IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 20, Issue 2 Ser.4 (February. 2021), PP 53-57
www.iosrjournals.org

Frequency of Non-Alcoholic Fatty Liver Disease in Patients with Type 2 Diabetes Mellitus and Its Relationship with Glycemic Status: an Observational Study

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Abstract:
Background*: Non-alcoholic fatty liver disease (NAFLD) and type 2 diabetes mellitus (T2DM) may coexist in many individuals. This study was conducted to observe the frequency of NAFLD in Bangladeshi T2DM patients and to compare the glycemic status in T2DM patients with and without NAFLD.*
Materials and methods: *Total 80 (eighty) previously known cases of T2DM were included as per inclusion and exclusion criteria. All patients underwent abdominal ultrasound to detect fatty liver. NAFLD was diagnosed after excluding other causes of liver diseases. Clinical and biochemical data were recorded and compared among T2DM patients with and without NAFLD.*
Results: *Overall frequency of NAFLD in T2DM was 60%. Frequency among male and female T2DM patients was comparable (58.1% vs 62.2%, P 0.714). Frequency increases with age and highest frequency was found in age group 50-59 years (62.2%). Body mass index (BMI) and SGPT were significantly higher in NAFLD compared to non-NAFLD where age, duration of diabetes, fasting plasma glucose (FPG), plasma glucose 2 hours after breakfast (ABF) and HbA1c were comparable (BMI 27.8±4.9 vs 24.7±3.2 kg/m^2, P 0.006; SGPT 47.0±25.3 vs 31.9±13.3 IU/L, P 0.001; age 52.5±8.2 vs 51.1±9.2 years, P 0.349; duration of DM 5.1±3.8 vs 5.7±3.1 years, P 0.460; FPG 9.1±2.8 vs 9.4±2.1 mmol/L, P0.220; ABF 14.7±4.8 vs 14.8±3.6 mmol/L, P 0.092; HbA1c 8.9±1.9 vs 8.8±1.2%, P 0.065 respectively).*
Conclusions: *NAFLD is very common in Bangladeshi T2DM patients. Degree of hyperglycemia is comparable in T2DM patients with and without NAFLD.*
Keywords:*Non-alcoholic fatty liver disease (NAFLD), Type 2 diabetes mellitus (T2DM), Glycemic status, Insulin Resistance, Metabolic syndrome.*

Date of Submission: 29-01-2021 Date of Acceptance: 14-02-2021

I. Introduction

Non-alcoholic fatty liver disease (NAFLD) is a common metabolic disorder involving liver which is now considered as the most common cause of chronic liver disease[1]. NAFLD is characterized by accumulation of excess fat in liver in the absence of excess alcohol consumption with exclusion of identifiable causes of chronic liver disease[2]. NAFLD includes a series of pathological conditions of liver which range from simple steatosis (NAFL), nonalcoholic steatohepatitis (NASH), cirrhosis of liver and hepatocellular carcinoma[2]. Prevalence of NAFLD varies in different studies conducted on population of different ethnicities. Population of South East Asian region has more risk of developing NAFLD than other ethnic population. Some studies in Indian subcontinent suggested that prevalence of NAFLD varies from 16% to 32% in urban population and 9% to 16% in rural population[3,4,5]. Exact prevalence of NAFLD is not known in Bangladesh. One study suggested 33.86% of Bangladeshi population is affected with NAFLD[6].

As there is a close relationship between metabolic syndrome (MS) and NAFLD, it is often considered as hepatic manifestation of metabolic syndrome. As hyperglycemia is an important component of MS, NAFLD and type 2 diabetes mellitus (T2DM) may coexist in many individuals. Many studies found higher prevalence of NAFLD in patients with T2DM. One meta-analysis suggested overall prevalence of NAFLD in T2DM is about 54%[7]. Exact prevalence of NAFLD in Bangladeshi T2DM patients is still unknown. Very few studies had been conducted in this issue. Moreover relationship of NAFLD with glycemic status in type 2 diabetic patients is still controversial. This study was conducted to observe the frequency of NAFLD in T2DM patients and to compare different parameters of glycemic status including fasting plasma glucose (FPG), plasma glucose 2 hours after breakfast (ABF) &glycated hemoglobin (HbA1c) in T2DM patients with and without NAFLD.

