Original Research Article

Prevalence of Non-Alcoholic Fatty Liver Disease and Associated Factors among Type 2 Diabetics of Kanchipuram: A Hospital Based Cross-Sectional Study

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Abstract

Background: Non-alcoholic fatty liver disease (NAFLD) was practically unheard of even 30 years ago, but is now considered one of the most common "new-world" phenomenon causing chronic liver disorders in developed and developing countries. A hospital based cross-sectional study was conducted to determine the total prevalence of NAFLD and associated factors in diabetics attending tertiary care hospital in Kanchipuram, Tamil Nadu.

Materials and methods: A hospital based cross-sectional study was done for a period of 1and ½ year from January 2019 to July 2020 on 300 adults aged above 20 years, with history of diabetes more than two years and on medication and no history of alcohol consumption. Examination of patient included general examination and system examination along with recording of vitals like hemoglobin, metabolic parameters like fasting blood sugar, postprandial blood sugar, glycated hemoglobin, routine urine examination, liver enzymes and ultrasonogram of abdomen performed by radiologist were taken. It was analyzed using SPSS version 22.

Results: A total of 300 patients with Type 2 DM attending OPD of tertiary care hospital in Kanchipuram were included in the study. Out of the 300, 160 (53%) were males and 140 (47%) were females. 81 (27%) were without NAFLD and 219 (73%) were with NAFLD according to USG reports. Most of the patients belonged to the age group 45-65 years (63%), 147 (49%) lived in urban area, 123 (41%) were employees, 150 (50%) BMI was from 18-24.9, 78 (26%) were diabetic for 5 years, 138 (46%) were taking metformin for type 2 diabetes. The comparison of lipid profile, liver

enzymes and fasting blood glucose levels with USG report mild, moderate AND severe fatty liver. The results were significant only fasting blood glucose levels (p-0.04).

Conclusion: The results of the present study clearly demonstrate that the prevalence of NAFLD in adults of Kanchipuram have some definite risk factors which leads to increasing burdens to chronic liver disease in Indian population.

Key words

Non-alcoholic Fatty Liver Disease, Type 2 DM, Liver Enzymes, Lipid Profile.

Introduction

Non-alcoholic fatty liver disease (NAFLD) was practically unheard of even 30 years ago, but is now considered one of the most common "new-world" phenomenon causing chronic liver disorders in developed and developing countries [1, 2]. It has been estimated that NAFLD together with the epidemic of obesity, will be a major cause of liver-associated morbidity and mortality by 2030 [3]. NAFLD is defined as the presence of _≥5% of hepatic steatosis (HS), in the absence of competing liver disease etiologies, such as chronic viral hepatitis, use of medications that induce steatosis such as amiodarone or tamoxifen, and other chronic liver diseases, such as autoimmune hepatitis, hemochromatosis, Wilson's disease, or significant alcohol consumption. The U.S. Guideline for NAFLD (endorsed as the American Association for the Study of Liver Diseases, American College of Gastroenterology, and American Gastroenterological Association NAFLD Guideline defines significant alcohol use as current or recent alcohol consumption of >21 drinks/week in men and >14 drinks/ week in women.

According to the results of previous studies in different parts of the world, prevalence of NAFLD is 36.8% in Mediterranean region, 5%–24% in China), 20%–40% in Europe, 9%– 30% in Japan, 16%–32% in Indian urban areas, and 9% in Indian rural areas. The least prevalence rate in Asian countries is 5% in Singapore [4-6]. Prevalence of NAFLD is related to several factors such as age, gender, ethnicity, presence of sleep apnea and endocrine system disorders (e.g., hypothyroidism, hypopituitarism, hypogonadism, and polycystic ovarian syndrome) [7]. It is also strongly associated with obesity, insulin resistance, type 2 diabetes mellitus, and metabolic syndrome [6].

