Observational Study of Serum Alanine Aminotransferase (ALT), Serum Aspartate Aminotransferase (AST) and Serum Alkaline Phosphatase (ALP) Levels in Type 2 Diabetic Patients

Himanshu Jindal[1], Abhilasha Singh[2], Rajan Goyal[3], Abhishek Kamendu[4]

[1, 3, 4] Department of General Medicine, Narayan Medical College and Hospital, Jamuhar, Sasaram, Bihar, India.
[2]Department of Physiology, Narayan Medical College and Hospital, Jamuhar, Sasaram, Bihar, India.

ABSTRACT

BACKGROUND

The relationship between liver enzymes like alanine aminotransferase (ALT), aspartate aminotransferase (AST), Alkaline phosphatase (ALP) and diabetes has been studied, but the results of these are inconsistent. Several prospective studies have reported that ALT was associated with incident diabetes. We wanted to study the levels of serum alanine aminotransferase (ALT), serum aspartate aminotransferase (AST) and serum alkaline phosphatase (ALP) in patients of Type 2 DM.

METHODS

This is a hospital based observational study which was conducted in Narayan Medical College and Hospital, Jamuhar, Sasaram, Rohtas, Bihar. Alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), glycosylated haemoglobin (HbA1c), FBS, PPBS, total bilirubin, and hepatitis B surface antigen (HBsAg) were determined in all study participants.

RESULTS

The mean value was 96.35, 67.37, 152.78 and 1.098 for AST, ALT, ALP and total bilirubin. On multivariate analysis for effect of FBS, PPBS, HbA1c on the value of AST weak correlation was found with R square of 0.11. On the effect of FBS, PPBS, HbA1c on the value of ALT we found weak correlation with an R square of 0.079.

CONCLUSIONS

There is a weak correlation between deranged liver enzyme (AST, ALT and ALP) with HbA1c, FBS and PPBS. But still, liver functions should be monitored in diabetic patients.

KEYWORDS

ALT, AST, Diabetes, HbA1c, FBS, PPBS

Corresponding Author:
Dr. Abhishek Kamendu,
Associate Professor,
Department of General Medicine,
Narayan Medical College and Hospital, Jamuhar, Sasaram - 821115,
District - Rohtas, Bihar, India.
E-mail:
abhishekkamendu1980@gmail.com

DOI: 10.18410/jebmh/2020/584

How to Cite This Article:
Jindal H, Singh A, Goyal R, et al. Observational study of serum alanine aminotransferase (ALT), serum aspartate aminotransferase (AST) and serum alkaline phosphatase (ALP) levels in type 2 diabetic patients. J Evid Based Med Healthc 2020; 7(48), 2852-2855. DOI: 10.18410/jebmh/2020/584

Submission 17-06-2020,
Peer Review 23-06-2020,
Acceptance 22-07-2020,
Published 30-11-2020.

BACKGROUND

Diabetes Mellitus (DM) is a spectrum of metabolic disorders represented by defect in metabolism of carbohydrate, lipid, and protein with increased blood glucose. This is mainly due to absolute or relative deficiency of insulin secretion. Type 2 DM is the more prevalent than other type of diabetes caused by resistance to insulin action and also inadequate insulin secretion.[1]

It is associated with insulin resistance i.e. lowering effect of insulin to the peripheral tissues generally skeletal muscle, adipose tissues and liver and / or secretory defect i.e. low secretion of insulin due to beta cell defect causes suppression of hepatic glucose production. Whereas liver plays an important role in hepatic glucose regulation in both fasting (via decrease insulin and increase glucagon causes glycogenolysis and gluconeogenesis) and non-fasting state (via increase insulin and decreases glucagon level).[2]

The liver is the mainstay in the regulation of carbohydrate metabolism, because it uses glucose for its energy requirement, as well as it also stores glucose as glycogen for future needs. It is an important organ for gluconeogenesis. This type of actions makes liver more susceptible to metabolic diseases as in patients of diabetes.

