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ORIGINAL ARTICLE

The Frequency of Abnormally High Liver Enzymes and their Connection to Type 2 Diabetes Mellitus

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ABSTRACT

Objective: The purpose of this research is to measure liver enzyme activity in Pakistani people with type 2 diabetes.
Study Design: Cross sectional
Place and Duration: The study was conducted in department of Pathology Women Medical& Dental College Abbottabad from January 2022 to June 2022.
Methods: 400 people were enlisted for the study (200 in the healthy control group I, and another 200 with type 2 diabetes). Alkaline phosphatase (ALP), alanine aminotransferase (ALT), and aspartate aminotransferase (AST) were assessed, as was body mass index (BMI). We also checked total protein (TP), albumin, and fasting blood glucose (FBG), and we tested glycosylated haemoglobin (HbA1c). Averages and standard deviations were used to describe quantitative data, whereas frequencies were used to characterize qualitative information. Tests for associations, significance, and correlations between groups were conducted using the Pearson/Spearman correlation test, the unpaired t-test, and the Chi-squared test. Statistical significance was defined as a P-value less than.05. Each piece of information was put via SPSS 24.0 for statistical analysis.
Results: Among 200 patients of Type 2 DM females were higher in numbers than males. Type 2 DM patients had a mean age of 48.8 years (SD 11.12), whereas the healthy population had a mean age of 40.6 years (SD 11.3) (P .0001). AST activity in Type 2 DM was found to be similar to that of healthy individuals (P =.060). Type 2 DM is associated with elevated levels of ALT, total bilirubin, and alkaline phosphatase when compared to healthy controls (P .0001). Hepatic enzyme levels were abnormal in 60% of those with type 2 diabetes compared to 30% of those without the disease.
Conclusion: Liver function tests (LFTs) were shown to be significantly abnormal in the diabetic community as a whole, demonstrating widespread co-existing derangements. It is possible that early diagnosis and therapy might benefit from a thorough workup in such patients. Furthermore, reducing liver-related morbidity and mortality in Type 2 DM would benefit from early diagnosis and therapy of aberrant liver parameters.
Keywords: Liver Hepatic pathology, Diabetes mellitus type 2, Liver function tests

INTRODUCTION

It is becoming clear that NAFLD is the leading cause of chronic liver disease in both Western countries and the rest of the globe [1]. The absence of alcoholic liver damage is a hallmark of this condition. From basic steatosis to NASH to fibrosis to cirrhosis and its consequences such decompensation and hepatocellular carcinoma (HCC), NAFLD encompasses a wide range of liver diseases [2, 3]. As time goes on, this is projected to overtake all others as the primary reason people seek a liver transplant.

Most people with NAFLD have no symptoms and are diagnosed after abnormal liver investigations show up on routine laboratory evaluation. In particular, there is an increase in alanine aminotransferase (ALT) and aspartate aminotransferase (AST), two liver enzymes. Aminotransferase levels may not consistently predict the severity of inflammation and cirrhosis [3], and they may not be increased in all cases of nonalcoholic fatty liver disease.

One of the main causes of death and disability worldwide, diabetes mellitus is a major public health concern [4, 5]. About one in eleven adults worldwide would have diabetes mellitus, according to the International Diabetes Federation (IDF) [6]. South-East Asian countries are particularly affected by diabetes [6], and low- and middle-income countries account for over 80% of all diabetic subjects. Liver diseases such NAFLD, hepatocellular carcinoma, and cirrhosis have all been linked to diabetes [3, 7, 8].

In the diabetic population, these liver disorders are among the leading causes of death. Changes in liver enzyme levels [9], which are biological markers connecting liver disease and diabetes, are useful indicators of liver damage in NAFLD. The importance of liver enzymes in diabetes risk assessment has received a lot of attention. Many studies have found an association between diabetes and increased liver enzymes [10], although the results are contradictory. High levels of AST, ALT, and GGT have been linked to diabetes in certain research [11]. Another study found that levels of GGT, ALT, and ALP rose significantly but AST did not [12].

Given that assessing GGT and ALT includes well-standardized, easy, affordable, and regular assays with no necessity for fasting prior to venipuncture[13], it is of clinical interest to study if these practical biomarkers might assist identify persons at higher risk of developing T2D. There was a discrepancy in the existing data, with some studies showing that GGT and/or ALT significantly improved T2D prediction and others not finding such a correlation. Furthermore, a recent study in a white and African-American population suggested that ALT 26 IU/L considerably improved diabetes prediction, although a Japanese study has discovered a far lower cut-off value for ALT (13 IU/L). [14] The Asians acquire type 2 diabetes at a lower body mass index (BMI) than individuals of Western cultures is consistent with this difference, suggesting that the liver may play a more major role in the development of T2D in relatively slim Asian people. There is, however, a lack of evidence to support this claim. Furthermore, to the best of our knowledge, no study has yet examined the association between GGT and ALT and the risk of T2D or the levels at which they may serve as a threshold for T2D prediction in a Chinese population.

