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Prevalence of Non-Alcoholic Fatty Liver Disease and Its Correlation with Coronary Risk Factors in Patients with Type 2 DM

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ABSTRACT

Background: *Type 2 diabetics appear to be at greater risk of Non-alcoholic Fatty Liver Disease (NAFLD) and certainly of fibrosis and cirrhosis development. Type 2 diabetes and NAFLD are more common than previously thought, especially in India. To find out if there is a connection between NAFLD and Cardiovascular Disease (CVD) in a large group of type 2 diabetics, the current study was designed.* ***Aim:*** *1) To study the prevalence of NAFLD by USG in patients with type 2 diabetes mellitus. 2) To correlate NAFLD with coronary artery disease and coronary risk factors in patients with type 2 diabetes mellitus.* ***Methods:*** *This was an observational, cross-sectional, open-labeled, single-centric, parallel-design study conducted in the department of general medicine of a tertiary care hospital among patients with type 2 Diabetes Mellitus (DM).* ***Results****: Among the 120 patients that took part in the study, there were 69 NAFLD patients and 51 non-NAFLD patients. Individuals with NAFLD had a significantly longer mean diabetes duration. In the NAFLD group, the prevalence of hypertension, obesity, visceral obesity, and metabolic syndrome was greater. The NAFLD group had much worse glycemic control. Sr. HDL and Sr. Triglyceride levels were found to be greater in the NAFLD group, whereas Sr. LDL levels were found to be higher in the non-NAFLD group, and Total cholesterol levels were practically comparable in both groups. ALT and AST values were higher in NAFLD patients than in non-NAFLD patients.* ***Conclusion:*** *The prevalence of NAFLD increases dramatically in the presence of type 2 diabetes, with the majority of patients affected in the fourth decade of life. Obesity, hypertension, and dyslipidemia were considerably more prevalent with NAFLD compared to subjects without NAFLD.*

Keywords:: Non-Alcoholic Fatty Liver Disease (NAFLD), Diabetes, Hypertension, Obesity, Dyslipidemia

INTRODUCTION

Nonalcoholic fatty liver disease (NAFLD) is a group of disorders characterized histologically by macrovesicular hepatic steatosis that affects people who do not consume alcohol in proportions that are typically thought to be damaging to the liver [1]. The prevalence of NAFLD in the general population has been reported to be in the 15%-30% range in many countries, and it is virtually certainly growing [2-4]. It is frequently linked to obesity, type 2

diabetes, dyslipidemia, and insulin resistance, all of which are components of the metabolic syndrome, lending credence to the idea that NAFLD is the hepatic manifestation of the syndrome [5-8].

People with type 2 diabetes appear to have an increased likelihood of acquiring NAFLD and certainly a higher risk of developing fibrosis and cirrhosis when compared to nondiabetic patients [5-8]. Recent studies further suggest that the presence of NAFLD in type 2 diabetes may be associated with an elevated risk of Cardiovascular Disease (CVD) independent of metabolic syndrome components [9,10]. However, if these findings are right, they suggest that detecting NAFLD in type 2 diabetes may aid in CVD risk prediction, with substantial therapeutic implications. As a result, identifying those with NAFLD would also identify a subset of diabetic patients who should be addressed with more extensive medication to reduce their risk of future CVD events. The "exact" prevalence of NAFLD in type 2 diabetes is uncertain, particularly in India. As a result, the current study was designed to investigate the prevalence of NAFLD and whether there is a link between NAFLD and CVD in a large cohort of type 2 diabetic people.

METHOD

The current study was an observational, cross-sectional, open-labeled, single-centric, parallel-design study conducted in the department of general medicine of a tertiary care hospital after approval from the institutional ethics council. In this study, 120 type 2 diabetes mellitus patients admitted to a medical care unit or attending a diabetic OPD who were non-alcoholic, had no viral or autoimmune hepatitis serological markers, and had no evidence of genetic/metabolic liver disease were enrolled at random. In all recruited patients, a meticulously detailed history was collected, with special emphasis paid to alcohol consumption, and an abdominal ultrasound was conducted.

The study group was divided into 2 subgroups:

- NAFLD- Patients with USG evidence of fatty changes in the liver.
- Non-NAFLD- Patients without any USG evidence of fatty changes in the liver.

RESULTS

There were 69 NAFLD patients and 51 non-NAFLD individuals among the 120 patients participating in the study. The prevalence of NAFLD was highest in the fourth decade of life, followed by the fifth decade. Male predominance was seen in our study sample, with 58.23% incidence among NAFLD patients, however, this was not statistically significant (p=1.0) among patients in either category (Table 1).