Liver disorder is very commonly seen in patients with type 2 diabetes. This consists of abnormal liver enzymes, Non-Alcoholic Fatty Liver Disease (NAFLD), cirrhosis, hepatocellular carcinoma, and acute hepatic failure. There is also an unexplained association of diabetes with hepatitis C. Non-alcoholic fatty liver disease is also a reason of chronic liver disease associated with diabetes and obesity both. With no intervention, NAFLD will eventually lead to stage of Non-Alcoholic Steato-Hepatitis (NASH). NASH is main reason of end-stage liver disease and also a contributor of cardiovascular disease in type 2 diabetes mellitus.[4]

The association between hepatic enzymes including alanine transaminase (ALT), aspartate transaminase (AST) and Alkaline phosphatase (ALP) and incident of diabetes have been examined, but the results are not conclusive. Many studies have reported that ALT was associated with incident of diabetes[5], but this association was not significant in a study of 4,201 French men and women.[6] Hanley et al.[7] and Fraser et al.[5] found that AST independently predicted incident diabetes in 906 Non-Hispanic Americans, 3,041 British women, and 9,337 Americans (7,495 white and 1,842 black), respectively. However, others showed that AST did not predict incident diabetes.[8] Majority of research done on this topic indicate that deranged liver enzyme levels, such as level of ALT, AST, and ALP, in the serum are a frequent findings in type 2 DM. It suggested that serum levels of liver enzymes are strongly associated with blood sugar level and / or magnitude of insulin resistance.[9]

Liver enzyme i.e., serum alanine aminotransferase, serum aspartate aminotransferase act as hepatocellular, whereas serum alkaline phosphatase acts as biliary function marker. Normally aminotransferase acts like other protein, distributed in plasma and interstitial fluid. Generally ALT level is more than the AST level as AST is cleared more rapidly by reticuloendothelial system as compare to ALT.[10]

Alanine aminotransferase is a cytoplasmic enzyme found mainly in liver whereas aspartate aminotransferase is a cytoplasmic and mitochondrial enzyme found in many organs like cardiac, skeletal muscle, liver, kidney, brain and erythrocytes therefore ALT is more specific marker for the liver injury.

Alkaline phosphatase is a type of isoenzyme and its source is mainly liver and bone. In liver ALP exists on canalicular membrane of the hepatocytes and ALP clearance from serum is by biliary tract and disease in hepatobiliary tract mainly biliary system causes increase in ALP level.[11]

In the present study, various liver enzyme levels studied are mainly AST level, ALT level, and ALP level. A scientific attempt has been made to find out correlation between type 2 diabetes mellitus and liver enzyme levels and its effect on the liver and to see whether there is any relationship between the severities of diabetes on liver functions.

METHODS

This is a hospital based observational study which was conducted in Narayan Medical College and Hospital, Jamuhar, Sasaram, Rohtas, Bihar. Conducted from Oct 2019 to Jun 2020. Consecutive 200 patients with type 2 DM who satisfied the inclusion and exclusion criteria were selected from OPD of Narayan medical college and recruited in the study. The study was approved by the IEC (Institutional Ethical Committee).

After taking structured medical history, detailed physical examination, including measurements of Body Mass Index (BMI), was done on the selected subjects. All of them had their ALT level, AST level, ALP level, glycosylated haemoglobin (HbA1c) and hepatitis B surface antigen (HBsAg) done. The reference levels were as follows: ALT: 10 - 40 international units per litre (IU / L), AST: 10 - 35 IU / L, and ALP: 80 - 290 IU / L. These were estimated in Beckman Coulter AU2700 Plus autoanalyzer using commercially available kits (Beckman Coulter, USA). The serum levels of AST, ALT, and ALP were considered elevated when their levels were higher than their respective reference ranges. Levels of FBS, PPBS and HbA_1c and total bilirubin were also recorded.

Inclusion Criteria

The patients with confirmed diabetes mellitus or newly diagnosed diabetes mellitus by WHO criteria (1999), fasting plasma venous glucose of 126 mg / dl or random or two hour post prandial plasma blood glucose of 200 mg / dl.

Exclusion Criteria

The diabetic patients with history of alcohol intake, hepatotoxic drugs like amiodarone, anti-tuberculous drugs, history of liver diseases or clinical evidence of acute hepatitis, those who were found to have evidence of hepatitis B and C virus infection (HBsAg positive and HCV antibody positive) were excluded from this study.

