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PREVALENCE OF NONALCOHOLIC FATTY LIVER DISEASE AMONG TYPE 2 DIABETIC POPULATION

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ABSTRACT

Objective to study the prevalence of non-alcoholic fatty liver disease (NAFLD) among type-2 Diabetic patients in this part of Andhra Pradesh. All the patients of type-2 diabetes (n=1337) who came to the OP Department were screened. The patients who fulfilled the inclusion and exclusion criteria were subjected to detailed history, physical examination and ultrasound scan of the liver. A total of 1219 patients were enrolled into the study. Hepatic steatosis was detected in 963 patients. The prevalence of NAFLD was 79% among the type-2 diabetic patients and NAFLD was the most common cause (91%) of fatty liver on ultrasound scan. The prevalence of NAFLD was more common in the age group of 40-59 Years. Conclusion: Patients with type-2 diabetes very frequently suffer from NAFLD.

INTRODUCTION

Nonalcoholic fatty liver disease (NAFLD) is emerging as the most common chronic liver condition in India and across the globe in recent years due to increasing prevalence of diabetes, obesity and metabolic syndrome. The histological spectrum of NAFLD ranges from steatosis to steatosis with evidence of hepatocellular inflammation and damage [nonalcoholic steatohepatitis (NASH)]. The prevalence of NAFLD has been reported to be in the 15–30% range in the general population in various countries (1). It is projected that NAFLD will be the leading cause of liver cirrhosis in the near future (2). Non-diabetics seem to have a less risk of acquiring NAFLD when compared to patients with type 2 diabetes. The actual prevalence of NAFLD in type 2 diabetics is not known. The few available studies have small sample size and have been undertaken in highly selected populations (3) (4), which are a poor reflection of the actual status of NAFLD (5).

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This present study was undertaken to determine the prevalence of NAFLD in this part of Andhra Pradesh, India.

METHODS AND MATERIAL

This study was conducted in 1219 outpatients attending the Department of General Medicine in a tertiary care hospital (Gayatri Vidya Parishad hospital) in Vizag for a period of one year between 1st January 2015 and 31st December 2015. Patients were assigned to the type 2 diabetes group if they were previously diagnosed as having diabetes and at some time in their disease, other than a time consistent with “the honeymoon period” were managed with diet and exercise alone or with oral hypoglycemic agents or were noncompliant with their insulin regimen for more than 3 weeks preceding admission. Patients with newly diagnosed diabetes were assigned to the type 2 group if they tested negative for autoimmune antibody or if they had phenotypic features of type 2 diabetes (such as obesity, acanthosis nigricans, or a family history of type 2 diabetes). Based on recent evidence that indicates similar biochemical profiles and physical characteristics, patients with idiopathic type

1diabetes (type 1B) were included in the type 2 diabetes subgroup for purposes of analysis. Patients less than 18 years and those who were not willing to participate in the study were excluded. According to standardized procedure the following information was recorded prospectively: (1) Demographics (2) BMI (3) Diabetes duration (4) Medications (5) Smoking status and alcohol consumption (6) Blood pressure (7) HbA1c (8) Fasting Lipid Profile.

BMI was calculated according to the following standard formula: **BMI =**

(Weight in Kilograms / (Height in Meters x Height in Meters))

Waist circumference was measured in a standing position at the level of the umbilicus. Liver function tests were evaluated on fasting blood samples. Serology for viral hepatitis B and C was performed in all the cases.

