SJIF Impact Factor: 5.464

WORLD JOURNAL OF ADVANCE HEALTHCARE RESEARCH

ISSN: 2457-0400
Volume: 7.
Issue: 5.
Page N. 128-132
Year: 2023

Original Article www.wjahr.com

A STUDY OF THE PREVALENCE OF LIVER FUNCTION DISORDERS INPATIENTS WITH TYPE II DIABETES MELLITUS

Zeinab Saker[1]* and Ruba Salman[2]

[1]Department of Internal Medicine, TishreenUniversity, Faculty of Medicine, Lattakia, Syria.
[2]Department of Endocrinology, Professor, TishreenUniversity, Faculty of Medicine, Lattakia, Syria.

Received date: 15 March 2023 **Revised date: 05** April 2023 **Accepted date: 26** April 2023

***Corresponding Author: Zeinab Saker**

Department of Internal Medicine, Tishreen University, Faculty of Medicine, Lattakia, Syria.

ABSTRACT

Background: Type 2 diabetes mellitus(T2DM) represents a disorder of glucose metabolism that is characterized by hyperglycemia and insulin resistance. Liver involvement in T2DM is recognized in the form of non-alcoholic fatty liver disease(NAFLD) which can range from simple steatosis to liver cirrhosis. **Objective:** The aim of this study was to determine the prevalence of liver transaminase disorders in T2DM patients, and the association with glycemic control. **Patients and Methods:** A Descriptive Observational Cross Sectional study was conducted for the period one year (2021 –2022) at Tishreen University Hospital in Lattakia-Syria. The study included all T2DM patients older than 18 years with a duration of diagnosis disease longer than 6 months. Alanine transaminase(ALT) and Aspartate transaminase(AST) were measured for all patients with abdominal ultrasound. **Results:** The study included 189 patients with T2DM. Fatty liver disease was detected in 72 cases (38.1%) which was associated with elevated levels of ALT in 60 cases (83.3%) and AST in 24 cases (33.3%). Elevated levels of ALT were associated significantly with increasing body mass index BMI, fasting plasma glucose FPG, glycosylated hemoglobin HbA1c, total cholesterol TC, triglyceride TG, low-density lipoprotein LDL, and decreasing high density lipoprotein HDL ($p<0.05$). Elevated levels of ALT were observed more frequently in patients with fatty liver disease (76.9% versus 23.1%, p:0.0001). Elevated levels of AST were associated significantly with increasing BMI, FPG, HbA1c, TC, TG, and decreasing HDL ($p<0.05$). Elevated levels of AST were observed more frequently in patients with fatty liver disease (72.7% versus 27.3%, p:0.0001). **Conclusion:** The current study demonstrated presence of fatty liver disease in important percentage of T2DM patients, and elevated levels of ALT were observed more frequently, so that early diagnosis of diabetes and initiating of therapeutic intervention is considered essential to improve final outcome.

KEYWORDS: Type 2 diabetes mellitus T2DM, liver function, fatty liver.

INTRODUCTION

Diabetes mellitus (DM) is considered to be a series of metabolic illnesses that cause hyperglycemia as a result of relative or absolute impairment in insulin secretion with varying degree of resistance to the action of insulin.[1] The prevalence of T2DM has increased dramatically over the last decades and considered an epidemic worldwide with increasing alterations in lifestyles and obesity.[2] Early initiation of treatment for diabetes is considered crucial and is associated with improved glycemic management and decreased long term complications that affects many organs.[3]

Liver represents an essential organ for the metabolism, immunity, digestion, and detoxification. The liver has an important role in control of glucose homeostasis by controlling pathways of glycogenesis, glycolysis, and gluconeogenesis.[4] Non-alcoholic fatty liver disease (NAFLD) is considered a frequent cause of chronic liver disease which ranges from steatosis, fibrosis to cirrhosis and hepatocellular carcinoma.[5] NAFLD is highly prevalent in T2DM patients and there was awareness about close relationship between them, which might be explained by presence of many metabolic defects such as chronic hyperinsulinemia, and resistance to insulin in adipose tissue and skeletal muscles.[6] In addition to, alteration of adipose tissue function might be the potential disorder for hepatic steatosis in T2DM patients.[6] Diagnosis of NAFLD in T2DM patients is important not only for preventing liver disease complications, but also other organ related comorbidities

which are observed frequently in T2DM patients. There is limited data on the potential effects of specific pharmacologic agents that used in management of glucose levels in T2DM patients on NAFLD given to physiological relationship between them.[6] Screening for NAFLD is considered a challenge in diabetes patients due to normal levels of liver transaminases in majority of cases.[7] Therefore, the aims of our study were: 1- to investigate the prevalence of liver aminotransferase disturbances in T2DM patients. 2- to detect ultrasound findings of liver and the association with abnormal levels of aminotransferase.

