Biochemical Evaluation of Some Liver Enzymes in Type 2 Diabetes Mellitus Iraqi Patients

Ali Abdul Hussain Kasim*
Mohammed M. Mohammed**
**Department of Clinical Laboratory Sciences, collage of pharmacy, University of Baghdad, Iraq.*
*** Department of Clinical Pharmacy, collage of pharmacy, University of Al-Mustansiryah, Iraq.*

الخلاصة:

الكبد هو العضو الرئيسي المسؤول عن أيض الكلوكوز. هذه الوظيفة الأساسية للكبد جعلته عرضة للإصابة بالأمراض خاصة في الاشخاص المصابين بالاضطرابات الأيضية ومرض السكري.

أظهرت دراسات عديدة أن مرض السكري يرتبط مع ارتفاع مخاطر مرض الكبد المزمن، سرطان الكبد الأولي والموت نتيجة تليف الكبد.

الهدف من الدراسة هو تقييم بعض الانزيمات الكبدية في المرضى العراقيين المصابين بمرض السكري المزمن من النوع الثاني (T2DM) ومقارنتها مع الأشخاص الغير مصابين بالمرض.

شملت الدراسة (60) ستون مريضا عراقيا مصابين بداء السكري المزمن من النوع الثاني، و(60) ستون شخصا من الأصحاء كمجموعة سيطرة، وتم قياس مستويات (Glucose, AST, ALT, GGT , ALP).

أظهرت النتائج ان متوسط قيم ALT ، AST وGGT في T2DM أعلى بكثير من تلك التي في مجموعة السيطرة ($P\leq 0.001$ ل ALT و GGT و $P\leq 0.05$ لAST) وفي المقابل، أظهرت الدراسة انه لا يوجد فرقا معنويا في قيم ALP بين مجموعتي الدراسة.

إن نتائج هذه الدراسة جاءت موافقة لتقارير سابقة أظهرت معدلات انتشار عالية وغير طبيعية لإنزيمات الكبد في المرضى الذين يعانون من داء السكري من النوع 2 في شعوب أخرى.

Abstract:

Liver is the main organ of glucose storage as glycogen and metabolism. This key function of liver exposes it to many types of diseases with metabolic disorders, particularly diabetes.

Many studies had showed that; diabetes is associated with high risk of chronic liver disease, primary liver cancers and liver cirrhosis. However, most of these studies were performed in Western countries, and there is a lack of information from Iraq.

The aim of the study is to evaluate some hepatic enzymes in Iraqi patients with chronic type 2 diabetes mellitus (T2DM) compared with healthy volunteers.

Sixty Iraqi subjects with type 2 DM, and sixty healthy volunteers as control group were included in this study. The levels of (Glucose, ALT, AST, GGT, and ALP) were measured.

The mean values of concentration levels of ALT, AST and GGT were significantly higher in T2DM than the control group ($P \leq 0.001$ for ALT, GGT and $P \leq 0.05$ for AST). In contrast, there is no significant difference in ALP levels in the two study groups.

The results of this study are in accordance with previously reported high prevalence rates of abnormal liver enzymes in patients with type 2 diabetes mellitus in other populations.

Introduction:

Liver is the main organ of glucose metabolism; where glucose uptake, storage, synthesis, and metabolism occurs[1]. This key function of the liver exposes it to diseases in subjects with metabolic disorders, particularly diabetes mellitus (DM)[2]. Diabetes mellitus is associated with non-alcoholic fatty liver disease (NAFLD) including its sever form, non-alcoholic steatohepatitis (NASH)[3,4].

Among DM patients, the risk of chronic liver disease is doubled, independent of alcoholic liver disease or viral hepatitis[5]. DM also increases the risk of primary liver cancers[5-7] and liver cirrhosis[8,9]. However, most of these studies were performed in Western countries [10-18], and a lack of information from Iraq.

The most common liver function tests include the serum amino-transferases, alkaline phosphatase, bilirubin, albumin, and prothrombin time. Aminotransferases, such as alanine aminotransferase (ALT) and aspartate aminotransferase (AST), measure the concentration of intracellular hepatic enzymes that have leaked into the circulation and serve as a marker of hepatocyte injury. Alkaline phosphatase (ALP), γ-glutamyl transpeptidase (GGT), and bilirubin act as markers of biliary function and cholestasis. Albumin and prothrombin reflect liver synthetic function[19].

