IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 13, Issue 1 Ver. VII. (Jan. 2014), PP 26-30
www.iosrjournals.org

Serum Acid Phosphatase Activity in Diabetes Mellitus

Sonam Tashi Dolma[1], Davina Hijam[1], David Gangte[1], Ng. Arunkumar[1], Abhishek Dubey[1], Asitava Roy[1], Heirangkhongjam Lakhipyari[1], T.h Ibetombi Devi[1]

[1]*Department of Biochemistry, Regional Institute of Medical Sciences, Imphal, Manipur, India-795004*

Abstract: *Lysosomal enzymes acid phosphatase show increase in diabetes mellitus and this is closely related to diabetic metabolic alterations. This was a cross- sectional study conducted on 50 diabetic subjects (25 patients with complications and 25 patients without complications) in RIMS hospital during the period from September 2010 to August 2012. Twenty five age and sex matched healthy individual were taken as controls. Glycosylated haemoglobin (HbA1c) was estimated by Fast Ion Exchange Resin Method. Acid Phosphatase was estimated by colorimetric kit method. The difference in the level of Fasting Blood Sugar(FBS), Postprandial Blood Sugar(PPBS) and HbA1c between control, diabetic groups without and diabetes with complication groups was significant statistically (P<0.001) indicating a poor control of glucose in the study group.*

There was a significant difference in the level of Acid Phosphatase in control, diabetic group without complication and diabetes with complication(2.03±0.73, 4.58±0.68, 8.61±1.05IU/L) respectively. The comparison of serum acid phosphatase level in male and female subjects in the study groups was insignificant. Statistically significant increase in serum acid phosphatase level was observed in the diabetes with complication compared to those without the complication (P <0.001). There was a significant positive correlation of acid phosphatase with fasting blood sugar, postprandial blood sugar and glycosylated haemoglobin. Acid phosphatase can be used as an index for the development, control of diabetes and prognosis of diabetic complications.

Key Words: *Acid phosphatase, Diabetes*

I. Introduction

Diabetes Mellitus is one of the most common non-communicable diseases globally, and is the fourth or fifth leading cause of death in most developed countries, with evidence that it is epidemic in many industrialised and developing countries.[1]It is a chronic disorder characterized by hyperglycaemia resulting from insulin deficiency and hyperglycaemia which has a high risk of developing complications for eyes, kidneys, peripheral nerves, heart and blood vessels.[2]

Lysosomal enzyme like acid phosphatase show change in diabetes mellitus. Human acid phosphatase is normally found at low concentrations. However, pronounced changes in their synthesis occur in particular diseases, where unusually high or low enzyme expression is seen as part of the pathophysiological process.[3] Different forms of acid phosphatase are found in different organs, and their serum levels are used as a diagnostic tool for many diseases. Acid phosphatase is nonspecific enzyme which cleaves many different phosphate esters. The exact biochemical role of acid phosphatase is somewhat obscure but is thought to be mainly a digestive enzyme.

Acid phosphatase is found to be elevated in diabetes mellitus. The higher activity of acid phosphatase found in vasculopathic diabetes would indicate that in these patients the activation process is not restricted to the enzymes capable of degrading mucopolysaccharides and gycloproteins which accumulate in the walls of diseased vessels, but also involves a variety of lysosomal hydrolases as a non specific phenomenon. Lysosomal enzymes activation in diabetes is also apparently linked to both the degree of metabolic decompensation and presence of vasculopathies [4]. On the basis of these considerations, the study was conducted to see the activitiy of serum acid phosphatase in diabetes with or without vasculopathies in Manipur where incidence of diabetes is very high and as no such study has been carried out before.

II. Aims And Objects

To estimate serum acid phosphatase in diabetic patients (with complications and without complications) and to compare the levels with that of controls

III. Materials And Methods

The study was Cross-sectional study carried out in the Department of Biochemistry in collaboration with the Department of Medicine, Regional Institute of Medical Sciences, Imphal, Manipur, India during the period from September 2010 to August 2012.

