Prevalence of Non-alcoholic Fatty Liver Disease in Type 2 Diabetes Mellitus and its Association with Ischemic Heart Disease

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Abstract

Introduction: NAFLD disease entity comprises of Fatty Liver, Steatohepatitis, Cirrhosis as the disease progresses. NAFLD is the outcome of imbalance between mechanisms of triglyceride synthesis and triglyceride disposal. Diabetes Mellitus is an important risk factor for development of NAFLD, which enhance the lifetime risk of developing NAFLD by production of Cytokines that lead to insulin resistance and oxidative stress. Association of NAFLD with TYPE-2 DIABETES MELLITUS and Metabolic Syndrome makes the patient more prone to develop Ischemic Heart Disease. Hence it is important to establish the prevalence of NAFLD in Diabetics and to find out its association with Ischemic Heart Disease.

Objectives: 1. To find out prevalence of NAFLD in patients with TYPE-2 Diabetes Mellitus.
2. To find out association of IHD with NAFLD.

Methodology: A cross sectional study involving 300 patients was conducted in JLN Hospital Ajmer. It Included patients fulfilling inclusion criteria after ruling out the exclusion criteria. An initial screening in the form of detailed history taking and clinical examination was carried out to include/exclude the patients in the study. The Investigations used such as HbA1c, USG, 2D Echocardiography.

Results: among 300 patients studied NAFLD was present in 166 patients, it was absent in 134 patients, hence the prevalence of NAFLD was 55.3%. In our study, the prevalence of IHD was found 36.7% in total study participants. Statistically significant (P value <0.001) higher prevalence (51.8%) in NAFLD group than Non-NAFLD group (17.9%) was found in our study.

Conclusion: In our study it was observed that there is high prevalence of NAFLD in diabetic population. And being a state of ectopic fat deposition, NAFLD itself works as an independent risk factor for developing IHD.

Keywords: Diabetes Mellitus, Non-alcoholic fatty liver disease, ischemic heart disease, insulin.

Introduction

NAFLD is currently one of the most common causes of derangements in Liver functions. The spectrum of NAFLD includes nonalcoholic fatty liver, and non-alcoholic steatohepatitis (NASH), with or without fibrosis and cirrhosis. NAFLD is the outcome of imbalance between mechanisms of triglyceride synthesis and triglyceride disposal. Secondary causes of fatty infiltration must be checked out before NAFLD is diagnosed, such as lipodystrophy, malnutrition, Cushing's disease, and steatogenic drugs (corticosteroids, amiodarone, methotrexate, tamoxifen, and antiretroviral therapy) [1]. Type 2 Diabetes Mellitus is the leading disorder of our generation. Diabetes Mellitus is an important risk factor for development of NAFLD, which enhances the lifetime risk of developing NAFLD by production of Cytokines that lead to insulin resistance and oxidative stress. Population and hospital-based studies from the West report that around 10–24% of general population, and 57–74% of obese individuals may have NAFLD And the corresponding rates for NASH are 3–4%(in general population) and 15–20%(in obese individuals) respectively [2].

Association of NAFLD with TYPE-2 DIABETES MELLITUS and Metabolic Syndrome makes the patient more prone to develop Ischemic Heart Disease [3]. The prevalence of NAFLD is also variable in different studies. We carried out a cross sectional study to find out prevalence of NAFLD in Diabetic patients and to find out the association of NAFLD with IHD.

Materials and Methods

The cross sectional study consisting of 300 diabetic patients in the age group between 20-80 years fulfilling diagnostic criteria of diabetes mellitus, was conducted at JLN Medical College and Hospitals, Ajmer between September 2021 to September 2022. Exclusion criteria were 1) patients with daily alcohol consumption of >20g. 2) Patients with evidence of acute or chronic viral hepatitis. 3) Patients with evidence of Liver disease due to any other cause such as malignancies, Liver abscesses, Hemochromatosis, Wilson's disease. 4) Patients who are on hepatotoxic medications. 5) Patients having derangement of hepatic functions due to any other febrile illnesses/diseases. These 300 patients underwent ultrasonography, out of which 166 patients had fatty infiltration of liver including 5 patients with coarse echotexture of liver suggesting cirrhosis. It is known that ultrasonography has a sensitivity of ~90% and a specificity of ~95% in detection of moderate and severe hepatic steatosis, although ultrasonography is not totally sensitive, particularly when hepatic fat infiltration on liver biopsy is <30%. The presence of IHD was confirmed by reviewing hospital medical records of all patients and by a thorough physical examination that also included vascular laboratory studies (electrocardiogram and 2D- echo-Doppler, which were performed for all participants). Data on IHD were collected for those with and without NAFLD. These patients were subjected to a detailed history and physical examination.

