Original Article

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Evaluation of Liver Enzymes Activities Among Type 2 Diabetic Patients Attending Alribat University Hospital, Khartoum State

Ayat Ali Eltayeb[1], Shereen Faisal[1], AbdElkarimA.Abdorabo[1], Suhair A.Ahmed[1], RimazGurashi[1], GadAllahModawe[2]

[1]AlNeelain University, Faculty of Medical Laboratory Science, Clinical Chemistry Department, Khartoum, Sudan.

[2] Omdurman Islamic University, Faculty of Medicine and Health Sciences, Biochemistry Department.

ABSTRACT

Background: Diabetes mellitus is a metabolic disease known as chronic hyperglycemia, resulting from defective insulin action and secretion. Various studies have documented liver disease as a major cause of mortality in patients with type 2 diabetes. Notably, the liver plays an important role in the maintenance of normal glucose levels during fasting as well as in the postprandial period.

Aim: To evaluate the levels of liver markers in patients with type 2 diabetes in Khartoum state.

Patients and Methods: Across-sectional study was conducted at Alribat University Hospital, Sudan, from January 2018 to April 2019.A total of 100patients were included in the study.This sample included 50 patients who had beenpreviously diagnosed with type 2 diabetes and a similar number of age- and gender-matched healthy control participants. Serum liver markers concentrations were estimated using an enzymatic method in a fully automated biochemistry analyzer (Cobas 3546). The data were analyzed using SPSS version 20.

Results: The majority of patients were aged more than 55 years. The serum levels of aspartate aminotransferase (AST) in the type 2 diabetesgroup and the control group were 31.26±10.34 and 20.35 ± 6.48, respectively(p-value= 0.00).The serum levels of alanine aminotransferase (ALT) in the type 2diabetic patients and control participants were 33.74±6.48 and 19.70±6.23, respectively(p-value= 0.00).The serum levels of ALP in the type 2 diabetes group and the control group measured 125.20±49.61 and 87.90±24.35, respectively(p-value = 0.00).The serum levels of γ-glutamyl transferase (GGT) in the type 2 diabetes patients and control participants were 47.72±9.01 and 43.48±8.63, respectively(p-value= 0.026). Moreover, the mean body mass index (BMI) in the type 2 diabetesgroup and the control group was 26.36±5.94 and 19.19±2.67, respectively (p-value= 0.00), and the correlation between the duration of disease and liver enzymes GGT, ALT,AST, and ALP were 0.47,0.34,0.57,0.93, respectively. The current study demonstrated insignificant correlation between the serum levels of GGT and ALT and the BMI of patients with type 2 diabetes (p-value= 0.83,0.863); however, significant correlation was detected between serum levels of AST and ALT and the BMI of the patients (p-value= 0.002,0.032).

Conclusion: In the present study, a significant increase in the level of liver enzymes ALT, AST, GGT, and ALP was observed in type 2 diabetic patients when compared to the normal group. Thus, these liver enzymes can be used as biomarkers for the assessment of type 2 diabetes.

Keywords: Liver enzymes, Diabetes mellitus, Sudanese patients

Corresponding author:*GadAllahModawe,gadobio77@hotmail.com.*

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INTRODUCTION

Diabetes mellitus is a disorder of carbohydrate metabolism characterized by the impaired ability of the body to supplyor respond to insulin and thereby maintain proper levels of glucose within the blood. Type 2 diabetes is caused by impairment in the β-cells' function and capacity to secrete sufficient insulin, coupled with a decline in target tissue sensitivity to insulin. According to the International Diabetes Federation (IDF), about 1 in 11 adults worldwide are affected by diabetes mellitus, and over 90% of them have type 2 diabetes.[1,2]The incidence of diabetes and associated disorders in thepopulation has increased substantially in the last decades. It is a major cause of morbidity and mortality, though these outcomes are not due to the immediate effects of the disorder. Instead, they are related to the diseases that develop as a result of chronic diabetes mellitus.[3]This heterogeneous metabolic disorder, especially uncontrolled diabetes, can affect many organs including the liver, whichregulates carbohydrate, lipid, and protein metabolism.[4]Elevated serum levels of liver enzymes, particularlyaspartate aminotransferase (AST), alanine aminotransferase (ALT), and γ-glutamyltransferase (GGT),have beencommonly observed in diabetes.[5]Studies have found that type 2 diabetes is associated with a clinical spectrum of liver abnormalities collectively known as non-alcoholic fatty liver disease. These studies emphasized the body mass index (BMI) as the most important variable of liver abnormalities,especially when correlated with glycemic control status by determining glycosated heamoglbulin .[6,7]Therefore, this study aimed to estimate the levels of liver markers in type 2 diabetes patients. We estimated the levels of liver enzymes, ALT, AST, GGT, and alkaline phoshatase as liver markers, and we investigated other variables such as age, gender, duration of the disease,and BMI.[8,9]The objective of the present study was to evaluate the levels of liver markers in patients with type 2 diabetes in the Khartoum state.

