Scholars Journal of Applied Medical Sciences
Abbreviated Key Title: Sch J App Med Sci
ISSN 2347-954X (Print) | ISSN 2320-6691 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

Biochemistry

Pattern of Liver Enzymes in Type -2 Diabetes Mellitus Subjects with and without Dyslipidemia

Dr. Shahanaz Akter[1*], Dr. Manindra Nath Roy[2], Dr. Farzana Afroze[3], Dr. Sumi Dey[4], Dr. Most. Tasnim Ara Jhilky[5], Afsana Akhter[6]

[1]Lecturer, Department of Biochemistry, Mugda Medical College, Dhaka, Bangladesh
[2]Professor and Head, Department of Biochemistry, United Medical College. Dhaka, Bangladesh
[3]Assistant Professor (Cc), Department of Biochemistry, Monno Medical College, Dhaka, Bangladesh
[4]Lecturer, Department of Biochemistry, Jashore Medical College, Jashore, Bangladesh
[5]Lecturer, Biochemistry Department, Mugda Medical College, Dhaka, Bangladesh
[6]Lecturer, Department of Biochemistry, Sir Salimullah Medical College, Dhaka, Bangladesh

DOI: 10.36347/sjams.2024.v12i06.005 | **Received:** 24.04.2024 | **Accepted:** 01.06.2024 | **Published:** 05.06.2024

***Corresponding author:** Dr. Shahanaz Akter.
Lecturer, Department of Biochemistry, Mugda Medical College, Dhaka, Bangladesh

Abstract **Original Research Article**

Background: Type 2 diabetes mellitus (T2DM) is a major public health concern affecting millions of people worldwide. It is associated with dyslipidemia and disturbed liver function. Pattern of liver enzymes and its association with dyslipidemia in T2DM has been reported in limited studies. ***Objective:*** This study was aimed to evaluate the pattern of liver enzymes in T2DM subjects with and without dyslipidemia. ***Methods:*** This cross sectional analytical study was conducted in the department of Biochemistry of Sir Salimullah Medical College from March, 2021 to February, 2022. Sampling technique was purposive convenient. According to inclusion and exclusion criteria 100 study subjects were taken in this study, among them 50 T2DM subjects without dyslipidemia were taken as Group A and 50 T2DM subjects with dyslipidemia were taken as Group B. All study subjects were briefed about the study and written consent were taken. After taking informed written consent, their BMI was recorded. Fasting samples were collected from each study subject with full aseptic precaution. Fasting plasma glucose (FPG), glycosylated haemoglobin (HbA1c), fasting lipid profile, and liver enzymes (ALT, AST and GGT) were measured in Group A and Group B. Categorical variables were expressed as frequency and percentage. Continuous variables were expressed as mean ± standard deviation. Unpaired t-test, chi-square test, Fisher's exact test and pearson's correlation coefficient test were used for comparison of means and strength of association, where appropriate. All statistical tests were consideded at 5% level of significance. ***Results:*** The biochemical parameters FPG, HbA1c, TC, TG, LDL-C, ALT, GGT were significantly higher in Group B compared to Group A. However, mean value of HDL-C was significantly lower in Group B than Group A. Out of 100 subjects overall 6 (12%) subjects in Group A and 47 (94%) subjects in Group B had at least one or more elevated liver enzymes. ALT and GGT had a significant positive correlation with TC, TG, LDL-C and a significant negative correlation with HDL-C. ***Conclusion:*** Liver enzymes (ALT and GGT) are elevated in type 2 diabetes mellitus subjects with dyslipidemia while they remain almost normal in type 2 diabetics without dyslipidemia. Moreover, elevated liver enzymes (ALT and GGT) are associated with dyslipidemia in type 2 diabetes mellitus.

Keywords: Liver Enzymes, Type -2 Diabetes Mellitus, Dyslipidemia.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is the most common type of diabetes that covers about 90% of all diabetic cases [1]. T2DM is a heterogenous, multifactorial, polygenic disease characterized by a defect in insulin secretion (the beta-cell secretory defect) and action (insulin resistance), which results in elevated blood glucose [2]. In the initial stages of the disorder, glucose tolerance remains near-normal. Despite insulin resistance as the pancreatic beta cells compensate by increasing insulin production. A gradual fall in beta cells function causes the development of an intermediate hyperglycemic state, in which blood glucose level is higher than normal but does not reach the level of diabetes. The disease ultimately progresses towards complete beta-cell dysfunction leading to overt diabetes [3]. No single cause is adequate to explain the progression from normal glucose tolerance to diabetes. The fundamental molecular defects are insulin resistance

and impaired insulin secretion, which results from a combination of environmental and genetic factors [4].

