Evaluation of Serum Transaminases in Type 2 Diabetes Mellitus
K.V.N. Mallikarjuna Rao¹*, Surya Meenakshi Devi Pusapati², N. Lakshmana Kumar³

ABSTRACT

Background: Liver is the central hub for metabolism. Liver dysfunction in diabetes mellitus is one of the major causes of morbidity and mortality. Periodical evaluation of transaminases helps in early diagnosis of liver dysfunction. Aim: The aim of the present study is to measure aspartate transaminase (AST) and alanine transaminase (ALT) in known cases of type 2 diabetes mellitus (T2DM) and to compare the values with matched controls. Settings and Design: Institutional cross-sectional observation study. Methods & Material: Study was done in 100 known cases of T2DM and in 30 controls. Age, AST, ALT and fasting plasma glucose (FPG) were recorded, analysed and compared between two groups. Statistical Analysis: Data was analysed using Microsoft Excel 2007 and SPSS trial version 16.0. Results: Significant difference between FPG, AST, ALT and age were observed between two groups (P < 0.05). Conclusion: The results from our study showed that there are elevated levels of ALT and ASTs among T2DM patients when compared with normal individuals.

KEYWORDS: Diabetes mellitus, Aspartate transaminase (AST), Alanine transaminase (ALT), Age, Fasting plasma glucose (FPG), Nephropathy, Ischaemic heart disease

INTRODUCTION

Diabetes mellitus is a chronic metabolic state characterised by hyperglycaemic leading to micro- and macrovascular complications like nephropathy, retinopathy, ischaemic heart disease, peripheral vascular disease and increased risk of infections, leading to impaired quality of life [1]. Current estimates suggest that there are 170 million people suffering worldwide from diabetes, and it may reach to 266 million by year 2030 [2]. Asians have strong genetic susceptibility for type 2 diabetes mellitus (T2DM) [2]. Indians, in particular, are at higher risk of diabetes at younger age with a low degree of obesity and hence are at higher risk of chronic diabetic complications.

The liver is a key organ involved in the glucose metabolism and energy homeostasis. Major amount of carbohydrates absorbed from gastrointestinal tract undergoes hepatic processing and subsequent storage as glycogen or metabolism into amino acids or fatty acids. Liver diseases are often overlooked as a complication of diabetes. VERONA a place in Italy were diabetes population–based study has shown that standardised mortality rate from cirrhosis was higher than cardiovascular disease in diabetes [3]. Though the association of diabetes with cirrhosis has been recognised for more than 100 years, liver disease in diabetes remains underestimated [4].

Chronic liver disease is often identified by asymptomatic elevation of alanine transaminase (ALT) and aspartate transaminase (AST) during routine serum investigations, but more often such slight increase in their levels are overlooked. Nonetheless, there is evidence to suggest that mild elevation in the levels of these enzymes may be a marker for liver disease [5]. Abnormal liver-function tests are common in diabetes mellitus and more so in patients with type 2 diabetes than type 1 diabetic

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patients [6,7]. Elevation of the levels of ALT and AST was found to be in the range of 7.8–31.5% in T2DM [8–11]. Existing literature suggests that liver enzyme abnormalities together with T2DM constitute an increased risk for cardiovascular disease [12,13] and renal disease [14]. This makes diagnosis of non-alcoholic fatty liver disease (NAFLD) in T2DM patients not only essential for prevention of hepatic complications but also important for prevention of cardiovascular disease and renal dysfunction.

With this background, the present study was aimed at estimating the levels of serum transaminases among type 2 diabetic patients and comparing them with control population.

Diabetes mellitus is associated with liver disorders which include elevation of liver enzyme levels, NAFLD, and chronic liver disorders like hepatitis C infection, cirrhosis and hepatocellular carcinoma [3,15,16]. NAFLD is a common liver disease and may originate from simple steatosis, or severe non-alcoholic steatohepatitis (NASH) or advanced fibrosis and cirrhosis [17].

