Assessment of Liver Disorders in Patients of Type 2 Diabetes Mellitus: A Hospital Based Study

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ABSTRACT

Background: Non-alcoholic steatohepatitis (NASH) is commonly associated with type 2 diabetes mellitus (DM). Prevalence of NASH in type 2 DM has not been well studied and there is an epidemic rise in type 2 DM in Asian and Western populations. Its association with chronic liver disease in the form of NASH makes it an important health problem. Hence, we have studied its prevalence and correlation of biochemical parameters with histological grades of non-alcoholic fatty liver disease (NAFLD) in otherwise asymptomatic type 2 DM patients.

Materials & Methods: One hundred and twenty-five individuals were screened. N=30 individuals were excluded due to history of alcohol intake or liver disease as a result of other causes. N=95 non-alcoholic individuals with type 2 DM underwent abdominal ultrasonography (US abdomen). N=28 patients had evidence of fatty liver on US abdomen, and 16 of these 28 patients underwent liver biopsy.

Results: Out of 125 patients enrolled with the suspicion of Nonalcoholic Fatty Liver Disease (NAFLD) and Non-alcoholic steatohepatitis in patients of Type 2 Diabetes Mellitus, female patients were 70 (56%) and male patients 55 (44%). The prevalence of NAFLD was found to be more in females n=40 than males n=30. N=16 patients were undergone liver biopsy for the suspicion NASH. Out of 22 patients suspected, only 9 patients were found to be having NASH.

Conclusion: We conclude that the prevalence of NASH is high in type 2 DM patients and liver biopsy is the only investigation to differentiate between non-alcoholic fatty liver and steatohepatitis.

Key words: Dyslipidaemia, Liver disorders, Type 2 DM

INTRODUCTION

Type 2 diabetes mellitus (T2DM), insulin resistance (IR), obesity, metabolic syndrome and NAFLD are particularly closely related. Non-alcoholic fatty liver disease (NAFLD) is a chronic liver disease that might affect up to one-third of the adult population in industrialised countries. It is a form of liver disease observed in middle aged patients with abnormal liver biochemical test results and histologic evidence of alcoholic hepatitis but with no history of alcohol abuse.[1] The spectrum of NAFLD includes, simple steatosis without evidence of cell injury, which tends to be stable over time, to steatohepatitis, which progress to cirrhosis.[2] Non-alcoholic fatty liver disease (NAFLD) has become over the last decade the most common form of chronic liver disease in children and adults. It is tightly associated with obesity and threatens to become a serious public health problem. Non-alcoholic liver disease is an important cause of liver disease in India. Epidemiological studies suggest its prevalence in around 9% to 32% of general population, but with a higher prevalence in overweight / obesity and diabetes.[3]

Non-alcoholic fatty liver disease is commonly associated with obesity, type 2 diabetes, dyslipidaemia and insulin resistance – components of the metabolic syndrome. This strongly supports the notion that NAFLD is the hepatic manifestation of metabolic syndrome.[4]

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associated with type 2 diabetes mellitus (DM). Prevalence of NASH in type 2 DM has not been well studied and there is an epidemic rise in type 2 DM in Asian and Western populations. Its association with chronic liver disease in the form of NASH makes it an important health problem. Indian population has a higher body fat content and abdominal adiposity; the latter is particularly associated with insulin resistance and hence NAFLD. Moreover with increasing incidence and prevalence, the perception of NAFLD being a benign condition of little clinical significance is rapidly changing. The overall prevalence of NAFLD in western countries varies from 15-40% and in Asian countries from 9-40%. In India too, NAFLD is emerging as an important cause of liver disease. Epidemiological studies suggest the prevalence of NAFLD to be around 9-32% in general Indian population, with a higher incidence amongst overweight/obese and diabetic/ prediabetic patients. So, this study is conducted to estimate the prevalence of NAFLD as diagnosed by ultrasound examination of liver, in type 2 diabetes. Therefore, these patients can be treated earlier and prevented from going into cirrhosis.

METHODS
This prospective study was designed to enroll known T2DM patients (duration ≥3 years), in age group of 25-65 years, attending outpatient Medicine department of Dept. of General Medicine, KIMS, Bhubaneswar. The study was approved by the ethics committee of the hospital and informed consent was obtained from all the subjects. On the basis of inclusion and exclusion criteria, 125 T2DM patients enrolled over the period of 6 months and underwent complete medical and physical examination at the time of enrollment. The history of medication and alcohol consumption and other relevant details were obtained.