II. Material And Methods

This cross sectional observational study was conducted in department of Endocrinology and Gastroenterology of US- Bangla Medical College and Hospital from July 2019 to March 2020. Previously known cases of T2DM with age 35 to 75 years were enrolled as study sample. Patients with history of alcohol and hepatotoxic drug intake were excluded. Patients with family history of chronic liver diseases other than NAFLD and who were positive for viral marker screening like HBsAg or anti HCV were also excluded. Pregnant and lactating mother or previously known case of liver and renal diseases or patients suffering from any acute illness or chronic diseases or patients who refused to take part in the study were not enrolled. Total 80 (eighty) cases of T2DM were taken as per inclusion and exclusion criteria. Various demographic, anthropometric and biochemical data was recorded in a data collection sheet. Standing height and weight were measured in centimeters (cm) and kilograms (kg) respectively by appropriate measuring scale and body mass index (BMI) was measured by the formula: BMI (kg/m^2)= weight (kg)/ [height (m)]^2. Blood samples for FPG, HbA1c and SGPT were collected after overnight fasting at least for 8 hours. Blood sample for ABF was collected 2 hours after taking usual breakfast. FPG, ABF, HbA1c and SGPT were measured by enzymatic method in SeLECTRA PRO M, France

All patients underwent ultrasonography (USG) of whole abdomen for detecting NAFLD by an ultrasound machine Mindray DC-30, China. NAFLD was classified based on standard USG criteria. Grade 1 (mild steatosis) includes slightly increased hepatic echogenicity with normal vessels and absent posterior attenuation. Grade 2 (moderate steatosis) includes moderate increase of hepatic echogenicity with partial dimming of vessels and early posterior attenuation. Grade 3 includes diffuse increased hepatic echogenicity with absence of visible vessels and heavy posterior attenuation. All USG was done by an expert radiologist with same machine.

After editing and coding, data were entered and analyzed by using Statistical Package for the Social Science (SPSS version 22.0). Quantitative data were expressed as mean ± standard deviation (SD) and were compared between NAFLD group and non-NAFLD group using student's t test. Qualitative variables were expressed as frequencies in percentages and were compared by $\chi 2$ test. A *P* value less than 0.05 was considered as statistically significant.

III. Result

Total 80 (eighty) cases of type 2 DM were included in the study where 43 were male and 37 were female. Figure 1 shows, total 48 cases had USG evidence of NAFLD (60%).

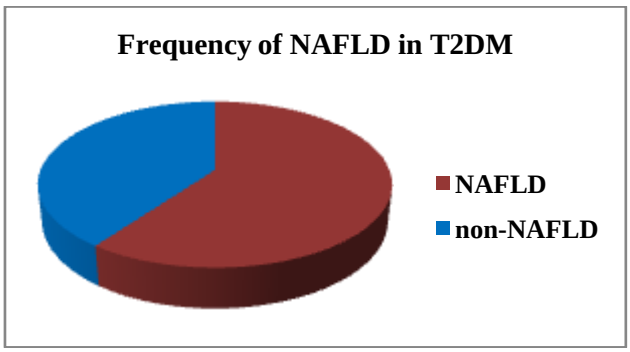

Figure 1: Frequency of NAFLD in T2DM patients

Figure 2 shows USG grading of fatty liver among T2DM patients which indicates most of cases are grade 1 (75%) where grade 2 and 3 contributes very few case (20.8% and 4.2% respectively).

