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A Study on the Interplay of Abnormal Serum Hepatic Enzymes, Lipid Levels, and Glycemic Control in the Young South Indian Diabetics.

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Abstract:

Diabetes Mellitus is a metabolic disorder caused by insufficient insulin production or ineffective insulin use, leading to hyperglycemia. The aim of this study was to explore the relationship between abnormal serum hepatic enzymes, lipid levels, and glycemic control in young South Indian diabetics (20-40 years). A total of 191 participants were included in the study, with 107 males (56%) and 84 females (44%). HbA1c levels >6.5% were measured using the immunoturbidimetric method on the Mindray BS-600 machine. In addition to glycemic control, liver enzymes such as Aspartate aminotransferase (AST), Alkaline phosphatase (ALP), Gamma-glutamyl transferase (GGT), Alanine

aminotransferase (ALT), albumin, and lipid profiles including total cholesterol, HDL, and LDL levels were also measured to assess metabolic disturbances in these young diabetic individuals. In this study, HbA1c values for males aged 21-30 and 31-40 were 9.46 ± 2.15 and 9.24 ± 1.87, respectively, while for females, they were 9.94 ± 2.48 and 8.99 ± 1.71. Liver markers like AST ($p = 0.11$), ALT ($p = -0.01$), and GGT ($p = 0.03$) showed weak or negligible correlations with HbA1c. In contrast, Total Cholesterol ($p = 0.55$) and LDL ($p = 0.50$) showed moderate positive correlations with HbA1c, indicating significant cardiovascular risks ($p < 0.05$). Triglycerides ($p = 0.007$) and HDL ($p = 0.29$) showed weak correlations.

To conclude, the study highlighted a significant relationship between HbA1c and lipid markers, with moderate positive correlations to Total Cholesterol and LDL, indicating cardiovascular risk. However, correlations with liver markers (AST, ALT, GGT, albumin) were weak or negligible. Future research should have focused on liver dysfunction and lipid imbalances in diabetes.

Key words:

Diabetes Mellitus, Liver markers, Lipid profile, HbA1c, Young diabetic population, Chronic liver disease (CLD), Atherogenic dyslipidemia.

Introduction:

Diabetes Mellitus is a metabolic disorder characterized by hyperglycemia, where blood sugar levels are abnormally high due to dysfunction of pancreatic β-cells. The primary cause of this condition is either insufficient insulin production or the body's inability to effectively use insulin. This impaired insulin function disrupts various metabolic processes, ultimately leading to the development and progression of diabetes mellitus (1). According to the International Diabetes Federation (IDF), Diabetes Mellitus (DM) affected over 463 million people globally in 2019. The prevalence of the disease is on a rapid rise, with projections suggesting that more than 700 million individuals will be living with diabetes by 2045(2).

The liver plays a significant role in the development of this disorder (3). However, diabetes mellitus has been suggested as a potential risk factor for chronic liver disease (CLD). Additionally, liver cirrhosis (LC) has been found to promote the development of diabetes due to the liver's impaired function, leading to the term "hepatogenous diabetes" (HD)(4).The liver is a key organ responsible for glucose and lipid metabolism and is also impacted by metabolic syndrome. Liver enzymes such as Aspartate aminotransferase (AST), Alkaline phosphatase (ALP), Gamma-glutamyl transferase (GGT), albumin, and Alanine aminotransferase (ALT) are crucial indicators of liver function, often used to diagnose liver diseases. Elevated levels of these enzymes are linked to metabolic syndrome and other conditions like dementia, stroke, and liver injury (5). Recent research has identified liver enzymes as biomarkers for metabolic syndrome and its clinical outcomes (6). The relationship between liver enzymes and metabolic syndrome stems from their influence on factors such as obesity, liver fat accumulation, and blood sugar levels. Abnormalities in these factors contribute to the development of metabolic syndrome. Higher levels of liver enzymes are also associated with elevated blood pressure and triglyceride levels, both of which are components of metabolic syndrome (7).