Type 2 DM has been linked with dyslipidemia and the elevation of some liver enzymes. It is associated with abnormalities of both quantity and quality of lipoproteins due to increased transportation of fat to the liver [5]. The term diabetic dyslipidemia comprises a triad of raised triglycerides, increased concentration of small dense low-density lipoprotein cholesterol (LDL-C) and reduced high-density lipoprotein cholesterol (HDL-C) [6]. Dyslipidemia in diabetic patients results from insulin deficiency or insulin resistance that promotes lipolysis in the visceral adipocytes and increases the flux of free fatty acids in plasma and liver. Moreover, T2DM with dyslipidemic patients also have a higher prevalence of abnormal liver function tests due to direct hepatotoxic effect of fatty acid on liver when produced in excess [5]. They may suffer from an entire spectrum of liver diseases including non-alcoholic fatty liver disease, non-alcoholic steatohepatitis, cirrhosis, hepatocellular carcinoma and hepatic failure [7]. Non-alcoholic fatty liver disease is the scope of chronic liver disease in T2DM patients which is characterized by excess deposition of fat in the liver. Serum alanine aminotransferase (ALT) and gamma-glutamyl transferase (GGT) are good biomarkers of NAFLD. Hepatocytes damage or increased membrane permeability of hepatocytes due to inflammatory assault causes the release of these enzymes into the blood [4].

Various studies showed that ALT and GGT are the predictive markers of NAFLD in T2DM patients with dyslipidemia. This is due to insulin resistance which results lipolysis and excess deposition of fat on liver and together create inflammatory affect, oxidative stress and lead to elevate liver enzymes [8]. Though liver enzymes elevated and the disease progresses to hepatic failure, in most of the cases there may have no virtual symptoms. Thus asymptomatic individuals with mild elevation of liver enzymes reveals the chances of liver disease, mainly NAFLD in T2DM with dyslipidemia [9]. However, as per our knowledge no such study was reported in our country. Therefore, this cross sectional analytical study was designed to elucidate the pattern of liver enzymes (ALT, AST and GGT) in type 2 diabetes mellitus subjects with and without dyslipidemia.

Objective

To assess the liver enzyme patterns in individuals with Type 2 Diabetes Mellitus, both with and without dyslipidemia.

METHOD

This cross sectional analytical study was done at Department of Biochemistry of Sir Salimullah Medical College, Dhaka during the period of March, 2021 to February, 2022. 50 subjects were included for each group comprising a sample size of 100. Subjects of Type-2 diabetes mellitus with the age range of 30 to 59 yrs. Sampling technique applied purposive convenient sampling technique applied for this study. Study subjects were divided in 2 groups. Group A- Type 2 diabetes mellitus (T2DM) subjects without dyslipidemia. Group B- Type 2 diabetes mellitus (T2DM) subjects with dyslipidemia

Selection of Subjects:

Inclusion Criteria:

1. Subjects of T2DM with age range of 30 to 59 years irrespective of gender.
2. Duration of diabetes not less than 3 years.

Exclusion Criteria:

1. T2DM with any complications.
2. Patients with history of jaundice, liver cirrhosis and liver cancer, and conditions which may raise liver enzymes like acute hepatitis and chronic hepatitis (HBV and HCV).
3. Underweight and obese subjects.
4. Hypertension.
5. Pregnancy.
6. Patients with a history of lipid lowering agents within six months and drugs affecting liver enzymes: Amiodarone, Methotrexate, Pioglitazone, Tamoxifen, or other hepatotoxic drugs.
7. Patients with history of alcohol intake.

Variables of the Study:

1. Age
2. Gender
3. Body mass index (BMI)
4. Blood pressure: Systolic and diastolic blood pressure
5. Duration of diabetes mellitus
6. Fasting plasma glucose (FPG)
7. HbA1c
8. Serum fasting lipid profile include
   - Total cholesterol (TC)
   - Triglyceride (TG)
   - Low density lipoprotein-cholesterol (LDL-C)
   - High density lipoprotein-cholesterol (HDL-C)
9. Serum liver enzymes include
   - Alanine aminotransferase (ALT)
   - Aspartate aminotransferas (AST)
   - Gamma-glutamyl transferase (GGT)

Study Procedure:

Subjects were selected from the outpatient department of Medicine and Endocrinology, Sir Salimullah Medical College and Mitford Hospital, Dhaka. Ethical permission was taken from the Ethical Review Committee of Sir Salimullah Medical College. After proper counselling objectives, study's risk and the procedure were explained in detail to all participants.

Only voluntary participants were recruited for this study. They had the freedom to withdraw themselves from the study at any stage. Informed written consent was taken from all respondents. Socio-demographic and other relevant data were taken and recorded in the data collection sheet with a pretested questionnaire.

Measurement of BMI: Height was measured (without shoes) by measuring tape in centimeters. Body weight was measured in light clothing and without shoes. Weight was recorded in kilogram. BMI was calculated as weight in kilogram divided by height in meter square.

Blood Pressure Measurement: BP was measured after at least 5 minutes rest in a chair with feet on the floor and arm supported at heart level using a manual sphygmomanometer. Readings were taken two times five minutes apart. An average of two readings was taken for analysis.

Blood Sample Collection:

Fasting blood samples were collected from all study subjects. They were allowed to fast overnight (10 – 12 hours). Under all aseptic precaution 6 ml of venous blood was taken in different vacutainer tube by vacutainer needle. 2 ml of blood was collected into a vacutainer tube coated with dried sodium fluoride-potassium oxalate mixture for estimation of FPG and then 2 ml of blood was collected into an EDTA containing vacutainer tube for estimation of HbA1c. The remaining 2 ml of blood was collected into a plain tube and allowed to clot.

