Journal of Research in Applied and Basic Medical Sciences 2023; 9(4): 272-279

Original Article

RABMS Journal of Research in Applied and Basic Medical Sciences

Pattern of Serum Liver Enzymes in the Patients with Type 2 Diabetes Mellitus

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Abstract

***Background & Aims*:** The liver plays an important role in the regulation of glucose concentration and metabolism. Diabetic patients develop abnormalities in liver enzymes affecting the liver and its function. A recent study shows the association between liver enzymes and diabetes mellitus (DM) which leads to diabetic neuropathy, nephropathy, and retinopathy if left untreated. The aim of the present study was to determine the impairment of liver enzymes in the patients with diabetic individuals compared to non-diabetic individuals.

***Materials & Methods*:** This is a cross-sectional study that was carried out at the Star Hospital, Sanepa, Lalitpur, Nepal, from June 2021 to August 2021. A total of 260 participants were included in this study, out of which, 135 were known diabetic cases and 125 were nondiabetic control. Fasting plasma glucose was analyzed with semi-automated analyzer STAT Fax 3300 by GOP-POD method and liver enzymes were analyzed by IFCC method. An Independent T-test was applied. Statistical analysis was done with SPSS version 16.0.

***Results*:** The prevalence of elevated liver enzymes was significantly higher in diabetic individuals compared to nondiabetic ones. ALT, AST, and ALP were raised by 28.8%, 23.7%, and 48.8%, respectively among the patients with DM. significant increases in AST and ALT was observed in men compared to women, but changes in ALP level was insignificant when compared by gender. A significant elevation of AST and ALP was seen in diabetic patients compared to controls ($P<0.05$).

***Conclusion*:** Positive correlation was found between fasting sugar, ALT, AST, and ALP. Similarly, a positive correlation was found between HbA1C and liver enzymes (AST< ALT and ALP).

***Keywords*:** Diabetes Mellitus, Liver Enzymes, Plasma, Serum

Received 06 March 2023; accepted for publication 25 August 2023

Introduction

Diabetes mellitus (DM) is one of the major and common non-communicable diseases. Type 2 diabetes is the most common form, as is found in 90% of total cases in diabetic patients (1). Since the liver plays a major role in the regulation of carbohydrate metabolism, there exists an association between diabetes and liver injury (2). Type 2 diabetes is also characterized by hyperglycemia, and is linked with hyperlipidemia or the disturbance in various liver enzymes as shown in different studies. Disturbances in Liver function tests are recognized in some diabetic patients (3).

The liver enzymes, AST, ALT, and ALP are routinely measured to evaluate liver function. AST, ALT, and ALP are also considered the markers of the hepatocellular health (4). ALT is considered the most specific marker of the liver function test, as it is primarily found in the organ itself; however, AST and ALP are also found in other tissues and are so considered as the non-specific markers of the liver function tests (5). GGT is the least specific marker of the liver function test (LFT) in the context of this study, since various studies have shown its independent elevation without any correlation with type 2 diabetes. GGT is seen to be mainly elevated in the patients with pre-hepatic, hepatic, or post-hepatic illness (for example jaundice) (6).

LFTs includes measuring AST, ALT, ALP, and GGT. The type 2 diabetic patients more frequently had elevated ALT and GGT levels than those with type 1 diabetes (7). However, increases in LFTs were rarely more than twice the upper limit of normal (8). The management of liver injury associated with diabetes is a global problem until now, and successful diagnosis and treatment are not yet available (9).

Liver function tests can be performed in diabetic patients, and the prevalence can be measured. Increased activity of the liver enzymes such as AST, ALT, ALP, and γ-GT is the indicator of hepatocellular injury (10, 11). Increased activity of these markers are associated with insulin resistance, metabolic syndrome, and type 2 diabetes (12). The fasting glucose level of the patient with type 2 diabetes will be correlated with various liver enzymes such as AST, ALT, and ALP. GGT is also a marker of liver injury but, however, will be excluded in this study since it is the most non-specific marker of hepatocellular injury and is mostly related to the biliary tract function. Various studies have also known the independency of increase of GGT with type 2 diabetic patients (13).

