



Nonalcoholic Fatty Liver Disease (NAFLD) in Saudi Patients with T2DM in Jazan Region: Prevalence and Associated Factors

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Authors' contributions

This work was carried out in collaboration between all authors. Authors EE, HA, HO and IB prepared the project proposal and designed the research paper. Authors EE, YS, AT, TH, MM, SEA and MSM assisted with the data collection and analysis. Authors EE, HA, HO, IB, YS, AT, TH, MM, SEA and MSM wrote the manuscript and provided significant input. All authors read and approved the final manuscript.

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ABSTRACT

Backgrounds: Non-alcoholic fatty liver disease (NAFLD) has become one of the major health problems world widely, especially among communities with sedentary lifestyle. The main objectives of this study were to know the prevalence of NAFLD among Saudi patients with T2DM in Jazan region and to determine the most important associated factors.

Materials and Methods: A cross sectional study targeted 230 type 2 diabetic patients, who attended Diabetic Center at Jazan General Hospital. All participants were screened for NAFLD

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using abdominal ultrasonography in addition to clinical and laboratory workup. Descriptive statistics, Chi square/Fisher exact test and logistic regression were utilized for data analysis.

Results: The prevalence of fatty liver in the present study was 47.8% (95% CI 41.1–54.6), with no significant difference between males 49.1% (95% CI 40.0–58.3) and females 46.3% (95% CI 36.6–56.3). The prevalence of NAFLD was found to be 52.9% among patients whose ages range between 40-59 years. Factors associated with NAFLD were found to be age, uric acid, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) (p -value<0.05 for all).

Conclusion: NAFLD is tremendously common among people with type 2 diabetes in Jazan region and the major associated factors were age, obesity, uric acid and elevated liver enzymes. There was no positive correlation between the presence of fatty liver and duration of DM or the degree of glycemic control.

Keywords: Non-alcoholic fatty liver disease; T2DM.

1. INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is the most common chronic liver disease in the industrialized Countries, also it is the major cause of cryptogenic cirrhosis (accounts for >50% of cases). 20 to 40% of adults in western countries have NAFLD of which 10 to 20% are having Nonalcoholic steato-hepatitis (NASH). Progression of NASH to cirrhosis has been reported at between 5% and 25% over a period of 10 years [1]. NAFLD is a disease that can occur in all sexes, ages, and ethnic groups. The major risk factors of NAFLD are: obesity, hyperlipidemia, Diabetes Mellitus (DM) and metabolic syndrome (insulin resistance syndrome) which represent the strongest risk factor [2]. Due to epidemics of DM and Obesity in industrialized countries, this will also lead to a dramatic rise in the prevalence of NAFLD in these Countries [3]. There is a very high rate of NAFLD in patients with T2DM [4].

In the Kingdom of Saudi Arabia, a prevalence of 7–10% has been documented in the general population. NAFLD, as detected by ultrasound, is common in Saudi patients with type 2 diabetes [5,6].

The majority of patients with NAFLD have no specific symptoms and are usually detected incidentally because of abnormal liver function tests or hepatomegaly. Deranged liver biochemistry is seen in 50% of patients with NAFLD. Imaging studies are usually needed during the evaluation process. Ultrasonography shows a "bright" liver with increased echogenicity, it has a sensitivity & specificity approaching 90%. Fatty livers have lower density than splenic density on computed tomography (CT) and fat appears bright in T1-weighted magnetic resonance images (MRIs).

No medical image however is helpful to distinguish simple steatosis from advanced NASH [7,8,9]. NAFLD is a benign condition whereas NASH may progress to cirrhosis, liver cell failure, and hepatocellular carcinoma. Although liver biopsy is the most reliable tool for determining the presence of NASH and fibrosis in patients with NAFLD, is generally limited by cost, sampling error, and the related morbidity and mortality [10,11]. The main objectives of this study were to determine the prevalence of NAFLD among patients with type 2 diabetes in Jazan region, and to know the most important associated factors.

