

PRESENCE OF NON-ALCOHOLIC FATTY LIVER DISEASE IN PATIENTS OF UNCONTROLLED AND CONTROLLED TYPE 2 DIABETES MELLITUS

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ABSTRACT

Objectives: To determine the presence of non-alcoholic fatty liver disease in patients of uncontrolled and controlled type 2 diabetes mellitus.

Study Design: Cross sectional study.

Place and Duration of Study: Jinnah Allama Iqbal Institute of Diabetes and Endocrinology (JAIDE)/Jinnah Hospital Lahore, from Sep 2017 to Nov 2017.

Material and Methods: Our study included 127 patients between 25-75 years of age and of either gender who presented in Jinnah Allama Iqbal Institute of Diabetes and Endocrinology (JAIDE) during the year of 2017. Patient details including demographic data, HbA1c and blood glucose random were collected. Nonalcoholic fatty liver disease (NAFLD) was diagnosed on ultrasonography as per criteria. The data were analyzed in SPSS version 21. Quantitative data were presented as mean and standard deviation and qualitative data as frequency and percentages. Chi-square test was used to assess any statistical significance with p -value ≤ 0.05 .

Results: Among 127 patients, with mean age of 45.1 ± 9.3 years, males were 38.6% and females were 61.4%. The average duration of diabetes was 6.3 ± 4.5 years. Mean blood sugar random was 300 ± 113 mg/dL and mean HbA1c was $9.3\% \pm 2.1$. Overall, NAFLD status was found in 100 (78.7%) and it was negative in 27 (21.3%). Out of 101 patients with uncontrolled diabetes, 98% patients were positive for NAFLD, while in 26 patients with controlled diabetes, NAFLD was found only in 2% patients showing statistically significant results ($p < 0.000$).

Conclusion: Non-alcoholic fatty liver disease is more prevalent in patients with uncontrolled type 2 diabetes mellitus as compared to controlled diabetics.

Keywords: Diabetes mellitus, HbA1c, Non-alcoholic fatty liver disease, Steatosis.

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INTRODUCTION

Nonalcoholic fatty liver disease (NAFLD) is one of the common causes of chronic liver disease, and its prevalence in general population estimates about 20-30% and this further increases upto 70-90% in patients with obesity or type 2 diabetes mellitus^{1,2}.

NAFLD ranges from less serious problem like steatosis to significant disease in the form of steatohepatitis, hepatic cirrhosis and end stage liver disease leading to liver failure, at times requiring transplantation. Various factors contribute to and have some association with the development of NAFLD. Epidemiological data

fully support a bi-directional relationship between NAFLD and type 2 DM. Stated otherwise, NAFLD is associated with established Type 2 DM in cross-sectional studies and precedes the development of type 2DM in follow-up studies³.

The pathogenesis of NAFLD appears to involve a two-hit hypothesis. The first hit is the accumulation of excessive free fatty acid within the hepatocytes due to impaired insulin action following a secondary event of oxidative stress, resulting in nonalcoholic steatohepatitis⁴. Hyperinsulinemia induces insulin resistance by inhibiting the beta oxidation of free fatty acid which ultimately is re-esterified into triacyl glycerides and deposited into the liver. Increased lipotoxicity leads to a condition of mitochondrial dysfunction thereby releasing the reactive oxygen species. The free radicals released by reactive

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oxygen species causes inflammation by activating the inflammatory cytokines leading to hepatic injury⁵.

Various diagnostic modalities have been used for the diagnosis of NAFLD. It includes routine liver markers in blood, liver biopsy, ultrasonography, CT scan and magnetic resonance imaging. Although liver biopsy is gold standard but it is more invasive while other investigations like CT scan or MRI are expensive⁶. However, ultrasonography is a safe, non-invasive, radiation free, cost effective and easily available modality. Ultrasound abdomen has sensitivity and specificity ranging from 60–94% and 84–95%, respectively⁷. Sonographic features of NAFLD include attenuation of image, diffuse echogenicity, uniform heterogeneity, subcutaneous depth of more than 2 cm and liver covering the entire field⁸.

We estimated the occurrence of NAFLD in patients with type 2 DM, particularly those with poor glycemic control. There is an increased risk for development of NAFLD secondary to diabetes, and there is evidence that NAFLD conversely is a risk factor for the development of Type 2 DM. In a study comparing NAFLD patients and control subjects, none of whom had diabetes at baseline, those with NAFLD were more likely to have diabetes and metabolic syndrome when re-evaluated eleven years later⁹.

Diagnosis and treatment of nonalcoholic fatty liver disease can have a major impact on management of patients with type 2 DM and it can help to improve their overall disease outcome.

The objective of this study was to determine the presence of non-alcoholic fatty liver disease in patients of uncontrolled and controlled type 2 diabetes mellitus.

