

Research Article

**A case control study on evaluation of liver enzymes in patients
of type-II diabetes mellitus**

**¹Shahnaz Noor, ²Shahbaz Ahmed Qureshi,
and ³Abdul Hameed**

¹Assistant Professor, Department of Pathology
Quaid-e-Azam Medical College, Bahawalpur

²Associate Professor, Department of Gastroenterology & Hepatology
Quaid-e-Azam Medical College, Bahawalpur

³Associate Professor, Department of Medicine
Shahida Islam College, Lodhran

[Received: 20/12/2018; Accepted: 21/01/2019; Published: 23/01/2019]

ABSTRACT

Objective: To evaluate the liver enzymes in patients of type-II diabetes mellitus presenting at tertiary care hospital.

Material and methods: This case control study was conducted at Department of Gastroenterology & Hepatology, Bahawal Victoria Hospital, Bahawalpur from July 2017 to January 2018 over the period of 6 months. Total 100 type-II diabetics (cases) having age between 30-70 years either male or female were selected. Total 100 non-diabetics were also selected as controls. Liver enzymes were assessed in cases and controls.

Results: Mean fasting plasma glucose levels in cases and controls were 182.28±8.42 mg/dl and 96.79±1.05 mg/dl statistically significant difference of mean plasma glucose levels between both groups was detected with p value 0.0001. Mean post prandial plasma glucose levels in cases were 257.8±14.9 mg/dl and mean post prandial plasma glucose levels in controls were 136.6±5.3 mg/dl and the difference was statistically significant with p value 0.001. Aspartate amino transferase levels in cases and controls were 47.55±4.69 U/L and 33.51±2.33 U/L respectively.

Conclusion: Results of present study showed that diabetics were found with high value of liver enzymes as compared to non-diabetics. Difference of liver enzymes values between the cases and controls was statistically significant. 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.

Key words: liver enzymes, diabetes mellitus, NAFLD

INTRODUCTION

Diabetes is one of the major non – communicable diseases, whose prevalence is increasing exponentially. Globally, Type 2 Diabetes Mellitus is the most common form accounting for about 90% of all the cases.¹ There exists an association between diabetes and liver injury as diabetes

mellitus is known to be associated with a number of liver disorders, including isolated elevation of liver enzyme levels, nonalcoholic fatty liver disease (NAFLD), and other chronic liver disorders like hepatitis C infection (HCV) and cirrhosis.² The liver has a central role in glucose

homeostasis in the fasting and post prandial concentrations and in liver diseases, this hepatic carbohydrate metabolism is generally altered.³ There is evidence that the disturbance in hepatic glucose metabolism may be involved in the pathogenesis of Type 2 Diabetes Mellitus.⁴ It is stated that the disturbances in liver function tests are well recognized in some diabetic patients.⁵ Increased activities of liver enzymes such as Alanine transaminase (ALT), Aspartate transaminase (AST) and Gamma glutamyl transferase (GGT) which are indicators of hepatocellular injury, are associated with insulin resistance and Type 2 Diabetes Mellitus.⁶ It was found in a study of 35 patients that HBA1c results should be used in patients with advanced liver disease when evaluating long term glucose control in such patients.³ Further, increased levels of ALT, AST and GGT are known to be markers of nonalcoholic fatty liver disease (NAFLD).⁷ There is increased prevalence of NAFLD in the Diabetes Mellitus and it is regarded as a predisposing factor for insulin resistance and hyperinsulinemia.⁸

MATERIAL AND METHODS

This case control study was conducted at Department of Gastroenterology & Hepatology, Bahawal Victoria Hospital, Bahawalpur from July 2017 to January 2018 over the period of 6 months. An approval was taken from institutional review committee and written informed consent was taken from every patients. Total 100 type-II diabetics (cases) having age between 30-70 years either male or female were selected. Total 100 non-diabetics were also selected as controls. Patients with history of alcohol consumption, patients taking hepatotoxic drugs like amidarone, antituberculous drugs, Pregnant women patients with history of liver disease including clinical or biochemical evidence of acute hepatitis, autoimmune hepatitis, primary liver cirrhosis, hemochromatosis or Wilson disease, subjects with positive hepatitis B and C virus infection (seropositive for HBsAg and HCV antibodies) were excluded from the study.