Even though, it has been perceived as a major public health problem of developed and western world, it has emerged as a major public health problem in Asian countries, including India [8] but the exact large-scale prevalence studies are scarce on Indian population. Among the general population, the reported prevalence varied from 9% in rural populations to 32% in urban populations. As per SPRINT study, which was one of the large scales multicentric study from 101 cities across India, the overall prevalence of NAFLD was 56.5% among T2DM patients aged between 25 to 84 years. The prevalence was lowest at 44.1% in western India to as high as 72.4% in northern states [9, 10]. With this background, we conducted a hospital based cross-sectional study to determine the total prevalence of NAFLD and associated factors in diabetics attending tertiary care hospital in Kanchipuram, Tamil Nadu. The results of the study can further help in combining with other studies which can help in policy making by means of reliable methods.

Aim and objectives

- To determine the prevalence of NAFLD among diabetics, attending OPD of tertiary care hospital in Kanchipuram, Tamil Nadu.
- To determine the factors associated with NAFLD in diabetics**.**

Materials and methods

Study Setting: A tertiary care hospital in Kanchipuram, Tamil Nadu.
Study Period: For a period of one and half year from January 2019 to July 2020.
Study Design: A hospital based cross-sectional study.
Source Population: The source for the selection was all type 2 diabetic patients on follow-up treatment at the hospital.
Study Population: The selected type 2 diabetic subjects were considered as the study population

Sample Size Determination: Sample size was not determined initially. Rather, all type 2 diabetic patients on follow-up during the study period were randomly approached and requested for their consent to participate in the study. After their consents were obtained, the patients were evaluated for eligibility to be enrolled into the study. Nearly 500 type 2 diabetic patients gave their consent to participate. However, based on the inclusion criteria we set for analysis of NAFLD, 300 type 2 diabetic patients were eligible for the study.
Sampling Technique: Convenience Sampling.

Inclusion criteria

- Adults aged above 20 years
- Both male and female
- History of diabetes more than two years and on medication and no history of alcohol consumption

Exclusion criteria

- Patients with daily alcohol consumption of >20g or with evidence of acute or chronic viral hepatitis or liver disease due to any other cause were excluded from the study.
- Patients who were on hepatotoxic medications were also excluded.

Data Collection: Permission was obtained from the ethical review board of the hospital prior to study. Informed consent had been obtained from all the participants before getting information from them. Upon recruitment, name, age, sex, BMI, was taken using a proforma. Interviewers checked medication consumed physically. The data were collected by clinical nurses selected from assessing anthropometric measurements among selected type 2 diabetic patients. Data collectors were given training for three days about data collection procedures and research ethics. In addition, the process of data collection was supervised by investigators in rotation.

Examination of patient also included general examination and system examination along with recording of vitals like hemoglobin, metabolic parameters like fasting blood sugar, postprandial blood sugar, lipid profile, routine urine examination, ultrasonogram of abdomen performed by radiologist were taken.

Definitions in study

NAFLD-diagnostic criteria

- Alcohol consumption <20g/d,
- USG Abdomen suggestive of fatty liver.

Diagnostic criteria of diabetes mellitus (ADA guidelines 2011) [11]

- A1C ≥6.5%. The test should be performed in a laboratory using a method that is National Glycohemoglobin Standardization Program(NGSP) certified and standardized to the Diabetes Control and Complications Trial(DCCT) assay.* or
- Fasting plasma glucose FPG ≥126 mg/dl (7.0 mmol/l). Fasting is defined as no caloric intake for at least 8 h.* or
- 2-h plasma glucose ≥200 mg/dl (11.1 mmol/l) during an oral glucose tolerance test (OGTT). The test should be performed as described by the World Health Organization, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.* or
- In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥200 mg/dl

(11.1 mmol/l) Symptoms of diabetes plus RBS >or equal to 200 mg/dl or,

- (*In the absence of unequivocal hyperglycemia, result should be confirmed by repeat testing)

Study variables: The liver status (being without NAFL, being mild NAFL, moderate NAFL, severe NAFL), fasting blood glucose are dependent variable while independent variables were BMI, age, sex, and duration of diabetes. Liver status was considered as outcome variable. Demographic variables like age, gender, BMI, residence occupation, Duration of DM, alcohol consumption, were considered as Primary explanatory variables.

