

## Original Research Article

## Detection of Non-Alcoholic Fatty Liver Disease in Patients with Type-2 Diabetes Mellitus

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**Abstract:** **Background:** Non-Alcoholic Fatty Liver Disease (NAFLD) is defined as excessive fat in the liver that is not caused by excessive alcohol consumption. Recent studies have shown that NAFLD can predict the onset of diabetes and vice versa and that one ailment might act as a progression factor for the other. The paper aims to find out the various risk factors associated with developing Non-Alcoholic Fatty Liver Disease (NAFLD) in patients with type 2 Diabetes Mellitus to prevent both hepatic and systemic flares. **Material and Method:** A prospective cross-sectional observational study was conducted around 950 known patients of type 2 Diabetes Mellitus attending the outpatient Diabetes clinics during a period of May 2019 to May 2021 at NIMS Medical College & Hospital. Among them, 150 patients, willing to participate were selected as per inclusion and exclusion criteria. **Results:** A statistically significant difference was observed between the study groups in relation to Total Bilirubin, Direct Bilirubin, Indirect Bilirubin, serum proteins, Albumin, AST, ALT, Alkaline Phosphatase as the p-value calculated to be <0.05. **Conclusions:** The study showed people with high glycemic index have a higher chance of developing the disease. Thus tighter control of blood glucose level is the key to prevention. Obesity, uncontrolled diabetes, deranged lipid profile and abnormal liver enzymes are some of the risk factors for developing NAFLD. Thus screening must include all this risk factors and management strategies should address them separately.

**Keywords:** NAFLD, Diabetes Mellitus, AST, ALT.

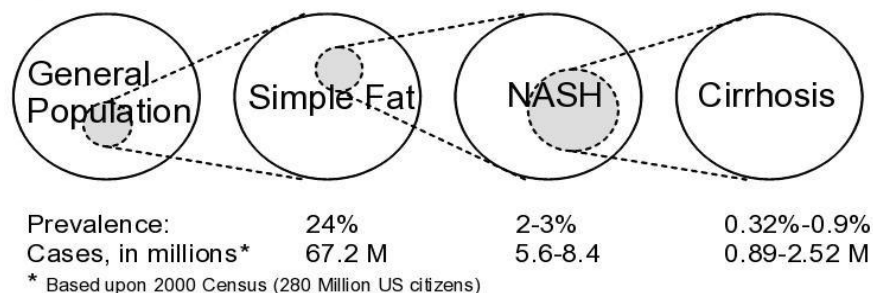
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## INTRODUCTION

Non-Alcoholic Fatty Liver Disease (NAFLD) is defined as excessive fat in the liver (more than 5% of liver weight or more than 5% of hepatocytes affected) that is not caused by excessive alcohol consumption. It is a clinicopathological entity with a broad histological spectrum that begins with basic steatosis to nonalcoholic steatohepatitis (NASH), severe fibrosis, and, in rare cases, cirrhosis [1]. The fraction of hepatocytes harboring fat droplets is used to determine steatosis. A lower limit of 5% of hepatocytes has been

proposed. NAFLD is most common liver diseases, affecting 20-30% of the general population in Western countries, even in this part of the world, detection rates vary from 8.7% to 32% [2].

Insulin resistance, oxidative stress and subsequent lipid peroxidation, pro-inflammatory cytokines, adipokines, and mitochondrial dysfunction have been highlighted in recent investigations and all have a role in the development and progression of NAFLD.



**Figure 1: NAFLD**

Recent studies have shown that NAFLD can predict the onset of diabetes and vice versa and that one ailment might act as a progression factor for the other [3, 4]. Although the connection is most likely due to "common soil," it's also plausible that diabetes interacts with NAFLD via specific pathogenic mechanisms [5]. Though the incidence of abnormal liver enzymes in diabetic patients ranges from 7.2 percent to 22.9 percent, the prevalence of NAFLD in these patients is mainly unclear because it is usually asymptomatic and is not detected by conventional tests. There is, however, a definite link between diabetes and non-alcoholic fatty liver disease (NAFLD).

In this context, future challenges for researchers and clinicians will include raising awareness of the link between diabetes and NAFLD. Thus, the paper aims to find out the various risk factors associated with developing Non-Alcoholic Fatty Liver Disease (NAFLD) in patients with type 2 Diabetes Mellitus to prevent both hepatic and systemic flares.