Diabetic patients are more likely to develop abnormal cholesterol levels (atherogenic dyslipidemia), which increases their risk of major blood vessel diseases like heart disease and stroke, as well as smaller blood vessel complications such as nerve damage (neuropathy) and kidney problems (nephropathy)(8,9). Atherogenic dyslipidemia is marked by elevated triglycerides (TG), low levels of high-density lipoprotein (HDL), and high levels of low-density lipoprotein (LDL) in the blood (10). Some research suggests that HbA1c can be a reliable predictor of both dyslipidemia and heart disease (11,12). However, while HbA1c is commonly used to monitor blood sugar control and related diabetes complications, some studies question its link to dyslipidemia (13,14,15,16,17,18)

Glycated hemoglobin (HbA1c) reflects an individual's average blood sugar levels over the past three months. Since the early 2000s, the American Diabetes Association has recommended it as an alternative to glucose tolerance tests for diagnosing and monitoring diabetes and prediabetes. (19) People with diabetes, as identified by elevated HbA1c levels, often show abnormal cholesterol and liver function, putting them at a high risk for heart and liver diseases (20)

Materials

This prospective cross-sectional study was conducted at a tertiary care center in Chennai, South India, between August 2023 and August 2024. It included diabetic patients aged 20 to 40 years who visited the hospital during the study period and consented to participate. Participants were carefully selected by excluding non-diabetics, smokers, alcohol consumers, and individuals with conditions such as endocrine or genetic disorders, or those on steroid medications. Only those with an HbA1c level above 6.5%, indicating poor glycemic control, were included in the study.

Methods

This cross-sectional study was conducted at Sree Balaji Medical College and Hospitals among outpatients attending routine diabetic check-ups. The study focused on diabetic individuals aged 20 to 40 years with HbA1c levels exceeding 6.5%. The exclusion criteria included non-diabetic individuals, smokers, alcoholics, patients with known liver diseases, individuals with diagnosed endocrine or genetic disorders, and those on steroid medication. The data was collected using a structured questionnaire.

Clinical Biomarkers & Statistical Analyses:

HbA1c levels were assessed through the immunoturbidimetric technique on the Mindray BS-600 system. Fasting and postprandial glucose concentrations were measured via the glucose oxidase-peroxidase (GOD-POD) method. Aspartate aminotransferase (AST), alanine transaminase (ALT), and alkaline phosphatase (ALP) were evaluated using the International Federation of Clinical Chemistry (IFCC) protocol, while gamma-glutamyl transferase (GGT) was determined through the SZASZ method. Albumin levels were measured using the bromocresol green assay, total cholesterol via the cholesterol oxidase-peroxidase (CHOD-POD) method, triglycerides through the glycerol-3-phosphate oxidase (GPO-POD) assay, and LDL and HDL were directly measured on the Mindray BS-600 system.

The study's statistical analyses were performed using SPSS Statistics version 26 to ensure precise data interpretation and reliable results.

Human Ethics:

The Institutional Ethics Committee granted approval for this study in August 2023 (Ref.No.002/SBMCH/IHEC/2023/1994).

Standard Reference range:

The reference values for this study are as follows: HbA1c should be below 6.5%, fasting blood glucose between 70 and 99 mg/dL, and postprandial blood glucose under 140 mg/dL. For liver enzymes, the normal ranges are AST: <35 U/L for men and <34 U/L for women, ALT: <45 U/L for men and <34 U/L for women, and ALP: 53-128 U/L for men and 42-98 U/L for women. Albumin levels should range from 3.5-4.6 g/dL, total cholesterol below 200 mg/dL, triglycerides between 150-199 mg/dL, LDL below 100 mg/dL, and HDL between 40-60 mg/dL.