Levels of glycosylated hemoglobin (HbA1C), aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase, total bilirubin, serum albumin, platelet count, prothrombin time (PT), total cholesterol, high density lipoprotein (HDL) cholesterol and triglycerides were measured

using standard techniques from fasting samples of these patients. LDL cholesterol levels were calculated using the Friedewald's formula. Serological markers of viral (HBsAg and HCV antibodies) and autoimmune hepatitis (antinuclear antibody, antimitochondrial antibody and anti-smooth muscle antibody) were estimated. Fatty liver was defined as the presence of an ultrasonographic pattern consistent with "bright liver," with evident ultrasonographic contrast between hepatic and renal parenchyma, vessel blurring, and narrowing of the lumen of the hepatic veins. Statistical analysis was performed using SPSS 20 software and the analyzed data was expressed in percentages. P-value equal to or less than 0.05 were considered to be significant.

Results

In our study, among 300 patients studied NAFLD was present in 166 patients, it was absent in 134 patients, hence the prevalence of NAFLD was 55.3%. In our study, among 300 subjects, the prevalence of NAFLD was found slightly higher in female (57.1%) compare to 53.8% in male.

This distribution was not statistically significant (P value >0.05). Age, Duration of Diabetes, Sex preponderance, Level of liver enzymes(AST and ALT) were not statistically significant in our study. In

comparison of parameters such as Total Cholesterol, HDL Cholesterol, LDL Cholesterol, Triglycerides, HbA1c between NAFLD and Non NAFLD groups, only HbA1c and LDL were found to be statistically significant (p value <0.05), rest other parameters were statistically not significant.

In our study, the prevalence of IHD was found 36.7% in total study participants. IHD was present in 86 out of 166 NAFLD patients (51.8%), it was present in 24 out of 134 non NAFLD patients (17.9%) depicting NAFLD as a risk factor for presence of IHD, Odds ratio = 4.927 (95% confidence interval: 2.882 to 8.424) Chi-square = 35.241 with 1 degree of freedom; P <0.001.

In our study, all above risk factors were found higher in NAFLD group than Non-NAFLD group. Among these risk factors serum HbA1c >7 was present in 54 (32.5%) NAFLD patients having IHD, 28 (20.9%) non NAFLD patients having IHD.

It was also observed that high LDL (>130 mg %) were found in 64 patients (38.6%) with NAFLD patients having IHD, 34 (25.4%) non NAFLD patients having IHD. This describes the risk factors serum HbA1c >7 and high LDL to be statistically significant (P value <0.05) and rest other risk factors to be statistically insignificant.

Table1: Age Distribution Between NAFLD and Non-NAFLD Group.

Age-group	Group					
	NAFLD		**Non-NAFLD**		**Total**	
N	%	N	%	N	%	
640 years	42	25.30%	28	20.90%	70	23.30%
41-50 years	60	36.10%	46	34.30%	106	35.30%
51-60 years	42	25.30%	36	26.90%	78	26.00%
>60 years	22	13.30%	24	17.90%	46	15.30%
Total	166	100.00%	134	100.00%	300	100.00%

Table 2 : Prevalence of NAFLD (Gender Distribution)

	NAFLD	Non NAFLD
Female	80(57.1%)	60(42.9%)
Male	86(53.8%)	7446.2%)
Total	166(55.3%)	134(44.7%)

Table 3: Comparison of Laboratory Parameters Between NAFLD And Non-NAFLD Group.

	NAFLD		Non-NAFLD		P value
	Mean	SD	Mean	SD	
FBS	106.27	11.55	106.46	9.52	0.874
PPBS	212.59	27.57	215.01	23.6	0.42
HbA1c	6.79	0.49	6.62	0.39	0.001
SCOT	30.61	10.16	30.55	6.72	0.951
SGPT	30.52	9.87	31.37	9.9	0.457
T. Cholesterol	217.54	34.32	214.69	37.68	0.493
TG	269.63	69.67	260.39	65.76	0.243
HDL	46.54	11.91	47.4	13.83	0.563
LDL	130.07	88.12	114.9	30.06	0.048

Table 4: Prevalence Of Ischemic Heart Disease In NAFLD And Non-NAFLD Group.