## MATERIAL AND METHODS

A prospective cross-sectional observational study was conducted around 950 known patients of type 2 Diabetes Mellitus attending the outpatient Diabetes clinics during a period of May 2019 to May 2021 at NIMS Medical College & Hospital. Among them, 150 patients, willing to participate were selected as per inclusion and exclusion criteria.

### Inclusion Criteria

- Diagnosed case of type 2 Diabetes Mellitus according to ADA Guidelines 2011. Fasting Plasma Glucose (FPG) > 126 mg/dl (7mmol/l), or an Oral Glucose Tolerance Test, plasma glucose levels exceeded 200 mg/dl (11.1mmol/l) after 2 hours, or HbA1C > 6.5%.
- BMI of 25kg/m<sup>2</sup> or more.
- Patients without history of alcohol consumption of more than 30mg/day for men and more than 20 mg/day for women.
- Persons with no previous history of jaundice, viral hepatitis or use of hepatotoxic drugs.
- Whose USG suggest features of Fatty Liver Changes.

### Exclusion Criteria

- Prior history of icterus.
- History of alcohol consumption in a quantity more than that mentioned in the inclusion criteria.
- History of use of drugs causing LFT abnormalities (Hepatotoxic drugs).
- Hepatitis B, Hepatitis C and HIV cases.

### Data Collection

A questionnaire containing socio-demographic details as age, gender, duration of diabetes mellitus, anti-diabetic medication intake, history of alcohol use with its duration and quantity were collected from the enrolled participants. The sample population was divided into two independent study groups depending upon USG findings suggestive of Fatty Liver Disease including diabetic patients with NAFLD and without NAFLD.

Anthropometric measurements were taken for their weight, height, BMI, waist circumference, hip circumference and waist-hip ratio.

Blood samples were collected after 10 hours fasting. Fasting plasma glucose (FPG), Post prandial plasma glucose (PPPG) by hexokinase (enzymatic UV) method, HbA1c by affinity chromatography, total bilirubin, direct bilirubin, indirect bilirubin, albumin, globulin, SGOT, SGPT, alkaline phosphate, lipid profile tests were estimated. Ultrasonography was also done by Model-MINDRAY DC-7(High End Digital Colour Doppler Machine with 5Probes).

Informed consent was taken from each of the participants of the study. Ethical approval for conducting the study was obtained from Institutional Ethical Committee. Statistical analysis was performed by using Statistical Software for Social Sciences (SPSS)-17 (© SPSS Inc. Chicago, USA). Continuous data was expressed as mean and standard deviation and analyzed using Student's T Test. Meanwhile, categorical data was expressed as proportions and analyzed using Pearson's Chi Square Test. A P- value less than 0.05 was considered significant at 95% confidence interval.

## RESULTS

Among 150 diabetic patients, we figured out the cases with or without NAFLD, which is shown in the Figure no.2. The result showed that 51 diabetic patients of 50-59 age group did not have NAFLD,

whereas 12 patients of same age group having NAFLD. The mean age group of with NAFLD was  $54.86 \pm 11.89$  years with range 23-78years and that of the patients without NAFLD was  $53.64 \pm 8.65$  years.

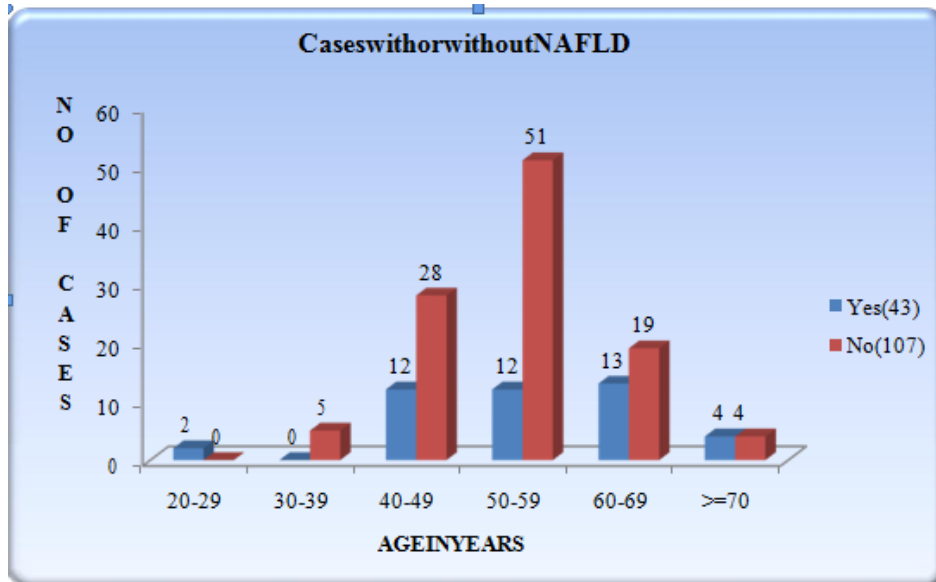


Figure 2: Cases as Per Presence or Absence of Disease

In this study, a statistically significant difference was observed between the study groups in relation to Total Bilirubin, Direct Bilirubin, Indirect

Bilirubin, serum proteins, Albumin, AST, ALT, Alkaline Phosphatase as the p-value calculated to be  $<0.05$  (Table 1).

