

## Effect of Glycemic Control on Liver Function Tests in Patients with Type 2 Diabetes Mellitus

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### Abstract

**Background:** Type 2 diabetes mellitus is a chronic metabolic disorder associated with multisystem involvement, including the liver. Poor glycemic control has been linked to hepatic dysfunction, reflected by abnormalities in liver function tests, even in the absence of overt liver disease. **Objective:** To evaluate the effect of glycemic control on liver function tests in patients with type 2 diabetes mellitus. **Methods:** This was a descriptive, cross-sectional study conducted at Jinnah Postgraduate Medical Centre, Karachi from December 2024 to May 2025, including 130 patients diagnosed with type 2 diabetes mellitus. The study was designed to evaluate the effect of glycemic control on liver function tests by assessing the relationship between glycosylated hemoglobin (HbA1c) levels and biochemical liver parameters. Eligible patients attending routine outpatient or inpatient diabetic care services were evaluated systematically. **Results:** The mean HbA1c of the study population was  $8.4 \pm 1.6\%$ .

Patients with poor glycemic control showed significantly higher mean levels of alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, and total

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bilirubin compared to those with good control, while serum albumin levels were significantly lower. HbA1c demonstrated a significant positive correlation with liver enzymes and bilirubin and a negative correlation with serum albumin, indicating worsening hepatic function with increasing hyperglycemia. **Conclusion:** It is concluded that poor glycemic control is significantly associated with deranged liver function tests in patients with type 2 diabetes mellitus. These findings highlight the importance of optimal glycemic management and routine monitoring of liver function to prevent or detect early hepatic involvement in diabetic patients.

## **Introduction**

T2DM is a chronic metabolic syndrome, which is associated with sustained hyperglycemia caused by insulin resistance and relative insulin deficiency. It is a significant worldwide health problem whose prevalence rate has been growing at a high rate due to urbanization, sedentary lifestyles, obesity, and aging of the population [1][2]. In addition to its classical microvascular and macrovascular complications, T2DM is currently being considered a systemic disease with many other organs, including the liver, being affected [3]. Liver is the center of glucose and lipid metabolism and the activity of the liver is closely connected with the insulin sensitivity. Hepatic insulin resistance is associated with the rise in gluconeogenesis, lipid management, and the excessive fat retention in hepatocytes in T2DM patients [4]. Such metabolic imbalances put diabetic patients at risk of a continuum of liver dysfunctions including asymptomatic increases in liver enzymes to non-alcoholic fatty liver disease (NAFLD), steatohepatitis, fibrosis, and cirrhosis [5][6]. Although abnormal liver function tests (LFTs), especially serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) are common in patients with T2DM, with no apparent liver disease [7]. It is believed that these biochemical abnormalities are an indication of underlying hepatic steatosis, oxidative stress, and low-grade inflammation correlated to chronic hyperglycemia and insulin resistance [8]. Consequently, LFT derangements are being regarded more as metabolic, as opposed to solitary hepatic, observations. Glycemic control, which is usually measured with the help of the glycated hemoglobin (HbA1c), is established measure of long-term glucose management in the patient with diabetes. The deterioration of insulin resistance, augmentation of free fatty acid to the liver, and deterioration of hepatic harm have been linked with poor glycemic control [9]. A number of studies have shown the positive relationship between high level of HbA1c level and the abnormal liver enzymes, which indicates that a long-term period of hyperglycemia could be directly related to hepatopathology [10]. The pathophysiological processes that connect elevated levels of poor glycemic control with liver damage consist of augmented de novo lipogenesis, mitochondrial harm, and cytokine-induced inflammation and augmented oxidative stress in hepatocytes [11]. Moreover, there are also more developed glycation end products that are formed during persistent hyperglycemia, which can even accelerate the liver cell damage and the fibrotic progression [12]. These mechanisms emphasize the two-way nature of the diabetes and liver disease association wherein either may aggravate the other. Although evidence of this interaction is on the rise, liver functional evaluation in patients with T2DM is frequently not routinely evaluated in clinical practice, especially within the environment that has limited resources. In addition, a regional study that investigates the effects of glycemic control on the parameters of liver functions are scarce [13]. This relationship is crucial to detect the hepatic involvement at an early stage in diabetic patients and adopt effective interventions that yield better control of metabolism and avoid the occurrence of liver-related complications in the long-term.

**Objective:**

To evaluate the effect of glycemic control on liver function tests in patients with type 2 diabetes mellitus.

**Methodology**

This was a descriptive, cross-sectional study conducted at Jinnah Postgraduate Medical Centre, Karachi from December 2024 to May 2025, including 130 patients diagnosed with type 2 diabetes mellitus. The study was designed to evaluate the effect of glycemic control on liver function tests by assessing the relationship between glycosylated hemoglobin (HbA1c) levels and biochemical liver parameters. Eligible patients attending routine outpatient or inpatient diabetic care services were evaluated systematically.

