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A Cross-Sectional Study on Prevalence of Elevated Liver Enzymes and their Association with Type 2 Diabetes Mellitus

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Abstract

Background: Diabetes mellitus poses a significant global health challenge, with Type 2 Diabetes Mellitus (T2DM) being particularly prevalent and on the rise, especially in low and middle-income countries. Liver enzymes, such as aspartate aminotransferase (AST), alanine aminotransferase (ALT), and γ-glutamyl transferase (GGT), are vital indicators of liver health and metabolism, often showing elevated levels in individuals with diabetes. Despite the public health importance of this relationship, comprehensive research, especially in Bangladesh, remains limited. This study aimed to address this gap by evaluating liver enzyme levels and their correlation with T2DM. ***Objective:*** The objective of this study was to assess the frequency of elevated liver enzymes and their association with T2DM. ***Method:*** A cross-sectional study was conducted in a tertiary hospital in Dhaka from May to August 2023. The study included 192 participants with T2DM and an equal number of control participants without diabetes. Liver enzymes (AST, ALT, and GGT) were measured, and statistical analysis was performed using independent t-tests. ***Results:*** The study found that persons with Type 2 Diabetes Mellitus (T2DM) had significantly higher levels of Aspartate Aminotransferase (AST) and Alanine Aminotransferase (ALT) compared to the control group ($p < 0.001$). Nevertheless, there was no substantial disparity in GGT levels seen between the two groups ($p = 0.065$). Individuals with T2DM had a considerably higher mean fasting blood glucose level compared to controls ($p < 0.001$). The liver function test results of the participants with type 2 diabetes mellitus (T2DM) were substantially higher compared to the control group. The serum alanine aminotransferase (ALT) level was 46.06 ± 22.38 IU/L and the serum aspartate aminotransferase (AST) level was 42.94 ± 19.08 IU/L, with a p-value of less than 0.001. However, there was no significant association between the gamma-glutamyl transferase (GGT) level in both study groups, with a p-value of 0.065. ***Conclusion:*** Elevated levels of AST and ALT are common in individuals with T2DM, indicating potential liver dysfunction. Liver enzyme testing may serve as a valuable tool in the assessment and management of diabetes-related complications.

Keywords: Type 2 Diabetes Mellitus, Liver enzymes, aspartate aminotransferase (AST), alanine aminotransferase (ALT).

INTRODUCTION

Diabetes mellitus is a diverse set of illnesses characterised by consistently high levels of glucose in the blood due to problems with the production or effectiveness of insulin, which in turn affects the metabolism of carbohydrates, lipids, and proteins [1, 2]. Type 2 diabetes is the result of β-cells being unable to operate properly and produce enough insulin, combined with a decrease in the ability of target tissues to respond to insulin (insulin resistance) [3, 4]. Worldwide, type 2 diabetes is a prevalent non-communicable illness that is rapidly growing and impacting a substantial population. The issue is quickly becoming a significant worldwide health concern and is on track to become widespread by

2030, particularly in low and medium income nations [1, 5, 6].

Diabetes, a metabolic condition, impacts various organs, including the liver, which has a crucial role in regulating the metabolism of carbohydrates, lipids, and proteins [7]. Diabetes often leads to an increase in the levels of certain enzymes in the blood, specifically aspartate aminotransferase (AST), alanine aminotransferase (ALT), and γ-glutamyltransferase (GGT) [8, 9]. Alanine aminotransferase and aspartate aminotransferase are highly specific indicators of liver damage. Alanine aminotransferase is found in the cytoplasm of liver cells, while aspartate aminotransferase is positioned in the mitochondria [10, 11]. A recent analysis indicates a strong correlation between elevated levels of ALT and AST and the presence of insulin resistance, type 2 diabetes mellitus (T2DM), and metabolic syndrome [9, 12]. Gamma-glutamyltransferase (GGT) is situated on the outer surface of the majority of cells and facilitates the absorption of glutathione, a crucial element of cellular antioxidant defences [13-15]. An elevation in GGT concentration has been considered a more reliable indicator of liver damage caused by alcohol-related liver illness compared to hepatic injury associated with diabetes [14]. Despite diabetes being a significant public health issue in Ethiopia, there is a severe lack of well-documented and up-to-date articles on the connection between diabetes and liver injury/dysfunction. Given the lack of sufficient research completed thus far, our current study aims to address the existing gap in understanding the relationship between liver marker enzymes and T2DM. Hence, our objective was to evaluate liver enzyme tests, including ALT, AST, and GGT, and their correlation with Type 2 diabetes in comparison to control groups without diabetes.

