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Study Of Non Alcoholic Fatty Liver Disease With Fibroscan In Patients Of Type 2 Diabetes Melitus

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Abstract

India is becoming the world's diabetic capital. The prevalence of NAFLD in TYPE 2 diabetes mellitus is 59.67% as per studies conducted in Indian populations. NAFLD represents a continuum from simple steatosis to non alcoholic Steatohepatitis and cirrhosis. NAFLD and type 2 diabetes mellitus are common condition that often coexists and can act synergistically to cause adverse events.

The presence of NAFLD in. type 2 diabetes mellitus can lead to substantial risk
of liver fibrosis. Advanced liver fibrosis is associated with overall and liver related mortality. Fibroscan is a non invasive tool which measures the hepatic stiffness.

The aim of study is to assess to screen people of type 2 diabetes mellitus for NAFLD with fibroscan.

Keywords: NAFLD, Diabetes Melitus, Fibroscan

Introduction

Non-alcoholic fatty liver disease (NAFLD) is the most common cause of chronic liver disease worldwide, with a global prevalence of 25.2%.Non-alcoholic fatty liver disease is characterized by: (i) the presence of hepatic steatosis, as determined by imaging or histological diagnosis; (ii) no history of excessive alcohol drinking or the consumption of <140 g/week ethanol intake for men (<70 g/week for women) in the past 12 months; and (iii) no competing etiologies for hepatic steatosis and no coexisting causes for chronic liver disease. Clinically, NAFLD patients tend to have components of metabolic syndrome such as obesity, type 2 diabetes mellitus (T2DM), hyperlipidemia (HL) and hypertension (HT). Among these comorbidities, T2DM seems to be the most important risk factor for having NAFLD and nonalcoholic steatohepatitis (NASH) and the most important clinical predictor of adverse clinical outcomes such as advanced hepatic fibrosis and mortality.

The gold standard method for diagnosis of NAFLD is liver biopsy, which provides quantification of all qualities of the disease: steatosis, hepatocellular injury (NASH) and fibrosis, i.e., the degree of scarring in the liver. Despite being highly informative, the utility of liver biopsy is limited by its invasiveness, especially considering the high prevalence of the disease. In addition to liver biopsy, steatosis can be assessed with non-invasive imaging modalities such as ultrasonography of liver. Liver fibrosis can be non-invasively estimated using 1D ultrasonography transient elastography (TE; FibroScan, Echosens, Paris, France). Fibroscan (transient elastography) measures liver stiffness through estimation of velocity of propagation of a shear wave through liver tissue. The value depends on the viscoelastic properties of the liver. The recent EASL-EASD-EASO Clinical Practice Guidelines for management of NAFLD and EASL-ALEH Clinical Practice Guidelines for evaluation of liver disease severity concluded that this technique is an acceptable non-invasive procedure for identification of cases at high risk of advanced fibrosis and cirrhosis.[28,29]

The only curative treatment for end-stage cirrhosis is liver transplantation, for which NAFLD is currently

the most rapidly increasing indication Due the growing epidemic of NAFLD and lack of treatment options, there has been everlasting search into the risk factors and pathophysiologic mechanisms leading to NAFLD and its progression. One such risk factor significantly affecting NAFLD is Type 2 Diabetes Mellitus. However, not much studies are available in this regard, especially from our region. Therefore, the present study was planned to assess the prevalence of Non Alcoholic Fatty Liver Disease in patients of Type 2 Diabetes Mellitus.

Aim Of The Study

To find out the prevalence of Non Alcoholic Fatty Liver Disease in the patients of Type 2 Diabetes Mellitus using Fibroscan.

Objectives

To assess the degree of fibrosis of Liver by Fibroscan in the patients of Type 2Diabetes Mellitus with NAFLD (in patients who can afford to do the test).

To study the various risk factors associated with Liver fibrosis in patients ofType 2 Diabetes Mellitus with NAFLD.

Materials And Method

This observational, single centred, cross sectional study was conducted under the Department of Medicine, MGM Medical College and Hospital, Navi Mumbai. Prior approval of Institutional Ethics Committee was taken before start of the study. A written signed informed consent was taken from all the patients prior to their enrolment in the study.

Study Design

Observational, Single centre, Cross-sectional study

Study Site

Department of Medicine, MGM Medical College and Hospital, Navi Mumbai.

Duration Of Study

March 2020 – October 2021

Study Population

26 cases of Type 2 Diabetes Mellitus attending the Medicine OPD during the study period and meeting the inclusion and exclusion criteria.