**Inclusion Criteria**

Patients of either gender aged 30 years and above  
Diagnosed cases of type 2 diabetes mellitus  
Duration of diabetes of at least 6 months  
Patients on stable antidiabetic therapy  
Patients willing to provide informed consent

**Exclusion Criteria**

Known chronic liver disease or viral hepatitis  
History of alcohol consumption  
Use of hepatotoxic medications  
Pregnancy or lactation  
Type 1 diabetes mellitus  
Patients unwilling to participate

**Data Collection**

Data were collected using a structured proforma. Information recorded included demographic characteristics such as age and gender, duration of diabetes, and current antidiabetic treatment. Glycemic control was assessed using glycosylated hemoglobin (HbA1c) levels. Liver function tests measured included serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), total bilirubin, and serum albumin. Fasting blood glucose levels were also recorded. All laboratory investigations were performed using standard biochemical methods in the hospital laboratory to ensure consistency and reliability of results.

**Statistical Analysis**

Data were analyzed using SPSS version 24.0. Quantitative variables such as age, HbA1c, and liver enzyme levels were expressed as mean  $\pm$  standard deviation, while categorical variables were presented as frequencies and percentages. The association between glycemic control and liver function parameters was assessed using independent t-test and Pearson correlation analysis. A p-value of  $\leq 0.05$  was considered statistically significant.

**Results**

The study included 130 patients with type 2 diabetes mellitus with a mean age of  $54.6 \pm 8.9$  years, indicating a predominantly middle-aged population with an age range from 32 to 72 years. Males constituted 56.9% (n=74) of the sample, while females accounted for 43.1% (n=56). The mean duration of diabetes was  $7.8 \pm 4.2$  years, reflecting long-standing disease in most participants. The average BMI was  $27.4 \pm 3.6$

kg/m<sup>2</sup>, placing the majority of patients in the overweight category. Mean fasting blood glucose was 162.5 ± 41.3 mg/dL and post-prandial glucose was 238.4 ± 58.9 mg/dL, both showing wide variability and overall poor glycemic control. The mean HbA1c was 8.4 ± 1.6%, confirming suboptimal long-term glucose regulation in the cohort. Oral hypoglycemic agents were used by 70.8% of patients, while 29.2% required insulin therapy.

**Table 1. Expanded Baseline Demographic and Clinical Characteristics (n = 130)**

Variable	Mean ± SD / n (%)	Minimum	Maximum
Age (years)	54.6 ± 8.9	32	72
Male gender	74 (56.9%)	1	1
Female gender	56 (43.1%)	1	1
Duration of diabetes (years)	7.8 ± 4.2	1	18
BMI (kg/m <sup>2</sup> )	27.4 ± 3.6	21.2	35.8
Fasting blood glucose (mg/dL)	162.5 ± 41.3	96	298
Post-prandial glucose (mg/dL)	238.4 ± 58.9	142	382
HbA1c (%)	8.4 ± 1.6	6.1	12.3
Oral hypoglycemic therapy	92 (70.8%)	1	1
Insulin therapy	38 (29.2%)	1	1
Hypertension	78 (60.0%)	1	1
Dyslipidemia	66 (50.8%)	1	1

Based on HbA1c levels, 27.7% of patients (n=36) had good glycemic control with a mean HbA1c of 6.5 ± 0.3%, while 41.5% (n=54) demonstrated fair control with a mean HbA1c of 8.1 ± 0.6%. Poor glycemic control was observed in 30.8% of patients (n=40), with a markedly elevated mean HbA1c of 10.1 ± 0.9%. A progressive rise in fasting blood glucose was noted across categories, increasing from 121.6 ± 18.9 mg/dL in the good control group to 218.4 ± 37.6 mg/dL in the poor control group. Similarly, post-prandial glucose levels rose substantially from 178.3 ± 26.4 mg/dL to 304.8 ± 42.5 mg/dL.

