



Alteration of liver function and glyated haemoglobin (HbA_{1c}) in type 2 Diabetic Mellitus

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Abstract

Alanine aminotransferase (ALT) is the most specific marker of hepatic pathology. Glutamyl transferase (GGT) is considered to be a sensitive indicator of liver damage but not specific. Obesity also has major affects on GGT. The National Cholesterol Education Program has proposed a definition of the metabolic syndrome to help identify individuals at risk for both coronary heart disease and type 2 diabetes. A total of 90 subjects (60 type 2 diabetic subjects, 30 healthy subjects) in an age group of 30 – 75 years satisfying inclusion criteria were selected for the study. Biochemical parameters like fasting and post prandial blood sugar, total serum cholesterol, total triglycerides, HDL, LDL, HbA_{1c}, ALT, AST and GGT were measured using quantitative enzymatic method in Dimension – R fully automated biochemistry analyzer. In our study the Mean \pm S.D values of Gamma Glutamyl Transferase, Alanine Aminotransferase, Aspartate Amino Transferase and Glycated Haemoglobin (HbA_{1c}) was significantly elevated among cases when compared to controls (p value <0.001). The Mean \pm S.D value of HbA_{1c} was elevated in cases when compared to controls. (p value <0.001). Increase in the levels of ALT and GGT in our study supports the theory that the liver functions may get altered due to diabetes.

Key words: Glycated Haemoglobin (HbA_{1c}), Type 2 Diabetic Mellitus Gamma Glutamyl Transferase, and Aspartate Amino Transferase.

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Introduction

The International Diabetes Federation (IDF) estimates that 285 million people around the world have diabetes [1]. This total is expected to rise to 560 million within 20 years. Each year an additional 8-10 million people develop diabetes. India leads the world with largest number of diabetic subjects earning the dubious distinction of being termed the “diabetes capital of the world” [2]. According to the Diabetes Atlas 2006 published by the International Diabetes Federation, the number of people with

diabetes in India currently around 40.9 million is expected to rise to 69.9 million by 2025 unless urgent preventive steps are taken [3]. Alanine aminotransferase (ALT) is the most specific marker of this hepatic pathology. Glutamyl transferase (GGT) is considered to be a sensitive indicator of liver damage but is not specific [4]. Obesity also has major affects on GGT. A number of prospective studies have shown raised GGT or ALT to predict the development of type 2 diabetes independent of BMI and alcohol intake.[5] In our earlier study, raised GGT level was shown to be an independent risk factor for type 2 diabetes, and we hypothesized that GGT might be a marker for visceral and hepatic fat deposition (steatosis) and, by inference, a marker of hepatic insulin resistance [6].

A number of cross-sectional studies have since shown relationships between GGT and ALT and the metabolic syndrome and insulin resistance, suggesting that GGT/ALT may serve as a marker for insulin resistance [7]. Moreover, studies have suggested that hepatic inflammation may be another possible mechanism by which elevated hepatic

enzyme levels are related to diabetes risk [8]. Few studies have examined the role of insulin or inflammation in the link between hepatic enzymes and the risk of diabetes, although elevated ALT has shown to be associated with increased risk of diabetes independent of insulin sensitivity and C-reactive protein [9]. The National Cholesterol Education Program has proposed a definition of the metabolic syndrome to help identify individuals at risk for both coronary heart disease and type 2 diabetes [10].

Materials and Methods

Subjects were chosen from type 2 diabetes and apparently healthy population who visited Sri Ramachandra Medical centre, Chennai for master health check up. With the consent of the subjects and the approval of medical officers and ethical committee, access to values on biochemical tests, BMI and Duration of diabetes and an aliquot of blood sample of the subjects were obtained for the study. People with carcinomas and patients who have undergone treatment for cancer or any other surgical procedures are excluded. Subjects without any known chronic or acute diseases or illness were considered for the study. 90 subjects (60 type 2 diabetic subjects, 30 healthy subjects) in an age group of 30 – 75 years satisfying the above criteria were selected for the study. Fasting and post prandial blood were collected between 8 am and 12 pm from all recruited patients. About 5 ml peripheral blood sample (by standard venous puncture) was collected by the technical staff of Sri Ramachandra Medical Centre, Chennai in a clean and sterilized plain vacutainer. The serum was separated by centrifuging the samples at 2500 rpm for 10 minutes and collected in microfuge tubes.