Inclusion Criteria

1. Patients who were known cases of Type 2 Diabetes Mellitus.
2. Patients who were newly diagnosed Type 2 Diabetes Mellitus.
3. Patients of either gender within the age group of 30 to 75 years.

Exclusion Criteria

1. Patients with other types of diabetes like Type 1 DM, gestational diabetes,Maturity Onset Diabetes of Young, LADA, steroid induced diabetes, etc.
2. Patients with history of alcohol consumption or any other addictions.
3. Pregnant patients.
4. Patients who were positive for HbsAg, HCV, or had any history of any otherchronic liver diseases, jaundice, hepatitis.
5. Patients who were on Methotrexate, Estrogen, Cortisol, CCBs, Amiodarone,Valproic acid, antiviral medications, etc.
6. Patients who do not consent to participate in the study.

Sample Size

26 patients of. Type 2 DM attending to the Medicine OPD during the study period, were included in the study

Investigation

Laboratory investigations were carried out. 10ml blood sample was collected and divided into plain bulb, EDTA bulb and fluoride bulb for further evaluation.

1. EDTA bulb – HbA1C
2. Plain bulb – Lipid profile, LFT, RFT, electrolytes, HBsAg, Anti HCV.
3. Fluoride bulb – FBS, PPBS

The laboratory investigations were carried out as follows:

1. HbA1c estimation was done by enzymatic assay method on automated analyser.
2. Plasma sugar was carried out by glucose oxidase and peroxidase method.

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3. LFT and RFT were carried out by enzymatic method.
4. Total cholesterol was estimated by using liquid Cholesterol reagent set for determination of Total Cholesterol based on Enzymatic method using Cholesterol Esterase, Cholesterol Oxidase and Peroxidase on automated analyser.
5. Triglycerides was estimated by Glycerokinase Peroxidase-Peroxidase method on automated analyser.
6. HDL cholesterol was estimated by Phosphotungstic Acid method on automated analyser.
7. LDL was calculated using formula Total Cholesterol - (VLDL + HDL).
8. Serum electrolytes were assessed.
9. Urine sugars and proteins were assessed by the dipstick test.
10. All patients were tested for HBsAg and Anti HCV antibody by immunoassay.
11. All investigations were done in Biochemistry Laboratory of MGM Hospital, Kamothe.

All the patients underwent USG abdomen to assess the liver. Affording patients also underwent Fibroscan. USG and fibroscan were done under the Department of Radiodiagnosis, MGM Hospital, Kamothe.

Ultra Sonography – Ultrasound of the abdomen is routinely used to evaluate NAFLD , but a liver biopsy is considered the gold standard for

the diagnosis of NAFLD. Fatty liver can be diagnosed by the presence of at least two of the following three abnormal findings on abdominal ultrasonography :

1. increased echogenicity of the liver near-field region with deepattenuation of the ultrasound signal;
2. hyperechogenity of liver tissue (“bright liver”), as often comparedto hypoechogenity of the kidney cortex; and
3. vascular blurring.

The fatty liver was graded as grade 1,2,3 according to report given by experienced radiologist. Ultrasonography has a sensitivity of 90% and specificity of 95% in detection of moderate and severe hepatic steatosis.

NAFLD can be classified based on standard ultrasonographic criterion

1. GRADE 1 fatty liver – mild steatosis
2. GRADE 2 fatty liver – moderate steatosis
3. GRADE 3 fatty liver – severe steatosis

Fibroscan -

Fibroscan was done in patients who could afford the test.

Patients were asked to be on fasting for at least for 3 hrs before the fibroscan is being done. It was performed by a single experienced operator using fibroscan 530 compact with a standard M probe. Liver stiffness measurement (LSM) was measured with 10 successful measurements and mean of all values is taken.

Fibro Scan Grading

1. F1 – No Significant Fibrosis - <7 kilo pascals
2. F2 – Significant Fibrosis - >7 kilo pascalsAll the data was recorded in excel sheet and analysed.

Stastical Analysis

The data was analyzed using statistical software (IBM SPSS, IBM Corporation, Armonk, NY, USA). Descriptive statistics: The

Numerical/Continuous data were expressed as Mean ± Standard Deviation and the Categorical data were expressed as Percentages.

Analytical statistics: The Numerical/Continuous data were analysed by the ‘Unpaired t test’ and the Categoricaldata were analysed by the

Chi square test (Fischer’s exact test was used when more than 20% of cells had value less than 5). P value of less than 0.05 was considered as “statistically Significant” and indicated by “*” in the Tables. Bar charts and Pie

diagrams were used for the presentation of the data as applicable.

Table1: Distribution of the study population according to the demographic characteristics and results of Fibroscan.