PATIENTS AND METHODS

Study population: This study was a comparative cross-sectional hospital-based study.It was performed atAlribat University Hospital, Sudan, January from 2018 to April 2019. A total of 100 participants were recruited as the study sample, including 50 Sudanese patients previously diagnosed with type 2 diabetes mellitus used the case group and 50 healthy individuals used as control group.

Inclusion and exclusion criteria: Patients diagnosed with type 2 diabetes mellitus were included in this study. On the other hand,patients with a history of liver diseases and severely debilitating diseases such as cancer or severeanemia (hemoglobin<10 g/dl) were excluded; additionally, weexcludedpatients with clinical and subclinical hypothyroidism and patients with any history of taking tamoxifen, corticosteroids, and amiodarone.

Data collection and blood sampling: The data for each group were collected from a direct questionnaire and then entered into an excel sheet. Demographic data included age, gender, and BMI. Under aseptic and antiseptic precautions, blood specimens were collected in a heparinized tube at room temperature and centrifuged for 10

minutes at 3500rpm. All the precautions were taken according to the Clinical and Laboratory Standards Institute criteria. Serum liver markers and HbA1c concentrations were estimated using an enzymatic method in a fully automated biochemistry analyzer (Cobas 3546).

Quality control: Normal and pathological control materials were used to evaluate the working solutions and the testing samples. All precautions were takenand quality mattersconsidered according to manufacturing instructions.

Ethical consideration: Ethical permission was obtained from relevant authorities. Samples were collected after a written agreement assigned with laboratory administrations. This study was approved by the ethical committee of the Faculty of Medical Laboratory Science (Clinical Chemistry Department) of Al Neelain University, 2018.

Data analysis: The data obtained were expressed as mean ± SD. Statistical analyseswere performed using the Statistical Package for the Social Sciences (SPSS) version 20. Differences in mean values between the groups were measured using an independent t-test.

RESULTS

As illustrated in Figure1,the patients were of varied age groups, the youngest being 23 years and the oldest 63 years of age. High incidence was reported in the age group below 55 years (26 patients [52%]), while a lower incidence was reportedin the age group above 55 years.The age groups were match between study populations . (20[40%]) had normal body mass, while 18(36%) were overweight, and 12 patients (24%) were obese. As detailed inTable 1,the mean ±SD of BMI, AST,ALT, ALP, and GGT in the case group measured 26.36±5.94, 31.26±10.34, 33.74±6.48, 125.20±49.61, 47.72±9.01, respectively. On the other hand, the mean ±SD of BMI, AST,ALT, ALP, and GGT in the control group.
measured19.19±2.67,20.35±6.48,19.70±6. 23, 87.90±24.35, and 43.48±8.63, respectively. The BMI, AST, ALT, and ALP were significantly higher in the case group compared to the control group with a p-value= 0.000, while GGT was significantly higher in diabetic patients than the healthy individuals with a p-value= 0. 026.Table 2shows the activity of liver enzymes according to age. The activity of ALP and GGT demonstrated a significant difference between the age groups of the patients, while the BMI, AST, and ALT were insignificantly different.Table 3 reports the activity of liver enzymes according to the gender of the patients.The activity of ALP and GGT reported a significant difference between the age groups of the patients, while the BMI, AST, and ALT were insignificantly different.Furthermore, Table 4 shows the correlation between liver enzymes and HbA1c. No association between the activity of GGT, ALT, ALP, and HbA1c was observed, while aweak negative correlation between AST activity and HbA1c was detected. Figure 2 illustrates the correlation between the liver enzymes and the duration of the disease. Evidently, A gradual association between the levels of GGT, ALT, AST, and ALP and the duration of the disease was detected. Moreover, the activity of ALP and AST was gradually associated with the BMI; however, no correlation between the activity of GGT and ALT and the BMI was observed.