PATIENTS AND METHODS

After approval from hospital ethical committee and informed written consent from the patients, 127 patients with a known history of type 2 diabetes mellitus aged between 25–75 years and belonging to either gender were included

in the study. Uncontrolled diabetes mellitus was defined as HbA1c >6.5% and blood sugar random of >180mg/dL, while controlled diabetes was defined as HbA1c <6.5% and blood sugar random of <180mg/dL. Nonalcoholic fatty liver disease (NAFLD) was diagnosed as presence of fatty liver on ultrasonography described as features of attenuation of image quickly within 4–5 cm of depth, diffuse echogenicity & brightness within the first 2–3 cm of depth and uniform heterogeneity with thick subcutaneous depth of more than 2 cm with no visible edges⁸. Patients having viral hepatitis B or C and history of primary biliary cirrhosis, Wilson's disease, hemochromatosis, and autoimmune hepatitis and patients taking medications that can account for steatosis (e.g. tamoxifen, amiodarone, methotrexate) during the previous year were excluded from study. Data were analyzed in SPSS version 21. Quantitative data were presented as mean and standard deviation and qualitative data as frequency and percentages. Chi-square test was used to assess any statistical significance with *p*-value ≤0.05.

RESULTS

There were 127 patients included in the study, with mean age of 45.1 ± 9.3 years, males were 49 (38.6%) and females were 78 (61.4%). The average duration of diabetes was 6.3 ± 4.5 years. Mean blood sugar random was 300 + 113 mg/dL with more than 80% patients having BSR of above 180mg/dL. Mean HbA1c was 9.3% ± 2.1 and 79.5% patients had HbA1c >6.5% (table-I). Overall, NAFLD status was found in 100 (78.7%) and it was negative in 27 (21.3%) patients. Regarding diabetes control and presence of NAFLD, 101 patients with uncontrolled diabetes, 98% patients had NAFLD, and among 26 patients with controlled diabetes, NAFLD was found only in 2% patients showing statistically significant results (*p*<0.000) (table-II).

DISCUSSION

Nonalcoholic fatty liver disease (NAFLD) is defined by fatty change in liver in the absence of alcohol use and other etiologies of liver disease. It

is a growing public health problem worldwide. Liver steatosis often causes no symptoms at all but when it progresses to symptomatic disease and fibrosis, it leads to poor prognosis. Recent evidence has shown a close relationship between hyperglycemia and NAFLD and its progression

Table-I: Demographic and clinical profile of subjects.

Variables (n= 127)	Frequency	Percentage (%)
Age (years)		
Mean=45.1, SD =9.3		
25 - 50 years	88	69.3
51 - 75 years	39	30.7
Gender		
Male	49	38.6
Female	78	61.4
Duration of Diabetes (years)		
Mean=6.3 SD=4.5		
<10 years	107	84.3
11-20 years	20	15.7
Blood Sugar Random (mg/dL)		
Mean=300, SD=113		
<180 mg/dL	26	20.5
>180 mg/dL	101	79.5
HBA1c		
Mean=9.3, SD= 2.1		
<6.5%	26	20.5
>6.5%	101	79.5
NAFLD Status		
Yes	100	78.7
No	27	21.3

Table-II: Diabetes status and NAFLD status (chi-square).

Diabetes Status	NAFLD Status		p-value
	Yes	No	
Uncontrolled	98 (98%)	03 (11%)	p=0.000
Controlled	02 (2%)	24 (89%)	
Total	100	27	

to advanced disease. Dysfunctional adipose tissue, found in obesity, type 2 DM and NAFLD, impairs glucose and lipid metabolism by two ways: Firstly, acting as an endocrine organ & releasing a number of fat-derived cytokines and secondly, by free fatty acid induced ectopic fat deposition and lipotoxicity^{9,10}.

This study proved significant relationship between presence of NAFLD and its progression in patients with uncontrolled diabetes mellitus

and it supports the previous data available in other studies. As for example, Wong *et al* observed in a cross-sectional series of non-diabetic individuals that impaired glucose tolerance (IGT) or impaired fasting glucose (IFG) alone occurred in 25% of patients with simple steatosis versus 55% of those with non-alcoholic steatohepatitis¹¹. In type 2 diabetic patients with or without obesity, up to 30% have fat with inflammation, 25% have associated fibrosis, and 1-8% have cirrhosis¹².

Regarding the role and importance of ultrasonography in diagnosis of NAFLD, it is pertinent to mention that, it is an easily available, non-invasive radiological modality which can detect the features of NAFLD to much confidence with high level of sensitivity and specificity suggesting it an acceptable first-line screening tool for NAFLD^{13,14}. In addition to that, ultrasonography is more cost effective when compared with CT scan or MRI as a diagnostic tool¹⁵. Despite the fact that liver biopsy is gold standard and most accurate to diagnose NAFLD but it is more invasive and carries significant risk of procedural complications¹⁶.

These patients may benefit from more careful surveillance and early treatment interventions. Our findings have significant clinical and public health implications suggesting the screening for NAFLD in uncontrolled diabetic patients. The detection of NAFLD on ultrasonography should alert the clinicians treating diabetes and it could be the starting point of new research to improve interventions for decreasing progression of NAFLD to hepatic cirrhosis in diabetic patients^{17,18}.

CONCLUSION

Non-alcoholic fatty liver disease is more prevalent in patients with uncontrolled type 2 diabetes mellitus as compared to controlled diabetics.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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