum cholesterol (more than 200 mg/dl)	24(16.5%)	18(12.4%)	.18
Serum alkaline posphatase (more than 300 u/l	8(5.5%)	05(3.4%)	.21
ALT(more than 40 u/l)	6(4.1%)	6(4.1%)	.23

Table-3: Frequency of NAFLD in diff. age groups

Age group	Diabetic patients (No)	Percentages
30-39	16	11
40-49	78	53.7
50-59	29	20
60-69	12	8.2
70 and above	10	6.8

The major complaints were fatigue, generalized weakness, anorexia, pain right upper abdomen and itching (Table-1). This table also shows the comparison of frequencies of these features with the patients having no fatty liver disease.

Table 3 shows the frequency of NAFLD in different age groups of the patients. This study shows that NALFD is more frequent in the age range of 40 to 49 which is about 54% (n=78) while it is least in the extremes of ages (Table-3).

Serum albumin and serum bilirubin were normal in all the study patients while other biochemical derangements are given in Table-2. Subjects without FLD were significantly more likely to be male, older, and non obese compared with those who developed NAFLD. Obesity, triglyceride and total cholesterol level were higher in frequency in patients with NAFLD. The rest of the comparison showed no significant differences in symptoms/signs and biochemical parameters between the two groups (Table-2).

There was no difference in the apparent severity of diabetes as shown by the comparison of HbA1c values between the two groups. Further more, the treatment regimens needed for diabetes, hypertension and hyperlipidemia were similar between the two groups (Fig-1).

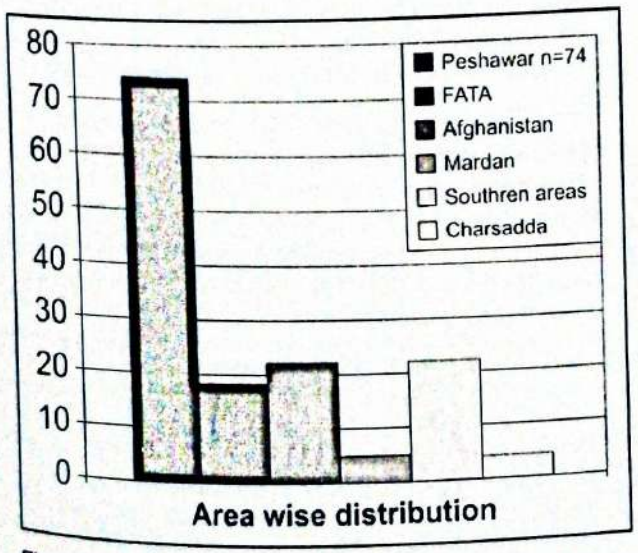

Fig-1: Showing frequency of NAFLD according to area

CONCLUSION:

Non alcoholic fatty liver disease is quit a common problem in the type 2 diabetic patients. It is more common in the urban population than rural population. Obesity, high triglyceride and cholesterol levels are associated with NALFD, therefore controlling these factors may prove beneficial for decreasing the frequency of NALFD in type 2 diabetic patients.

DISCUSSION:

Non-alcoholic fatty liver disease (NAFLD) is a common liver disorder. It is mainly seen in obese and diabetic patients. Varying prevalence rates have been reported in various studies. As NAFLD is common and generally asymptomatic in patients with diabetes mellitus, the clinical significance of NAFLD has traditionally been overlooked. A recent study from Japan in apparently healthy individuals has reported the prevalence of NAFLD as 29%.[9] An Italian study reported it to be 20%.[10] The frequency of NAFLD reported in general population of USA is 20%[11]. A study from Karachi, Pakistan conducted by Luxmi et al, [12] in 120 diabetic patients described the frequency of NAFLD as 60.8% and Akber et al from Saudi Arabia as 55%[13] in Type-2 diabetics. Gupta et al from India report it to be 49% in diabetics [14]. These studies correlates with data obtained from the present study (54%).

Various studies described NAFLD as asymptomatic which may be true in initial phase but patients may present with fatigue and heaviness in right upper abdomen later on. In our study fatigue was noted as the most common complaint associated with NAFLD. A study by Wing-kin syn et al described fatigue as an important symptom and pain right upper abdomen in 33% of the patients.[15] Heaviness and pain in right upper abdomen is due to stretching of the liver capsule which is correlated with the amount of fat present in the liver.[16,17] Diabetes mellitus is an important risk factor for NAFLD.

