Research Paper

Volume : 4 | Issue : 2 | February 2015 • ISSN No 2277 - 8179

A STUDY OF LIVER DYSFUNCTION DETERMINANTS IN NORMAL AND TYPE 2 DIABETIC SUBJECTS IN INDIAN POPULATION

Medical Science

KEYWORDS : Type-2 Diabetes mellitus and LFT

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ABSTRACT

The association of abnormal liver function tests are not uncommon encounter in diabetes mellitus patients. Previous data on evaluation of liver function tests in patients with type 2 diabetes mellitus showed considerable debates, so this study was conducted to evaluate the liver function test abnormalities in patients with type 2 DM in India. It is a case control comparative study included biochemically and clinically confirmed 50 cases of Type 2 DM (age ranges 12-60Years) and results are compared with 50 age and sex matched healthy controls. LFTs were performed using standard methods. Our study shows that serum AST,ALT,ALP,GGT and bilirubin significantly increase and total protein was significantly decrease in type 2 DM patients when compared to control subjects.Thus the emerging evidence suggests the abnormal LFTs may be marker for diagnosis and prognosis of diabetes mellitus.

INTRODUCTION

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.(1) In the health care delivery system worldwide, cases of diabetes mellitus and its associated clinical conditions are increasing on daily basis. Type 2 DM is a heterogeneous, multifactorial, polygenic disease characterized by a defect in insulin secretion (the beta cell secretory defect) and action (insulin resistance) which results in elevated blood glucose.(2) 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.(1)

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). Diabetes is more prevalent in men than women.

There exists an association between diabetes and liver injury. Liver plays a major role in the regulation of carbohydrate homeostasis. Hepatocellular glycogen accumulation leads to hepatomegaly and liver enzyme abnormalities in poorly controlled diabetes patients. In hyperglycemic states, there will be intracellular glycogen accumulation in the hepatocytes due to increased glycogen synthesis, causing typical biochemical findings of mild to moderately elevated aminotransferases, normal liver synthetic function, with or without mild elevations of alkaline phosphatase. All these biochemical disturbances and hepatomegaly are found to be reversible with good glycemic control. (3)

Several biochemical tests are useful in the evaluation and management of patients with hepatic dysfunction. Liver Function Tests (LFTs) are commonly used in clinical practice to screen for liver disease. The most common LFTs include the serum aminotransferases (ALT, AST), alkaline phosphatase, bilirubin and albumin. Increased activities of liver enzymes such as aspartate aminotransferase (AST), alanine aminotransferase (ALT) and GGT are indicators of hepatocellular injury. Increased activity of these markers is associated with insulin resistance.(4)

Individuals with type II 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 resistance. Aminotransferases, such as alanine aminotransferase (ALT) and aspartate aminotransferase (AST), measure the concentration of intracellular hepatic enzymes that have leaked into circulation and serve as a marker of hepatocyte injury. Alkaline phosphatase, GGT, and bilirubin act as markers of biliary function and cholestasis. Albumin reflect liver synthetic function. Chronic mild elevation of transaminases are frequently found in type 2 diabetic patients.(5)

Many reports are available which correlate liver function tests in diabetes mellitus. The studies are controversial for derangement of liver function tests in diabetes mellitus. Hence the present study is undertaken to determine liver function tests in type II diabetes mellitus.

MATERIAL AND METHODS

The present study was conducted on 50 clinically established diabetic patients. The patients were diagnosed depending on the results of clinical examinations, blood HBA1C and serum fasting and post-prandial glucose levels. The subjects selected for the study were grouped as follows:

Group I : Healthy control subjects (n=50) (Age 36-60 years)

GroupII : This group consists of type 2 (NIDDM) diabetic subjects (n=50) (Age 36-60 years)

Exclusion Criteria:- The alcoholics, subjects with systemic and other hepatic disease, pregnant women, patients with infectious diseases, post operative patients, smokers, patients on drugs (except antidiabetic therapy),genetic disorders and age <36 years and >60 years were excluded from study.