Objective

Evaluating the Frequency of Elevated Liver Enzymes and Their Correlation with Type 2 Diabetes Mellitus.

METHOD

A cross-sectional study was carried out in tertiary hospital, Dhaka between May and August 2023. The sample size, denoted as n, was calculated using the formula for a single population proportion: n = Z^2 * p * (1 - p) / d^2. In this formula, Z represents the Z score at a 95% confidence interval, which is equal to 1.96 with a power of 0.80. The variable p represents the prevalence, which is set at 50%, and d represents the marginal error, which is 5% (0.05). The formula N = (1.96)^2 * 0.5 * (1 - 0.5) / 0.05 calculates the value of N. The equation 2 equals 384. In conclusion, a grand total of 384 individuals were chosen for the study by the utilisation of the basic random sampling method. We selected an equal number of individuals for both the case group (diabetes) and the control group (seemingly healthy), with 192 participants in each group.

Participants who had been diagnosed with diabetes mellitus according to the World Health Organisation (WHO) guidelines [16], and had a fasting plasma venous glucose level of ≥ 7 mmol/L (126 mg/dL) or a random plasma venous glucose level of ≥ 11.1 mmol/L (200 mg/dL), were included in the study. However, participants with a history of liver disease, alcohol intake, hepatotoxic drug use, clinical evidence of acute hepatitis, hepatitis B or C virus infection, and clinical or subclinical hypothyroidism were excluded.

The interviewer was specifically designed to gather information that assists in evaluating participants based on the eligibility requirements. Each volunteer participant had 5 millilitres (5 mL) of venous blood taken using disposable plastic syringes. The blood was transferred into flat containers and then subjected to centrifugation following coagulation. The serum was stored at a temperature of -20 °C in a sterile environment at the laboratory of the University of Gondar Compressive Specialised Hospital until the analysis was conducted. The levels of SGOT, SGPT, and GGT were measured utilising enzymatic assays using the A25 Bio-system human (German). The reference values for each test were determined based on the enzymatic test of the A25 Bio-system human (German) kit. Data quality management/control refers to the process of ensuring that data is accurate, reliable, and consistent throughout its lifecycle. Data collectors and supervisors received training on the study's objectives, data collection procedures, laboratory analysis, and ethical considerations. The sample was received, logged, and handled in accordance with the standard operating procedure. Supervisors and investigators closely monitored and supervised the data collection process. The standard operational method was implemented during the pre-analytic, analytic, and post-analytic stages of laboratory services, which had a significant impact on the overall quality of the laboratory analysis. The data was further processed and verified to ensure consistency and detect anomalies.

The data were entered twice and processed using Epi Data 3.1 (Jens M. Lauritsen & Michael Bruus). They were then uploaded to SPSS version 20 (IBM, New York, U.S) and reported as mean ± SD values. The statistical study involved conducting an independent t-test to determine the disparity between the two unpaired groups. A p-value of 0.05 was deemed to be statistically significant.

RESULTS

The results revealed that among the patients group (n = 192), 63% were male and 37% were female, while in the control group (n = 192), 60.4% were male and 39.6% were female. The mean age of the patients was 55.76 years with a standard deviation of 10.11, whereas the mean age of the control group was 50.93 years with a standard deviation of 5.41. Regarding education, the majority of patients had primary school

education (35.9%), followed by secondary school and college education (35.9%), while in the control group, primary school education was also predominant (40.1%), followed by secondary school and college education (28.1%). In terms of occupation, the most common occupation among patients was being a merchant (47.9%), followed by civil servant (37.5%), while in the control group, merchants also constituted the largest proportion (41.1%), followed by civil servants (33.3%).