Statistical Analysis

It was done using SPSS 20 (Chicago, IL, USA) software package and all $p < 0.05$ were considered as statically significant. In the study, the relationship between liver enzymes in non-diabetic and diabetic subjects was analysed by Pearson correlation coefficients. The relationships multiple linear regression and partial correlations were used after adjusting for covariates. The results were presented as mean levels ± SE.

RESULTS

Basic Characteristics of Study Subjects	Mean	Range
Age (yrs.)	54.97 ± 11.90	35 - 80
BMI (Kg / m^2)	25.77 ± 3.305	19 - 31
Duration of Diabetes (yrs.)	5.71 ± 4.71	0 - 15
FBS (mg / dl)	202.38 ± 73.38	84 - 431
PPBS	262.27 ± 83.12	146 - 514
HbA1c	8.91 ± 1.976	6 - 15
AST	70.91 ± 135.91	10 - 790
ALT	49.63 ± 69.46	6 - 356
ALP	137.2 ± 141.59	55 - 711

Table 1. Characteristics of Study Subjects

In this study total 200 study subjects were studied, in which 121 male (60.5 %) and 79 female (39.5 %) were there. Mean age of study subjects were 54.97 ± 11.90 yrs. (range 35 - 80 yrs.), having BMI 25.77 ± 3.305 (range 19 - 31). The average duration of diabetes in our study subjects was 5.71 ± 4.71 yrs. with range 0 - 15 yrs. The mean value of FBS, PPBS and HbA1c were 202.38 ± 73.38, 262.27 ± 83.12 and 8.90 ± 1.976. The mean value of AST 70.91 ± 135.91, ALT 49.63 ± 69.46 and ALP was 137.2 ± 141.59.

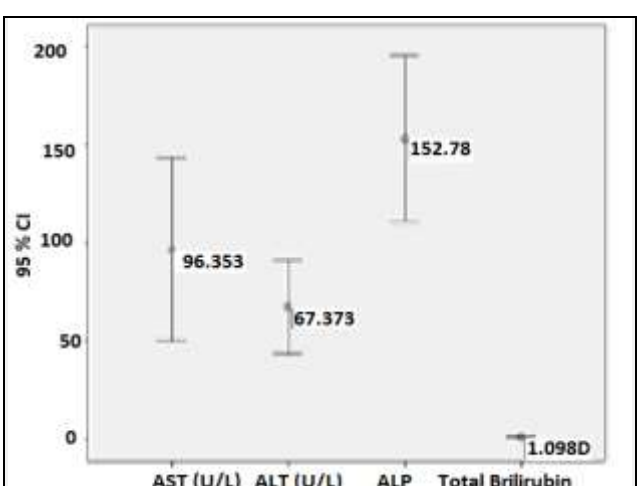

Figure 1. Shows Error Plot Graph of Liver Enzymes in the Study Subjects

The Mean value were 96.35, 67.37, 152.78 and 1.098 for AST, ALT, ALP and Total Bilirubin

Figure 2 shows the correlation between AST and HbA1c, the correlation between AST and HbA1c is very weak, with R square 0.01. When we do multivariate analysis for effect of FBS, PPBS, HbA1c on the value of AST we found weak correlation with R square 0.11. Figure 3 shows the correlation between ALT and FBS, the correlation between ALT and FBS is very weak, with R square 0.03. When we do multivariate analysis for effect of FBS, PPBS, HbA1c on the value of ALT we found weak correlation with R square 0.079.

