*Original Article*

# Serum Alanine Transaminase Level in Type 2 Diabetes Mellitus and It's Relationship with Glycemic Status

Karmakar P[1], Islam MZ[2], Sultana D[3], Hossain N[4], Afrin N[5], Akhter S[6], Iqram T[7], Siddique MAA[8]

**Abstract**

***Background:*** *Type 2 diabetes mellitus is a complex heterogeneous group of metabolic conditions characterized by increased levels of blood glucose due to impairment in insulin action and/or insulin secretion. The liver plays a major role in the regulation of carbohydrate metabolism, as it uses glucose as a fuel. Type 2 DM has been linked with dyslipidemia and elevation of some liver enzymes. Alanine Transaminase (ALT) is said to be a more specific enzymatic marker for liver injury. So, the objective of the present study is to assess the serum ALT level in type 2 diabetes mellitus and non-diabetic people and see its relationship with glycemic status.* ***Materials and Methods:*** *This was a hospital based cross-sectional comparative study comprising hundred (100) diagnosed type 2 diabetic patients and non-diabetic people aged between 31 and 70 years. This study was carried out in the department of Biochemistry, Eastern Medical College and department of Medicine, Eastern Medical College Hospital, Cumilla, Bangladesh from July 2022 to June 2023 with ethical clearance from respective IERB. Samples were taken by non-probability convenient sampling. Important variables in this study were FPG, HbA1c%, serum ALT and duration of diabetes.* ***Results:*** *Serum ALT level increased in 83% of type 2 diabetic cases and 24% in non-diabetic people. Serum ALT levels were significantly higher in type 2 diabetic patients than non-diabetic people (58.46±18.89 vs 33.93±15.02 U/L) and there were significant differences of serum ALT levels between good and poor control diabetes patients (42.40±11.05 vs 60.24±18.78 U/L). This study showed a positive correlation of serum ALT with FBS ($p<0.00001$), HbA1c% ($p=0.02$) and duration of diabetes ($p=0.008$) in the study cases.* ***Conclusion:*** *The results of the present study concluded that serum ALT levels were significantly increased in type 2 diabetic patients. Serum ALT is widely available and considered as a more specific marker for liver disease.*

**Key words:** Serum ALT, HbA1c%, Type 2 DM.
**Received:** March 05, 2024; **Accepted:** March 25, 2024
**DOI:** https://doi.org/10.3329/emcj.v9i2.76935

## Introduction

Diabetes mellitus is a heterogeneous group of disorders characterized by persistent hyperglycemia with carbohydrate, lipid and protein metabolism resulting from defects in insulin secretion and/or insulin action[1-2]. Globally, type 2 diabetes is one of the most common non-communicable diseases that is caused by impaired β-cells function and capacity to secrete sufficient insulin, coupled with a decline in target tissue sensitivity to insulin (insulin resistance)[3-4]. This metabolic disorder (diabetes) affects many organs, including the liver, which plays a key role in the regulation of carbohydrate, lipid and protein metabolism[5].

The liver is an insulin sensitive organ, that plays an important role in maintenance of normal glucose levels during fasting as well as in the postprandial period[6]. Glycogenesis, glycogenolysis, gluconeo genesis, lipid metabolism and insulin degradation take place in the liver[7]. The liver enzymes, aspartate amino transferase (AST), alanine aminotransferase (ALT), Alkaline phosphatase (ALP) and gamma glutamyl transferase (GGT) are routinely used in evaluation of liver function.

Alanine aminotransferase (ALT) is a cytoplasmic enzyme found mainly in liver whereas aspartate aminotransferase (AST) 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[8]. The upper normal limit of serum alanine aminotransferase is set at 40 U/L[9]. Alkaline phosphatase (ALP) is a type of iso-enzyme, and its

[1]Pijush Karmakar, Associate Professor, Department of Biochemistry, Eastern Medical College, Cumilla, Bangladesh.
[2]Md. Zakirul Islam, Professor, Department of Pharmacology & Therapeutics, Eastern Medical College, Cumilla, Bangladesh.
[3]Dalia Sultana, Assistant Professor, Department of Biochemistry, Eastern Medical College, Cumilla, Bangladesh.
[4]Nadia Hossain, Assistant Professor, Dept. of Biochemistry, Chittagong Maa-o-Shishu Hospital Medical College, Chattogram, Bangladesh.
[5]Nahida Afrin, Assistant Professor, Department of Biochemistry, Rangamati Medical College, Rangamati, Bangladesh.
[6]Salma Akhter, Assistant Professor, Department of Biochemistry, Central Medical College, Cumilla, Bangladesh.
[7]Towhidul Iqram, Assistant Professor, Department of Physiology, Eastern Medical College, Cumilla, Bangladesh.
[8]Md. Asraful Alam Siddique, Assistant Professor, Department of Anatomy, Eastern Medical College, Cumilla, Bangladesh.

