e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2024; 16(1); 1325-1329

Original Research Article

Study of Correlation of Non-Alcoholic Fatty Liver Disease and Neuropathy in Type 2 Diabetes Mellitus

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Received: 25-10-2023 / Revised: 23-11-2023 / Accepted: 26-12-2023
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Conflict of interest: Nil

Abstract:

Introduction: According to the World Gastroenterology Organization's global guidelines, the overall prevalence of NAFLD is about 4% to 46% across the world. Considering the concept of bidirectional relationship between NAFLD and type 2diabetes mellitus, assessing the hepatic status for fatty infiltration could be an ideal marker of insulin resistance in type 2 diabetes mellitus and its complications. Objectives: To determine the correlation if any, between non-alcoholic fatty liver disease and microvascular complications in type 2 diabetes mellitus.

Methodology: A Cross Sectional study conducted in Department of General Medicine at the teaching hospital of Mandya Institute of Medical Sciences between June 2020 to May 2021. Study population were All Non-alcoholic Diabetic patients diagnosed to have a Fatty liver on USG. A minimum sample size of 78 was required for the study. Purposive sampling was used. Appropriate statistical tools were used in analyzing the data. The level of significance[α] was 5% i.e., p-value <0.05 is considered statistically significant.

Results: In the study, all the participants were diagnosed with non-alcoholic fatty liver disease. Grade 1 NAFLD was observed in majority of the participants i.e., about 53.8% cases. Followed by Grade 2 around 34% and 10% cases had Grade 3 NAFLD. In assessing the association between diabetic complications in type 2 diabetic patients NAFLD, there exists statistically significant relation, all the three microvascular complications namely neuropathy.

Conclusion: The study concludes that increased severity of NAFLD with increase in the age, blood sugar level, and triglyceride level. Direct correlation between NAFLD and neuropathy due to type 2 diabetes mellitus.

Keywords: Diabetes Mellitus, Non-Alcoholic Fatty Liver Disease, Micro Vascular Complications, Type 2 DM.

Introduction

According to the World Gastroenterology Organization's global guidelines, the overall prevalence of NAFLD is about 4% to 46% across the world [1]. Number of studies conducted in Indian population, concluded that the prevalence rate of NAFLD was about 9-32% and with a higher incidence of NAFLD among Type 2 Diabetes mellitus individuals found to be 12.5% to 87.5% [2].

Wide variety of fatty liver changes, from steatosis to steatohepatitis, cirrhosis and hepatocellular carcinoma is included under the term NAFLD, in the absence of alcohol intake [3]. Only recently, NAFLD has been increasingly recognized as the liver disease component of metabolic syndrome [4]. Number of studies has concluded that T2DM patients appear to have an increased risk of developing NAFLD than non-diabetic subjects and certainly the risk of developing fibrosis and cirrhosis is greater [3]. Current preclinical data suggest hyperinsulinemia and selective hepatic sensitivity to insulin leads to increased adipose tissue lipolysis and increased fatty acid delivery to liver, enhancing stimulation of hepatic lipid synthesis. Moreover, increased cellular oxidant stress leading to fibrosis by activation of hepatic stellate cells [5] has been implicated as the key for progression of NAFLD. The primary mechanism by which NAFLD contributes to type 2 diabetes mellitus is by increasing insulin resistance [6] and pancreatic beta cell lipo-toxicity caused by sustained elevation in FFAs formed from lipolysis of adipose tissue resulting in defective insulin secretion [7].

Ultrasonography of abdomen seems to be a non-invasive, cost effective, simple procedure to detect

the fatty changes in liver [8]. Therefore, considering the concept of bidirectional relationship between NAFLD and type 2diabetes mellitus, assessing the hepatic status for fatty infiltration could be an ideal marker of insulin resistance in type 2 diabetes mellitus and its complications. [9-15]

Materials and Methods

This is a Cross Sectional study was conducted in the Department of General Medicine at the teaching hospital of Mandya Institute of Medical Sciences among All Non-alcoholic Diabetic patients diagnosed to have a Fatty liver on USG Abdomen. A minimum sample size of 78 was required for the study.

Inclusion Criteria:

- Non-alcoholic individuals and Diagnosed cases of Diabetes Mellites in the age group of 18-65 years with USG abdomen showing Hyper-echoic liver suggestive of Fatty liver
- Patients who give informed consent.

Exclusion Criteria:

- Patients who are positive for HBs Ag or Anti-HCV antibodies
- Patients who have abnormal iron work up (High S. Iron, High S. Ferritin, Low TIBC)
- Pregnant women.

Tools Used:

Investigations

FBS: Enzymatic End Point Method (Hexokinase/G-6-PDH) was used for quantitative determination of plasma glucose in human serum by using kit manufactured by Abbott Ltd.