Data Analysis: The collected data was checked for completeness, inconsistency and outliers by looking at their distribution. Incomplete and inconsistent data were excluded from the analysis. It was analysed using SPSS [12] version 22.

Descriptive analysis was carried out by mean and standard deviation for quantitative variables, frequency and proportion for categorical variables.

All Quantitative variables were checked for normal distribution within each category of explanatory variable by using visual inspection of histograms and normality Q-Q plots. Shapiro-wilk test was also conducted to assess normal distribution. Shapiro wilk test p value of >0.05 was considered as normal distribution.

For normally distributed Quantitative parameters the mean values were compared between study groups using ANOVA (>2 groups).

Results

A total of 300 patients with Type 2 DM attending OPD of tertiary care hospital in Kanchipuram were included in the study. Out of the 300, 160 (53%) were males and 140 (47%) were females. Most of the patients belonged to the age group 45-65 years (63%), 147 (49%) lived in urban area, 123 (41%) were employees, 150 (50%) BMI was from 18-24.9, 78 (26%) were diabetic for 5 years, 138 (46%) were taking metformin for type 2 diabetes (**Table - 1**).

Table - 1: Distribution of baseline characteristics study population (N=100).

Parameter	**Summary**
Age group	
< 25 years	9 (3%)
25 - 44 years	54 (18%)
45 - 64 years	189 (63%)
> 65 years	48 (%16)
Gender	
Male	160 (53%)
Female	140 (46%)
Residence	
Rural	120 (40%)
Urban	147 (49%)
Others	33 (11%)
Occupation	
Employee	123 (41%)
Farmer	87 (29%)
Merchant	45 (15%)
Student	21 (7%)
House wife	24 (8%)
BMI (kg/m^2) (mean ± SD)	26.01 ± 4.43
<18	45 (15%)
18 to 24.9	150 (50%)
25 to 29.9	84 (28%)
>=30	21 (7%)
Duration of DM (in years)	
<2	60 (20%)
2 to 5	63 (21%)
5 to 7	78 (26%)
>7	66 (33%)
Drug history	
Metformin	138 (46%)
Other combinations	162 (54%)

Table - 2 results show the comparison of lipid profile, liver enzymes and fasting blood glucose levels with USG report of mild, moderate, severe fatty liver, the results were significant only fasting blood glucose levels (p-0.04).

Table – 3 shows 81 (27%) were without NAFLD and 219 (73%) were with NAFLD according to USG reports. The prevalence of NAFLD according to severity, 102 (34%) were mild, 90 (30%) were moderate and 27 (9%) had severe NAFLD.

Discussion

Non-alcoholic fatty liver disease is the most serious liver disorder and cause of cirrhosis among type two diabetic patients [13]. Setting the objective of evaluating the prevalence of NAFLD and associated factors in type 2-Diabetic patients attending the tertiary care hospital, Kanchipuram, we evaluated 300 type 2 diabetic patients who fulfilled the inclusion criteria. A number of studies have shown the link between Type 2 DM and NAFLD 73%of the study participants had NAFLD along with type 2 diabetic mellitus. The present finding is almost closer to research done in type 2 diabetic patients attending diabetic clinic of a tertiary care hospital in Mangalore (75% prevalence) by Shivananda Pai M, et al. [14]. This could be due to lack of liver checking habits as evidenced by the study participants' and. might be due to low attention given by health sector on fatty liver disease.

Table - 2: Lab parameter of NAFL disease compared with Ultrasonographic report among diabetics (N=300).

Parameter	Liver status				P-value
	Normal (N=81)	Mild fatty (N=102)	Moderate fatty (N=90)	Sever fatty (N=27)	
Fasting blood glucose (mg/dl)	165.21±1.22	179.44±1.32	188.56±1.21	175.80±1.67	0.04
Aspartate aminotransferase (u/l)	28.82±1.92	35.61±5.24	35.48±2.24	21.24±1.52	0.28
Total protein (gm/dl)	8.28±0.34	8.24±0.28	8.08±0.23	8.95±0.89	0.42
Total cholesterol (mg/dl)	189.89±14.29	198.47±10.42	179.39±11.86	191.99±26.87	0.51
High density lipoprotein (mg/dl)	39.21±1.57	37.72±1.80	36.94±2.12	32.30±2.90	0.39
Low density lipoprotein (mg/dl)	118.34±7.30	112.51±5.64	110.80±8.37	109.01±9.34	0.25

Table - 3: Distribution of study subjects according to prevalence of NAFLD based on USG report (300).