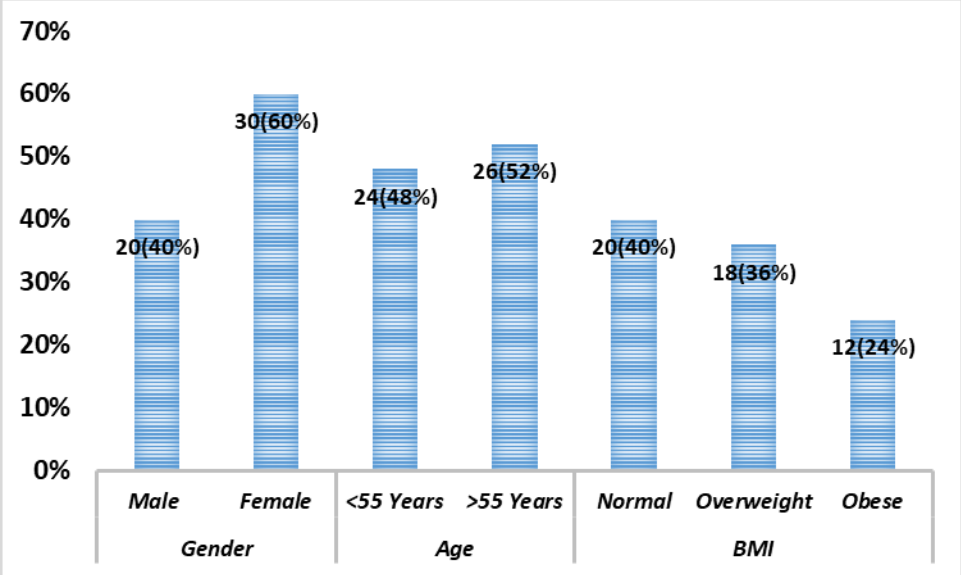


Figure 1: Gender ,Age and BMI among study population .

Table 1: Comparison of the means of the study parameters betweenthe case and control group.

Parameters	Case (Mean±SD) N=50	Control (Mean±SD) N=50	*P-value*
BMI	26.36±5.94	19.19±2.67	0.000
AST U/L	31.26±10.34	20.35±6.48	0.000
ALT U/L	33.74±6.48	19.70±6.23	0.000
ALP U/L	125.20±49.61	87.90±24.35	0.000
GGT U/L	47.72±9.01	43.48±8.63	0.026

Table 2: Comparison of the study parameters within the type 2 diabetes patients group according toage.