Serum and plasma were separated after centrifugation at 3000 rmp for 10 minutes and were collected in labelled eppendrofs. FPG and HbA1c were performed immediately. Eppendrofs with serum were stored in refrigerator at -20°C until assay. Serum lipid profile and liver enzymes (ALT, AST and GGT) of all samples were estimated following standard methods. All the tests were done in the Biochemistry laboratory of Sir Salimullah medical college, Dhaka.

Laboratory Analysis:

1. Estimation of fasting plasma glucose: Glucose oxidase method
2. Estimation of HbA1c: Immunofluorescence method
3. Estimation of serum total cholesterol: Enzymatic end point method
4. Estimation of serum fasting TG: Enzymatic (GPO-PAP) method
5. Estimation of fasting HDL-C: Enzymatic (CHOD-PAD) method
6. LDL-C was calculated from total cholesterol, HDL-C, and TG using Friedewald's formula Serum ALT: Kinetic method
7. Serum AST: Kinetic method
8. Serum GGT: Kinetic end point method

FPG, serum lipid profile and liver enzymes were analyzed by semi auto biochemistry analyzer (Humalyzer 3000, Germany). HbA1c was determined by Getein 1100, (China).

Data Collection and Processing:

After relevant information was recorded systematically in a pre-designed standard data sheet and then data were checked, edited and processed.

Data Analysis:

Data was analyzed with the help of software SPSS (Statistical Package for Social Sciences) version 22. Categorical variables were expressed as frequency and percentage. Continuous variables were expressed as mean ± standard deviation. Unpaired t-test was performed to compare mean values of baseline and biochemical variables between two groups. For categorical variables chi-square test and Fisher's exact test were done. To determine correlation between continuous variables, Pearson's correlation coefficient test was carried out. The p value of <0.05 was considered as statistically significant.

RESULTS

Table-1 showed the distribution of study subjects according to age and gender. It was observed that majority subjects belonged to age group of 40-49 years, 26 (52%) in Group A and 22 (44%) in Group B. Among 100 study subjects, 28 (56.0%) and 30 (60%) were male in Group A and Group B respectively. In regard to age and gender, no significant difference was seen between two groups.

Table I: Distribution of the study subjects according to Age and Gender (n=100)

	Group A (n=50) number (%)	Group B (n=50) number (%)	p-value
Age (years)			
30 - 39	10 (20.0)	7 (14.0)	
40 - 49	26 (52.0)	22 (44.0)	0.137
50 - 59	14 (28.0)	21 (42.0)	
Gender (%)			
Male	28 (56.0)	30 (60.0)	0.685
Female	22 (44.0)	20 (40.0)	

Chi-Square test was done to measure the level of significance.

Table-2 showed that mean±SD values of FPG and HbA1c were significantly higher (p<0.001) in Group B compared to Group A.

Table-2: Comparison of glycemic status between Group A and Group B (n=100)

Glycemic status	Group A (n=50) Mean ± SD	Group B (n=50) Mean ± SD	p-value
FPG (mmol/L)	6.15 ± 2.41	11.10 ± 3.76	**<0.001**
HbA1c (%)	6.34 ± 1.48	8.47 ± 1.59	**<0.001**

Figure-1 showed that mean±SD values of TC and LDL-C were significantly higher (p<0.05) in dyslipidemic group than normolipidemic group. There was also significant difference in respect of TG (204.38±52.95 vs 178.76±44.58). However, mean±SD values of HDL-C decresed (p<0.001) significantly in T2DM with dyslipidemia compared to T2DM without dyslipidemia.

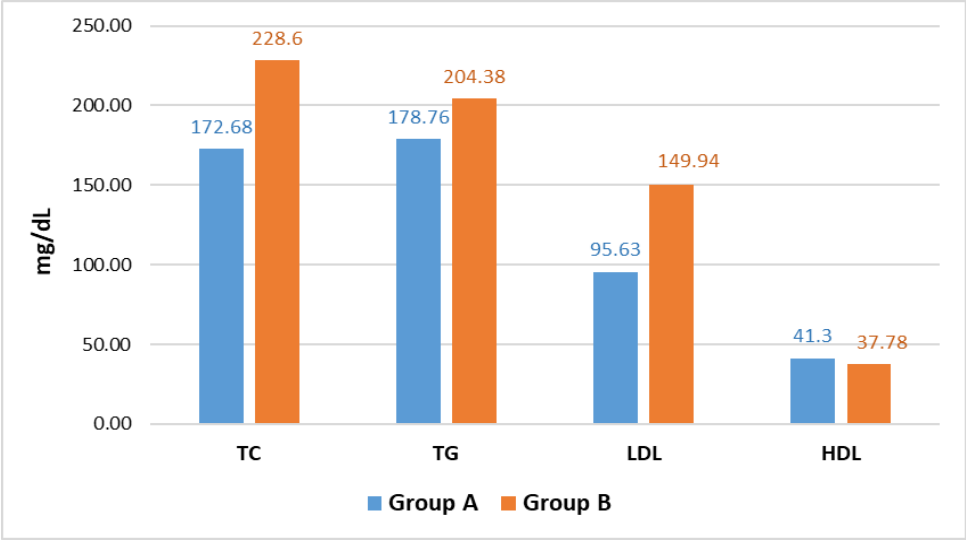


Figure 1: Bar diagram showing mean values of lipid profile level in Group A and Group B

Figure-2 showed that mean±SD values of ALT and GGT were significantly more (p<0.001) in Group B than Group A. However, there was no significant difference in case of AST between two groups.

