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ORIGINAL ARTICLE

Non-Alcoholic fatty liver disease in type 2 diabetes mellitus: A dangerous duo.

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ABSTRACT… Objective: To determine the frequency of nonalcoholic fatty liver disease in type 2 diabetes mellitus. **Study Design:** Cross sectional study. **Setting:** Department of Medicine Ayub Teaching Hospital Abbottabad. **Period:** August 2018 to Feb 2019. **Material & Methods:** A total of 153 patients, who were diagnosed case of diabetes were studied for the presence of NAFLD. Ultrasound abdomen was used to detect NAFLD. Data was recorded on a pro forma and analyzed using SPSS 20 version. **Results:** Out of 153 patients, there were 73 males (45.8%) whiles 83 females (54.2%). Patients were aged 30 – 80 years with mean ± SD as 54.60± 11.277 years. The mean duration of diabetes was 7.18±6.95 years. In our study 54.9 % (84) of the patients were having fatty liver on U/S scan, 35.3% have abnormal lipid profile and 35.3 % (54) were hypertensive, out of which 59.3% (32) were having fatty liver on scan with P value of 0.424. **Conclusions:** Type 2 diabetes patients have increased risk of development of NAFLD, prevalence being 54.9%. Post-menopausal females and those with dyslipidemia have more risk of developing of NAFLD among diabetics.

Key words: Metabolic Syndrome, Nonalcoholic Fatty Liver Disease, Type 2 Diabetes Mellitus.

INTRODUCTION

Nonalcoholic fatty liver disease (NAFLD) is the most prevalent form of liver diseases in western world.[1] It is defined as "the presence of increased hepatic fat content, which is mainly stored in the form of neutral lipids within intracellular droplets and is not explained by at risk of alcohol.[2]

The prevalence of NAFLD in general population lies in range of 15-30% in various countries.[3-5] Its spectrum ranges from simple fatty liver changes to nonalcoholic steatohepatitis (NASH), which can lead to end stage liver disease (i.e. cirrhosis, liver failure and hepatocellular carcinoma (HCC).[6] NAFLD is a hepatic presentation of metabolic syndrome and is closely related to other components of syndrome, which include type 2 diabetes mellitus (T2DM), insulin resistance, increased body mass index (BMI) and dyslipidemias.[7-12]

NAFLD and T2DM are the most common diseases of western world[13] and there exists a complex bidirectional relationship between them.[12,14-17] The prevalence of NAFLD in T2DM patients is 59.67% and this is expected to escalate further in near future.[13] Recent data suggests that both T2DM and NAFLD share common pathophysiological pathways (i.e. pro-fibrotic and pro-inflammatory) and cardio metabolic risk factors.[12,14-17] Patients with T2DM have higher risks of developing NAFLD and there are 2 to 4 times increased risk of progressing to life threatening end stage liver disease.[17-20]

The purpose of our study was to know the frequency of fatty liver disease in DM and its correlation with different parameter. The aim was that if we find a higher prevalence then we can recommend to the health authorities to devise a plan and give recommendations where by all the diabetic patients are regularly screened for NAFLD, and appropriate measures are taken to prevent or manage them. Thus our study would

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help in the better management of DM and its complication like fatty liver disease which can become fatal causing liver failure.

MATERIAL & METHODS

This cross sectional study was performed on all diagnosed diabetic patients admitted in the Medical units or presenting to the medical OPD of Ayub Teaching Hospital Abbottabad. The study was conducted from 1st August 2018 to 28th February 2019. One hundred and fifty three patients were included through non probability consecutive sampling. After getting approval from the hospital ethics committee, data was collected and an informed consent was taken from the patient or his/her next of kin. A detailed history was taken and complete physical examination was performed including measurement of the patient's weight and height to find body mass index (BMI). Age limit was defined and data was collected from all patients whether it was newly diagnosed or old diabetics, aged 30 years and above. Sample size was calculated with WHO sample size formula with prevalence of NAFLD of 59.6% with 7.79% Standard error.[13] Those who had history of alcohol drinking, liver cirrhosis, hepatocellular carcinoma, liver viral infection (hepatitis B and C positive), previous history of cholecystectomy and liver failure were excluded from sample size. A strict exclusion criterion was used to control confronting. Those taken in sample size were sent for ultrasound (U/S) to radiology department to look for fatty liver disease on U/S scan. The scan was performed by same radiologist on every patient. Patient's kidney function test and lipid profile and alkaline transaminase was send to hospital laboratory and was performed by same biochemist.