The aim of this study was to correlate liver enzymes with type 2 diabetic patients attending Star Hospital. The correlation study of liver enzymes is found to be conducted previously worldwide but is not sufficient in the context of Nepal. The site of this study is chosen to be Star Hospital since there is sufficient patient flow with type 2 diabetes in this hospital which will be enough to conduct the study. Also, diabetic patients from different districts of Nepal are getting treatment from Star hospital, which will make it relevant to conduct the study among the patients from different places in Nepal.

Materials & Methods

A quantitative type of hospital-based cross-sectional study was carried out in the Department of Biochemistry, Modern Technical College, Sanepa, Lalitpur, Nepal, on Type 2 diabetic patients attending Star Hospital, Sanepa from June to August 2021. 260 participants were enrolled. Out of 135 typed 2 diabetic patients, 125 were control subjects who were healthy controls enrolled in the study by a convenient Sampling Technique whose age group was above 40 years.

Ethical consideration was obtained from the Institutional Review Committee (IRC) of Star Hospital Research Center (SHRC). Written consent was taken from Star Hospital. Oral and written consent were also obtained from the participants who were included in the study.

Venous blood was collected from the median cubital vein by sterilizing the local area with an alcohol pad. Then, the venous blood was allowed to rest for clot formation and serum were recovered by centrifugation at 2000 rpm for 5-10 minutes. Then the different parametric test was performed.

Blood glucose estimation was done by GOD/POD (glucose oxidase/peroxidase) method where GOD acts on glucose to form gluconic acid and hydrogen peroxide. Peroxidase acts as hydrogen peroxide to form water and oxygen. 4-amino antipyrine reacts with oxygen to form a pink colored complex. The formation of pink color is directly proportional to the concentration of glucose present in serum. The intensity of the color is measured at 540 nm of colorimeter.

Serum Alanine aminotransferase (ALT) estimation by IFCC method: ALT or SGPT catalyzes the transfer of amino group from alanine to α-ketoglutarate forming pyruvate and glutamate. The

absorbance of the colored product is measured in a spectrophotometer at 340 nm wavelengths.

Serum Aspartate aminotransferase (AST) estimation by IFCC method: AST or SGOT catalyzes the transfer of the amino group from aspartate to α-ketoglutarate, forming oxaloacetate and glutamate. The absorbance of the color produced is measured in a spectrophotometer at 340 nm wavelength.

Serum Alkaline Phosphatase (ALP) estimation: Alkaline Phosphatase cleaves p-nitrophenyl phosphate (p-NPP) into p-nitrophenol and phosphate. P-nitrophenol is a yellow color compound in an alkaline medium and absorbs light at 405 nm. The rate of increase in absorbance at 405 nm is proportional to alkaline phosphatase in the specimen.

All the data were entered in the MS excel and further statistical analysis was done in the statistical package for social science (SPSS) version 16. Frequency and chi-square test were measured. P values less than 0.05 were considered significant.

Results

A total study comprises 260 participants; of which, 151 were male with mean age of 57.1±16.0 years and 109 were female with mean age of 58.2±16.2 years. ALT and AST of males are significantly higher than females, but changes in ALP level was insignificant as shown in table 1. Out of 135 cases of Type 2 diabetes, 74 were male and 61 were female with mean age of 60.3±15.1 years. Similarly, 125 controls were taken out, of which, 77 were male and 48 were female with mean age of 54.7±16.6. Significant elevation of AST and ALP was found in the case group compared to control group, and ALT was found insignificant, as shown in table 2. Significant elevation of AST, ALT, and ALP was found in the patients with poor glycemic control than the patients with good glycemic control, as shown in table 3.

A statistically significant correlation was found between HbA1C and ALP (r=0.141, p=0.023), as shown in figure 1. Similarly, positive Correlation was found between HbA1C and AST, which was statistically significant (r=0.161, p=0.010), as shown in figure 2. Positive statistically significant correlation was found between HbA1C and ALT, which was r=0.119 and p=0.016, as shown in figure 3. Positive Correlation was found between fasting sugar and ALP, which was statistically significant (r=0.162, p=0.009), as shown in figure 4. Positive Correlation was found between fasting sugar and AST, which was statistically significant (r=0.171, p=0.006), as shown in figure 5. Positive Correlation was found between fasting sugar and ALT, which was statistically significant (r=0.133, p=0.032), as shown in figure 6.

