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Original Research Article

The Liver Aminotransferase Levels in Diabetes Patients

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Abstract

This study aim toinvestigate the levels ofliver aminotransferase in patients with diabetes and the effect of glycemic control on the levels of these enzymes.The study was conducted on 115 persons, 19 poorly controlled diabetic patients (glucose>300 mg/dl), 25 moderately controlled diabetic patients (glucose 200-300 mg/dl), 21 well controlled diabetic patients (glucose < 200 mg/dl), and 50healthy non diabetic subjects as normal control. Serum glucose, ALT and ASTwere assessed in all groups.There was no statistically difference in ALT and AST levels between control and total diabetes patient groups. Poorly controlled diabetic patients demonstrated highly significantly increase of ALT and AST when compared with the other two patient groups (well and moderate controlled diabetic). But there is no significant statistic for these enzymes between well and moderate controlled diabetic groups. In conclusion,increased levels of ALT and ASTmay contributory factor to induced liver disease observed in poorly glycemic control patients.

Key words: diabetes, Alinine aminotransferase, aspartate aminotransferase.

دراسة مستويات أنزيمات الكبد (الامينوترانزفيريز) في مرضى السكر

الخلاصة

يهدف هذا البحث الى دراسة مستويات انزيمات الكبد الامينوترانزفيريزفي مرضى السكر ومدى تأثير تنظيم السكر على مستويات هذه الانزيمات. أجريت هذه الدراسة على ١١٥ شخص, ١٩ مريضا ضعيفي السيطرة على تنظيم السكر (مستوى السكر أكثر من ٣٠٠ ملغم/ديسي لتر), ٢٥ مريضا معتدلي السيطرة على تنظيم السكر (مستوى السكر ٢٠٠ – ٣٠٠ ملغم/ديسي لتر), ٢١ مريضا جيدة التنظيم للسكر (مستوى السكر أقل من ٢٠٠ ملغم/ديسي لتر) و ٥٠ شخص أصحاء وغير مصابين في مرض السكر شكلوا مجموعة سيطرة. تم قياس مستوى كل من السكر وأنزيمات الامينوترانزفيريز في مصل جميع الاشخاص.

أظهرت النتائج بان ليس هنالك فرق معنوي في مستويات هذين الانزيمين بين مجموعة المرضى الكلية ومجموعة السيطرة ولكن هنالك زيادة معنوية عالية في مستويات الانزيمين بين مجموعة المرضى ضعيفة السيطرة على تنظيم السكر و مجموعتي المرضى الاخريين(المعتدلة والجيدة الانتظام للسكر). لكن ليست هنالك علاقة معنوية لمستويات هذه الانزيمات عند مقارنتها بين مجموعة المرضى معتدلة السيطرة على تنظيم السكر ومجموعة المرضى جيدة التنظيم للسكر.

نستنتج ان زيادة مستويات انزيمات الامينوترانزفيريز في مرضى السكر يعتبر عامل مشارك في مخاطر ظهور أمراض الكبد في المرضى ضعيفي السيطرة على تنظيم السكر.

Introduction

The liver has a central role in glucose homeostasis. Glycogenesis, glycogenolysis, gluconeogenesis, lipid metabolism, and insulin degradation take place in the liver [1].

In liver diseases, hepatic carbohydrate metabolism is commonly disturbed. Andre et al found there is no specificity in liver disease to be associated with diabetes mellitus [2].

insulin/glucagon ratio and altered portal insulin levels may affect liver function and integrity in diabetic patients [3].

Several biochemical tests constitute what are called the "liver function tests" can give different information about hepatic dysfunction. The abnormal levels in plasma enzyme activity generally indicate liver cell membrane damage rather than hepatic function capacity [4, 5].

Aminotrasferase, such asalinine aminotransferase (ALT) and aspartate aminotransferase (AST) estimate the level of enzymes of intracellular hepatic which have leakage into the blood stream so serve as a biomarker of hepatocyte injury [6].

In cases of infective conditions or inflammatory, there is a damage to the cytoplasmic membrane; which leak to contents of cell causes a marked rise in plasma ALT than AST activities.Whereas in situation of infiltrative disorders characterized by damage in cytoplasmic membranes and mitochondrial, the proportionally is change to elevation in plasma AST than ALT activity [7, 8].

Recently severalreports have reported that there is an association between occurrence of non-insulin dependent diabetes mellitus and elevated level of liver enzymes, especially aminotransferases in different ethnics [9,10].

The aim of the present study is to measure the levels of ALT and ASTenzymes among diabetic subjects and then compare them with normal subjects and if there is an effect for glycemic control on levels of these enzymes.

Materials and Methods

A total number of 115 subjects participated in this study from October 2013 to April 2014. From those 65patients with diabetes (aged 25-60 years, 22 male and 28 female, duration of diabetes 6 months – 18 years) and 50 subjects apparently healthy controls (aged 23- 60 years, 32 male and 18 female).

A diagnosis of diabetes was made according to the World Health Organization criteria (i.e., a doctor's diagnosis and/or fasting plasma glucose greater than 126 mg/dl). Clinical data of all patients which included sex, age, duration of diabetes, family history of diabetes and liver diseases, as well as a history of medication were obtained by reviewing the medical records and direct patient interview.