Informed consent was secured from all subjects for participating in the study. Individuals in control group were matched with the patients for their place of residence and sex.

Blood samples were obtained by antecubital vein puncture, between 8 and 9 AM after an overnight fast (10-12 hours). Standard aseptic precautions were taken and samples with signs of hemolysis were discarded. The blood was centrifuged at 3000 rpm for 15 minutes (40C) and serum was stored at -40C until the day of the test.

Serum were subjected for estimations including Blood Glucose,(fasting and post prandial), serum Total and direct bilirubin, serum AST, ALT, Total protein, Albumin, ALP, GGT by using commercially available kits and methods on fully auto analyser .Serum Indirect bilirubin, Globulin and A:G ratio were estimated by standard calculative methods.

RESULT AND DISSCUTION

The mean±SD value of AST in healthy control subjects was 26.64±.9U/L, and in type II diabetes mellitus subjects was 38.0±10.0 U/L. SGOT level showed highly significant increase (P<0.01) in type II diabetes mellitus subjects when compared with healthy controls.(Table)

The mean±SD value of ALT level in healthy control subjects was 21.52±7.9 U/L, in type II diabetes mellitus subjects was 36.0±13.25 U/L.SGPT level showed highly significant increase (P<0.01) in type II diabetes mellitus subjects when compared to healthy control subjects.

The mean±SD value of ALP in healthy control subjects was 71.36±11.17 U/L and in type II diabetes mellitus subjects was 95.1±15.65 U/L. On comparing type II diabetes mellitus subjects with healthy control subjects, the ALP values of type II diabetes mellitus subject was increased significantly(P<0.05) (Table).

The mean±SD value of GGT level in healthy control subjects was 29.4±5.09 U/L,in type II diabetes mellitus subjects was 42.9±10.91 U/L. GGT level showed highly significant increase (P<0.01) in type II diabetes mellitus subjects when compared to healthy control subjects.(Table)

The mean±SD value of Total serum Bilirubin in healthy control subjects was 0.66±0.23 mg/dl and in type II diabetes mellitus subjects was 1.08±0.90. On comparing type II diabetes mellitus subjects with healthy control subjects, the total serum bilirubin values were observed statistically significant (P<0.05) (Table).

The mean±SD value of Total protein in healthy control subjects was 7.09±0.53 gm/dl and in type II diabetes mellitus subjects was 6.69±0.56 gm/dl. The Total protein level showed significant decrease (P<0.05) in type II diabetes mellitus subjects when compared to healthy control subjects (Table).

BIOCHEMICAL PARAMETERS IN HEALTHY CONTROLS(GROUP-I) AND TYPE II DIABETES MELLITUS SUBJECTS (GROUP II)

Parameters	Mean±S.D. (Group I)	Mean±S.D. (Group II)	P value by 't' test
Glucose (f) (mg/dl)	88.0±11.47	209.0±103.0	-
Glucose (PP) (mg/dl)	117.0±6.84	288.0±106.0	-
Total S. Bilirubin (mg/dl)	0.66±0.23	1.08±0.90	P<0.05
Direct S. Bilirubin (mg/dl)	0.19±0.07	0.28±0.18	P<0.05
Indirect S. Bilirubin (mg/dl)	0.46±0.14	0.75±0.78	P>0.05
A.S.T. (U/L)	26.64±4.9	38.0±10.0	P<0.01
A.L.T. (U/L)	21.52±7.9	36.0±13.25	P<0.05
Total protein (gm/dl)	7.09±0.53	6.69±0.56	P>0.05
Albumin (gm/dl)	4.31±0.26	4.29±0.32	P>0.05
Globulin (gm/dl)	2.98±0.35	3.02±0.49	P<0.05
A : G Ratio (gm/dl)	1.28±0.20	1.32±0.28	P>0.05
ALP (U/L)	71.36±11.17	95.1±15.65	P<0.01
GGT (U/L)	29.4±5.09	42.9±10.91	P<0.05