Fasting blood sample was drawn for plasma glucose, Post prandial plasma glucose, Aspartate amino transferase, Alanine amino transferase and Alkaline phosphatase and send to laboratory for analysis. Lab findings were noted on pre-designed proforma along with demographic profile of the individuals.

All the collected data was entered in SPSS version 20 and analyzed. Mean and SD was calculated for numerical data and frequencies and percentages were calculated for categorical data. Comparison of numerical variables between cases and controls was done by using t test. P value ≤ 0.05 was taken as statistically significant.

RESULTS

Mean fasting plasma glucose levels in cases and controls were 182.28 ± 8.42 mg/dl and 96.79 ± 1.05 mg/dl statistically significant difference of mean plasma glucose levels between both groups was detected with p value 0.0001. Mean post prandial plasma glucose levels in cases were 257.8 ± 14.9 mg/dl and mean post prandial plasma glucose levels in controls were 136.6 ± 5.3 mg/dl and the difference was statistically significant with p value 0.001. Aspartate amino transferase levels in cases and controls were 47.55 ± 4.69 U/L and 33.51 ± 2.33 U/L respectively. Difference between cases and controls for Aspartate amino transferase was statistically significant with p value 0.0256. In cases, mean Alanine amino transferase level was 45.66 ± 3.2 U/L and in cases was 44.13 ± 4.47 U/L and difference was not significant statistically. Mean Alkaline phosphatase levels in 103.45 ± 7.6 U/L in cases and in controls was 71 ± 2.224 U/L and the difference was statistically significant with p value 0.002. (Table 1)

Odds ratio for ALT and AST are calculated and given in Table 2 and Table 3. It is evident from Table 2 that AST levels were high in 23 (23%) of diabetics and 18 (18%) of non-diabetics. Odds ratio showed a higher risk of liver enzyme elevation in diabetics. Risk of elevation of AST was found to be 1.65 times high. Table 3 shows that ALT levels were high in 69 (69%) of

diabetics and 36 (36%) of non-diabetics. Risk of elevation of ALT was 1.25 times high in diabetics compared to non-diabetics.

Table 1: Laboratory parameters of diabetic patients and controls

Lab parameters	T2DM (n = 100)	Non-diabetic (n = 100)	P value
Fasting plasma glucose (mg/dl)	182.28±8.42	96.79±1.05	<0.0001
Post prandial plasma glucose (mg/dl)	257.8±14.9	136.6±5.3	<0.0001
Aspartate amino transferase (U/L)	47.55±4.69	33.51±2.33	0.0256
Alanine amino transferase (U/L)	45.66±3.2	44.13±4.47	0.51
Alkaline phosphatase (U/L)	103.45±7.6	71±2.224	0.0002

Table 2: Odd's ratio for aspartate amino transferase

Parameter	Cases	Controls
Increased aspartate amino transferase	23 (23%)	18 (18%)
Normal aspartate amino transferase	134	100

Table 3: Odd's ratio for alanine amino transferase

Parameter	Cases	Controls
Increased alanine amino transferase	69 (69%)	36 (36%)
Normal alanine amino transferase	31 (31%)	64 (64%)

DISCUSSION

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. 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 serum ALT values between 1 and 2.5 times upper normal limit.⁹ Asymptomatic individuals with mild elevations of ALT and AST revealed that 98% had liver disease, fatty liver disease and chronic hepatitis.¹⁰ The most common cause of a mild elevation of serum ALT is non-alcoholic fatty liver disease, which is the most prevalent liver disease in type 2 diabetes.¹¹

Odds ratio (OR) for AST suggest that the risk of development of liver disease is 1.65 times in diabetics as compared to controls. Odds ratio for ALT suggest that risk of liver disease is 1.25 times in diabetics. A similar finding was noted in a previous study.¹² A study by Gupte et al, reported that 49% patients with DM had evidence of fatty liver; of these 32% underwent liver biopsy.¹³ 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 author's 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. Present 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.¹⁴

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.¹⁵In type 2 diabetic patients with or without obesity, up to 30% have fat with inflammation, 25% have associated fibrosis, and 1-8% have cirrhosis.¹⁶⁻¹⁸

CONCLUSION

Results of present study showed that diabetics were found with high value of liver enzymes as compared to non-diabetics. Difference of liver enzymes values between the cases and controls was statistically significant. 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.

