

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

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Abstract:

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

Materials and Methods: All patients who are diagnosed with non-alcoholic fatty liver on USG abdomen in our hospital shall be explained about this study. Informed consent shall be obtained from those who agree to participate in the study. Information will be collected through a pre-tested and structured proforma for each patient. In the first part, data regarding identifier details like name, age, phone number, inpatient number, date of admission, etc., will be obtained. In the second part, information about the chief complaints, history of presenting illness, past history, will be obtained. Details regarding the general condition of the patient will be obtained. In the third part, General physical examination including anthropometry and relevant systemic examination is undertaken. In the fourth part, patient is subjected to fundoscopy, urine for micro albuminuria study for estimating the micro vascular complications, which is then correlated with the presence of fatty liver.

Results: 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 analysing 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. Fundoscopy was performed to assess the severity of diabetic retinopathy among the participants in the study. Accordingly, only 39.5% of the participants were found to be normal. Majority of the participants were diagnosed as non-progressive diabetic retinopathy. Whereas among those who were categorized as Grade 2 and Grade 3, majority were suffering from progressive diabetic retinopathy. Such that the analysis for any association between fundoscopy results and the severity of NAFLD, there exists statistically significant relation, thereby suggesting that more progressive the retinopathy, more was the severity of NAFLD in the study.

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; The increased severity of NAFLD with increase in the age, blood sugar level, and triglyceride level. There is also direct correlation between NAFLD and microvascular complications due to type 2 diabetes mellitus which include diabetic retinopathy.

Keywords: Non-alcoholic fatty liver disease, Retinopathy, Type 2 diabetes mellitus.

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Introduction

NAFLD is defined as fatty infiltration of liver exceeding 5-10% of the total weight and involving more than 30% of the hepatocytes in a liver lobule with fat deposits mostly in the form of macrovesicular steatosis in the absence of significant alco-

hol intake. [1] A non-alcoholic state is defined as either total abstinence from alcohol or with alcohol intake of <20gm/day (males) and <10gm/day (females). [2] Fatty liver is pathologically designated as fatty degeneration of the liver and called as fatty

change, fatty infiltration, fatty metamorphosis or fatty steatosis of liver – all terms entitled to define the accumulation of fat within the hepatocytes. [3] NAFLD is a multisystem illness that affects extra-hepatic organs and regulatory pathways in addition to the liver. [4] It raises the risk of type 2 diabetes, cardiovascular and cardiac disease, chronic kidney disease, sleep apnoea, small bowel bacterial overgrowth and colorectal cancers, osteoporosis, psoriasis, and various endocrinopathies such as metabolic syndrome, polycystic ovary syndrome, hypothyroidism, and hypopituitarism, and has a causal link in sleep apnoea. [5]

Men have a higher prevalence of NAFLD and NASH than women, while women have a higher rate of progression to advanced fibrosis. [6] Women have a lower risk of NAFLD during their reproductive years, but after menopause, the protective effect wears off, and women have the same prevalence of NAFLD as males. [7]

Type 2 diabetes accounts for 90% of all diabetes cases. [8] Type 2 diabetes mellitus impairs both basal insulin secretion and hepatic insulin sensitivity. As insulin sensitivity declines, endogenous insulin production rises to maintain normal fasting plasma glucose levels. The compensatory insulin secretion decreases as the disease advances and fasting, and post-meal plasma glucose levels rise. [9]

Diabetic retinopathy is a well-known, sight-threatening chronic microvascular condition that affects nearly all diabetic individuals at some point. Diabetic retinopathy is the most common cause of blindness worldwide. [10] Diabetic retinopathy becomes more common as diabetes progresses and the patient ages. In patients with newly diagnosed type 2 diabetes, diabetic retinopathy is an independent risk factor for subclinical atherosclerosis. As a result, even in the early stages of diabetes, a diagnosis of diabetic retinopathy may necessitate a more thorough cardiovascular examination. [11]

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

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:

Fundoscopy: Direct Ophthalmoscopy with dilated pupils was done to diagnose diabetic retinopathy.

Data collection: All patients who are diagnosed with non-alcoholic fatty liver on USG abdomen in our hospital shall be explained 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 reasons.

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, proportion, 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: 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 2: 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 3: Prevalence of diabetic complications among the study participants

Diabetic complications	Frequency (N)	Percentage (%)
Diabetic Retinopathy	Non-Progressive	41
	Progressive	22
		51.3
		27.5

Table 4: Association between funduscopy results and grades of NAFLD

Funduscopy	Non-Alcoholic Fatty Liver Disease		
	Grade 1	Grade 2	Grade 3
Normal (N=17)	17 (39.5%)	0 (0.0%)	0 (0.0%)
NPDR (N=41)	26 (60.5%)	13 (44.8%)	2 (25.0%)
PDR (N=22)	0 (0.0%)	16 (55.2%)	6 (75.0%)
p-value	<0.001		

Funduscopy was performed to assess the severity of diabetic retinopathy among the participants in the study.

Accordingly, only 39.5% of the participants were found to be normal. Majority of the participants were diagnosed as non-progressive diabetic retinopathy. Whereas among those who were categorized as Grade 2 and Grade 3, majority were suffering from progressive diabetic retinopathy.

Such that the analysis for any association between funduscopy results and the severity of NAFLD, there exists statistically significant relation, thereby suggesting that more progressive the retinopathy, more was the severity of NAFLD in the study.

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Table 5: Association between glycated hemoglobin and grades of NAFLD

NAFLD	Mean HbA1C (%)	Standard Deviation	p-value
Grade 1 (N=43)	7.21	0.97	<0.001
Grade 2 (N=29)	12.18	1.96	
Grade 3 (N=8)	15.58	0.80	

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 $\pm 3.32\%$.

The minimum and maximum values were 5.6 and 16.6, respectively. On comparing the HbA1C 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 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.

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 [12] 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 [13] where males were predominant comparatively. However, in case of Grade 3, females comprised about three quarters of the present study population. In the study, the risk of developing complications of diabetes mellitus such as diabetic

retinopathy was assessed by fundoscopy, clinical screening, and urine investigation for albumin respectively. Based on the findings from these tests, the prevalence of diabetic retinopathy was found to be more than three fourth of the study population. Whereas in the study by Afarideh M et al [14], the prevalence of diabetic retinopathy was around 28.48%.

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 [15]

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 relevant biochemical investigations were performed among the participants in the study, 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 past three months in around 73.8% of participants. On other hand, the triglyceride level was exceeding in all 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; The increased severity of NAFLD with increase in the age, blood sugar level, and triglyceride level. There is also direct correlation between NAFLD and microvascular complications due to

type 2 diabetes mellitus which include diabetic retinopathy.

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