Results

Sex Distribution:

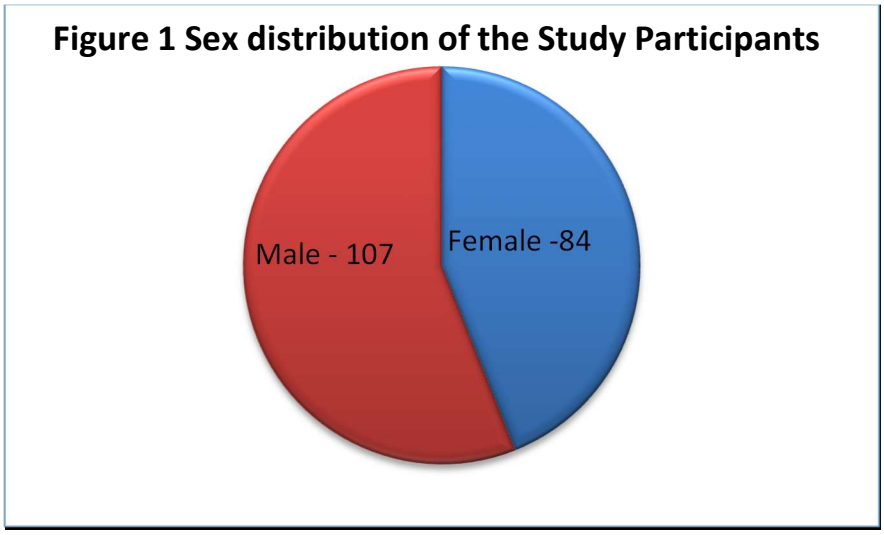


Table 1 presents the mean and standard deviation (SD) values for HbA1c and liver markers (AST, ALT, ALP, GGT, and albumin) across different age groups and sexes.

HbA1c: Males aged 21-30 had a mean of 9.46 ± 2.15, and those aged 31-40 had a mean of 9.24 ± 1.87. For females, HbA1c in the 21-30 group was higher at 9.94 ± 2.48, while in the 31-40 group, it was lower at 8.99 ± 1.71, indicating a slight decrease with age in females.

AST (Aspartate Transaminase): Males in the 21-30 age group had a mean of 34.62 ± 13.61, rising to 37.92 ± 16.2 in the 31-40 group. Females had lower AST levels, with a mean of 30.5 ± 12.86 in the 21-30 group, increasing to 37.9 ± 23.07 in the 31-40 group.

ALT (Alanine Transaminase): Males aged 21-30 had a mean of 39.06 ± 11.88, increasing to 44.1 ± 10.18 in the 31-40 age group. Females had lower ALT levels, with 33.86 ± 14.12 in the 21-30 group, and 41.67 ± 16.67 in the 31-40 group, showing an increase with age.

ALP (Alkaline Phosphatase): Males aged 21-30 had a mean of 101.92 ± 26.69, increasing to 107.1 ± 18.85 in the 31-40 group. Females had slightly higher ALP levels, with 107.34 ± 25.48 in the 21-30 group, and 108.48 ± 21.59 in the 31-40 group.

GGT (Gamma-Glutamyl Transferase): Males had a mean of 49.27 ± 39.98 in the 21-30 age group, which decreased to 44.41 ± 12.74 in the 31-40 group. Females had lower GGT levels, with 40.38 ± 12.66 in the 21-30 group, and 46.85 ± 46.61 in the 31-40 group, showing a slight increase with age.

Albumin (ALB): Males had a mean of 4.48 ± 0.52 in the 21-30 group, and 4.58 ± 0.54 in the 31-40 group. Females had slightly lower albumin levels, with 4.36 ± 0.7 in the 21-30 group, and 4.23 ± 0.47 in the 31-40 group, showing a small decrease with age. (Figure 2&4)

Table 1 Mean and Standard deviation of HbA1c & Liver Markers

Parameter	Sex	Age Group	Mean	Standard Deviation
HbA1c	Male	21-30	9.46	2.15
		31-40	9.24	1.87
	Female	21-30	9.94	2.48
		31-40	8.99	1.71
AST	Male	21-30	34.62	13.61
		31-40	37.92	16.2
	Female	21-30	30.5	12.86
		31-40	37.9	23.07
ALT	Male	21-30	39.06	11.88
		31-40	44.1	10.18
	Female	21-30	33.86	14.12
		31-40	41.67	16.67
ALP	Male	21-30	101.92	26.69
		31-40	107.1	18.85
	Female	21-30	107.34	25.48
		31-40	108.48	21.59
GGT	Male	21-30	49.27	39.98
		31-40	44.41	12.74
	Female	21-30	40.38	12.66

