Original Article

Incidence of Non Alcoholic Fatty Liver Disease in Type II Diabetes Mellitus Patients

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ABSTRACT

Objective: To assess the incidence of non alcoholic fatty liver disease in type II diabetes mellitus patients.
Study Design: Prospective / Observational Study
Place and Duration of Study: This study was conducted at the Department of Medicine, Nishtar Hospital Multan, from April 2017 to December 2017.
Materials and Methods: A total no. of 176 took part in the study. Patients were divided into two equal groups on the basis of presence or absence of NAFLD. 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 $HbA1_c$ were the variables calculated. All the data was subjected to statistical analysis by using computer software SPSS version 23. Chi square test was applied and P value less than or equal to 0.05 was taken as significant.
Results: The mean age, BMI, plasma AST, plasma ALT, plasma ALP, duration of type 2 DM and fasting plasma glucose of non NAFLD patients was 59.15±5.63 years, 32.03±5.32 kg/m^2 , 19.68±2.22, 19.87±1.71, 62.32±12.84, 8.40±3.71 years, 124.57±5.66 mg/dl respectively. While, the mean age, BMI, plasma AST, plasma ALT, plasma ALP, duration of type 2 DM and fasting plasma glucose of NAFLD patients was 61.55±8.00 years, 32.05±6.24 kg/m^2, 23.03±2.56, 27.28±1.94, 75.19±21.30, 8.12±1.28 years, and 137.45±5.07 mg/dl respectively. The mean albumin (g/dl), plasma cholesterol, plasma triglyceride, plasma LDL-C and plasma HDL-C of non NAFLD patients was 4.20±0.64 g/dl, 150.65±28.44, 114.04±5.99, 87.25±18.16 and 42.97±11.40 respectively. HbA1c was 9.1% (n=8). While, the mean albumin (g/dl), plasma cholesterol, plasma triglyceride, plasma LDL-C and plasma HDL-C of NAFLD patients was 3.80±0.69 g/dl, 158.62±42.02, 150.07±9.03, 87.0±27.89 and 40.76±10.46 respectively. HbA1c was 6.8% (n=6)
Conclusion: Conclusion from results of this study can be made that NAFLD has a high incidence in patients with type II diabetes mellitus.
Key Words: Non-Alcoholic Fatty Liver Disease, Diabetes Mellitus, Non-Alcoholic Steatohepatitis

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INTRODUCTION

In United States of America and many other parts of the world Non-alcoholic fatty liver disease 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 non alcoholic steatohepatitis. This complication can lead to further serious and more chronic complications like cirrhosis of liver and even development of

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hepatocellular carcinoma. Drugs used in the treatment of type two diabetes mellitus have been shown to be effective in improving conditions like NAFLD and NASH [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.

MATERIALS AND METHODS

This study was conducted in Nishtar Hospital Multan from April 2017 to December 2017. It is a prospective study with sample size of 176. Sample size was calculated from the reference study by Paola Portillo Sanchez et al [9]. Non probability consecutive sampling technique was used to collect the sample size. Ethical approval for this study was obtained from the Hospital Ethics Committee. Informed consent was taken prior to the inclusion in the study.

All the patients included in our study have had diabetes mellitus for more than five years. Patients were excluded on the basis of following 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 $HbA1_c$ 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.

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.

RESULTS

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

Table No.1: Demographic Characteristics among the study groups

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	87.5% (n=77)	80.7% (n=71)	χ^2=1.52, p=0.216
Female	12.5% (n=11)	19.3% (n=17)	
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

Table No.2: Demographic Characteristics

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	85.2% (n=75)	81.8% (n=72)	χ^2=0.372, p=0.542
Anti-Hypertensive medications	86.4% (n=76)	84.1% (n=74)	χ^2=0.181, p=0.671
Statin Use	75% (n=66)	83% (n=73)	χ^2=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)	χ^2=0.310, p=0.577

The mean albumin (g/dl), plasma cholesterol, plasma triglyceride, plasma LDL-C and plasma HDL-C of non NAFLD patients was 4.20±0.64 g/dl, 150.65±28.44, 114.04±5.99, 87.25±18.16 and 42.97±11.40 respectively. HbA1c was 9.1% (n=8). Treatment with metformin was 85.2% (n=75). Anti-hypertension medications and use of statin use was 86.4% (n=76) and 75% (n=66) respectively. While, the mean albumin (g/dl), plasma cholesterol, plasma triglyceride, plasma ldl-C and plasma HDL-C of NAFLD patients was 3.80±0.69 g/dl, 158.62±42.02, 150.07±9.03, 87.0±27.89 and 40.76±10.46 respectively. HbA1c 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 2).

DISCUSSION

NAFLD and NASH 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, 13, 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 amino transferases 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 non alcoholic fatty liver disease or non alcoholic 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

Conclusion from results of this study can be made that NAFLD has a high incidence in patients with type II diabetes mellitus and that it occurs with normal levels of aminotransferases in plasma. Therefore its presence should not be ruled out if these markers are normal in type II diabetes mellitus patients. Moreover obesity is also a risk factor for the development of NAFLD in type II diabetes mellitus.

Author's Contribution:

Concept & Design of Study:	Muhammad Tahir
Drafting:	Muhammad Tahir, Muhammad Waqas
Data Analysis:	Muhammad Waqas, Namra Anam

Revisiting Critically:	Muhammad Tahir, Muhammad Waqas
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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