The pathophysiology of this illness involves the liver significantly. However, the liver is not spared from the lethal effects of type 2 diabetes. A recent study found that up to 70% of patients with cirrhosis also had type 2 diabetes, which may have contributed to the onset and development of their condition [15]. It is not yet understood what causes changes in liver biomarkers in people with diabetes.

Using this as a starting point, the current study seeks to determine how often aberrant LFT parameters are among people with diabetes. Inasmuch as we are aware, there is a dearth of statistics pertaining to people. Consequently, the current study aimed to learn how common LFT abnormalities are among diabetics and if there is a connection between LFT parameters and high blood sugar levels in T2DM patients, all with the hopes of giving doctors new tools to better treat the condition.

MATERIAL AND METHODS

This cross-sectional study was conducted at Department of Pathology Women Medical& Dental College Abbottabad from January 2022 to June 2022 and comprised of 400 patients. Patients having a history of liver illness, alcohol use, hepatotoxic drug use, acute hepatitis, participants with a presentation of viral infection including such hepatitis B and C, and patients with a history of thyroid dysfunction were not permitted to participate in the present study.

All ages, from 18 to 75, were represented among the patients. Fasting venous plasma glucose (FPG) 126 mg/dL (7.0 mmol/L) was required for inclusion in the trial. Participants having a confirmed diagnosis of diabetes mellitus or newly diagnosed diabetes utilizing American Diabetes Association (ADA) screening criteria were eligible to participate. Blood samples (5 mL) were drawn from the participants' veins and placed in a sterile vacutainer tube with the help of single-use syringes that had been previously sterilized. Serum was separated from whole blood by centrifuging it at 2000g for 10 minutes while. The serum samples were frozen at -20 °C until further testing could be done. Total bilirubin, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, total protein, were assessed using an semiautomated biochemistry analyzer (Microlab 300), and haemoglobin A1c was evaluated using a Special chemistry analyzer Finecare.

In this analysis, we utilized the following reference intervals: TB cutoffs are as follows: ALT >45 U/L in men and >34 U/L in women; AST cutoffs are as follows: >35 U/L in men and >31 U/L in women; and ALP cutoffs are as follows: >129 U/L in men and >104 U/L in women. Fasting glucose levels above 126 mg/dL were used to diagnose type 2 diabetes, as recommended by the American Diabetes Association.

Means and standard deviations (SDs) were used to characterize quantitative variables, whereas frequencies (%) were used to illustrate qualitative ones in the current investigation. The relationship between liver enzymes and underlying diseases was calculated using Pearson's correlation coefficient. We tested the anthropometric factors for statistical significance using the independent sample t-test. Prevalence differences between the sexes were analyzed using the chi-squared test. It was determined that a P-value of less than.05 indicated statistical significance. IBM's SPSS software, version 23 was used for the statistical analysis.

RESULTS

Among 200 patients of T2DM females were higher in numbers than males while in control group males were higher in numbers. T2DM patients had a mean age of 48.8 years (SD 11.12), whereas the healthy population had a mean age of 40.6 years (SD 11.3) (P .0001). Mean BMI in group I was 25.3±6.21 kg/m^2 and in group II mean BMI was 26.9±11.29 kg/m^2. There were 130 (65%) patients in group I and 125 (62.5%) cases in group II had rural residency.(table 1)

Table-1: Demographically detailed of enrolled cases

Variables	Control Group	Diabetic Group
Gender		
Male	122 (61%)	65 (32.5%)
Female	78 (39%)	135 (67.5%)
Mean age (years)	40.6±11.3	48.8±11.12
Mean BMI (kg/m^2)	25.3±6.21	26.9±11.29
Place of Living		
Rural	130 (65%)	125 (62.5%)
Urban	70 (35%)	75 (37.5%)

AST activity in T2DM was found to be similar to that of healthy individuals (P =.060). Fasting blood glucose and haemoglobin A1c levels were found to be statistically substantially higher in T2DM patients compared to healthy controls (P .0001). T2DM is associated with elevated levels of ALT, total bilirubin, and alkaline phosphatase when compared to healthy controls (P .0001).(table 2)

Table-2: Comparison of lab results in both groups

Variables	Control Group	Diabetic Group
AST **(U/L)**	30.8±7.26	32.9±13.03
Fasting Glucose **(mg/dL)**	99.19±9.44	200.7± 19.74
HbA1c **(%)**	5.1 ±1.30	9.2 ±3.70
ALT (U/L)	30.01±7.19	37.8±5.27
total bilirubin	0.55 ±0.03	0.71±0.09
alkaline phosphatase**(U/L)**	90.3±20.41	106.7±17.49
Albumin (mg/dL)	43.4±3.36	42.8±17.81

