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Research Article

Diabetes Mellitus

Alterations in liver enzymes in type 2 diabetes mellitus

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Introduction: Liver plays an important role in regulation of blood glucose in fed state as well as in fasting. Diabetes mellitus can result as a consequence of liver disorder and vice versa. Objective of our study is to compare the liver enzymes in type 2 diabetic patients as compared to non-diabetic patients. **Methodology:** A case- control study was conducted in the Department of Biochemistry, Karwar Institute of Medical Sciences, Karwar from January 2015 to December 2015. We collected the data of 54 diabetic patients and 57 healthy people as controls. Random blood glucose, aspartate aminotransferase (AST), alanine amino transferase (ALT) and alkaline phosphatase (ALP) were estimated in the study subjects. **Results:** We found that AST levels (33.38±2.19 U/L) in diabetics extremely significantly high as compared to controls (24.82 ± 0.95 U/L). ALT levels were also extremely significantly high in diabetics, 27.69±1.96 U/L as compared to 19.32±1.22 U/L in controls. Correlation study showed a weak positive correlation between AST, ALT and blood glucose. Odds ratio showed a higher risk of liver disorder in diabetics. **Conclusion:** Diabetics had high liver enzymes as compared to non-diabetics. An association was found between type 2 diabetes mellitus and liver enzymes.For better characterization of cause and effect, further studies need to be done on alterations in liver function tests along with the histopathological analysis of liver biopsy samples.

Keywords: Hepatic Enzymes, Diabetes Mellitus, Risk of liver disorders

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Introduction

Liver disease is an important cause of death in type 2 diabetes mellitus. A population-based diabetes study by De Marco et al [1] reported that cirrhosis was the fourth leading cause of death and accounted for 4.4% of diabetes related deaths. In another prospective cohort study Balkau B et al suggests that cirrhosis accounted for 12.5% of deaths in patients with diabetes [2]. Virtually the entire spectrum of liver disease is seen in patients with type 2 diabetes. This includes abnormal liver enzymes, nonalcoholic fatty liver disease (NAFLD), cirrhosis, hepatocellular carcinoma, and acute liver failure. In addition, there is an unexplained association of diabetes with hepatitis C. The prevalence of cirrhotic patients developing diabetes is 12.3 % – 57% [3]. Thus, patients with diabetes have a high prevalence of liver disease and patients with liver disease have a high prevalence of diabetes. Elevation of serum alanine aminotransferase (ALT), while uncommon in apparently normal subjects is common in patients with type 2 diabetes [3]. A clinical trial report suggests that 2- 24% of screened type 2 DM patients had liver enzyme tests above the upper limit of normal [4]. In this study, investigators noted that 5% of the patients had concomitant liver disease at baseline. Another report involving multiple clinical trials with type 2 diabetes suggests that diabetics had higher levels of serum alanine amino transferase (ALT), aspartate aminotransferase (AST), or alkaline phosphatase than the normal limits [5].

Liver has an important role in the carbohydrate metabolism and regulation of blood glucose. It is the major site for glycogenesis and gluconeogenesis. This function of liver makes it susceptible in diabetes mellitus [6]. Increased activity of the liver enzymes is associated with Insulin resistance [7]. The cause and effect relationship between diabetes mellitus and liver diseases are well documented. But less explored area in the field of research in our settings.

Objectives

Aim of our study is to compare the liver enzymes in type II diabetic patients as compared to non-diabetic healthy volunteers. We also would like to find out the association between type 2 diabetes and liver enzyme levels.

Methodology

Study design: A case- control study was conducted in the Department of Biochemistry, Karwar Institute of Medical Sciences, Karwar from January 2015 to December 2015. Institutional ethics committee approval has been sought before starting the study.

Group I: Type II diabetic patients irrespective of their treatment.
Group II: non- diabetic, healthy volunteers.

We collected the data of 54 patients in group I and 57 controls in group II. Sample size is calculated by using suitable formula .Diabetes mellitus (DM) is diagnosed as per American Diabetic Association guidelines 2016 [8].

Inclusion criteria for patients: Type II diabetic patients with a mean age of 52.3±1.7.

Exclusion criteria for patients: Type I diabetics, alcoholics, smokers, hypertensives, those with liver disorders, patients on hepatotoxic drugs and those with any other systemic illnesses.

Inclusion criteria for controls: healthy volunteers, non-diabetic, nonalcoholic individuals.

Group I subjects had a mean age of 52.3±1.7 years, 64% of them being males and 36% being females.
Group II had a mean age of 47.8±2.1 years, 72% being men and 28% women.