Table-1: Demographic status of the study group

Characteristics	Patient (n = 192) N (%)	Control (n = 192) N (%)
Sex		
M	121(63%)	116 (60.4%)
F	71 (37%)	76 (39.6%)
Age (Mean ± SD)	55.76 ± 10.11	50.93 ± 5.41
Education		
Illiterate	40 (20.8)	39(20.3)
Primary school	69 (35.9)	77(40.1)
Secondary school and college	69 (35.9)	54(28.1)
Degree and above	14 (7.3)	22(11.5)
Occupation		
Farmer	17 (8.9)	17(8.9)
Merchant	92 (47.9)	79(41.1)
Civil servant	72 (37.5)	64(33.3)
Student	6(3.1)	12(6.3)
Other	5 (2.6)	20(10.4)

Out of the participants with diabetes, 93 individuals (48.4%) had elevated serum AST levels, while out of the control group, 8 individuals (4.2%) had elevated serum AST levels. Out of all the cases of diabetes, 77 (40.1%) had high levels of serum ALT, while all 192 (100%) individuals in the control group had normal ALT values. Furthermore, 3 individuals (1.6%) with diabetes and 1 individual (0.5%) from the control group exhibited increased serum GGT levels.

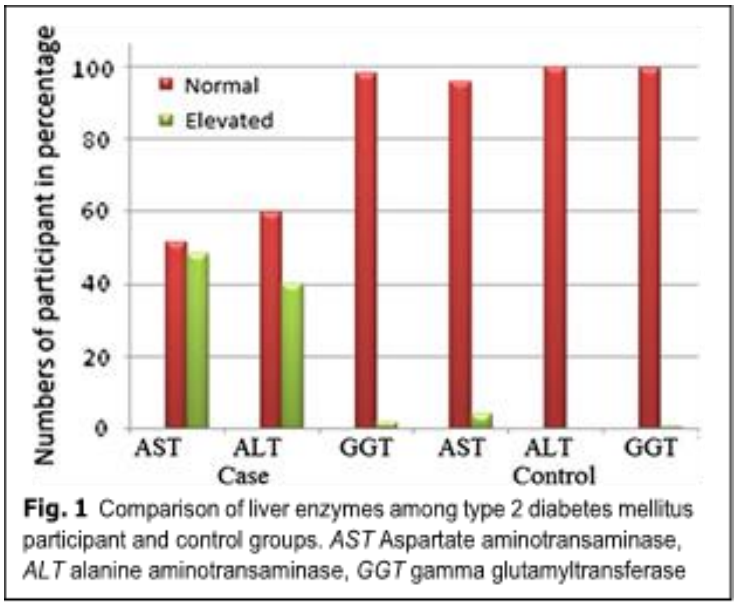

Fig. 1 Comparison of liver enzymes among type 2 diabetes mellitus participant and control groups. *AST* Aspartate aminotransaminase, *ALT* alanine aminotransaminase, *GGT* gamma glutamyltransferase

Figure-1: Comparison of liver enzymes among type 2 diabetes mellitus participant and control groups. AST Aspartate aminotransaminase, ALT alanine aminotransaminase, GGT gamma glutamyltransferase

The average values of ALT and AST were markedly elevated in individuals with type 2 diabetes compared to the control group ($P < 0.001$), as indicated in Table 2. There was no significant association between the GGT level of the control group and that of the diabetic individuals ($P = 0.065$). The average fasting blood glucose level in individuals with T2DM was substantially greater than that of the control group ($P \leq 0.001$).

Table-2: Biochemical parameters among diabetes and control participant (as mean ± SD) (N = 384)

Parameters	DM participants (mean ± SD)	Control group (mean ± SD)	*P* value	Laboratory reference range
FBS(mg/dl)	189.80 ± 64.45	89.52 ± 10.81	< 0.001	60–110 mg/dL
AST(IU/L)	42.94 ± 19.08	20.34 ± 9.90	< 0.001	0–37 U/L
ALT(IU/L)	46.06 ± 22.38	22.66 ± 9.45	< 0.001	0–42 U/L
GGT	21.98 ± 8.36	20.28 ± 9.63	0.065	0–48 U/L