Table 1. Baseline Characteristics by Gender

Parameters	Male	Female	P-value
Age(years)	57.1±16.0	58.2±16.2	0.606
Sugar F(mg/dl)	140.1±65.6	130.1±51.5	0.188
Sugar PP(mg/dl)	193.2±107.8	184.4±93	0.493
Hba1c(%)	6.5±2.2	6.2±1.7	0.202
AST(IU/L)	23.9(18.0,35.6)	19.0(15.5,28.3)	0.006
ALT(IU/L)	29.3(20.2,42.4)	23.0(16.3,35.9)	0.009
ALP(IU/L)	222.7±80.7	247.3±180.4	0.140

Table 2: Correlation of Biochemical Parameters between Case and Control

Parameters	Case	Control	P-value
Age(years)	60.3±15.1	54.7±16.6	0.005
Sugar F(mg/dl)	176.7±57.8	92.2±14.6	0.000
Sugar PP(mg/dl)	264.6±89.3	108.9±19.2	0.000
Hba1c(%)	7.8±1.9	4.9±0.5	0.000

Parameters	Case	Control	P-value
AST(IU/L)	24.2(17.2,40.1)	20.0(16.1,27.5)	0.04
ALT(IU/L)	26.5(19.8,44.0)	26.0(16.3,40.0)	0.113
ALP(IU/L)	260.9±170.5	203.4±61.6	0.000

Table 3: Baseline characteristics based on Glycemic Status

Parameters	HbA1c>7.0% (Poor Glycemic Control)	HbA1c<7% Good Glycemic Control)	P-value
Age(years)	60.3±15.5	54.7±16.6	0.005
Sugar F(mg/dl)	176.6±57.8	92.2±14.5	0.000
Sugar PP(mg/dl)	264.5±89.3	108.8±19.2	0.000
HbA1c(%)	7.8±1.9	4.9±0.6	0.000
AST(IU/L)	28.2(17.4,50.7)	20.0(16.6,28.1)	0.010
ALT(IU/L)	29.3(19.9,51.0)	25.8(17.7,37.8)	0.033
ALP(IU/L)	260.9±170.5	203.4±61.6	0.000

