ORIGINAL ARTICLE

Oman Medical Journal [2022], Vol. 37, No. 2: e350

Prevalence of Non-alcoholic Fatty Liver Disease among Patients with Diabetes Mellitus Attending Primary Health Care Centers in Bahrain

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ARTICLE INFO

Article history:
Received: 19 February 2021
Accepted: 10 October 2021

Online:
DOI 10.5001/omj.2022.53

Keywords:
Diabetes Mellitus; Non-alcoholic Fatty Liver Disease; Prevalence; Risk Factors; Bahrain.

ABSTRACT

Objectives: To identify the prevalence of non-alcoholic fatty liver disease (NAFLD) among patients with type 2 diabetes mellitus (T2DM) in Bahrain and to assess the risk factors for the same. ***Methods***: This retrospective cross-sectional study investigated a random sample of patients who were treated for T2DM during 2018 at non-communicable disease clinics in primary health centers in Bahrain. Cases of 382 patients who underwent abdominal ultrasonography were selected for the study. The collected patients' data were statistically analyzed. Prevalence of NAFLD among T2DM patients and the possible risk factors were assessed. ***Results:*** The mean age of the study population (N = 382) was 59.0±12.0 years. The majority (61.5%) were women. Hypertension (57.9%) was the most prevalent associated condition. Most patients were either overweight (30.5%) or obese (58.3%). Fatty liver was found in 68.1% patients based on ultrasound imaging. Elevated alanine aminotransferase was found in 75 (21.0%) out of 357 (93.5%) patients who were tested for the same. The significant risk factors identified for fatty liver were female ($p = 0.013$), high body mass index (BMI) ($p < 0.001$), high waist circumference ($p = 0.011$), and high triglyceride levels ($p = 0.043$). Binary logistic regression identified BMI as an independent risk factor for fatty liver ($p = 0.005$). ***Conclusions:*** The prevalence of NAFLD among patients with T2DM in Bahrain is high, and comparable to the levels reported in other studies. Female and high BMI, waist circumference, and triglyceride level are risk factors for NAFLD, while BMI is an independent risk factor.

Non-alcoholic fatty liver disease (NAFLD) is defined as the presence of ≥ 5% steatosis, usually detected by radiological imaging in absence of any secondary causes of fat accumulation in the liver such as alcohol, drugs, or autoimmunity.[1,2] The term describes a spectrum of progressive liver disease ranging from simple steatosis, non-alcoholic steatohepatitis, and fibrosis to liver cirrhosis. It is the leading cause of liver diseases worldwide and is emerging as the premier cause for end stage liver disease.[3] The presence of NAFLD increases liver-related morbidities and mortalities. It also increases risk of comorbidities like diabetes mellitus and cardiovascular diseases.[1] In patients with NAFLD, half of the deaths are related to cardiac disease and malignancies. Early identification of NAFLD can help improve the patient outcome through prevention and treatment.[4]

NAFLD has been recognized as the hepatic component of metabolic syndrome.[5] It is prevalent among obese people and those with type 2 diabetes mellitus (T2DM) irrespective of their degree of obesity.[6] The association of NAFLD with T2DM is due to the compensatory hyperinsulinemia resulting from insulin resistance leading to progressive defective lipid metabolism and triglyceride accumulation in the liver, or to β-cell dysfunction, leading to aggravation of T2DM, which in turn puts further pressure on the liver.[7]

The prevalence of NAFLD is increasing in developed countries with their growing obesity epidemic.[1] Bahrain is also following that trend. According to the International Diabetes Federation,

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the number of diabetics in Bahrain is projected to reach 156 000 out of an estimated adult population of 1.56 million by 2030.[8] As NAFLD and T2DM tend to co-exist, the prevalence of NAFLD in countries like Bahrain is expected to be high.[9]

However, there is a dearth of literature on the prevalence of NAFLD in Bahrain. The aim of this study is to narrow the information gap by assessing the prevalence of NAFLD among patients with T2DM who utilize the primary health care services in Bahrain.

