Original Research

Predictors of non-alcoholic fatty liver disease and non-alcoholic steatohepatitis in patients with type-2 diabetes mellitus

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Abstract

Background: Hepatic steatosis in Non-Alcoholics may range from a 'benign' indolent deposition of fat [known as non-alcoholic fatty liver diseases (NAFLD)] to severe lipotoxicity-induced steatohepatitis with neuroinflammation [known as non-alcoholic steatohepatitis (NASH)]. NASH is an overlooked complication of Type-2 diabetes mellitus (T2DM) that if missed may carry serious long-term consequences.

Objectives: To determine the Predictors of Non-alcoholic fatty liver disease and Non-alcoholic steatohepatitis in patients with Type-2 Diabetes Mellitus.

Materials and Methods: Fatty liver Disease by Ultrasonography & various other relevant factors (clinical and biochemical) were measured in all study subjects. These parameters were compared among two study groups i.e. (NAFLD and normal Liver). The statistical analyses were done using Statistical Analytic system (SAS), Chi-square test & Fisher Exact test were applied.

Results: Incidence of Non-alcoholic fatty liver disease in our study is around 62 (59.7%) of which 37 (55%) are males and 25 (45%) are females. The incidence of Non-alcoholic steatohepatitis in this study is around 22 (25.5%) of which 15 are males and 7 are females. BMI and WC values are significantly higher in the fatty liver group than normal group. (p<0.011 and p<0.001 respectively).

Conclusion: The prevalence of NAFLD is high amongst T2DM patients and, considering the increased liver mortality among these patients, NAFLD should be actively sought out and treated in patients with diabetes. Insulin resistance does not seem to be correlated with the presence of NAFLD among T2DM patients.

KEY WORDS: Type-2 Diabetes Mellitus (T2DM), Nonalcoholic Fatty Liver Disease (NAFLD), Homeostasis Model Assistant–Insulin Resistance (HOMA-IR), Quantitative Insulin Sensitivity check Index (QUICKI)

Introduction

The non-alcoholic fatty liver disease (NAFLD) is most frequent chronic liver disease growing rapidly parallel to that of obesity during recent decades worldwide.[1-3] When associated with Type-2 diabetes mellitus (T2DM) and obesity, NAFLD prevalence is growing up to 75-90%.[4-7] NALFD includes nonalcoholic steatohepatitis (NASH), nonalcoholic fatty liver, liver cirrhosis and hepatocellular carcinoma.[8]

Obesity, Type-2 diabetes, and hyperlipidemia are recognized as risk factors for NAFLD.[9] Insulin resistance is frequently detected in patients with NAFLD, as it is in those without obesity and diabetes.[10] An increasing number of patients have been described with normal body mass index (BMI), although these individuals may have central adiposity and occult insulin resistance.[11]

The standard technique used to identify NAFLD is a liver biopsy, which is not feasible as it is an invasive and an expensive procedure to perform in such a large number of

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patients.[12] Investigation and monitoring of the liver metabolic function and early detection of liver lipid accumulation having great importance. This study was designed is to know the predictors for Non-alcoholic fatty liver disease and Non-alcoholic steatohepatitis in patients with Type-2 Diabetes Mellitus.

Materials and Methods

The cases for the study were selected from patients with Type-2 diabetes mellitus diagnosed by standard criteria above the age of 40 years who attended the MNR Medical College and Hospital. This study is a prospective observational study, where continuous data is enumerated which fulfills the inclusion criteria. This study was conducted during October 2012 to September 2015.

Inclusion Criteria:

- Patients of age above 30 years with Type-2 diabetes mellitus on oral hypoglycemic drugs.

Exclusion Criteria:

- Any quantity of alcohol consumption based on careful history.
- Usage of drugs known to cause steatosis is including Amiodarone, Corticosteroids, Tamoxifen, Methotrexate and high dose Estrogen.
- Significant co-morbidities precluding a liver biopsy
- History of jejunoileal bypass or extensive small bowel resection.
- Patients with Type-2 diabetes mellitus on insulin therapy.

After an overnight fast, serum samples were obtained from all subjects for liver function tests (aspartate aminotransferase [AST], alanine aminotransferase [ALT], and alkaline phosphatase), serum lipid profile (total cholesterol, triglycerides, high-density lipoprotein cholesterol [HDL-C] and low-density lipoprotein cholesterol [LDL-C]), fasting blood glucose (FBS), serum insulin level and hemoglobin A1c (HbA1c).

