

**OCCURRENCE OF NAFLD IN THE PATIENTS SUFFERING FROM TYPE II
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ABSTRACT

Objective: To assess the prevalence of non-alcoholic fatty liver disease in type II diabetes mellitus patients.

Study Design: A Prospective Observational Study. **Place and Duration:** Department of Medicine Sheikh Zayed Hospital Rahim Yar, from June 2018 to January 2019. **Methodology:** Patients presenting with diabetes mellitus type II were divided into two equal groups on the basis of presence or absence of non-alcoholic fatty liver disease. Age, gender, BMI, Plasma aspartate aminotransferase, Plasma alanine aminotransferase, Plasma alkaline phosphatase, duration of type II diabetes mellitus, fasting plasma glucose, serum albumin, plasma cholesterol, plasma triglycerides, Plasma LDL-C, Plasma HDL-C and HbA_{1c} were the variables calculated. **Results:** The mean age was 59.15±5.63 years, BMI 32.03±5.32 kg/m², Plasma AST 19.68±2.22, Plasma ALT 19.87±1.71, Plasma ALP 62.32±12.84, duration of type 2 DM was 8.40±3.71 years and fasting plasma glucose of non NAFLD patients was 124.57±5.66 mg/dl. While, the mean age was 61.55±8.00 years, BMI 32.05±6.24 kg/m², plasma AST 23.03±2.56, plasma ALT 27.28±1.94, plasma ALP 75.19±21.30, duration of type 2 DM 8.12±1.28 years and fasting plasma glucose of NAFLD patients was 137.45±5.07 mg/dl. The mean albumin (g/dl) was 4.20±0.64 g/dl, plasma cholesterol was 150.65±28.44, plasma triglyceride 114.04±5.99, plasma LDL-C 87.25±18.16 and plasma HDL-C of non NAFLD patients was 42.97±11.40. HbA_{1c} in non NAFLD was 9.1%. While, the mean albumin was (g/dl) 3.80±0.69 g/dl, plasma cholesterol 158.62±42.02, plasma triglyceride 150.07±9.03, plasma LDL-C 87.0±27.89 and plasma HDL-C of NAFLD patients was 40.76±10.46. HbA_{1c} of NAFLD patients was 6.8%. **Conclusion:** Non Alcoholic Fatty Liver Disease has a high prevalence in patients with type II diabetes mellitus having normal aminotransferases.

KEYWORDS: Prevalence, Non-Alcoholic Fatty Liver Disease, Diabetes Mellitus, Non-Alcoholic Steatohepatitis, Aminotransferases, Alanine Aminotransferase, Aspartate Aminotransferase, Plasma Glucose.

INTRODUCTION

In United States of America and many other parts of the world Non-alcoholic fatty liver disease (NAFLD) is considered to be the most common cause of chronic liver disease.^[1] Despite this fact, very little information regarding relation between type two diabetes mellitus and non-alcoholic fatty liver disease has been known. Use of aminotransferases as screening tools for its diagnosis.^[2] has shown that its prevalence ranges from 15-20%.^[3] or may be less but contrary to these tests liver ultrasound has shown greater prevalence of non-alcoholic fatty liver disease among type two diabetes patients i.e. 20-46%. Prevalence was reported to be 34% when gold standard techniques like, magnetic resonance imaging and spectroscopy were used for screening.^[4] Obesity is also one of the major risk factors for the

development of NAFLD as evident from the various studies present in previous literature.^[5]

Liver plays an important role in pathophysiology of type two diabetes mellitus as it is involved in the development of insulin resistance.^[6] Underlying mechanism which causes fatty changes in the liver of the patient suffering from type two diabetes mellitus is not fully understood. Hepatic fat accumulation, inflammatory signals from different types of immune cells and energy metabolism changes are thought to be the few reasons for development of NAFLD in T2DM. Mitochondrial function, lipotoxins, adipocytes and cytokines have been thought to be involved in both the development of NAFLD and type diabetes mellitus.^[7] Non diabetic patients suffering from NAFLD have insulin resistance. Similarly, patients suffering from type diabetes mellitus often develop non-alcoholic fatty liver disease due to

insulin resistance and might undergo inflammatory changes and develop nonalcoholic steatohepatitis. This complication can lead to further serious and more chronic complications like cirrhosis of liver and even development of hepatocellular carcinoma. Drugs used in the treatment of type two diabetes mellitus have been shown to be effective in improving conditions like NAFLD and Non-alcoholic steatohepatitis.^[8]

Although there are evidences present to establish the relation between type to diabetes and liver fibrosis and steatohepatitis but in settings of normal aminotransferases very little literature have been published. Current study is conducted to determine the prevalence of non-alcoholic fatty liver disease among patients of type II diabetes mellitus and different parameters which are altered during development of this change in bodies of the patients. Rationale of our study is to find prevalence of NAFLD in patients of type II diabetes mellitus in local population as even though multiple studies have provided this correlation but in our local settings such evidence and correlation needs to be established so that screening for liver disease among the patients of type II diabetes mellitus can be improved. In this study the prevalence of non-alcoholic fatty liver disease in type II diabetes mellitus patients and comparison of the clinical findings among diabetic patients with NAFLD and without NAFLD will be performed.