2. PATIENTS AND METHODS

2.1 Study Design, Participants and Setting

A cross-sectional study targeted 230 Saudi patients, who attended Diabetic Center at Jazan General Hospital. The main inclusion criteria were adult patients (18 years and above), with T2DM, while patients with coexisting liver disease and those who consume alcohol or taking steatogenic drugs were excluded from the study. The study took place at Jazan general hospital, during the period between January to June 2013. Jazan region is one of the thirteen regions of the Kingdom of Saudi Arabia. It is located on the tropical Red Sea coast in southwestern Saudi Arabia. Jazan covers an area of 11,671 square kilometers, including 5,000 villages and towns.

2.2 Sample Size and Design

A representative sample of 230 participants was calculated, depending on 95% confidence interval, error not more than 7%, and non-response rate of 15%. Since there is no prior

estimate for the prevalence of NAFLD among population of Jazan region an estimate of 50% was utilized using sampling formula for a single cross-sectional survey. Patients were selected using a systematic random sampling method to ensure high degree of randomization.

2.3 Laboratory, Physical Examination and Socio-demographic Data

Clinical data were collected from all participants, including: age, gender, duration of DM, body mass index (BMI), drug history, history of alcohol consumption and the presence of systemic hypertension. Laboratory data involved: complete blood counts, Liver function tests (Alanine aminotransferase = ALT, Aspartate aminotransferase= AST, alkaline phosphatase=ALP), Renal function tests, Fasting blood glucose, Glycated HbA1c, lipid profile (Low density cholesterol= LDL, High density cholesterol=HDL, Triglycerides=TG),uric acid(UA)and serology for hepatitis B and C.

Weight, standing height was measured in a standardized fashion by a trained examiner. The standing height measurement was made at minimal inspiration to the nearest 0.1cm. Body mass index (BMI) was calculated as weight (kg)/height (m²). Patients with BMI less than 25 were classified as normal, over 25 classified as overweight and patients with a BMI over 30 classified as obese.

2.4 Ultrasonographic Examination

All subjects were screened for NAFLD by a single, expert radiologist using a sensitive Ultrasound machine: Toshiba. Aplio XG, probe 305 hz. B mode, (m mode. Dual, panoramic). Fatty liver was diagnosed in the presence of increased hepatic echogenicity compared to the spleen or the kidneys. The diagnosis of NAFLD was based on the American association for the study of liver disease (ASSLD) guidelines for the assessment and management of NAFLD [12,13].

2.5 Statistical Analysis

Data were analyzed using SPSS version 20 (SPSS Inc, Chicago, IL, USA)). Data analysis involved descriptive statistics as well as inferential statistics. Descriptive statistics included a simple tabulation, frequencies, proportion for categorical variability including cross-tabulations. Differences in proportions were compared for significance using the Chi

Square test, with a significance level set at p . value<0.05. We also performed an independent t test to assess differences in numerical variables between patients with and without NAFLD. The logistic regression model was also used to evaluate factors associated with NAFLD. Adjusted odds ratios (ORs) and their 95% confidence intervals were reported.

2.6 Ethical Approval

The study proposal and instrument were approved by the Jazan University's review board (IRB) and voluntary informed consents were getting from all patients enrolled in the study. Before the data collection started permission was also obtained from the Directorate of Health in Jazan region. The data was anonymized to protect participants as no names were required.

3. RESULTS

A total of 207 (90%) out of 230 participants were included in this study, (90%).The 23 (10%) patients were excluded from the study because their records were not complete. Table 1 shows some background characteristics of the study population. Almost 67.6% of study participants were between (40-59) years, while about 54.1% were males and the majority 54.6% reported that they have T2DM for period more than 10 years.