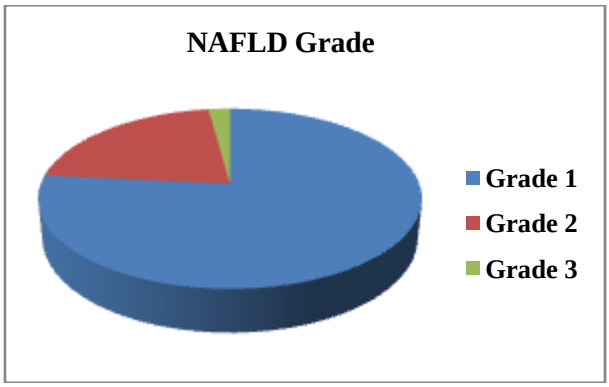

Figure 2: Distribution of USG based different grade of fatty liver among type 2 diabetic patients

Figure 3 shows sex distribution of NAFLD in type 2 diabetes patients which shows 25 male patients and 23 female patients had NAFLD (58.1% and 62.2% respectively; *P* 0.714).

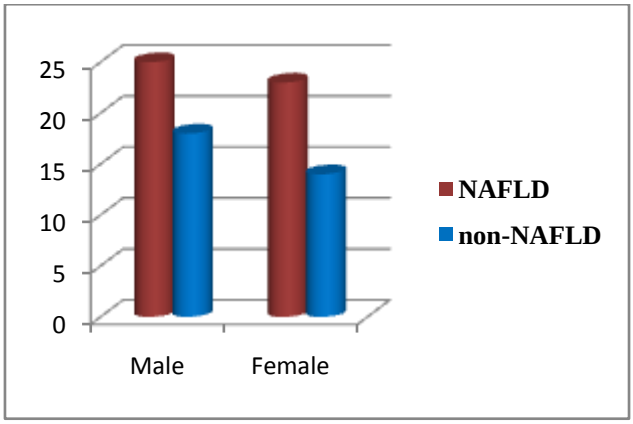

Figure 3: Sex distribution of study subjects with and without NAFLD

Table 1 shows age group wise distribution of study subjects. It shows relatively higher frequency of NAFLD in elderly T2DM patients than young individuals although difference was not significant. NAFLD in T2DM was most frequently observed in age group 50-59 years (62.2%).

Table 1

Age distribution of T2DM patients with and without NAFLD

Age groups (years)	Total (n=80)	NAFLD (n=48)	Non-NAFLD (n=32)	*P* value
<40	4	2(50%)	2(50%)	0.967
40-49	29	17(58.6%)	12(41.4%)	
50-59	37	23(62.2%)	14(37.8%)	
≥60	10	6(60%)	4(40%)	

Percentage measured from individual age group total
***P* <0.05 is statistically significant**

Table 2 shows comparison of different characteristics of type 2 diabetic patients with and without NAFLD which indicates significantly higher BMI and SGPT in NAFLD group, where different measures of glycemic status including FBG, ABF, HbA1c and duration of diabetes are comparable between the groups.

Table 2

Comparison of different demographic, anthropometric and biochemical data between T2DM patients with and without NAFLD

Characteristics	NAFLD (n=48)	Non-NAFLD (n=32)	*P* value
Age (years)	52.5±8.2	51.1±9.2	0.349
BMI (kg/m^2)	27.8±4.9	24.7±3.2	0.006*
Duration of DM (years)	5.1±3.8	5.7±3.1	0.460
SGPT (IU/L)	47.0±25.3	31.9±13.3	0.001*
FBG (mmol/L)	9.1±2.8	9.4±2.1	0.220
ABF (mmol/L)	14.7±4.8	14.8±3.6	0.092
HbA1c (%)	8.9±1.9	8.8±1.2	0.065

***P* <0.05 is statistically significant**

IV. Discussion

NAFLD represents a spectrum of disorders characterized by predominantly macro-vesicular steatosis in liver which occurs in persons in the absence of consumption of alcohol in amounts assumed harmful to liver[8]. As NAFLD and T2DM both are associated with metabolic syndrome, these common disorders may exist together. This study was conducted to observe the frequency of NAFLD as diagnosed by USG among the patients of T2DM and to compare different anthropometric and biochemical data between T2DM patients with and without NAFLD.