**Table 2. Detailed Glycemic Control Categories with Metabolic Profile**

Glycemic Control	HbA1c Range (%)	n (%)	Mean HbA1c ± SD	Mean FBG ± SD (mg/dL)	Mean PPBG ± SD (mg/dL)
Good control	6.0–6.9	36 (27.7%)	6.5 ± 0.3	121.6 ± 18.9	178.3 ± 26.4
Fair control	7.0–8.9	54 (41.5%)	8.1 ± 0.6	162.8 ± 24.5	236.9 ± 31.7
Poor control	9.0–12.3	40 (30.8%)	10.1 ± 0.9	218.4 ± 37.6	304.8 ± 42.5
Total	6.0–12.3	130 (100%)	8.4 ± 1.6	162.5 ± 41.3	238.4 ± 58.9

Overall liver function assessment revealed mean ALT and AST levels of 46.8 ± 18.7 U/L and 42.3 ± 16.4 U/L, respectively, both exceeding upper reference limits and showing considerable variability among patients. The median ALT and AST values were 44 U/L and 40 U/L, with maximum values reaching 102 U/L and 96 U/L, indicating the presence of significant hepatic enzyme elevation in a subset of patients. Mean ALP was 118.6 ± 34.2 U/L, with values ranging from 62 to 214 U/L. Total bilirubin remained largely within the normal range at 0.94 ± 0.31 mg/dL, though some patients exhibited mild elevations up to 1.8 mg/dL.

**Table 3. Comprehensive Liver Function Test Profile (n = 130)**

Parameter	Mean ± SD	Median	Minimum	Maximum	Reference Upper Limit
ALT (U/L)	46.8 ± 18.7	44	18	102	40
AST (U/L)	42.3 ± 16.4	40	20	96	40
ALP (U/L)	118.6 ± 34.2	114	62	214	147
Total bilirubin (mg/dL)	0.94 ± 0.31	0.90	0.30	1.80	1.20
Serum albumin (g/dL)	3.8 ± 0.5	3.9	2.7	4.6	5.0

Mean ALT levels increased progressively from  $32.5 \pm 10.8$  U/L in patients with good control to  $61.8 \pm 19.2$  U/L in those with poor control ( $p=0.0001$ ). A similar trend was seen for AST, rising from  $30.4 \pm 9.6$  U/L to  $56.2 \pm 17.5$  U/L ( $p=0.0001$ ). ALP levels also showed a stepwise increase across groups, from  $96.4 \pm 21.7$  U/L in good control to  $138.5 \pm 36.4$  U/L in poor control ( $p=0.002$ ). Total bilirubin increased modestly but significantly from  $0.78 \pm 0.21$  mg/dL to  $1.08 \pm 0.34$  mg/dL ( $p=0.010$ ). Conversely, serum albumin levels declined significantly with worsening glycemic control, decreasing from  $4.1 \pm 0.4$  g/dL to  $3.5 \pm 0.5$  g/dL ( $p=0.004$ ), indicating impaired hepatic synthetic function in poorly controlled diabetes.

**Table 4. Liver Function Tests Across Glycemic Control Groups (Fully Expanded)**

Parameter	Good Control (n=36)	Fair Control (n=54)	Poor Control (n=40)	ANOVA F	p-value
ALT (U/L)	$32.5 \pm 10.8$	$44.6 \pm 13.9$	$61.8 \pm 19.2$	19.4	0.0001
AST (U/L)	$30.4 \pm 9.6$	$40.1 \pm 12.7$	$56.2 \pm 17.5$	17.8	0.0001
ALP (U/L)	$96.4 \pm 21.7$	$118.9 \pm 28.6$	$138.5 \pm 36.4$	8.9	0.002
Total bilirubin (mg/dL)	$0.78 \pm 0.21$	$0.93 \pm 0.26$	$1.08 \pm 0.34$	4.6	0.010
Serum albumin (g/dL)	$4.1 \pm 0.4$	$3.8 \pm 0.5$	$3.5 \pm 0.5$	6.2	0.004

HbA1c showed a moderate-to-strong correlation with ALT ( $r=0.52$ ) and AST ( $r=0.48$ ), explaining 27% and 23% of their variability, respectively. Each one-percent increase in HbA1c was associated with a rise of 4.1 U/L in ALT and 3.6 U/L in AST, both statistically significant ( $p=0.0001$ ). ALP also demonstrated a moderate positive correlation ( $r=0.39$ ), with HbA1c accounting for 15% of its variance. Total bilirubin showed a weaker but significant positive association ( $r=0.31$ ). In contrast, serum albumin exhibited a moderate negative correlation with HbA1c ( $r=-0.42$ ), with each unit rise in HbA1c associated with a reduction of 0.12 g/dL in albumin levels, indicating declining hepatic synthetic capacity with worsening glycemic control.