		31-40	46.85	46.61
Albumin (ALB)	Male	21-30	4.48	0.52
		31-40	4.58	0.54
	Female	21-30	4.36	0.7
		31-40	4.23	0.47

Table 2 presents the mean and standard deviation (SD) of cardiac markers, including Total Cholesterol (TC), Triglycerides (TG), High-Density Lipoprotein (HDL), and Low-Density Lipoprotein (LDL), across different age groups and sexes.

Total Cholesterol (TC): Males aged 21-30 had a mean of 218.69 ± 57.75, while those aged 31-40 had 231.69 ± 40.93. For females, the mean was 227.96 ± 48.19 for 21-30 years and 220.97 ± 44.39 for 31-40 years, indicating a slight increase in TC with age, especially in males.

Triglycerides (TG): Males aged 21-30 had a mean of 164.96 ± 47.98, increasing to 178.44 ± 63.47 in the 31-40 age group. Females showed similar trends, with 177.25 ± 63.63 for 21-30 years and 183.43 ± 66.8 for 31-40 years, showing an increase with age in both sexes.

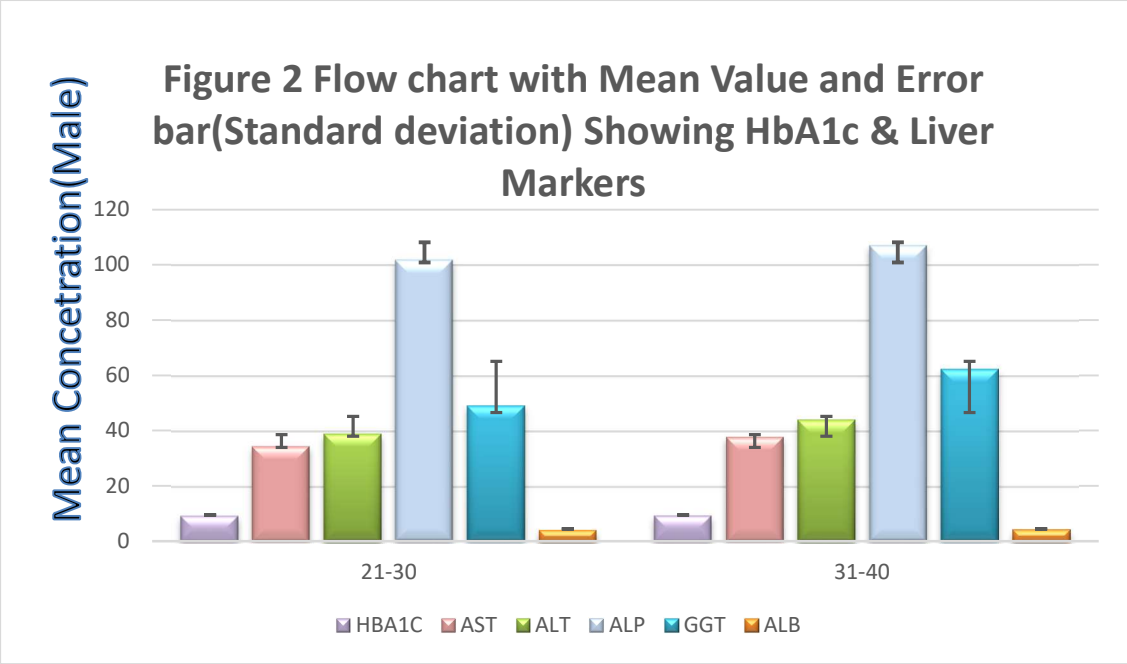
HDL: Males had a mean of 39.58 ± 4.38 in the 21-30 group and 40.35 ± 5.73 in the 31-40 group. Females had 40.26 ± 4.36 in the 21-30 group and 39.53 ± 3.46 in the 31-40 group, indicating slight variations with age and sex.

