ORIGINAL RESEARCH PAPER

General Medicine

PREVALENCE OF NAFLD IN DIABETIC PATIENTS IN A TERTIARY CARE HOSPITAL, SOUTHERN RAJASTHAN

KEY WORDS: Diabetes mellitus, NAFLD, NASH

Lapsiwala Yash Y.	Resident, Dept. Of General Medicine & Therapeutics, GMCH, Udaipur.
Shrimali Lalit*	Professor, Dept. Of General Medicine & Therapeutics,GMCH, Udaipur *Corresponding Author

ABSTRACT

Non alcoholic fatty liver disease is an emerging risk factor for Cirrhosis and liver malignancy. The incidence of NAFLD is more in obese and diabetic patients. The current study is undertaken to determine the prevalence of NAFLD in diabetic patients. The relationship of NAFLD with variables like sex, age and number of years since diagnosis of diabetes was also noted. Total 100 known diabetic patients admitted at Geetanjali Hospital, Udaipur, were studied for USG diagnosed fatty liver. It was observed that 39 % diabetic patients had NAFLD. The incidence increased with rising age, and also with duration of diabetes. Thus all diabetic patients should be screened for fatty liver so that its progress to NASH and cirrhosis can be prevented.

INTRODUCTION

Diabetes Mellitus is a very common endocrine and metabolic disease worldwide. The prevalence of DM has risen dramatically over the past two decades, from an estimated 30 million cases in 1985 to 382 million in 2013.[1] Based on current trends, the International Diabetes Federation projects that 592 million individuals will have diabetes by the year 2035.[2]

Liver disease may cause or contribute to, be coincident with, or occur as a result of diabetes mellitus. There exists an association between diabetes and liver injury.[3] Normal functioning of liver is essential for the maintenance of blood glucose levels and for a continued supply of glucose to organs that require it as energy source. This central role of the liver in glucose homeostasis explains the pathogenesis of glucose intolerance in liver diseases. Hepatocellular glycogen accumulation leads to hepatomegaly and liver enzyme abnormalities in poorly controlled diabetes patients.[3]

Liver can also be affected by steatosis or accumulation of fat, a condition known as non-alcoholic fatty liver disease (NAFLD). It is a well-recognized complication of diabetes with frequency of 40–70%.[3] Increased transport of fatty acids to the liver, enhanced hepatic fat synthesis, and decreased oxidation or removal of fat from the liver lead to fat accumulation in the liver. Nonalcoholic fatty liver disease (NAFLD) is the main cause of chronic liver disease associated with diabetes and obesity. Without treatment, compensated steatosis in NAFLD will eventually lead to decompensated steatosis with necroinflammation and fibrosis, i.e. stage of non-alcoholic steatohepatitis (NASH). NAFLD and NASH increase the risk of liver cancer.[3]

Liver imaging techniques like Ultrasound or CT can be used for diagnosis of NAFLD or NASH. MRI is more sensitive for the diagnosis. But definitive diagnosis of NASH requires liver biopsy. However, new imaging methods like transient elastography, Fibro scanning and plasma biomarkers such as cytokeratin-18 fragments (marker of hepatocytes apoptosis) are emerging as alternative diagnostic techniques.[4] Because of easy availability and cost benefits, USG can be readily used for the diagnosis of NAFLD.

AIMS AND OBJECTIVES

1) To determine the frequency of Ultrasonography diagnosed NAFLD in indoor patients with Diabetes mellitus.
2) To study the relationship between NAFLD and age and sex of the diabetic patients.
3) To study the relationship between NAFLD and number of years since diagnosis of DM.

MATERIALS AND METHODS

1. Study design and Subjects

This was a hospital based cross sectional retrospective study which was conducted at Geetanjali Medical College and Hospital, Udaipur, Rajasthan, after approval from the ethical committee. Total 100 Indoor patients, who were diabetic were enrolled as per the inclusion and exclusion criteria as defined below, during the

period of January 2017 to October 2018. Subjects were recruited according to simple random sampling method. Ultrasound examination for changes of NAFLD was carried out by qualified radiologists for all these patients.

2. Selection Criteria

2.1. Inclusion Criteria

1. All patients with confirmed diabetes mellitus by WHO criteria (2014), Fasting plasma venous glucose of ≥ 7 mmol/l (126 mg/dl) or Two hours post prandial plasma venous glucose of ≥ 11.1 mmol/l (200 mg/dl) or HbA1c value more than 48 mmol/mol (6.5%).
2. All diabetics irrespective of glucose control.
3. All diabetics irrespective of treatment.

2.2. EXCLUSION CRITERIA

1. Patients with history of alcohol intake.
2. Patients taking hepatotoxic drugs.
3. Past history of liver diseases or acute hepatitis.
4. Patients having evidence of hepatitis B or C virus infection.