Elevated activities of two serum transaminases, ALT and AST, may be associated with liver disease [8–11]. Chronic elevations of transaminases usually reflect insulin resistance [18]. Patients with an AST:ALT > 1 have more fibrosis and more progressive disease [19]. Normally, the liver maintains blood-glucose concentration in fasting and postprandial states. Diminished effect of insulin on liver leads to glycogenolysis and increases hepatic glucose production. Abnormalities of lipolysis and triglyceride storage in insulin-sensitive tissue, such as the adipose tissue, are early manifestations of insulin resistance and can be detected prior to fasting hyperglycaemia. The precise environmental, metabolic and genetic factors and series of events that lead to the insulin resistance are not understood fully [20]. There is an increased frequency of tumour necrosis factor alpha promoter sequence polymorphism was found in NASH patients, suggesting a possible genetic link to fatty liver in insulin-resistant states [21]. Impaired insulin signalling and hepatocyte injury are the reasons for elevated transaminases [22].

Development of liver disease with an incidence rate 0.53 per 100 person-years was reported with problems of hepatitis, gallbladder disease and hepatocellular carcinoma [23]. Obese type 2 diabetes individuals have shown significant elevation of transaminases [24]. A study has shown that prevalence of elevated transaminases is 5% in type 2 diabetes, and most of them have attained normal levels with appropriate diabetic treatment [25]. Filipinos with type 2 diabetes have shown higher prevalence (16%) of elevated transaminases [26]. Severity is more in children of 9–18 years age group with type 2 diabetes. A total of 49% cases have shown elevated transaminases with more proneness for development of NASH which may be due to childhood obesity [27]. Different studies have shown prevalence rates ranging from 2 to 24% of elevated transaminases in T2DM [28].

**MATERIAL AND METHODS**

An institutional study was carried out in 100 known cases of T2DM cases attending the OPDOUT PATIENT DEPARTMENT of medical college attached teaching hospital, and 30 control subjects (both females and males) aged between 18 and 70 years were selected. The purpose of the study was explained, and consent was taken from all the subjects. Institutional ethics committee approval was obtained. The data collected includes age, duration of diabetes, any history of previous liver disease, any history of hypertension and alcohol consumption. Study period – 1 year.

Known cases of T2DM attending the OPD are included in the present study.

Known cases of hepatic disease, alcoholics and hypertension are excluded from the study.

Cases were selected based on the simple random sampling and were taken up for the further processing. Age and sex matched controls were selected from the
same geographical area. 5 ml of venous blood was collected in fasting state. Serum was separated within hour by centrifugation and used for study. Fasting plasma glucose was estimated using glucose oxidase method where glucose oxidase converts glucose to gluconic acid and hydrogen peroxide, and in the presence of peroxidase to produce red quinoneimine dye. This dye has absorbance maximum at 505 nm (500–550 nm). The intensity of the colour complex is directly proportional to concentration of glucose in specimen [29]. A sample volume of 0.01 ml and reagent volume of 1.0 ml is taken, and the concentration of glucose is estimated using a wavelength of 505 nm with Blank absorbance limit <0.300 Abs.

The serum that is obtained by centrifugation is treated with ALT reagent where ALT present in the sample catalyses the transfer of amino group from L-alanine to alpha ketoglutarate forming pyruvate and L-glutamate. Pyruvate in the presence of NADH nicotinamide adenine dinucleotide hydroxide and lactate dehydrogenase (LDH) is reduced to L-lactate. In this reaction, NADH is oxidised to NAD Nicotinamide adenine dinucleotide (NAD). The reaction is monitored by measuring the rate of decrease in absorbance at 340 nm due to oxidation of NADH to NAD. A sample volume of 25 µl and working reagent volume of 500 µl are taken, and the level of ALT is measured using wavelength of 340 nm for a kinetic interval of 60 s. The values obtained are compared between diabetics and non-diabetics.