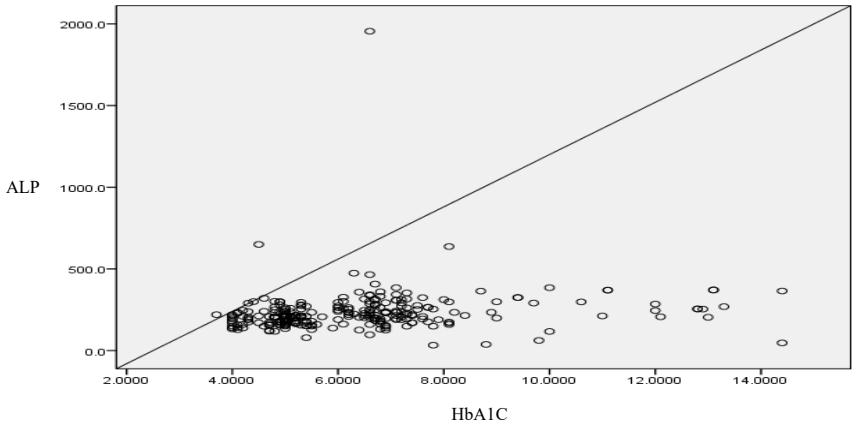

Fig. 1. Correlation between HbA1C and ALP in Type 2 diabetic patients

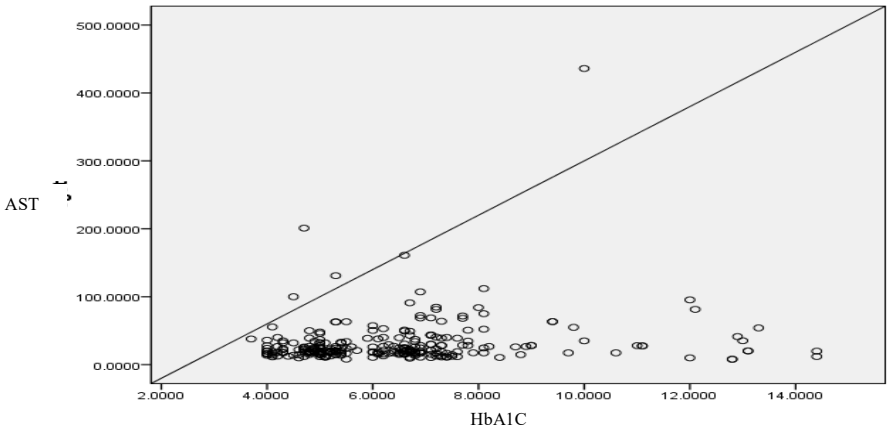

Fig. 2. Correlation between AST and HbA1C

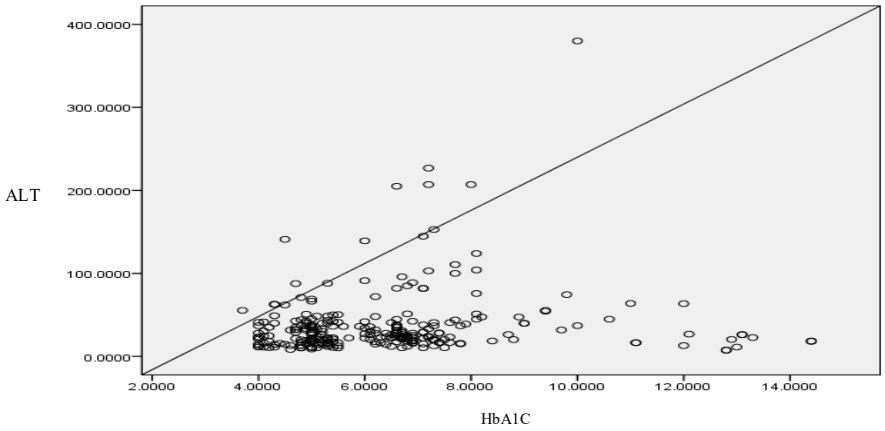

Fig. 3. Correlation between ALT and HbA1C

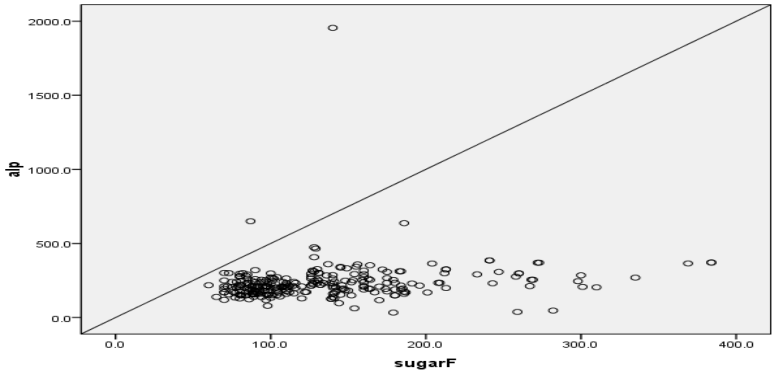

Fig. 4. Correlation between Fasting sugar and ALP

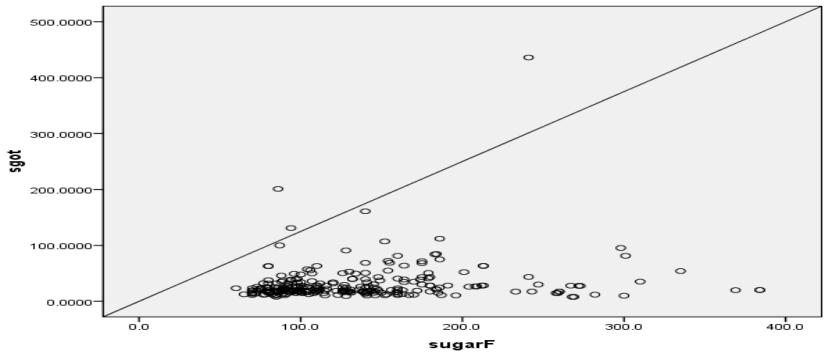

Fig. 5. Correlation between Fasting sugar and AST

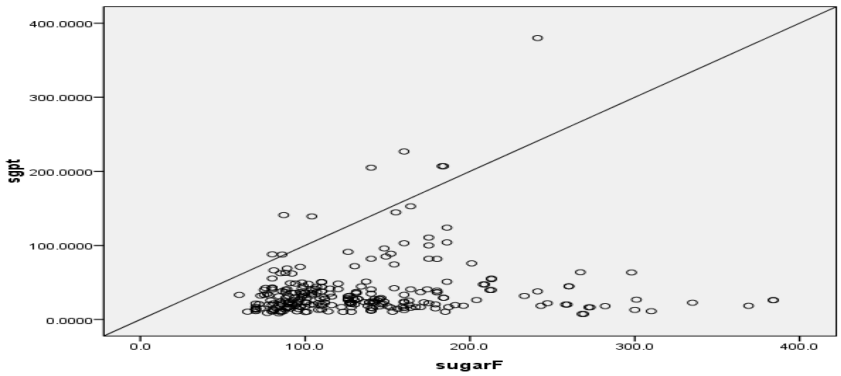

Fig. 6. Correlation between Fasting Sugar and ALT

Discussion

The prevalence of type 2 diabetes mellitus (T2DM) is around 4.5% in the adult population as per the data reported by IDF atlas 2013 in Nepal and its trend is escalating (14). A higher incidence of liver function test abnormalities has been associated with individuals suffering from T2DM than individuals without diabetes. In studies conducted by GetnetTeshome et al. and Shiful Islam et al. among diabetic patients, at least one liver enzyme was raised above the upper limit of the normal range (1, 15).

In our study, the prevalence of elevated liver enzymes is raised by ALT (28.8%), AST (23.7%), and ALP (48.8%) out of 135 Type II diabetic patients. Our results support the finding of a study done by Roshan Takelmayam et al. which also shows raised ALT and AST by 56% and 20%, respectively, although the study shows normal ALP levels (16). Similar study was conducted by Ghimire et al. in Nepal which reported a high prevalence of LFT abnormalities (about 62.3%) in 162 Type II diabetic patients, that have increased ALT, AST, and ALP by 15%, 13%, and 9% respectively (17). Also, Ni et al. performed a study on 81 type II diabetic patients in Malaysia, and reported that about 18%, 12%, and 15% have abnormal liver function tests in ALT, AST and ALP, respectively (18).

The increased incidence of LFT abnormalities has been associated with T2DM in studies conducted by Shiful Islam et al. in Bangladesh (1). These increase in liver enzymes in diabetic patients could be because of chronic disease and insulin resistance, leading to an increase of fatty acids with toxic effect on hepatocytes. All of these are responsible for the increase in transaminase and reduced synthetic functions of the liver (19).