OBSERVATION AND RESULTS

Out of the total 100 patients enrolled, 52 patients were male and 48 patients were female. 11 patients (6 Male, 5 female) were less than 40 years of age; 23 patients (8 male, 15 female) were between 41-50 years of age; 25 patients (13 male, 12 female) were between 51-60 years of age and 41 patients (25 male, 16 female) were in the age group of more than 60 years, with mean age of all patients being 56.740 ± 12.466 years.

Table 1: Sex Wise Age Distribution

Age group	Male		Female		Total	
	Number	%	Number	%	Number	%
≤40 Years	6	11.53%	5	10.41%	11	11%
41-50 Years	8	15.38%	15	31.25%	23	23%
51-60 Years	13	25%	12	25%	25	25%
>60 years	25	48.07%	16	33.33%	41	41%
Total	52		48		100	100%
Mean±SD	58.154±13.725		55.208±11.027		56.740±12.528	

Detailed history was taken about the number of years since diagnosis of DM. 60 patients out of total 100 were diagnosed as having DM for less than 5 years. 28 patients were diagnosed before 6-10 years while 12 patients had DM for more than 10 years. The mean number of years since diagnosis of DM was 5.391 years.

Out of the total 100 patients, only 6 had HbA1c ≤7. While 28 patients had HbA1c between 7 and 8, 9 patients had between 8 and 9, 11 patients had between 9 and 10 and majority 46 patients had HbA1c ≥10. The Mean HbA1c was 10.212±2.855.

USG diagnosed NAFLD was categorized in only two categories, Positive or Negative. Various grades and severity of NAFLD was not

taken in to consideration. Out of total 100 patients, 39 patients had NAFLD. The P value was 0.027, which suggests significant correlation.

Out of total 52 males, 15 patients had NAFLD (28.84%), whereas out of 48 female patients, 24 had NAFLD (50%). This suggests that incidence of NAFLD in female diabetic patients was significantly higher than male patients. The P value was 0.030, which suggests significant correlation.

In the age group of ≤40 years, 1 out of 11 patients had NAFLD (9.09%). In the age group of 41-50 years, 6 out of 23 (26.08%), in the age group of 51-60 years, 12 out of 25 (48%) and in the age group of >60 years, 20 out of 41 (48.78%) had NAFLD. This shows that the incidence of NAFLD increases with age. The P value 0.041 suggests a significant correlation.
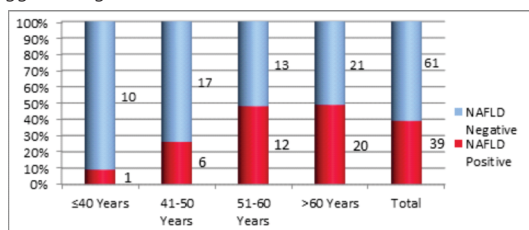
Figure 1: Incidence of NAFLD in different age groups

In the group of <5 years since diagnosis of DM, 16 patients out of 60 had NAFLD (26.66%). In 5-10 years group, 14 out of 28 (50%) and >10 years group, 9 out of 12 (75%) had NAFLD. This clearly shows that incidence of NAFLD increases rapidly with number of years since diagnosis of DM. The P value 0.003 suggests significant correlation.

Table 2: NAFLD incidence with number of years since diagnosis of DM

Number of years since diagnosis of DM	Total	NAFLD	NAFLD Percentage
< 5 Years	60	16	26.66%
5-10 years	28	14	50%
>10 Years	12	9	75%
Total	100	39	39%
P value		0.003	

DISCUSSION:

In our study, out of 100 diabetic patients, NAFLD on USG was found in 39 patients. Ajay Duseja, PGIMER, Chandigarh, concluded that prevalence of NAFLD is around 9% to 32% of general population in India.[5] He also quoted that Type 2 DM is a major risk factor for presence and severity of NAFLD. They found that 35 of 40 (88%) nonalcoholic patients with DM had fatty liver on USG. In a study from Mumbai, 49 of 100 patients with DM had fatty liver on USG.[6] Our findings correlates with these findings.

We observed that Out of total 52 males, 15 patients had NAFLD (28.84%), whereas out of 48 female patients, 24 had NAFLD (50%). This suggests that incidence of NAFLD in female diabetics is significantly higher than males. Summart U et al. had studied 34709 normal populations for incidence of NAFLD. They concluded that 22.9% females and 18.3% males had NAFLD.[7] Although, Amrapurkar, Kamani et al. had done random study on 1168 otherwise healthy population and they found NAFLD more prevalent in males then females (24.6% and 13.6% respectively).[8] In another study by Mohan V. et al., 35.1 % males and 29.1 % females had NAFLD in general population.[9] Thus our findings do not correlate with these studies possibly because of smaller sample size in our study. Dai W. et al. had done Meta analysis of 24 studies involving 35499 diabetes patients, and they reported incidence of NAFLD in diabetes patients in 60.11 % of males and 59.35% of females.[10] Gender difference in the prevalence of NAFLD in T2DM patients could be attributed to the gender differences in hormone levels and lipid levels. Specifically, female hormones may play a potentially protective role in NAFLD.[11] Wang Z had concluded in his similar study that NAFLD is more prevalent in post-menopausal

women.[12] Our study group had 48% females with mean age 56.74 years. Thus in our study group majority of the females were in postmenopausal age group. This correlates with above studies.