Hepatic enzyme levels were abnormal in 60% of those with type 2 diabetes compared to 30% of those without the disease.(figure-1)

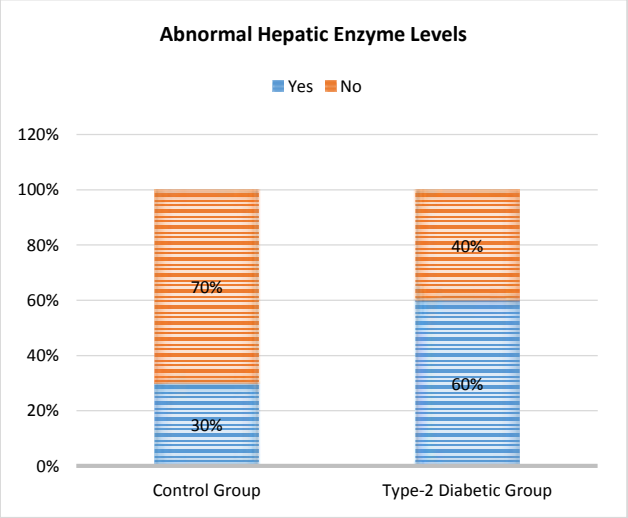

Figure-1: Comparison of enzyme levels among both groups

DISCUSSION

In order to shed light on the prevalence and nature of hepatic dysfunctions in people with diabetes, the current investigation was conducted. Results demonstrate that patients with Type 2 DM have abnormalities in LFT. A substantial connection was also reported between increased expression in T2DM patients, as we observed in the present study [16], confirming the results of a previously published study between liver enzymes and T2DM in the Ethiopian community. The authors have previously looked at hepatic enzyme activity in T2DM patients and found a high frequency of NAFLD [17]. Our findings are consistent with those of a prior study [18] that employed an increased AST enzyme as a marker for predicting the likelihood of developing diabetes. First, this anomaly may be due to the accumulation of fat in the liver, a condition known as nonalcoholic fatty liver disease (NAFLD). Another recent cross-sectional study indicated that T2DM patients are more likely to have abnormal LFTs than healthy people. [19] Inflammation of the liver, which disrupts liver function and causes a shift in liver biomarkers, is another potential explanation [20]. In addition, excessive quantities of fatty acids can cause membrane rupture in cells, as well as the activation and inhibition of crucial steps in the regulation of many metabolic processes, as well as mitochondrial malfunction [21].

In current study 200 diabetic and 200 control patients were included. Among 200 patients of T2DM females were higher in numbers than males. T2DM patients had a mean age of 48.8 years (SD 11.12), whereas the healthy population had a mean age of 40.6 years (SD 11.3) (P .0001). These findings were comparable

to the previous studies.[22,23] As much as 71.2% of the general population and 70.0% of the T2DM population in previous study have abnormal LFTs. [24]. We found a similar pattern of abnormal liver parameters in our investigation, albeit at a lower (60%) incidence rate than was shown in the aforementioned study. Further, between 50 and 70 percent of people with diabetes have abnormal LFTs reported. [25]

Twenty-two percent of participants in a research conducted in Sudan by Idris et al. [26] had at least one abnormal liver function test. Diabetics have an ALT rise of up to 4.5 times that of the general population, as demonstrated by Harris et al. [27]. The present research was bolstered by a UK study of 959 diabetic patients, which found that whereas 15.7% of diabetics had elevated ALT levels, 10.4% of patients had elevated alkaline phosphatase levels, and only 3.9% had hyperbilirubinemia [28]. Another Iranian study found that 10.4% and 3.3% of the diabetic population experienced an increase in ALT and AST, respectively [29]. Another study reported a statistically significant increase in ALT (57%) and AST (46%), as compared to non-diabetic controls with DM [30].

As appropriate surrogate markers of NAFLD, which is characterized by hepatic fat buildup, elevated GGT and ALT levels were associated to T2D development. [31] Fat accumulation in organs other than the liver is a risk factor for type 2 diabetes, and NAFLD may be an indicator that this has occurred. [31] A Korean study, on the other hand, found positive correlations between GGT/ALT and T2D risk in people who did not have fatty liver, implying the existence of other routes. [32]

CONCLUSION

Liver function tests (LFTs) were shown to be significantly abnormal in the diabetic community as a whole, demonstrating widespread co-existing derangements. It is possible that early diagnosis and therapy might benefit from a thorough workup in such patients. Furthermore, reducing liver-related morbidity and mortality in T2DM would benefit from early diagnosis and therapy of aberrant liver parameters.

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