ORIGINAL ARTICLE

SERUM HEPATIC ENZYMES LEVEL IN TYPE 2 DIABETES MELLITUS IN A TERTIARY LEVEL HOSPITAL

K Fatema[1], D Parvin[1], S Islam[2], MSR Hossain, MA Rumman[4]
F Afroz[5], F Quamrunnahar[6], N Sultana[7]

[1]Dept of Biochemistry, NICVD, Dhaka; [2]Dept of Cardiology, NICVD, Dhaka; [3]Dept of Microbiology, Sheikh Hasina Medical College, Tangail; [4]Dept of Biochemistry, Dhaka Central International Medical College, Dhaka; [5]Dept of Biochemistry, Dhaka Medical College, Dhaka; [6]Dept of Clinical Pathology, NICVD, Dhaka; [7]Dept of Biochemistry, Dhaka Medical College, Dhaka

ABSTRACT

Diabetes mellitus is one of the most common non-communicable diseases globally. Magnitude of DM in developing countries including Bangladesh is rising rapidly. Several studies across the world have reported the association of higher serum hepatic enzyme levels with type 2 DM which may be an expression of excess deposition of fat in the liver. Thus, serum hepatic enzyme levels may serve as a marker of insulin resistance in the liver and may predict the prognosis and complications in type 2 DM individuals. The present cross-sectional study was conducted in the Department of Biochemistry, Dhaka Medical College, Dhaka from July' 2015 to June' 2016 to find out the association of serum hepatic enzyme levels with type 2 DM individuals in a tertiary level hospital. A total number of 100 subjects were selected with the age ranging from 30 to 60 years. Among them, 50 diagnosed type 2 DM individuals were included in the Group A and 50 apparently healthy individuals were selected as Group B for comparison. The study parameters were fasting plasma glucose (FPG), HbA1c, ALT, AST, ALP and GGT. The mean($\pm$SD) serum ALT, AST, ALP and GGT concentration (U/L) in cases were 46.28$\pm$.81, 28.17$\pm$10.08, 118.26$\pm$16.08 and 36.98$\pm$10.08 respectively and mean($\pm$SD) serum ALT, AST, ALP and GGT concentration(U/L) in controls were 29.54$\pm$8.56, 24.54$\pm$6.89, 96.68$\pm$14.36 and 23.82$\pm$6.98 respectively. The present study showed that higher levels of serum hepatic enzymes (ALT, AST, ALP and GGT) were present in subjects with type 2 diabetes mellitus. Among these parameters, ALT, ALP and GGT showed positive correlation with FPG and HbA_{1c} in both groups but AST showed no correlation with FPG and HbA_{1c}.

Key Words: Diabetes Mellitus, Serum Hepatic Enzymes

Introduction

Diabetes mellitus is a metabolic disorder characterized by the presence of hyperglycemia due to defective insulin secretion, defective insulin action or both. The long-term persistence of this disorder can cause susceptibility to specific complications and also foster artherosclerosis. Diabetes mellitus is associated with a broad range of clinical presentations, from being asymptomatic to ketoacidosis or coma, depending on the degree of metabolic derangements[1]. Diabetes Mellitus is the single most important metabolic disease, widely recognized as one of the leading cause of death and disability worldwide. The World Health

Organization estimated that the total number of people with DM is projected to rise from 171 million in 2000 to 366 million in 2030[2]. Distributive pattern of diabetes shows higher rates among people of developing countries. The world wide prevalence of DM in adults is expected to rise from 5.0% in 2003 to 6.2% in 2030. The largest proportional and absolute increase will occur in developing countries, where the prevalence will rise from 4.2% to 5.6% in 2030[3]. Diabetes mellitus is epidemic in many developing and industrializing countries. Nearly 80% of people with diabetes live in low and middle-income countries. China and India hold the first and second position having 98.4 and 65.1 million of total cases of DM respectively among adult populations (20 to 79 years) in 2013[4]. As apart of South-East Asia, in Bangladesh the magnitude of DM is also rising. Type 2 diabetes mellitus is characterized by three biochemical abnormalities: peripheral insulin resistance, impaired insulin secretion and excessive hepatic glucose production. The pancreatic Beta cell dysfunction is thought to be primarily responsible for the progression of T2DM[5]. The reduced insulin secretion resulting from Beta cell dysfunction is assumed to be the most direct and most important cause of clinical hyperglycemia. It has been reported that the Beta cell capacity is relatively low in Asian people compared to those of Western individuals[6]. Therefore, it is assumed that insulin secretory dysfunction may play a more important role in the progression of DM in our population[7].