METHODS

This retrospective cross-sectional study investigated medical files of patients diagnosed with T2DM who attended the non-communicable disease (NCD) clinics in the primary health care centers (PHCs) in Bahrain between January and March 2018. PHCs were selected for the study as they are the cornerstone of Bahrain's health care system, with 28 centers distributed across this island nation with a population of 1.33 million.[8] Each PHC has a NCD clinic staffed by family physicians and specialized nurses.

The sample was randomly selected from a list of all the 6730 diabetic patients who attended NCD clinics in all the 28 PHCs in Bahrain during the study period. The patients' names were listed on a Microsoft Excel file and a random number was generated for each record. Out of these, 2500 records were selected to calculate the required sample size at 95% confidence interval with 5% confidence level. Only patients with abdominal ultrasonography (USG) were included in the study. As the prevalence of fatty liver cases was unknown, their proportion was set at 50%. The optimal sample size was calculated to be N = 382.

Sociodemographic data of the selected 382 patients such as age, sex, and nationality were collected. The patients' USG reports were gathered with anthropometric data such as weight, height, and body mass index (BMI). Laboratory data collected related to diabetes included last fasting blood sugar, last glycosylated hemoglobin (HbA_{1c}), last lipids profile, the last liver function profile, and viral hepatitis B and C serology. Liver biopsy results were reviewed.

The data was entered in Microsoft Excel and then transferred to SPSS program version 21 (SPSS Inc., Chicago, IL, USA) for statistical analysis.

Descriptive statistics for sociodemographic data such as sex and nationality were calculated. Numerical variables were presented as mean and standard deviation (SD) or median and range. The patients were segregated into four groups based on their BMI (underweight, normal, overweight, and obese), and their number and percentage were calculated. Patients were considered to have a metabolic syndrome if, in addition to T2DM, they had at least two of the following: blood pressure ≥ 130/85 mmHg or were on antihypertensive treatment; triglycerides ≥ 1.7 mmol/L or receiving a fibrate; high density lipoprotein (HDL) cholesterol <1.04 mmol/L for men or 1.29 mmol/L for women; waist circumference >102 cm for men or 88 cm for women, according to Adult Treatment Panel III (ATP III) criteria.[10]

Abdominal ultrasound reports were grouped into four categories: normal, with hepatomegaly alone, with combined fatty liver and hepatomegaly, and fatty liver alone; then the number and percentage of each group was reported. In addition, fatty liver was graded using specific characteristics found in ultrasound such as greater echogenicity of the liver parenchyma relative to the renal cortex of the right kidney, along with visibility and sharpness of the diaphragm and hepatic veins' interface.[11] Accordingly, the severity of hepatic steatosis was classified into four grades: Grade 0, no steatosis: liver and renal cortex of the same echogenicity; Grade 1, mild steatosis: slightly brighter liver as compared to the renal cortex, clear diaphragm visualization, and interface of hepatic veins with sharp contours; Grade 2, moderate steatosis: brighter liver with attenuated ultrasound beam at deeper parts of the liver, diaphragm and hepatic veins still visible but with blunted contours; Grade 3, severe steatosis: very bright liver, severe ultrasound beam attenuation, diaphragm or hepatic veins not visible.[11] Among the patients who developed hepatic fibrosis, cirrhosis and malignancy were also reported.

The laboratory data like lipids and blood sugar levels were grouped as controlled or uncontrolled according to the diabetes guidelines followed in the PHCs. The liver enzyme levels were categorized as normal or abnormal (elevated).

Univariate analysis was used to study the relationships between different factors or associations including demographic, anthropometric, laboratory factors, use of lipid lowering agents, tobacco

smoking, adherence to dietary advice (daily five portions of fruits/vegetables), physical activity recommendations (30 minutes daily, five days per week), and the presence or absence of fatty liver. Student's *t*-test, Fisher's exact test, and Mann-Whitney U test were used. Risk factors found to be significant in the univariate analysis, with no multicollinearity using a variation inflation factor (VIF) > 8, were included in a binary logistic regression to find the independent risk factors for fatty liver. The threshold for statistical significance was set at 0.050.