The overall prevalence of diabetes in Iraq was 2.18%. The rates were greater in urban than rural areas (2.53% and 1.58% respectively), and in the South/Centre than in Kurdistan (2.30% and 1.43% respectively). The rates of diabetes increase markedly in the 30-49 age group, assumed to indicate the onset of type 2 diabetes. More increases in the rates were seen after age 50, with a prevalence rate of 14.38 % [20].

With no doubt the risk of morbidity due to diabetes is increasing. Therefore, the comprehensive studies of DM and its impacts are needed to be

undertaken. The aim of our study was evaluating some hepatic enzymes in Iraqi patients with long standing type 2 diabetes compared to healthy volunteers.

Materials and Methods:

Sixty Iraqi subjects with type 2 DM attending; the Specialist Center for Endocrine Glands and Diabetes (Alresafah-Baghdad), and sixty healthy volunteers as control group were included in this study. The type 2 diabetic patients chosen (called T2DM in the study), are suffering from diabetes for at least 5 years. Thirty of whom are males and thirty are females. All the subjects in T2DM group are on glibinclamide alone or glibinclamide plus metformin as treatment for diabetes. Subjects with history of liver disease, or severe debilitating diseases such as cancers were excluded. Also we excluded subjects with history of taking tamoxifen, corticosteroids, amiodaron, statins or any medication that is known to alter the hepatic enzymes level. None of the subjects participated in this study is an alcohol drinker.

In the laboratory investigation, serum Glucose, ALT, AST, GGT, and ALP were measured using end-point enzymatic (for serum glucose) and end-point colorimetric (for hepatic enzymes) spectrophotometry, using kits purchased from Biomaghreb® (Biomaghreb,Tunis, Tunisia). All reagents used were of analytical grade.

Statistical Analysis:

Microsoft office excel software 2007 for windows was used for all statistical analysis. Differences between T2DM and control group were evaluated by the student's t-test. The level of significance was set at $P \leq 0.05$.

Results:

In the present study, the average age was 59±6.3 years, ranging between 40 and 65 years in T2DM and 53±8.5 years in a range of 39 through 60 in control group. The mean duration of diabetes was 7.73±4.32 years, ranging of 5 through 20 years. Body mass index (BMI) (kg/m^2) calculated as the ratio of weight (kg) to the square of height (meters) of the T2DM and the control groups was 27.7±3.21 and 24.23±4.6 kg/m^2 respectively.

The concentration levels of ALT, AST, GGT, ALP and serum glucose in T2DM and the control group is presented in Table-1. The mean values of ALT, AST and GGT were significantly higher in T2DM than that in the control group ($P \leq 0.001$ for ALT, GGT and $P \leq 0.05$ for AST). In contrast, ALP has showed no significant difference between the study groups. The mean value of serum glucose level was clearly higher in T2DM than in the control group (Table-1 and Figure-1).

	T2DM [Mean±SD]	Control [Mean±SD]
FBG(mg/dl)	142.2±12.13**	85.2±3.83
ALT(U/L)	24.79±9.07**	19.35±6.1
AST(U/L)	25.53±8.56*	22.24±5.82
GGT(U/L)	34.17±5.48**	27.43±8.06
ALP(U/L)	93.75±13.21	91.74±17.72

Table-1: The levels of FBG, ALT, AST, GGT and ALP in T2DM patients and control group.

