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Original Research Article

Frequency of Abnormally Elevated Liver Enzymes in Patients with Type 2 Diabetes Mellitus Presenting to Tertiary Care Hospital Mardan

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Abstract:
Objective: To determine the frequency of elevated liver enzymes in patients with type 2 diabetes mellitus. **Study Design:** A descriptive study with cross-sectional design. **Place and Duration of Study:** Medicine Department, Mardan Medical Complex, carried out from 13th September 2025 till 13th December 2025. **Methodology:** 189 patients type 2 diabetes mellitus were taken by consecutive sampling. Those having liver disease, alcohol use, hepatotoxic medicines, acute hepatitis, hepatitis B or C infection, and subclinical hypothyroidism were not included. Demographic information and BMI was recorded. Serum bilirubin, alanine aminotransferase, aspartate aminotransferase and alkaline phosphatase levels were checked. Abnormal liver enzymes were defined if any two of tested enzymes were above reference limits. Data was analysed with IBM Statistical Package for the Social Sciences version 23. Chi-square test or Fisher's exact test was used, where $p<0.05$ was taken as significant. **Results:** Mean age of patients was 45.05 ± 8.72 years, while mean body mass index was 25.14 ± 2.73 kg/m^2. There were 101 (53.4%) males and 88 (46.6%) females. Elevated liver enzymes were observed in 74 (39.2%) patients. In patients above 45 years, frequency was more compared with those ≤45 years, 63 (48.1%) versus 11 (19.0%), respectively ($p<0.001$). Elevated enzymes were also more in females, 44 (50.0%), compared with males, 30 (29.7%) ($p=0.004$). **Conclusion:** Elevated liver enzymes were frequently seen in type 2 diabetes mellitus patients and showed significant association with older age, female gender and increased BMI.

Keywords: Diabetes mellitus, Liver enzymes, Liver function tests, Obesity, Type 2 diabetes mellitus

INTRODUCTION

Diabetes mellitus is one of the most prevalent metabolic diseases, where the blood glucose level stays high due to insufficient production of insulin or problems with its functioning.1 Type 2 diabetes mellitus is the most widespread kind of diabetes and is caused by insulin resistance and insufficient production of this hormone.2 It is becoming increasingly prevalent worldwide due to old age, obesity, bad diet, lack of exercise and other factors.3 Uncontrolled diabetes may influence various organs of the body, resulting in such complications as cardiovascular disorders, kidney, nervous, eye or liver dysfunction. It is often connected with obesity and abnormal lipid levels.4

Diabetes mellitus type 2 may affect the normal functioning of the liver and may cause liver enzyme changes.5 Insulin resistance causes fat deposition in the liver and thus, it can promote the occurrence of liver diseases associated with steatohepatitis due to metabolic dysfunction.6 High blood sugar and elevated fatty acids cause oxidative stress and inflammation in the hepatic cells, causing the leakage of liver enzymes in the bloodstream.7 Hence, patients with diabetes mellitus type 2 may have elevated liver enzymes including alanine aminotransferase,

aspartate aminotransferase, alkaline phosphatase, and gamma-glutamyl transferase.8 The levels of enzyme elevation may differ depending on the patient's glycaemic control, obesity, duration of diabetes, lipid metabolism and liver disease.

An abnormally high liver enzyme level means that there is an abnormal high amount of one or more liver enzymes associated with either liver damage or cholestasis in a patient.9 The reason for the rise in the enzyme level in patients suffering from type 2 diabetes mellitus could be the presence of fatty liver, inflammation, insulin resistance or any other liver conditions.10 Alanine aminotransferase and aspartate aminotransferase are two common tests used to measure liver damage whereas alkaline phosphatase and gamma-glutamyl transferase levels may rise because of cholestatic or any other liver condition.

Objective

This study need arises from the increasing incidence of type 2 diabetes mellitus and its potential impact on the functioning of the liver. Abnormally high levels of liver enzymes may develop in diabetic patients due to fatty liver, insulin resistance, and other changes in metabolism; however, these changes may go undetected in most diabetic patients. Testing of liver enzymes will assist in diagnosing early liver involvement in diabetic patients. There is a lack of local data on the incidence of abnormally high levels of liver enzymes in diabetic patients.

