Original Article

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To Study the Occurrence of Non-Alcoholic Fatty Liver Disease (NAFLD) in Type 2 Diabetes Mellitus.

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Abstract

Background: Macrovascular and Microvascular complications are well evaluated in DM but NAFLD is the most neglected and unevaluated complication among DM.Fibroscan is the non-invasive method for assessing liver fibrosis which has high reproducibility and accuracy**Subjects and Methods:** It was a Case Control study. Fibrosis was assessed by fibroscan and was then quantified. **Results:** In our study there was a significant difference seen among the different grades of fibrosis among controls and cases (p=0.004). The mean fibrosis score too was high among cases (13.498) as compared to controls (6.052). The overall prevalence of NAFLD (F2-F4) was found to be 50% among cases as compared to 14% in controls.**Conclusion:** Diabetes has a significant etiological role in occurrence of NAFLD in population. Fibroscan has a substantial role in screening and diagnosing diabetics for NAFLD and fibrosis, thus advocating its use is recommended to prevent understudied and unrecognized complication of DM preventing mortality and morbidity.

Keywords: NAFLD, Diabetes, Fibroscan,LSM, Fibrosis.

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Introduction

NAFLD is spiking the clinical importance lately, due to increased inclination towards sedentary life style &rising trend of diabetes in our country with huge negligence in understanding the severity of the disease.Diabetics are usually screened for the known complications both macro and microvascular. Majority of the time patients are neglected for liver related complications that manifests as NAFLD,which is the silent complication on rise. NAFLD (Non- alcoholic liver disease) is gamut extending from NAFL (non- alcoholic fatty liver) to NASH (non- alcoholic steato-hepatitis), which has proclivity to evolve to liver cirrhosis, hepatocellular carcinoma (HCC).[1]

Liver biopsy is the gold standard for establishing NAFLD but being an invasive technique it is usually not accepted by patients and related to even complications, hence a non-invasive technique is needed. Transient elastography by Fibroscan is the non-invasive method for assessing liver fibrosis which has high reproducibility and accuracy.[2]

Aim

- To study the occurrence of NAFLD (Non-Alcoholic Fatty Liver Disease) in Type 2 Diabetes Mellitus.

Objectives

- To screen Type 2 Diabetes Mellitus patients for Liver Stiffness Measure (LSM) by Fibroscan.
- To study various correlates of LSM in Type 2 Diabetes Mellitus patients.

Subjects and Methods

This study was conducted in the Department of Internal Medicine, Teerthanker Mahaveer Medical College and Research Centre, Moradabad. Our study is of Case-control type which was done over the span 1 year**.** Fifty cases and Fifty controls were taken from both OPD and IPD setting in TMMC & RC, Moradabad, U.P. Patients were selected on the basis of Inclusion & Exclusion criteria.

Inclusion Criteria

a) **Cases:** Patients aged from ≥18 years up to 70 years with type 2 diabetes who attended OPD and admitted in IPD at Teerthanker Mahaveer Medical College & Research Centre, Moradabad are considered as Cases.
b) **Controls:** Patients aged from ≥18years up to 70 years without diabetes who attended OPD and admitted in IPD at Teerthanker Mahaveer Medical College & Research Centre, Moradabad are considered as Controls.

Exclusion Criteria

a. Subjects who are known case of malignancy,
b. HbsAg Positive (hepatitis B surface antigen) or Anti HCV reactive (antibody against hepatitis C virus),

c. Other causes of fatty liver (eg, consumption of amiodarone and tamoxifen) are excluded,
d. Males who had intake of >20 g and women who had intake of >10 g of alcohol over 24 hours are excluded

Case definition

Cases will be who are known case of diabetes mellitus (taking oral hypoglycemics) or newly diagnosed and newly diagnosed will diagnosed by following criteria:[3]

- Symptoms of diabetes plus random blood glucose concentration ≥11.1 mmol/L (200 mg/dL) or
- Fasting plasma glucose ≥7.0 mmol/L (126 mg/dL) or
- HbA1c ≥ 6.5% or
- 2-h plasma glucose ≥11.1 mmol/L (200 mg/dL) during an oral glucose tolerance test

Methodology

All the subjects, relevant detailed history was obtained along with salient clinical findings according to the pre-designed proforma, FIBROSCAN and laboratory reports of the patients was collected and analyzed. All the cases and controls underwent Fibroscan which is non-invasive method for assessing Liver Fibrosis which is measured in kPa (kilo Pascals) by using suitable probe. Face-to-face interviews from both cases and controls and records. Data which was collected, was entered in Microsoft Excel Word Spreadsheet on regular basis. Data was organized in tabular form. Data was evaluated using SPPS version 18. Significant tests were applied. The difference was considered statistically significant at $p < 0.05$.

