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LIVER DYSFUNCTION IN DIABETIC PATIENTS ADMITTED IN REFERRAL HOSPITAL

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Background: Liver function tests (LFTs) are group of tests that help in diagnosis, monitoring therapy, and assessing prognosis of liver disease. To estimate liver function tests in diabetic patients attending OPD of Central Referral Hospital, Sikkim, India. **Methods:** This study was conducted in Central Referral Hospital, Gangtok, Sikkim, India between October 2007 to April 2008. A total of 150 diabetic patients and 50 controls were taken to assess the liver function tests (LFTs) by measuring Aspartate aminotransferase (AST), Alanine aminotransferase (ALT), Alkaline phosphatase (ALP) & total bilirubin (TB). **Results:** Total Bilirubin (TB) was found to be elevated in maximum number of patients, 84 (56%) out of 150 patients and followed by both AST and ALT, 39 (26%) each out of 150 patients. **Conclusion:** LFTs in type-2 diabetic patients are found to be statistically significant when compared with normal healthy controls

Keywords: type-2 diabetes mellitus; liver function tests; Sikkim

INTRODUCTION

Liver plays a major role in metabolism and has a number of functions in the body, including glycogen storage which is made from sugars, helping to process fat and proteins from digested food, making proteins that are essential for blood to clot, decomposition of red blood cells, hormone production and detoxification.[1]Diabetes mellitus, long considered a disease of minor significance to world health, is now emerging as one of the main threats to human health in the 21st century. The past two decades have seen an explosive increase in the number of people diagnosed with diabetes world-wide. The World Health Organization (WHO) estimated that there were 135 million diabetics in 1995 and this number would increase to 300 million by the year 2025. India leads the world today with the largest number of diabetics in any given country. It has been estimated that in 1995, 19.4 million individuals were affected by diabetes in India and these numbers are expected to increase to 57.2 million by the year 2025 (one sixth of the world total).[2]

The liver plays a central and crucial role in the regulation of carbohydrate metabolism. Its normal functioning is essential for the maintenance of blood glucose levels and of a continued supply to organs that require a glucose energy source. Liver disease occurring as a consequence of diabetes mellitus includes glycogen deposition, steatosis and nonalcoholic steatohepatitis (NASH), fibrosis and cirrhosis, biliary disease, cholelithiasis, cholecystitis, complications of therapy of diabetes (cholestatic and necroinflammatory).[3]

Liver function tests (LFTs) are commonly used in clinical practice to screen for liver disease, monitor the progression of known disease, and monitor the effects of potentially hepatotoxic drugs. Individuals with diabetes have a higher incidence of liver function test abnormalities than individuals who do not have diabetes. Mild chronic elevations of transaminases often reflect underlying insulin résistance. The most common LFTs include the serum aminotransferases alkaline phosphatase, bilirubin, albumin, and prothrombin time. Aminotransferases, such as alanine amino transferase (ALT) and aspartate aminotransferase (AST), serve as a markerof hepatocyte injury. Alkaline phosphatase (ALP), γ-glutamyl trans-peptidase (GGT), and bilirubin are markers of biliary function and cholestasis. Chronic mild elevation of transaminases is frequently found in type-2 diabetic patients.[4]

Diabetes mellitus (DM) is associated with non-alcoholic fatty liver disease (NAFLD) including its severe form, non-alcoholic steato hepatitis (NASH). Among patients with diabetes, the risk of chronic liver disease is doubled, independent of alcoholic or viral hepatitis.[5] This study was conducted to examine the dysfunction of LFT in diabetic patients of Sikkimese population

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PATIENTS AND METHOD

A total of 150 type 2 diabetic patients and 50 healthy controls who visited the OPD of Central Referral Hospital, Gangtok, Sikkim, India from October, 2007 to April 2008 irrespective of drugs and diet taken were included in the study. Ethical approval for the study was taken from the institutional research ethical committee. All these patients were referred to Clinical Biochemistry Laboratory for estimation of fasting blood glucose (FBS), Post-Prandial blood glucose (PPBS), aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP) and total bilirubin (TB). Blood glucose estimation was carried out by glucose oxidase (GOD)/ peroxidase (POD) method, amino transferases (AST & ALT) and alkaline phosphatase (ALP) were estimated by the method recommended by International Federation of Clinical Chemistry (IFCC) and total bilirubin (TB) level by Malloy & Evelyn method. AST, ALT & ALP were expressed in International Unit/Liter while concentration of blood glucose and total bilirubin were expressed in milligram/deciliter (mg/dl). The data was analyzed using Statistical Package for the Social Sciences (SPSS) for Windows Version 16.0. Data are presented as mean ± SD or as a percentage (%). A p value < 0.05 is considered to be statistically significant.

