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Prevalence of Non-Alcoholic Fatty Liver Disease in Type 2 Diabetic Patients at a Tertiary Health Centre of Eastern India

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Abstract **Original Research Article**

Introduction: Non-alcoholic fatty liver disease (NAFLD) is one of the most common causes of chronic liver disease globally. The prevalence of NAFLD is estimated to be around 9-32% in the Indian population. A higher incidence rate is reported in obese and diabetic patients. Common complications reported with type 2 Diabetes Mellitus includes nephropathy, retinopathy, neuropathy, coronary artery disease, peripheral vascular disease and increased risk of infections however NAFLD is generally overlooked even though chronic liver disease carries significant morbidity and mortality. ***Objective:*** The aim of the study was to determine the prevalence of NAFLD in type 2 diabetic patients visiting Patna Medical College and Hospital for treatment using noninvasive and simple NAFLD Score. ***Method:*** The prospective, observational, cohort study was done in Department of Medicine, Patna Medical College and Hospital, between January 2018 till June 2018. All patients with minimum duration of 3 years of type 2 diabetes mellitus and who presented at our medical OPD for the treatment/follow up on Fridays, between January 2018 to June 2018 were included in the study. The required data was tabulated and analyzed using statistical tool. ***Result:*** A total of 413 patients were included in the study and when categorized using NAFLD score, 52.06% (215 of 413) patients had indeterminate or F3 to F4 grade liver fibrosis whereas 47.96% (198 of 413) patients were categorized into F0-F2 grade of liver fibrosis. ***Conclusion:*** The study highlights the prevalence of NAFLD in T2DM population besides demonstrating associated risk factors in our subset of T2DM patients.

Keywords: NAFLD, NAFLD Score, Type 2 Diabetes Mellitus.

INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is a chronic liver disease which includes histologically as well as clinically different non-alcoholic entities; fatty liver (NAFL, steatosis hepatis) and steatohepatitis (NASH-characterised by hepatocyte ballooning and lobular inflammation ± fibrosis) which has the potential to progress to cirrhosis and rarely even hepatocellular cancer [1,2]. It is one of the most common causes of chronic liver disease in Western world, with an increasing prevalence [3]. In a study, the prevalence was found to vary with ethnicity, ranging from 45% in Hispanics to 33% in whites and 24% in blacks [4]. Another study concluded that the survival of patients with non-alcoholic steatohepatitis (NASH) was decreased and that these patients died significantly more often from CHD and other liver-related problems [5].

NAFLD can occur in association with multiple diseases affecting the liver, however the increase in prevalence of NAFLD is contributed to its pathophysiologic association with type 2 DM (T2DM) and obesity. In a study, the prevalence of NAFLD in obese type 2 diabetic patients has been estimated to be above 70% [6].

The exact pathogenesis of NAFLD is not fully understood, even though insulin resistance appears to be a contributing factor, and obesity is the most common cause of the insulin resistant state. With progressive obesity, alterations in lipid metabolism along with inflammation in adipose tissue and other sites of fat deposition leads to insulin resistance secondary to post-receptor abnormalities in insulin signalling pathways [7]. The increased circulating free fatty acid levels related to diminished suppression of adipose tissue lipolysis by insulin, result in increased delivery of free fatty acids to the liver and hence increased synthesis of excess triglyceride in the liver and deposition of excess liver fat. As observed in euglycemic insulin clamp study, insulin resistance is not only a factor in obesity and diabetes, but also could be an underlying mechanism for NAFLD even in non-obese individuals without diabetes [8].

Several scoring systems like APRI, FIB4, ELF (Enhanced Liver fibrosis), and NAFLD Score have been developed to determine the severity of fibrosis each having their own advantages and shortcomings. NAFLD score is a simple scoring system based on routine laboratory investigations along with the age and BMI of the patient [9]. A Japanese study validated the NAFLD Score and found an acceptable sensitivity, specificity, and positive and negative predictive values for advanced liver fibrosis of 100%, 83%, 63%, and 100%, respectively [10].

The present study was hence undertaken to determine the prevalence of NAFLD in patients with Type 2 DM treated at our hospital based on NAFLD score.

