Prevalence of non-alcoholic fatty liver disease in patients with type 2 diabetes mellitus and its correlation with the complications in a tertiary care hospital of southern Tamil Nadu

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Abstract
Background: Non alcoholic fatty liver disease (NAFLD) is a relatively common and "silent" disease, which has gained special attention over the recent years, due to its serious impact on public health being appreciated increasingly. Despite the exponential increase in the research going on in this field, still there are various queries which remain unclear. In this study the prevalence of non alcoholic fatty liver disease in patients with type 2 diabetes mellitus is studied **Methodology:** 100 patients with type 2 diabetes were included in the study. They were screened for NAFLD using ultrasound abdomen. Serum triglycerides was checked. Correlation between the triglycerides and fatty liver was analysed. Informed consent was obtained from all the individuals. The participants were selected from out patients attending the medical and medical gastroenterology outpatient clinic and in patients admitted in the medical ward. **Results:** In this study the prevalence of non alcoholic fatty liver disease was found to be 65%.those patients found to have Non-alcoholic fatty liver disease, also found to have elevated non HDL C. Serum triglycerides were normal in patients who don't have fatty liver disease. **Conclusion**: In our study, we found that all patients with non alcoholic fatty liver disease, had elevated triglycerides with 100% correlation. Non HDL-C is a better predictor of cardiovascular risk and steato hepatitis in patients with NAFLD. Hence lowering Non HDL cholesterol has a beneficial role in the treatment. Early diagnosis and treatment of NAFLD can reduce cardiovascular risk in patients with diabetes.
Key Word: fatty liver disease.

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Access this article online	
Quick Response Code:	Website: www.medpulse.in
	Accessed Date: 02 July 2019

INTRODUCTION

A Non-alcoholic fatty liver disease (NAFLD) is a relatively common and "silent" disease, which has gained special attention over the recent years, due to its serious impact on public health being appreciated increasingly. The prevalence of NAFLD has been reported to be 15 – 30% in the general population in various countries and is increasing. Compared with non-diabetic subjects, people with type 2 diabetes appear to have an increased risk of developing NAFLD. Recent studies show that NAFLD was independently associated with an increased prevalence of CAD, Chronic Kidney Disease and Retinopathy in diabetic patients.

AIMS AND OBJECTIVES

To study the prevalence of non-alcoholic fatty liver disease in type 2 diabetic patients and the correlation of non-alcoholic fatty liver disease and serum triglycerides and its complications.
Background: The prevalence of NAFLD in India is around 10–32%[3,4,5]. According to the NHANES data, the prevalence of NAFLD has been increasing over the past 3 decades accounting to nearly 50 to 75% of chronic liver disease during those time periods. Diabetes, central obesity, insulin resistance and dyslipidemias are common predisposing factors. India has the largest number of

people with diabetes in the world. Asian Indians are more prone to have insulin resistance and have increased waist circumference and visceral fat. With increasing obesity and diabetes mellitus, there is a high possibility of the prevalence of fatty liver increasing further.

MATERIALS AND METHODOLOGY

100 patients with type 2 diabetes were included in the study. They were screened for NAFLD using ultrasound abdomen. Serum triglycerides was checked. Correlation between the triglycerides and fatty liver was analysed. Informed consent was obtained from all the individuals. The participants were selected from out patients attending the medical and medical gastroenterology outpatient clinic and in patients admitted in the medical ward.

Inclusion criteria: Type 2 diabetic patients coming to KKGMCH with age more than 40 years were included.

Exclusion criteria: Those patients with history of any quantity of alcohol consumption, Chronic liver disease, Usage of drugs known to cause steatosis including Amiodarone, Corticosteroids, Tamoxifen, Methotrexate and high dose Estrogen, History of jejuno ileal bypass or extensive small bowel resection and pregnant women were excluded.

RESULTS

The total study population was 100. Out of which 65 were cases with NAFLD and 35 were controls without NAFLD. The general details of the study population are given in table 1 (given below). Our study population had a mean age of 54 yrs. Most of the population belonged to the age group between 40-60 years. Out of the total 68 were females and 32 were males. Characteristics of cases