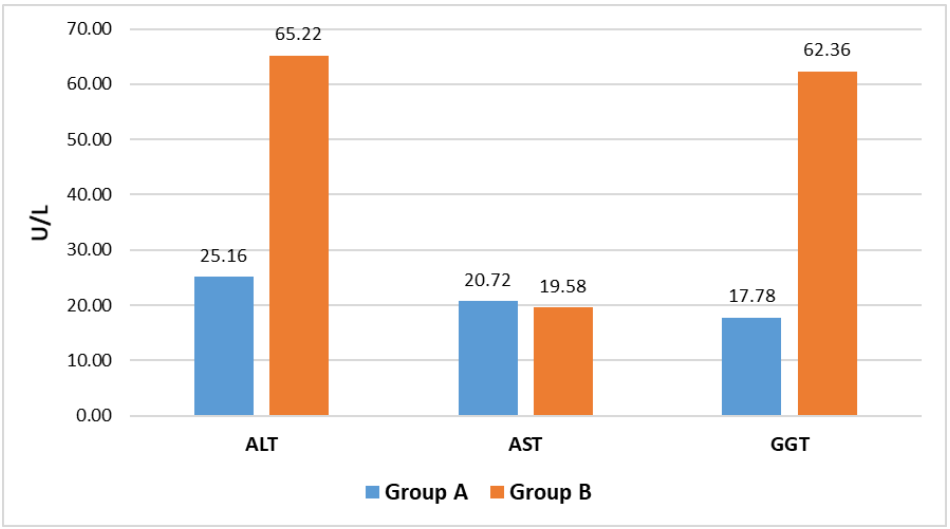
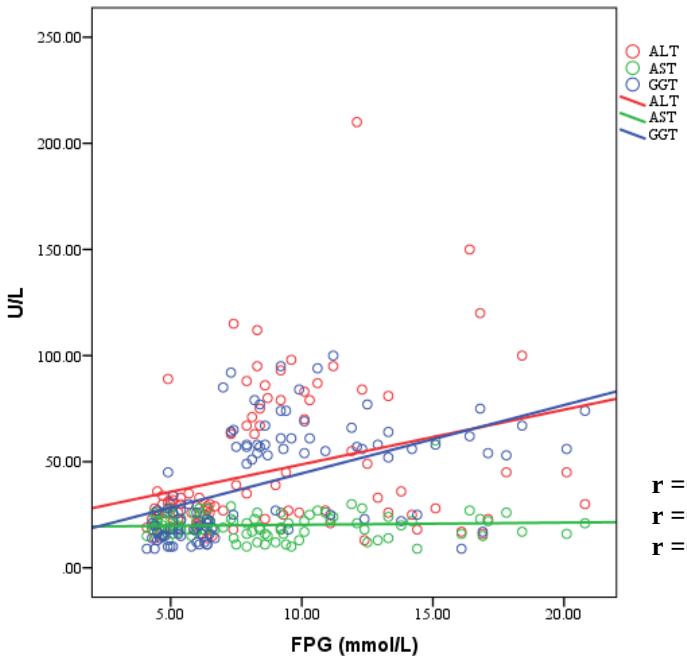


Figure 2: Bar diagram showing mean values of serum liver enzymes (ALT, AST and GGT) in Group A and Group B

Table-3 and figure-3 showed correlation of ALT, AST and GGT with different variables. Serum ALT and GGT had significant positive correlation with FPG, HbA1c, TC, TG and LDL-C. But they were negatively correlated (p<0.001) with HDL-C. AST did not show significant correlation with any variables.

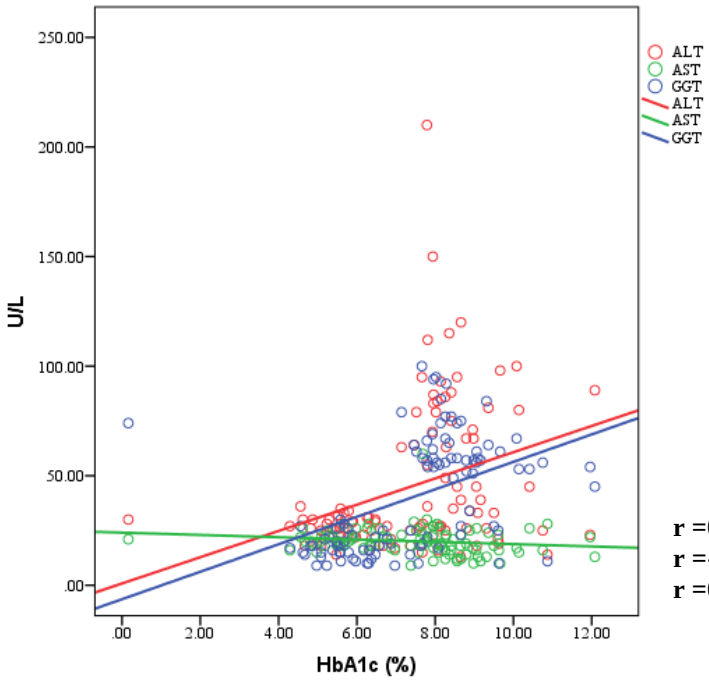
Table-3: Correlation of Liver enzymes (ALT, AST and GGT) with biochemical variables in study subjects (n=100)