LDL: Males had a mean of 135.65 ± 36.81 for 21-30 years, increasing to 139.99 ± 28.87 in the 31-40 group. Females had 138.91 ± 32 in the 21-30 group, decreasing to 132.55 ± 29.34 in the 31-40 group, showing a slight decrease in LDL with age in females. **(Figure 3&5)**

Table 2 Mean and Standard deviation of Lipid Profile

Parameter	**Sex**	**Age Group**	**Mean**	**Standard Deviation**
Total Cholesterol (TC)	Male	21-30	218.69	57.75
		31-40	231.69	40.93
	Female	21-30	227.96	48.19
		31-40	220.97	44.39
Triglycerides (TG)	Male	21-30	164.96	47.98
		31-40	178.44	63.47

	Female	21-30	177.25	63.63
		31-40	183.43	66.8
HDL	Male	21-30	39.58	4.38
		31-40	40.35	5.73
	Female	21-30	40.26	4.36
		31-40	39.53	3.46
LDL	Male	21-30	135.65	36.81
		31-40	139.99	28.87
	Female	21-30	138.91	32
		31-40	132.55	29.34



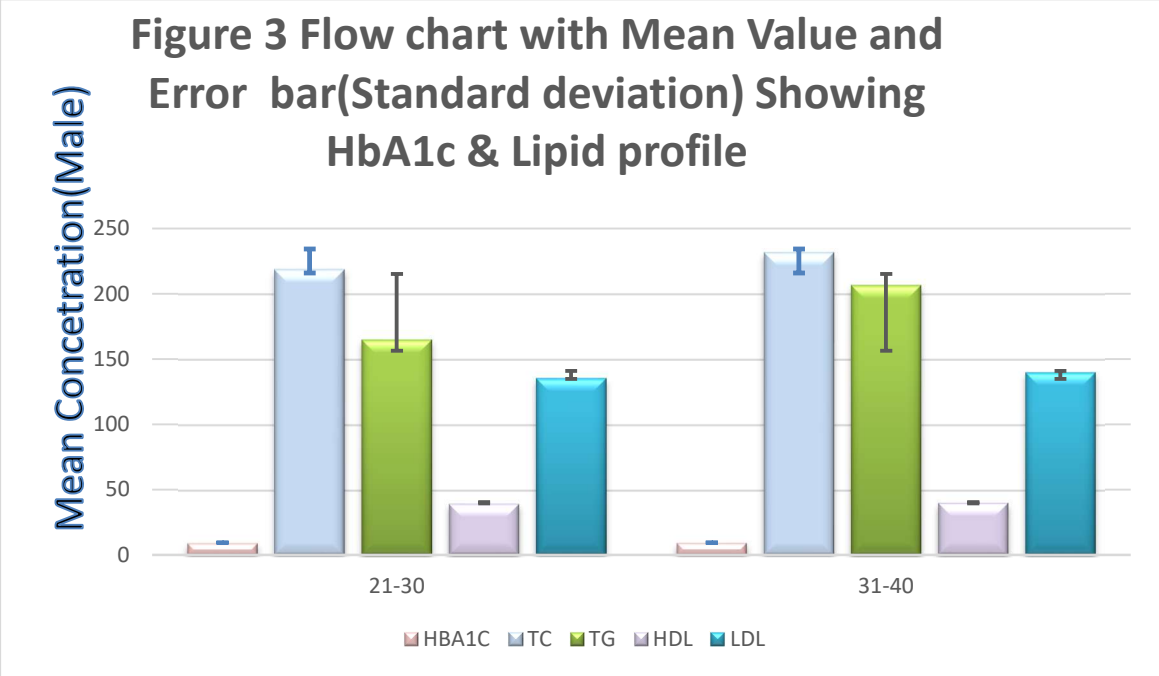


Figure 3 Flow chart with Mean Value and Error bar(Standard deviation) Showing HbA1c & Lipid profile
Mean Concetration(Male)
250
200
150
100
50
0
21-30
31-40
HBA1C
TC
TG
HDL
LDL