GROUP	N	IHD	%
NAFLD	166	86	51.8%
Non NAFLD	134	24	17.9%
Total	300	110	36.7%

Table 5: Prevalence of Risk Factors For IHD Between NAFLD And Non-NAFLD Groups.

Risk factors		NAFLD		Non-NAFLD		P value
		N	%	N	%	
HbA1c	> 7	54	32.50%	28	20.90%	0.025
T. Cholesterol	>200 mg%	124	74.7%,	92	68.70%	0.247
TG	>150 mg%	160	96.40%	126	94.00%	0.336
HDL	<40 mg%	64	38.60%	46	34.30%	0.450
LDL	> 130 mg%	64	38.60%	34	25.40%	0.022

Discussion

In our study, the prevalence of NAFLD is 55.3% whereas NAFLD was not found in 44.7% of the study participants. Similar to our study, in the study by AK Agarwal *et al* [2], the prevalence of NAFLD, was 57.2%. In our study the mean age of study participants was 48.48 ± 10.54 years. Age ranged from 28 to 84 years. It was observed in our study that non-NAFLD group had statistically not significant (P value >0.05) higher mean age than NAFLD group. The mean age for NAFLD group was 47.53±10.08 years, and for non NAFLD group it was 49.66±10.54 years. The majority of cases in our study were in age group 41-50 years in 106(35.3%) patients. This distribution was found not to be statistically significant (p value >0.05). In the study comparable to our study, Md Shahimur Parvez *et al* [4]. found that NAFLD group included 62 patients with mean age

45.8±12.46 years and non-NAFLD group of 38 subjects with mean age 45.32±10.56 years.

In our study, the prevalence of NAFLD was found slightly higher in females 57.1% compare to 53.8% in males. This distribution was not statistically significant (P value >0.05). In the study comparable to ours, by Sven H Loosen *et al* [5], the prevalence was slightly higher in females than males, 45.6% of NAFLD patients were females and 44.4% were males.

In our study, mean HbA1c was 6.79±0.49% in NAFLD group and 6.62±0.39% in non NAFLD group respectively which is higher in NAFLD patients than non-NAFLD, this data is statistically significant (P value <0.05). In the study by Targher G *et al* [1], the mean HbA1c is 7.3±1.1% in NAFLD group, 6.7±0.6% in non NAFLD group respectively.

In our study in NAFLD group, mean LDL levels were 130.07±88.12 mg%. In the study by Chatrath H *et al* [6], The dyslipidemia in NAFLD is characterized by increased serum triglycerides, increased low-density lipoprotein (LDL nontype A) particles, and low high-density lipoprotein (HDL) cholesterol, which is comparable to our study in terms of LDL.

In our study, the prevalence of IHD was found 36.7% in total study participants. IHD was present in 86 out of 166 NAFLD patients (51.8%), and in 24 out of 134 non NAFLD patients (17.9%) which was statistically significant (P value <0.001) in NAFLD group. In the study by AK Agarwal *et al* [7] the prevalence of CAD was 60.5% in NAFLD group and 45.2% in non NAFLD group, which is comparable to our study.

In our study among the risk factors for IHD in NAFLD patients, only HbA1c and LDL were statistically significant. Which was comparable to the study by Amna S Butt *et al* [8]

Conclusion

There is a pressing unmet requirement to determine the prevalence of NAFLD in the type 2 diabetic patients and to figure out its association with IHD. It has only recently been recognized that NAFLD represents an important burden of disease for patients with type 2 diabetes(considered as liver manifestation of metabolic syndrome), but the magnitude of the problem of NAFLD in patients with type 2 diabetes is currently unknown.

It is also becoming evident that NAFLD is related to IHD in people with type 2 diabetes , but further research in this area is required to ascertain whether NAFLD is a (independent) cardiovascular risk factor. Indeed, the effect of NAFLD on IHD risk deserves particular attention in view of the implications for screening/ surveillance strategies in the growing number of patients with NAFLD. So that the diabetic population can be saved from this risk.

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