VOLUME - 11, ISSUE - 04, APRIL - 2022 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

Diabetology

A HOSPITAL BASED STUDY IN TERTIARY CARE CENTRE IN NORTH INDIA: PREVALENCE OF NAFLD IN PATIENTS OF PREDIABETES AND DIABETES

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ABSTRACT

Background: Non-alcoholic fatty liver disease (NAFLD) is the most common liver disease in developed countries and now becoming in developing countries also. Central Obesity and sedentary life style is usually associated with NAFLD.There are a lot of study has been done regarding prevalence of NAFLD in diabetes but lesser study available for prediabetes. In different studies reviewed by us, prevalence of NAFLD in diabetic subjects has been reported to range from 26.5% to 86.7%1,2,3. In prediabetic patients this prevalence has been seen to range from 48.24% to 68%4,5,6. **OBJECTIVE:** To assess the prevalence of Non-Alcoholic Fatty Liver Disease (NAFLD) in prediabetes and diabetes patients. **RESEARCH DESIGN AND METHODS**: A cross sectional study was conducted at SRN Hospital, Prayagraj. A total of 100 prediabetic and 100 diabetic patients were enrolled in the study. Patients on the basis of HbA1c(glycated hemoglobin) are divided in to two groups, prediabetic and diabetic group. Patients with known case of liver disease, taking steroid and regular alcohol intake were excluded from study. Ultrasonography B mode used for detection of fatty liver infiltration and their grading. **RESULT**: Prevalence of NAFLD was 48% in prediabetic and 54% in diabetic group. In prediabetic group, 32% had grade 1, 13% had grade 2 and 3% had grade 3 NAFLD whereas in diabetic group 34% had grade 1, 18% had grade 2 and 2% had grade 3 NAFLD. In the present study, we found that diabetic patients as compared to pre-diabetic patients were significantly older, had a higher proportion of males and higher BMI(Body mass index). **Conclusion:** There was no significant difference between two groups for association of NAFLD and its severity. Higher BMI is associated with higher chances to get NAFLD and diabetes mellitus in future.

KEYWORDS : Non-Alcoholic Fatty Liver Disease, Prediabetes, Type 2 Diabetes.

INTRODUCTION

Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycemia.The worldwide prevalence of DM has risen dramatically over the past two decades, from an estimated 108 million cases in 1980 to 415 million in 2017[7].Based on current trends, the IDF projects that 642 million individuals will have diabetes by the year 2040[7]. NAFLD is strongly correlated with insulin-resistant states such as obesity, metabolic syndrome, and type 2 diabetes mellitus(T2DM). Hepatic steatosis in the absence of secondary cause of fat accumulation in liver is called non-alcoholic fatty liver disease (NAFLD). It has been shown that insulin resistance can increase the peripheral lipolysis, triglyceride synthesis and hepatic uptake of free fatty acid which ultimately leads to NAFLD. The simple accumulation of triglyceride within hepatocytes (hepatic steatosis) is on the most clinically benign extreme of the spectrum[8].On the opposite, most clinically ominous extreme, are cirrhosis and primary liver cancer.

Stages of NAFLD:

1. Steatosis: Hepatic steatosis is initial stage. This is where excess fat builds up in the liver cells but is considered harmless. There are usually no symptoms and you may not even realise you have it until you find it incidentally on ultrasonography.

2. Steatohepatitis: Only a few people with simple fatty liver enter in next stage, known as non-alcoholic steatohepatitis (NASH). NASH is a more aggressive form of the condition, where the liver has become inflamed. A person with NASH may have a dull or aching pain felt in the top right of their abdomen.

3. Fibrosis: Some people with steatohepatitis go on to develop fibrosis, which is where persistent inflammation in the liver results in the generation of fibrous scar tissue around the liver cells and blood vessels. This fibrous tissue replaces some of the healthy liver tissue, but there is still enough healthy tissue for the liver to continue to function normally.

4. Cirrhosis: Most severe stage characterized by bands of scar tissue, nodules (containing regenerating hepatocytes and disruption of the architecture of entire liver. Liver shrinks and becomes lumpy, this is known as cirrhosis. Cirrhosis tends to occur after many years of liver inflammation.The damage caused by cirrhosis is permanent and can't be reversed.

MATERIAL AND METHODS

Study Design: A cross sectional study was conducted at Swaroop Rani Hospital, MLNMC Prayagraj. In which 100 prediabetic and 100 diabetic patients (on the basis of HbA_1c level)were enrolled in the study. Patients with age 18 years or more who have been diagnosed as prediabetic (HbA_{1c} 5.7-6.4%) and diabetic ($HbA_{1c} \geq 6.5\%$) were included. Patients with known metabolic disorders, cardiovascular disease, morbid obesity (BMI >35 kg/m^2) and liver dysfunction or patients taking steroids regularly for different indications or having a history of alcohol intake (>50 ml per week) and patients refusing to participate in the study were excluded.

