

Hepatic Enzymes in Type 2 Diabetes

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Seventy six patients classified as having type 2 diabetes (mean age 56.7 ± 3.25 years; duration of type 2 diabetes 9.47 ± 3.87 years) were studied along with forty normal subjects for the prevalence of abnormal aminotransferase (AST and ALT) activities. Of those with type 2 diabetes, 45 patients used insulin in addition to diet and hypoglycemic drugs. None of the patients had known chronic liver disease. Hemoglobin A_{1c} averaged 10 ± 2.0 vs. 6 ± 1.11 . The type 2 diabetic patients had elevated ALT (48 %) more frequently than AST (25 %). Elevated aminotransferases were twice the upper limit of normal in majority of the patients.

Key Words: Alanine and Aspartate aminotransferases, Glycated hemoglobin, Type 2 diabetes.

INTRODUCTION

Patients with type 2 diabetes experience disturbances of metabolism that lead to microvascular and macrovascular organ damage¹. An association between diabetes, liver injury and elevated serum activity of two aminotransferases, aspartate aminotransferase (AST) and alanine aminotransferase (ALT), occurs more occasionally in diabetics than in the general population². In the present study, the levels of hepatic enzymes alanine aminotransferase and aspartate aminotransferase in type 2 diabetic patients have been compared with those in subjects without type 2 diabetes.

EXPERIMENTAL

Physician-diagnosed seventy-six type 2 diabetic patients (55 % male) attending District Head Quarter Hospital, Faisalabad, Pakistan were studied along with forty non-diabetic volunteers, taken as control. The participants, after written consent, were interviewed for obtaining demographic history.

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None of the patients and control subjects had hepatitis B or C viral infection or known chronic liver disease. Data on alcohol consumption habits showed that all the subjects were non-drinkers. Of those with type 2 diabetes, 45 patients used insulin in addition to diet and hypoglycemic drugs, which were not altered throughout the course of the study. Briefly, alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were measured using standard kit (Biocon) by reaction rate assay based on the conversion of NADH to NAD⁺. HbA_{1c} was measured as described earlier³. Plasma glucose and erythrocyte sedimentation rate (ESR) were measured by standard kit (Biocon) method and Westergren method⁴, respectively.

All the analyses were conducted in Enzyme Research Laboratory, Department of Chemistry and Biochemistry, University of Agriculture, Faisalabad, Pakistan with adherence to quality control procedures. The institutional upper limit of normal (ULN) of ESR and HbA_{1c} was 30 mm/1st hour and 6 %, respectively. For AST and ALT, ULN was 25 U/L and that of plasma glucose was 140 mg/dL.

Compiled data are expressed as mean \pm standard deviation. Statistical analysis involved t-test to identify the difference between two groups with significance level set at $p \leq 0.01$.

RESULTS AND DISCUSSION

Over the past several decades, incidence of diabetes has reached epidemic levels in Pakistan⁵. Public health concerns are increasing due to numerous interconnected health consequences including hypertension, heart disease, hepatic dysfunction and renal failure. The present study aims at investigation of the prevalence of two hepatic aminotransferases (ALT, AST) in type 2 diabetic patients in local population as it is not known, if any such study has been conducted in this region. Increased levels of all the measured parameters were found in type 2 diabetic patients as compared to the normal subjects (Fig. 1).

Patients studied (55 % male) had a mean age of 56.7 ± 3.25 years compared to that of 52.6 ± 9.48 years in control and had mean duration of type 2 diabetes 9.47 ± 3.87 years. About 29 % patients were active smokers compared to only 9 % control subjects. 45 Type 2 diabetics used insulin in addition to diet and oral hypoglycemic drugs compared to only three persons who received lipid-lowering therapy.

Prevalence of raised blood glucose levels in type 2 diabetics compared to those without diabetes (228.39 ± 55.35 mg/dL vs. 112.13 ± 12.87 mg/dL, $p = 0.000$) was indicator of poor glycemic control as glycated hemoglobin averaged 10 ± 2.0 % vs. 6 ± 1.11 % ($p = 0.000$) in patients and normal persons, respectively. 29 patients (38 %) had HbA_{1c} > 10 %.

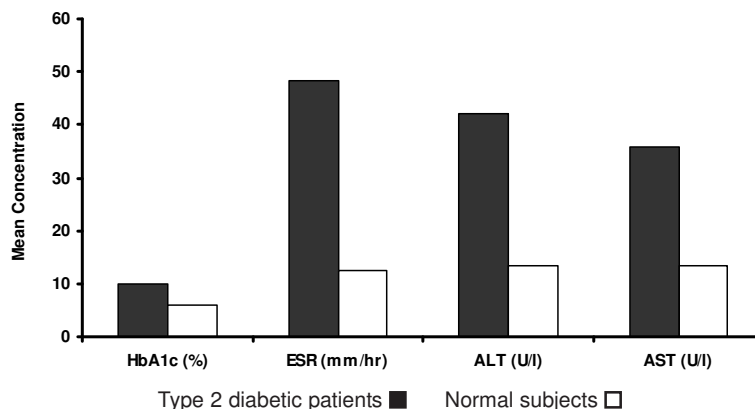


Fig. 1. Comparison of HbA_{1c}, ESR, ALT and AST levels in diabetic and normal participants

Mean ESR in case and normal subjects was 48.36 ± 1.77 vs. 12.37 ± 2.34 ($p = 0.000$), respectively. Although erythrocyte sedimentation rate (ESR) is a basic, economical test in clinical medicine that is used in diagnosis, monitoring diseases activity and response to therapy, it is not sensitive or specific for any particular pathological condition. Poor glycemic control results in significant changes of erythrocyte membrane fluidity, erythrocyte deformability and antioxidant status⁶. However, an increased ESR may occur in many different clinical settings and therefore, higher measurements of ESR among type 2 diabetic patients in the present study were irrelevant as an isolated laboratory value as described in literature^{7,8}.

Mean ALT was significantly higher in type 2 diabetic patients than that in controls (42.18 ± 12.63 U/L vs. 13.45 ± 3.6 U/L, $p = 0.000$). 36 Patients (48 %) had raised ALT (> 25 U/L) including 76 % whose ALT was twice the upper limit of the normal. In a similar study by West *et al.*⁹, the ALT was 3-4 times higher in patients with either type 1 or type 2 diabetes than that in the general population. Harold *et al.*¹⁰ also assessed that type 2 diabetic patients (mean HbA_{1c} 8.5-9.0 %) had serum ALT values 1-2.5 times the upper limit of the reference.

Activity of AST in type 2 diabetic and control persons was significantly different (35.89 ± 9.47 U/L vs. 13.35 ± 3.53 U/L, $p = 0.000$) (Fig. 1). Only 25 % patients showed elevated AST concentrations including 52 % patients exhibiting AST twice the upper limit of normal.

Belfiore *et al.*¹¹ categorized ALT and AST as enzymes whose activities correlate with blood sugar and may increase during ketotic episodes. Reichling and Kaplan¹² evaluated the elevated serum activity of AST as indicator of liver disease while Hanley *et al.*¹³ confirmed an independent predictivity of AST for incident diabetes.

Although the mechanism of the relation between hepatic enzymes and diabetes is not clear, the results of the present study support further investigation into long-term hepatic outcome associated with type 2 diabetes.

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