The liver enzymes ALT, AST, ALP and GGT are routinely used in the evaluation of liver function. Serum AST and ALT levels are considered as the markers of hepatocellular health, whereas serum ALP and GGT level indicates biliary tract obstruction. Increased activities of liver enzymes such as AST, ALT, ALP and GGT are the indicators of hepatocellular injury and cholestasis. Increased activity of these markers is associated with T2DM[8]. Elevated ALT level may be considered as a consequence of hepatocyte damage due to NAFLD. This may further enhance fatty infiltration and decreased hepatocyte integrity. Alanine aminotransferase (ALT) might also be upregulated as a compensatory response to the impaired hepatic insulin signaling or alternatively, may leak more easily out of the hepatocytes because of fatty infiltrations and subsequent damage[9]. Aspartate aminotransferase (AST) is present in tissues of the liver, heart, skeletal muscles, kidneys, brain, pancreas, lungs and in white and red blood cells. The association between serum AST and T2DM has been controversial but a recent meta analysis suggested that elevated AST is associated with increased risk of T2DM after controlling for potential confounding factors[10]. Alkaline phosphatase (ALP) is a hydrolytic enzyme serine protease acting optimally at pH 10. T2DM subjects may also exhibit elevated ALP. Hepatosteatosis and insulin resistance in T2DM subjects may be responsible for this elevation[11,12]. Elevation of GGT is a marker of the presence of insulin resistance. An elevation of GGT is closely related to hepatic steatosis. Excess fat in the liver may enhance oxidative stress, leading to over consumption of GSH (Glutathione) with a compensatory increase in GGT synthesis. A higher GGT production could be secondary to a low-grade hepatic inflammation induced by hepatic steatosis[13]. Therefore, this study is aimed to find out the association of liver enzymes with T2DM patients in Bangladesh.

Materials and Method

This cross-sectional study was conducted in the Department of Biochemistry, Dhaka Medical College, Dhaka from July' 2015 to June' 2016. A total number of 100 study subjects attending in OPD of the Department of Endocrinology and Metabolism, DMCH were selected purposively. Among them 50 diagnosed cases of T2DM were selected as cases with a age range 30 to 60 years

(Groups-A) and 50 age-matched apparently healthy subjects were taken as controls (Groups-A). Type 2 DM patients with pre-existing chronic kidney disease, chronic liver disease, chronic obstructive pulmonary disease, smokers, alcoholics and having acute infectious diseases were excluded from the study by history, clinical examination and relevant laboratory investigations. With all aseptic precautions, after an overnight fast, blood sample was collected from all the study subjects for estimation of HbA1c, FPG, serum ALT, serum AST, serum ALP and serum GGT. Statistical analysis was performed by using the SPSS version21. All data were processed to compute mean and standard deviation. Difference of mean between two groups were compared by unpaired Student's 't' test. Determinations of correlation between variables were done by Pearson's correlation coefficient (r) test. For all statistical analysis $p < 0.05$ was considered as significant.

Results

In this cross-sectional study, 50 diagnosed T2DM patients and 50 apparently healthy subjects were enrolled on the basis of their clinical and laboratory diagnostic criteria. Table I shows general characteristics of the study population in both groups. The age, gender and BMI were matched between Group A and Group B.