and controls was compared and mentioned in tables given below. Serum triglycerides were elevated only in those patients with non-alcoholic fatty liver disease. Mean BMI was 25.54. The mean waist circumference was 92 cm. The mean systolic and diastolic blood pressures were 138mmHg and 84 mmHg respectively. Regarding the blood investigations the mean fasting blood sugar was 149 mg/dl. The mean AST and ALT levels were 40 and 41 respectively. Looking into the lipid profile the mean total cholesterol was 203.05(+/- 34.83), LDL 100.25(+/- 28.33), HDL 46.34 (+/- 6.027) and triglycerides 167.53 (+/- 53.939). On comparison of the demographic profile with the presence or absence of NAFLD the mean age of the cases and controls were 54.35 and 53.54 respectively. The mean BMI among the cases were 26.32 and that among the controls were 24.12 ($p<0.001$). The waist circumference among the cases were 95.2 and that among the controls were 86.26 ($p<0.001$). The mean duration of Diabetes among the cases and controls were almost the same 6yrs. The mean blood pressure among the cases and controls were 141/86 and 131/80mmHg ($p<0.05$). The mean fasting blood sugar was 161 among cases and 126.31 among controls. The mean AST levels were 44.38 and 31.74 among cases and controls respectively. The mean ALT levels were 47.41 among the cases and 27.48 in the control group. The mean LDL levels were 103.12 and 94.91 among the cases and controls respectively. The mean HDL levels were 45.37 among the cases and 48.14 among the controls ($p<0.05$). The mean Triglycerides were markedly high the cases 185.72 than in controls 133.74 ($p<0.001$).
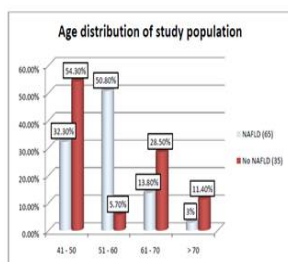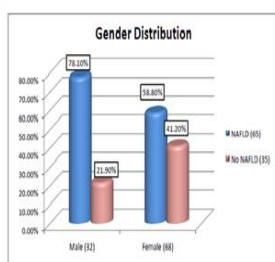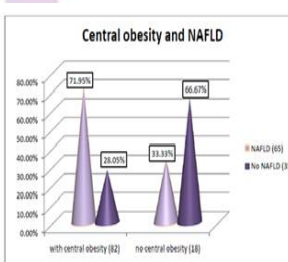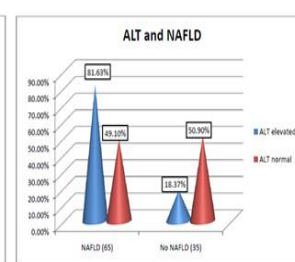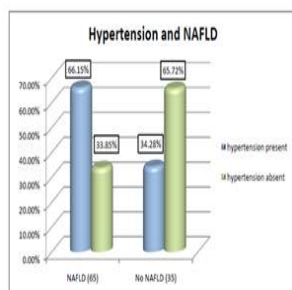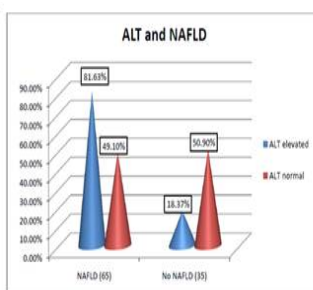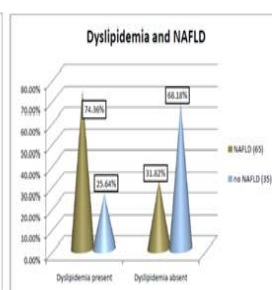

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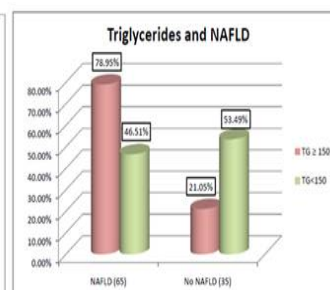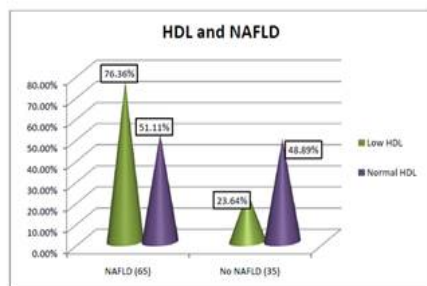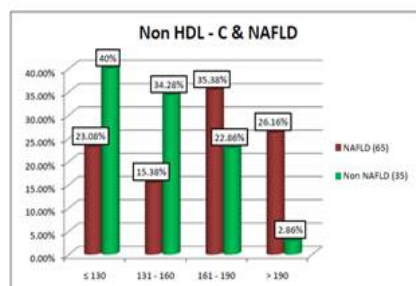