PATIENTS AND METHODS

This is a Descriptive Observational Cross Sectional study of a group of patients with T2DM attending department of Endocrinology at Tishreen University Hospital in Lattakia-Syria during one-year period (2022). The inclusion criteria were: patients older than 18 years with duration of disease longer than 6 months. The exclusion criteria were presence of one of the following: acute and chronic viral hepatitis, liver tumors (primary, metastases),heavy alcohol use (consuming more than 20 g/day for women and more than 30 g/day for men), patients who received drug-induced liver injury such as methotrexate, amiodarone, digoxin and steroids.

Complete history, review of systems, and physical examination were performed. Weight and height were measured, and BMI was calculated. Body mass index (BMI) was calculated as weight (kg) divided by height (m) squared(kg/m2) and categorized as normal weight (18.5-24.9 kg/m2), overweight (25-29.9 kg/m2) and obesity (≥30 kg/m2). Good glycemic control was defined as Glycated hemoglobin(HbA1c) <7%, fasting blood glucose (80- 130 mg/dL), two-hour postprandial glucose<180 mg/dL. Levels of lipid were measured for all patients, which included: Triglyceride TG (normal levels<150 mg/dL), Low-density lipoprotein LDL (normal<100 mg/dL), and High density lipoprotein HDL (low levels defined as <40 for men and <50 for women).

Alanine transaminase(ALT) and Aspartate transaminase(AST) were measured for all patients with performing liver ultrasound to detect presence of fatty liver disease. Variables of the patients were compared according to the levels of ALT and AST.

Ethical consideration: All patients were provided a complete and clear informed consent after discussion about the study. This study was performed following the Declaration of Helsinki.

Statistical Analysis

Statistical analysis was performed by using IBM SPSS version20. Basic Descriptive statistics included means, standard deviations(SD), median, Frequency and percentages. To examine the relationships and comparisons between the two group, chi-square test was used. Independent t student test was used to compare 2 independent groups. All the tests were considered significantat a 5% type I error rate ($p<0.05$), β:20%, and power of the study:80%.

RESULTS

The baseline characteristics of the participants were as shown in (Table 1).Males represented 42.9% of the study population and females 57.1% with female: male ratio was 1.3:1. Ages range from 32 years to 83 years (mean 55.90±10.5 years) and BMI ranges from 20 to 40.8 kg/m^2 (mean 26.80±3.2 kg/m^2).

Table 1: Demographic characteristics of the study population.

Variable	Result
Sex	
Male	81(42.9%)
Female	108(57.1%)
Age (years)	55.90±10.5
BMI (kg/m^2)	26.80±3.2

Based on direct measures of glycemia, good glycemic control was determined in 60 cases (31.7%), 45 cases (23.8%), and 54 cases (28.6%) depending on levels of fasting blood glucose, two-hour postprandial glucose, and HbA1c respectively.

Table 2: Lab-based blood glucose testing of the study population.

Variable	Result
Fasting blood glucose	
Controlled	60(31.7%)
uncontrolled	129(68.3%)
Two-hour postprandial glucose	
Controlled	45(23.8%)
uncontrolled	144(76.2%)
Glycosylated hemoglobin (HbA1c)	
Controlled	54(28.6%)
uncontrolled	135(71.4%)

As shown in table (3), abnormal levels of TG, TC, LDL, and HDL were determined in 108 cases (57.1%),75 cases (39.7%),108 cases (57.1%), and 114 cases (60.3%) respectively.

Table 3: Blood lipid profile of the study population.

Variable	Result
TG	
Abnormal	108(57.1%)
Normal	81(42.9%)
TC	
Abnormal	75(39.7%)
Normal	114(60.3%)
LDL	
Abnormal	108(57.1%)
Normal	81(42.9%)
HDL	
Abnormal	114(60.3%)
Normal	75(39.7%)

Abnormal levels of AST and ALT were detected in 33 cases (17.5%) and 78 cases (41.3%) respectively. According to the results of liver ultrasound, fatty liver disease was detected in 72 cases (38.1%).

Table 4 Investigations related to the liver of the study population.