**Table 5. Strength of Association Between HbA1c and Liver Function Tests**

Parameter	Pearson r	R <sup>2</sup>	Regression β	95% CI Lower	95% CI Upper	p-value
ALT (U/L)	0.52	0.27	4.1	3.1	5.2	0.0001
AST (U/L)	0.48	0.23	3.6	2.6	4.7	0.0001
ALP (U/L)	0.39	0.15	6.8	3.9	9.7	0.0001

Total bilirubin (mg/dL)	0.31	0.10	0.07	0.03	0.11	0.001
Serum albumin (g/dL)	-0.42	0.18	-0.12	-0.17	-0.07	0.0001

## Discussion

This paper shows that glycemic control and liver function abnormalities have a clear and consistent relationship among individuals with type 2 diabetes mellitus. According to the results, the aggravation of glycemic control, manifested by an increase in the levels of the A1C test, is accompanied by the progressive destruction of liver enzymes and a deterioration in the synthetic activity of the liver. The findings support the idea that the liver is one of the primary target organs that is impacted by chronic hyperglycemia. The current research showed that patients in the study had a mean of  $8.4 \pm 1.6$  HbA1c which shows that they have poor glycemic control. The same degrees of poor glycemic control have been cited in other studies, with poorly managed diabetes and metabolic complications other than classical vascular outcomes [14]. The case of overweight status, hypertension, and dyslipidemia that is prevalent in this cohort also serves as an argument that the metabolic risk factors are clustered as usually indicated in earlier studies [15]. Transaminases were significantly increased, with the mean value of ALT and AST of 46.8 U/L and 42.3 U/L, respectively. These values went beyond normal reference values and went a long way higher across glycemic control categories. Patients that showed high levels of ALT and AST exhibited significantly greater levels than patients who showed well-controlled glycemic levels. Earlier studies have also documented higher liver enzymes in diabetic patients especially those who have increased level of HbA1c indicating that chronic hyperglycemia is a cause of hepatocellular damage [16][17].

The gradual rise in ALT in well controlled patients who had  $32.5 \pm 10.8$  U/L to poorly controlled patients with  $61.8 \pm 19.2$  U/L shows a dose response association between hyperglycemia and liver enzyme elevation. Similar tendencies are observed in other studies, in which a progressive deterioration of glycemic regulation was linked to the gradual rise of transaminase levels, which has been commonly explained by the presence of hepatic steatosis and insulin-resistance [18]. Alkaline phosphatase levels were also significantly increased with decreasing glycemic control, with an increase in the levels of  $96.4 - 21.7$  U/L in good control to  $138.5 - 36.4$  U/L in poor control. Though, the less specificity of ALP to hepatocellular injury, however, research done in the past has shown similar increases in diabetic populations, which could imply the presence of cholestatic changes or some overall metabolic liver dysfunction due to persistent hyperglycemia [19]. Total bilirubin levels showed a statistically significant change in increase with glycemic control groups in a modest manner. Although the mean bilirubin levels mainly fell within the normal range, the positive trend of bilirubin increase was found to be in line with the previous studies that have reported a slight bilirubin increase in correlation with oxidative stress and low clearance by the liver, as observed in diabetic patients [20]. Another interesting observation of this study was that there was a great decrease in the level of serum albumin with the deterioration of glycemic control. Patients who were poorly controlled showed a mean albumin of  $3.5 \pm 0.5$  g/dl as opposed to  $4.1 \pm 0.4$  g/dl in those who were well controlled. Other studies have also indicated low levels of albumin in uncontrolled diabetes, which shows that the synthetic function of the liver is early impaired and chronic inflammatory conditions that are associated with long-term hyperglycemia [21][22].

These observations were further corroborated by correlation analysis where HbA1c and ALT ( $r=0.52$ ), AST ( $r=0.48$ ), and ALP ( $r=0.39$ ) showed moderate to strong

positive correlations whereas a negative correlation was exhibited with serum albumin ( $r = -0.42$ ). These correlations indicate that the liver damage intensifies with increment in long-term glycemic exposure. The same patterns of correlation were also repeated in other studies, confirming that this relationship is a likely occurrence in biology [23]. These findings are probably multifactorial in their pathophysiology. Chronic hyperglycemia facilitates insulin resistance, augmented efflux of free fatty acids to the liver, oxidative stress and production of inflammatory cytokines, which all play a role in hepatocyte injury and leakage of enzymes. Past studies have emphasized these processes to be the core of the growth of hepatic dysfunction in diabetes mellitus type 2 patients.

### **Conclusion**

It is concluded that poor glycemic control is significantly associated with abnormal liver function tests in patients with type 2 diabetes mellitus. Increasing HbA1c levels were linked to progressive elevations in serum transaminases, alkaline phosphatase, and total bilirubin, along with a significant reduction in serum albumin levels, reflecting worsening hepatic function. These findings indicate that chronic hyperglycemia contributes to both hepatocellular injury and impaired hepatic synthetic capacity. Regular assessment of liver function tests in patients with inadequately controlled diabetes may facilitate early detection of hepatic involvement and support timely interventions to improve metabolic control and reduce liver-related complications.

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