Determination Of Nafld And Diabetic Status

Determination of non-alcoholic fatty liver disease was done by carrying out an abdominal ultrasound. B-mode USG was used to subjectively estimate the degree of fatty infiltration in the liver. "The grading of liver steatosis was based on features including liver brightness, contrast between the liver and the kidney, ultrasonographic appearance of the intrahepatic vessels, liver parenchyma and diaphragm. Steatosis was graded as follows: Absent (score 0) when the echotexture of the liver is normal; mild (score 1), when there is a slight and diffuse increase of liver echogenicity with normal visualization of the diaphragm and of the portal vein wall; moderate (score 2), in case of a moderate increase of liver echogenicity with slightly impaired appearance of the portal vein wall and the diaphragm; severe (score 3), in case of marked increase of liver echogenicity with poor or no visualization of portal vein wall, diaphragm, and posterior part of the right liver lobe[9].

Diabetic status was ascertained using the following criteria[10].

- HbA_{1c} 5.7-6.4% - Prediabetes
- $HbA_{1c} \geq 6.5\%$ - Diabetes

Level of glycemic control based on fasting and post-prandial blood sugar levels was also assessed

Fasting blood sugar

- < 100 mg/dl - Non-diabetic
- 100-125 mg/dl - Prediabetic
- >125 mg/dl - Diabetic

Post prandial blood sugar

- <140 mg/dl - Non-diabetic
- 140-199 mg/dl - Prediabetic
- >200 mg/dl - Diabetic

RESULTS

Total 200 cases were enrolled in the study, out of which 100 (50%) were prediabetic and remaining 100 (50%) were diabetic using HbA1c criteria as described in the materials and method section (Fig.1).

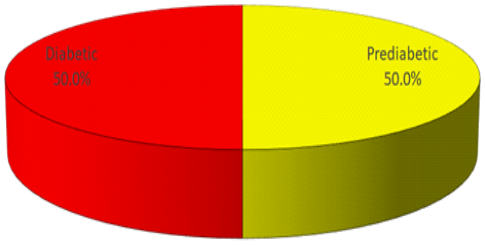

Fig. 1: Group wise distribution of study population

According to fasting blood glucose criteria, a total of 87 (43.5%) were normal, 59 (29.5%) were prediabetic and 54 (27%) were diabetic .According to post-prandial blood glucose criteria, a total of 56 (28.0%) were normal, 103 (51.5%) were prediabetic and 41 (20.5%) were diabetic (Table 1).

Table 1: Distribution of study population according to diabetic status using fasting and post-prandial blood glucose levels

SN	Variable	No. of cases	Percentage
1.	Fasting blood glucose		
	Normal (<100 mg/dl)	87	43.5
	Prediabetes (100-125 mg/dl)	59	29.5
	Diabetes (>125 mg/dl)	54	27.0
2.	PP Glucose		
	Normal (<140 mg/dl)	56	28.0
	Prediabetes (140-199 mg/dl)	103	51.5
	Diabetes (>200mg/dl)	41	20.5

Comparison of Demographic Profile of Cases in two study groups

Age of patients ranged from 18 to 81 years. Age of prediabetic patients ranged from 18 to 79 years with a mean age of 54±13.22 years. Age of diabetic patients on the other hand ranged from 31 to 81 years with a mean of 62.32±12.19 years. On evaluating the data statistically, the difference between two groups was found to be significant (p<0.001) (Table 2).

Table 2: Comparison of Demographic Profile of Cases in two study groups

SN	Variable	Prediabetes (n=100)		Diabetes (n=100)		Statistical significance	
		No.	%	No.	%	χ^2	'p'
1.	Mean age ± SD (Range) in years	54.00±13.22 (18-79)		62.32±12.19 (31-81)		't'=4.626; p<0.001	
2.	Sex						
	Male	51	51.0	66	66.0	4.634	0.031
	Female	49	49.0	34	34.0		

Comparison of BMI Profile of Cases in two study groups

Body mass index of patients ranged from 22 to 32 kg/m2. Only 39 patients in prediabetic and 26 in diabetic group had BMI in 18.5-24.99 kg/m2 range. Proportion of those with BMI ≥25 kg/m2 was 61% in prediabetic and 74% in diabetic group. Statistically this difference was significant (p=0.023). As far as mean BMI was concerned, it was also significantly higher in diabetic (26.76±1.87kg/m2) as compared to that in prediabetic (25.98±2.55 kg/m2) (p=0.014).(Table 3;Fig.2).