According to guidelines from the National Heart, Lung, and Blood Institute (NHLBI) and the American Heart Association (AHA), metabolic syndrome is diagnosed when a patient has at least 3 of the following 5 conditions:

- Fasting glucose ≥100 mg/dL (or receiving drug therapy for hyperglycemia)
- Blood pressure ≥130/85 mm Hg (or receiving drug therapy for hypertension)
- Triglycerides ≥150 mg/dL (or receiving drug therapy for hypertriglyceridemia)
- HDL-C < 40 mg/dL in men or < 50 mg/dL in women (or receiving drug therapy for reduced HDL-C)
- Waist circumference ≥102 cm (40 in) in men or ≥88 cm (35 in) in women; if Asian American, ≥90 cm (35 in) in men or ≥80 cm (32 in) in women

Ultrasound scanning of the liver was done by an experienced radiologist, who had no information of the patient details. The diagnosis of fatty liver was made on the basis of characteristic ultrasound features (5) (6). The echogenicity of the normal liver equals or minimally exceeds that of the renal cortex or spleen. Intrahepatic vessels are sharply demarcated, and posterior aspects of the liver are well depicted (

Figure 1). Fatty liver was diagnosed if liver echogenicity exceeds that of renal cortex and spleen and there was attenuation of the ultrasound wave, loss of definition of the diaphragm, and poor delineation of the intrahepatic architecture. To avoid false-positive interpretations, fatty liver was not considered if only one or two of these criteria were fulfilled.

Figure 1. Normal appearance of the liver at US. The echogenicity of the liver is equal to or slightly greater than that of the renal cortex (rc)

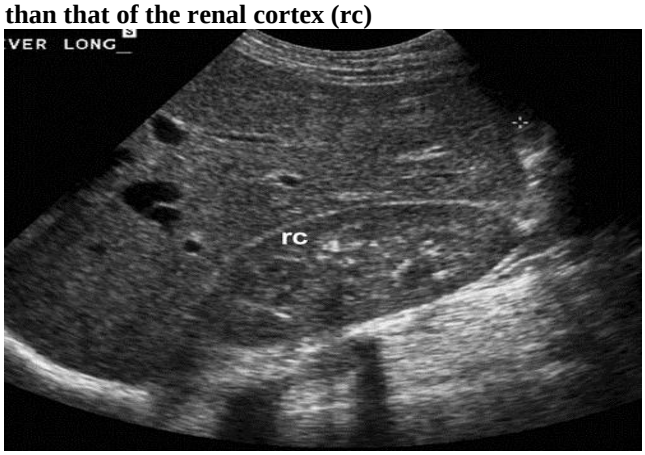
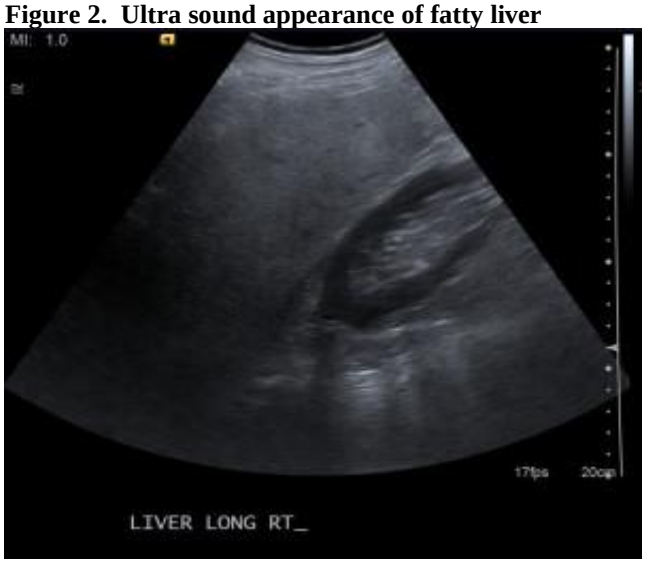