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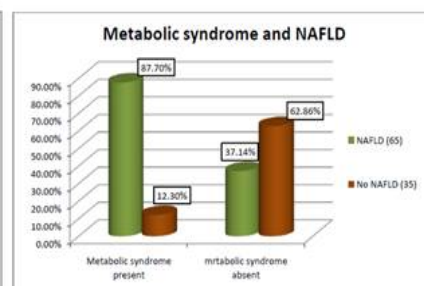Figure 8:

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DISCUSSION

Fatty liver is a very common incidental finding which is usually neglected. But now it needs to be given special attention as it is considered to be a forerunner of many diseases especially coronary artery disease. A large number of various studies conducted across the world have shown that NAFLD is associated with obesity, diabetes, insulin resistance and dyslipidemia which are factors which in association with fatty liver make a person vulnerable to develop cardio vascular diseases. Thus these individuals have a lesser life span when compared with those without the above mentioned risk factors. In this study the diagnosis of NAFLD was made based on the ultra-sonographic evaluation of the abdomen. Due to ethical reasons the gold standard test of liver biopsy was not done in the study group. But still USG has a sensitivity of 80% and specificity of 99%.[1,2] The prevalence of NAFLD among patients with diabetes in India is reported to be between 12.5% to 87.5%.[3,4,5] "A study by Mohan et al showed the prevalence of NAFLD to be 54.5%, which was significantly higher in patients with diabetes".[5] "Prashanth et al found a high prevalence of NAFLD and NASH in type 2 diabetics, which increased with multiple components of the metabolic syndrome". "A study conducted by Shobha Luxmi et al showed a 60.8% prevalence of NAFLD among patients with diabetes"39. In this study the prevalence was found to be 65% among patients with diabetes which correlated with the above-mentioned studies. Most of the previous studies conducted in India have shown a higher prevalence of NAFLD among males than in females[6]. This study also showed a higher prevalence of 78.1% among males than the prevalence of 58.8% among the females. The average age of the patients with NAFLD was 54.35 yrs. "Previous studies have shown that the prevalence of fatty liver increases with age and majority of cases occur between 40 and 60 years"[5,7] In our study also the prevalence of NAFLD was high between 41-60 yrs. The average duration of diabetes was found to be around 6.5 years in both the cases and controls. There was no 71 significant correlation between the duration of diabetes and prevalence of NAFLD. p value = 0.668. On

analyzing the anthropometry of the population, 58% of the total study population were obese, 27% were overweight and only 15% had a normal BMI. The mean BMI of the patients with fatty liver was found to be 26.32. Their mean waist circumference was 95.2 cm which was higher than the ethnic specific cut off by the IDF. About 82.76% of patients with obesity and 71.95% of them with truncal obesity were found to have fatty liver for which there was significant correlation as compared to previous studies41. Obesity was defined as BMI ≥25 and if overweight individuals were also included in this category the significance might increase further. Fatty liver was prevalent in about 78.18% of the patients who had hypertension and there was significant statistical correlation for this. About 88% of the study population had inadequate glycemic control among which 71.59% had NAFLD which may be considered as an indicator of insulin resistance in these patients. Inadequate glycemic control also had a significant correlation with the prevalence of NAFLD.72 p <0.05. Only fasting and post prandial blood sugar levels were estimated and HBA1C levels were not evaluated. Dyslipidemia was prevalent in about 78% of the study group of which 78.36% had NAFLD. Based on the above statistical evidence since most of the patients had poor glycemic control, hypertension and dyslipidemia it is possible to arrive at a conclusion that patients with these comorbid conditions are at a higher risk of developing NAFLD. Regarding lipid profile low HDL, elevated total cholesterol, LDL and triglycerides were seen in 42%, 62%, 55% and 67% respectively. Among these low HDL, elevated total cholesterol and triglycerides had a statistically significant correlation with the prevalence of NAFLD. Elevated LDL did not correlate with prevalence of NAFLD. About 78.95% of patients with hypertriglyceridemia were found to have NAFLD (p<0.001) with the mean Triglycerides level being 185.72. This was consistent with findings reported in previous studies conducted by Angulo et al42, Donnelly et al43 and Sharabi et al44.73 About 60% of the fatty liver subjects had low HDL levels and the mean HDL was 45.37 and there was a significant negative correlation