DISCUSSION

The average age of the diabetic group and the control group in the current study were 56 and 52 years, respectively. Acute and subclinical liver cell dysfunction may affect the regulation of blood sugar levels. Given that liver enzymes are not the sole indicators of liver damage, it is evident that they also possess a prognostic value in evaluating the seriousness of diabetes. Insulin resistance is a common characteristic of type 2 diabetes mellitus (T2DM), indicating an imbalance in the liver's regulation of glucose levels [17]. Glycation is the prevailing complication of type 2 diabetes mellitus (T2DM) that leads to oxidative stress in tissue [18]. Oxidative stress and cytokine production in the liver lead to changes in liver enzymes as a result of hepatocellular damage [19, 20]. Therefore, the dysregulation of blood glucose management leads to further consequences, as it plays a crucial part in this process [21]. This disorder leads to the atypical release of liver enzymes into the bloodstream, causing them to increase in level. The current study aimed to evaluate the levels of liver enzymes, specifically ALT, AST, and GGT, in individuals with type 2 diabetes mellitus (T2DM) who were matched for age and sex, as well as in a control group consisting of individuals who were considered to be in good health.

Out of the diabetes cases, 93 individuals (48.4%) had elevated serum AST levels, while in the control group, 8 individuals (4.2%) had elevated serum AST levels. Out of the case groups, 77 individuals (40.1%) had higher levels of serum ALT, while all 192 individuals (100%) in the control group had normal values. The findings revealed a substantial rise in the mean values of AST and ALT in individuals with T2DM compared to the control group. The results of our research were consistent with a study carried out in Iraq and India, which found a significant correlation between the increase in AST and ALT levels and the presence of T2DM [20, 22]. Similarly, a recent study conducted in Myanmar and Singapore found that the average levels of ALT and AST among patients with diabetes fell within the normal range [23]. Contrary to our results, the amount of GGT showed a statistically significant association with T2DM in the two studies mentioned above [20]. Abnormally high levels of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were seen in 18.5% and 14.8% of the people with type 2 diabetes mellitus (T2DM), respectively [24]. India has reported a similar discovery, where they examined 90 individuals with type 2 diabetes mellitus (T2DM) for liver enzyme alanine aminotransferase (ALT), and compared them to a control group of 90 healthy participants [20].

Among the participants with type 2 diabetes mellitus (T2DM), 40% had significantly high levels of serum ALT (alanine aminotransferase) at an average of 71.65 ± 23.3 [10, 24]. Similarly, our findings were consistent with a research conducted on individuals with diabetes from Sudan and 50 control people who were apparently healthy. The study findings indicated that the average levels of ALT and AST were notably elevated in individuals with T2DM compared to the control group [9, 12]. Despite the fact that the average readings fell within the normal range, 11 patients with type 2 diabetes (22%) had abnormal liver enzymes, with at least one or more being affected [12, 25]. However, this investigation found no significant association between GGT and the risk of diabetes. On the other hand, a different study found that GGT was strongly linked to the risk of diabetes in participants, as compared to the control group [13]. This study proposed that an elevation in GGT concentration served as a sensitive and early indicator of the onset of diabetes.

We conducted a study to assess the occurrence of heightened levels of liver marker enzymes in individuals with Type 2 Diabetes Mellitus (T2DM). This could be attributed to the elevated impact of glycogen and insulin on hepatic cells. The key metabolic process is the rise of glycogenolysis, which is the breakdown of stored glycogen, and gluconeogenesis, which is the creation of glucose from non-carbohydrate precursors [26]. Therefore, the increase in the supply of substrate (such as alanine) and the conversion of alanine to glucose may be regulated as a compensatory mechanism in response to impaired hepatic insulin communication transduction. This impairment allows the enzyme to escape from hepatocytes, primarily due to the accumulation of fat and injury to hepatic cells [23]. An excessive buildup of fat and its release in hormone-responsive organs (such as the liver) and liver cells indicate a metabolic shift due to insulin resistance, which is detected before an increase in fasting blood sugar levels. Insulin resistance causes an excessive release of free fatty acids, leading to the mobilisation of fat and the toxicity of liver cells [20]. The increase in transaminase enzyme levels is strongly correlated with liver cell destruction. Hepatic cell injury occurs as a result of the rupture of a plasma membrane under high concentrations of metabolites, leading to the loss of mitochondrial functions and the inactivation of regulating metabolic enzymes [27].

CONCLUSION

Overall, this study found a clear link between the increase in liver enzyme levels (ALT and AST) and the presence of type 2 diabetes mellitus, as compared to the control group. Thus, liver enzyme testing may play a beneficial role in the management of diabetes.

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