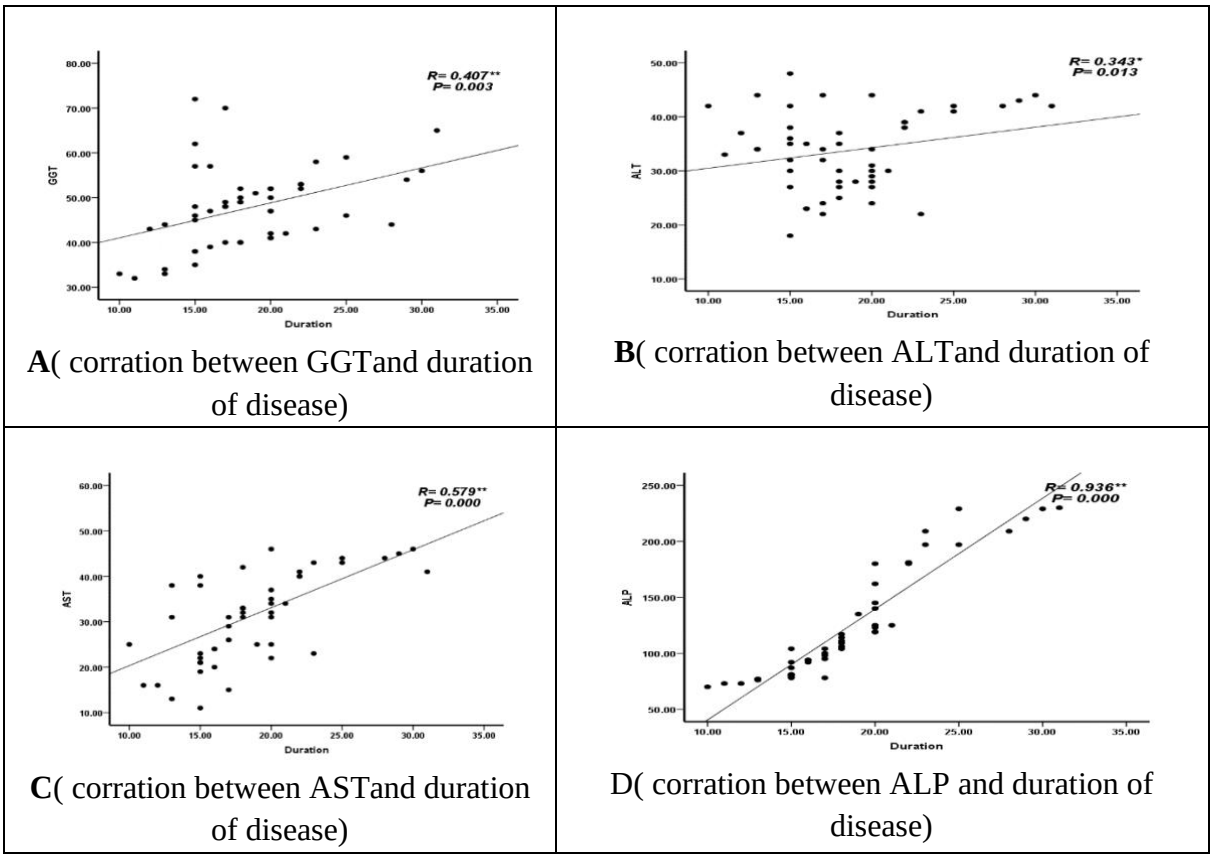
Parameters	<55 Years (Mean±SD)	>55 Years (Mean±SD)	*P-value*
BMI	25.5±6.3	27.2±5.6	0.334
AST U/L	28.5±11.2	33.8±8.9	0.074
ALT U/L	33.5±6.4	33.9±8.2	0.826
ALP U/L	100.0±30.3	148.5±52.9	0.000
GGT U/L	43.3±7.6	51.8±8.3	0.000

Table 3: Comparison of liver enzymes and BMI among pateints group according to gender**.**

Parameters	Male (Mean±SD)	Female (Mean±SD)	*P-value*
BMI	26.1±5.8	26.8±6.3	0.674
AST U/L	31.8±9.9	30.5±11.1	0.656
ALT U/L	34.0±7.1	33.2±50.3	0.762
ALP U/L	133.2±50.3	113.2±47.1	0.032
GGT U/L	51.9±8.1	41.4±6.1	0.000

Table 4: Correlation between the liver enzymes and the HbA1c among pateints patients .

Parameters	*R-value*	*P-value*
GGT U/L	-0.078	0.588
ALT U/L	-0.145	0.315
AST U/L	-0.297*	0.036
ALP U/L	-0.124	0.389



A(corration between GGTand duration of disease)

B(corration between ALTand duration of disease)

C(corration between ASTand duration of disease)

D(corration between ALP and duration of disease)

Figure 2: Correlations among theGGT, AST,ALT, and ALP levels and the duration of the disease.

DISCUSSIONS

Increased levels of liver enzymes even within the reference range are associated with an increased risk of type 2 diabetes. Hepatic fat accumulationis one of the well-known complications of diabetes type 2 with a reported frequency of 40–70%. If fat in the hepatocytes is accompanied by excess inflammation and steatonecrosis, it should be considered a cause ofchronically increased liver enzymes in asymptomatic diabetic patients.[10]In type 2 diabetic patients with or without obesity, up to 30% have fat with inflammation, 25% have associated fibrosis, and 1–8% have cirrhosis.[11-13] The present study was conducted to evaluate the abnormality of liver functions within type 2 diabetic patients by measuring the activity of liver enzymes.This cross-sectional study

recruited 50 patients with diabetes type 2 for the study group and 50 healthy individualsfor the control group.Blood samples were collected from the study and control groups, and the activity of the ALT, AST,ALP,and GGT was measured andthen statistically analyzed.