Data was analyzed using SPSS 20.0. Quantitative variables like age and dyslipidemia were described as mean + standard deviation. Categorical variables like gender, fatty liver disease were described as frequencies and percentages. Data was stratified by gender and BMI, and duration of DM and analyzed. To know the significant difference between fatty liver disease by gender, hypertension, dyslipidemia and BMI, chi square test at 5% significant level was used.

RESULTS

The study sample consists of 153 patients of either sex who had been diagnosed with diabetes mellitus. The youngest study participant was 30 years old and the age of the oldest study participant was 80 years with mean ± SD as 54.60± 11.277 years. There were 73 males (45.8%) whiles 83 females (54.2%).Mean duration of diabetes was 7.18±6.95 years. In our study 54.9 % (84) of the patients were having fatty liver on U/S scan, 35.3% have abnormal lipid profile and 35.3 % (54) were hypertensive, out of which 59.3% (32) were having fatty liver on scan with P value of 0.424. 66% of patients were using oral anti-diabetics while 53.6% were using insulin. In 75.81 % (116) of the patients kidney functions (urea, creatinine) was abnormal with correlation with fatty liver disease was not significant with P value of 0.102. The basic characteristic of patient is shown in Table-I, while the association of duration of Diabetes with NAFLD is shown in Figure-1, while Table-II shows association between BMI and NAFLD.

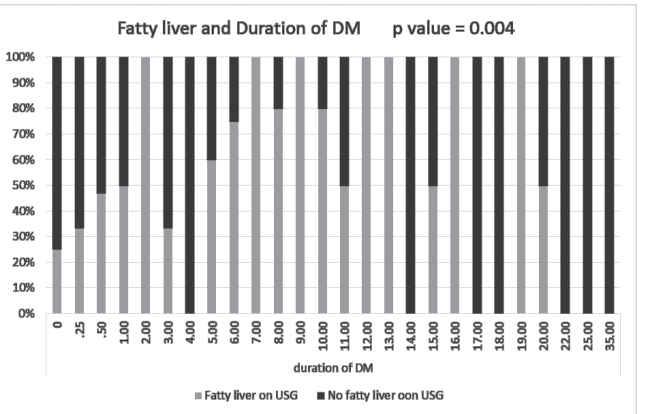

Figure-1. Association of fatty liver with duration of diabetes:

DISCUSSION

NAFLD is the commonest form of CLD worldwide. T2DM is not only an important risk factor for NAFLD but it also speeds up the progression of liver disease in NAFLD. Despite of these facts NAFLD in T2DM is usually overlooked by endocrinologists as well as by medical physicians in their clinical practice.[21]

Our study is an initiative towards screening the vast subject of liver diseases in T2DM found in Pakistan.

		Total	Fatty Liver on USG		P-Value
			Yes (%)	No (%)	
Patient Gender	Male	70	30(42.9)	40(57.1)	.006
	Female	83	54(65.1)	29(34.9)	
Oral Anti Diabetic Agents	Yes	101	60(59.4)	41(40.6)	.119
	No	52	24(46.2)	28(53.8)	
Insulin Usage	Yes	82	56(68.3)	26(31.7)	<.001
	No	71	28(39.4)	43(60.6)	
Dyslipidemia	Yes	54	44(81.5)	10(18.5)	<.001
	No	99	40(40.4)	59(59.6)	
ALT	Normal	149	80(53.7)	69(46.3)	.066
	Raised	4	4(100)	0	

Table-I. Demographics and basic characteristics of patients. The Chi-square statistic is significant at the 0.05 level.

