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Deranged Liver Function Tests in Type 2 Diabetes: A Retrospective Study

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ABSTRACT

Background: Liver associated disorders like altered LFTs such as alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and gamma-glutamyltranspeptidase (GGT) in the serum, fatty liver disease, cirrhosis, hepato-cellular carcinoma and acute liver failure are a common occurrence in type 2 DM.
Aim and Objective: To assess the association between liver function parameters and type 2 diabetes (T2D) in a north Indian population.
Material and Methods: The study was conducted among 133 Type 2 DM patients in the department of Biochemistry, Pt. B.D Sharma Postgraduate Institute of Medical Sciences, Rohtak, Haryana, India. Data from type 2 DM diagnosed patients was retrospectively reviewed. Reports of outpatient fasting serum glucose and LFTs (which included serum levels of total bilirubin, AST, ALT, ALP, and albumin) were compiled. LFTs were advised to these patients as a part of routine screening.
Results: It was found that the frequencies of elevated Bil, elevated ALT, elevated AST, elevated ALP and diminished albumin were 31.5%, 52.6%,59.3%, 42.1% and 73.6% respectively in the Type 2 DM cases. Moreover, the concentration of S. ALP correlated significantly with the random serum glucose levels. The correlation was significantly positive in the diabetic cases ($r = 0.20$, $P < 0.05$).
Conclusion: The current study highlights the importance of liver function monitoring in patients with type 2 DM. This report would be helpful inencouraging the clinicians to give interest in monitoring this neglected diabetic hepatic complication in individuals suffering from type 2 DM.

Keywords- Type 2 Diabetes, liver function, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, diabetes mellitus.

INTRODUCTION

Diabetes mellitus (DM) refers to a group of metabolic disorders characterized by hyperglycemia with disturbances in carbohydrate, lipid, and protein metabolism due to absolute or relative deficiency of insulin secretion. Type 2 DM is the more prevalent variety of DM caused by resistance to insulin action and inadequate compensatory insulin secretory response. [1]

The prevalence of diabetes worldwide was estimated to be 2.8% in 2000 and 4.4% in 2030 and it has been found to be more prevalent in men than women. The total number of diabetes is projected to increase from 171 million in 2000 to 366 million in 2030. [2]

The liver plays a central role in maintaining glucose homeostasis. Loss of insulin effect on the liver leads to glycogenolysis and an increase in hepatic glucose production. The precise genetic, environmental, and metabolic factors and sequence of events that lead to the underlying insulin resistance, however, is not fully understood. [3]

Liver associated disorders like altered LFTs such as alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and gamma-glutamyltranspeptidase (GGT) in the serum, fatty liver disease, cirrhosis, hepato-cellular carcinoma and acute liver failure are a

common occurrence in type 2 DM. [4,5] Chronic hyperinsulinemia and relative insulin resistance is associated with increased lipogenesis and associated fatty changes. Moreover, accumulation of free fatty acid is known to be toxic to hepatocytes leading to increased oxidative stress levels and increase in proinflammatory cytokine – Tissue Necrotic Factor. [6]

MATERIALS AND METHOD

The study was conducted among 133 Type 2 DM patients in the department of Biochemistry, Pt. B.D Sharma Postgraduate Institute of Medical Sciences, Rohtak, Haryana, India.

Data from type 2 DM diagnosed patients was retrospectively reviewed. Reports of outpatient fasting serum glucose and LFTs (which included serum levels of total bilirubin, AST, ALT, ALP, and albumin) were compiled. LFTs were advised to these patients as a part of routine screening.

The LFTs were estimated in auto-analyzer (RandoxSuzuka, United Kingdom, model no. 6L7WD5J) using kits provided by Randox laboratories .Quality control was done to ensure the validity of the test results using third party control materials (Randox, UK and Christian Medical College, Vellore). The normal reference ranges used for this study were as follows: Total bilirubin: 0.3–1 mg/dL, ALT: 0–35 U/L, AST: 0–35 U/L, ALP: 30–120 U/L, and albumin: 3.5–5.5 g/dL. [7] The serum levels of total bilirubin, AST, ALT, and ALP were considered deranged when they were more than the respective reference ranges while the levels of albumin were considered deranged when they were less than the reference range. For categorization of type 2 DM from total population, the type 2 DM diagnostic criteria provided by the IDF was used. [8]

Statistical Analysis: Appropriate statistical analysis was done using SPSS. Graphs were prepared using Excel 2010.

RESULTS

Table 1: Frequency of normal and abnormal liver function tests in the study sample

Parameter	Normal (Total = 133)	Abnormal
Total Bilirubin	91 (69.5%)	42(31.5%)
AST	54 (40.7%)	79(59.3%)
ALT	63 (47.4%)	70(52.6%)
ALP	77 (57.9%)	56(42.1%)
Albumin	32(26.4%)	98(73.6%)

Table 1 shows the normal and abnormal LFT values in the total 133 cases. The table shows that the frequencies of elevated Bil, elevated ALT, elevated AST, elevated ALP and diminished albumin were 31.5%, 52.6%, 59.3%, 42.1% and 73.6% respectively.

The most common abnormality in liver function test was the decreased values of S.albumin, in 98 patients (73.6%) whereas, elevated T.Bil in 42 patients(31.5%) was the least common abnormality observed.

Table 2: Mean values of liver function tests in the study cases

Parameter	Mean±SD
Total Bilirubin	1.05±1.38
AST	123.42±227.46
ALT	130.85±263.32
ALP	144.20±84.22
Albumin	3.09±1.06

Table 2 shows that the mean value of all the parameters of liver function test was deranged in the all the diabetic cases. It was found that the mean value of T.Bil,S ALT, S. AST, S. ALP and S. Albumin were 1.05±1.38, 123.42±227.46, 130.85±263.32, 144.20±84.22, 3.09±1.06 respectively.