Table 2 shows the Level of the prevalence of NAFLD among study participants by Selected Characteristics. The overall prevalence of NAFLD in Jazan Region was 47.8%, which is higher among the age group (40-59 years old. The prevalence was higher among males (49.1%; 95% CI: 40.0-58.2) than females (46.3%; 95% CI: 36.6-56.3), but without significant differences (P. value = 0.689). According to BMI the prevalence of NAFLD, showed high rates among, both overweight and obese, (56.1%; 95% CI: 53.7-79.6) and (49.1%; 95% CI: 19.4-95.6) respectively, without significant differences between the different BMI categories (P. value = 0.360).

Table 3 provides the biochemical tests and other variables for males, females and total study participants. According to the table in males, the average age of the subjects with NAFLD was 50.5±2.00, and 56.9±1.78 in those without NAFLD. In females, the average age in NAFLD and the non NAFLD group was 51.8±1.42 and 53.1±1.53 respectively. There were statistical

differences in age, weight-to-height ratio, UA, AST and ALT between NAFLD group and non NAFLD group for the study participants. There was no significant difference in Cr. Metabolic factors such as BMI, TG, TC and FPG between participants with NAFLD and non NAFLD group.

Table 4 illustrates the results of the multivariate logistic regression analysis. The analysis shows only age has statistically significant association with NAFLD (OR 2.08 (.988-4.414); P. value .040), FBG and LDL and BMI, although they showed increased OR, but without significant impact on NAFLD.

4. DISCUSSION

Non-alcoholic fatty liver disease (NAFLD) is defined as having hepatic steatosis, either by imaging or by histology in the absence of secondary hepatic steatosis like alcohol consumption, use of steatogenic drugs or hereditary disorders [12].

In the present study, which enrolled 207 patients with T2DM the prevalence of NAFLD among them was 47.8%. This is in keeping with what was documented in the literature.

Table 1. Background characteristics of studied population

Characteristics	No	%
Age groups		
Less than 40	5	2.4
40-59	140	67.6
60+	62	30.0
Gender		
Male	112	54.1
Female	95	45.9
DM duration		
Less than 5 years	40	19.3
5-9 Years	54	26.1
10 years and more	113	54.6
BMI categories		
Normal	34	16.4
Overweight	66	31.9
Obese	53	25.6
Missing	54	26.1
Exercise		
Regular	52	25.1
Irregular	60	29.0
No exercise	59	28.5
Missing	36	17.4
Total	207	100

Table 2. Prevalence of NAFLD in Jazan region by selected characteristics

Characteristics	N-positive/ N-tested	Prevalence	95% CI	P. value
Age groups (n=207)				
Less than 40 years	(3/5)	60.0	(22.2-88.1)	0.050
40-59 years	(74/140)	52.9	(44.6-80.9)	
60+ years	(22/62)	35.5	(24.7-47.9)	
Gender (n=207)				
Male	(55/112)	49.1	(40.0-58.2)	0.689
Female	(44/95)	46.3	(36.6-56.3)	
DM duration				
Less than 5 years	(22/40)	55.0	(40.6-74.5)	0.228
4-9 Years	(29/54)	53.7	(50.2-79.8)	
More than 10 years	(97/109)	42.2	(45.3-66.6)	
BMI categories				
Normal	(14/34)	41.2	(44.1-69.6)	0.360
Overweight	(37/66)	56.1	(53.7-79.6)	
Obese	(26/53)	49.1	(19.4-95.6)	
Exercise				
Regular	(28/52)	53.8	(52.9-80.4)	0.122
Irregular	(21/60)	35.0	(35.8-66.6)	
No exercise	(28/59)	47.5	(42.1-70.9)	
Overall prevalence	(99/207)	47.8		

Table 3. Comparisons of biochemical tests and metabolic characteristics of subjects according to gender