The study population consisted of 50 type 2 diabetes mellitus patients (25 without complication and 25 with complication: microvascular and macrovascular) greater than 18 years of age, irrespective of sex, caste and creed, and willing to participate from different areas of Manipur and attending Diabetic Clinic or admitted in the Medical ward of RIMS, Imphal were included in the study group. Another 25 age and sex matched healthy individuals free from any systemic disease were taken as control group.

Exclusion Criteria: Individuals suffering from carcinoma, chronic diseases like, rheumatoid arthritis, COPD, coronary artery disease, active MI, Pagets disease or hyperparathyroidism, diseases of blood cells, such as sickle cell disease or multiple myeloma were excluded from the study.

All the selected patients had given voluntary consent before start of the study. The study was done after obtaining the approval from Institutional Ethical Committee of RIMS.

A detailed history of the patients was taken. Personal history of smoking, consumption of alcohol, presence or absence of obesity and family history of diabetes, hypertension or coronary heart disease were also recorded.

Weight, height, body mass index (BMI) was measured once at the beginning of the study. BMI was calculated as weight (kg) divided by the square of the height (m^2).

Nephropathy was defined as proteinuria >1+ on dipstick with no abnormal findings on urinary examination. Neuropathy (peripheral) was defined as absent touch or vibratory sensations of the feet. Retinopathy was defined by presence of varying degrees of microaneurysms, haemorrhages, exudates, venous changes, new vessel formation, and retinal thickening. Patients with a history of CAD and stroke were taken as having macrovascular complication.

Four ml of fasting blood was collected by venipuncture from each patient and controls. About 2ml of blood was collected in plain vial for the estimation of acid phosphatase, about 1 ml in fluoride vial for the estimation of blood glucose. One ml of blood was collected in EDTA vial for the estimation of HBA1C. Another 2ml of venous blood was collected in fluoride vial after 2 hours of intake of normal meal to estimate the post prandial blood sugar. The blood sample collected in the plain vial was centrifuged immediately. All the tests were carried out on the same day. The chemicals and reagents used in the study were of analytical grades.

Fasting Blood glucose was estimated by GOD PAP Method[5] using Liquicolor Kit manufactured by HUMAN, Germany. HbA1c was estimated by Fast Ion Exchange Resin Separation Method as described by Goldstein DE, Little RR & Widdmayer HM.[6] by using Glycosylated Haemoglobin Test Kit manufactured by HUMAN WIESBADEN, Germany.Acid Phosphatase was estimated by the method of Hillmann G and Klin Z[7] using colorimetric kit manufactured by Human Company, Germany.

Reference Values

Total acid phosphatase			
Assay temperature	25°C	30°C	37°C
Men up to(IU/L)	3.6	5.0	6.5
Women up to (IU/L)	3.0	4.2	5.5

IV. Statistics

Statistical analysis was performed using SPSS 17 version statistical tests like χ^2-test, independent t-test, ANOVA (F-test) and correlation coefficient 'r' are applied whenever found suitable and necessary. The P-value less than 0.05 was considered significant.

V. Results

It was observed that the number of females was more than that of male in both the control group (60%) and diabetic without complications (52%) which is quite in contrast to diabetes with complications where the number of male (76%) was more than that of female (24%).

Thirty two percent of diabetic without complications belong to age group of 50 to 59 years and 60 to 69 years, followed by 20% in the age group of 40-49 years. In the diabetes with complication group, majority (36%) cases were in the age group of 60-69 years. Age expressed in mean ± SD in male and female control were 65.2 ± 8.44, 56.27 ± 5.93 and in diabetic without complication and diabetic with complication cases were 58 ± 9.4, 57.62 ± 13.5 and 63.68 ± 9.98, 59.17 ± 9.02 respectively, but these difference are not statistically significant (P>0.05), indicating that both groups are of comparable age.