PPBS: Enzymatic End Point Method (Hexokinase/G-6-PDH) was used for quantitative determination of plas-ma glucose in human serum by using kit manufactured by Abbott Ltd.

HbA1C: Enzymatic method of the estimation of the glycated Hb is used.

Serum Triglycerides: Enzymatic method was used for the quantitative determination of triglyceride in human serum using Glycerol Phosphate Oxidase – Phenol Amnio-phenazone (GPO-PAP) end point method, manufac-tured by Abbott Ltd

Ultrasound abdomen: was done by the qualified radiologist for the diagnosis of the NAFLD

The Michigan Neuropathy Screening Instrument (MNSI) is used to assess distal symmetrical peripheral neu-ropathy in diabetes. It includes two separate assessments: one patient history based and secondly physicians' examination-based screening.

In this study, the second half which includes a lower extremity examination- inspection and assessment of vibra-tory sensation and ankle reflexes by physician was used.

Data collection: All patients who are diagnosed with non-alcoholic fatty liver on USG abdomen in our hospital shall be ex-plained about this study. Informed consent shall be obtained from those who agree to participate in the study. Ultrasonography is the most widely used imaging technique for the detection of fatty liver. The overall sensitivity, specificity, positive likelihood ratio and negative likelihood ratio of ultrasound for the detection of moderate-severe fatty liver, compared to histology (gold standard), are 84.8% (95% confidence interval: 79.5-88.9), 93.6% (87.2-97), 13.3 (6.4-27.6), and 0.16 (0.12-0.22) respectively. Confirmation of fatty liver by biopsy and histopathological examination, although considered gold standard, is not practically done for ethical rea-sons.

Statistical methods to be employed: The data will be entered in excel sheet and presented in the form of percentages, frequencies and figures such as tables, charts and graphs. Data will be analyzed using SPSS software. Descriptive statistics like percentage, pro-portion, central tendency, SD and inferential statistics like chi-square test to know the association and t-test to know the difference between two means and other suitable tests will be applied and depicted via bar charts, pie charts. Correlation between Non-Alcoholic Fatty Liver Disease and Micro vascular complications in Type 2DM will be calculated.

Using descriptive statistics like proportion, percentage, mean and standard deviation and inferential statistics like chi-square, t-test, and other suitable statistical tools will be applied. The level of significance[α] was 5% i.e., p-value <0.05 is considered statistically significant.

Results

Table 1: Distribution of the study participants based on the grades of non- alcoholic fatty liver disease

NAFLD	Frequency (N)	Percentage (%)
Grade 1	43	53.8
Grade 2	29	36.3
Grade 3	8	10.0
Total	**80**	**100.0%**

In the study, based on the findings from ultrasonography of whole abdomen, all the participants were diagnosed with non-alcoholic fatty liver disease. Further, on analyzing the severity of the condition, Grade 1 was observed

in majority of the participants i.e., about 53.8% cases. The next common finding was Grade 2 which comprised about more than one third of the study population. Remaining 10% cases suffered with the most severe form i.e., Grade 3 NAFLD.

Table 2: Association between age of the study participants and grades of NAFLD

NAFLD	Mean Age (in years)	Standard Deviation
Grade 1 (N=43)	42.95	7.30
Grade 2 (N=29)	52.10	8.34
Grade 3 (N=8)	55.75	6.90

The mean age of the participants in the study was 47.55 years with a standard deviation of around ±9.11 years. The minimum age and maximum age of the study participants were 30 years and 65 years, respectively.

Table 3: Association between gender of the study participants and grades of NAFLD

Gender	Non-Alcoholic Fatty Liver Disease		
	Grade 1	Grade 2	Grade 3
Male (N=49)	29 (67.4%)	18 (62.1%)	2 (25.0%)
Female (N=31)	14 (32.6%)	11 (37.9%)	6 (75.0%)

In the study, majority of the participants were males. Even on comparing with respect to the severity of non-alcoholic fatty liver disease, males were predominant in both Grade 1 and Grade 2. However, in case of Grade 3, females comprised about three quarters of the population.

Table 4: Prevalence of diabetic complications among the study participants

Diabetic complications	Frequency (N)	Percentage (%)
Diabetic Neuropathy	55	68.8

Table 5: Association between neuropathy status and grades of NAFLD

NAFLD	Mean Michigan NSI	Standard Deviation	p-value
Grade 1 (N=43)	2.52	1.28	
Grade 2 (N=29)	6.71	0.97	
Grade 3 (N=8)	7.56	0.42	**<0.001**

Michigan Neuropathy Screening Instrument was used in the study to assess the severity of neuropathy among the study participants. The mean value was 4.54 with a standard deviation of around ±2.47. The minimum and maximum values were 1 and 8, respectively. On comparing the neuropathy status of the participants in the study with respect to the severity of non-alcoholic fatty liver disease, using one way ANOVA, it was found that there exists statistically significant relation. Thus it is evident that more severe the neuropathy among the participants more was the severity of NAFLD.