Overweight was defined as a body mass index (BMI) between 23 and 25 kg/m^2, and obesity as BMI equal or above 25 kg/m^2. Patients were considered centrally obese if the waist circumference was greater than 80 cm in females and 90 cm in males. Patients with one of the criteria: LDL-C >100 mg/dL, total cholesterol >200 mg/ dL, triglycerides >150 mg/dL, or HDL-C < 40 mg/dL in males and <50 mg/dL in females were considered to have dyslipidemia. Homeostasis Model Assistant–Insulin Resistance (HOMA-IR) and Quantitative Insulin Sensitivity check Index (QUICKI) were calculated as measures of insulin resistance and sensitivity using following formula:

HOMA-IR = [fasting insulin (μU/mL) × fasting glucose (mmol/L)]/22.5.

QUICKI = 1/ [log (fasting insulin (μU/mL)) ± log (glucose (mg/dL))].

All subjects underwent abdominal ultrasonography by the radiologist for evidence of fatty liver disease, based on ultrasonographic findings (diffuse increase in echogenicity as compared to that of the spleen or renal cortex).

Results

Among 90 patients with mean age of 55.96±11.65 years, 56 (60%) subjects were males and 36 (40%) subjects were females.

Discussion

The present study consisted 90 patients with T2DM, the prevalence of NAFLD based on abdominal ultrasound examination was 59.7%. This is similar to a study by Angulo P et al, which have reported the prevalence of NAFLD among DM patients at approximately 50% (range: 21-78%).[13] However, a study by Rubinstein et al. and in the present study, it has been suggested that both sexes might be afflicted equally.[14] The mean age of patients in both the NAFLD and non-NAFLD groups was 55.37±10.95 and 57.25±13.22, respectively which was not statistically different (p=0.482).

Table 1: Enzymes of patients studied

Enzymes	Number of patients (n=90)	%	Mean ± SD
SGOT (IU/L)			
• <10	1	1.1	34.94±18.41
• 10-42	63	69.7	
• >42	26	28.7	
SGPT (IU/L)			
• <3	-	-	39.00±14.84
• 3-33	34	37.6	
• >33	56	62.0	
Alkaline Phosphates (IU/L)			
• <20	-	-	164.86±63.38
• 20-125	30	33.3	
• >125	60	66.6	

Table 2: HOMA-IR & QUICKI of patients studied

HOMA-IR & QUICKI	Number of patients (n=90)	Percentage	Mean ± SD
HOMA-IR			
• <3	4	4.4	8.47±4.45
• 3-5	24	26.4	
• 5-10	42	46.2	
• >10	20	22.0	
QUICKI			
• <0.3	60	66.6	0.28±0.01
• >0.3	30	33.4	

In the present study, there were no significant sex differences in the incidence of NAFLD between the two groups (p= 0.92), however, the prevalence of NAFLD among men and women varied in different clinical studies. In a study by Sanyal et al, NAFLD was considered to be more common among women, whereas, it was reported to be more prevalent among men by Williams CD et al.[15,16]

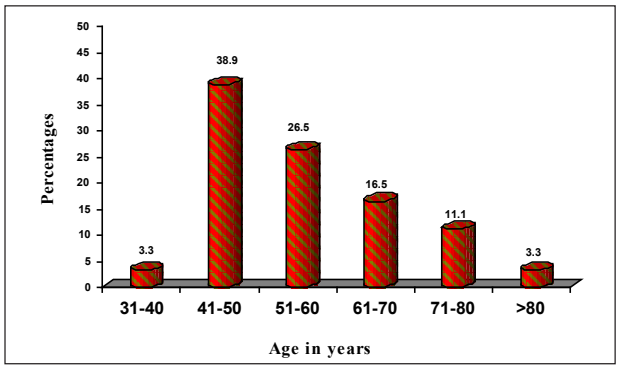

Figure 1: Age distribution of patients studied

To identify NAFLD ultrasound was used, which has a sensitivity and specificity of 89% and 93%, respectively, in detecting liver steatosis showed by Bacon BR et al.[17] In fact, imaging tests are insensitive when the degree of steatosis is less than 33%.Therefore, our figures may be an underestimation of the true prevalence of NAFLD in T2DM patients. Our findings indicate that the prevalence of NAFLD is much higher in patients with T2DM than in the general population. Due to the significant rate of increased liver-related morbidity and mortality in T2DM patients, it is important to discover and treat this condition. Unfortunately, with the possible exception of weight loss among obese subjects, there is no established treatment for NAFLD. Many researchers have studied insulin sensitizers, antioxidants, and other agents with various