**Address of Correspondence:** Dr. Pijush Karmakar, Associate Professor, Department of Biochemistry, Eastern Medical College, Cumilla, Bangladesh. Mobile: +8801619150410. Email: dr.pijushkk@gmail.com

source is mainly liver and bones[8]. Gamma glutamyl transferase (GGT) is found in liver and other tissues also[10].

Patients with type 2 diabetes are frequently diagnosed with liver disease. This consists of abnormal liver enzymes, Non-Alcoholic Fatty Liver Disease (NAFLD), cirrhosis, acute hepatic failure and hepatocellular carcinoma[11]. The association between hepatic enzymes including alanine transaminase (ALT), aspartate transaminase (AST) and Alkaline phosphatase (ALP) and incident of diabetes have been examined. Most of the research done on this topic indicates that deranged liver enzyme levels, such as level of ALT, AST and ALP, in the serum are a frequent finding 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[12]. It has also been suggested that increases in ALT, a gluconeogenic enzyme whose gene expression is inhibited by insulin, may reflect impaired insulin signaling rather than liver damage alone[13].

The present study aimed to evaluate one of the most important liver function tests i.e. serum ALT level in patients with long-standing type 2 diabetes mellitus and also compared the serum ALT level with good and poor glycemic control.

## Materials and Methods

This cross-sectional study was carried out in Eastern Medical College Hospital from July 2022 to June 2023. Ethical clearance for this study was taken from the IERB of Eastern Medical College, Cumilla. A hundred (100) diagnosed type 2 diabetic patients and 100 non-diabetic people with the age range of 31 to 70 years were selected by non-probability convenient sampling. Data were collected by pre-designed questionnaire containing all the variables of interest and fulfilling the exclusion & inclusion criteria for the study population. Patients with active hepatitis, known cases of hepatitis B and C positive, cirrhosis of liver and carcinoma were excluded from the study. Informed consent from each subject was taken before the collection of samples. Under all aseptic precaution fasting venous blood samples were taken from each participant using sterile disposable syringe. Then FBS, HbA1c%, serum bilirubin and serum ALT were measured. Plasma glucose was measured by glucose oxidase method using multichannel auto analyzer. Serum bilirubin was measured in Siemens biochemistry autoanalyzer. Serum ALT level was measured by enzymatic method (modified IFCC) in Siemens biochemistry autoanalyzer. HbA1c% was measured by Biorad D10 analyzer by HPLC method. All the data was processed and analyzed using Microsoft Excel and IBM-SPSS v22.0 for Windows. Statistical inference was based on a 95% confidence interval and p-value <0.05 was regarded statistically significant. Variables were expressed as mean ± standard deviation (SD). To see the statistical differences student's 't' test was used and to see the correlation Pearson's correlation coefficient was used. The summarized data were presented in the form of tables and figures.

## Results

In this cross-sectional comparative study, hundreds (100) diagnosed type 2 diabetic patients were taken in which 59 were male and 41 were female. Besides of 100 non-diabetic people 47 were male and 53 were female (figure-1). The mean age was 48.97 ± 9.67 years in the diabetic group and 42.42 ± 11.24 years in the non-diabetic group. Serum ALT level was found to be increased in 83% of type 2 diabetic cases and 24% in non-diabetic people (table-I).