Results

The results of our study are enlisted below. The various demographical profile of our subjects is tabulated [Table 1]. The distribution of diabetics and non-diabetics among urban and rural areas. 64% diabetics were residing in urban areas in vicinity of Moradabad and adjacent districts in comparison to 36% cases who were residing in rural areas. Non-Diabetics 52% were residing in rural areas whereas 48% controls were residing in urban areas.

Table 1: Demographic Profile of Subjects

Variables	Sub-groups	Total (n=100)	Percentage (%)
Age (in years)	18-30	14	14
	31-40	22	22
	41-50	30	30
	51-60	21	21
	>60	13	13
	Mean±SD	45.83±12.65	
Gender	Female	49	49
	Male	51	51
Education Qualification	Illiterate	48	48
	Primary	30	30
	High School	15	15
	Graduate	7	7
Marital Status	Unmarried	12	12
	Married	88	88
Religion	Hindu	55	55
	Muslim	45	45
Residence	Rural	44	44
	Urban	56	56

Table 2: Comparison between Cases and Controls among different liver stiffness groups

Variable	Type of case	Fibrosis Grade										P value
		F0		F1		F2		F3		F4		
		Mean	Std. Deviation	Mean	Std. Deviation	Mean	Std. Deviation	Mean	Std. Deviation	Mean	Std. Deviation	
Age	Cases	52.06	9.98	52.00	10.92	50.40	5.90	50.00	10.61	53.87	9.49	<0.001
	Controls	38.30	11.73	43.00	15.97	39.25	14.10	43.50	14.20	39.67	12.66	
BMI	Cases	22.47	2.84	25.68	5.77	23.66	5.05	28.56	6.95	26.61	6.27	0.472
	Controls	23.48	4.22	28.70	3.56	22.05	4.39	25.58	6.77	25.60	5.38	
SGOT	Cases	28.06	13.75	23.00	12.51	22.20	6.94	43.40	20.50	58.09	45.11	0.208
	Controls	32.33	14.98	40.73	27.24	390.25	470.10	44.50	16.98	66.33	26.41	
SGPT	Cases	32.56	19.55	28.56	22.23	24.80	14.31	47.00	25.00	59.69	47.41	0.175
	Controls	38.55	29.45	50.40	53.17	361.00	416.50	43.25	18.03	75.00	74.51	
Hb	Cases	11.88	1.67	11.53	1.89	8.74	2.42	11.14	0.85	11.27	2.86	0.001
	Controls	12.71	2.27	13.32	1.41	10.70	2.41	13.13	1.77	13.77	2.15	
SBP	Cases	122.38	11.51	121.33	14.93	128.00	21.68	149.20	18.79	126.53	19.03	0.459
	Controls	122.18	14.52	128.00	14.97	116.50	13.99	136.00	24.87	133.33	15.28	
DBP	Cases	74.88	7.93	77.11	8.95	80.00	14.14	92.80	12.46	78.53	10.10	0.659
	Controls	76.61	9.96	82.00	9.80	75.00	5.77	84.50	12.69	76.67	11.55	

BMI, body mass index; SGOT, serum glutamate oxaloacetic transaminase; SGPT, serum pyruvate transaminase; Hb,hemoglobin;SBP,systolic blood pressure; DBP,diastolic blood pressure

Our study depicts the distribution of Hemoglobin as mean Hb value among cases was 11.244±2.25 whereas among controls the mean Hb was 12.720±2.19, mean SGOT value among cases was 37.11±30.46 juxtaposed to controls was 64.99±152.51, SGPT mean values among cases was 40.65±33.11 in comparison to controls was 68.33±139.30. Our study also depicts the distribution of cases and controls according to hypertension as following i.e. 74% did not have hypertension out of which 38% were cases and 36% were controls, 26% had hypertension out of which 24% were cases and 28% were controls. [Table 2]

The distribution of duration of DM was as 46% in time span of 6-10 years of duration of DM , 38% in time span of 1-5 years of duration of DM ,16% in time span of >10 years of

duration of DM. The mean duration of DM in our study was 7.52 +/- 4.46 years with no significant variation among different fibrosis grade.

Table 3: Distribution of subjects according to NAFLD on Fibroscan.[4]

Fibrosis Grade (kPa)	Cases (%)	Control (%)	Total (%)	p-value
F0 (0-5.9)	16(32%)	33(66%)	49(49%)	P=0.004
F1 (6-6.9)	9(18%)	6(12%)	15(15%)	
F2 (7-8.6)	5(10%)	4(8%)	9(9%)	
F3 (8.7-10.2)	5(10%)	4(8%)	9(9%)	
F4 (>10.3)	15(30%)	3(6%)	18(18%)	
Mean±SD	13.498±17.18	6.052±2.08	9.775±12.73	