REFERENCES

1. Wu Y, Ding Y, Tanaka Y, Zhang W. Risk factors contributing to type 2 diabetes and recent advances in the treatment and prevention. *International journal of medical sciences*. 2014;11(11):1185.
2. Benedict M, Zhang X. Non-alcoholic fatty liver disease: An expanded review. *World journal of hepatology*. 2017 Jun 8;9(16):715.
3. Rui L. Energy metabolism in the liver. *Comprehensive physiology*. 2011 Jan 17;4(1):177-97.
4. Lee PG, Halter JB. The pathophysiology of hyperglycemia in older adults: clinical considerations. *Diabetes Care*. 2017 Apr 1;40(4):444-52.
5. Limdi JK, Hyde GM. Evaluation of abnormal liver function tests. *Postgraduate medical journal*. 2003 Jun 1;79(932):307-12.
6. Wang YL, Koh WP, Yuan JM, Pan A. Association between liver enzymes and incident type 2 diabetes in Singapore Chinese men and women. *BMJ Open Diabetes Research and Care*. 2016 Sep 1;4(1):e000296.
7. Sanyal D, Mukherjee P, Raychaudhuri M, Ghosh S, Mukherjee S, Chowdhury S. Profile of liver enzymes in non-alcoholic fatty liver disease in patients with impaired glucose tolerance and newly detected untreated type 2 diabetes. *Indian journal of endocrinology and metabolism*. 2015 Sep;19(5):597.
8. Leite NC, Villela-Nogueira CA, Cardoso CR, Salles GF. Non-alcoholic fatty liver disease and diabetes: from physiopathological interplay to diagnosis and treatment. *World Journal of Gastroenterology: WJG*. 2014 Jul 14;20(26):8377.
9. Lebovitz HE, Kreider M, Freed MI. Evaluation of liver function in type 2 diabetic patients during clinical trials: evidence that rosiglitazone does not cause hepatic dysfunction. *Diabetes Care*. 2002 May;25(5):815-21.
10. Hultcrantz R, Glaumann H, Lindberg G, Nilsson LH. Liver investigation in 149 asymptomatic patients with moderately elevated activities of serum aminotransferases. *Scand J Gastroenterol*. 1986 Jan; 21(1):109-13.
11. Harris MI, Flegal KM, Cowie CC, Eberhardt MS, Goldstein DE, Little RR, et al. Prevalence of diabetes, impaired fasting glucose, and impaired glucose tolerance in U.S. adults. The Third National Health and Nutrition Examination Survey, 1988-1994. *Diabetes Care*. 1998 Apr; 21(4):518-24.
12. Adiga U, Malawadi BN. Alterations in liver enzymes in type 2 diabetes mellitus. *Biomedical Review: J Basic Applied Med Sci*. 2016;3(1):13-6.

13. Gupte P, Amarapurkar D, Agal S, Baijal R, Kulshrestha P, Pramanik S, et al. Non-alcoholic steatohepatitis in type 2 diabetes mellitus. *J GastroenterolHepatol*. 2004 Aug 1;19(8):854-8.
14. Paola PS, Kenneth C. Treatment of NAFLD in patients with type 2 diabetes mellitus. *Clin Diabetes Endocrinol*. 2016;2:9.
15. Sheth SG, Gordon FD, Chopra S. Nonalcoholic steatohepatitis. *Ann Internal Med*. 1997 Jan 15;126(2):137-45.
16. Andersen T, Gluud C. Liver morphology in morbid obesity: a literature study. *Int J Obesity*. 1984;8(2):97-106.
17. Kern WH, Heger AH, Payne JH, DeWind LT. Fatty metamorphosis of the liver in morbid obesity. *Arch Pathol*. 1973 Nov;96(5):342-6.
18. Nasrallah SM, Wills CE Jr, Galambos JT. Hepatic morphology in obesity. *Dig Dis Sci*. 1981 Apr;26(4):325-7.