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ORIGINAL RESEARCH

Study of correlation of non-alcoholic fatty liver disease (NAFLD) with micro and macrovascular complications of type 2 diabetes mellitus (T2DM)

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Abstract

Introduction: Non-alcoholic fatty liver disease is characterised as a common liver disorder that is very strongly associated with insulin resistance and type-2 diabetes mellitus. The aim of this study is to assess the association between NAFLD and micro- and macrovascular complications of diabetes.

Materials and Methodology: 100 patients with ultrasound evidence of NAFLD were ascertained to group - 1 and another comparative group of 100 patients (group - 2) were randomly selected from patients with normal liver ultrasound. Each patient's baseline demographic data, age, sex, location, and duration of diabetes, history of previous illness, medication they were currently taking as well as anthropometric measurements including height and weight were recorded. Body mass index (BMI) was calculated.

Results: The study comprised of 100 patients observed with type – 2 diabetes and the average age of the study participants was 58.09 ±6.1 years. When comparing the gender orientation, 43 (43%) of study participants are reported as males and the remaining 57 (57%) were females. Out of the total 100 participants, sixty nine patients were diagnosed with fatty liver disease and the remaining thirty one were not reported with fatty liver when screened through ultrasonography. The mean age of the all the study participants were 55.75 ± 6.09 and 54.56 ± 5.52 and the duration of diabetes was seemed to be relatively longer in patients with NAFLD. (11.86 ± 4.09, $p<0.0001$).

Conclusion: NAFLD should be included in future preventive public health initiatives, and the affected individuals should be motivated to adapt a healthier lifestyle.

Keywords: NAFLD, type-2 diabetes, insulin resistance

Introduction

Non-Alcoholic Fatty Liver Disease (NAFLD) is a common liver disorder that is strongly associated with insulin resistance and Type 2 Diabetes Mellitus (T2DM).[1]Definition of Nonalcoholic Fatty Liver Disease NAFLD is defined as hepatic steatosis diagnosed either by histology/imaging with macro vesicular steatosis in >5% of hepatocytes according to histological analysis or by proton density fat fraction or >5.6% as assessed by proton magnetic resonance spectroscopy (MRS) or quantitative fat/water selective magnetic resonance imaging (MRI) with no secondary cause for steatosis.[2]Type 2 diabetes mellitus (T2DM) and NAFLD share insulin resistance as a common pathophysiological mechanism, and each of these two diseases affects the development of the other. Recent studies have

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suggested that NAFLD is often present as a comorbidity in T2DM patients. The mutual interrelationship between these conditions is shown by findings suggesting that T2DM can exacerbate NAFLD by promoting progression to non-alcoholic hepatosteatosis or fibrosis, while NAFLD causes the natural course of diabetic complications to worsen in T2DM patients. It remains unknown whether one disease is the cause of the other or vice versa.[3]

Obesity and physical inactivity are interlinked risk factors for the development of diabetes and both are clearly implicated in an individual's risk of developing NAFLD. Obesity is well known to correlate with both NAFLD prevalence and severity. In a study of patients who had liver biopsies while undergoing elective abdominal surgery, the BMI was strongly correlated with NASH[7]and in a separate study intra-abdominal fat was associated with non-alcoholic steatohepatitis (NASH).[4]

The prevalence is reported higher among patients with diabetes mellitus and obesity ranging from 35% to 75% in various studies. The prevalence of NAFLD is on rise in Asian countries which may be attributed to the improvement of life style, the change of dietetic structure and the application of new diagnostic techniques.[5] Some patients with NAFLD develop necro-inflammatory changes in the liver called Non Alcoholic Steatohepatitis (NASH) and a fraction of those will develop cirrhosis, This progressive fibrotic disease can progress to end stage liver disease.[6]

This study was conducted to know the frequency of NAFLD in type 2 diabetic patients and to see whether the presence and severity of NAFLD are related to diabetic metabolic status and to the occurrence of chronic micro and macrovascular degenerative complications. Currently, there is a lack of information on association between NAFLD and macro vascular complications in Indian scenario. Hence the aim of this study is to assess the association between NAFLD and micro- and macrovascular complications of diabetes.