Table 6: Biochemical profile of the study participants

Biochemical Profile		Frequency (N)	Percentage (%)
FBS	≤130 mg/dL	30	37.5
	>130 mg/dL	50	62.5
PPBS	≤180 mg/dL	20	25.0
	>180 mg/dL	60	75.0
HbA1C	≤7%	21	26.3
	>7%	59	73.8
Triglyceride	≤149 mg/dL	0	0.0
	>149 mg/dL	80	100.0

In the study, the relevant biochemical investigations were performed among the participants. Such that the blood sugar profile was estimated which showed that fasting blood sugar was not under control in nearly two third of study population while post prandial blood sugar was off the limits in three fourth of them. Even the blood sugar was not under control in the last three months in around 73.8% of participants as the glycated hemoglobin was above 7% in these individuals. On other hand, the triglyceride level was exceeding in all the participants.

Discussion

In the study, on analyzing the severity of non-alcoholic fatty liver disease among the participants, Grade 1 was observed in majority i.e., about 53.8% cases. The next common finding was Grade 2 which comprised about more than one third of the study population. Remaining 10% cases suffered with the most severe form i.e., Grade 3 NAFLD.

The mean age of the participants in the study was 47.55 years with a standard deviation of around ±9.11 years. The minimum age and maximum age of the study participants were 30 years and 65 years, respectively. This resembles the study by Arase Y et al [16] where the mean age was around 48.0 years with a standard deviation of around ±8.4 years.

Majority of the participants in the study were males. Even on comparing with respect to the severity of non-alcoholic fatty liver disease, males were predominant in both Grade 1 and Grade 2. This is quite similar to the study by Targher G et al [17] where males were predominant comparatively. However, in case of Grade 3, females comprised about three quarters of the present study population.

The study analysed for any association between complications of diabetes mellitus and the severity of NAFLD, there exists statistically significant relation, thereby suggesting that more severe the complications of diabetes mellitus, more was the severity of NAFLD in the study. This was proven by the observations from the study by Somalwar et al [18] and Afarideh M et al [19].

On observing the severity of NAFLD among those participants who were suffering from more than one complication of diabetes mellitus, the study found that as the grades of NAFLD increased, the complications were present more in number. Such that the analysis for any association between co-existence of diabetic complications and the severity of NAFLD, there exists statistically significant relation, thereby suggesting that NAFLD was more severe among those who had more than one diabetic complication. Again, the study observed the severity of NAFLD among those participants who were suffering from either all three complication of diabetes mellitus or none, and found that as the grades of NAFLD increased, the complications were present more in number, whereas completely contrast among those without any complications. Such that the analysis for any association of grades of NAFLD with both presence and absence of all diabetic complications, there exists statistically significant relation, thereby suggesting that controlling the blood sugar, prevents the diabetic complications, further avoiding the progression into the severity of NAFLD.

The glycated hemoglobin of the participants was measured in the study to understand the control of blood sugar over the period of 3 months. The mean HbA1C value was found to be 9.85% with a standard deviation of around ±3.32%. Whereas in the study by Targher G et al [17], the mean HbA1C was quite lower than the present study with the value of 7.20%. On further comparing the HbA1C with respect to the severity of NAFLD, using one way ANOVA, it was found that there exists an extremely significant relation which was proven statistically. Thus, it is evident that the severity of NAFLD was more with the increase in the HbA1C of the participants. This is justified by the study by Afarideh M et al [19], which showed that HbA1C was more among those who were suffering from the severity of the condition.

On estimating the triglyceride level in the study, the mean value was found to be 192.15 mg/dL with a standard deviation of around ±23.29 mg/dL. This is quite higher compared to the findings from the study by Arase Y et al [20], where the mean triglyceride value was 164 mg/dL with a standard deviation of around ±117 mg/dL. On comparing the triglyceride level of the participants with respect to the severity of NAFLD, using one way ANOVA, the study found an extremely significant relation which was proven statistically. Thus, it is evident that the severity of NAFLD was more with the increase in the triglyceride level of the participants.

Conclusion

On observing type 2 diabetes mellitus patients who were diagnosed with non- alcoholic fatty liver based on the findings from USG abdomen, the study found; Increased severity of NAFLD with increase in the age, blood sugar level, and triglyceride level. Direct correlation between NAFLD and neuropathy due to type 2 diabetes mellitus.

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