RESULTS

Patients' demographic data are shown in Table 1. Most patients (n = 362; 94.8%) were Bahraini while 5.2% of patients (n = 20) were non-Bahraini —five from Pakistan, four from India, two from Egypt, two from Syria, one each from Iraq, Saudi Arabia, Philippine, and Bangladesh; nationalities of three patients were not specified. The mean age of the patients was 59.0 ± 12.0 years and most were women (n = 235; 61.5%).

Hypertension and hypothyroidism were the most prevalent associated conditions and were found in 221 (57.9%) and 35 (9.2%) patients, respectively. Thirty-nine patients (10.2%) had other associated diseases as shown in Table 1. Five patients had breast cancer (two of whom underwent mastectomy, two received chemotherapy, and one received radiotherapy) while one patient underwent angiography. Symptomatic hypoglycemia was reported in 36 (9.4%) patients. None had a history of alcohol consumption. One patient had a family history of dyslipidemia.

More than half of the patients (n = 212; 55.5%) were adherent to their prescribed medications. Regarding counseling, 191 (50.0%) patients received foot care advice. Counseling on diet and tobacco restriction were given to 291 (76.2%) and 24 (6.3%) patients respectively.

Anthropometric parameters, blood pressure, and laboratory findings are shown in Table 2. Metabolic syndrome was present in 216 (56.5%) of the entire cohort. BMI data of 338 (88.5%) patients was available, most of whom were either overweight (n = 103; 30.5%) or obese (n = 197; 58.3%), while 37 (10.9%) had normal BMI, and one patient was underweight. HbA_{1c} level data were available for 222 (58.1%) patients, among whom blood sugar was controlled in 120 (54.1%) and uncontrolled in 102 (45.9%). Fasting blood sugar data was available for 315 (82.5%) patients, of whom 159 (50.5%) were uncontrolled while 156 (49.5%) were controlled. ALT results were available for 357 (93.5%) patients, among whom elevated ALT was found in 75 (21.0%) while 282 (79.0%) had normal ALT (normal being < 33 U/L for females and < 41 U/L for males). Of the 91(23.8%) patients who were tested for hepatitis B, and 89 (23.3%) for hepatitis C, two tested positive for each condition.

Fatty liver was detected using abdominal USG

Table 1: Demographic data of the study population.

Variables	n (%)
Nationality	
Bahraini	362 (94.8)
Non-Bahraini	20 (5.2)
Age, year, mean ± standard deviation	59.0 ± 12.0
Sex	
Female	235 (61.5)
Male	147 (38.5)
Associated diseases	
Hypertension	221 (57.9)
Hypothyroidism	35 (9.2)
Others*	39 (10.2)
Current medications	
Hypoglycemic drugs	342 (89.5)
Anti-hyperlipidemia medications including statin	295 (77.2)
Antihypertensive medications	221 (57.9)
Insulin	54 (14.1)
Aspirin	49 (12.8)
Lifestyle	
Tobacco smoking	41 (10.7)
Diet (5 fruit/vegetable portions per day)	166 (43.5)
Physical activity (30 minutes per day, 5 days per week)	98 (25.7)
Cardiovascular risk	
Not calculated	189 (49.5)
≤ 10	118 (30.9)
11– 20	45 (11.8)
21– 30	15 (3.9)
31– 39	3 (0.8)
≥ 40	12 (3.1)
Family history of cardiovascular death	259 (67.8)

** Sickle cell disease: 7; breast cancer: 5; hyperuricemia: 5; rheumatoid arthritis: 3; osteoporosis: 2; benign prostatic hypertrophy 2; gastritis: 2. One patient each had dust allergy, anemia, kidney stone, migraine, psoriasis, Parkinson disease, pancreatitis, epilepsy, coronary artery bypass grafting, sickle cell trait, thyroid cancer, psychiatric disease, and bronchial asthma.*

Table 2: Anthropometric parameters, blood pressure, and laboratory findings of the 382 patients.