METHODOLOGY

This prospective observational study was conducted in Sheikh Zayed Hospital Rahim Yar Khan from June 2018 to January 2019. Sample size (n=176) was calculated from the reference study by Paola et al.^[9] Non probability consecutive sampling technique was used to collect the sample size.

All the patients included in our study have had diabetes mellitus for more than five years. Exclusion criteria; prior history of alcohol consumption, history of any chronic liver disease, type I diabetes mellitus or any other serious illness of heart, lungs or kidney. Patients were divided into two equal groups Non-NAFLD group and NAFLD group on the basis of the presence of non-alcoholic fatty liver disease. Diagnosis of non-alcoholic fatty liver disease was made by measuring total body fat by dual energy x-ray absorptiometry and by measuring

liver triglyceride content with the help of magnetic resonance spectrometry. Diagnosis of NAFLD was considered if liver triglyceride content was more than 5.5%.

Age, gender, BMI, plasma AST, plasma ALT, plasma ALP, duration of type II diabetes mellitus, fasting plasma glucose, serum albumin, plasma cholesterol, plasma triglycerides, plasma LDL-C, plasma HDL-C and HbA_{1c} were the variables calculated at the start of the study and at the end of the study. Other than the variables just mentioned treatment with metformin, antihypertensive drugs use and statin use was also taken into account and analyzed in each patient presenting as type II diabetes mellitus. All the data was measured and recorded in form of a performed performa which contained information regarding all the variables to be assessed in this study. Data was collected by the researcher himself.

Data Analysis: After recording and measuring the data regarding these variables, all the data was subjected to statistical analysis by using computer software SPSS version 23. Frequency and percentage was calculated for categorical variables and mean and standard deviation was calculated for continuous variables. Chi square test was applied and P value less than or equal to 0.05 was taken as significant.

RESULT

A total number of 176 patients were enrolled in this study. Patients was divided into two equal groups i.e. 88 (n=50%) in each, non NAFLD and NAFLD respectively. The mean age was 59.15±5.63 years, BMI 32.03±5.32 kg/m², plasma AST 19.68±2.22, plasma ALT 19.87±1.71, plasma ALP 62.32±12.84, duration of type 2 DM was 8.40±3.71 years and fasting plasma glucose of non NAFLD patients was 124.57±5.66 mg/dl. There were 77 (87.5%) males and 11 (12.5%) females. While, the mean age was 61.55±8.00 years, BMI 32.05±6.24 kg/m², plasma AST 23.03±2.56, plasma ALT 27.28±1.94, plasma ALP 75.19±21.30, duration of type 2 DM 8.12±1.28 years and fasting plasma glucose of NAFLD patients was 137.45±5.07 mg/dl. There were 71 (80.7%) males and 17 (19.3%) females. The difference was statistically significant, except gender (p=0.216) and duration of type 4 DM (p=0.499). (Table-I).

Table I: Frequency of Demographic Characteristics among the both groups (N=176).

Characteristics	Non NAFLD (n=88)	NAFLD (n=88)	Test of Sig.
Age (years)	59.15±5.63	61.55±8.00	t=-2.29, p=0.023
Gender			
Male	77 (87.5%)	71 (80.7%)	$\chi^2=1.52, p=0.216$
Female	11 (12.5%)	17 (19.3%)	
BMI (kg/m ²)	32.03±5.32	32.05±6.24	t=-3.45, p=0.001
Plasma AST	19.68±2.22	23.03±2.56	t=-9.26, p=0.000
Plasma ALT	19.87±1.71	27.28±1.94	t=-26.83, p=0.000
Plasma ALP	62.32±12.84	75.19±21.30	t=-4.45, p=0.000

Duration of type 2 DM (years)	8.40±3.7	8.12±1.28	t=0.677, p=0.499
Fasting Plasma glucose (mg/dl)	124.57±5.66	137.45±5.07	t=-15.38, p=0.000