Our study shows us a statistically proven alliance among insulin users with LSM (p-: 0.016). All the cases were using oral anti diabetics drugs but among cases only 24% were using insulin. It was observed that LSM was towards higher side amid insulin users when juxtaposed to non-insulin users.
The distribution of Diabetics as per the quantification of HbA1c levels and the mean HbA1c level among diabetics in our study is 9.51+/- 2.43. It was also seen that there was no significant variance seen among the HbA1c levels and mean score of LSM (p=0.144). Moreover, the mean score did not have significant variation for different fibrosis grades.
There was a significant difference seen among the different grades of fibrosis among controls and cases in our study (p=0.004). Among cases F4 grade of fibrosis was seen in 30% subjects whereas it was seen only in 6% in controls. The mean fibrosis score was high among cases (13.498) as compared to controls (6.052). [Table 3] The grading used for fibrosis was based on the basis used by Wong et al. as mentioned in [Table 3]
Our study depicts the distribution of BMI among cases and controls as follows i.e among diabetics (cases) 40% were quantified as obese, 30% were quantified as normal, 22% were quantified as overweight, 8% were quantified as underweight. Among Non-Diabetics (controls) 48% were quantified as obese, 28% were quantified as normal, 14% were quantified as overweight, 10% were quantified as underweight.
There was no significant difference seen between mean blood fasting glucose levels and different fibrosis groups. The mean duration of fasting blood glucose levels among cases was 160.32 mg/dl with no significant variation among different fibrosis grade.

Discussion

In our study the prevalence of NAFLD was found to be 50% among cases (diabetics) and 22% among controls (non-diabetics). The study place, Moradabad, displayed that the NAFLD was more prevalent among diabetics with statistically significant relationship. In a study by Agarwal AK. et al,[5] 124 participants (74 males & 50 females) with T2DM were assessed, with prevalence of NAFLD being 57.2%.
In our study the mean age of cases having fibrosis was 50.4 years (F2), 50 years (F3) and 53.87 years (F4). In a study done by Tomeno W et al,[6] there were a total of 27 participants who had NAFLD, out of which 12 were males and 15 females, the mean age group of participants having NAFLD in this study was 55.8 ± 14.9 years.

BMI and Fibrosis

In our study 62% cases and 62% controls had higher BMI for their age and height. Our study previewed no significant difference (p=0.472) between BMI and different fibrosis grades among cases and controls. Patients with high BMI and diabetes are the ideal patient to undergo Fibroscan to assess fibrosis.

HbA1c and Fibrosis

It was seen that there was no significant difference seen among the HbA1c levels and mean score of LSM (p=0.144) in our study. Moreover, the mean score did not have significant variation for different fibrosis grades among cases. This can be explained by the concept that LSM which is an irreversible entity and HbA1c which can vary with treatment, so significant relationship is unlikely to be present.

Fibroscan and NAFLD

In our study there was a significant difference seen among the different grades of fibrosis among controls and cases (p=0.004). Among cases F4 grade of fibrosis was seen in 30% subjects whereas it was seen only in 6% in controls. The mean fibrosis score too was high among cases (13.498) as compared to controls (6.052). The overall prevalence of NAFLD (F2-F4) was found to be 50% among cases as compared to 14% in controls. This result concluded that diabetes plays a pivotal role in occurrence of NAFLD. In usual clinical practice fibrosis LSM 7-9kpa is used as grading for NAFLD which amounted to our group F2 and F3, which amounts to 20% of the diabetic group. Fibroscan being a non-invasive and user-friendly tool, clinicians should use it for liver stiffness assessment in diabetics patients for recognizing the evil effect of DM on liver. It is well known that insulin resistance induces ED (endothelial dysfunction) in liver which progresses to state of pro-fibrogenic, pro-inflammatory and pro-thrombotic environment impairing the liver repair, progressing to steatosis and further to steatohepatitis and cirrhosis.

Insulin and Fibrosis

Relation between Insulin and Fibrosis in our Study pictures a statistically proven alliance among insulin users with LSM (p-: 0.016). It was observed that LSM was towards higher side among insulin users when juxtaposed to non-insulin users. It is postulated that poor diabetes control which is explained by administration of insulin and not controlled by Oral Anti Diabetics drugs, can lead to progression to NAFLD and even advanced fibrosis.

Conclusion

We included the two categories of patients that were diabetics and non-diabetics. They were evaluated and underwent the routine investigations, BMI measurements.

The both clusters underwent Fibroscan. There data was collected and tabulated and was analyzed. We then compared our study with various other studies who also studied on the prevalence of NAFLD in Diabetics using various other techniques.

Diabetes has a significant etiological role in occurrence of NAFLD in population. Fibroscan has a substantial role in screening and diagnosing diabetics for NAFLD, therefore advocating its use is recommended to prevent understudied and unrecognized complication of DM preventing mortality and morbidity, by the physicians.

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