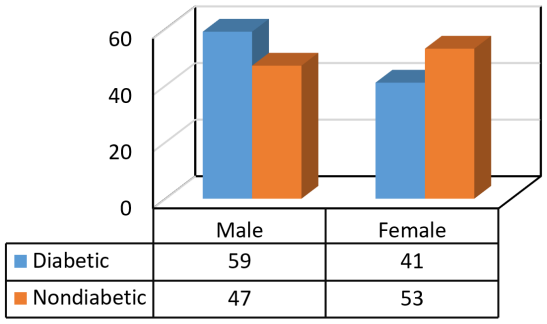


**Figure-1: Pie chart shows the gender distribution of the study population (n=200)**

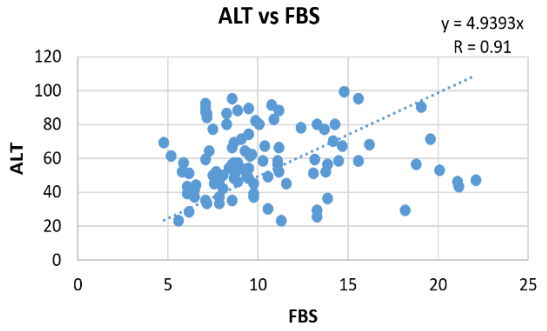


**Figure-2: Correlation between serum ALT and FBS in cases (n=100)**

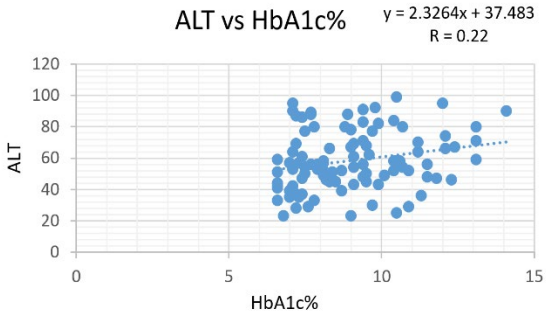


**Figure-3: Correlation between serum ALT and HbA1c% in cases (n=100)**

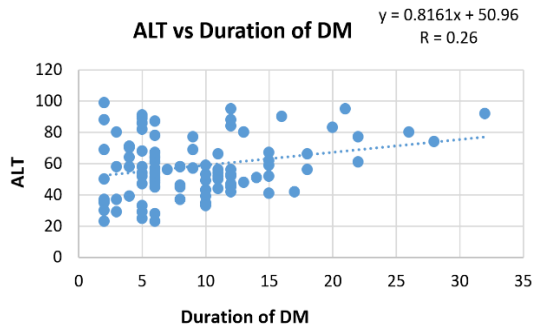


**Figure-4: Correlation between serum ALT and duration of diabetes in cases (n=100)**

Table-II shows that there were significant differences of FBS and HbA1c% in between type 2 diabetic patients and non-diabetic people. Table-II also demonstrates that serum ALT levels were significantly higher in type 2 diabetic patients than those of non-diabetic people in this study (58.46 ± 18.89 vs 33.93 ± 15.02 U/L). Besides, there was no significant difference in serum bilirubin level in type 2 diabetic patients and non-diabetic people. In table-III ALT levels were compared between good and poor diabetic control groups and showed that serum ALT levels were significantly higher in poorly controlled type 2 diabetic patients in comparison to good control diabetic patients (60.24 ± 18.78 vs 42.40 ± 11.05 U/L). Figure-2, 3 and 4 showed that there was significant correlation among serum ALT with FBS (p<0.00001), HbA1c% (p=0.02) and duration of diabetes (p=0.008) in the cases.

**Table-I: Serum ALT level in between type 2 diabetic patients and non-diabetic people (n=200)**

| S. ALT (U/L) | Type 2 Diabetic (n=100) | Non-diabetic (n=100) | χ2 Value | p-value (Significance) |
|---|---|---|---|---|
| Increased (>40 U/L) | 83 (83%) | 24 (24%) | 69.96 | p<0.00001 (Significant) |
| Normal (≤40 U/L) | 17 (17%) | 76 (76%) | | |
| **Total** | **100 (100%)** | **100 (100%)** | | |

**Table-II: Comparison of FBS, HbA1c% and serum ALT between type 2 diabetic patients and non-diabetic people (n=200)**

| Variables | Type 2 Diabetic (n=100) Mean±SD (Range) | Non-diabetic (n=100) Mean±SD (Range) | p-value | Significance |
|---|---|---|---|---|
| FBS (mmol/l) | 10.49±3.91 (4.8-22.1) | 5.39±0.45 (4.3-6.0) | p<0.00001 | Significant |
| HbA1c (%) | 9.02±1.82 (6.6-14.1) | 5.38±0.22 (4.6-5.6) | p<0.00001 | Significant |
| S. Bilirubin (mg/dl) | 0.46±0.24 (0.1-0.9) | 0.49±0.22 (0.1-0.9) | p=0.293 | Not Significant |
| S. ALT (U/L) | 58.46±18.89 (23-99) | 33.93±15.02 (17-88) | p<0.00001 | Significant |