Fatty Liver on Scan	Body Mass index (BMI)					P-Value
	Underweight <18.5 %(n)	Normal 18.5-24.9 %(n)	Overweight 25-29.9 %(n)	Obese 30-34.9 %(n)	Severely Obese 35-39.9 %(n)	
Yes	50%(2)	54.3%(38)	50.9%(28)	72.7%(16)	0.0%(0)	0.226
No	50%(2)	45.7%(32)	49.1%(27)	27.3%(6)	100%(2)	

Table-II. Association of BMI with fatty liver disease.

According to our study the overall prevalence of NAFLD in T2DM is 54.9%, which is similar to global prevalence of NAFLD in T2DM i.e. 55.5%.[22] Our results are also consistent with its prevalence in US i.e. 51.8%. Pooled prevalence of NAFLD in T2DM according to one another meta-analysis conducted in 2017 was 59.69%.[23] However, our result contradicts the study conducted by Targher G et al in 2007; according to them the prevalence is found to be 69.5%.[24] Slight variations among studies have been found and this is due to reason we used ultrasound as diagnostic tool for determining NAFLD while other studies used other parameters too like aminotransferases level, liver biopsy, ^{1}H-nuclear magnetic resonance spectra of the liver.

Our study suggests that NAFLD is more prevalent in females (65.1%) than males (42.9%) that totally contradicts results of studies done in past. According to Targher G et al prevalence of NAFLD was 71.1% in men and 68% in women.[24] 2017 meta-analysis conducted by Dai W and colleagues also depicted same results i.e. the pooled prevalence was 60.11% and 59.35% in male and female T2DM patients, respectively.[23] These studies showed that female gender is a protective factor for NAFLD and this is due to reason female hormones are protective in nature. Also higher triglyceride to high density lipoprotein ratio in males than females make them more vulnerable to NAFLD. One reason why we found higher NAFLD ratio in female is that in our study most of the females were aged over 45 and most of them were in post-menopausal stage.

Our study also suggests that elements of metabolic syndrome (dyslipidemia, hypertension and higher BMI) are also independent risk factors for development of NAFLD among T2DM patients. Though our results for hypertension and higher BMI are not statistically significant ($p>0.05$) but they are consistent with results of previous studies done by Björkström K et all[25], Dai W et all[23] and Portillo-Sanchez P et all.[26]

Raed et al[27] observed that the serum levels of aminotransferases in diabetic patients have no relationship with the prevalence of NAFLD in diabetics. This finding is in accordance with our study as we have observed that 53.7% of diabetic patients with NAFLD had raised ALT levels compared to 46.3% diabetic patients who did not have NAFLD ($p=.066$).

We observed that patients who were on insulin were less likely to develop NAFLD compared to patients on oral anti diabetic drugs. This finding was statistically significant (p=<.001). Further studies need to be done to confirm this finding.

Our study has certain strengths. NAFLD comprises a spectrum of diseases ranging from simple fatty liver to steatohepatitis to liver cirrhosis. Its association with type 2 diabetes mellitus has been well documented. However, no study to date was performed on its prevalence in the Hazara division. Secondly, we found that the frequency of NAFLD is very high (54.9%) and therefore we recommend a regular NAFLD screening program in patients with diabetes mellitus. Finally, we have provided important inferences regarding usage of insulin, BMI and dyslipidemia association with NAFLD. These findings need further evaluation and assessment.

Our study is not without limitations. First our sample size was small and secondly our sample mostly consist of diabetics with age between 50 to 70 years with diabetes duration of 10 to 15 years and old aged people with higher duration either did not cooperate or did not give consent to be part of study.

CONCLUSIONS

T2DM patients have increased risk of development of NAFLD, prevalence being 54.9%. Post-menopausal females have more risk than males and elements of metabolic syndrome i.e. increased BMI, hypertension and dyslipidemia being independent risk factors for increase chances of development of NAFLD among diabetics.

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AUTHORSHIP AND CONTRIBUTION DECLARATION

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2	Sabir Khan Khattak	Data collection, Statistical analysis, Manuscript / Study design.	
3	Asim Ali Shah	Proof reading, Literature review.	
4	Ayesha Akhtar	Data collection, Study Methodology, Proof reading.	