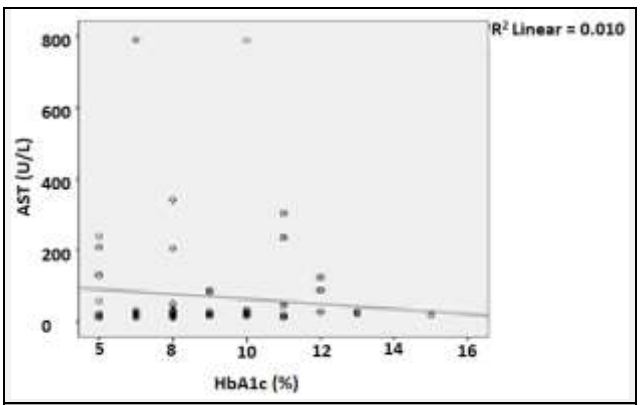

Figure 2. Correlation between HbA1c and AST

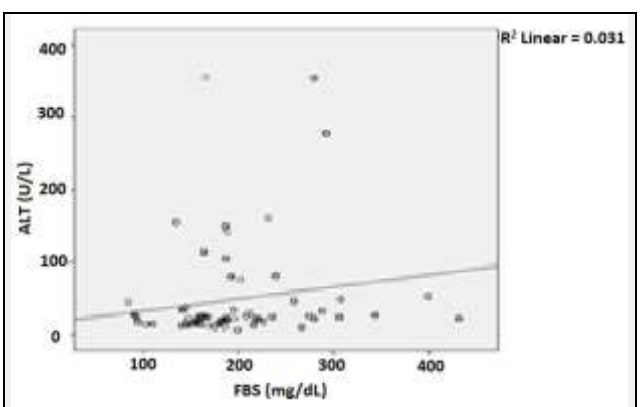

Figure 3. Correlation between FBS and ALT

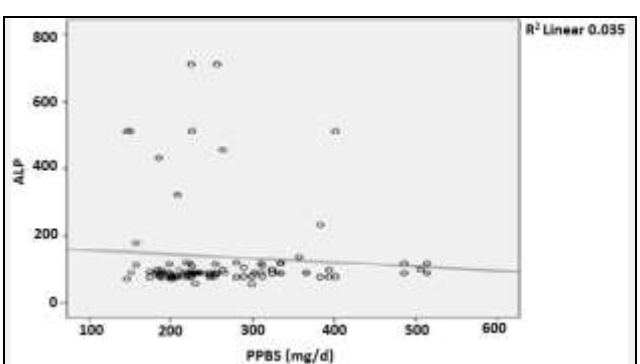

Figure 4. Correlation between PPBS and ALP

Figure 4 shows the correlation between ALP and PPBS, the correlation between ALP and PPBS is very weak, with R square 0.005. When we do multivariate analysis for effect of FBS, PPBS, HbA1c on the value of ALP we found weak correlation with R square 0.015.

DISCUSSION

This study was conducted to assess the liver enzymes in type 2 DM. This study was conducted at tertiary medical centre of south Bihar on type 2 DM. In this study total 200 study subjects were studied, in which 121 males (60.5 %) and 79 females (39.5 %) were there. Mean age of study subjects was 54.97 ± 11.90 yrs. (range 35 - 80 yrs.), other studies

conducted on this topic such as Alam J et al[3] also show male preponderance. Diabetes prevalence also increases with age. The average duration of diabetes in our study subjects was 5.71 ± 4.71 yrs. with range 0 - 15 yrs. The mean value of FBS, PPBS and HbA1c were 202.38 ± 73.38, 262.27 ± 83.12 and 8.90 ± 1.976. Other similar studies such as by Chadrasekhar GS[12] FBS was 182.28 ± 8.42, whereas PPBS was 257.8 ± 14.9, study by Gohel VD[4] shows RBS were 166.54 ± 31.2, study by Bora K et al[9] shows FBS was 175.11 ± 58.54 in male and 214.58 ± 82.11 in female.

In our study the mean value of AST 70.91 ± 135.91, ALT 49.63 ± 69.46 and ALP was 137.2 ± 141.59. Other study such as by Gohel VD[4] shows ALT was 35.25 ± 10.80 and serum ALP was 171.89 ± 80.88. Chandrasekhar GS[12] shows AST 47.55 ± 4.69, ALT was 45.66 ± 3.2 and ALP was 103.45 ± 7.6.This is almost in accordance with our study.