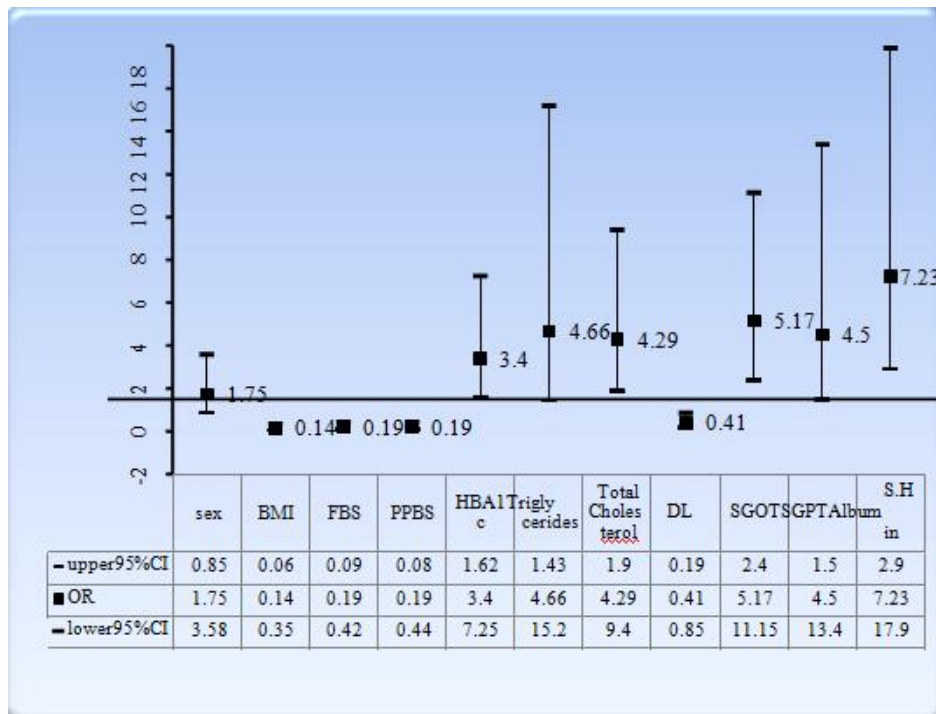


Table 1: Error bar showing unadjusted ODDS RATIO and 95% Confidence Interval of Risk Factors and NAFLD

## DISCUSSION

In our study out of 150 diabetic patients (62 males and 88 females) included in the study 43 have

features of fatty liver and 107 have normal liver profile in ultrasonography. A similar study by Ghobad Abangah *et al.*, showed a male detection of 65.7 % and

a female detection of 34.3% [6]. The overall detection of NAFLD in India is 8.7 to 32% [7]. Cortez-Pinto *H et al.*, showed a detection of 33% [8]. Another study in Japanese population showed that detection of NAFLD increased to 43% in individuals with impaired fasting glucose and 62% in individuals with type 2 diabetes mellitus [9]. The detection in Rajasthan is 24.5 % [2]. The outcome of our study is slightly more at 28.66 % which may be explained on the basis of the fact that the participants were mostly central government employees residing in a local area and hence contributing factors like sedentary lifestyle, central obesity and raised BMI were expected to be more in this population.

#### **NAFLD with Age and Gender**

The mean age (mean  $\pm$  SD) of the patients with NAFLD was 54.86  $\pm$  11.89 years with range 23-78 years and that of the patients without NAFLD was 53.64  $\pm$  8.65 years. There was no significant difference in the mean age of the two groups ( $p > 0.05$ ). Detection in males ( $n = 62$ ) – 51.2 % and that of females is ( $n = 88$ ) – 48.8%. Dhupal *et al.*, showed a similar trend in male and female detection. The mean age of the patients was 49.14 years with male to female ratio of 3:4 [10]. A number of studies in different countries documented that the detection of NAFLD in men was significantly higher than in women [11].