The diabetes patients were classified as regards diabetic control into three groups on the basis of their blood sugar level [11]:

Group 1: Well controlled (glucose < 200 mg/dl), consisted of 21 patients (12 males and 9 females).

Group 2:Moderately controlled (glucose 200-300 mg/dl), consisted of 25 patients (9 males and 16 females).

Group 3: Poorly-controlled (glucose> 300 mg/dl), consisted of 19 patients (12 males and 7 females).

The glucose assay was performed by using a kit from randox type which determines glucose level depending on the enzymatic oxidation for glucose in the presence of glucose oxidase enzyme.

The activities of ALT and AST enzymes were estimated as liver function tests using a randox kit which determine their levels by monitoring concentrations of pyruvate hydrazone and oxaloacetate hydrazone formed respectively when adding 2,4-dinitrophenyl hydrazine.

Statistical evaluation was performed using the SPSS for windows version 18. Student's *t*-test has been applied to compare between groups. The significant test was applied at $p < 0.05$.

Results

There was no significantly difference in age and sex distribution between healthy control and diabetes patients groups (table 1).

Table 1: Demographic features of the study groups

Parameters		Diabetic patient groups			Healthy Control group (N = 50)
		Group 1 (N = 21)	Group 2 (N = 25)	Group 3 (N = 19)	
Sex	Male	12	9	12	32
	Female	9	16	7	18
Age		41.95 ± 8.54	45.36 ± 7.96	47.24 ± 7.82	40.37 ± 6.48

Table 2 shows the mean and standard deviations of serum FBS, ALT and AST in healthy control and all patients with diabetes groups.

FBS levels were significantly higher ($p<0.0001$) in the total patient groups than in control group.

There was no statistically difference in ALT and AST levels between control and total patient groups.

Table 2 also shows levels of ALT and AST in relation to severity of diabetes assessed by fasting blood sugar levels. It was observed that there was increase in the levels of ALT and AST with increasing severity of diabetes. The difference in the values of these parameters between group 3 and groups 1 and 2 was highly statistically significant ($p<0.001$). But there was no statistically difference in the levels of these parameters between group 1 and group 2.

Table 2: laboratory data of control and all patients with diabetic

	Diabetes patient groups				Healthy control group N = 50
	Group 1 N = 21	Group 2 N = 25	Group 3 N = 19	Total N = 50	
FBS (mg/dl)	174.09 ± 18.29	232.76 ± 27.47	387 ± 52.29	210.7 ± 57.41*** a	89.14 ± 6.06
ALT (U/l)	9.47 ± 1.86	10.84 ± 2.03	14.26 ± 1.52** b	10.43 ± 2.39	9.76 ± 1.74
AST (U/l)	8.95 ± 1.71	9.24 ± 1.83	13.63 ± 1.80** b	9.02 ± 2.06	8.08 ± 1.32

a Types diabetic patients vs. healthy control group (P***<0.0001)
b Types group 3 vs. groups 1 and 2 (p**<0.001)

Discussion

In the present study, although the means of ALT and AST enzymes were within normal range but we noted some values of these enzymes in the patients group more than the normal range (28% for ALT and 12% for AST). However these increasing values were not more than one times of the upper limit of normal range.

These data is in agreement with recent study in Sudan, where 50 diabetes patients and 30 normal control subjects were tested for liver function, although the means of ALT and AST were falling

within the normal range. Overall 11 patients (22%) had at least one or more abnormal liver function test enzymes [12].

Similar finding was also present in a study by Han Ni et al, in which the means of ALT and AST were within normal range among 81 diabetes patients. Raised ALT and AST were noted in 18.5% and 14.8% respectively in patient group [13].

Abnormal liver function tests in diabetes patients can be attributed to several factors, the most common cause is nonalcoholic fatty liver disease (NAFLD). Although the pathogenesis of this disease is still unclear, it is characterized by accumulation of triglycerides within the hepatocytes. Insulin resistance is thought to play an important role in the triglyceride accumulation. Excess intracellular fatty acids, oxidant stress, ATP depletion, and mitochondrial dysfunction all contribute to hepatocytes injury and inflammation followed by fibrosis [14].

Present study also investigate the effect of glycemic control on the liver function in diabetic group and noted that there is a significantly elevated in ALT and AST levels associated with poor glycemic control group this result is agreement with other studies [15,16].

In diabetic patients with poor glycemic control, two combined events are usually present, promoting hepatic glycogen deposition: hyperglycemia and consequent large amount of insulin. In hyperglycemia, glucose passively enters the hepatocytes by insulin-independent transporter (GLUT2), and it is rapidly phosphorylated, with inhibition of its release from hepatocytes [17].

The glucokinase (GCK) convert the glucose into the G6P, with subsequent trapping in the hepatocytes. Then, an increased insulin administration promotes the polymerization of G6P in glycogen, driving the large amount of glycogen synthesis in the presence of high cytoplasmic glucose concentrations [18].

Therefore, glycogen is trapped within the hepatocytes as a result of a combination of both hyperglycemia and insulin treatment. The consequent liver damage becomes evident with the blood release of aminotransferases [19].

In conclusion, we have shown that there is elevated in serum ALT and AST levels in poor glycemic patients thus screening for these two enzymes can be a useful test in diabetic population to prevent future complications.

In the future, we should be evaluate levels other liver function tests on diabetes patients and study if there is effect of them on the pathogenesis of that disease.

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