Characteristics	Male			Female			Total		
	NAFLD present	NAFLD absent	P. value	NAFLD present	NAFLD absent	P. value	NAFLD present	NAFLD absent	P. value
Age (years)	50.5±2.00	56.9±1.78	0.011	51.8±1.42	53.1±1.53	0.565	50.8±1.2	55.1±1.2	0.015
BMI (kg/m ²)	28.8±0.69	28.5±0.88	0.775	29.9±0.97	28.7±0.78	0.348	29.2±0.56	28.6±0.58	0.816
W/H (kg/m)	0.47±0.01	0.47±0.02	0.772	0.47±0.01	0.44±0.01	0.093	0.47±0.01	0.45±0.01	0.016
TG (mmol/L)	157.1±7.8	151.9±11.5	0.700	156.7±7.4	165.4±10.1	0.490	157.0±5.4	158.8±7.4	0.843
TC (mmol/L)	202.3±8.0	185.3±4.9	0.077	208.1±7.1	222.2±8.1	0.195	205.0±5.4	202.4±5.0	0.724
UA (µmol/L)	5.6±0.40	6.4±0.60	0.167	5.6±0.60	5.3±0.34	0.698	5.7±0.3	5.8±0.3	0.047
CR (µmol/L)	0.9±0.01	0.9±0.09	0.244	1.4±0.62	0.68±0.02	0.047	1.1±.29	0.82±0.05	0.362
AST (U/L)	31.8±2.4	26.10±2.3	0.092	29.1±2.21	21.7±1.73	0.009	30.6±1.6	23.8±1.4	0.000
ALT (U/L)	36.3±2.5	29.4±2.4	0.048	34.2±2.72	23.3±2.00	0.002	35.3±1.8	26.3±1.6	0.000
ALP	79.4±4.8	80.5±5.5	0.881	90.8±5.19	84.6±4.39	0.370	84.6±3.5	82.4±3.5	0.630
FBG (mmol/L)	197.4±13.3	205.2±15.0	0.699	201.6±13.55	203.8±14.9	0.913	199.2±9.4	204.5±10.5	0.709

Values, mean±standard error of the mean (S.E.M).BMI: body mass index; W/H: weight to height ratio; TG: Triglycerides; TC: total cholesterol; UA: Uric acid; FPG: Fasting plasma glucose; CR: Creatinine; HDL: High Density Lipoprotein cholesterol; LDL: Low Density Lipoprotein cholesterol. ALT(alanine aminotransferase); AST (aspartate aminotransferase)

Table 4. Factors associated with NAFLD among the studied patients

Factor	Odds ratio (95% CI)	P value
Age>40 years	2.08 (.988-4.414)	0.040
Fasting glucose>110 mg/dL	1.35 (.514-3.576)	0.539
BMI>kg/m ²	1.56 (.688-3.539)	0.287
Total cholesterol>200mg/dL	0.938 (.508- 1.731)	0.838
LDL>160 mg/dL	2.32 (.205-26.287)	0.496
HDL<40mg/dL	0.904 (.276-2.965)	0.869
Triglyceride>150 mg/dL	1.013 (.536-1.914)	0.968

A previous study, conducted in Saudi Arabia in 2003 by Akbar and Kawther, showed NAFLD prevalence of 55% among 116 patients with type 2 diabetes. Female gender and obesity were the two common features of patients with NAFLD in that study [4].

Worldwide many previous ultrasonographic studies of patients with diabetes have shown NAFLD prevalence ranging from 21 to 78% with an approximate average of 50% [14,13,15,16].

In another study, 127 of 204 diabetic patients showed fatty changes on ultrasound, and 87% of the patients with fatty liver who underwent liver biopsy had histologic confirmation of NAFLD [17]. The actual prevalence of NAFLD among diabetic patients is usually underestimated in ultrasonographic studies as compared with studies that rely on the histological diagnosis (liver biopsy), however ultrasonography is safe and cost effective for screening a large number of patients, whereas liver biopsy is limited by cost and associated morbidities [2,13].