**Table-III: Comparison of serum ALT between good and poor control diabetes (n=100)**

| Variable | Good Control (n=10) Mean±SD (Range) | Poor Control (n=90) Mean±SD (Range) | p-value | Significance |
|---|---|---|---|---|
| S. ALT (U/L) | 42.40 ± 11.05 (23-99) | 60.24 ± 18.78 (23-59) | p=0.004 | Significant |

**Discussion**

The liver plays a pivotal role in regulating the metabolism of carbohydrates as it utilizes glucose to meet its energy requirements, as well as it also stores glucose as glycogen for future needs. It is an important organ for gluconeogenesis. This type of action makes the liver more susceptible to metabolic diseases as in patients with diabetes[14]. Liver disease is more common 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. NAFLD is also a reason for chronic liver disease (CLD) associated with diabetes and obesity. With no intervention, NAFLD will eventually lead to a stage of Non-Alcoholic Steato-Hepatitis (NASH). NASH is the main reason for end-stage liver disease and a contributor to cardiovascular disease in type 2 diabetes mellitus[12].

Liver enzyme i.e., serum alanine aminotransferase, serum aspartate aminotransferase serves as hepatocellular markers, while serum alkaline phosphatase serves as a biliary function marker. Generally, ALT level is more than the AST level as AST is cleared more rapidly by reticuloendothelial system as compared to ALT[15]. Alanine aminotransferase (ALT) is a cytoplasmic enzyme

primarily located in the liver. So, ALT is a more specific marker for liver injury[8]. Alanine aminotransferase (ALT) concentration is considered as raised when ALT is >40 U/L[9].

In this study, among the diabetic cases 83% of patients had elevated serum ALT level while in non-diabetic people 24% had elevated ALT. A similar study was conducted by Gohel, et al.[12] and found that 39% diabetic patients had elevated ALT while in control group 6% people had elevated ALT. Other studies by Azeez, et al.[16], Singh, et al.[17], Ghimire, et al.[18], Shibabaw, et al.[19] and Han, et al.[20] and observed increased level of serum ALT in 57%, 52.6%, 46.66%, 40.1%, and 18.5% respectively among the patients with diabetes compared to non-diabetic people. The mean level of serum ALT in type-2 diabetic patients was 58.46±18.89 U/L and in non-diabetic people it was 33.93±15.02 U/L. Serum ALT in type 2 diabetic cases was 35.25±10.80 U/L in the study by Gohel, et al.[12], 47.86±33.66 U/L in the study by Mathur, et al.[21], 45.66±3.2 U/L in the study by Chandrashekhar.[22], 46.06±22.38 IU/L in the study by Shibabaw, et al.[19] and 39.00 ± 24.21 U/L in the study by Rashid, et al[23]. This is nearly consistence with our study.

Cho, et al.[24] found increased activity of liver enzymes, notably ALT, was associated with a twofold increase in the risk of type 2 diabetes independently of conventional risk factors and serve as a useful marker to identify individuals at high risk of type 2 diabetes in Asian populations. Abnormal liver enzyme levels in diabetes patients can be due to several factors. Firstly, hyperinsulinemia might directly lead to hepatic insulin resistance along with fatty liver. This increased fat deposition in liver is toxic to hepatocytes, leading to an increase in various transaminases level and decreased anabolic capacity of liver. Secondly, insulin-resistance also leads to an increase in level of proinflammatory cytokines like Tumor Necrosis Factor (TNF). Additionally, this could aggravate hepatocellular damage. NAFLD is one of the hepatic complications of diabetes mellitus with metabolic syndrome and ALT has been used as a marker of NAFLD[25].