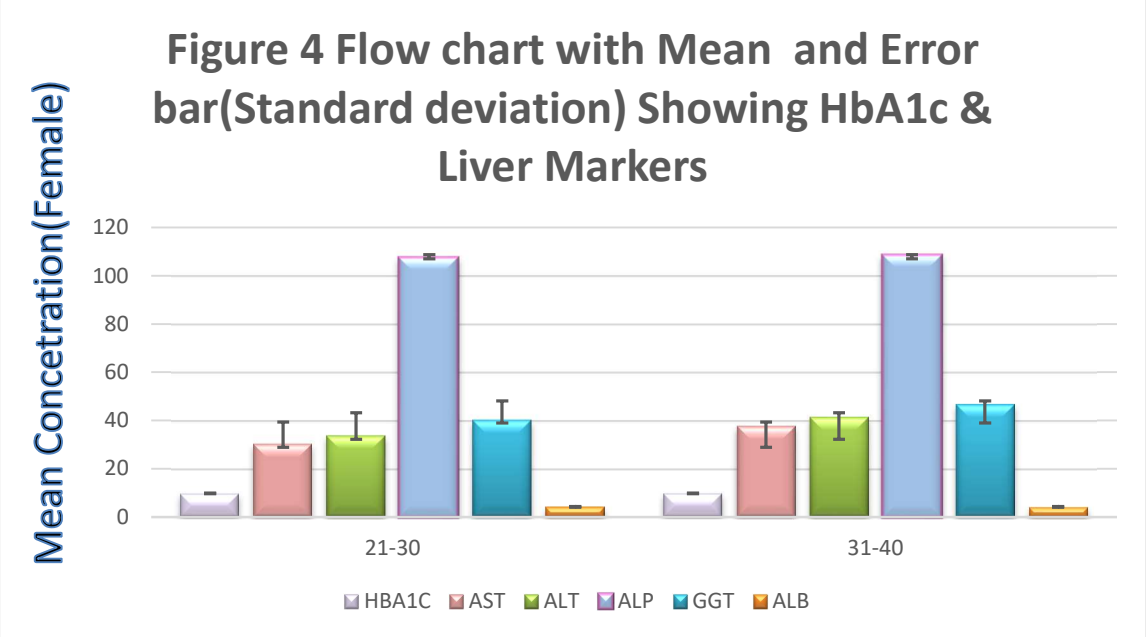
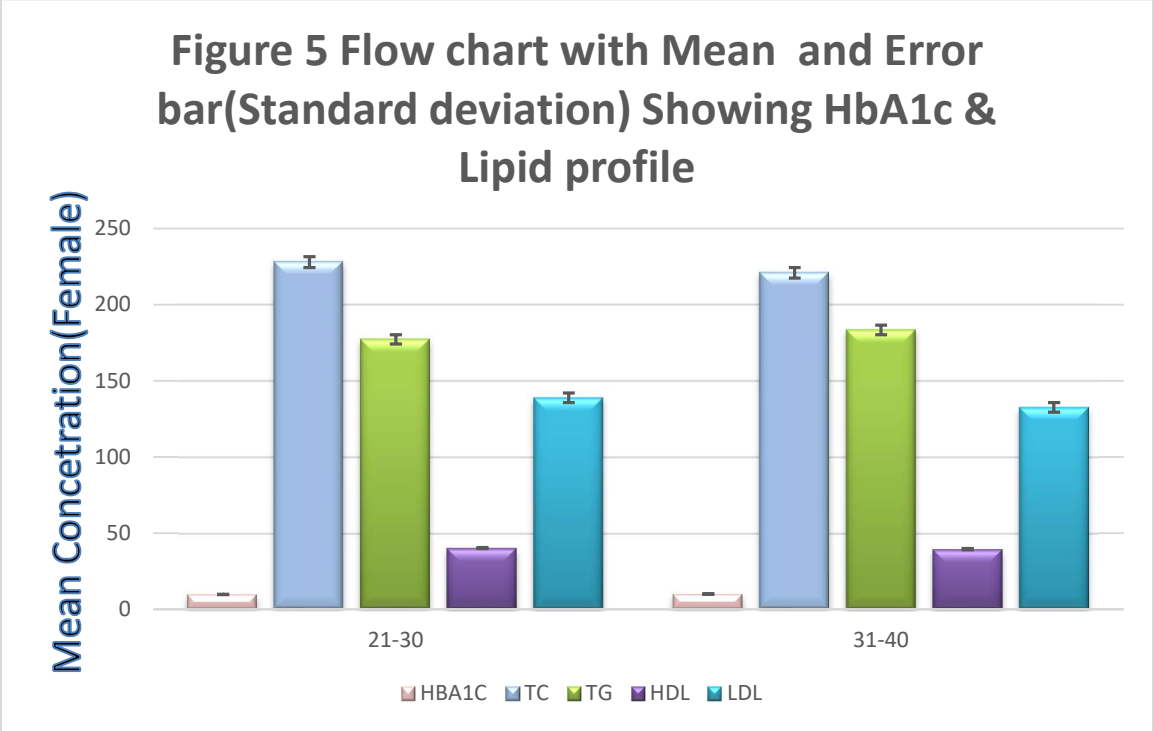