The mean albumin (g/dl) was 4.20±0.64 g/dl, plasma cholesterol was 150.65±28.44, plasma triglyceride 114.04±5.99, plasma LDL-C 87.25±18.16 and plasma HDL-C of non NAFLD patients was 42.97±11.40. HbA1c in non NAFLD was 9.1% (n=8). Treatment with metformin was 75 (85.2%). Anti-hypertension medications and use of statin use was 86.4% (n=76) and 75% (n=66) respectively While, the mean albumin was (g/dl) 3.80±0.69 g/dl, plasma cholesterol 158.62±42.02,

plasma triglyceride 150.07±9.03, plasma LDL-C 87.0±27.89 and plasma HDL-C of NAFLD patients was 40.76±10.46. HbA1c of NAFLD patients was 6.8% (n=6). Treatment with metformin was 81.8% (n=72). Anti-hypertension medications and use of statin use was 84.1% (n=74) and 83% (n=73) respectively. The difference was statistically significant albumin (p=0.000) and plasma triglyceride (p=0.000). (Table-II).

Table II: Treatment History and Lipid Profile in Both groups (N=176).

Characteristics	Non NAFLD (n=88)	NAFLD (n=88)	Test of Sig.
Albumin (g/dl)	4.20±0.64	3.80±0.69	t=3.94, p=0.000
treatment with metformin	75 (85.2%)	72 (81.8%)	χ²=0.372, p=0.542
Anti-Hypertensive medications	76 (86.4%)	74 (84.1%)	χ²=0.181, p=0.671
Statin Use	66 (75%)	73 (83%)	χ²=1.67, p=0.195
Plasma cholesterol	150.65±28.44	158.62±42.02	t=-1.47, p=0.143
Plasma triglyceride	114.04±5.99	150.07±9.03	t=-31.17, p=0.000
Plasma LDL-C	87.25±18.16	87.0±27.89	t=0.070, p=0.944
Plasma HDL-C	42.97±11.40	40.76±10.46	t=1.34, p=0.181
HbA1c %	9.1% (n=8)	6.8% (n=6)	χ²=0.310, p=0.577

DISCUSSION

Non Alcoholic Fatty Liver Disease and Non-alcoholic steatohepatitis are complications of diabetes mellitus and as our results have shown that most of the laboratory findings in people with NAFLD and without NAFLD are almost similar except few, it is important to advise more sensitive and specific methods for the diagnosis of NAFLD in patients with type two diabetes mellitus. There was difference present among the two groups discussed in this study in terms of plasma aminotransferases suggesting that their levels in NAFLD group, even though differ from the levels of plasma aminotransferases in non NAFLD patients but are not high enough to alarm the clinicians about the presence of a fatty liver disease. Plasma triglycerides were also significantly higher in patients with diagnosed NAFLD. Another striking finding in these results is the presence of statistically significant difference among the two groups in terms of fasting blood glucose suggesting that NAFLD is associated with poor glycemic control in patients with type II diabetes mellitus.

Despite being closely related entities not many studies has shown the evidence of presence of Non-alcoholic fatty liver disease in patients with type II diabetes mellitus with normal aminotransferases. Most of the clinicians and physicians believe that ultrasounds and aminotransferases levels which are commonly used in the diagnosis of liver diseases are not sensitive when used for the diagnosis of non-alcoholic fatty liver disease.^[10] Our study was done to find out the prevalence of non-alcoholic fatty liver disease not only because NAFLD or NASH is caused by type two diabetes mellitus.^[11] but also because NASH and NAFLD can

also precipitate micro and macro vascular diseases of type two diabetes mellitus.^[12 - 14] NAFLD and type II diabetes mellitus are closely associated with each as diabetes mellitus can lead to NAFLD and NAFLD when present can increase the risk of developing type two diabetes mellitus.^[15,16] Multiple studies have suggested the presence of liver fibrosis and steatosis in obese patients with type two diabetes mellitus but prevalence is still uncertain as tests for diagnosis of NAFLD and NASH that is ultrasound has very low sensitivity and specificity.^[17]

Multiple studies have shown that NASH and NAFLD usually presents with normal levels of plasma aminotransferases^[18, 19] but very little number of studies have shown whether NAFLD or NASH with normal aminotransferases is associated with type II diabetes mellitus, therefore, leaving a large gap in knowledge in terms of diagnosing the asymptomatic patients with diabetes who might have nonalcoholic fatty liver disease or nonalcoholic steatohepatitis. Only one previous study has results consistent with results of this study, which showed very high prevalence of NAFLD in patients with type two diabetes mellitus.

CONCLUSION

Non Alcoholic Fatty Liver Disease has a high prevalence in patients with type II diabetes mellitus having normal aminotransferases.

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