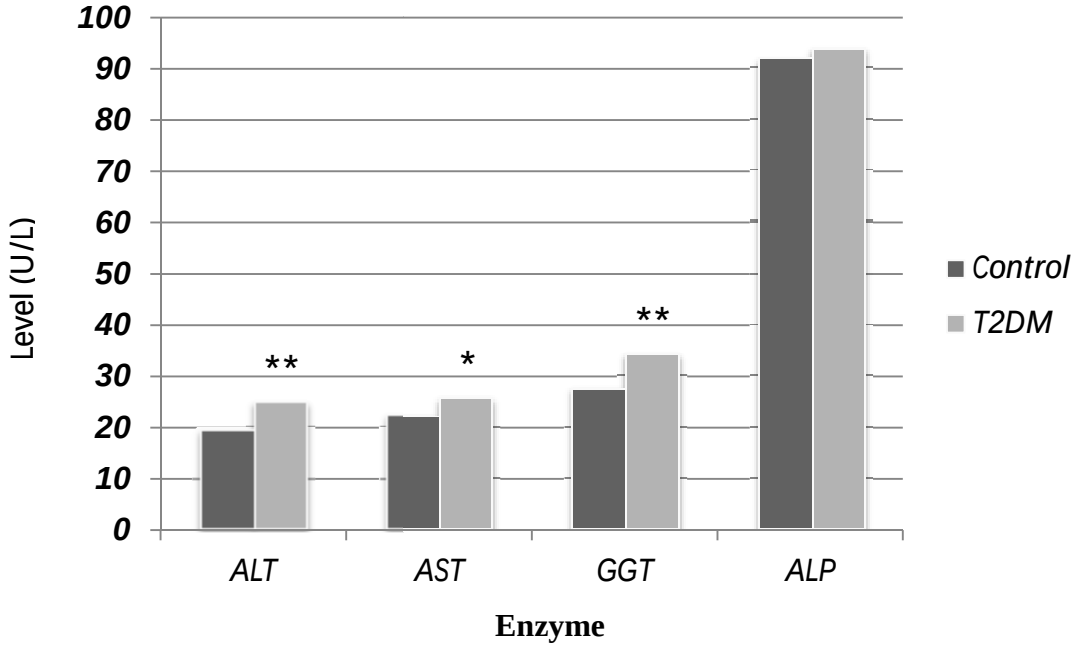

Figure-1: ALT, AST, GGT and ALP levels (U/L) ALP in T2DM patients and control group.
*P ≤ 0.05
**P ≤ 0.001

Discussion:

Although abnormal concentration levels of hepatic enzymes in type 2 diabetic patients have been reported for over two decades, these are limited to a few reports mainly from western countries, with little or no data available from Middle East, including Iraq.

Although the differences were statistically significant, the means of ALT, AST and GGT were within the normal values. Our results is in agreement with Salmela et al[15], who found in a study carried out in Finland that 57% of the

175 diabetic outpatients (100 subjects) had at least one abnormal liver enzyme level; 27% (48 subjects) had at least two abnormal liver enzymes level. Our results also agree with Nannipieri et al[21], in a study carried out in Mexico city, he stated that an elevated serum ALT level is greater among persons with type 2 diabetes, those who are overweight or obese, men, and those who consume more than three drinks per day. Meltzer and Everhart[22] previously noted a greater prevalence of abnormal ALT levels among Mexican American with diabetes.

Many perspective studies reported that increased levels of serum GGT, even within its normal range, showed a dose-response relationship with the incidence of type 2 diabetes. This association is independent of well-known predictors for diabetes such as, age, body mass index, and also other factors associated with GGT levels such as alcohol consumption and liver damage[23-27]. Our results regarding ALP and transaminases disagree with Paruk et al[28], whose study results showed that; the most frequently encountered abnormalities in South African patients with type 2 diabetes mellitus, were those of GGT and ALP, rather than ALT abnormalities. This may be attributed to the fact that alcohol intake was not considered in their study.

In patients with asymptomatic abnormal liver enzymes, NAFLD was the most common diagnosis when detailed investigations were conducted[29-31]. Although the etiology of the abnormal liver enzymes in patients with type 2 diabetes mellitus may be varied, the most common cause is assumed to be NAFLD. In general, the prevalence of NAFLD has been shown to be high in patients with type 2 diabetes mellitus, and is almost universal in morbidly obese subjects with type 2 diabetes mellitus[32-34].

In conclusion, our results were in accordance with previously reported high prevalence rates of abnormal liver enzymes in patients with type 2 diabetes mellitus in other populations. Further large scale study, including DM patients (type 1 and 2) from different parts of Iraq is needed to establish our findings and to use these results as a reference records for this type of disease.

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