	ALT		AST		GGT	
	r	p-value	r	p-value	r	p-value
FPG	0.305	<**0.01**	0.064	0.529	0.506	<**0.001**
HbA1c	0.330	<**0.001**	-0.154	0.126	0.458	<**0.001**
TC	0.550	<**0.001**	0.030	0.769	0.651	<**0.001**
TG	0.337	<**0.001**	0.175	0.082	0.321	<**0.001**
LDL-C	0.547	<**0.001**	-0.066	0.514	0.656	<**0.001**
HDL-C	-0.468	<**0.001**	-0.016	0.871	-0.431	<**0.001**



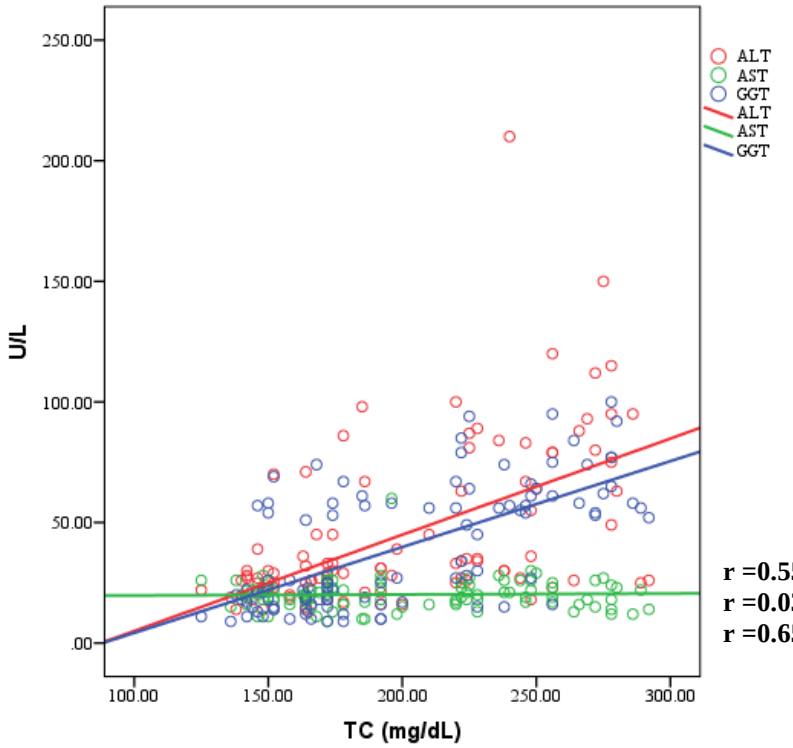
r =0.305; p <0.01(ALT)
r =0.064; p <0.529(AST)
r =0.506; p <0.001(GGT)

Figure 3a: Scattered diagram showing correlation of ALT, AST and GGT with FPG



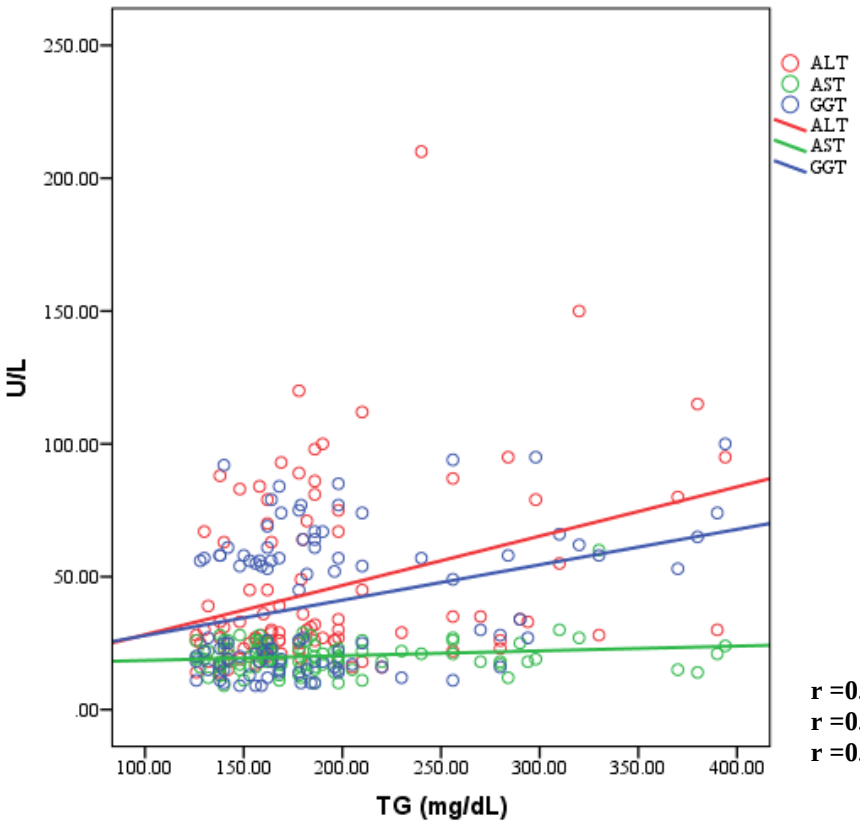
r =0.33; p <0.001(ALT)
r =-0.154; p <0.126(AST)
r =0.458; p <0.001(GGT)