with the prevalence of NAFLD. Thus like in other previous studies this study also showed that fatty liver negatively correlated with plasma HDL levels[8,9,10]. Around 64.62% of fatty liver subjects had high total cholesterol levels and the mean was 210.15 in them. There was a significant positive correlation with total cholesterol levels and fatty liver. P<0.001. About 53.85% of subjects with fatty liver had elevated LDL levels and the mean LDL level was 103.12 in them. But LDL levels did not have a significant correlation with the prevalence of NAFLD (p=0.45) as in previous studies. This was in concordance with the previous studies conducted by Giovanni Targer *et al*45 and Vijay Viswanathan *et al*28. About 71 % of the study population had high Non HDL-C levels. Among them, 22%, 31% and 18% had mild, moderate and severely high Non HDL-C levels. About 76.92% of patients with NAFLD had high Non HDL-C levels. More than 60% of these patients had moderate to severely high levels of Non HDL-C. There was a significant statistical correlation 74 between Non HDL-C and NAFLD. p value = 0.002. "Zelber *et al* has shown that Non HDL-C independently predicts new onset NAFLD46." Our results were in concordance with the above study and the study conducted by Sangyeoup *et al*47. ALT levels were found to be high among 61.54% of individuals in the fatty liver group than 25.71% in the non fatty liver group. The mean ALT level was 47.41 in the fatty liver group which was higher than that of non fatty liver group. Moreover this study showed a significant correlation with high ALT levels and fatty liver (p<0.001). This was consistent with the results of various previous studies26. AST levels were found to be high among 70.77 % of individuals with fatty liver and 40 % in the non fatty liver group. Mean AST level was 44.38 in the fatty liver group. But, this study did not show significant correlation between AST levels and fatty liver (p=0.14) The presence of Metabolic Syndrome was evaluated according to IDF criteria. About 86.15% of individuals in the fatty liver group had 75 Metabolic Syndrome against 37.14% in the non fatty liver group. (Fig: 14, Table: 15) In this study, Metabolic Syndrome had a positive correlation with the prevalence of NAFLD. This was in concordance with previous study by Marchesini *et al*48. Regarding the prevalence of the complications of diabetes about 16%, 22%, 21% and 28% had CAD, retinopathy, neuropathy and nephropathy respectively. About 23.08% of individuals with NAFLD had Coronary Artery Disease against only 2.9% in the Non NAFLD group. There was a significant positive correlation with NAFLD and CAD (p = 0.044). This would probably be explained by the higher prevalence of dysglycemia and components of Metabolic Syndrome, which favors early onset atherosclerosis in these patients.

Around 27.69% of the patients with fatty liver were found to have diabetic retinopathy against 11.43% in the non fatty liver group. But, there was no significant correlation with the prevalence of NAFLD and diabetic retinopathy (p = 0.201). About 26.15% of individuals with NAFLD were found to have developed diabetic neuropathy against only 11.43% in the non NAFLD group. This also did not show a significant 76 correlation (p = 0.244). About 29.23% of the patients with NAFLD had diabetic nephropathy against 25.71% in the non NAFLD group. This study failed to show a significant correlation between NAFLD and diabetic retinopathy. Overall, among the complications of diabetes, only Coronary Artery Disease showed a positive correlation with NAFLD. The other complications like retinopathy, neuropathy and nephropathy did not have a significant correlation with NAFLD. This was only partially consistent with the results of the study conducted by Viswanathan *et al*28. The limitations of this study are as follows: There was a selection bias as all the participants were included from a tertiary care hospital, sex distribution was unequal with less number of male participants, other tests like anti nuclear antibody, anti smooth muscle antibody, anti mitochondrial antibody, serum ferritin were not done, the gold standard test of liver biopsy was not done due to ethical reasons and fatty liver was diagnosed only by ultrasound. Hence, the results could not be compared with the severity of NAFLD.

CONCLUSION

The prevalence of NAFLD was found to be 65% in the study population. Body Mass Index, waist circumference and uncontrolled hypertension were higher in the fatty liver group. Dyslipidemia especially hyper triglyceridemia and low HDL were strongly associated with NAFLD. Non HDL-C is considered as a better predictor of cardiovascular risk and steato hepatitis in patients with NAFLD. Hence lowering Non-HDL cholesterol has a beneficial role in the treatment. Metabolic Syndrome had a significant association with NAFLD. Diabetic complications like Coronary Artery Disease had a statistically significant correlation with NAFLD. All patients with Diabetes should be screened for NAFLD, because these patients develop diabetes related complications earlier. Early diagnosis and treatment of NAFLD can reduce cardiovascular risk in patients with diabetes

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Source of Support: None Declared
Conflict of Interest: None Declared