In this study serum ALT was significantly higher in patients with poor control diabetes as compared to patients with good control. The findings of the present study is in agreement with that of Cho, et al.[24] and Chandra, et al[26]. This study also showed that there was a significant positive correlation of serum ALT with FBS and HbA1c%. This similar correlation was also observed in other studies[12,27,28]. Alam, et al.[29] in their study showed that serum ALT level was elevated in type 2 diabetic cases in comparison to non-diabetic subjects. But they have failed to show any correlation of serum ALT with FBS and HbA1c%. Serum ALT levels were positively correlated with duration of diabetes in this study cases. A similar finding was also observed by Gohel, et al.[12] and Odewabi, et al.[27] in their studies.

## Conclusion

Liver function tests are frequently used in clinical practice to diagnose liver disease, monitor the course of known diseases, and monitor the effects of hepatotoxic drugs. Serum ALT is a widely available and more specific marker for liver disease. Even a minor elevation of ALT is a good predictor of morbidity from liver disease.

## Conflict of interest

The authors declared that they have no conflict of interest.

## Acknowledgement

Authors acknowledged the patients who gave their permission to sample collection for the study and the scholars whose articles are cited and included in references to this manuscript.

## References

1. Whiting DR, Guariguata L, Weil C, Shaw J. IDF diabetes atlas: global estimates of the prevalence of diabetes for 2011 and 2030. Diabetes Res Clin Pract. 2011; 94 (3): 311-21. doi: 10.1016/j.diabres.2011.10.029.
2. Chen L, Magliano DJ, Zimmet PZ. The worldwide epidemiology of type 2 diabetes mellitus-present and future perspectives. Nat Rev Endocrinol. 2012; 8 (4): 228-36. doi: 10. 1038/nrendo.2011.183.
3. Centers for Disease Control and Prevention (CDC). Prevalence of overweight and obesity among adults with diagnosed diabetes-United States, 1988-1994 and 1999-2002. MMWR Morb Mortal Wkly Rep. 2004; 53 (45): 1066.
4. Bluestone JA, Herold K, Eisenbarth G. Genetics, pathogenesis and clinical interventions in type 1 diabetes. Nature. 2010; 464 (7293): 1293-300. doi: 10.1038/nature 08933.
5. Levinthal GN, Tavill AS. Liver disease and diabetes mellitus. Clin Diabetes. 1999; 17 (2): 73-93.
6. Traupe T, Gloekler S, de Marchi SF, Werner GS, Seiler C. Assessment of the human coronary collateral circulation. Circulation. 2010; 122 (12): 1210-20. doi: 10.1161/ CIRCULATIONAHA.109.930651.
7. Wannamethee SG, Shaper AG, Lennon L, Whincup PH. Hepatic enzymes, the metabolic syndrome, and the risk of type 2 diabetes in older men. Diabetes Care. 2005; 28 (12): 2913-8. doi: 10.2337/diacare.28.12.2913.
8. Lowe D, Sanvictores T, Zubair M, John S. Alkaline Phosphatase. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2024 Jan.