This study showed high frequency of raised triglyceride and cholesterol level in the patients of NAFLD as compared to those without NAFLD which is in accordance with the other literature in Pakistan.[8] Other biochemical parameters like alanine aminotransferase (ALT) and alkaline phosphatase were not significantly raised in the patients of NAFLD as compared to those with no NAFLD in this study. Other literature reported raised ALT in significant number of fatty liver patients.[18] Normal ALT has also been reported in NAFLD by other studies.[9]

REFERNCES

1. Stefan N, Kantartzis K, Ha"ring H.Causes and metabolic consequences of fatty liver disease,Endocrine Reviews 29, 2008-2009;(7):939-60
2. Tolman KG, Fonseca V, Dalpiaz A, Tan MH. Spectrum of liverdisease in type 2 diabetes and management of patients with diabetes and liver disease. Diabetes Care 2007;30:734-43
3. Ali R, Cusi K. New diagnostic and treatment approaches in nonalcoholic fatty liver disease (NAFLD). Ann Med 2009;41 (4):265-78
4. Bugianesi E, Vanni E, Marchesini G. NASH and the risk of cirrhosis and hepatocellular carcinoma in type 2 diabetes. Curr Diab Rep 2007;7: 175-80
5. Traghr G.MarraF, Marchesini G. Increased risk of cardiovascular disease in nonalcoholic fatty liver disease: causal effect or epiphenomenon? Diabotologia 2008;51: 1947 -53
6. Targher G,Chonchol M,Bertolini I.Increaased risk of CKD among type 2 Diabetics with non-alcoholic fatty liver disease. J;Am Soc Neprol2008;19:1964-70
7. Cusi.K.Non-alcoholic fatty liver disease in type 2 diabetes mellitus,Current opinion in endocrinology. Diabetes and Obesityr2009April;16(2):I41-9
8. Luxmi S, Sattar RA, Ara J. Association of non-alcoholic fatty liver with type 2 diabetes mellitus. JLUMHS 2008; 188-93.
9. Jimba S, Nakagami T, Takahashi M. Prevalence of non-alcoholic fatty liver disease and its association with impaired glucose metabolism in Japanese adults. Diabet Med 2005; 22:1141-45.
10. Bedogni G, Miglioli L, Masutti F. Prevalence of and risk factors for non-alcoholic fatty liver disease: the Diaonysos nutrition and liver study. Hepatology 2005; 42:44-52.
11. Ford ES, Giles WH, Dietz WH. Prevalence of metabolic syndrome among US adults: findings from the 3rd National health and nutrition examination survey. JAMA 2002;287:356-9.
12. Luxmi S, Sattar RA, Ara J. Association of non-alcoholic fatty liver with type 2 diabetes mellitus. JLUMHS 2008;188-193.
13. Akber DH, Kawther AH. Non-alcoholic fatty liver disease in Saudi type 2 diabetic subjects attending a medical outpatient clinic. Diabetes Care 2003; 26:3351-65.
14. Gupta P, Amarapukar D, Agal S, Baijal R, Kulshreshtta P, Pramik S, et al. Non-alcoholic steato-hepatitis in type 2 diabetes mellitus. J Gasteroentrol Hepatol 2004; 19:854-58.
15. Syn WK, Nightingale P, Bateman JM. Non-alcoholic fatty liver disease in a district general hospital: clinical presentation and risk factors. Hepatol Int 2008; 2:190-95.
16. Podolsky DK. Infiltrative, genetic and metabolic diseases affecting the liver: In; Kasper DL, Fauci NS, Longo DL, Braunwald E, Hauser SL, Jameson JL. Harrison's principles of Internal Medicine. McGraw Hill Medical Publishing; 16th edition 2005; Vol II: 1869-73.
17. Bacon BR, Farahvash MJ, Janney CG, Newuschwander-tetri BA. Non-alcoholic steato-hepatitis: An expanded clinical entity. Gastroenterology 1994; 107:1103-09.
18. Tolman KG, Fonseca V, Tan MH *et al.* Narrative review: hepatobiliary disease in type 2 diabetes mellitus. Ann Intern Med 2004; 141:946–56.