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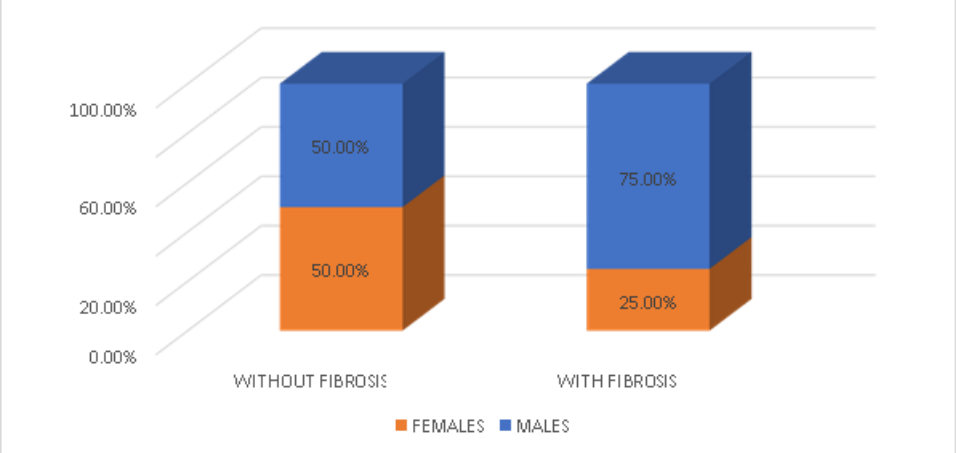
PARAMETER	WITHOUT FIBROSIS	WITH FIBROSIS	P Value
MEAN AGE (years)	54.83 ± 6.72	44.25 ± 10.19	**0.004***

Inference - Mean age of patients of NAFLD having fibrosis was 44.25 ± 10yrs as compared to 54.83 ± 6.72yrs in patients without fibrosis.

Table 2 : Gender wise distribution of the study population according to the results of Fibroscan

GENDER	WITHOUT FIBROSIS(< 7KPa)		WITH FIBROSIS(>7KPa)		TOTAL	
	N	%	N	%	N	%
FEMALES	9	34.62%	2	7.69%	11	42.31%
MALES	9	34.62%	6	23.07%	15	57.69%
TOTAL	**18**	69.24%	**8**	30.76%	**26**	100%
P value	**0.234**					
Statistical Significanc	**Not Statistically Significant**					

Graph 1 : Gender wise distribution of the study population according to the results of Fibroscan



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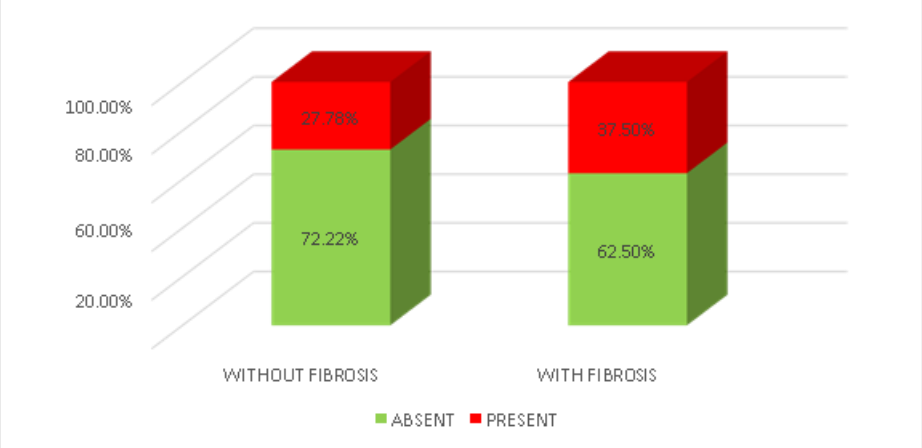
Inference – Prevalence of males (75%) patients was higher than females (25%) patients among the patients of NAFLD with fibrosis.

Table 3: Distribution of the study population according to the presence of hypertension and results of Fibroscan

HYPERTENSION	WITHOUT FIBROSIS		WITH FIBROSIS		TOTAL	
	N	%	N	%	N	%
ABSENT	13	50%	5	19.23%	18	69.23%
PRESENT	5	19.23%	3	11.54%	8	30.77%
TOTAL	18	69.24%	8	30.76%	26	100%
P value	0.620					
Statistical Significance	Not Statistically Significant					

Graph 2 : Distribution of the study population according to the presence of hypertension and results of Fibroscan.



Inference - Hypertension was present in 37.5% of the patients of NAFLD with fibrosis, was found to be higher when compared to patients without fibrosis(27.78%).

