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Comparative Study of Liver Enzymatic Panel: Focus on Serum AST, ALT, ALP AND GGT with the Severity of Type II Diabetes Mellitus

Kiranjeet Kaur[1], JasdeepSingh Sandhu[2*], Narendra Kumar Sah[3]
[1]Professor, Department of Biochemistry, Maharishi Markandeshwar Medical College & Hospital, Solan, HP, India
[2]Associate. Professor, Department of Physiology, Maharishi Markandeshwar Medical College & Hospital, Solan, HP, India
[3]Assistant Professor, Department of Biochemistry, Maharishi Markandeshwar Medical College & Hospital, Solan, HP, India

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***Corresponding author**
JasdeepSingh Sandhu

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Abstract: Diabetes mellitus, a global problem, affects the functions of the liver characterized by altered metabolism and glucose homeostasis. The relationship of increase in various liver enzymes in type 2 diabetes mellitus, causing hepatocytes dysfunction is not well established. The present study was carried out to focus on various liver enzymes like aspartate amino transferase (AST), alanine amino transferase (ALT), alkaline phosphatase (ALP) and gamma glutamyl trans peptidase (GGT) and to find out correlation, if any, between type 2 diabetes mellitus and liver functions and its effect over the liver. The present study also focuses whether there is any relationship between the severities of Type 2 diabetes mellitus on liver functions. The present study was a case-control study and was carried out on 40 diagnosed cases of type 2 diabetes mellitus with age group of 30-80 years and 15 healthy controls who were age and sex matched. Serum was collected from blood sample of all the 55 subjects and was sent for biochemical investigations. In the present study, mean Fasting blood sugar (FBS) and Post-prandial blood sugar (PPBS) of type 2 diabetic subjects was found to be 195.45 ± 53.39 & 283.27 ± 74.57 as compared to controls 78.66 ± 10.30 & 118.13 ± 10.78. It was observed that liver enzymes (AST, ALT, ALP & GGT) were not significantly raised in mild diabetic subjects ($p > 0.05$) as compared to controls, whereas, these enzymes were significantly increased in moderate and severe diabetic subjects as compared to controls. Liver dysfunction has significant relationship with the severity of type 2 diabetes mellitus.
Keyword: Diabetes mellitus, aspartate amino transferase (AST), alanine amino transferase (ALT), alkaline phosphatase (ALP) and gamma glut amyl Tran's peptidase (GGT), Liver dysfunction.

INTRODUCTION

Diabetes mellitus is a metabolic disorder characterized by hyperglycemia and glycosuria resulting from defective insulin secretion or insulin action or both leading to disturbances in carbohydrate, protein and fat metabolism [1].

World Health Organization (WHO) predicts that the number of people with diabetes is to double in the next couple of decades and the major brunt of this will be borne by the developing countries. In fact, diabetes has long passed the stage of being an epidemic in India. India shall have approximately 57.2 million diabetics by the year 2025[2].

A major component of the diabetic state is disturbance in the carbohydrate metabolism and liver is an organ to play an important role in metabolism and glucose homeostasis. Altered portal insulin levels and the insulin/glucagon ratio may influence hepatocytes function and integrity in diabetic patients and predispose them to various hepatic disorders [3]. Disturbances of liver function in some patients with diabetes mellitus is well-recognized but the precise relationship of diabetes mellitus to liver dysfunction has not been established[4,5]. The liver is probably the single most important regulatory site of glucose metabolism and in patients with liver disease, disturbance of carbohydrate metabolism is common [6, 7].

In a study carried out by Diamond, he expressed that despite the diversity of functions of liver, a high volume of blood bilirubin in diabetics indicate liver damage [8]. Also, longer the duration of diabetes and older the patients, the more frequently does the hepatic dysfunction become demonstrable [9].

Increased activity of serum β-glucuronidase, N-acetyl-β glucuronidase may be linked to the increased susceptibility of diabetics to atherosclerosis. Increased activity of β-glucuronidase has been related to underlying liver involvement. The enhanced activity of alkaline phosphatase has been interpreted as the increased phosphatase activity in tissues in the diabetic state. The increased enzyme activities (Aspartate aminotransferase, Alanine aminotransferase, Glutamate and is citrate dehydrogenase and Arginase) reflect the association with the complicated diabetic disease [10].

In the present study, various liver function tests studied are aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP) and gamma glutamyltranspeptidase (GGT) and attempt has been made to find out correlation between type 2 diabetes mellitus and liver functions and its effect on the liver and to see whether there is any relationship between the severity of diabetes on liver functions.