Variables	Mean	SD	Median	Minimum	Maximum	Tested patients n (%)
Body mass index, kg/m^2	32.4	7.1	31.3	17.7	67.8	338 (88.5)
Waist circumference, cm	106.9	17.0	105.0	50.0	200.0	209 (54.7)
Systolic blood pressure, mmHg	133.9	16.5	133.4	94.0	206.0	370 (96.9)
Diastolic blood pressure, mmHg	73.4	10.1	74.0	52.0	108.0	370 (96.9)
Hemoglobin level, g/dL	12.4	2.0	12.6	5.5	19.0	107 (28.0)
Fasting blood sugar, mmol/L	7.7	2.6	7.1	3.2	19.6	315 (82.5)
Hemoglobin A_{1c}, mmol/mol	55.4	17.9	52	13.1	130.0	222 (58.1)
Cholesterol level, mmol/L	4.4	1.0	4.3	1.3	8.5	301 (78.8)
Low density lipoprotein level, mmol/L	2.4	0.9	2.3	0.6	7.1	270 (70.7)
High density lipoprotein level, mmol/L	1.2	0.4	1.1	0.3	2.9	283 (74.1)
Triglyceride level, mmol/L	1.7	1.0	1.5	0.5	9.9	291 (76.2)
Total serum protein, g/L	73.0	5.0	73.0	40.0	86.0	362 (94.8)
Serum albumin, g/L	43.0	3.0	43.0	21.0	52.0	370 (96.9)
Serum globulin, g/L	30.0	5.0	30.0	8.0	48.0	363 (95.0)
Total bilirubin, µmol/L	11.0	11.0	8.0	0.0	120.0	351 (91.9)
Alkaline phosphatase, U/L	83.0	48.0	77.0	0.0	642.0	356 (93.2)
Alanine aminotransferase, U/L	30.0	41.0	21.0	7.0	591.0	357 (93.5)
Gamma glutamyl transferase, U/L	60.0	109.0	30.0	0.0	1512.0	367 (96.1)

SD: Standard deviation.

in 260 (68.1%) patients, 105 (39.9%) of whom had an associated hepatomegaly. Nine (2.4%) patients had an isolated hepatomegaly, three (0.8%) had hepatic hemangioma, one (0.3%) had liver cirrhosis secondary to hepatitis C infection, one (0.3%) had liver metastasis secondary to breast cancer, and one had small hepatic cyst. The remaining, 107 (28.0%) patients had normal liver. No patient had hepatic fibrosis or hepatocellular carcinoma on USG. Classifying according to ultrasonographic grading of hepatic steatosis, 122 (31.9%) patients had no hepatic steatosis on USG (grade 0), 26 (6.8%) had mild steatosis (grade 1), two (0.5%) had moderate steatosis (grade 2), and 38 (9.9%) had severe steatosis (grade 3), while the rest 194 (50.8%) patients had fatty liver of unspecified grades. For the two patients with hepatitis B, one had diffuse fatty liver and one had normal liver ultrasound, while both patients with hepatitis C had fatty liver.

Fifty-eight (15.2%) patients had computed tomography (CT) (one of them had magnetic resonant imaging scan (MRI)) that confirmed the ultrasound findings.

Elevated ALT was found in 67 out of 241 (27.8%) patients with fatty liver compared to only 8 out of 116 (6.9%) patients without fatty liver ($p < 0.001$). One female with hepatitis B had high ALT and liver biopsy performed in the secondary healthcare which showed hepatic fibrosis and cirrhosis. She was on regular antiviral medication (Tenofovir 300 mg daily).

Results of univariate analysis of possible risk factors of fatty liver are shown in Table 3. Female ($p = 0.013$), high BMI ($p < 0.001$), high waist circumference ($p = 0.011$), and high triglyceride level ($p = 0.043$) were significant risk factors for fatty liver. High ALT ($p < 0.001$) and gamma-glutamyl transferase (GGT) ($p < 0.001$) were also significantly associated with fatty liver. The significant risk factors were tested for multicollinearity (VIF > 8) between each other and were put into a logistic regression model. Accordingly, BMI was found to be an independent risk factor for fatty liver ($p = 0.005$) [Table 4].