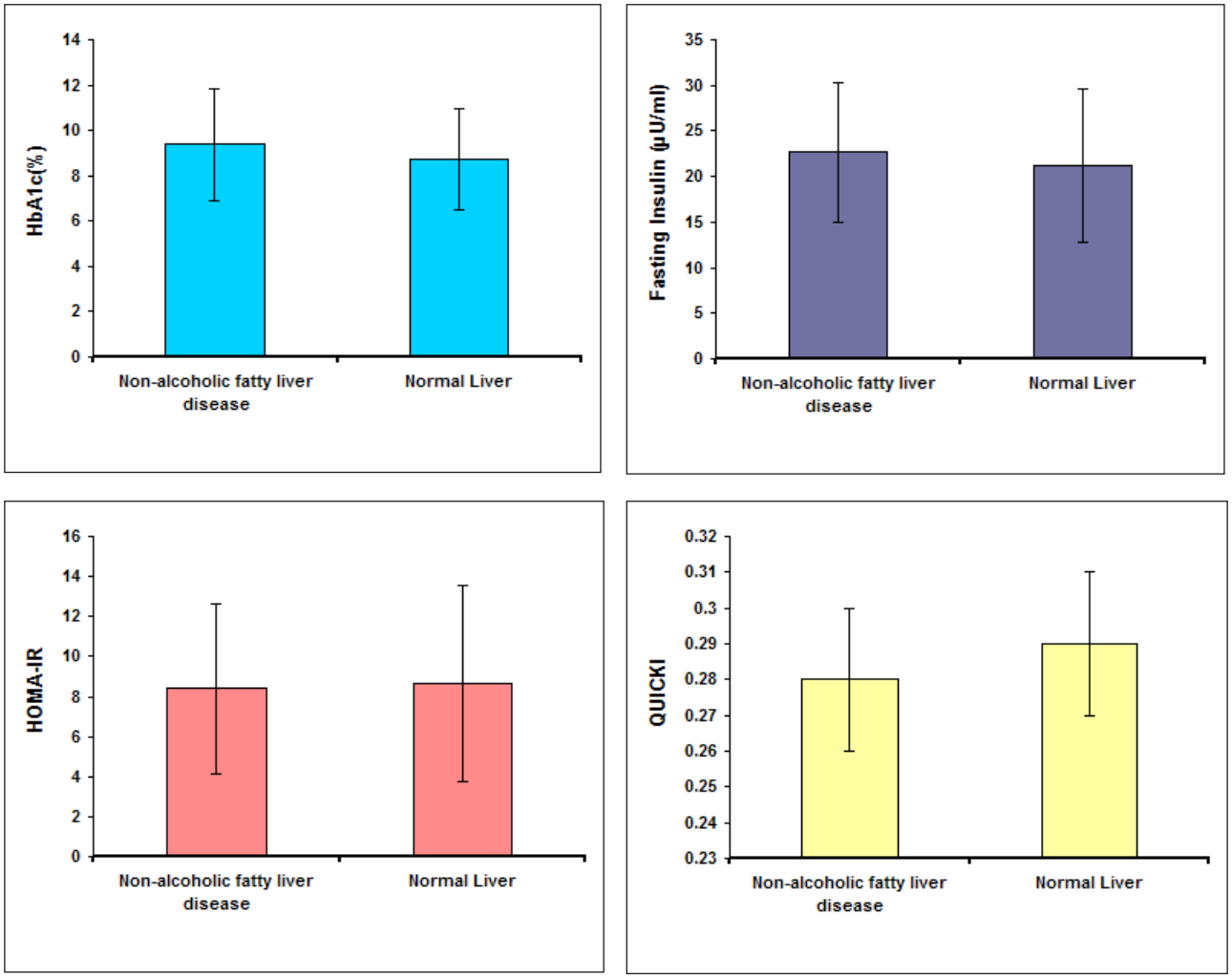

Figure 2: Showing Insulin resistance parameters according to USG abdomen

Table 3: Showing socio-demographic variables according to USG abdomen

Variables	USG abdomen		*p*-value
	Non-alcoholic fatty liver disease (*n*=62)	Normal Liver (*n*=28)	
Age in years	55.37±10.95	57.25±13.22	0.482
Gender			
Male	37(59.7%)	17(60.7%)	0.926
Female	25(40.3%)	11(39.3%)	
Height (cm)	5.54±0.19	5.57±0.21	0.538
Weight (kg)	72.32±11.39	69.43±10.25	0.253
BMI(kg/m^2)	25.30±3.62	24.03±3.19	0.116
Waist circumference(cm)	97.75±5.93	93.28±5.31	0.001**
HIP (cm)	94.98±7.27	91.23±6.60	0.022*
Waist/HIP ratio	1.03±0.07	1.03±0.08	0.721

Table 4: Showing clinical variables according to USG abdomen

Clinical variables	USG abdomen		*p*-value
	Non-alcoholic fatty liver disease (*n*=62)	Normal Liver (*n*=28)	
Duration of DM (yrs.)	10.87±4.99	11.46±6.37	0.634
Total cholesterol (mg/dL)	173.21±46.51	173.52±48.63	0.977
Triglycerides (mg/dL)	157.65±98.68	138.41±91.58	0.384
HDL(mg/dL)	37.73±11.46	42.21±17.55	0.152
LDL(mg/dL)	104.67±42.17	105.90±38.92	0.896
SGOT (Iu/L)	37.95±18.86	28.28±15.73	0.020*
SGPT (IU/L)	41.50±14.62	33.46±14.05	0.017*
ALP (IU/L)	173.53±70.05	145.67±40.09	0.053+

rates of success; however, a universally effective treatment remains to be identified.