#### **NAFLD and HbA1c Level**

The mean HbA1c level (mean  $\pm$  SD) of study population was 7.47  $\pm$  1.28 % with range of 6.6-11.5 % and the median was 6.8 %. The mean HbA1c level (mean  $\pm$  SD) of patients with NAFLD was 7.93  $\pm$  1.33%, whereas the patients without NAFLD was 7.29  $\pm$  1.217%. The difference in these two groups was statistically significant ( $p < 0.001$ ). Chehrehat *et al.*, showed significant association of NAFLD and HbA1c levels with a P value of 0.012 [12].

#### **NAFLD and BMI**

There was significant association between BMI and NAFLD in our study. Proportion of subjects with BMI  $> 24.9$  was significantly higher in patients with NAFLD than in patients without NAFLD. The mean BMI (mean  $\pm$  SD) of study population was 27.55  $\pm$  2.55 kg/m<sup>2</sup> with range of 24.34 – 38.09 kg/m<sup>2</sup> and a median value of 26.89 kg/m<sup>2</sup>. The mean BMI (mean  $\pm$  SD) of patients with NAFLD was 29.10  $\pm$  2.83 kg/m<sup>2</sup> and that of patients without NAFLD was 26.96  $\pm$  2.14 kg/m<sup>2</sup>. The difference in these two groups was statistically significant ( $p < 0.001$ ), which was supported by the study of Nigam *et al.*, 2013 [13].

#### **NAFLD and Lipid Profile:**

The mean Serum Triglyceride (mean  $\pm$  SD) of patients with NAFLD was 117.00  $\pm$  35.63 mg/dl and that of patients without NAFLD was 100.40  $\pm$  24.63 mg/dl. The difference in these two groups was statistically significant ( $p < 0.01$ ). Abandah *et al.*, and Dhupal *et al.*,

also showed significant association with a P value of 0.05 and  $< 0.011$  respectively [6, 10].

The mean Serum Total Cholesterol (mean  $\pm$  SD) of the patients with NAFLD was 188.07  $\pm$  47.36 mg/dl and that of patients without NAFLD was 165.15  $\pm$  35.75 mg/dl. The difference in these two groups was statistically significant ( $p < 0.001$ ). Odds ratio as per a study by Mohan V *et al.*, of elevated TC ( $> 200$  mg/dl) is 1.45 - 1.8 [14]. However, another study by Ghobad Abandah *et al.*, showed no significant association [6].

#### **NAFLD and Liver Function Tests**

The mean SGOT (mean  $\pm$  SD) of study population was 40.81  $\pm$  10.79 IU/l with range 15 -78 IU/l and a median value of 40.0 IU/l. The mean SGOT (mean  $\pm$  SD) of patients with NAFLD was 43.42  $\pm$  12.06 IU/l and that of patients' without NAFLD was 39.76  $\pm$  10.10 IU/l. The difference in these two groups was statistically significant ( $p < 0.0001$ ). This was supported by a study of Nigam *et al.* in 2013 which showed a significant association of SGOT with NAFLD with a P value of 0.005 [13].

On the other hand, the mean SGPT (mean  $\pm$  SD) of study population was 34.07  $\pm$  9.49 IU/l with range 16 - 67 IU/l and a median value of 33.0 IU/l. The mean SGPT (mean  $\pm$  SD) of patients with NAFLD was 37.77  $\pm$  10.321 IU/l and that of patients without NAFLD was 32.59  $\pm$  8.762 IU/l. The difference in these two groups was statistically significant ( $p < 0.007$ ). As per a study of Mofrad P *et al.*, the entire histologic spectrum of NAFLD can be seen in individuals with normal ALT values [15]. Similar studies showed significant association between SGPT with NAFLD [6, 13, 16].

## **CONCLUSION**

NAFLD is a part of wide spectrum of disease whose end point may progress to cirrhosis of liver to even hepato-cellular carcinoma. Identifying the risk factors of this disease will help in its screening and early detection which in turn will help to prevent more serious complications. The study showed people with high glycemic index have a higher chance of developing the disease. Thus tighter control of blood glucose level is the key to prevention. Obesity, uncontrolled diabetes, deranged lipid profile and abnormal liver enzymes are some of the risk factors for developing NAFLD. Thus screening must include all this risk factors and management strategies should address them separately.

Finally it is strongly recommended to undertake larger scale community based studies involving this particular subset of population with long term follow up for better understanding about the community burden, natural course and risk factors of this disease.



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