Table 1 Baseline demographic characteristics (n=120) (p-value < 0.05 considered statistically significant)

Age-wise distribution			
Age (years)	**NAFLD**	**Non-NAFLD**	
31-40	13	13	
41-50	21	18	
51-60	19	18	
61-70	16	2	
Gender wise distribution			
Gender	**NAFLD**	**Non-NAFLD**	**p-value**
Male	42	30	1
Female	27	21	

Individuals with NAFLD had a considerably longer mean duration of diabetes than those without (p<0.001). There was no significant difference in the number of smokers between the NAFLD and non-NAFLD groups (p=0.88), but the prevalence of hypertension (81.15% *vs* 49.01% ; p<0.001), obesity (BMI>25 kg/m^2) (60.86% *vs* 37.25%; p<0.001), metabolic syndrome (73.91% *vs* 27.45%; p<0.001). Poor glycemic control, as measured by HbA1c levels, was substantially greater in the NAFLD group than in the non-NAFLD group (p=0.035) (Table 2).

Table 2 Comparison of features (p-value<0.05 considered statistically significant)

Features	NAFLD (n=69)	Non-NAFLD (n=51)	p-value
Duration of DM (years)	7.96 ± 2.212	4.67 ± 1.352	<0.001
Presence of Clinical features (n)	58	51	0.008
Smoking	60	43	0.88
Hypertension	56	25	<0.001
BMI >25 kg/m²	42	19	<0.001
Metabolic Syndrome	51	14	<0.001
HbA1c (>7%)	43	21	0.035
LDL cholesterol >160 mg/dl	25	29	0.03
HDL (<50 mg/dl in females and <40 mg/dl in males)	47	14	<0.001
Total cholesterol >200 mg/dl	26	21	0.84
Triglyceride >150 mg/dl	48	15	<0.001
ALT (> 50 IU/l in males and >35 IU/l in females)	12	2	0.04
AST (>40 IU/l)	11	0	0.008

Sr. HDL (40 mg in men and less than 50 mg in females) was observed to be higher in the NAFLD group (68.11% vs.27.45%; p=0.001). Similarly, Sr. Triglyceride >150 mg/dl was found to be higher in NAFLD (69.56% *vs* 29.41% p<0.001), but S. LDL >160 mg/dl was found to be higher in the NAFLD group (36.23% *vs* 56.86%; p=0.03), and Total cholesterol >200 mg/dl was found to be almost identical in both groups (42.6% *vs* 41.12%; p=0.84). 17.39% of NAFLD patients had elevated ALT levels (>50 U/l in males and >35 U/l in females), whereas 3% of non-NAFLD patients had elevated ALT levels (p=0.004). Similarly, 15.94% of NAFLD patients and none of the non-NAFLD patients had increased AST levels (>40 IU/l) (p=0.008) (Table 2).

DISCUSSION

In our study, 69 of 120 type 2 DM patients attending Diabetic Clinic had NAFLD, indicating that the prevalence of NAFLD was 57.5%. This is in line to studies conducted by Agarwal A. K., et al and Targher, Gioanni et al, which found NAFLD in 57.2% and 69.5% of type 2 DM patients, respectively. In general, 70%-75% of type 2 diabetic people may have some degree of NAFLD [11-13]. The prevalence was observed to be almost in the same range in studies undertaken by Luxmi et al, Mohan, V. et al and Kalra, Sanjay, et al [14-16]. In addition, studies have found that, when compared to nondiabetic subjects, people with type 2 diabetes tend to have a higher risk of acquiring NAFLD and, without a doubt, a higher risk of developing fibrosis and cirrhosis [17-21].

The majority of patients were in their fourth decade of life, with a male predominance. According to Targher, Gioanni et al, the prevalence of NAFLD increases with age and males predominate, with 71.1% and 68% with type 2 DM having NAFLD. Amarapurkar, Deepak, et al found comparable findings to ours, with peak incidence in the fourth to sixth decade and male preponderance. It is proposed that circulating oestrogen levels within a physiological

range may be responsible for a "protective" effect on the development of steatosis (owing to both NAFLD and, presumably, HCV genotype 1) [22].

The majority of NAFLD patients, 58 out of 69, or 84.05%, were asymptomatic, whereas some experienced symptoms such as fatigue, malaise, fullness of the abdomen, and right upper quadrant pain. Newton J, L and Bogdanova, Katerina, et al also showed that the majority of individuals with NAFLD do not present with symptoms directly related to their underlying liver disease [23-24].