The study conducted by Han Ni et al. in Myanmar shows raised levels of ALT and AST with 18.5 and 14.9 percents, respectively (18). Similarly, the same result was seen in the study by Sanjay Kumar Jha et al (20). Most of the previous studies analyzed AST, ALT, and GGT in T2D individuals, and only a few studies included ALP.

In contrast to our study, AST was not significantly correlated with HBA1C in a study conducted by AL-Jamil et al. in 2014 (21). A research from the western part of Nepal described a significant increase in ALT and ALP but AST did not elevate significantly in a diabetic patient when compared to the control group (22). A study conducted by Bora et al. in India and Balogun et al. in Nigeria reported a high prevalence of deranged LFTs of about 71.2% and 70%, respectively 23, 24).

The contrast in the above-mentioned study may be because of different populations, methodologies, and pathophysiological conditions.

Conclusion

In the present study, a significant increase in the level of liver enzymes, ALT, AST, and ALP was observed in type 2 diabetic patients when compared to

healthy individuals. Hence, we found an association between the level of liver enzymes, ALT, AST, and ALP and type 2 diabetes mellitus.

Liver enzymes can be used as a biomarker for the assessment of type 2 diabetes, and it is possible to monitor complications of type 2 diabetes along with the study of serum liver enzymes through liver function tests.

Acknowledgments

The authors like to acknowledge all the helping hands that helped to shape up the work to make it successful.

Data availability

The raw data supporting the conclusions of this article are available from the authors upon reasonable request.

Conflict of interest

None of the authors have any interest that conflicts with this study.

Funding/support

Nine

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