Table 3: Comparison of BMI Profile of Cases in two study groups

SN.	BMI Category	Prediabetes (n=100)		Diabetes (n=100)		Statistical significance	
		No.	%	No.	%	2	'p'
1.	18.5-24.99 kg/m²	39	39.0	26	26.0	7.507	0.023
2.	25.0-29.99 kg/ m²	56	56.0	73	73.0		
3.	≥30 kg/ m²	5	5.0	1	1.0		
	Mean BMI±SD (Range) kg/ m²	25.98±2.55 (22-32)		26.76±1.87 (24.01-31.81)		t=2.472; p=0.014	

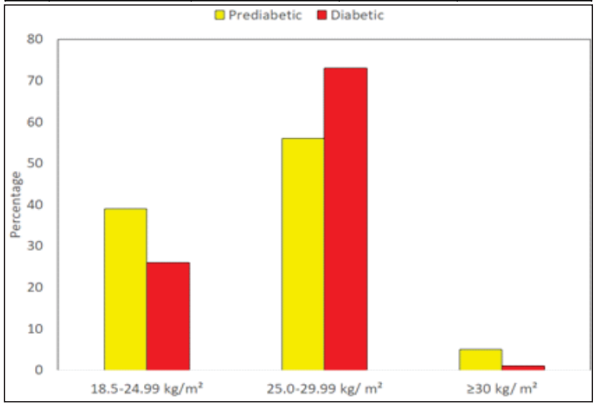

Fig. 2: Comparison of BMI status of prediabetic and diabetic patients

Majority of prediabetic patients did not have NAFLD (52%). Prevalence of Grade 1, 2 and 3 NAFLD was 32%, 13% and 3% respectively in prediabetic group. On the other hand majority of diabetic patients (54%) had NAFLD. Prevalence of Grade 1, 2 and 3 NAFLD was 34%, 18% and 2% respectively in diabetic group. Statistically, there was no significant difference between two groups with respect to prevalence of NAFLD and its grades (p=0.697) (Table 4; Fig.3).

Table 4: Comparison of two groups for NAFLD and its grades

SN	NAFLD and its grade	Prediabetes (n=100)		Diabetes (n=100)	
		No.	%	No.	%
1.	No NAFLD	52	52.0	46	46.0
2.	NAFLD Grade 1	32	32.0	34	34.0
3.	NAFLD Grade 2	13	13.0	18	18.0
4.	NAFLD Grade 3	3	3.0	2	2.0

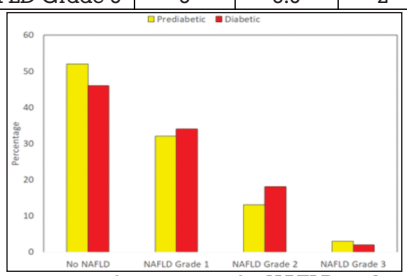

Fig. 3: Comparison of two groups for NAFLD and its grades

DISCUSSION

Relationship between non-alcoholic fatty liver disease and insulin resistance is considered to be bidirectional11. Pathogenesis of NAFLD is quite complex, no doubt systemic insulin resistance is a major driver, however, accumulation of lipids, oxidative stress, diet, microbial activity and genetic variation also have a dominant role12. Their coexistence may be primarily attributable to sharing of the pathogenic abnormalities of excess adiposity and insulin resistance13. However, it is difficult to find out which of these is predecessor of the other. In fact obesity is considered to be a more determining factor than diabetes. NAFLD prevalence in obese individuals is reported to be in 75-95% range14,15 whereas it is reported to affect nearly 50-75% of diabetic patients only16,17. In the present study we observed the prevalence of NAFLD was 48% in prediabetic and 54% in diabetic group . Compared to the present study, Mohan et al.18 in their study reported the prevalence of NAFLD in diabetic and prediabetic patient as 54.5% and 33% respectively and found this difference to be significant statistically. Additionally In another study, Kim et al.19 too found this difference to be 8.9% only between those with impaired fasting glucose and diabetes mellitus respectively and did not find such huge difference as observed by Mohan et al.18 in their study. In the present study, though we could not find a significant difference in prevalence of NAFLD between prediabetic and diabetic patients, however, some interesting facts emerged while evaluating this relationship. In the present study, we found that diabetic patients as compared to pre-diabetic patients were significantly older, had a higher proportion of males, higher BMI. These findings are interesting from the point of view that they tend to explain the higher risk of NAFLD in diabetic as compared to non-diabetic patients. In fact a number of previous studies have shown high prevalence of NAFLD even in normoglycemic individuals. Rajput and Ahlawat4 in a recent study reported the prevalence of NAFLD in 26% of normoglycemic individuals as compared to 59% prediabetic patients.

CONCLUSION

Prevalence of NAFLD was 48% in prediabetic and 54% in diabetic group. In prediabetic group, 32% had grade 1, 13% had grade 2 and 3% had grade 3 NAFLD whereas in diabetic group 34% had grade 1, 18% had grade 2 and 2% had grade 3 NAFLD. There was no significant difference between two groups for prevalence of NAFLD and its severity. On evaluating the association of NAFLD with different clinico-demographic variables, older age, a higher proportion of males and higher BMI were significantly associated with higher risk of NAFLD.

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