Table 4 : Distribution of the study population according to the BMI and results of Fibroscan

PARAMETER	WITHOUT FIBROSIS	WITH FIBROSIS	P Value

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2 **BMI (kg/m)**	24.01 ± 1.94	25.92 ± 3.61	**0.090**

Inference - BMI was found to be higher among the patients of NAFLD with fibrosis, as compared to patients of NAFLD without fibrosis.

Table 5 : Distribution of the study population according to the liver function tests andresults of Fibroscan

PARAMETER	WITHOUT FIBROSIS	WITH FIBROSIS	P Value
T. BILI (mg/dL)	0.65 ± 0.30	0.73 ± 0.35	**0.553**
D. BILI (mg/dL)	0.17 ± 0.12	0.18 ± 0.14	**0.890**
ID. BILI (mg/dL)	0.48 ± 0.21	0.54 ± 0.23	**0.484**
SGOT (U/L)	23.22 ± 5.87	23.88 ± 6.29	**0.800**
SGPT (U/L)	21.72 ± 5.82	23.75 ± 8.36	**0.481**
ALK PO (IU/L)	115.00 ± 33.82	119.88 ± 26.03	**0.721**
T. PROTEIN (g/dL)	7.28 ± 0.64	7.31 ± 0.49	**0.909**
ALBUMIN (mg/dL)	3.87 ± 0.53	3.86 ± 0.47	**0.967**

Inference - liver function tests were almost similar in the patients of NAFLD with fibrosis and without fibrosis.

Table 6 : Distribution of the study population according to the renal function testsand results of Fibroscan

PARAMETER	WITHOUT FIBROSIS	WITH FIBROSIS	P Value
UREA (mg/dL)	33.50 ± 14.06	33.63 ± 12.14	**0.983**
CREATININE (mg/dL)	0.85 ± 0.22	0.62 ± 0.30	**0.041***
BUN (mg/dL)	14.46 ± 8.25	17.06 ± 5.02	**0.421**
URIC ACID (mg/dL)	5.10 ± 1.90	4.82 ± 1.32	**0.706**

Inference –Among the patients of NAFLD with fibrosis, there was no significant difference in the renal parameters as compared to patients without fibrosis.

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Table 7 : Distribution of the study population according to the electrolytes and resultsof Fibroscan

PARAMETER	WITHOUT FIBROSIS	WITH FIBROSIS	P Value
SODIUM (mEq/L)	134.39 ± 3.81	135.88 ± 4.97	**0.411**
POTASSIUM (mmol/L)	4.39 ± 0.41	4.21 ± 0.40	**0.306**

Inference - Among the patients of NAFLD with fibrosis, there was no significant difference in electrolyte values as compared to patients without liver fibrosis.

Table 8 : Distribution of the study population according to the blood sugar levels andresults of Fibroscan

PARAMETER	WITHOUT FIBROSIS	WITH FIBROSIS	P Value
HbA1c (%)	9.90 ± 2.51	9.00 ± 2.31	**0.396**
FBS (mg/dL)	187.03 ± 68.29	148.53 ± 57.31	**0.178**
PLBS (mg/dL)	291.08 ± 100.32	257.31 ± 89.31	**0.422**

Inference

1. HbA1C levels were almost similar in both the groups
2. Fasting blood sugar was found to be higher in patients of NAFLD withoutfibrosis however this result could not attain statistical significance.

Table 9 : Distribution of the study population according to the lipid profile andresults of Fibroscan

PARAMETER	WITHOUT FIBROSIS	WITH FIBROSIS	P Value
T-C (mg/dL)	162.62 ± 36.80	155.88 ± 41.50	**0.682**
HDL-C (mg/dL)	46.44 ± 13.59	41.00 ± 6.44	**0.295**
LDL-C (mg/dL)	74.33 ± 31.37	55.20 ± 21.95	**0.133**

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VLDL-C (mg/dL)	42.40 ± 17.75	59.67 ± 38.42	**0.125**
TRIGLYCERIDES (mg/dL)	212.00 ± 88.76	217.50 ± 74.53	**0.880**

Inference – lipid profile values among the patients of NAFLD with fibrosis, were almost similar to those patients without liver fibrosis.

Discussion

Type 2 Diabetes Mellitus with NAFLD is considered as a multifactorial disease with genetic and environmental factors. Insulin Resistance is considered as a key risk factor for the occurrence and development of T2DM with NAFLD. IR in the peripheral tissue and liver is one of the main causes of this condition, leading to the increase in circulating glucose levels and lipid substrates for lipid accumulation in the liver.

