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Research Article

**THE PREVALENCE OF NON-ALCOHOLIC FATTY LIVER
DISEASE IN TYPE II DIABETES MELLITUS PATIENTS IN
LAHORE**

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Abstract:

Introduction: Nonalcoholic fatty liver disease (NAFLD) is diagnosed when >5% hepatic macrovesicular steatosis identified either by histology or imaging in absence of alcohol intake. NAFLD has been regarded as a hepatic manifestation of metabolic syndrome and has been found to be associated with obesity, diabetes mellitus type 2 (T2DM). The aim of this study was to evaluate the frequency of NAFLD in diabetic patients of Northern Pakistan and assess the determining factors.

Methods: A cross-sectional, observational study was conducted in Punjab Ranjers Teaching Hospital, Lahore for duration of six months from 1st November 2019 to 30th April 2020. Consecutive, non-probability sampling technique was adopted. All patients of age 30 years or above, of both genders, known cases of T2DM for at least one year, and strictly non-alcoholic presenting in the outpatient department were included. Their demographic, clinical, and biochemical profile was recorded. Data was entered and analyzed using SPSS for Windows version 20.0.

Results: The study was completed by 145 participants. There were 67 (46.2%) males and 78 (53.8%) females. The mean age of the participants was 57.3 ± 12.5 years (range: 30-78 years). The mean duration of diabetes was 8.8 ± 6.2 years (range: 2-18 years). Mean BMI was 30 ± 5.5 , and HbA1c was 7.9 ± 2.1 (range: 7.3-8.8).

Conclusion: Type – 2 diabetic patients with metabolic syndrome having raised BMI, serum cholesterol and triglycerides are more prone to NAFLD. Currently T2DM patient are not routinely screened for NAFLD.

Keywords: Diabetes mellitus (DM), Fatty liver, Hepatic steatosis, NAFLD

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INTRODUCTION:

Nonalcoholic fatty liver disease (NAFLD) is diagnosed when >5% hepatic macrovesicular steatosis identified either by histology or imaging in absence of any secondary cause such as alcohol intake^[1]. It comprises of a spectrum of diseases including simple steatosis, nonalcoholic steatohepatitis (NASH), advanced fibrosis, cirrhosis, and hepatocellular carcinoma. NAFLD has been regarded as a hepatic manifestation of metabolic syndrome and has been found to be associated with obesity, diabetes mellitus type 2 (T2DM), and dyslipidemia^[2].

NAFLD has become a global health concern with a pooled prevalence of 25% among the general population diagnosed by imaging^[3]. In T2DM, the prevalence of NAFLD is as high as 56%^[4]. In 20% biopsy-proven NASH cases in asymptomatic T2DM, liver function tests (LFTs) were in range^[5], which indicates that liver enzymes alone are not an efficacious indicator of intrahepatic fat accumulation. In presence of T2DM, NAFLD worsens glycemic control and predisposes to diabetic complications including chronic kidney disease and cardiovascular complications^[4]. High serum triglycerides and serum alanine aminotransferase (ALT) were also associated with NAFLD in T2DM patients. These patients were more prone to obesity especially increased waist circumference^[6].

Despite such a glaring incidence of NAFLD in T2DM and establishment of its grave implications on the progression of diabetes, the guidelines recommending NAFLD screening in diabetic patients are controversial. American Association for the Study of Liver Diseases (AASLD) does not routinely recommend NAFLD screening in T2DM in view of lack of evidence regarding cost-effectiveness and long-term benefits of screening^[7]. The European Association for the Study of the Liver (EASL) recommended NAFLD screening in T2DM, even if serum LFTs are in range in view of its high incidence^[8].

The incidence of NAFLD has been studied in the diabetic population of Pakistan. The reported incidence has been as high as 60-72% in Southern Pakistan^[9, 10]. The aim of this study was to evaluate the frequency of NAFLD in diabetic patients of Northern Pakistan and assess the determining factors.

MATERIAL AND METHODS

A prospective, cross-sectional, observational study was conducted in Punjab Ranjers Teaching Hospital, Lahore for duration of six months from 1st November 2019 to 30th April 2020. The study was approved by institutional review board. Informed consent was attained from all participants.

Consecutive, non-probability sampling technique was adopted. All patients presenting in the outpatient department of age 30 years or above, of both genders, known cases of T2DM for at least one year, and strictly non-alcoholic were invited to participate. Patients with known liver disorders such as hepatitis and others were excluded. Current or previous alcohol drinkers were excluded. Patients taking steroids, statins, pioglitazone, amiodarone, and oral contraceptive pills were excluded as all these drugs alter serum LFTs. Pregnant women were not included. Patients of type 1 diabetes were also excluded.

For all patients who were included after fulfilling the inclusion criteria and providing written informed consent, blood samples were obtained for serum lipid profile and serum LFTs according to the standard hospital procedure. Upper abdominal ultrasound (US) with Sonoline 450 (B-Mode probe 3.5 MHZ) was done to identify hepatic steatosis.

A semi-structured proforma was used to record their demographic data – age, gender, body weight and height, clinical data – duration of diabetes, comorbidity status, presenting complaints and biochemical profile – glycosylated hemoglobin (HbA1c), serum LFTs and lipid profile of the patients. SPSS for Windows version 20.0 was used enter and analyze the data. For categorical variables frequencies and percentages were calculated. For continuous variables mean and standard deviation (SD) was calculated.