Glucose was estimated by GOD – POD enzymatic method, cholesterol, TGL, HDL, LDL were estimated by using commercially available kit in them market. VLDL was calculated by using Friedrickson formula. Glycated haemoglobin (HBA_{1C}) was measured by using HPLC. ALT, AST and GGT were estimated on Dimension-R clinical chemistry system with the kits available for the quantitative determination in human serum or plasma.

Results

In our study the Mean ± S.D values of Gamma Glutamyl Transferase, Alanine Aminotransferase, Aspartate Amino Transferase and Glycated Haemoglobin (Hba_{1c} was significantly

elevated among cases when compared to controls (*p* value <0.001). The Mean ± S.D value of Hba_{1c} was elevated in cases when compared to controls. (*p* value <0.001).

Discussion

In the present study, the levels were found the markers of liver injury, including elevated concentrations of aspartate aminotransferase (AST) and alanine aminotransferase (ALT), suggest a risk of type 2 diabetes. Levels of AST and ALT were positively associated with type 2 diabetes and are known to independently predict type 2 diabetes statistically significant compared to controls. Ohlson et al found elevated ALT in non diabetic Swedish men to be a risk factor for type 2 diabetes. It has been hypothesized that elevation in ALT, a gluconeogenic enzyme whose gene transcription is suppressed by insulin, could indicate impairment in insulin signaling, rather than purely hepatocyte injury. [11] Higher ALT has been found to be a risk factor for type 2 diabetes and indicates a potential role of increased hepatic gluconeogenesis and or inflammation in the pathogenesis of type 2 diabetes.

Biochemical parameters	Type-2 diabetes N=30 Mean ± SD	Controls N=30 Mean ± SD	P value
Fasting Glucose (mg/dl)	146.53±49.72	95.6±9.05***	<0.001
Postprandial Glucose (mg/dl)	216.73±71.90	120.23±18.60***	<0.001
HbA _{1C} (%)	8.32 ±2.05	5.89±0.44***	<0.001
Cholesterol (mg/dl)	178.15±41.30	168.8±28.00	NS
Triglycerides (mg/dl)	124.55±48.45	131.43±72.16	NS
HDL (mg/dl)	44.63±19.45	42.9±9.99	NS
LDL (mg/dl)	111.15±36.12	108.96±28.3	NS
ALT (IU/L)	45.23±15.22	44.9±13.73	NS
AST (IU/L)	26.16±15.18	25.4±7.19	NS
GGT (IU/L)	48.56±47.77	36.04±14.93	NS

Table 1: Showing the mean and standard deviation values of all the measured parameters among cases and controls.

A number of cross – sectional studies have shown relationships between GGT and ALT and the metabolic syndrome and insulin resistance, suggesting that GGT / ALT may serve as a marker for insulin resistance [12]. Studies have also suggested that hepatic inflammation may be another possible mechanism by which elevated hepatic enzyme levels are related to diabetes risk.[13] A number of prospective studies have shown raised GGT or ALT to predict the development of type 2 diabetes independent of BMI and alcohol intake.[14] A complementary relationship observed between ALT, and uric acid levels with respect to glycaemic

status and duration of diabetes in our study is in agreement with the above studies linking ALT with insulin resistance and metabolic syndrome.[15] Some studies have showed no relationships between elevated ALT and diabetes.[16] The ethnic differences in levels of visceral fat (which probably plays a major role in the relationship between ALT and diabetes) may account for the differing outcome in various studies [17]. In the present study, the glycaemic status of the patient group did not exhibit any correlation with their BMI status, whereas a correlation was observed with respect to their ALT levels. Altered portal insulin levels and the insulin/glucagon ratio may influence hepatocyte function and integrity in diabetic patients and predispose them to various hepatic disorders.[18] Although no specific liver disease is known to be associated with diabetes mellitus, altered hepatic glucose metabolism may be involved in the pathogenesis of non insulin dependent diabetes [19]. Disturbances in liver function test (LFT) are well recognized in some diabetic patients [20].

Conclusion

Levels of ALT and GGT were found to be altered in type 2 diabetes subjects. Present study a marginal increase was observed in the levels of ALT and GGT supporting the theory that the liver functions may get altered due to diabetes.

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