Growing evidence clearly shows that NAFLD is a multiorgan disease, supporting a strong link between NAFLD and cardiovascular diseases (CVDs), Type 2 Diabetes Mellitus, chronic kidney disease (CKD), extrahepatic malignancies (eg., colorectal cancer), obstructive sleep apnea (OSA), and various endocrinopathies (e.g., thyroid dysfunction, polycystic ovarian syndrome (PCOS), osteoporosis, psoriasis, hypothyroidism, and iron overload).

[169] Although the primary site of NAFLD is the liver, the most common causes of mortality are CVDs, followed by extrahepatic malignancies such as colorectal cancer and then liver-related complications (cirrhosis and HCC). Nevertheless, the high incidence and rapid progression of NAFLD in cases with T2DM indicates a unifying underlying pathophysiologic mechanism. Not much studies have been conducted in this regard. Therefore, the present studywas conducted to study the prevalence of NAFLD in cases of T2DM.

A total of 100 cases of T2DM were included in the present study after obtaining ethics clearance and written informed consent. Demographic details and relevant histories were recorded. Physical examination was done. Laboratory findings were recorded. All patients underwent USG scan and affording patients underwent Fibroscan. NAFLD was diagnosed on the basis of ultrasonographic evidence of fatty liver. All data was entered in excel and analysed. The findings are summarised in the following sections.

Demographics:

Fibroscan and Fibrosis: In the present study, fibroscan could be done in 26% of the cases due to financial constraints. Amongst the NAFLD cases undergoing Fibroscan, fibrosis was present in 30.76% of the cases.

Hypertension: In the present study, hypertension was present in 40% of the total cases. Hypertension was present in 50 percent of patients with NAFLD.

When assessed with respect to fibrosis, the prevalence of hypertension was similar in the cases having fibrosis and in the cases without fibrosis; P value: 0.620.

BMI: In the present study, it was observed that the BMI in the cases with normal liver scan was lower (23.61 ± 1.90 kg/m2) than the cases with NAFLD (25.72 ± 2.03 kg/m2); P value: less than 0.001.

When assessed with respect to fibrosis, the BMI was similar in the cases having fibrosis and in the cases without fibrosis; P value: 0.090.

Laboratory investigations: In the present study, it was observed that uric acid was higher in the cases having NAFLD (6.02 ± 2.33 mg/dL) as compared to the normal cases (5.03 ± 1.53 mg/dL); P value: 0.021.

Among the studies on relationship between NAFLD and uric acid most displayes strong association between hyperuricemia and NAFLD. Thus ,as a risk factor, uric acid might develop as one prediction marker for the occurrence and severity of NAFLD incidences, which implies that uric acid may be a potential therapeutic target for NAFLD, especially in patients with hyperuricemia. However ,the potential mechanism of how uric acid contribute to NAFLD pathology is far from beingclarified and further

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studies are required to investigate the mechanism. In the study conducted by Zhang C. et al, there was a strong association between hyperuricemia and NAFLD. These findings were similar to our present study.

When assessed according to the diabetic profile, the mean levels of HbA1c, FBS and PLBS were significantly higher in the cases having NAFLD than the normal cases; P value: less than 0.001.

When assessed according to the lipid profile, the mean levels of total cholesterol, LDL cholesterol, VLDL cholesterol and triglycerides were significantly higher in the cases having NAFLD than the normal cases; P value: less than 0.05. HDL cholesterol was similar in both the groups; P value: more than 0.05.

Rest all parameters, viz., LFT, RFT and serum electrolytes were similar in both the groups; P value: more than 0.05.

Thus, it is seen the present study that in T2DM patients, increased HbA1c, FBS, PLBS, Uric acid, lipid profile are associated with NAFLD. Hepatic transaminases (SGOT and SGPT) and other liver and renal function tests may be normal.

Limitations: The present study was a single centre study and was limited by the OPD attendance of the patients. It was a time bound study.Therefore, the results may not be generalized.

Summary Of Results

1. A total of 26 patients underwent fibroscan of which only 8 patients showed fibrosis and 18 patients had no liver fibrosis.
2. In patients who underwent fibroscan , the mean age of patients having fibrosis was younger than the patients not having fibrosis.
3. In patients who underwent fibroscan ,males had higher prevalence of fibrosis as compared to females.
4. Hypertension was equally present in both group patients' i.e with fibrosis and without fibrosis.
5. Patients with higher BMI has shown significant fibrosis on fibroscan.
6. Among the patients who underwent fibroscan and who were diagnosed to have liver fibrosis there was no statistically significant derangement in the laboratory parameters in both the groups.

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