RESULTS:

The study was completed by 145 participants. There were 67 (46.2%) males and 78 (53.8%) females. The mean age of the participants was 57.3 ± 12.5 years (range: 30-78 years). The mean duration of diabetes was 8.8 ± 6.2 years (range: 2-18 years). Mean BMI was 30 ± 5.5 , and HbA1c was 7.9 ± 2.1 (range: 7.3-8.8). Demographic and clinical characteristics are shown in table 1.

Baseline Characteristics		Frequency (%)
Gender	Male	67 (46.2%)
	Female	78 (53.8%)
Age, years	Mean	57.3 ± 12.5
	30-39	16 (11%)
	40-49	78 (53.7%)
	50-59	29 (20%)
	60-69	12 (8.2%)
	70 and above	10 (6.8%)
Co-morbidity status	Hypertension	
	Ischemic heart disease	
	Others	
Diabetic complications	Peripheral neuropathy	
	Peripheral arterial disease	
	Chronic renal disease	
	Retinopathy	
Body mass index, kg/m²	Mean	30 ± 5.5
	Less than 30	71 (49.0%)
	30 and above	74 (51.0%)
Presenting complaints	Generalized itching	
	Generalized weakness	93 (64.1%)
	Fatigue	100 (68.9%)
	Right upper abdominal heaviness	
	Right upper abdominal pain	

On abdominal US, 74 (51.0%) patients were diagnosed with NAFLD. Among these patients, 73 (97.3%) had mild hepatomegaly on US. None of the patients in non-NAFLD group had hepatomegaly. In NAFLD group the mean liver size was 17.2 ± 3.1 cm as compared to 13 ± 2.4 cm in the non-NAFLD group. The characteristics of both groups are compared in table 2.

Patient characteristics		NAFLD (%)	Non NAFLD (%)	P value
Gender	Male			
	Female			
Age, years	Mean			
	30-39			
	40-49			
	50-59			
	60-69			
	70 and above			
Co-morbidity status	Hypertension			
	Ischemic heart disease			
	Others			
Diabetic complications	Peripheral neuropathy			
	Peripheral arterial disease			
	Chronic renal disease			
	Retinopathy			
	Mean			

Body mass index, kg/m²	Less than 30			
	30 and above			
Presenting complaints	Generalized itching			
	Generalized weakness	46		
	Fatigue	53		
	Right upper abdominal heaviness	32%		
	Right upper abdominal pain	42%		
Biochemical profile	Triglycerides (>150 mg/dl)	47 (32.4%)	39 (26.8%)	
	Cholesterol (>200 mg/dl)	24 (16.5%)	18 (12.4%)	
	Alkaline phosphatase (>300 u/l)	8 (5.5%)	5 (3.4%)	
	Alanine Aminotransferases (>40 u/l)	6 (4.1%)	6 (4.1%)	

NAFLD was less common in old age men ex-smoker or current smoker.

Prevalence of HTN, Hyper triglyceridemia HDL and cholesterol had no significant difference in patients having NAFLD compared to those who don't have NAFLD. Similarly, there was no difference in the apparent severity of diabetes with HbA1c values between the two groups. Further, the treatment regimens for diabetes and use of medication for hypertension and hyperlipidemia were similar between the two groups.

DISCUSSION:

The incidence of NAFLD among our diabetic population is high.

It is predicated that the prevalence of NAFLD and its complications is increasing and will be double by the year 2025.⁹ By understanding, the difference in prevalence of hepatic steatosis and steatosis related liver injury in different ethnic people will help to develop new treatment options and prevention method. NAFLD which is common hepatic disorder is commonly seen in obese and diabetic patients.

Different studies showed different prevalence in different area. Usually NAFLD is asymptomatic in Diabetic patient. A study was done in Karachi by Luxemi et al. which examined 120 diabetic patients and found that 60.8% had NAFLD.¹⁰

A study was also conducted in Japan in which impaired glucose metabolism was independently detected in healthy middle-aged Japanese adults with 29% prevalence of NAFLD¹¹. Another study which was conducted in Italy showed the prevalence of 20%.¹² Mean while in US 20% of the general population had NAFLD.¹³ Akbar et al in Saudi Arabia done a study in type 2 DM and found that

55% had NAFLD.¹⁴ In India Gupta et al study showed that 49% of Diabetic patients had NAFLD.¹⁵ In our study, the Frequency of NAFLD is 51% which is close to the results from India and other studies conducted in Pakistan. We took abdominal ultrasound as sole entity for the diagnosis of NAFLD, which is having high sensitivity and specificity if the liver fat content is more than 33% but if the liver fat content is less than 33% then liver biopsy is the best diagnostic tool.

NAFLD patients are asymptomatic in initial phase but later on they become symptomatic with main complaints of fatigue and right upper abdomen heaviness which is evident from multiple studies. In our study fatigue was noted as chief complaint in 145 diabetics, out of which, 53 were having fatty liver. Generalized body weakness was observed in 93, out of which 46 (31.7%) were having NAFLD. Among patients with fatty liver disease, pain right upper abdomen was present in 42 and heaviness in right upper abdomen in 32 (64.70%). Most of the symptoms in NAFLD were because of stretching of the liver capsule i.e. right upper abdomen pain and heaviness. Result from wing kin synetal shows that fatigue and heaviness were the two important symptoms of the 33% patients¹⁶. Diabetic's mellitus is an important risk factor for NAFLD.

CONCLUSION:

Type – 2 diabetic patients with metabolic syndrome having raised BMI, serum cholesterol and triglycerides are more prone to NAFLD. Currently T2DM patient are not routinely screened for NAFLD.

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