In the present study NAFLD was found more in the age groups between 40-59 years (52.9% of patients). In many studies, fatty liver was mostly found in the middle age groups [13,18,19]. However, some studies have shown that the prevalence of NAFLD correlates with progression of age [20]. We have no explanation for that.

In this study, the average age of the subjects with NAFLD was 50.5±2.00, whereas 56.9±1.78 in those without NAFLD. In terms of gender no significant changes, however the prevalence was slightly more in males. Prevalence in males was 49.1%, whereas it was 46.3% in females. Many studies have shown that NAFLD is more common in men [21,22].

Obesity is a common and well reported risk factor for NAFLD. Also, overweight and visceral obesity are recognized risk factors for NAFLD. In

patients with morbid obesity the prevalence of NAFLD can be more than 90% and up to 5% of patients may have liver cirrhosis [23,4].

In the current study there is a significant correlation between an increase in BMI and the presence of NAFLD (56.1% of studied patients had overweight, whereas 49.1% were obese with OR=1.56), however, no significant differences between the different BMI categories (P=0.360). Leite and colleagues, Akbar and Kawther, Merat et al. and Shahbazian et al. have shown similar results to ours regarding the strong correlation between obesity and NAFLD [24,5,13,15].

Hypertriglyceridemia and low serum HDL-cholesterol level are very common in individuals with NAFLD. The prevalence of NAFLD in patients with dyslipidemia was estimated to be 50% [25].

In contrast to the previous studies, there was no significant difference in dyslipidemia between participants with NAFLD and non-NAFLD group in our study.

Other factors found to be significantly associated with NAFLD in the current study were elevation in serum transaminases (ALT, AST) and uric acid (UA), with P-value of <0.05 for both. There were statistical differences in UA, AST and ALT between NAFLD group and non NAFLD group. Similar results were reported in Leite et al. [24] study. It has been well-documented that hyperuricemia is associated with components of metabolic syndrome including DM, dyslipidemia and obesity [26]. On the other hand, some studies have shown a significant association between hyperuricemia and NAFLD in subjects without metabolic syndrome. In those studies, hyperuricemia correlated with severity of NAFLD on ultrasonography [27].

In individuals with NAFLD elevation in transaminases (ALT, AST), having reversed AST/ALT ratio and diabetes are considered as

non-invasive biomarkers for NASH and fibrosis, however, for confirmation of NASH still liver biopsy remains the gold standard method [1]. So in the future more large prospective study based on a highly sensitive and specific non-invasive biomarker for NASH such as Cytokeratine-18(CK 18) need to be conducted in Saudi patients with diabetes in order to determine the prevalence of NASH among them [28].

Although the majority of participants (54% of study patients) had reported a longer duration of diabetes (10 years or more) we found no direct correlation between duration of T2DM, state of glycemic control and presence of NAFLD. These findings were consistent with what was reported in the previous studies [5,13].

Management of patients with NAFLD is directed towards the treatment of liver disease and the associated metabolic factors such as DM, obesity and dyslipidemia. Many pharmacological agents have been tried for treatment of NAFLD, but the most effective ones are Pioglitazone and Vitamin E (Tocopherol), which are considered only for those with biopsy-proven NASH. However, vitamin E is not recommended for diabetic patients, in addition the long-term safety of Pioglitazone is not ensured [12].

Perhaps the main strength of this study is that it is the first study to investigate prevalence of NAFLD in Jazan region; however, some significant limitations should be mentioned. The first obvious limitation of the study was its study design; the cross sectional study design may not be suitable for assessing associations between NAFLD and other explanatory variables. Also the study sample may not be well representative for all Jazan populations since the study was conducted in one hospital of the region.

5. CONCLUSION

NAFLD is extremely common in patients with T2DM. Age, high liver enzymes (ALT, AST) and high serum uric acid are the major associated factors. More attention needs to be paid towards diabetic patients with fatty liver in order to minimize the risk of progression to cirrhosis and its serious sequelae.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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