METHODOLOGY

A cross sectional research was carried out in Medicine Department of Mardan Medical Complex. The duration of study was from 13th September 2025 till 13th December 2025. Adult patients with Type 2 Diabetes Mellitus who visited outpatient department for regular follow up or for other complaints were taken in this research.

Before starting the research, ethical permission was taken from the ethical review board of the hospital. The study was started after approval of synopsis and all work was done according to ethical rules and requirements of the hospital.

Sample size was estimated by WHO sample size calculator. Confidence level was kept 95%, margin of error was 7% and expected frequency of raised liver function tests among diabetic patients was taken as 60%.11 The sample size obtained was 189 patients. The 7% margin of error was used due to less availability of suitable patients. Consecutive non-probability sampling method was used for taking the patients in the study.

Patients from 18 to 60 years age were included and both males and females were taken. All patients were already diagnosed cases of Type 2 Diabetes Mellitus. Those patients who had previous liver disease, history of alcohol use, use of medicines which can damage liver, acute hepatitis, hepatitis B or hepatitis C infection were not included. Patients with history of subclinical hypothyroidism were also excluded. Type 2 Diabetes Mellitus was defined in patients already diagnosed as diabetic and using metformin, with fasting blood glucose more than 140 mg/dl and HbA1c above 7.0%.

Written informed consent was obtained from the patients or their attendants before collecting the information. Data was collected on a pre-designed proforma. Demographic details and clinical information was obtained from every participant and inclusion and exclusion criteria was checked. Age, gender and body mass index were recorded. BMI was calculated by dividing the weight in kilograms with height in meter squared.

After examination and assessment, around 5–10 ml venous blood was taken from each patient using routine venipuncture procedure. The samples were placed in plain vacutainer tubes and transferred to pathology laboratory for biochemical testing. Total bilirubin, Alanine Transaminase (ALT), Aspartate Aminotransferase (AST) and Alkaline Phosphatase (ALP) were tested from serum with the help of automated biochemistry analyser. Raised liver enzymes was considered when any two of the tested liver enzymes were above the laboratory reference limits. The reference values used were total bilirubin 0.3–1 mg/dL, ALT more than 45 U/L for males and more than 34 U/L for females, AST more than 35 U/L for males and more than 31 U/L for females, while ALP more than 129 U/L for males and more than 104 U/L for females.

The data was entered into IBM SPSS version 26 and analysis was performed. Numerical variables such as age, BMI and liver function test values were shown as mean with standard deviation. Categorical variables such as gender and raised LFTs were shown in frequencies and percentages. Possible effect of age, gender and BMI was controlled by stratification. After stratification, Chi-square test or Fisher exact test was applied as suitable. Statistical significance was considered when p-value was less than 0.05.

RESULTS

A total of 189 patients were included in the study. The mean age of the participants was 45.05 ± 8.72 years, with a mean BMI of 25.14 ± 2.73 kg/m^2. The mean values for liver enzymes were as follows: alanine aminotransferase (ALT) were 40.58 ± 13.18 U/L, aspartate aminotransferase (AST) were 32.46 ± 9.23 U/L, and alkaline phosphatase (ALP) were 110.37 ± 27.12 U/L. With regards to gender distribution, majority of the patients were male, accounting for 101 (53.4%) of the total sample, whereas female patients were 88 (46.6%) (Table 1).

Table 1. Patient Demographics n=189

Demographics	Mean ± SD
Age (years)	45.05 ± 8.72
BMI	25.14 ± 2.73
ALT (U/L)	40.58 ± 13.18
AST (U/L)	32.46 ± 9.23
ALP (U/L)	110.37 ± 27.12
Gender	
Male n (%)	101 (53.4%)
Female n (%)	88 (46.6%)

With respect to the frequency of abnormally elevated liver enzymes, it was found that 74 (39.2%) of the patients had raised liver function tests (LFTs), whilst 115 (60.8%) had normal LFTs, out of total 189 patients (Table 2).

Table 2. Frequency of Abnormally Elevated Liver Enzymes in Patients with Type 2 Diabetes Mellitus.