Our findingsdemonstrated a significant elevation in the activity of the liver enzymes with a p-value of 0.000, 0.000, 0.000, and 0.026 for ALT, AST, ALP, and GGT, respectively. These findings align with previous studies,[14-17]which reported that AST (SGOT) and ALT (SGPT) are sensitive indicators of liver damage of diseases.[18]The rough endoplasmic reticulum is remarkably decreased as a consequence of increased glucose concentration.[19]Furthermore, a decreased number of mitochondrial cristae and changednuclear membranes in hyperglycemia can lead to abnormal liver function.[20,21]Additionally, diabetes and liver function appear to be interrelated, where hyperglycemia in type 2 diabetes can cause liver dysfunction; in turn, liver dysfunction can further aggravate insulin resistance and hepatic glucose metabolism issues. Elevated blood glucose levels can create glucotoxicity and in parallel initiate lipogenesis and lipotoxicity. The combination of glucotoxicity and lipotoxicitystimulatesthe inflammatory process and releases cytokines such as interleukins and tumor necrosis factors.[22]A recent study further provided causal evidence for the association between GGT and insulin resistance.[23]

Elevated levels of ALT, AST, and GGT reflect an excess fat deposition in the liver, which is a conditionknown asnon-alcoholic fatty liver disease. This non-alcoholic fatty liver disease is foundwith metabolic syndrome, which refers to some cardiovascular risk factors related tocentral obesity,insulin resistance,dyslipidemia, hypertension, and type 2 diabetes mellitus.[24,25]Serum GGT works asan intracellular antioxidant defensemechanism with the primary function of regulating intracellular glutathione levels.[26]Elevation ofoxidative stress may contribute to the development of diabetes,[27]and chronic oxidative stress results in declined responsiveness to insulin, finally leading to T2D.[28]

The increased levels of ALP found in our type 2 diabetes patients are consistent with previous studies where ALP was found to be elevated in diabetic subjects, ALP in the liver was found to be associated with the cell membrane, which adjoins the biliary canaliculus, and high serum levels of the liver isoenzyme indicate cholestasis rather than simply damage to the liver cells.[29]

Furthermore, our study demonstrates a significant increase in the levels of ALP and GGT in the older diabetics group (> 55years) with p-value 0.00 and 0.00 for ALP and GGT, respectively, and the male group within the study population with p-value 0.03 and 0.00 for ALP and GGT, respectively.However, these findings disagree with a previous study that found that the increased age wassignificantly associated with elevated levels of ALT, AST, and GGT.[30]Moreover, another study found that the prevalence of increased liver enzymes in the group of patients with type 2 diabetes was higher in the female than in the male participants.[31]On the other hand, a studyfound that the increase in ALT,AST, and GGT levels was higher in males with type 2 diabetes.

Furthermore, our results reported a significant correlation between AST activity and HbA1C with a p-value of 0.036, and this is in linewith a previous report.[17]Additionally,our findings demonstrate a significant correlation between all study parameters(ALT, AST, ALP, and GGT activity) and the duration of the disease, which also aligns with a previous study.[32]

The mechanism of the accumulation of non-alcoholic fatty acids in the liver is caused by insulin resistance,whichactivates lipolysis, resulting in the accumulation of non-esterified fatty acids.[30]This enhanced fat accumulation in the liver is known to be directly toxic to hepatocytes.[33,34]

CONCLUSIONS

In the present study, a significant increase in the levels of liver enzymes ALT, AST, GGT, and ALP was observed in patients with type 2 diabetes compared to healthy individuals. Thus, these liver enzymes can be used as biomarkers for the assessment of type 2 diabetes.

Acknowledgments

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Competing Interests

None declared.

Availability of Data and Material

All data and materials associated with this paper are available through the corresponding author upon reasonable request.

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