Materials and methodology

100 patients with ultrasound evidence of NAFLD were ascertained to group - 1 and another comparative group of 100 patients (group - 2) were randomly selected from patients with normal liver ultrasound. Sample size was promptly determined by the formula n=4pq/e2. The study subjects were from age and duration matched diabetes group. This study is prospective observational study. This study elapsed for 6 months starting from September 2022 to March 2023. Data were collected from RIMS teaching hospital and informed consent was obtained from all the patients who had agreed and showed their willingness to participate in the study.

Certain inclusion criteria were followed in the study that included all the patients with clinically diagnosed type 2 DM combined with NAFLD will be enrolled for the present study. There are certain exclusion criteria also being followed in the study where in those patients giving a history of alcohol abuse, hepatitis or other liver diseases, obesity-related intestinal surgery, rapid weight loss in the obese and patients who are on hepato-toxic medication.

Each patient’s baseline demographic data, age, sex, location, and duration of diabetes, history of previous illness, medication they were currently taking as well as anthropometric measurements including height and weight was recorded. Body mass index(BMI) was calculated . Blood pressure was measured with a standard cuff sphygmomanometer in a seated position after a minimum rest period of 5 min and patient is considered hypertensive if systolic blood pressure reading≥140mmHg or diastolic blood pressure reading ≥90 mmHg in more than three occasions or if patients were receiving antihypertensive drug therapy.

Diagnosis of diabetes is made if the fasting plasma glucose is ≥126mg/dl or a non-fasting glucose>200mg/dl or a self-reported physician diagnosis or on treatment for diabetes.

Ultrasound imaging of the liver is done to diagnose NAFLD. Hepatic ultrasonography scanning is performed for all participants by a single experienced radiologist to avoid inter-

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observer variation, who will be blinded to subject's details. Hepatic steatosis is diagnosed by characteristic hyperechogenicity of liver relative to kidneys, ultrasound beam attenuation and poor visualization of intrahepatic structures.[7,8] Ultrasonography has a sensitivity of 89% and a specificity of 93% in detecting moderate-to-severe hepatic steatosis.[9]

Results

The study comprised of 100 patients observed with type – 2 diabetes and the average age of the study participants was 58.09 ±6.1 years. When comparing the gender orientation, 43 (43%) of study participants are reported as males and the remaining 57 (57%) were females. Out of the total 100 participants, sixty nine patients were diagnosed with fatty liver disease and the remaining thirty one were not reported with fatty liver when screened through ultrasonsography.

The mean age of the all the study participants were 55.75±6.09 and 54.56±5.52 and the duration of diabetes was seemed to be relatively longer in patients with NAFLD. (11.86±4.09, p<0.0001)

Table – 1 revealed the BMI, systolic & diastolic blood pressure between the two groups. BMI reported as 26.99±1.82 in group – 1 and 23.02±2.71. HbA1c was relatively higher in group-1 when compared with group – 2. Higher triglycerides were reported in group – 1 than group – 2. Total cholesterol and low HDL levels were relatively low between two groups.

Table – 2 summarised the multiple regression analysis. BMI (1.68, 95% CI-1.19-2.23). HbA1c showcased HbA1c levels on odds ratio 14.51, 9% CI - 3.07 '- 69.15, Triglycerides (OR=1.07, 1.04 – 1.13)

Table - 1: Details of demographic, hemodynamic and biochemical details of the study groups

Parameters	Group – 1	Group – 2	P - value
Age (years)	55.75±6.09	54.56±5.52	0.2612
Diabetes duration (years)	11.86 ± 4.09	7.23 ± 2.09	<0.0001
Waist circumference (cms)	93.71 ± 6.71	83.22 ± 5.07	<0.0001
BMI (Kg/m^2)	27.04± 1.82	23.03 ± 2.68	<0.0001
Systolic (mmHg)	147.62 ± 12.47	133.08 ± 9.11	<0.0001
Diastolic (mmHg)	92.09 ± 8.89	79.58 ± 6.81	<0.0001
HbA1c (%)	7.91 ± 0.61	6.75 ± 0.29	<0.0001
Triglycerides (mg/dL)	177.48 ± 18.97	140.53 ± 18.69	<0.0001
Total cholesterol (mg/dL)	255.32 ± 31.86	172.31 ± 36.79	<0.0001
HDL (mg/dL)	37.13 ± 5.82	45.62 ± 5.73	<0.0001
LDL (mg/dL)	111.73 ± 9.92	108.66 ± 7.37	0.0648