In our study the correlation between AST and HbA1c is very weak, with R square 0.01, other similar studies such as Alam J et al[3] found that there is higher prevalence of increased level ALT and AST in type 2 diabetic patients when compared to general population. Chandrasekhar GS[12] found in their study a significant elevation of ALT, AST and ALP levels were observed in diabetics, AST levels were 1.4 times high in diabetes patients as compared to normal controls. ALP levels were 1.45 times high in diabetes patients. Gohel VD[4] in their study found that among 39 % of patients had elevated ALT while in control group 6 % had elevated value. The chi square value is 19.512 at degree of freedom 1 the p value is 0.00011, so the test result is highly significant. Kalra S et al[13] reported out of total 924 T2DM patients, 522 (56.5 %) had NAFLD and out of 522 NAFLD patients 182 (34.9 %) had raised one aminotransferase either AST or ALT and 340 (65.1 %) had raised both aminotransferase

Abnormal liver enzyme levels in diabetes patients can be due to several factors. Firstly, hyperinsulinaemia might directly lead to hepatic insulin resistance along with fatty liver. This increased fat deposition in liver is toxic to hepatocytes, leading to increase in various transaminases level and decreased anabolic capacity of liver. Secondly, the insulin-resistance also leads to an increase in level of pro-inflammatory cytokines like Tumour Necrosis Factor (TNF). This may also contribute to hepatocellular injury. NAFLD is one of the hepatic complications of diabetes mellitus with metabolic syndrome and ALT has been used as a marker of NAFLD.

CONCLUSIONS

There is a weak correlation between deranged liver enzymes (AST, ALT and ALP) with HbA1c, FBS and PPBS. But still, liver function should be monitored in diabetic patients.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.
Financial or other competing interests: None.
Disclosure forms provided by the authors are available with the full text of this article at jebmh.com.

REFERENCES

[1] Singh A, Dalal D, Malik AK, et al. Deranged liver function tests in type 2 diabetes: a retrospective study. International Journal of Science & Healthcare Research 2019;4(3):27-31.
[2] Mathur S, Mehta DK, Kapoor S, et al. Liver Function in Type-2 diabetes mellitus patients. Int J Sci Stud 2016;3(10):43-47.
[3] Alam J, Mukti M, Hoque MM, et al. Liver function tests in diabetic and non-diabetic patients in Dhaka city of Bangladeshi population. Res Rev in BioSci 2013;7(4):147-152
[4] Gohel VD, Johnson B, Joshi V. Comparative study of liver function tests in diabetes type-2 patients and non-diabetics in Gujarat. Int J Basic Appl Physiol 2017;6(1):71-76.
[5] Fraser A, Harris R, Sattar N, et al. Alanine aminotransferase, gamma-glutamyltransferase and incident diabetes: the British Women's Heart and Health Study and meta-analysis. Diabetes Care 2009;32(4):741-750.
[6] Andre P, Balkau B, Born C, et al. Hepatic markers and development of type 2 diabetes in middle aged men and women: a three-year follow-up study -The D.E.S.I.R. Study (Data from an Epidemiological Study on the Insulin Resistance syndrome). Diabetes & Metabolism 2005;31(6):542-550.
[7] Hanley AJG, Williams K, Festa A, et al. Elevations in markers of liver injury and risk of type 2 diabetes: the insulin resistance atherosclerosis study. Diabetes 2004;53(10):2623-2632.
[8] Chen SC, Tsai SP, Jhao JY, et al. Liver fat, hepatic enzymes, alkaline phosphatase and the risk of incident type 2 diabetes: a prospective study of 132,377 adults. Scientific Reports 2017;7(1):4649.
[9] Bora K, Borah M, Chutia H, et al. Presence of concurrent derangements of liver function tests in type 2 diabetes and their relationship with glycemic status: a retrospective observational study from Meghalaya. J Lab Physicians 2016;8(1):30-35.
[10] Pratt DS. Sleisenger and Fordtran's Gastrointestinal and liver disease pathophysiology/diagnosis/ management. Chapter - 73. Liver chemistry and function tests. 10th edn. Elsevier Inc., 2016: 1243-1253
[11] Lowe D, Sanvictores T, John S. Alkaline Phosphatase. In: StatPearls Treasure Island (FL): StatPearls Publishing 2020 Jan.
[12] Chandrashekhar GS. Alterations of liver enzymes in T2DM: a case control study. Int J Adv Med 2018;5(6):1521-1524.
[13] Kalra S, Vithalani M, Gulati G, et al. Study of prevalence of Nonalcoholic Fatty Liver Disease (NAFLD) in Type 2 diabetes patients in India (SPRINT). Journal of The Association of Physician of India 2013;61(7):448-453.