Figure 3b: Scattered diagram showing correlation of ALT, AST and GGT with HbA1c



r =0.550; p <0.001(ALT)
r =0.030; p <0.769(AST)
r =0.651; p <0.001(GGT)

Figure 3c: Scattered diagram showing correlation of ALT, AST and GGT with TC



r =0.337; p <0.001(ALT)
r =0.175; p <0.082(AST)
r =0.321; p <0.001(GGT)

Figure 3d: Scattered diagram showing correlation of ALT, AST and GGT with TG

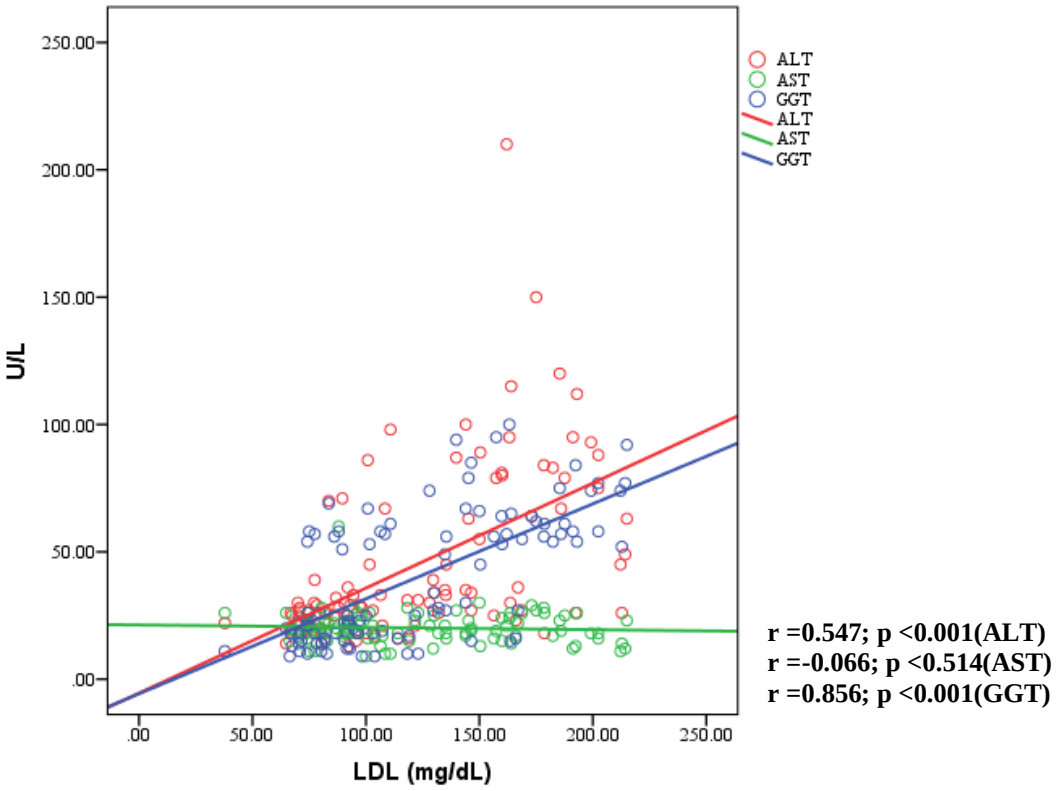


Figure 3e: Scattered diagram showing correlation of ALT, AST and GGT with LDL-C

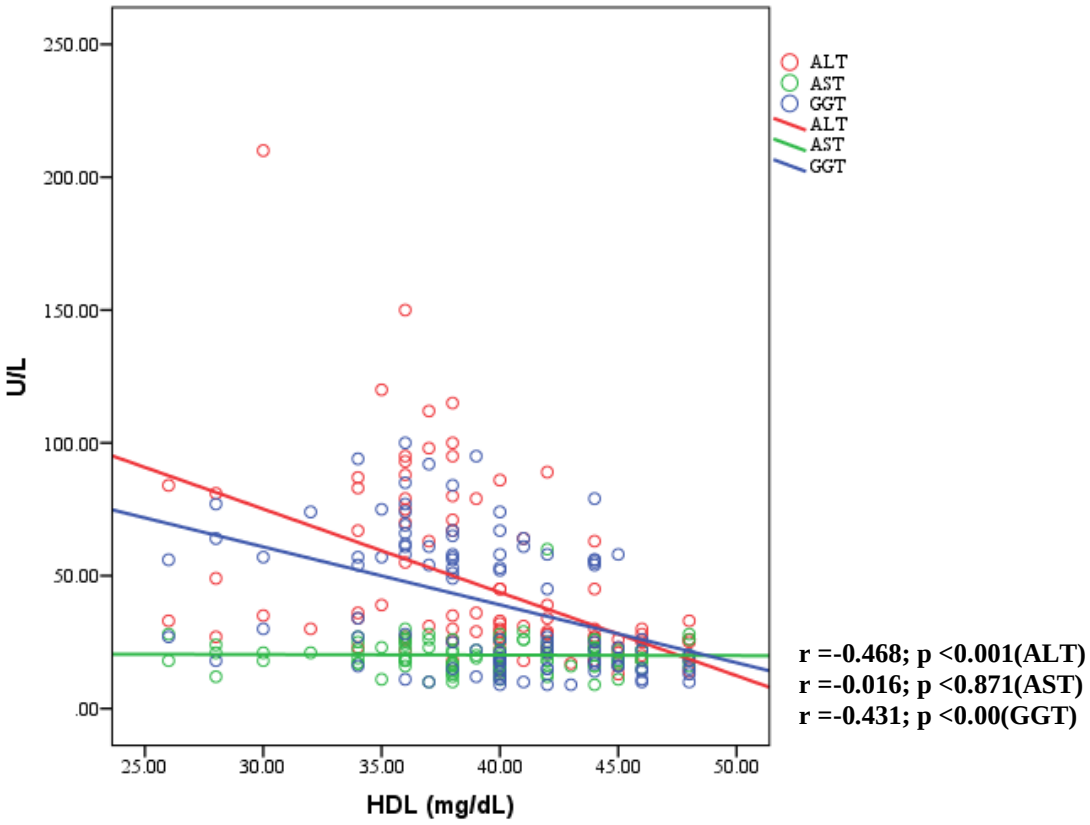


Figure 3f: Scattered diagram showing correlation of ALT, AST and GGT with HDL-C

Table-4 showed the distribution of study population according to liver enzymes status. Out of 100 subjects elevated ALT was observed in 6 and 36 subjects in Group A and Group B respectively. There was

significant association (p<0.001) of elevated ALT with dyslipidemia. However, no association was evident in case of AST. Increased GGT was seen in 43 diabetic subjects with dyslipidemia whereas none among those without dyslipidemia. Elevated GGT was significantly (p<0.001) associated with dyslipidemia.

Table-4: Distribution of the study population showing association of liver enzymes (ALT, AST and GGT) with dyslipidemia (n=100)

Liver Enzymes		Group A (n=50) number (%)	Group B (n=50) number (%)	p-value
ALT (U/L)	Normal	44 (88.0)	14 (28.0)	**<0.001**
	Elevated	6 (12.0)	36 (72.0)	
AST (U/L)	Normal	50 (100.0)	49 (98.0)	1.000
	Elevated	0 (0.0)	1 (2.0)	
GGT (U/L)	Normal	50 (100.0)	7 (14.0)	**<0.001**
	Elevated	0 (0.0)	43 (86.0)	

DISCUSSION

In this study, most of the study subjects were 40-49 years in both groups. One study reported almost identical age distribution of the study subjects [10]. It was evident from the study that number of male patients were more than female in both groups. This pattern of gender distribution is consistent with the other study [11]. However, females were more in the observation of another study [12].