The mean duration of DM was longer in those with NAFLD (7.96 years ± 2.21 years) than in those without NAFLD (4.67 years ± 1.35 years); $p<0.001$, which was similar to studies conducted by Targher, Gioanni, et al and Merat, Shahin, et al [21]. In his study, Chan, WahKheong, et al showed that NAFLD was not linked with length of DM but was associated with inadequate blood sugar control as evidenced by HbA1c level of 7.0% [25]. Also, the majority of NAFLD patients (56 out of 69; 81.15%) had hypertension, but the non-NAFLD patients (25 out of 51; 49.01 %) did not; p 0.001. Hypertension, a cardiac risk factor, was therefore common in NAFLD patients. Patients with NAFLD were more likely than those without the disease to have hypertension, according to a study by Agarwal A. K and colleagues. Kalra, Sanjay, et al. found that hypertension affected 64.4% of NAFLD patients and 55.5% of non-NAFLD patients [11,16]. Study by Vijay et al found that hypertension was more common in NAFLD patients (64.7%) than in non-NAFLD patients (40.8%) [26]. However, there was no significant difference in the number of smokers between NAFLD (13.04 %) and non-NAFLD type 2 DM (15.68 %) patients, which was similar to a study conducted by Chavez-Tapia, Norberto C., et al, but Agarwal A. K., et al reported 18.3 % of patients with type 2 DM with NAFLD were smokers and 7.5 % of patients with type 2 DM [11,27].

Glycemic control, as evaluated by HbA1c levels, was poorer in patients with NAFLD, with a mean HbA1c level of 7.15% ± 0.83% compared to patients without NAFLD, who had a mean HbA1c level of 6.70% ± 0.93%. The proportion of NAFLD patients with HbA1c values over 7 % (a sign of poor glycemic control) was 62.31%, compared to 41.17% of all patients ($p=0.035$). Many other studies have found that the mean HbA1c level in people with NAFLD is greater than in those without NAFLD. These findings were published by Agarwal A. K., et al, Targher, Gioanni et al, Juneja, Archana et al and Viswanathan, Vijay, et al [11,26,28]. NAFLD patients exhibited greater Triglyceride and lower HDL levels in our study, which was similar to studies conducted by Agarwal A. K, et al, Targher, Gioanni et al and Lv, Wen-Shan, et al. An investigation by Kalra, Sanjay and colleagues found that dyslipidemia was more common in the NAFLD group (59.6%) than in the non-NAFLD group (43.3%) [11,12,16,29].

The mean AST in the NAFLD group (40.77 IU/L ± 9.12 IU/L) was greater than in the non-NAFLD group (33.75 IU/L ± 6.25 IU/L), and the mean ALT in the NAFLD group (40.0 IU/L ± 9.12 IU/L) was higher than in the non-NAFLD group (33.75 IU/L ± 6.25 IU/L). Agarwal A. K. et al found that the mean AST in the NAFLD group (28.41 IU/L ± 1.4 IU/L) was greater than in the non-NAFLD group (22.8 IU/L ± 9.7 IU/L), and the mean ALT in the NAFLD group (35.2 IU/L ± 17.9 IU/L) was higher than in the non-NAFLD group (22.79.7 IU/L). This was very same to the study conducted by Viswanathan, Vijay et al, where the mean AST in the NAFLD group (37.624.9 IU/l) was greater than in the non-NAFLD group (27.617.6 IU/l), and the mean ALT in the NAFLD group (29.31 IU/L ± 17.9 IU/l) was higher than in the non-NAFLD group (22.4 ± 15.4) [26].

The Adult Treatment Panel III (ATP III) criteria was used to diagnose Metabolic Syndrome. According to the study, 51 out of 69 patients, or 73.91 % of those with NAFLD, had Metabolic Syndrome, while only 14 out of 51 patients, or 27.45 % of those without NAFLD, had Metabolic Syndrome. As a result, the prevalence of Metabolic Syndrome was considerably greater in the NAFLD type 2 DM group compared to the non-NAFLD type 2 DM group. There is a strong link between NAFLD and metabolic syndrome, with the prevalence of the condition being twice as high in the NAFLD group as in the controls. This study found that patients with ultrasound evidence of fatty liver had a higher prevalence of metabolic syndrome risk factors than controls. NAFLD is correctly referred to as the hepatic

component of metabolic syndrome. According to a study conducted by Agarwal A. K., et al, Targher, Gioanni et al, and Juneja, Archana et al, the prevalence of Metabolic Syndrome was considerably greater in NAFLD patients than in non-NAFLD patients [11,12,28].

There were certain limitations to this study that should be mentioned. Our study's cross-sectional methodology prohibits the discovery of causal or temporal relationships between NAFLD, metabolic syndrome, and coronary risk factors. NAFLD was diagnosed based on ultrasound imaging and the exclusion of other causes of chronic liver disease, however it was not confirmed by a liver biopsy.

CONCLUSION

Our study finds that the prevalence of NAFLD increases dramatically in the presence of type 2 diabetes, reaching 57.5 % in the fourth decade of life and being more common in males. Obesity, hypertension, and dyslipidemia were considerably more prevalent as coronary risk factors in patients with NAFLD compared to subjects without NAFLD.

DECLARATIONS

Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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