DISCUSSION

NAFLD is a common term used to describe a broad range of liver conditions characterized by excessive fat storage in liver cells in individuals who consume little or no alcohol.[4] The fact that insulin resistance is the most common risk factor for the development

Table 3: Univariate analysis of possible risk factors of fatty liver in 382 patients with diabetes.

Variables	Total	Abdominal ultrasound finding				*p*-value (95% CI)
	N (%)	Without fatty liver 22 (31.9%)		With fatty liver 260 (68.1%)		
		n (%)	Mean (SD)	n (%)	Mean (SD)	
Age	382 (100)	122 (31.9)	60.0 (13.0)	260 (68.1)	58.0 (11.0)	0.094[a] (-0.4–5.1)
Sex						
Female	235 (61.5)	64 (52.5)	-	171 (65.8)	-	0.013[b*]
Male	147 (38.5)	58 (47.5)	-	89 (34.2)	-	-
Body mass index, kg/m^2	341 (89.3)	105 (30.8)	30.2 (6.4)	236 (69.2)	33.4 (7.2)	<0.0001[c*]
Waist circumference, cm	209 (54.7)	69 (33.0)	103.4 (20.5)	140 (67.0)	108.6 (14.7)	0.011[c*]
Resting systolic blood pressure, mmHg	370 (96.9)	117 (31.6)	134.1 (19.5)	253 (68.4)	133.9 (14.9)	0.622[c]
Resting diastolic blood pressure, mmHg	370 (96.9)	117 (31.6)	72.9 (10.3)	253 (68.4)	73.6 (9.9)	0.434[c]
Hemoglobin level, g/dL	107 (28.0)	39 (36.4)	12.6 (1.6)	68 (63.6)	12.4 (2.2)	0.53 (-0.6–1.1)[a]
Fasting blood sugar, mmol/L	315 (82.5)	101 (32.1)	7.5 (2.9)	214 (67.9)	7.8 (2.5)	0.068[c]
Hemoglobin A_{1C}, mmol/mol	222 (58.1)	69 (30.1)	52.2 (18.9)	153 (68.9)	56.9 (17.3)	0.052[c]
Cholesterol level, mmol/L	301 (78.8)	96 (31.9)	4.3 (1.0)	205 (68.1)	4.4 (1.1)	0.632[c]
Low density lipoprotein level, mmol/L	270 (70.7)	86 (31.9)	2.2 (0.7)	184 (68.1)	2.5 (0.9)	0.057[c]
High density lipoprotein level, mmol/L	283 (74.1)	93 (32.9)	1.2 (0.4)	190 (67.1)	1.2 (0.3)	0.460[c]
Triglyceride level, mmol/L	291 (76.2)	90 (30.9)	1.7 (1.4)	201 (69.1)	1.7 (0.8)	0.043[c*]
Metabolic syndrome						
Yes	216 (56.5)	68 (31.5)	-	148 (68.5)	-	0.826[b]
No	166 (43.5)	54 (32.5)	-	112 (67.5)	-	
Total serum protein, g/L	362 (94.8)	115 (30.1)	73.0 (5.0)	247 (64.7)	74.0 (5.0)	0.094[c]
Serum albumin, g/L	370 (96.9)	118 (31.9)	43.0 (3.0)	252 (68.1)	43.0 (3.0)	0.236[c]
Serum globulin, g/L	363 (95.0)	116 (2.0)	30.0 (4.0)	247 (68.0)	31.0 (5.0)	0.211[c]
Total bilirubin, µmol/L	351 (91.9)	111 (29.1)	10.0 (8.0)	240 (62.8)	11.0 (12.0)	0.876[c]
Alkaline phosphatase, U/L	356 (93.2)	115 (30.1)	77.0 (31.0)	241 (63.1)	86.0 (54.0)	0.074[c]
Alanine aminotransferase, U/L	357 (93.5)	116 (30.4)	21.0 (10.0)	241 (63.1)	34.0 (49.0)	< 0.0001[c*]
Gamma glutamyl transferase, U/L	367 (96.1)	119 (31.2)	37.0 (40.0)	248 (64.9)	71.0 (128.0)	< 0.0001[c*]
Lipid lowering agents						
Yes	295 (77.2)	95 (32.2)	-	200 (67.8)	-	0.896[b]
No	87 (22.8)	27 (31)	-	60 (69)	-	
Tobacco smoking						
Yes	41 (11.1)	18 (43.9)	-	23 (56.1)	-	0.111[b]
No	327 (88.9)	101 (30.9)	-	226 (69.1)	-	
Following dietary advice						
Yes	166 (45.5)	58 (34.9)	-	108 (65.1)	-	0.260[b]
No	199 (54.5)	58 (29.1)	-	141 (70.9)	-	
Following physical activity advice						
Yes	98 (26.6)	31 (31.6)	-	67 (68.4)	-	1.000[b]
No	270 (73.4)	86 (31.9)	-	184 (68.1)	-	