A sample volume of about 25 µl and 500 µl of working reagent volume mainly containing L-aspartate is taken using wavelength of about 340 nm for a kinetic interval of 60 s. Aspartate aminotransferase (AST) catalyses the transfer of amino group from L-aspartate to U-ketoglutarate yield oxaloacetate and L-glutamate. The oxaloacetate undergoes reduction with simultaneous oxidation of NADH to NAD in the malate dehydrogenase catalysed indicator reaction. The resulting rate of decrease in absorbance at 340 nm is directly proportional to AST activity. LDH is added to prevent interference from endogenous pyruvate which is normally present in serum [30]. The values obtained are compared between diabetics and non-diabetics. For ALT and AST estimations, Erba Mannheim XL system packs were used and procured from Transasia Bio Medicals Ltd.

Data was analysed using Microsoft Excel 2007 & SPSS trial version 16.0. Continuous variables were expressed as mean ± standard deviation. Student t test was used to compare means of the two groups. Probability (P) value less than 0.05 was regarded as statistically significant.

RESULTS AND DISCUSSION

In the present study, out of 130 persons, 30 members are recruited as controls (n = 30), and 100 members as cases (n = 100). Group statistics are presented in Table 1. The results show that there is significant rise in the levels of AST and ALT in cases when compared with controls.

Table 1: Mean and S.D. of variables in controls and cases

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean ± S.D. (n = 30)</th>
<th>Mean ± S.D. (n = 100)</th>
<th>Significance (P Value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGE</td>
<td>35.80 ± 9.572</td>
<td>50.00 ± 9.209</td>
<td>0.00</td>
</tr>
<tr>
<td>FPG</td>
<td>83.33 ± 9.495</td>
<td>167.36 ± 53.114</td>
<td>0.00*</td>
</tr>
<tr>
<td>AST</td>
<td>27.70 ± 7.996</td>
<td>36.96 ± 22.892</td>
<td>0.032*</td>
</tr>
<tr>
<td>ALT</td>
<td>22.97 ± 8.348</td>
<td>39.14 ± 24.532</td>
<td>0.001*</td>
</tr>
</tbody>
</table>

*P < 0.05

This study showed that type 2 diabetic patients were likely to have higher levels of AST and ALT compared with non-diabetic individuals, even though the values are within the range (normal range for AST 4–45 IU/l and for ALT 3–40 IU/l) as prescribed by IFCC. This indicates that type 2 diabetic patients are likely to have progressive liver disease ranging from NAFLD to advanced fibrosis and cirrhosis which is often overlooked. Among ALT and AST enzymes, there was greater rise in the levels of ALT than AST, which supported the hypothesis that elevation of ALT is due to impairment in insulin signalling rather than purely hepatocyte injury [22]. Further, ALT plays a role in
gluconeogenesis and is more related to liver fat accumulation than AST [31]. Severe steatosis is denoted by a higher release of ALT enzyme in response to hepatocytes derangement which tends to occur early in the disease process. Therefore, minor elevations of this enzyme level may be a good predictor of mortality from liver disease [7,9,10,11]. In addition, chronic mild elevation of liver enzymes in T2DM patients also emphasises that T2DM has strong association with NAFLD, including its severe form NASH. Though the pathogenesis and sequence of events leading to NAFLD is not entirely understood, we can assume that liver-fat accumulation and progression of steatosis to NASH to be significant mechanisms [32].

One of the main limitations of the present study is that it was conducted on a small sample population with less number of subjects. The observations of the present study need to be confirmed on a large population.

The present study was undertaken to investigate the levels of serum transaminases among T2DM patients. From the results of the present study, it can be concluded that the serum levels of transaminases are significantly higher in diabetic patients than normal controls. Clinically, the increased levels of AST and ALT may possibly indicate a sign of unanticipated hepatic disorder, their frequent estimation in T2DM patients is warranted.

Periodical monitoring of transaminases and their relation to anti-diabetic medications, duration of diabetes along with measurement of serum lipids and ultrasound examination of liver will help in understanding the reasons for alteration of serum transaminases in individuals with T2DM.

REFERENCES


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