Figure 4 Flow chart with Mean and Error bar(Standard deviation) Showing HbA1c & Liver Markers
Mean Concetration(Female)
120
100
80
60
40
20
0
21-30
31-40
HBA1C
AST
ALT
ALP
GGT
ALB



The study showed varying correlations between HbA1c and metabolic parameters. Aspartate Transaminase (AST) had a weak positive correlation (p = 0.116), suggesting mild liver stress with higher HbA1c. Alanine Transaminase (ALT) (p =-0.011) and Gamma-Glutamyl Transferase (GGT) (p = 0.030) had negligible correlations. Alkaline Phosphatase (ALP) (p = -0.169) showed a weak negative correlation. Albumin (0.223) had a weak positive association. Total Cholesterol (p = 0.557) and LDL (p = 0.509) showed moderate positive correlations with HbA1c, indicating cardiovascular risk. Triglycerides (p = 0.007) and HDL (p = 0.298) showed negligible and weak positive correlations, respectively.

The strongest correlations of HbA1c are with **fasting glucose**, **postprandial glucose**, **total cholesterol**, and **LDL**, indicating that poor glycemic control is associated with higher levels of these parameters, which are risk factors for cardiovascular and metabolic complications in diabetes. Table 3

Table 3 Correlation between HbA1c & other Parameters

Parameter	**Correlation with HbA1c(p value)**	**Clinical Interpretation**
Aspartate Transaminase (AST)	0.116 (Weak Positive)	Slight association with liver enzyme AST; may indicate mild liver stress in patients with higher HbA1c.
Alanine Transaminase (ALT)	-0.011 (Negligible)	Almost no correlation with ALT, suggesting HbA1c does not strongly relate to ALT levels or liver health.

Alkaline Phosphatase (ALP)	-0.169 (Weak Negative)	Weak inverse association; higher HbA1c may have a minor effect on ALP, but not clinically significant.
Gamma-Glutamyl Transferase (GGT)	0.030 (Negligible)	No meaningful relationship with GGT, implying HbA1c has little association with this liver enzyme.
Albumin (ALB)	0.223 (Weak Positive)	Weak association with albumin; may indicate some relationship with protein levels, though not strong.
Total Cholesterol (TC)	0.557 (Moderate Positive)	Higher HbA1c levels are associated with elevated cholesterol, indicating increased cardiovascular risk.
Triglycerides (TG)	0.007 (Negligible)	Almost no correlation, suggesting HbA1c does not impact triglyceride levels significantly.
High-Density Lipoprotein (HDL)	0.298 (Weak Positive)	Slight positive association; higher HbA1c may relate to marginally increased HDL, though the link is weak.
Low-Density Lipoprotein (LDL)	0.509 (Moderate Positive)	Elevated HbA1c levels are associated with higher LDL, a risk factor for cardiovascular complications.