SD: standard deviation; CI: confidence interval.
*[a]student t-test; [b]Fisher's exact test; [c]Mann-Whitney U test. * p-value is statistically significant.*

Table 4: Binary logistic regression analysis of the selected risk factors of fatty liver in the 382 diabetic patients.

Variables	Adjusted odd ratio	95% CI	*p*-value
Sex	1.080	0.491–2.376	0.848
Body mass index, kg/m^2	1.147	1.042–1.263	0.005*
Waist circumference, cm	0.996	0.964–1.030	0.832
Triglyceride level, mmol/L	1.176	0.771–1.792	0.452

CI: confidence interval.
p-value is statistically significant.

of NAFLD is well-documented in literature. Both T2DM and NAFLD are sharing the same underlying mechanisms of insulin resistance, metabolic stress, and liver inflammation.[2] NAFLD per se is not a cause of insulin resistance but it has been proven to be a consequence of it.[6]

In the current study, the prevalence of NAFLD among patients with T2DM was found to be high. Of the 382 patients, 68.1% had fatty liver based on abdominal ultrasound imaging. Studies from Italy and Saudi Arabia also reported high prevalence of 59.6% and 72.8% respectively.[7,12] However, in a study from UK that investigated the prevalence of hepatic steatosis and NAFLD in type 2 diabetic patients, Williamson et al,[10] revealed a lower prevalence of NAFLD in 42.6% of 939 subjects examined. Moreover, a large meta-analysis of 86 studies comprising 8 515 431 individuals from 22 countries showed a global prevalence of NAFLD of 25.24% with highest prevalence in the Middle East and South America.[13] Our results were also similar to those of Mantovani et al,[14] who analyzed 19 observational studies with a total of 16 000 type 2 diabetic patients to find that those with NAFLD were 79.2% more likely to develop diabetes. Our results also support Targher and Byrne's finding that NAFLD worsens hepatic insulin resistance thereby increasing the odds of developing T2DM.[15] While these studies were conducted under different settings, they all demonstrated the relationship between fatty liver and T2DM, supporting the current results .

The current study showed the comorbidity of several other diseases among the 382 patients diagnosed with T2DM without history of alcohol consumption. Their main comorbidities were hypertension (57.9%) and hypothyroidism (9.2%). An earlier study by Talwalkar et al,[16] had also found similar prevalence of hypertension in their patients with T2DM, but significantly more hypothyroidism (24.8%).[16] An earlier study by Kim et al,[17] reported that comorbidity diseases among 20 314 subjects with T2DM were mainly hypertension, followed by gastritis and duodenitis, and lipidemias.

The present study identified various comorbidity conditions among its subjects, such as anemia, kidney stones, migraine, psoriasis, Parkinson disease, pancreatitis, sickle cell trait, thyroid cancer, rheumatoid arthritis, psychiatric disorders, and bronchial asthma. These comorbidities were insignificant in diabetic patients studied by Kim et al, who reported some others such as senile cataract, cerebral infarction, heart failure, and gastroesophageal reflux disease.