Raised LFTs	Frequency	% age
Yes	74	39.20%
No	115	60.80%
Total	189	100%

Regarding the association of raised LFTs with demographic factors, it was observed that patients aged more than 45 years had significantly higher frequency of raised LFTs as compared to those aged 45 years or below, that is 63 (48.1%) versus 11 (19.0%), and this difference were found to be statistically significant (p<0.001). With reference to gender, female patients were more frequently having raised LFTs as compared to male patients, that is 44 (50.0%) versus 30 (29.7%), and this association were also statistically significant (p=0.004). Furthermore, patients having BMI greater than 25 kg/m^2 were more likely to had raised LFTs as compared to those with BMI of 25 or below, that is 50 (53.2%) versus 24 (25.3%) and this finding were equally statistically significant (p<0.001) (Table 3).

Table 3. Association of Raised LFTs with Demographic Factors in Patients with Type 2 Diabetes Mellitus. n=189

Demographic Factors	Sub Groups	Raised LFTs		p-value
		Yes n(%)	No n(%)	
Age (years)	≤45	11 (19.0%)	47 (81.0%)	<0.001*
	>45	63 (48.1%)	68 (51.9%)	
Gender	Male	30 (29.7%)	71 (70.3%)	0.004*
	Female	44 (50.0%)	44 (50.0%)	
BMI (kg/m^2)	≤25	24 (25.3%)	71 (74.7%)	<0.001*
	>25	50 (53.2%)	44 (46.8%)	

*Chi-Square Test

DISCUSSION

In the present study the overall frequency of raised LFTs were found to be 74 (39.2%), which is considerably high and suggest that liver enzyme abnormalities are quite common amongst diabetic patients. This finding can be explained by the fact that chronic hyperglycaemia in type 2 diabetes leads to increased oxidative stress and lipid peroxidation within hepatocytes, which ultimately results in hepatocellular damage and raised liver enzymes.

With regards to age, patients above 45 years were more frequently having raised LFTs as compared to younger patients, that is 63 (48.1%) versus 11 (19.0%) and this were statistically significant (p<0.001). This could be because with increasing age, the insulin resistance becomes more pronounced and the duration of diabetes gets longer, both of which contributes to progressive liver damage over time.

Concerning gender, female patients were having higher frequency of raised LFTs as compared to male patients, that is 44 (50.0%) versus 30 (29.7%), which were statistically significant (p=0.004). A possible explanation for this finding is that female patients with type 2 diabetes are more prone to develop non-alcoholic fatty liver disease due to hormonal changes and differences in body fat distribution, particularly after menopause.

The present study found that 74 (39.2%) of the patients with type 2 diabetes mellitus were having raised LFTs, which is comparable to the findings of Siddiqa et al. 12 who also reported deranged LFTs in 39.2% of diabetic patients, suggesting that nearly two-fifth of the diabetic population are at risk of hepatic enzyme abnormalities. Similarly, Ndraha et al. 13 reported liver function abnormalities in 35.8% of their diabetic cohort, which is quite close to the present findings. However, Kouam et al. 14 reported

an overall abnormal liver enzyme profile in 56.5% of their patients, which is notably higher than the present study results. Burubu et al. 15 reported above-cutoff elevations in only 10% for ALT, which is lower than the present findings, whereas GGT was elevated in 66% of their patients. These differences could possibly be attributed to variations in sample size, patient demographics, duration of diabetes, and geographical differences in lifestyle and dietary habits amongst the study populations. Sarkar et al. 16 reported that amongst diabetic patients with clinically diagnosed hepatitis, 50.3% had elevated ALT and 66.4% had elevated AST, which are considerably higher than the present results and this difference is likely because their study population specifically included patients with concurrent hepatic disease, making direct comparison with the present general diabetic cohort less appropriate.