In this study, the study group is 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.
Data (risk factors and lab values) are collected and are compared between the two subgroups, to know the level of difference between them.
NASH will be suspected in a patient who is found to have elevations in liver tests such as alanine aminotransferase (ALT) or aspartate aminotransferase (AST). The only means of proving a confirmatory diagnosis of NASH will be done by liver biopsy. For a liver biopsy, a needle is inserted through the skin to remove a small piece of the liver. NASH will be diagnosed when examination of the tissue with a microscope shows fat along with inflammation and damage to liver cells. If the tissue shows fat without inflammation and damage, simple fatty liver or NAFLD is diagnosed.
We used data of liver enzyme abnormalities to characterize the prevalence, incidence, and risk factors for NAFLD in T2DM patients. The levels of Aspartate aminotransferase (AST) and Alanine aminotransferase (ALT) were measured. The elevation (value above normal) in aminotransferase levels was defined as per NHANES III criteria; corresponding to an AST >37IU/L or ALT >40IU/L for men and AST or ALT >31IU/L in women. The data processing was performed by capturing data into e-Case Report Forms. Data entered was checked by system design for completeness and integrity. Demographic data is presented as descriptive statistics. Sample studied was characterized by relative (%) and absolute (N) frequencies, for each of the qualitative variable.

RESULTS
A total of 125 patients, with more number of female patients 70 (56%) than male patients 55 (44%) were recruited with the suspicion of Nonalcoholic Fatty Liver Disease (NAFLD) and Non-alcoholic steatohepatitis in patients of Type 2 Diabetes Mellitus [Table 1].
Out of 125 patients enrolled in the study, n=70 (55%) T2DM patients (40 female/ 30 male), was identified as having NAFLD, based upon NHANES III criteria as described above. Data of these patients was analyzed further. The prevalence of NAFLD was found to be more in females n=40 than males n=30. Majority of the patients were found in 41-55 years age group followed by 25-40 years and least in 71-85 years age group [Table 1]. In the current study, elevation in AST and ALT levels, based on NHANES III criteria, were employed to estimate and characterize the prevalence of NAFLD in T2DM patients. The combined AST/ALT levels were more raised than AST and ALT alone [Table 2]. These levels were highly raised in patients of NASH confirmed by liver biopsy. Around 16 patients were undergone liver biopsy for the suspicion NASH. Out of 22 patients suspected, only 9 patients were found to be having NASH.

| Table 1: Demographic details of T2DM patients with NAFLD (n=125) |
|-------------------|--------------------|--------------------|--------------------|-------------------|
| Age Group  | Males n=55 | Females n=70 | Total n=125 |
| Non-NAFLD | Non-NAFLD | Non-NAFLD | Non-NAFLD | Non-NAFLD |
| 25-40 | 8 | 7 | 8 | 12 | 16 | 19 |
| 41-55 | 12 | 18 | 16 | 20 | 28 | 38 |
| 56-70 | 3 | 4 | 4 | 4 | 7 | 8 |
| 71-85 | 2 | 1 | 2 | 4 | 4 | 5 |

| Table 2: Prevalence of elevated aminotransferase levels in NAFLD patients |
|-------------------|--------------------|--------------------|
| LFT  | NAFLD Patients | Male | Female |
| Elevated AST  | 19 | 9 | 10 |
| Elevated ALT  | 12 | 5 | 7 |
| Elevated AST & ALT | 39 | 16 | 23 |

DISCUSSION
To best of our knowledge, there are no pan-India population-based studies on prevalence of NAFLD in T2DM population. This is the first cross sectional, multi-center study to report on prevalence of NAFLD in Indian T2DM population. The majority of epidemiological studies on NAFLD in general or in T2DM population in particular, are based on histological evidence of steatosis or fatty infiltration proven by imaging. This study makes the first effort to record the prevalence of NAFLD in T2DM patients on the basis of elevated aminotransferase levels.

In our study, overall prevalence of NAFLD in T2DM Indian population was found to be 96.5%, which is in line with prevalence of 54.5% described by Mohan et al, 10 but higher than the prevalence rate of 12.5%8 and 20% described in other studies. However, in the study by Prashanth et al,
87% T2DM patients had NAFLD on histology. Most of the studies in India have shown higher prevalence of NAFLD in males than in female population (M:F ratio of 2:1 approx.);[7,9,11] but our study revealed higher prevalence rate of disease in female (60%) than in male (54.3%) population, with same pattern reported from north and west part of the country.

CONCLUSION
We conclude that the prevalence of NASH is high in type 2 DM patients and liver biopsy is the only investigation to differentiate between non-alcoholic fatty liver and steatohepatitis.

REFERENCES