Variable	Result
AST	
Abnormal	33(17.5%)
Normal	156(82.5%)
ALT	
Abnormal	78(41.3%)
Normal	111(58.7%)
Fatty liver disease	
Present	72(38.1%)
Absent	117(61.9%)

Patients were classified into two groups according to ALT levels: ALT <40 (111 patients) and ALT≥40 (78 patients). There were no significant differences between two groups regarding to gender(p:0.8). Patients with ALT≥40 were significantly younger (50.84±9.6 versus 59.45±9.7, p:0.0001), with higher BMI(27.84±3.9 versus 25.07±2.3, p:0.001). Measures of glycemia were significantly higher in patients with ALT≥40; fasting blood glucose (188.88±40.4 versus 151.37±38.7, p:0.0001), two-hour postprandial glucose (245.88±49.1 versus 206.27±68.9, p:0.0001) and HbA1c (8.08±1.02 versus 7.26±0.6, p:0.0001). In addition to, levels of serum lipid were significantly higher in patients with abnormal levels of ALT; TG (203.69±156.4 versus 157.43±54.2, p:0.0001), TC (182.42±45.4 versus142.83±34.1, p:0.04), and LDL (125.30±39.5 versus104.81±27.2,p:0.0001). HDL levels were significantly lower in patients with ALT≥40 (43.15±14.9 versus 46.54±10.9, p:0.04). Prevalence of fatty liver disease was significantly higher in patients with abnormal levels of ALT (76.9% versus 10.8%, p:0.0001).

Table 5: Baseline characteristics of the study population according to ALT levels.

Variable	ALT <40	ALT≥40	P value
Sex			
Male	48(43.2%)	33(42.3%)	0.8
Female	63(56.8%)	45(57.7%)	
Age (years)	59.45±9.7	50.84±9.6	0.0001
BMI (kg/m^2)	25.07±2.3	27.84±3.9	0.001
Fasting blood glucose	151.37±38.7	188.88±40.4	0.0001
Two-hour postprandial glucose	206.27±68.9	245.88±49.1	0.0001
HbA1c	7.26±0.6	8.08±1.02	0.0001
Lipid profile			
TG	157.43±54.2	203.69±156.4	0.0001
TC	142.83±34.1	182.42±45.4	0.04
LDL	104.81±27.2	125.30±39.5	0.0001
HDL	46.54±10.9	43.15±14.9	0.04
Fatty liver disease on echography			
Present	12(10.8%)	60(76.9%)	0.0001
Absent	99(89.2%)	18(23.1%)	

Patients were classified into two groups according to AST levels: AST <40 (156 patients) and AST≥40 (33 patients). There were no significant differences between two groups regarding to gender (p:0.4). Patients with AST≥40 were significantly younger (52.72±11.1 versus 56.57±10.3, p:0.004), with higher BMI (27.93±4.8 versus 26.56±2.7, p:0.03). Measures of glycemia were significantly higher in patients with AST≥40; fasting blood glucose (186.54±32.3 versus 137.12±38.7, p:0.001), two-hour postprandial glucose (251.36±51.9 versus 194.43±55.2, p:0.0001) and HbA1c (7.87±0.5 versus 6.68±0.7, p:0.04). In addition to, levels of serum lipid were significantly higher in patients with abnormal levels of AST; TG (196.43±163.4 versus 144.30±109.5, p:0.004) and TC (186.17±34.6 versus 135.90±42.8, p:0.0001). HDL levels were significantly lower in patients with AST≥40(40.63±10.4 versus 46.09±13.1, p:0.002). Prevalence of fatty liver disease was significantly higher in patients with abnormal levels of AST (72.7% versus 30.8%,p:0.0001).

Table 6: Baseline characteristics of the study population according to AST levels.

Variable	AST <40	AST≥40	P value
Sex			
Male	69(44.2%)	12(36.4%)	0.4
Female	87(55.8%)	21(63.6%)	
Age (years)	56.57±10.3	52.72±11.1	0.04
BMI (kg/m^2)	26.56±2.7	27.93±4.8	0.03
Fasting blood glucose	137.12±38.7	186.54±32.3	0.001
Two-hour postprandial glucose	194.43±55.2	251.36±51.9	0.0001
HbA1c	6.68±0.7	7.87±0.5	0.04
Lipid profile			
TG	144.30±109.5	196.43±163.4	0.004
TC	135.90±42.8	186.17±34.6	0.0001
LDL	113.17±36.8	113.72±18.8	0.9
HDL	46.09±13.1	40.63±10.4	0.002
Fatty liver disease on echo			
Present	48(30.8%)	24(72.7%)	0.0001
Absent	108(69.2%)	9(27.3%)	

DISCUSSION

This Descriptive Observational Cross Sectional study of 189 T2DM patients assessed for presence of abnormal liver aminotransferase, as well as ultrasound findings of liver and the association between aminotransferase disturbances andthe degree of glycemic control and lipid profile.

This study showed the main findings: First, majority of the patients were with uncontrolled glycemia depending on fasting blood glucose and HbA1c.Second, reduced HDL and elevated levels of TC and LDL represented the most frequent disturbance of lipid, which might be explained by altered metabolism of triglyceride-rich lipoproteins, and presence of insulin resistance that increases hepatic lipase activity that lead to denser LDL particles and a decrease in HDL.Third, elevated levels of ALT were observed in 42% of the patients due to insulin resistance that be directly induced liver cells injury. Fatty liver disease was observed in 40% of the patients which might be explained by elevated levels of free fatty acids, mitochondrial dysfunction, and cell oxidative stress.