Table-I: General characteristics of the subjects in both groups (n = 100)

Parameters	Group A (n=50)	Group B (n=50)	p value
Age in years	35.26±9.5	34.3±8.7	0.604
mean±SD range	(30- 60)	(30-60)	
BMI in kg/m^2	28.3 ±4.08	27.4±3.55	0.104
mean±SD range	(20.34 - 37.5)	(19.3-36.7)	
Gender	n (%)	n (%)	
Male	28 (56%)	26 (52%)	0.68
Female	22 (44%)	24 (48%)	

Level of significance at p value < 0.05

Table II shows the mean values of hepatic enzymes levels in both groups. Mean(±SD) ALT, AST, ALP and GGT levels were significantly ($p < 0.05$) higher in Group A than that in Group-B.

Table-II: Hepatic enzymes of the subjects in both groups (n =100)

Parameters	Group A (n=50)	Group B (n=50)	p value
Serum ALT (U/L) Mean±SD (range)	46.28±11.81 (25.83-68.94)	29.54±8.56 (13.38-48.32)	<0.001^s
SerumAST(U/L)	28.17±10.08	24.54±6.89	<0.05^s
Mean±SD (range)	(16.7-40.78)	(7.01-41.82)	
Serum ALP (U/L)	118.26±16.08	96.68±14.36	<0.001^s
Mean±SD (range)	(79.03-152.13)	(65.35-127)	
Serum GGT (U/L)	36.98±10.08	23.82±6.98	<0.001^s
Mean±SD (range)	(11.71-60.81)	(10.51-36)	

Table III shows the correlation of FPG with ALT, AST, ALP and GGT. Pearson's correlation coefficient (r) test was performed to compare relationship between parameters. ALT and GGT positively correlated with FPG in both groups but this correlation was significant in Group A only. ALP positively correlated with FPG in both groups but not significantly. AST revealed no correlation with FPG in both groups.

Table-III: Correlation of FPG with serum ALT, AST, ALP and GGT

		Group			
		Group-B		Group-B	
		r value	p value	r value	p value
FPG vs.	ALT	0.285	<0.05^s	0.240	0.093^{ns}
	AST	0.035	0.809n^s	0.052	0.719^{ns}
	ALP	0.186	0.195n^s	0.167	0.246^{ns}
	GGT	0.312	<0.05^s	0.244	0.087^{ns}

Table IV shows the correlation of HbA_{1c} with ALT, AST, ALP and GGT. Pearson's correlation coefficient (r) test was performed to compare

relationship between parameters. ALT and GGT positively correlated with HbA1c in both groups but this correlation was significant in Group A only. ALP positively correlated with HbA_{1c} in both groups but not significantly. AST revealed no correlation with HbA1c in both groups.

Table-IV: Correlation of HbA_{1c} with serum ALT, AST, ALP and GGT

		Group			
		Group-B		Group-B	
		r value	p value	0.207	0.149^{ns}
HbA1c vs.	ALT	0.281	$<0.05^{s}$	0.032	0.825^{ns}
	AST	0.031	0.830^{ns}	0.143	0.321^{ns}
	ALP	0.167	0.246^{ns}	0.234	0.101^{ns}
	GGT	0.286	$<0.05^{s}$	0.207	0.149^{ns}

Discussion

The present study was undertaken to observe the association of serum hepatic enzymes with type 2 diabetes mellitus. For this purpose, a total number of 100 subjects were selected. Among them, 50 diagnosed type 2 DM subjects were considered as Group A and 50 age- matched apparently healthy individuals were included in Group B. Serum hepatic enzymes (ALT, AST, ALP and GGT) levels were estimated in all subjects to observe their hepatic enzyme status. In addition, fasting plasma glucose and HbA1c were also estimated to assess their glycemic status.