It was revealed from the study that subjects of both groups had similar pattern regarding duration of diabetes. Similar observation was evident in other studies [13-14]. However, it was not consistent with other study [15]. This may be due to progressive impairment of insulin secretion by β-cell with time, increase insulin resistance and a sudden decrease in insulin secretion. The exact mechanism by which altered lipid profile is more deranged with disease duration is not very well understood [14].

It was evident from the study that dyslipidemic patients had more serum ALT and GGT activities than the corresponding normolipidemic subjects. Moreover, a relationship between liver enzymes and lipid profile had been observed. Nearly similar results were reported by other studies [5]. These findings support the role of hepatic insulin resistance in the pathogenesis of NAFLD in diabetic patients with dyslipidemia [15-16]. Another study reported a correlation between ALT activity and increased fatty liver [17].

In the present study 36 (72%) of the dyslipidemic and 6 (12%) of the normilipidemic subjects had elevated serum ALT levels. In terms of GGT, 43 (86%) had elevated serum GGT among the diabetic subjects with dyslipidemia whereas all of the normilipidemic subjects had normal values. These findings were almost consistent with the observations of other investigators [18]. However, research in Singapore did not consistent with this study regarding ALT and GGT [19].

Thus, it is obvious from the study that ALT and GGT are elevated in dyslipidemic diabetic subjects as compared to normolipidemic diabetic patients. In addition, elevatved liver enzymes (ALT and GGT) are associated with dyslipdemia. In clinical practice, assay of liver enzymes along with lipid profile can be used as a routine test in T2DM patients for early detection of liver abnormality. This will help to prevent further progress to chronic liver disease.

CONCLUSION

In individuals with Type 2 Diabetes Mellitus (T2DM), liver enzymes show elevated levels particularly in the presence of dyslipidemia, whereas they tend to remain within normal ranges in those without dyslipidemia. Moreover, this elevation in liver enzymes, specifically alanine aminotransferase (ALT) and γ-glutamyltransferase (GGT), is closely associated with the presence of dyslipidemia in individuals with Type 2 diabetes.