Obesity is considered a predictor for T2DM (80%–85%) as well as NAFLD.[9] Obesity and overweight are increasing in Asian nations including Bahrain.[18] This is often considered a consequence of the recent economic prosperity in the region, which has led to sedentary behavior and increased consumption of food high in sugars and fats.[19] Most patients in our study were either overweight (30.5%) or obese (58.3%), which follows the worldwide trend towards increasing corpulence.[20] However, people with low BMI are not immune to NAFLD, as observed in Asian populations in whom there is a tendency toward lower BMI, but higher body fat percentage compared to Euro-American populations.[21] Non-obese NAFLD patients are likely to have adiposity risk factors such as increased waist circumference, skin fold thickness and body fat percentage.[22] Sarcopenic obesity, characterized by loss of skeletal muscle and gain of adipose tissue, is associated with severe NAFLD with poor outcome.[23,24] This condition was not observed in this study. In the current study, 16 of the 233 (6.9%) patients with NAFLD had normal BMI, but none had low BMI.

In the current study, being female was a significant risk factor for NAFLD. This finding might be explained by the fact that the prevalence of obesity is

twice among women than men in Asian countries.[18] However, Forlani et al,[7] from Italy reported more males than females to have the disease. Meanwhile studies by Williamson et al,[10] Mustapic et al,[11] and Alsabaani et al,[12] reported no significant difference based on sex.

In general population, NAFLD is associated with multiple metabolic comorbidities such as obesity, T2DM, hyperlipidemia, hypertension, and metabolic syndrome.[13] In the current study, univariate analysis revealed higher BMI, higher waist circumference, and higher triglyceride levels to be significant risk factors for fatty liver. BMI was the independent risk factor. These findings are supported by other studies.[7,10,12] A systematic review by Ashtari et al,[18] revealed that obesity, T2DM and metabolic syndrome are important risk factors for NAFLD in many countries including Asian countries. Williamson et al,[10] study of 939 patients with T2DM found that BMI, lesser duration of diabetes, HbA_{1c}, triglycerides, and metformin use, were independent predictors of NAFLD. Forlani et al,[7] study showed that impaired renal functions, higher albumin excretion, higher HbA_{1c} and blood pressure, HDL cholesterol, and poor quality of care were associated with NAFLD. Alsabaani et al,[12] study found high HDL cholesterol level to be protective against NAFLD in patients with T2DM. In recent years, intestinal microbiota has been investigated as a potential risk factor for NAFLD. Gut microbiota influences energy storage and lipid metabolism. It also affects choline metabolism, ethanol production, immune balance, and inflammation.[25] NAFLD is associated with gut dysbiosis and changes in the gut microbiota metabolic functions. Certain types of gut microbiota have been linked to NAFLD such as the role of *Bacteroides* in early NAFLD stages, and that of *Ruminococcus* in hepatic fibrosis.[26]

In the current study, high ALT and GGT were significantly associated with fatty liver (p <0.0001 for both). Elevated ALT was found in 75 (21.0%) of 357 tested patients with significantly higher mean ALT levels among those with NAFLD. Forlani et al,[7] also reported comparable ALT elevation (20.3%) among patients with T2DM.

In this study, the presence of fatty liver was evaluated radiologically, mainly by abdominal USG, along with CT scan or MRI in some patients. USG is known to underestimate the incidence of hepatic steatosis and under-diagnosis NAFLD especially when hepatic steatosis is < 20%.[27] However, in clinical practice, USG, CT scan, and MRI are the standard imaging modalities to diagnose NAFLD.[1] USG is easily available, cheap, and can be performed even at bedside.[1] Moreover, when sonographic features specific to NAFLD are standardized, ultrasound can achieve a high diagnostic accuracy.[27] Accordingly, to evaluate the prevalence of NAFLD in this study, we depended mainly on hepatic USGs, especially as we sourced our data from primary healthcare centers. The imaging facilities in the current study were similar to those in several previous studies as indicated in Byrne and Targher review.[2,11] Patients with advanced disease were referred to secondary healthcare facilities for further evaluations using other modalities including transient elastography or more invasive techniques such as liver biopsies. Liver biopsy is the gold standard to diagnose NAFLD. It confirms the diagnosis and evaluates the impact extent of the disease on the liver.[1]