In the present study, the mean(±SD) age of Group A and Group B were 35.26±9.5 years and 34.3±8.7 years respectively. There were 28 males and 22 females in the Group A and 26 males and 24 females in the Group B. The mean(±SD) of BMI was 28.3±4.08 and 27.4±3.55 in the Group A and Group B respectively. The age, gender and BMI of all the subjects in both groups were matched in this study. Nannipieri *et al.*[14] also found similar findings in their study. In contrast, Tohidi *et al.*[15] found significantly higher BMI in T2DM subjects than healthy individuals in a nested case control study conducted on 10,368 Iranin subjects. Type 2 DM subjects had significantly ($p<0.001$) higher mean FPG than adult normal individuals. These findings were similar to the findings by several studies[15-18]. In this current study, mean(±SD) HbA_{1c} in Group A and Group B were 7.26±0.34% and 5.03±0.45% respectively. Mean(±SD) HbA_{1c} was significantly ($p<0.05$) higher in the Group A than that in that Group B. Similar finding were in several studies[16,17]. According to this study, mean(±SD) serum ALT level was 46.28±11.81 U/L and 29.54±8.56 U/L in the Group A and Group B respectively. Mean(±SD) ALT level was significantly ($p<0.05$) higher in type 2 DM subjects than that of healthy individuals. Serum ALT level was also found significantly higher in type 2 DM subjects by various researchers similar to this study[14,16-19]. Contrary to this, Nakanishi *et al.*[20] found no significant changes of serum ALT level in type 2 DM subjects.

Mean(±SD) serum AST was 28.17±10.08 U/L and 24.54±6.89 U/L in the Group A and Group B respectively in this study. Mean(±SD) serum AST level was significantly ($p<0.05$) higher in type 2 DM subjects than that of adult normal individuals. Several studies also found significantly higher serum AST levels in T2DM subjects similar to present study[14,15,16,18,21]. In contrast, Nakanishi *et al.*[22] found no significant relation of serum AST with type 2 diabetes mellitus. In the present study, the mean serum ALP level was 118.26±16.08 U/L and 96.68±14.36 U/L in Group A and Group B respectively. Mean serum ALP level was significantly ($p<0.05$) higher in type 2 DM subjects when compared to adult normal individuals. Previous studies also found significantly higher serum ALP level in T2DM subjects in accordance with present study[14,17,18,20]. On the other hand, Nakanishi *et*

al.[20] found no significant association of serum ALP with type 2 diabetes mellitus. It was found in this study that the mean serum GGT level was 36.98±10.08 U/L and 23.82±6.98U/L in Group A and Group B respectively. Mean serum GGT level was significantly ($p<0.001$) higher in type 2 DM subjects than that of adult normal individuals. Several researchers also found significantly higher serum GGT level in T2DM subjects than normal individuals which is in agreement with present study[14,16,17,21].

In this study, Pearson's correlation coefficient (r) test was done to observe the relationship of FPG with serum ALT, AST, ALP and GGT level in both groups. In both groups, FPG level showed positive correlation with ALT, ALP and GGT and the correlations were found significant with ALT and GGT ($p<0.05$) only in the Group A. No correlation was found between FPG level and serum AST level in both groups. Almost similar types of findings have been reported by several studies[14,16,22]. Nakanishi *et al*.[20] found significant association of fasting glucose with GGT only but no association with ALT, AST and ALP in a cohort study carried out on 2918 Japanese male workers. Al-Jameil *et al*.[16] found significant positive correlation of HbA1c with ALT and GGT and very weak positive correlation with AST in a case control study conducted in Saudi Arabia.

In conclusion the present study shows that higher levels of serum hepatic enzymes (ALT, AST, ALPand GGT) ware present in subjects with type 2 diabetes mellitus. Among these parameters, ALT, ALP and GGT show positive correlation with FPG and HbA_{1c} in both groups but AST show no correlation with FPG and HbA_{1c}. Routine estimation of serum hepatic enzymes might be beneficial in subjects with type 2 diabetes mellitus to predict the onset of liver dysfunction due to diabetes mellitus.

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