REFERENCE

1. Magliano, D. J., Boyko, E. J., & Atlas, I. D. (2021). What is diabetes?. In *IDF DIABETES ATLAS [Internet]. 10th edition*. International Diabetes Federation.
2. Olokoba, A. B., Obateru, O. A., & Olokoba, L. B. (2012). Type 2 diabetes mellitus: a review of current trends. *Oman medical journal*, *27*(4), 269.
3. Kasper, J. S., & Giovannucci, E. (2006). A meta-analysis of diabetes mellitus and the risk of prostate cancer. *Cancer Epidemiology Biomarkers & Prevention*, *15*(11), 2056-2062.
4. Bin Dahman, L. S., Humam, M. A., Barahim, O. H., Barahman, O. M., & Balfas, M. A. (2021). Association between Liver Enzymes and Dyslipidemia in Yemeni Patients with Type Two Diabetes Mellitus. *Journal of Diabetes Mellitus*, *11*(02), 41-51.
5. Atiba, A. S., Oparinde, D. P., Babatunde, O. A., Niran-Atiba, T., Jimoh, A. K., & Adepeju, A. (2013). Liver enzymes and lipid profile among type

2 diabetic patients in Osogbo, Nigeria. *Greener Journal of Medical Sciences*, *3*(5), 174-8.
6. Adiels, M., Olofsson, S. O., Taskinen, M. R., & Borén, J. (2008). Overproduction of very low–density lipoproteins is the hallmark of the dyslipidemia in the metabolic syndrome. *Arteriosclerosis, thrombosis, and vascular biology*, *28*(7), 1225-1236.
7. Kashinakunti, S. V., Rangappa, M., & Kallaganada, G. S. (2017). Correlation between liver enzymes and lipid profile in type II diabetes mellitus–A case control study. *J. Biotechnol. Biochem*, *3*(5), 01-05.
8. Lee, D. H., Silventoinen, K., Jacobs Jr, D. R., Jousilahti, P., & Tuomileto, J. (2004). γ-Glutamyltransferase, obesity, and the risk of type 2 diabetes: observational cohort study among 20,158 middle-aged men and women. *The Journal of Clinical Endocrinology & Metabolism*, *89*(11), 5410-5414.
9. Harris, E. H. (2005). Elevated liver function tests in type 2 diabetes. *Clinical diabetes*, *23*(3), 115-119.
10. Aamir, A. H., Ul-Haq, Z., Mahar, S. A., Qureshi, F. M., Ahmad, I., Jawa, A., ... & Heald, A. H. (2019). Diabetes Prevalence Survey of Pakistan (DPS-PAK): prevalence of type 2 diabetes mellitus and prediabetes using HbA1c: a population-based survey from Pakistan. *BMJ open*, *9*(2), e025300.
11. Sisodia, R. K., & Chouhan, M. (2019). The study of correlation between Body Mass Index and glycemic control-HbA1c in diabetes type 2 patients.
12. Shahwan, M. J., Khattab, A. H., Khattab, M. H., & Jairoun, A. A. (2019). Association between abnormal serum hepatic enzymes, lipid levels and glycemic control in patients with type 2 diabetes mellitus. *Obesity Medicine*, *16*, 100137.
13. Shahwan, M. J., Khattab, A. H., Khattab, M. H., & Jairoun, A. A. (2019). Association between abnormal serum hepatic enzymes, lipid levels and glycemic control in patients with type 2 diabetes mellitus. *Obesity Medicine*, *16*, 100137.
14. Mandal, A., Bhattarai, B., Kafle, P., Khalid, M., Jonnadula, S. K., Lamicchane, J., ... & Gayam, V. (2018). Elevated liver enzymes in patients with type 2 diabetes mellitus and non-alcoholic fatty liver disease. *Cureus*, *10*(11).
15. Mehta, R. K., Koirala, P., Mallick, R. L., Parajuli, S., & Jha, R. (2021). Dyslipidemia in patients with type 2 diabetes mellitus in a tertiary care centre: a descriptive cross-sectional study. *JNMA: Journal of the Nepal Medical Association*, *59*(236), 305.
16. Ko, S. H., Park, S. A., Cho, J. H., Ko, S. H., Shin, K. M., Lee, S. H., ... & Ahn, Y. B. (2012). Influence of the duration of diabetes on the outcome of a diabetes self-management education program. *Diabetes & metabolism journal*, *36*(3), 222.
17. Al-Jameil, N., Khan, F. A., Arjumand, S., Khan, M. F., & Tabassum, H. (2014). Associated liver enzymes with hyperlipidemic profile in type 2 diabetes patients. *International journal of clinical and experimental pathology*, *7*(7), 4345.
18. Tolman, K. G., Fonseca, V., Tan, M. H., & Dalpiaz, A. (2004). Narrative review: hepatobiliary disease in type 2 diabetes mellitus. *Annals of internal medicine*, *141*(12), 946-956.
19. Nannipieri, M., Gonzales, C., Baldi, S., Posadas, R., Williams, K., Haffner, S. M., ... & Ferrannini, E. (2005). Liver enzymes, the metabolic syndrome, and incident diabetes: the Mexico City diabetes study. *Diabetes care*, *28*(7), 1757-1762.
20. Cho, N. H., Jang, H. C., Choi, S. H., Kim, H. R., Lee, H. K., Chan, J. C., & Lim, S. (2007). Abnormal liver function test predicts type 2 diabetes: a community-based prospective study. *Diabetes care*, *30*(10), 2566-2568.
21. Judi, L., Toukan, A., Khader, Y., Ajlouni, K., & Khatib, M. A. (2010). Prevalence of elevated hepatic transaminases among Jordanian patients with type 2 diabetes mellitus. *Annals of Saudi medicine*, *30*(1), 25-32.
22. Wang, Y. L., Koh, W. P., Yuan, J. M., & Pan, A. (2016). Association between liver enzymes and incident type 2 diabetes in Singapore Chinese men and women. *BMJ Open diabetes research and care*, *4*(1), e000296.