METHODS AND MATERIALS

The prospective, observational, cohort study was done in Department of Medicine, Patna Medical College and Hospital, between January 2018 till June 2018. All patients with minimum duration of 3 years of type 2 diabetes mellitus and who presented at our medical OPD for the treatment/follow up on Fridays, between January 2018 to June 2018 were included in the study. Detailed history and physical examination of the patients were done. The history of alcohol consumption was particularly asked for and those with affirmative reply were excluded from the study as also patients with known CLD and history of chronic viral hepatitis were not included in this study. Routine investigations including Complete Hemogram, Liver Function Test, Glycosylated Haemoglobin, Blood Sugar both Fasting and Post Prandial with drugs, Renal Function Test, Lipid Profile, Urine Analysis were done and based on which the NAFLD Score [9] of the patients were calculated.

The NAFLD Score was calculated by

NAFLD Score = -1.675 + 0.037 × Age (years) + 0.094 × BMI (kg/m^2) + 1.13 × IFG/diabetes (yes = 1, no = 0) + 0.99 × AST/ALT ratio – 0.013 × Platelet (×10^9/L) – 0.66 × Albumin (g/dL).

NAFLD Score Interpretation

The result obtained from the formula is placed in one of three categories

- Scores lower than -1.455 correlate with the absence of significant fibrosis (F0-F2 fibrosis);
- Scores from -1.455 to 0.675 correlate with an indeterminate score;
- Scores greater than 0.675 indicate the presence of significant fibrosis (F3-F4 fibrosis).

Chronic and sustained attacks on the liver during hepatic inflammations lead to the creation of scarring in the form of hepatic fibrosis.

The fibrosis process is a replacement of the damaged cells though the new cells do not maintain the hepatocyte functionality.

Hepatic fibrosis has five stages

- F0 and F1 are indicative of normal liver structure;
- F2 indicates light fibrosis;
- F3 is the stage where the fibrosis becomes severe;
- F4 is indicative of cirrhosis with extended scar tissue

The data of the patients were tabulated and analysed to calculate the prevalence of NAFLD in our subset of Type 2 Diabetes Mellitus patients.

RESULTS

During the study period, 576 patients of type 2 diabetes mellitus who met the inclusion criteria of the study were investigated. Altogether there was a dropout of 163 patients who were lost to follow up or who refused further investigations and hence data of 413 patients were analysed.

Table-1: Age, Sex Distribution and Duration since 1st diagnosed with diabetes

Total number of patients	413
Age Range & Mean Age	29 – 82 years; Mean 43.07±4.08 years
Sex Distribution (M:F)	271 Male, 142 Female (65.62% vs 34.38%)
Duration since 1st diagnosed with T2DM	6.14±2.08 years

Of the total 413 patients, the youngest patient was of 29 years of age and the oldest was 82 years of age with mean age of 43.07±4.08 years. 271 male and 142 female patients formed the study population. The average duration since diagnosis of T2DM was 6.14±2.08 years.

Table-2: NAFLD Score variables in the population

Mean Body Mass Index (in Kg/m^2)	29.16±3.65
Mean Aspartate Transaminase (in U)	59.07±11.04
Mean Alanine Transaminase (in U)	54.43±9.09
Mean Platelet (x10^9/L)	163±21.46
Mean Albumin (in g/dL)	31.03±2.45

The mean body mass index was found to be 29.16±3.65 kg/m^2. The mean BMI of female subgroup was higher when compared with the male counterpart (29.91±4.65 kg/m^2 vs 28.05±2.45 kg/m^2).

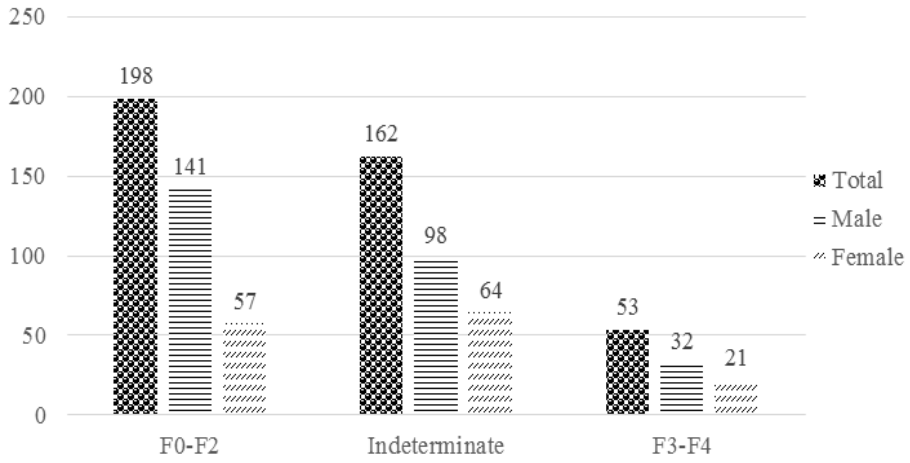

Chart-1: Patient distribution according to NAFLD score

413 patients when categorized using NAFLD score showed that 52.06% (215 of 413) patients had indeterminate or F3 to F4 grade liver fibrosis whereas 47.96% (198 of 413) patients were categorized into F0-F2 grade of liver fibrosis.