Table 3: Correlation analysis between random serum glucose and liver function tests

Parameter	Correlation coefficient ("r") value	P value
Total Bilirubin	0.017001	0.846
ALT	0.106901	0.221
AST	0.121486	0.164
ALP	0.202	0.002
Albumin	-0.21	0.812

Table 3 shows the correlation of random blood glucose with T.Bil, S.ALT, S.AST, S.ALP and S.Albumin. It was observed that the concentrations of S. ALP correlated significantly with the random serum glucose levels. The correlation was significantly positive in the diabetic cases ($r = 0.20$, $P < 0.05$). For the other components of LFTs,

none of the correlations were statistically significant (P > 0.05). It was found that the correlation was not statistically significant with the other parameters of LFT (p>0.05).

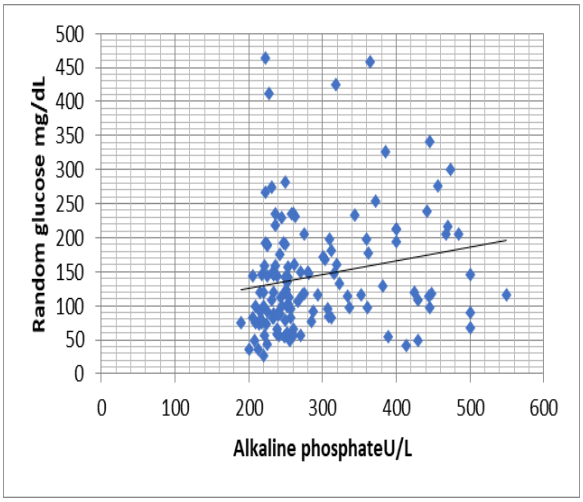

Figure 1: Correlation analysis between random serum glucose and liver function tests

DISCUSSION

The mean value of all the parameters of liver function test was deranged in the all the type 2 DM cases. It was found that the mean value of T.Bil, S. ALT, S. AST, S. ALP and S. Albumin were 1.05±1.38, 123.42±227.46, 130.85±263.32, 144.20± 84.22, 3.09±1.06 respectively. Moreover, a very high prevalence of abnormal LFTs was observed in patients with type 2 DM. S.albumin was the most commonly affected liver function test in 98 patients (73.6%) whereas, elevated T.Bil in 42 patients (31.5%) was the least common abnormality observed. Also, the S. ALP levels correlated significantly with the random serum glucose levels. The correlation was significantly positive in the type2 DM cases (r = 0.20, P < 0.05).

In support of our findings, Salmela et al studied the liver function tests of 175 diabetic patients without chronic liver disease, where 57% were found to have at least one abnormal LFT and 27% had at least two abnormal LFTs. However, these increases in liver function values were rarely more than two times of the upper limit of normal. [9] In another cross sectional study, which was conducted in Iran, a rise of ALT and AST in 10.4% and 3.3% of type 2 diabetes patients respectively was demonstrated. [10] Similarly, Studies conducted by Bora et al [11] in India and Balogun et al. in Nigeria [12] reported a high prevalence of deranged LFTs of about 71.2% and 70% respectively among the diabetic population. Ghimire et al observed increased level of ALT (57%) and AST (46%) among patients with diabetes mellitus. Moreover, a significant level of elevation in AST and ALT was observed among the patients with DM compared to non-diabetic controls (p<0.05). [13] Wang et al found that higher levels of ALT and GGT were significantly associated with increased risk of T2D (p for trend <0.001 for ALT, p for trend=0.03 for GGT), and the ORs (95% CIs) comparing highest versus lowest tertiles of ALT and GGT were 2.00 (1.01 to 3.96) and 2.38 (1.21 to 4.66), respectively. A null association was observed for AST, ALP, and LDH with T2D risk. Adding GGT (<23 vs≥23 IU/L) or ALT (<21 vs≥21 IU/L) to a prediction model resulted in significant gain in net reclassification improvement and integrated discrimination improvement of T2D prediction (all p<0.001). [14]

Abnormal liver function tests in diabetes patients can be attributed to several factors. Firstly, Hyperinsulinemia might directly lead to hepatic insulin resistance with associated fatty changes. This enhanced fat accumulation in liver is known to be directly toxic to hepatocytes, leading to increase in transaminases and diminished synthetic capacity of liver. [15] Secondly, The insulin-resistant state is also characterized by an increase in pro-inflammatory cytokines such as tumor necrosis factor (TNF), which may also contribute to hepatocellular injury. [16] Moreover, One of the hepatic manifestation of diabetes mellitus with metabolic syndrome is NAFLD and more specifically ALT has been used as a marker of NAFLD. [17] Recently, studies have revealed the association of hepatitis C virus infection in diabetes patients causing deranged LFTs. [18] Though relatively infrequent, statin therapy

can also contribute to abnormal liver function results. [19]

CONCLUSION

This study supports the previous studies reporting an association between abnormal liver function and type 2 diabetes, conducted in north Indian population. [20,21] The current study highlights the importance of liver function monitoring in patients with type 2 DM. This report would be helpful in encouraging the clinicians to give interest in monitoring this neglected diabetic hepatic complication in individuals suffering from type 2 DM. Moreover, timely diagnosis and management of the abnormal liver parameters may help to minimize liver related morbidity and mortality in diabetic population. Future attempts should be directed toward unraveling the causes of hepatic dysfunction in diabetics and examining the impact that hepatic involvement might have on the glycemic status. Further researches are needed to validate the findings, particularly the predictive utility of liver enzymes for T2D, and investigate the biological mechanisms for the associations.

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