Falchuk et al. (1980) [6] reported similar findings in which they showed elevated alkaline phosphatase levels in the range of 120-126 mU/ml. There was concomitant elevation of GGT. The SGOT and SGPT were also elevated in diabetes mellitus. Foster KJ et al. (1980) [7]assessed in 60 unselected diabetes patients and found GGT and alkaline phosphatase were elevated but rarely to more than twice the upper limit of normal which is in agreement with our findings. Our findings are in agreement with Everhart et al. (1995),[8] who states that elevated serum activity of two aminotransferases,(AST) and (ALT), is the most frequent measured indicator of liver disease and occurs in diabetes more frequently than general population

Noriyuki N.et al. (2004)[9] investigated the association between serum GGT and type II diabetes. The type II diabetes increased in correlation with the levels of serum GGT, ALT, AST and alkaline phosphatase. Sherif Gonem,(2007)[10]in UK by a cohort study of 959 diabetic patients over four year period, found 15.7% had raised ALT,10.4% had elevated alkaline phosphatase whereas only 3.9% had hyperbilirubinaemia. which also supports our findings. Sapna Smith Lal et al. (2009)[11] also reported that all diabetic subjects have significantly lower serum Total protein level as compared to non diabetic subjects. These studies also correlates with our findings.

Iman Mahomad Paruk et al.(2011)[12] analyzed liver function test abnormalities in 146 diabetes patients. Elevations of GGT, alkaline phosphatase and alanine transaminase were found when compared with subjects with normal results. This also correlates with our study. According to a study in Sudan by Idris A S et al.(2011),[13] where 50 diabetes patients and 30 normal control subjects were tested for liver function, the means of ALT, AST,GGT, total protein and albumin were reported to be significantly higher among diabetes compared to the control. However, the mean values were within the normal range, which also found the same results.

A similar study was done by Dhamyaa Hadi Salih in feb(2013) [14] studied on 55 blood samples and glucose, ALP,ALT ,AST were measured on these groups, and found that there is no significant difference between females and males in controls and patients, there is significant difference between the controls group and the patients and the correlation between the glucose and biochemical parameters were positive significant correlated with ALP,AST and ALT. Adeniran Samuel Atibaet al july (2013)[2] found the serum level of liver enzymes ALT, AST and ALP analyzed were significantly elevated in subjects than in the control group (12.69±6.75 vs 4.95±2.66 IU/L; p<0.05), (16.96±10.80 vs 7.83 IU/L±3.94,p<0.05) and (70.19±28.78 vs 23±8.77 IU/L; p<0.05) respectively, which also correlats with our study.

Hind M.et al.(2014)[15] studied on 120 type 2 diabetic subjects and 80 healthy control subjects and concluded that the means of ALT, AST, ALP, Total Protein, Albumin, and total bilirubin were significantly higher in patients than in the control (P<0.02), but direct bilirubin values were not significantly different, (P =0.37), which also supporative findings for us.

A similar study was done by Roshan Takhelmayum in 2014 [1], in which a total of 150

diabetic patients and 50 controls were taken to assess the liver function tests (LFTs) by measuring AST, ALT, Alkaline phosphatase & total bilirubin. Total Bilirubin 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 and concluded that LFTs in type-2 diabetic patients are found to be statistically significant when compared with normal healthy controls. It also correlats the study done by Razia Philip in 2014.[16]

It is difficult to assess the various liver function test in type II diabetes mellitus in a small study but inclusion of age and sex matched controls simultaneously and analyzing the statistical significance of difference between two groups leaves less chances for these results being a chance association. However, further elucidation is required in large cohort studies to draw conclusion on liver function tests in patients with diabetes mellitus on a firm ground in india.

Volume : 4 | Issue : 2 | February 2015 • ISSN No 2277 - 8179

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