Table-3: Sex Ratio, Age and BMI distribution as per NAFLD score category

F0 – F2 Grade	Male Female Ratio	71.21:28.79
	Mean Age	44.05±5.52 years
	Mean BMI	28.34±3.02 Kg/m^2
Indeterminate Grade	Male Female Ratio	60.49:39.51
	Mean Age	41.07±4.56 years
	Mean BMI	30.12±2.01 Kg/m^2
F3 – F4 Grade	Male Female Ratio	60.38:39.62
	Mean Age	46.45±2.03 years
	Mean BMI	31.45±2.78 Kg/m^2

Table-4: NAFLD Score wise mean HbA1c and incidence of dyslipidaemia

	Mean HbA1c	Dyslipidaemia	
		Present	Absent
Grade F0 - F2	7.01±0.12	104	94
Indeterminate Grade	7.42±0.9	97	65
Grade F3 - F4	7.98±0.8	41	12

DISCUSSION

The current study was undertaken to determine the prevalence of NAFLD in patients with type 2 diabetes mellitus being treated at Patna Medical College and Hospital, using simple, non-invasive NAFLD scoring system. The score is based on formula involving the age, BMI and few routine laboratory parameters of the patients, which are easily available throughout. The NAFLD score as validated by other studies is highly sensitivity, specificity, and with positive and negative predictive values [9, 10]. In the present global scenario were diabetes mellitus as emerged as an epidemic, its association with liver dysfunction has been widely studied [11-13]. It is imperative to determine the burden of such association of diabetes and fatty live disease in our society, for better disease management and health care.

The overall prevalence of NAFLD associated with type 2 diabetes mellitus in our study as calculated using the NAFLD score was found to be 52.06% which is in line with prevalence of 54.5% described by Mohan *et al.* [14] and 56.5% as found by Kalra *et al*. [15], but higher than the prevalence rate of 12.5% and 20% described in other studies [16, 17]. The male female ratio of patients found to have indeterminate or F3-F4 grade of liver fibrosis was 60.47:39.53. Several Indian studies have shown similar higher prevalence of NAFLD in males than in female population (M:F ratio of 2:1 approx.) [17-19].

Various studies had concluded that NAFLD is the most common cause of liver disease in the preadolescent and adolescent age group [18, 20, 21], however some studies have also shown that the

prevalence increases with increasing age. In the present study the prevalence of NAFLD was found to be higher in higher age group (Mean age 44.45±2.03 years for F3-F4, 41.07±4.56 years for indeterminate, 42.05±5.52 years for F0-F2 grade).

Association of obesity is an important factor for NAFLD in T2DM patients, and the same was evident in our study. The mean BMI showed an upward trend while comparing it across the NAFLD score grade, emphasizing major role of obesity. According to National Family Health Survey (NFHS-3) India of 2005-06, a greater number of females (13%) than males (9%) in India are overweight/obese [22]. In the present study as well, the percentage of female in Grade F3-F4 of liver fibrosis was highest and the gender specific BMI calculated for the grade was 33.04±2.34 Kg/m^2, thus reiterating the data of NFHS-3 that obesity is more prevalent in females.

The grade of NAFLD associated with T2DM was also found to be higher with higher HbA1c level. 138 patients (64.19%) out of 215 calculated to have NAFLD, were found to be suffering with dyslipidaemia, a finding in line with other studies [15].

All patients diagnosed with NAFLD associated with T2DM were further investigated and managed accordingly.

Conclusion

The study endpoint highlights the prevalence of NAFLD in T2DM population. The important limitation of the study is the follow up of such patients to determine the progression or regress of the disease with drugs and lifestyle modification which was not a part of the objectives, though it underscores the higher prevalence of NAFLD with T2DM which is further confounded by obesity and dyslipidaemia. The study results should sensitize the treating physicians to ascertain the prevalence of NAFLD in their diabetic patients using simple scoring system like NAFLD Score and to initiate prompt treatment.

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