RESULTS

The study was conducted on 150 type 2 diabetic patients. The mean ± SD age of type 2 diabetic patients 53.1 ± 7.61 ranging between 40-65 years while the mean ± SD age of healthy control subjects was 55.24 ± 9.13 ranging between 40-70 years. Out of 150 patients, 93 (62%) were males and 57 (38%) were females. Among the control subjects 32 (64%) were males and 18 (36%) were females as presented in Table 1.

Table 1
Age and sex distribution of study subjects

Characteristic	Control	Patients type-2 DM
Age (years)		
Mean ± SD	55.24 ± 9.13	53.1 ± 7.61
Range	40-70	40-65
Sex distribution		
Males	32 (64%)	93 (62%)
Females	18 (36%)	57 (38%)

All the tests (AST, ALT, ALP, TB), when compared with normal healthy control were found to be statistically significant (Table 2).

Table 2
Liver function tests of Type 2 diabetic patients and control subjects

Parameter	Control	Patients type-2 DM	p
FBS (mg/dl)	85.46 ± 11.52	204.30 ± 67.14	0.0001
95% CI	82.19-88.73	193.47-215.13	
PPBS (mg/dl)	171.30 ±14.41	298.70 ± 83.17	0.0001
95% CI	167.20-175.40	285.28-312.12	
AST (IU/dl)	20.44 ± 8.74	47.74 ± 41.42	0.0001
95% CI	17.95-22.93	41.06-54.42	
ALT (IU/dl)	20.00 ± 7.74	41.64 ± 36.14	0.0001
95% CI	17.80-22.20	35.81-47.47	
ALP (IU/dl)	68.50 ± 22.72	284.94 ± 221.34	0.0001
95% CI	62.04-74.96	249.23-320.65	
TB (mg/dl)	0.45 ± 0.19	1.40 ± 0.81	0.0001
95% CI	0.40-0.51	1.27-1.53	

Remarks:
FBS = fasting blood glucose, PPBS = Post-Prandial blood glucose, AST = aspartate aminotransferase, ALT = alanine aminotransferase, ALP = alkaline phosphatase, and TB = total bilirubin.

In both male and female, total bilirubin was found to be most elevated followed by AST (25.80%) in male and ALP (36.84%) in female. In total studied subjects, total bilirubin was found to be most elevated, i.e. 84 (56%) out of 150 patients (Table 3).

Table 3
Elevated LFT in male and female type-2 diabetic patients

Tests	Male	Female	Total
AST	24 (25.80%)	15 (26.31%)	39 (26%)
ALT	21 (22.58%)	18 (31.57%)	39 (26%)
ALP	15 (16.12%)	21 (36.84%)	36 (24%)
TB	39 (41.93%)	45 (78.94)	84 (56%)

DISCUSSION

It is found that 99 (66%) of the studied diabetic patients have abnormal liver function parameters. The most common abnormality is elevated total bilirubin level with 84 (56%) subjects. Serum bilirubin levels increases due to many causes and tend to increase in most liver diseases and result in jaundice.[6,7]Aminotransferases (AST & ALT) are elevated in 39 (26%) each. In the liver, ALT is exclusively cytoplasmic whereas AST is both cytosolic and mitochondrial. So an increase in serum ALT level is more specific for liver damage with exception in alcoholic hepatitis, hepatic cirrhosis and liver neoplasia. Other than viral and alcoholic hepatitis, nonalcoholic steatohepatitis is the most common cause of aminotransferase increases which is considered to be the most prevalent disease in type-2 diabetes.[7,8] Any diabetic patientfound to have a mild chronic elevation of ALT should have screeningfor treatable causes of other chronic liver diseases, particularlyhepatitis B, hepatitis C, and

hemochromatosis, which are found with increased incidence among diabetic patients.[9]

ALP activity is present in most organs of the body and elevations in serum ALP activity is commonly originate from the liver and bone. Increase in serum ALP activity tends to be more in extrahepatic obstruction than in intrahepatic obstruction. Increase may also be seen in patients with advanced primary liver cancer or widespread secondary hepatic metastases or can be seen as a consequence of reaction to drug therapy.[8] Our findings are almost similar to those conducted by Salmela et al., Ayman S. Idris et al. and Paruk IM et al except that it show a much higher prevalence rate of elevated LFT.[10-12]

CONCLUSION

Elevated LFTs percentage is more than any other studies conducted so far. It may be due to high drinking habit among the Sikkimese population, the liver function might have been deteriorated. This indicates that with the progress of diabetic condition the functioning of the liver is deteriorated more. Further studies are required to fully implicate liver dysfunction in diabetic patients.

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