Figure 2. Ultra sound appearance of fatty liver



Statistical analysis

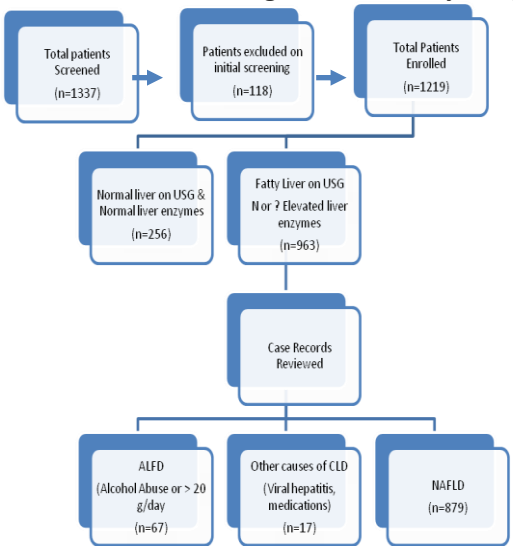
Data are means ± SD or proportions.

RESULTS

From 1st January 2015 to 31st December 2015, a total of 1337 patients were screened for the study. The main reasons for exclusion were that patients were not interested (n=26), type 1 diabetes (n=7), and did not undergo ultrasound examination (n=71) or having acute metabolic complications with or without co-morbid conditions (n=14).

A total of 1219 patients fulfilled the inclusion and exclusion criteria.

Figure 3. Flow Chart showing outline of study design



Of the 1219 patients, 608 (49.87%) were males and 611 females (50.13%).The mean age of patients was 53.2 years. The ages of the patients ranged from 16 years to 80 years with no significant difference between males and females.

Of the 1219 participants, 963 had hepatic steatosis on ultrasound with normal or elevated liver enzymes, whereas 256 had normal liver ultrasound scan as well as normal liver tests.

Among those with hepatic steatosis, 879 patients fulfilled the criteria for diagnosis of NAFLD. The rest 84 patients had other causes of chronic liver disease (alcoholics or who consumed >20g/day, n=67; viral hepatitis, n=7; miscellaneous, n=10). Thus the prevalence of NAFLD was 79%, and NAFLD accounted for the most common cause (91%) of fatty liver on ultrasound.

The prevalence of NAFLD was 54.6% in the age group of 40 –59 years and 65.4% among those aged >60 years; $P < 0.001$). For the purpose of analysis, the study participants were grouped into two according to NAFLD status: Group I – without fatty liver and Group II – with NAFLD (After exclusion of those with other known causes of chronic liver disease, n=84)

The baseline characteristics of the patients of both the groups are presented in Table 1. Individuals with NAFLD had a longer duration of diabetes than those without NAFLD. They also had poor glycemic control (average HbA_1c 7-8) and had higher values of liver transaminases (although 24% had normal serum alanine aminotransferase levels). The prevalence of metabolic syndrome was more in patients with NAFLD. No statistical difference was seen in the prevalence of NAFLD in both the sexes. The incidence of NAFLD is more in patients using insulin, antihypertensive and anti-platelet drugs.

Table 1. Baseline characteristics of the study participants, grouped according to NAFLD status

Variables	Without fatty liver	With NAFLD	p-value
Number of patients	256	879	
Sex (% men)	49	55	<0.001
Age (years)	51 ± 6	55 ± 3	<0.001
BMI (kg/m^2)	25.8 ± 3	28.3 ± 7	<0.001
Diabetes duration (years)	5 ± 3	11 ± 5	<0.001
Oral hypoglycemic users (%)	76	71	0.60
Insulin users (%)	13	29	<0.001
Antihypertensive drug users (%)	59	79	<0.001
Aspirin users	43	54	<0.001
Lipid-lowering drug users (%)	31	35	0.90
Current smokers (%)	29	33	0.7
Systolic blood pressure (mmHg)	132 ± 12	141 ± 13	<0.001
Diastolic blood pressure (mmHg)	85 ± 6	88 ± 15	<0.001
HbA1C (%)	7 ± 1.1	7.8 ± 1.8	<0.37
Triglycerides (mg/dl)	131 ± 14	167 ± 17	<0.001
HDL cholesterol (mg/dl)	45 ± 6	42 ± 7	0.043
LDL cholesterol (mg/dl)	116 = 17	137 = 21	0.30
Creatinine (mg/dl)	0.5 = 0.3	0.7 = 0.4	0.4
Asparate Aminotransferase (units/l)	27=4	31=7	0.05
ALT (units/l)	30 ± 5	35 ± 15	0.45
Elevated ALT (men >50 units/l; women >35 units/l) (%)	0	18	<0.001
ATP III–defined metabolic syndrome (%)	63	77	<0.001