Table - 2: Results of multiple logistic regression analysis

Parameters	Odds ratio (OR)	95% confidence levels	P - value
BMI	1.68	1.19 – 2.23	0.003
HbA1c	14.51	3.07 - 69.15	0.001
CAD	5.19	1.04 – 26.02	0.049
Triglycerides	1.07	1.04 – 1.13	0.001

Discussion

Non Alcoholic Fatty Liver Disease (NAFLD) is more frequently been noticed in type 2 diabetic patients and is meticulously now an important public health concern. Prevalence reports on NAFLD are widespread and similar statistics available on the association of NAFLD with diabetic micro- and macrovascular complications across Indian subcontinent.[6]

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Therefore this study had been revealed that the prevalence of NAFLD among the male hospitalized T2DM patients was 51.2% whereas in female patients (48.8%), but without any pronounced statistical significance. The average age of the patients was 55.15 ± 5.8 years (Ranging from 35 to 72). *Targher* et al reported that the prevalence of NAFLD gradually increased with age (i.e., 65.4% among participants aged 40-59 years and 74.6% among those aged ≥ 60 years; P<0.001).[10]*Duvnjak* et al in their study reported that the highest prevalence of NAFLD occurs in those aged between 40-60 years.[11]In our study, it has been revealed that prevalence rates of NAFLD increased significantly with the prolonged duration of diabetes. *Banerjee* et al researched and found that a longer duration of T2DM was significantly associated with NAFLD.[12]

NAFLD is an integral part of the metabolic syndrome which constituted a cluster of abnormalities such as dysglycemia, dyslipidemia, hypertension and obesity with insulin resistance as a major central pathogenic factor.[6].It has been reported in other studies[13, 14and] our study also reiterated and revealed high systolic and diastolic blood pressure in patients with NAFLD. Also it has been demonstrated that insulin resistance could possibly lead to higher free fatty acid load to the liver, consequently higher triglyceride synthesis and increased secretion of triglyceride from the liver. Moreover, the hypertriglyceridemia have been strongly in conjunction with liver fat accumulation.[1]Our study revealed that increased triglyceride levels (Mean ± SD, 177.48 ± 18.97) in diabetic fatty liver group as compared to non-fatty liver group (Mean ± SD, 140.53 ± 18.69) and the results were statistically significant (P value<0.0001). Additionally, the authors also found that HbA1c levels in fatty liver disease group were higher than non-fatty liver group, which confirmed the obvious dysglycemia in these patients (P value<0.0001). Diabetes mellitus and obesity may lead to increased liver fibrosis through different mechanism, the effect of these two conditions may be additive when they both exist in the same individual.[1]

Like in various other literatures, our results also stated that obesity, hyperglycemia and hyperlipidemia had an association with NAFLD. The prevalence of obesity as indicated by high BMI and waist circumference was significantly higher among subjects with NAFLD in our study. In a recent report, the prevalence of most of the cardio-metabolic risk factors was significantly higher in NAFLD subjects.[15]In a hospital-based study from North India, it was shown that 20% of NAFLD patients were overweight and 68% had obesity. Abnormal cholesterol, triglycerides, and HDL-cholesterol were present in 36%, 53%, and 66%, respectively in this study.[16] The above abnormalities were also seen in our study which was found to be statistically significant (P <0.0001).

Conclusion

The prevalence of obesity, hypertension and dyslipidemia were significantly higher in subjects with NAFLD compared to participants without NAFLD. Also the hepatic fat content could also be reversed based on the lifestyle changes and drugs administered. NAFLD should be included in future preventive public health initiatives, and the affected individuals should be motivated to adopt a healthier lifestyle.

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