Conclusion

It is concluded with the findings of the present study that, the prevalence of NAFLD is high amongst T2DM patients and, considering the increased liver mortality among these patients, NAFLD should be actively sought out and treated in patients with diabetes. Insulin resistance does not seem to be correlated with the presence of NAFLD among T2DM patients. It should be emphasized that the diagnosis of NAFLD in this study was based on ultrasonography findings, not on histology.

References

1. NCD-RisC. Trends in adult body mass index in 200 countries from 1975 to 2014. Lancet 2016, 387, 1377–1396.
2. Musso G, Gambino R, Cassader M, Pagano G. Meta-analysis: natural history of non-alcoholic fatty liver disease (NAFLD) and diagnostic accuracy of non-invasive tests for liver disease severity. Ann Med. 2011; 43:617–649.
3. Baumeister SE, Völzke H, Marschall P, John U, Schmidt CO, Flessa S, et al. Impact of fatty liver disease on health care utilization and costs in a general population: a 5-year observation. Gastroenterology. 2008; 134:85–94.
4. Gupte P, Amarapurkar D, Agal S, Baijal R, Kulshrestha P, Pramanik S, et al. Non-alcoholic steatohepatitis in Type-2 diabetes mellitus. J Gastroenterol Hepatol. 2004; 19:854–858.
5. Angulo P: Nonalcoholic fatty liver disease. N Engl J Med. 2002; 346:1221–1231,
6. Day CP: Non-alcoholic fatty liver disease: current concepts and management strategies. Clin Med. 2006; 6:19 –25.
7. McCullough AJ: Pathophysiology of nonalcoholic steatohepatitis. J Clin Gastroenterol 40 (Suppl. 1), 2006; S17–29.
8. Marchesini G, Marzocchi R, Agostini F, Bugianesi E: Nonalcoholic fatty liver disease and the metabolic syndrome. Curr Opin Lipidol, 2005; 16:421– 427.
9. Zelber-Sagi S, Nitzan-Kaluski D, Halpern Z, Oren R. Prevalence of primary non-alcoholic fatty liver disease in a population-based study and its association with biochemical and anthropometric measures. Liver Int 2006; 26: 856-863.
10. Chitturi S, Abeygunasekera S, Farrell GC, Holmes-Walker J, Hui JM, Fung C, Karim R, Lin R, Samarasinghe D, Liddle C, Weltman M, George J. NASH and insulin resistance: Insulin hypersecretion and specific association with the insulin resistance syndrome. Hepatology 2002; 35: 373-379.

11. Marchesini G, Marzocchi R, Agostini F, Bugianesi E. Nonalcoholic fatty liver disease and the metabolic syndrome. Curr Opin Lipidol 2005; 16: 421-427.
12. Bedogni G, Bellentani S, Miglioli L, Masutti F, Passalacqua M, Castiglione A, et al. The Fatty Liver Index: a simple and accurate predictor of hepatic steatosis in the general population. BMC Gastroenterol. 2006; 6:33.
13. Angulo P. Nonalcoholic fatty liver disease. N Engl J Med 2002; 346: 1221-1231.
14. Rubinstein E, Lavine JE, and Schwimmer JB. Hepatic, cardiovascular, and endocrine outcomes of the histological subphenotypes of nonalcoholic fatty liver disease. Paper presented at the Seminars in liver disease. 2008.
15. Sanyal AJ. AGA technical review on nonalcoholic fatty liver disease. Gastroenterology, 2002; 123:1705-25.
16. Williams CD, Stengel J, Asike MI, Torres DM, Shaw J, Contreras M, Landt CL, Harrison SAPrevalence of nonalcoholic fatty liver disease and nonalcoholic steatohepatitis among a largely middle-aged population utilizing ultrasound and liver biopsy: A prospective study. Gastroenterology 2011, 140, 124–131.
17. Bacon BR, Farahvash MJ, Janney CG, Neuschwander-Tetri B Nonalcoholic steatohepatitis: An expanded clinical entity. Gastroenterol.-Orlando 1994, 107, 1103–1109.

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