Most of the study patients were non-alcoholics (n = 963, 78.99%). Amongst the alcoholics only 7.1% of patients consumed >20 g/day of alcohol and the rest were taking minimal quantity (alcohol consumption <20 g/day; n=182, 14.93%).

DISCUSSION

NAFLD constitutes an important aspect of disease for patients with type 2 diabetes, but the prevalence of NAFLD in this patient population is currently unknown. A major finding of this study is that the prevalence of NAFLD in type 2 diabetic populations based on history and characteristic sonographic features is very high. Indeed, NAFLD is present in >70% of our study sample and represented the most common cause (91%) of fatty liver on ultrasound examination. In the present study, the prevalence of NAFLD based on abdominal ultrasound examination was 79%. This finding is similar to other studies (5). Prashanth et al found a high prevalence of NAFLD in type 2 diabetics which increased with various components of the metabolic syndrome (8). In a study by Mohan et al the prevalence of NAFLD (54.5%) was significantly higher in patients with diabetes compared to those with pre-diabetes (IGT or IFG) (33%), and normal glucose tolerance (NGT) (22.5%) (9). Gupte et al found that mild, moderate, and severe NAFLD in 65.5%, 12.5%, and 9.35% respectively in asymptomatic type 2 diabetics (10). BMI was significantly higher in patients with NAFLD (28.3±7) than those without NAFLD (25.8±3; p=0.001). Obesity is the most common entity associated with NAFLD that has been reported in other studies (11). There was no difference in HbA1c between the two groups (p=0.67). Although hyperglycemia has been reported in 20-75% of adult patients with NAFLD, we could not find any statistically significant difference in fasting blood sugar levels between the two groups (p=0.37) (11).Further studies may be required with large sample size to prove the presence or absence of any direct relationship between glycemic control and NAFLD. Among lipid parameters, only the mean triglyceride levels and mean HDL levels showed significant correlation with the presence of NAFLD (p=0.043). Mean cholesterol and LDL levels did not show a significant difference between the two groups. NAFLD is very frequently associated with deranged lipid levels. Studies have shown that 20-92% of patients diagnosed with NAFLD have hyperlipidemia including hypertriglyceridemia, hypercholesterolemia or both. In one study, almost 50% of the patients diagnosed with hyperlipidemia had NAFLD on ultrasound evaluations but only hypertriglyceridemia and not hypercholesterolemia, was shown to pose a risk of developing fatty liver disease.

The major limitation of the present study is that the diagnosis of NAFLD was based on ultrasound imaging and exclusion of other causes of chronic liver disease. The diagnosis was not confirmed by liver biopsy.

In clinical practice ultrasonography is the most common way of diagnosing NAFLD and has good sensitivity and specificity in detecting moderate and severe fatty liver (5). Indeed, it has been reported that the presence of >30% fat on liver biopsy is optimal for ultrasound detection of fatty liver, whereas ultrasonography is not totally sensitive, particularly when hepatic fat infiltration is <30% (7). Therefore, the frequency of NAFLD in patients with type 2 diabetes may be an underestimate of NAFLD.

CONCLUSION

The present study shows a greater extent of NAFLD in patients with type 2 diabetes than in the general population. It is important to properly evaluate and treat this condition in all patients with type 2 diabetes as NAFLD is linked with greater risk of liver related pathology in type 2 diabetes patients.

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CONFLICT OF INTEREST:
The authors declare that they have no conflict of interest.

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