Parameter	Summary
NAFLD	219 (73%)
No NAFLD	81 (27%)
Severity of NAFLD	
Normal	81 (27%)
Mild fatty	102 (34%)
Moderate fatty	90 (30%)
Sever fatty	27 (9%)

Obesity was reported as the risk factor for NAFLD. In many research findings, a fatty liver disease among type 2 diabetic patients was significantly associated with BMI [14]. In our findings, however, 150 (50%) of the participants had BMI in normal range (18.0-24.9) and only 21 (7%) patients were obese (BMI >30kg/m^2). The prevalence of NAFLD was highest in urban 147 (49%) which was similar to study by Chatterjee A, et al. [15] where the reported prevalence is ranged from 9% in rural populations to 32% in urban populations. In the current study, the proportion of male was slightly higher than the females. Many studies in the past had reported relatively higher risk of NAFLD in males compared to females. A study from south India had reported higher prevalence of 35.1% among men, compared to 29.1% in women [16].

In the current study, out of 300, 102 (34%) had mild fatty liver, 90 (30%) had moderate fatty liver and 27 (9%) had severe fatty liver that keeps on increasing till the age of 60 years. This finding is similar to a study done Sangeetha, et al. [17]. Severe grades of NAFLD were reported to be associated with coronary artery disease, even without metabolic syndrome by previous studies [18]. Hence studies have recommended screening of patients with higher grades of NAFLD for Coronary Artery Disease (CAD) [19] which was not considered in the present study.

The findings of the present study as seen with comparison among fasting blood sugar, liver enzymes and lipid profile with severity of NAFLD except blood sugar others were not significant which is in contrast to study done by Belay, et al. [14] were few factors were significant. This can be due to the fact that liver biopsy is the gold standard for diagnosing NAFLD. Out of 300, 78 (27%) were having diabetes since 5-7 years which is in similar to a study done by Anjana Prabhakar [20] were they showed the number of NAFLD increased with duration of diabetes. We interviewed for type of medicine taken by subjects which can help in treatment of NAFLD. 138 (46%) were taking Metformin which can help in treating NAFLD as proved by earlier studies [21]. We did not consider life style parameters like High vegetables intake, low non-veg intake, low oil consumption, regular physical activities which can decrease incidence of fatty liver. These were considered in a study by Sangeetha, et al. [17].

Limitations and recommendations

Limitations of the study were that the sample size is small. A larger sample size could have provided a greater statistical power and adjustment for potential confounders. The diagnosis of NAFLD was solely based on ultrasound imaging and exclusion of other causes of chronic liver disease. Still today gold standard for diagnosis of NAFLD is histological evaluation. Ultrasonography cannot differentiate NAFLD. These modalities are not the most sensitive, specific and predictive method for detecting (quantifying) liver. Non-alcoholic fatty liver diseases are the major risk factors for developing cardiovascular diseases stroke, peripheral vascular disease chronic kidney disease cirrhosis and liver cancer among type 2 diabetic patients which were not considered in the present study. Therefore, we recommend further research to know the pathogenesis and identify effective treatment options inclusive of NAFLD.

Conclusion

The results of the present study clearly demonstrate high prevalence of NAFLD in Kanchipuram type 2 diabetics and they have some definite risk factors like advance age, duration of diabetes, medication taken for diabetes etc. which leads to increasing burdens to chronic liver disease in Indian population. There is a need to understand the true impact of NAFLD especially among type 2 DM patients, which add much information to our current knowledge about the epidemiology of NAFLD in India as a whole. The causative mechanism driving NAFLD progression in T2DM and evaluating the results of newer anti-diabetic treatments and identification of additional novel targets would reduce disease burden.

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