If we consider different age groups, the incidence of NAFLD in age groups of ≤40, 41-50, 51-60 and >60 years was 9.09%, 26.8%, 48%,and 48.08% respectively. There is linear relationship of NAFLD with age in diabetic patients. In a similar study by Mayank Gupta et al., in diabetic patients, in the age groups of 25-34, 35-44, 45-54 and >55 years, NAFLD was found in 40%, 34%, 73%, and 89% of patients respectively.[13]

To evaluate the relationship of NAFLD with number of years since diagnosis of DM, we have divided the patients in the age groups of ≥ 5 years, 5-10 years and >10 years, and the incidence was 26.66%, 50% and 75% respectively. This establishes the linear relationship of NAFLD with number of years since diagnosis of DM.

CONCLUSION:
1. The incidence of NAFLD is more in diabetes patients as compared to general population.
2. The incidence of NAFLD is more in female than male diabetic patients.
3. The incidence of NAFLD increases with increasing age.
4. The incidence of NAFLD increases with increasing duration of diabetes.

REFERENCES
1. Kasper, D., Fauci,A., Hauser, S. et al.(2016). Harrison's principles of internal medicine. 19th ed. Mcgraw Hill, 2399.
2. International Diabetes Federation.(2017). IDF diabetes atlas 8th edition. Retrieved from https://www.idf.org.
3. Levinthal GN, Tavill AS. Liver disease and diabetes mellitus. Clinical Diabetes,17 (2),1-20.
4. Lomonaco, R., Chen, J., & Cusi, K. (2011). An endocrine perspective of nonalcoholic fatty liver disease (NAFLD). Therapeutic advances in endocrinology and metabolism, 2(5), 211-225.
5. Duseja, A. (2010). Nonalcoholic fatty liver disease in India–a lot done, yet more required! Indian Journal of Gastroenterology, 29(6), 217-225.
6. Gupte, P., Amarapurkar, D., Agal, S., Baijal, R., Kulshrestha, P., Pramanik, S., ... & Amarapurkar, A. (2004). Non-alcoholic steatohepatitis in type 2 diabetes mellitus. Journal of gastroenterology and hepatology, 19(8), 854-858.
7. Summart, U., Thinkhamrop, B., Chamadol, N., Khuntikeo, N., Songthamwat, M., & Kim, C. S. (2017). Gender differences in the prevalence of nonalcoholic fatty liver disease in the Northeast of Thailand: A population-based cross-sectional study. F1000Research, 6.
8. Amarapurkar, D., Kamani, P., Patel, N., Gupte, P., Kumar, P., Agal, S., & Deshpande, A. (2007). Prevalence of non-alcoholic fatty liver disease: population based study. Annals of hepatology, 6(3), 161-163.
9. Mohan,V., Farooq,S., Deepa,M., Ravikumar, R., Pitchumoni, C.1.(2009).Prevalence of non-alcoholic fatty liver disease in urban south Indians in relation to different grades of glucose intolerance and metabolic syndrome. Diabetes research and clinical practice,84(1),84-91.
10. Dai,W., Ye, L., Liu, A., Wen, S.W., Deng, J., Wu, X., Lai, Z.(2017). Prevalence of nonalcoholic fatty liver disease in patients with type 2 diabetes mellitus: A meta-analysis. Medicine,96(39).
11. Moon, S. S. (2013). Relationship between serum uric acid level and nonalcoholic fatty liver disease in pre-and postmenopausal women. Annals of Nutrition and Metabolism, 62(2), 158-163.
12. Wang, Z., Xu, M., Hu, Z., Hultström, M., & Lai, E. (2014). Sex-specific prevalence of fatty liver disease and associated metabolic factors in Wuhan, south central China. European journal of gastroenterology & hepatology, 26(9), 1015-1021.
13. Gupta, M., Mahavar, S., Chaturvedi,A., Chandra, R., Chauhan,G., Srivastava ,S., Sharma, R.(2017).Magnitude of non-alcoholic fatty liver disease (NAFLD) and concomitant risk factors in patients with type 2 diabetes mellitus. Int J Adv Med,4,1046-1052.