Available at: https://www.ncbi.nlm.nih.gov/books/NBK459201. [Accessed on August 12, 2023]
9. Kim HC, Nam CM, Jee SH, Han KH, Oh DK, Suh I. Normal serum aminotransferase concentration and risk of mortality from liver diseases: prospective cohort study. BMJ. 2004; 328 (7446): 983. doi: 10.1136/bmj.38050.593634.63.
10. Lee DH, Ha MH, Kim JH, Christiani DC, Gross MD, Steffes M, et al. Gamma-glutamyl transferase and diabetes-a 4-year follow-up study. Diabetologia. 2003; 46 (3): 359-64. doi: 10.1007/s00125-003-1036-5.
11. Zhang X, Yip TC, Tse YK, Hui VW, Li G, Lin H, et al. Duration of type 2 diabetes and liver-related events in nonalcoholic fatty liver disease: A landmark analysis. Hepatology. 2023; 78 (6): 1816-27. doi: 10.1097/HEP.0000000000000432.
12. Gohel VD, Johnson B, Joshi V. Comparative study of liver function tests in diabetes type-2 patients and nondiabetics in Gujarat. Int J Basic Appl Physiol. 2017; 6 (1): 71-6.
13. Bora K, Borah M, Chutia H, Nath CK, Das D, Ruram AA. 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): 30-5. doi: 10.4103/0974-2727.176227.
14. Han HS, Kang G, Kim JS, Choi BH, Koo SH. Regulation of glucose metabolism from a liver-centric perspective. Exp Mol Med. 2016; 48 (3): e218. doi: 10.1038/emm.2015.122.
15. Adams DH. Sleisenger and Fordtran's Gastrointestinal and Liver Disease. Gut. 2007; 56 (8): 1175. doi: 10.1136/gut.2007.121533.
16. Azeez FS, Saadi AM. Evaluation of Liver Function in Type 2 Diabetic Patients during Clinical Trials in Kirkuk City. Research J Pharm Tech. 2019; 12 (4): 1659-63. doi: 10.5958/ 0974-360X.2019.00278.6.
17. Singh A, Dalal D, Malik AK, Chaudhary A. Deranged liver function tests in type 2 diabetes: a retrospective study. Int J Med Sci Publ Health. 2019; 4 (3): 27-31.
18. Ghimire S, Shakya S, Shakya J, Acharya P, Pardhe BD. Abnormal Liver Parameters among Individuals with Type 2 Diabetes Mellitus Nepalese Population. Biochem Pharmacol. 2018; 7 (1): 2167-501. doi: 10.4172/2167-0501.1000243.
19. Shibabaw T, Dessie G, Molla MD, Zerihun MF, Ayelign B. Assessment of liver marker enzymes and its association with type 2 diabetes mellitus in Northwest Ethiopia. BMC Res Notes. 2019; 12 (1): 707. doi:10.1186/s13104-019-4742-x.
20. Han N, Htoo KS, Aung H. Determinants of Abnormal Liver Function Tests in Diabetes Patients in Myanmar. Int J Diabetes Res. 2012; 1 (3): 36-41. doi: https://doi.org/10.5923/j.diabetes.20120103.02.
21. Mathur S, Mehta DK, Kapoor S, Yadav S. Liver Function in Type-2 Diabetes Mellitus Patients. Int J Sci Stud. 2016; 3 (10): 43-7.
22. Chandrashekhar GS. Alterations of liver enzymes in T2DM: a case control study. Int J Adv Med. 2018; 5 (6): 1521-4.
23. Rashid MH, Haque MZ, Rahman MK, Mahbubur Rahman Khan M, Mahbubur Rahman ASM, Mamun-Al-Mahtab, et al. Study on Liver Dysfunction in Type 2 Diabetic Patients in Bangladesh. Euroasian J Hepatogastroenterol. 2016; 6 (1): 1-4. doi: 10.5005/jp-journals-10018-1155.
24. Cho NH, Jang HC, Choi SH, Kim HR, Lee HK, Chan JCN, et al. Abnormal Liver Function Test Predicts Type 2 Diabetes. Diabetes Care. 2007; 30 (10): 2566-8.
25. Jindal H, Singh A, Goyal R, Kamendu A. 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 Health. 2020; 7 (48): 2852-5.
26. Chandra KP, Shukla DK, Pawah AK. Comparative Study of Liver Function Parameters in Patients with Diabetes and Hypertension. J Med Sci Clin Res. 2016; 4 (12): 14723-7. doi: https://dx.doi.org/10.18535/jmscr/v4i12.67.
27. Odewabi AO, Akinola EG, Ogundahunsi OA, Oyegunle VA, Amballi AA, Raimi TH, et al. Liver Enzymes and its Corelates in Treated and Newly Diagnosed Type 2 Diabetes Mellitus Patients in Osogbo, Southwest, Nigeria. Asian J Med Sci. 2013; 5 (5): 108-12.
28. Alam MJ, Mukti MNM, Hoque MM, Karim MR, Islam MS, Mallik SC, et al. Liver function tests in diabetic and non-diabetic patients in Dhaka city of Bangladeshi population. Res Rev Biosci. 2013; 7 (4): 147-52.
29. Alam S, Raghav A, Reyaz A, Ahsan A, Ahirwar AK, Jain V, et al. Prevalence of elevated liver enzymes and its relationship with type 2 diabetes mellitus in North Indian adults. Metabol Open. 2021; 12: 100130. doi: 10.1016/j.metop.2021.100130.

**Citation of this article**
Karmakar P, Islam MZ, Sultana D, Hossain N, Afrin N, Akhter S, Iqram T, Siddique MAA. Serum Alanine Transaminase level in Type 2 Diabetes Mellitus and It's Relationship with Glycemic Status. Eastern Med Coll J. 2024; 9 (2): 68-72.