Discussion:

Our study shows elevated liver enzymes (AST, ALT, GGT) in both sexes of diabetic patients, with greater variability among older age groups and females. Young males exhibit higher GGT, indicating possible liver stress. ALP levels are slightly raised in older females, while albumin remains stable, suggesting age and gender-based liver function differences.

Mojgan's study found that elevated ALT, AST, GGT, and ALP levels are linked to higher diabetes odds in both sexes. Even normal-range elevations in ALT, GGT, and ALP were independently associated with increased diabetes risk, highlighting elevated liver enzymes as potential biomarkers for diabetes presence (21).

Thinbaijam's study suggests that elevated liver enzymes in T2DM patients may signal a greater risk for non-alcoholic fatty liver disease (NAFLD). This finding highlights the importance of regular liver health monitoring and management as essential components of diabetes care (22).

Our study also shows that both males and females have poor glycemic control, with females exhibiting higher HbA1c levels. Total cholesterol (TC) is elevated across all groups, with older males and young females at higher risk. Triglyceride (TG) levels are highest in older females, while HDL levels are suboptimal, especially in males. LDL is elevated across all age groups, indicating significant cardiovascular risk. HbA1c levels showed a positive correlation with lipid levels. Elevated lipid levels and poor glycemic control suggest increased risk for cardiovascular disease and metabolic

complications.

In the same way, Saera's study found that HbA1c positively correlated with cholesterol, triglycerides (TG), and LDL, and inversely with HDL, all with a significant p-value <0.05. TG levels were significantly higher in females, and metabolic syndrome showed a strong association with rising HbA1c, particularly in females (p=0.001) (23).

In the study by Abdulaziz Yahya et al., dyslipidemia was prevalent among diabetic patients, with over half having elevated LDL-c and most showing abnormalities in at least one lipid marker. HbA1c was positively correlated with both triglycerides and cholesterol, underscoring the critical link between glycemic control and lipid imbalances (24).

Overall, this study found a positive correlation between HbA1c levels and both liver markers and lipid profile, indicating that poor glycemic control is associated with liver dysfunction and lipid imbalances.

A study by Moyad found that mean Albumin, ALT, and AST levels were strongly associated with poorly controlled diabetes (HbA1c ≥ 7). Lipid profiles (TC, LDL-C, TG) were significantly linked to abnormal liver findings. The study concluded that liver biomarkers are significantly associated with type 2 diabetes (25).

A study by Rahanuma et al. in Bangladesh found high prevalence of dyslipidemia and liver enzyme abnormalities among participants. GGT levels were independently associated with all lipid components. The study suggests that dyslipidemic individuals are more likely to develop liver diseases, highlighting the need for larger studies to explore lipid-induced hepatic dysfunction mechanisms (26).

Limitation of the study:

The study's limitations include its cross-sectional design, small sample size, and lack of long-term follow-up data on diabetes progression.

Conclusion:

The study reveals a significant relationship between HbA1c and liver markers, as well as lipid profiles. Moderate positive correlations were found between HbA1c and Total Cholesterol (p = 0.557) and LDL (p =0.509), indicating cardiovascular risk with poor glycemic control. Weak or negligible correlations were observed with AST (p = 0.11), ALT (p = -0.01), GGT (p = 0.03) and albumin (p = 0.223). Triglycerides (p = 0.007) and HDL (p = 0.298) showed minimal associations, suggesting that glycemic control influences cardiovascular risk factors but has limited impact on liver function markers Future research should explore liver dysfunction, lipid imbalances, and their long-term effects on cardiovascular health in diabetes.

Abbreviations

CLD: Chronic liver disease

DM:Diabetes mellitus

SPSS:Statistical package for social sciences

IDF: International Diabetes Federation

HD: Hepatogenous diabetes

AST: Aspartate aminotransferase

ALP: Alkaline phosphatase

GGT: Gamma-glutamyl transferase

ALT: Alanine aminotransferase (ALT)

TC: Total Cholesterol

TG: Triglycerides

HDL: High Density Lipoprotein

LDL: Low Density Lipoprotein

NAFLD: Non-Alcoholic fatty liver disease

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None.

Conflict of interest disclosure

There is no Conflict of Interest.

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