Data collection and analysis: Data of age, gender, liver enzymes and blood sugar of patients were collected from our clinical biochemistry laboratory. Investigations were done by collecting two ml of venous blood sample in plain tubes by puncturing antecubital vein with aseptic precautions. Samples were centrifuged at 3000 rpm for 15 minutes. Plasma was analyzed for liver enzymes, AST, ALT and alkaline phosphatase with commercially available kits in fully automated chemistry analyzer, XL-640 [9-11]. Following ranges are considered to be normal for the liver enzymes;

AST – 5-37 U/L
ALT – 5 -35 U/L
Alkaline phosphatase – 25-147 IU/L

Statistical analysis: Data was analyzed by Student's unpaired't' test. $P< 0.05$ is taken as significant. Pearson's correlation coefficient, r (between -1 and +1) is calculated

To find the correlation of each parameter with blood glucose. Odds ratio was calculated to find out the relative risk.

Results

The results are expressed as mean ± standard error of mean (SEM) calculated for blood glucose, AST, ALT and alkaline phosphatase and are represented in the Table I.

Table I: Laboratory parameters of diabetic patients and controls.

Parameters	Type II Diabetes mellitus(Mean±SEM)	Controls (Mean±SEM)	P value
Random blood glucose (mg/dl)	207.03±9.60	101± 2.09	<0.0001*
AST (U/L)	33.38±2.19	24.82 ± 0.95	0.0004*
ALT (U/L)	27.69±1.96	19.32±1.22	0.0005*
Alkaline phosphatase (IU/L)	89.64±5.05	82.89±3.83	0.302

*Very highly significant

Pearson's correlation coefficients calculated to assess the correlation between blood glucose and AST as well as blood glucose and ALT were statistically insignificant. But there was a weak positive correlation between blood glucose and liver enzymes. Odds ratio for ALT and AST are calculated and given in Table II and Table III.

Table-II: Odds ratio for AST.

	Group I(Diabetes mellitus)	Group II (Controls)
Increased AST	15 (a)	4 (b)
Normal AST	39 (c)	53 (d)

Odds ratio = ad/bc = 15x53 /39x4 = 5.1

Table- III: Odds ratio for ALT.

	Group I (Diabetes mellitus)	Group II (Controls)
Increased ALT	12 (a)	5 (b)
Normal ALT	40 (c)	52 (d)

Odds ratio = ad/bc = ad/bc =12x52 / 40x5 = 3.12

Discussion

We found ALT and AST levels in the normal range, but AST levels were 1.3 times high in diabetes patients as compared to normal controls. ALT levels were 1.4 times high in diabetes patients. This suggests that diabetes patients have an inclined tendency towards alterations of liver enzymes.

There are several studies which report that there is an elevation in liver enzymes in diabetics. In a report involving clinical trials with type 2 diabetes patients, serum ALT, AST or alkaline phosphatase were 1-2.5 times higher than the upper normal. 5.6% had serumALT values between 1 and 2.5 time's upper normal limit [5]. Asymptomatic individuals with mild elevations of ALT and AST revealed that 98% had liver disease, fatty liver disease andchronic hepatitis [12]. The most common cause of a mild elevation of serum ALT is non-alcoholic fatty liver disease [13], which is the most prevalent liver disease in type 2 diabetes. Odds ratio (OR) for AST suggest that the risk of development of liver disease is 5 times in diabetics as compared to controls. Odds ratio for ALT suggest that risk of liver disease is 3 times in diabetics. A study by Gupte et al, reported that 49% patients with DM had evidence of fatty liver; of these 32% underwent liver biopsy [14]. In the biopsy report it was found that 66%, 13% and 9% showed mild, moderate and severe nonalcoholic steatohepatitis respectively and 22% showed fibrosis.

Since we have not assessed the histopathology of liver biopsy specimens, we cannot specify whether there is a fatty change or to which liver disorder they are prone. But comparatively high liver enzymes suggest a probable risk of chronic liver disease in future. Our study is supported by a recent review report by Paola et al suggests that patients with type 2 DM are at the highest risk of non-alcoholic steatohepatitis (NASH) , even in the setting of normal plasma aminotransferases [15]. However hepatic fat accumulation is a well-known complication of diabetes with a reported frequency of 40–70%. If fat in the hepatocytes is accompanied by lobular inflammation and steatonecrosis, it should be considered as a cause for chronically elevated liver enzymes in asymptomatic diabetic patients [16]. In type 2 diabetic patients with or without obesity, up to 30% have fat with inflammation, 25% have associated fibrosis, and 1–8% have cirrhosis [17-19]. Limitations of our study are small sample size and various confounding factors like obesity, metabolic syndrome and infection with hepatitis C, being not taken in to account.

Conclusion

We conclude that diabetic patients had high liver

Enzymes as compared to non-diabetics. An association was found between type 2 diabetes mellitus and liver enzymes. For better characterization of cause and effect further studies need to be done along with the assessment of blood coagulation, abdominal ultrasound, histopathology of liver biopsy and other parameters of liver profile need to be done.

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