Regarding age, patients above 45 years were more frequently having raised LFTs as compared to younger patients, that is 63 (48.1%) versus 11 (19.0%) and this were statistically significant ($p<0.001$). This finding is in agreement with Al-Naemi 17 who demonstrated that age had a significant effect on liver enzyme levels ($p=0.001$), suggesting that longer exposure to hyperglycaemia with advancing age leads to progressive hepatocellular damage via oxidative stress mechanisms. Kouam et al. 14 also reported that 66.5% of their patients were older than 60 years, further supporting the notion that older diabetic patients are more vulnerable to hepatic enzyme derangements. Bi et al. 18 also reported that the mean age of their type 2 diabetes group was 55.24±10.97 years, which is notably higher than the non-diabetic group mean age of 44.56±12.49 years, further suggesting that advancing age is an important contributing factor towards liver enzyme elevation in diabetic patients.

With regards to gender, female patients were more frequently having raised LFTs as compared to male patients, that is 44 (50.0%) versus 30 (29.7%), which were statistically significant ($p=0.004$). This is in contrast to Sarkar et al. 16 who reported higher enzyme levels amongst male diabetic patients and Das et al. 19 whose study population also showed male predominance in elevated transaminases. Burubu et al. 15 also included a slightly higher proportion of males (16 out of 30) in their diabetic group and Bi et al. 18 reported that their type 2 diabetes group comprised 64.33% males, both of which are in contrast to the present findings. The higher frequency amongst females in the present study could be explained by the hormonal differences, particularly oestrogen deficiency after menopause, which predisposes females to non-alcoholic fatty liver disease and subsequent liver enzyme elevation. Kouam et al. 14 also reported female predominance (75.9%) in their diabetic cohort and Ndraha et al. 13 similarly reported that 71.43% of their patients were female, both of which are somewhat in agreement with the present observation regarding female preponderance.

Concerning BMI, patients with BMI greater than 25 kg/m^2 were more frequently showing raised LFTs as compared to those with normal BMI, that is 50 (53.2%) versus 24 (25.3%) and this association were statistically significant ($p<0.001$). This finding is consistent with Al-Naemi 17 who demonstrated a significant effect of BMI on liver enzyme activity ($p<0.001$) and with Mandal et al. 20 who reported that patients with elevated ALT had a higher mean BMI of 30.2±7.5 kg/m^2 as compared to those with normal ALT, suggesting that increasing BMI directly correlates with worsening hepatic enzyme profile. Das et al. 19 also reported a significant positive correlation between BMI and ALT ($r=0.296$, $p=0.004$), further corroborating the present findings. Bi et al. 18 reported that fatty liver was present in 80% of their type 2 diabetes patients and that the mean BMI of the diabetic group was 27.12±3.59 kg/m^2, which is higher than non-diabetic controls and this supports the strong relationship between excess body weight, hepatic steatosis and raised liver enzymes. Kouam et al. 14 also identified BMI category as one of the five independent factors significantly associated with abnormal liver enzyme profiles ($p<0.001$) and Ndraha et al. 13 similarly reported that most of their patients were overweight or obese, collectively reinforcing the biological explanation that excess adipose tissue leads to increased flux of free fatty acids to the liver via hepatic steatosis, causing consequent elevation of liver enzymes.

The current research has many limitations that need to be discussed. Firstly, the study was carried out in one hospital, which limits its applicability to the wider population. Secondly, the number of patients was quite low (189 individuals) while a larger study involving several hospitals would be more applicable to the diabetic population. Thirdly, the factors like diabetes duration, HbA1c level, and the intake of hepatotoxic drugs were not considered, and they could affect liver enzymes level in diabetic individuals. Fourthly, the study was cross-sectional in nature; thus, the cause-and-effect relationship between type 2 diabetes and increased LFTs cannot be determined.

CONCLUSION

The current study has concluded out that abnormal elevation of liver enzymes is quite prevalent among patients suffering from type 2 diabetes mellitus and almost two-fifth of patients with type 2 diabetes had their LFTs raised. It was also found out that old age, female gender and high BMI were significantly associated with abnormal levels of liver enzymes among diabetic patients. There is a need for conducting more extensive multicenter studies in

order to have better understanding of the connection between type 2 diabetes and abnormal liver enzymes in Pakistani population.

Ethical Approval

Ethical approval for the research was taken from the Institutional Ethical Committee of the concerned hospital before starting the study.

Patients' Consent

Written informed consent was taken from all the participants before their inclusion in the study.

Competing Interests

The authors declare that there is no conflict of interest regarding this research.

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