MATERIALS AND METHODS

The present case-control study was conducted in Government Medical College; Patiala with 40 diagnosed cases of type 2 diabetes mellitus with age group of 30-80 years and 15 age and sex matched healthy controls. History was taken from all participated subjects with written consent forms. Patients with history of alcoholism and other liver disorders like cirrhosis, hepatitis were excluded from the study. Serum was collected from 55 subjects and following investigations were carried out:

- Fasting and post-prandial blood sugar (FBS & PPBS respectively) by Glucose oxidase and peroxidase (GOD/POD) method [11-13].
- Alkaline phosphatase (ALP) by King and Armstrong method [14].
- Aspartate transaminase (AST) &Alanine transaminase (ALT) by kinetic method according to the recommendations of International Federation of Clinical Chemistry (IFCC) [15].
- Gamma glutamyltransferase (GGT) by kinetic method according to SZASZ [16].

The severity of diabetes was divided into 3 grades according to modified Mathur *et al.* [17]

- Mild – Fasting blood sugar (FBS) as 140-200 mg%.
- Moderate – FBS as 201-300 mg%.
- Severe – FBS as ≥ 301 mg%.

RESULTS

Among 40 cases of type 2 diabetes mellitus, 19 were males and 21 were females. The mean FBS and PPBS of type 2 diabetic cases was found to be 195.45 ± 53.39 & 283.27 ± 74.57 as compared to controls 78.66 ± 10.30 & 118.13 ± 10.78. The mean serum ALP in type 2 diabetic cases was found to be 9.95 ± 4.16 with respect to controls 5.56 ± 1.15 showing statistically highly significant difference between type 2 diabetic cases and controls ($p<0.01$). The mean serum AST in type 2 diabetic cases was found to be 34.22 ± 10.11 with respect to controls 24.60 ± 9.21 showing statistically highly significant difference between type 2 diabetic cases and controls ($p<0.01$). Also, mean serum ALT in type 2 diabetic cases was found to be 37.10 ± 8.61 with respect to controls 29.40 ± 7.49 showing statistically highly significant difference between type 2 diabetic cases and controls ($p<0.01$). The mean serum GGT in type 2 diabetic cases was found to be 43.50 ± 17.46 with respect to controls 21.96 ± 6.62 showing statistically highly significant difference between type 2 diabetic cases and controls ($p<0.01$). These findings were in accordance with the study done by Mamta *et al.* [18] and Shipra *et al.* [19].

Table-1: Comparison of Serum Alkaline Phosphatase of Control Group V/s Study Group according to Severity of Diabetes

S. No.	Cases	No. of Patients	Mean ± SD	p Value
1.	Control (FBS 60-140 mg%) Mild Diabetics (FBS 141-200 mg%)	15 20	5.56±1.15 7.65±2.79	>0.05 Non-Significant
2.	Control (FBS 60-140 mg%) Moderate Diabetics (FBS 201-300 mg%)	15 13	5.56±1.15 9.52±2.62	<0.001 Highly Significant
3.	Control (FBS 60-140 mg%) Severe Diabetics (FBS >300 mg%)	15 7	5.56±1.15 12.24±2.69	<0.001 Highly Significant

Table-2: Comparison of Serum AST of Control Group V/s Study Group according to Severity of Diabetes

S. No.	Cases	No. of Patients	Mean ± SD	p Value
1.	Control (FBS 60-140 mg%) Mild Diabetics (FBS 141-200 mg%)	15 20	24.60±9.21 27.47±7.33	>0.05 Non-Significant
2.	Control (FBS 60-140 mg%) Moderate Diabetics (FBS 201-300 mg%)	15 13	24.60±9.21 36.52±9.03	<0.01 Significant
3.	Control (FBS 60-140 mg%) Severe Diabetics (FBS >300 mg%)	15 7	24.60±9.21 41.70±8.56	<0.01 Significant

Table-3: Comparison of Serum ALT of Control Group V/s Study Group according to Severity of Diabetes

S. No.	Cases	No. of Patients	Mean ± SD	p Value
1.	Control (FBS 60-140 mg%) Mild Diabetics (FBS 141-200 mg%)	15 20	29.40±7.49 30.21±4.99	>0.05 Non-Significant
2.	Control (FBS 60-140 mg%) Moderate Diabetics (FBS 201-300 mg%)	15 13	29.40±7.49 34.29±5.68	<0.05 Significant
3.	Control (FBS 60-140 mg%) Severe Diabetics (FBS >300 mg%)	15 7	29.40±7.49 45.50±8.38	<0.001 Highly Significant

Table-4: Comparison of Serum GGT of Control Group V/s Study Group according to Severity of Diabetes