The main treatment goals of NAFLD are to improve steatosis and to prevent disease progression.[1] Unless intervened early, NAFLD can progress to decompensated liver cirrhosis, liver failure, hepatocellular carcinoma, or even mortality.[2,9,28] As no single intervention can effectively cure NAFLD, modifying lifestyle and decreasing the risk factors are the keys of disease management.[1] Efforts should be made to encourage a healthy lifestyle—optimal physical activity and nutrition—by means of counseling, supplemented by educational material in non-technical language.[19] Many diabetic patients find it difficult to consistently maintain the recommended diet.[19] This may call for medications as the second line of NAFLD management and when indicated, surgical interventions.[1] In a recent metanalysis on antidiabetic medications, sodium glucose transporter 2 inhibitors (SGLT2Is) such as canagliflozin were found to improve liver functions among patients with T2DM.[29]

Early detection of NAFLD is essential to avoid the progression of the disease into decompensated liver cirrhosis and liver transplantation requirement.[28] With the rapid rise of obesity in Bahrain in tune with the global trends, NAFLD is expected to become the main indication for liver transplantation in the future.[1,9,28] Although liver transplantation is curative and has been shown to enhance survival in patients with advanced liver disease from any cause, patients with NAFLD face specific challenges.[28] First, there is

currently no appropriate pharmacotherapy to prevent the disease from progressing to advanced fibrosis. Second, patients with NAFLD are frequently older, obese, and have multiple comorbidities, raising the risk of mortality during and after liver transplantation. Third, increased prevalence of NAFLD in the donor population may have an adverse effect on potential liver graft availability and efficiency.[28]

Even though this study was performed following strict scientific procedures, it has limitations that need to be pointed out. Selection bias might have occurred due to a higher possibility of including exposed group with the outcome of interest as they have been investigated by abdominal ultrasound.[30] Being a retrospective study, the quality of the source records was essential. However, this could not be assured. Another limitation of this study relates to misclassification bias, a systematic error that can occur due to inaccurate categorization of the subjects.[31] Misclassification error could have led to the underestimation or overestimation of the effect of NAFLD on the occurrence of T2DM.[31] In addition, this study used a smaller sample compared to other studies.[10,14] Although the sample was adjudged appropriate for this study, a larger sample size would have strengthened the perception about the study's validity and improved its generalizability.

Despite limitations, the present study does advance the knowledge regarding the prevalence of NAFLD among diabetic patients in Bahrain and can help healthcare professionals and policymakers in optimizing high-quality care to diabetic patients. To our knowledge, this is the first study in Bahrain that focuses on NAFLD in patients receiving treatment for T2DM from primary health care facilities in the country. The outcome of this study may reinforce the need for diabetic patients to be mandatorily screened for NAFLD and other conditions identified in this paper. The current results have also the potential to enrich future updates to current clinical guidelines for treating T2DM. It can also serve as an impetus for early diagnosis of other less well-known comorbidities that negatively impact diabetic patients.

Further research is needed to determine if NAFLD increases the risk of diabetes or is an indicator for other comorbid diseases, as well as the extent to which the onset of T2DM is linked to different stages of liver disease. More regional (within Gulf Cooperation Council) and international comparative studies are also recommended to compare results from Bahrain with those from other populations.

CONCLUSION

The prevalence of NAFLD among adult patients with T2DM in Bahrain was found to be high, at 68.1%, which is comparable to those of other related studies. Female, high BMI, high waist circumference, and high triglyceride levels were significant risk factors for fatty liver. BMI stood out as an independent risk factor. High liver enzymes (ALT and GGT) were found associated with NAFLD. The growing epidemic of obesity and diabetes in Bahrain is likely to lead to even higher prevalence of NAFLD making it the most common cause for advanced liver diseases in the future. Further studies to assess the prevalence of NAFLD and the related comorbidities in the general population may help estimate the future burden on the health care system of Bahrain and be ready for the same.

Disclosure

The authors declare no conflicts of interest. No funding was received for this study.

Acknowledgments

The authors would like to thank the nursing staff and doctors in non-communicable disease clinics in the 28 primary health care centers in Bahrain for maintaining records in the patient files.

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