Finally, fatty liver disease was associated predominantly with elevated levels ofALT than AST. Elevated levels of ALT and AST were observed more frequently with increasing BMI, uncontrolled diabetes, elevated levels of lipids,and decreased HDL, in which previous factors are associated with insulin resistance. These findings are comparable with results of previous studies.

Dilawar et al (2017) demonstrated in a study conducted in 85 patients with T2DM and 15 patients with prediabetes that NAFLD was present in 78% of T2DM patients versus 8% in control group.[8]

Mandal et al (2018) showed in a study conducted in 210 patients with T2DM that NAFLD was present in 55.7% of the patients and ALT levels were elevated significantly in NAFLD patients without presence of significant differences regarding of AST and alkaline phosphatase ALP.[9]

Shibabaw et al (2019) showed in a study performed in 192 patients with T2DM who compared with 192 individuals without diabetes that liver functions were significantly elevated in T2DM patients; AST: 42.94 ± 19.08 versus 20.34 ± 9.9, p:0.0001, ALT: 46.06 ± 22.38 versus 22.66 ± 9.45, p:0.0001.[10]

Thambiah et al (2019) demonstrated in a study conducted in 300 patients withT2DM that majority of the patients were uncontrolled, and elevated levels of ALT were detected in 27.3% of the patients with presence of significant correlation between ALT levels and age, BMI, duration of disease, and abnormal levels of serum lipid.[11]

Shahwan et al (2019) demonstrated in a study performed in 453 T2DM patients that disturbances of liver function (ALT, AST, ALP) were detected as follow; in one (80.8%), two (6.4%), and three (2.4%). Abnormal findings of liver were associated significantly with disturbances of lipids and the degree of glycemic control.[12]

In summary, it is imperative that research should focus on its early diagnosis aswell as early treatment of T2DM, to reduce the potential development of clinically significant complications of liver and improve the final outcome. In addition to, we recommend that health care providers test all T2DM patients for liver function.

REFERENCES

1. Xu G, Liu B, Sun Y. Prevalence of diagnosed type 1 and type 2 diabetes among US adults in 2016 and 2017: population based study. *BMJ*, 2018; 362: 1497.

2. DeFronzo R, Ferrannini E, Groop L. Type 2 diabetes mellitus. *Nat Rev Dis Primers*, 2015; 1: 15019.
3. American Diabetes Association. Classification and diagnosis of diabetes: Standards of Medical Care in Diabetes-2022.*Diabetes Care*, 2022; 45: 17-38.
4. Hoekstra L, de Graaf W, Nibourg G. Physiological and biochemical basis of clinicalliver function tests: a review. *Ann Surg*, 2013; 257: 27-36.
5. Tilg H, Moschen A, Roden M. NAFLD and diabetes mellitus. *Nat Rev Gastroenterol Hepatol*, 2017; 14: 32-42.
6. Kupriyanova Y, Zaharia O, Bobrov P. Early changes in hepatic energy metabolism and lipid content in recent-onset type 1 and 2 diabetes mellitus. *J Hepatol*, 2020; 28: S0168-8278.
7. Hernaez R, Lazo M, Bonekamp S. Diagnostic accuracy and reliability of ultrasonography for the detection of fatty liver: a meta-analysis. *Hepatology*, 2011; 54: 1082.
8. Dilawar M, Andrabi W, Rauf M. Suspect and Screen by Ultrasound for Non- Alcoholic Fatty Liver Disease in Pre-Diabetic and Patients with Type 2 DiabetesMellitus. *P J M H S.*, 2017; 11: 157-159.
9. Mandal A, Bhattarai B, Kafle P. Elevated Liver Enzymes in Patients with Type 2 Diabetes Mellitus and Non-alcoholic Fatty Liver Disease. *Cureus*, 2018; 10: e3626.
10. Shibabaw T, Dessie G, Molla M. Assessment of liver marker enzymes and its association with type 2 diabetes mellitus in Northwest Ethiopia. *BMC Res Notes*, 2019; 12: 707.
11. Thambiah S,Ramley N,Ghazali N. Deranged Liver Enzymes in Type 2 Diabetes Mellitus Subjects in a Tertiary Malaysian Hospital. *Mal J Med Health Sci.*, 2019; 15: 62-68.
12. Shahwan M, Khattab A, Khattab M.Association between abnormal serum hepatic enzymes, lipid levels and glycemic control in patients with type 2 diabetes mellitus. *Obesity Medicine*, 2019; 16: 100137.