S. No.	Cases	No. of Patients	Mean ± SD	p Value
1.	Control (FBS 60-140 mg%) Mild Diabetics (FBS 141-200 mg%)	15 20	26.96±6.62 27.60±7.42	>0.05 Non-Significant
2.	Control (FBS 60-140 mg%) Moderate Diabetics (FBS 201-300 mg%)	15 13	26.96±6.62 40.05±6.22	<0.001 Highly Significant
3.	Control (FBS 60-140 mg%) Severe Diabetics (FBS >300 mg%)	15 7	26.96±6.62 44.40±13.98	<0.001 Highly Significant

DISCUSSION

Diabetes mellitus is characterized by persistent hyperglycemia with or without glycosuria due to absolute or relative deficiency of insulin hormone, thereby disturbing the intermediary metabolism. Liver is a prime organ that plays an important role in metabolism and homeostatic regulation of blood sugar. Thus, in liver diseases, hepatic carbohydrate metabolism is generally disturbed. Altered portal insulin levels and the insulin/glucagon ratio may influence hepatocytes function and integrity in diabetic patients and predispose them to various hepatic disorders, and lead to various structural and functional abnormalities.

The present study comprised of 40 subjects with type 2 diabetes mellitus from the OPD and various wards of Rajindra Hospital, Patiala and 15 ages and sex matched healthy controls. In the present study, the comparison of liver enzymatic panel was done with the severity of type 2 diabetes mellitus, and it was clear that the liver enzymatic panel was more significant in moderate and severe type 2 diabetics (Table 1).

These findings were in consistent with the study done by Bogach *et al.* that recorded that out of 16 cases, 6 had increased alkaline phosphatase level [20] Slamela *et al.* studied liver function tests in 175 diabetic patients and found abnormal values of serum alkaline phosphatase in 11 % of the patients[3]. Also, M Tibi *et al.* measured alkaline phosphatase in type-1, type-2 diabetes mellitus and non-diabetic control group and concluded that serum alkaline phosphatase was significantly higher in diabetic patients compared with control group [21]. Deepika G *et al.* in their comparative study on normal healthy subjects, diabetics with good glycemic control and without glycemic control, found significant elevation in serum ALP level in type II diabetes mellitus patients as compared to healthy normal subjects [22].

In the present study, serum AST and ALT were found to be statistically significantly increased ($p< 0.05$) in moderate and severe diabetics as compared to controls, whereas, serum AST and ALT were not statistically significantly increased in mild diabetes as compared to control ($p> 0.05$)(Table 2 & 3).

This was in accordance with the study done by Miralem *et al.* indicating that patients with diabetes mellitus (DM) type 2 and metabolic syndrome have higher levels of liver enzymes GGT, AST and ALT compared to patients with DM type 2 without metabolic syndrome [23]. Several studies concluded similar findings as: study done by Miyatake *et al.* who found higher hepatic enzymes level, AST, ALT and GGT in subjects with metabolic syndrome compared to control subjects[24], study done by Wedemeyer *et al* who found that elevated ALT level is also a risk factor for non-hepatic diseases including diabetes mellitus type 2, metabolic syndrome, cardiovascular diseases and malignancies[25], Goessling *et al.* confirmed that ALT is an independent predictor of metabolic syndrome and diabetes [26] and Kim *et al.* also confirmed that increased serum GGT and ALT levels are independent, additive risk factors for the development of type 2 diabetes mellitus in subjects without fatty liver or hepatic dysfunction[27].

In the present study, serum GGT was found to be highly statistically significant ($p < 0.01$) in moderate and severe diabetics as compared to controls, whereas serum GGT was found to be statistically non-significant in mild diabetics as compared to controls ($p > 0.05$)(Table 4).

These findings were in consistent with the study done by Sangappa *et al.* who found that all the liver parameters including AST, ALT& GGT were significantly high except ALP [28].

Philip R *et al.* in their study showed significant increase in AST, ALT and GGT ($p<0.01$) as compared to healthy controls [29]. Agarawal J in North India, reported serum levels of AST, ALT, ALP and GGT all were significantly elevated in type II diabetes mellitus patients as compared to controls($p<0.05$)[29].

CONCLUSION

The present study concluded the following:

- According to severity of diabetes, the liver enzymes (AST, ALT, ALP & GGT) were not significantly increased in mild diabetes ($p > 0.05$) when compared to controls.
- AST and ALT were significantly increased in moderate diabetes, whereas, the increase of ALP and GGT were highly significant.
- The increase of AST, ALT, ALP & GGT were highly significant in severe diabetes.

Based on these conclusions, liver dysfunction does occur in the setting of diabetes mellitus and have significant relationship with the severity of type 2 diabetes mellitus. Thus, we should keep in mind to focus on the liver enzymatic panel and controlling the blood sugar for longevity and good health.

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