It has been well established that patients with T2DM has higher prevalence of NAFLD than general population[7,9]. In this study, frequency of NAFLD in T2DM patients was 60%. A previous study in India found prevalence of NAFLD in T2DM was 56.5% which supports our result[11]. One meta-analysis also found pooled prevalence of NAFLD in type 2 diabetic individuals was about 54% which also supports our finding[7]. One recent study conducted in Bangladesh found slightly higher prevalence of NAFLD in T2DM (67%) than our finding[10]. Higher prevalence of NAFLD in T2DM may be due to its main pathogenesis, Insulin Resistance (IR). IR in liver and extra-hepatic tissues like adipose tissue and skeletal muscle act synergistically leading to systemic inflammation which causes the release of proatherogenic and nephrotoxic factors[12]. Increased influx of free fatty acid to ectopic tissue due to excessive lipolysis causes muscle and liver to develop IR and apoptosis[13]. Thus lipotoxic state in NASH results in hepatocyte necroinflammation[13]. Thus DM and IR do not only increases the chance to develop NAFLD, but also increases the progression of the disease to NASH and cirrhosis and thus increases the mortality and morbidity.

Some study like Kalra et al. found higher prevalence of NAFLD in female diabetic patients compared to male counterpart[10]. We found slightly higher frequency of NAFLD in female than male although difference was not significant. Khan MS et al. also observed same type of finding which supports our result[11]. Prevalence of NAFLD in male and female is still controversial. A meta-analysis suggested women have lower prevalence of NAFLD but higher risk of progression to NASH and cirrhosis[14].

It is established that prevalence of NAFLD increases with age. We also found higher frequency of NAFLD in T2DM patients in elderly groups. Highest frequency was found in age group 50-59 year (62.2%). Kalra et al. and Khan et al. found highest frequency in 61-70 years and 41-60 years age groups respectively[10,11]. Some studies suggested that age does not predict the presence and severity of NAFLD in T2DM patients[15].

Relationship between glycemic status in diabetic patients and NAFLD is still controversial. Afolabi BI et al. found that higher HgA1c, but not FPG and duration of diabetes is related to NAFLD in T2DM[16]. Ma H et al. found both FPG and HbA1c are significantly higher in NAFLD than non-NAFLD in elderly Chinese population[17]. In contrast to these findings, we observed comparable FPG, ABF and HbA1c among patients of T2DM with and without NAFLD. This finding is supported by Prashanth M et al. which suggest that FPG, ABF & HbA1c does not predict the presence and severity of NAFLD[15].

As main mechanism of development of NAFLD is underlying IR, which usually increases with time, duration of diabetes may have association with the presence of NAFLD. Interestingly we found comparable duration of DM in type 2 diabetic patients with and without NAFLD. However this finding is supported by Prashanth M et al. and Afolabi BI et al.[15,16].

This study has some limitations. Small sample size and lack of control group are the major limitations. We didn't consider different micro and macro vascular complications associated to diabetes in relation to NAFLD. Other components of metabolic syndrome like blood pressure and lipid profile were not considered.

V. Conclusion

NAFLD is very common in Bangladeshi patients with T2DM. Glycemic status and duration of diabetes do not predict the presence of NAFLD in T2DM. Study with a large sample size including age, sex & BMI matched control group should be conducted before giving definite conclusions.

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Mohammad AfjalHossain, et. al. "Frequency of Non-Alcoholic Fatty Liver Disease in Patients with Type 2 Diabetes Mellitus and Its Relationship with Glycemic Status: an Observational Study." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 20(02), 2021, pp. 53-57.