TABLE I -Summary of biochemical data in control, diabetes and diabetes with complication groups (values expressed in terms of Mean ± SD)

Parameters	Control (n=25) Mean ± SD	Diabetes without complication (n=25) Mean ± SD	P-Value	Diabetes with complication (n=25) Mean ± SD	P-Value
Fasting BS (mg/dl)	89.12±6.24	126.68±15.70[a***]	<0.001	166.44±7.99[b***]	<0.001
Postprandial BS (mg/dl)	124.16±7.11	203.6±37.64 [a***]	<0.001	271.12±26.16 [b***]	<0.001
HbA1c (%)	4.78±0.27	9.57±1.34 [a***]	<0.001	12.71±0.99 [b***]	<0.001
Acid phosphatase (IU/L)	2.03±0.73	4.58±0.68 [a***]	<0.001	8.61±1.05 [b***]	<0.001

a: comparison between control and diabetes
b: comparison between control and diabetes with complication; *** P value <0.001

Table I shows that, the difference in the level of FBS, PPBS and HbA1c between control and study groups were significant statistically (P<0.001) indicating a poor control of diabetes in the study group. A statistically significant difference was detected in acid phosphatase levels between the three groups (P<0.001).

Table II-Mean ± SD of Acid Phosphatase Level categorized on the basis of sex

Study Subjects	Sex	Number (%)	Serum Acid Phosphatase level (IU/L)	P-value
=Control (n=25)	Male	10(40)	2.08±0.77	0.747
	Female	15(60)	1.98±0.73	
Diabetes without complication (n=25)	Male	12(48)	4.63±0.69	0.700
	Female	13(52)	4.53±0.69	
Diabetes with complication (n=25)	Male	19(76)	8.57±1.13	0.744
	Female	06(24)	8.73±0.85	

Table II shows that the comparison of serum acid phosphatase levels in male and female subjects in both the study groups and control group was insignificant.

Table III -Comparison of serum FBS, PPBS, HbA1c and acid phosphatase levels in diabetes without and with complication group

Parameter mean ± SD	Diabetes without complications (n=25)	Diabetes with complication (n=25)	P value
FBS (mg/dl)	126.68±15.70	166.44±7.99	< 0.001
Postprandial BS (mg/dl)	203.6±37.64	271.12±26.16	<0.001
HbA1c(%)	9.57±1.34	12.71±0.99	< 0.001
Acid Phosphatase (IU/L)	4.58±0.68	8.61±1.05	< 0.001

There was significant increase of FBS, PPBS and HbA1c (P<0.001) in diabetic with complication indicating a more poor control of blood sugar. (Table III). Statistically significant increase in serum acid phosphatase levels was observed in the diabetes with complication compared to those without the complication .

Table IV:-Distribution of diabetic cases by serum Acid Phosphatase levels

Serum Acid phosphatase (IU/L)	No. of diabetic cases (n=50)	Percentage (%)	Acid Phosphatase Level(Mean ± SD)
< 4.00	4	8%	3.7 ± 0.12
4.01-6.00	22	44%	4.73 ± 0.6
6.01-8.00	4	8%	7.68 ± 0.25
>8.00	20	40%	9 ± 0.4

Table IV show that 44% diabetic cases have serum acid phosphatase level in the range 4.01 – 6IU/L.

Table V-Correlation of serum acid phosphatase with age, diabetes duration, FBS, PPBS and HbA1c

Parameter	Control (n=25)		Diabetes without complications (n=25)		Diabetes with complications (n=25)	
	Correlation coefficient 'r'	P-value	Correlation coefficient 'r'	P-value	Correlation Coefficient 'r'	P-value
Age (yr)	0.088	0.677	0.182	0.383	0.133	0.527
Diabetes duration (yr)	------	------	-0.067	0.752	-0.101	0.630
Fasting BS(mg/dl)	0.271	0.190	0.720**	<0.001	0.445*	0.026
Postprandial BS (mg/dl)	0.186	0.373	0.590**	0.002	0.551**	0.004
HbA1c (%)	0.003	0.991	0.748**	<0.001	0.584**	0.002

**Correlation is significant at the 0.01 level; *Correlation is significant at the 0.05 level.

In diabetes group without complication and diabetes with complication group, here was a significant positive correlation of acid phosphatase with fasting blood sugar, postprandial blood sugar and glycosylated haemoglobin. (Table V)

VI. Discussion

In the present study, 52% of diabetics without complication were female and 48% were males. This finding is consistent with the statement that type 2 diabetes mellitus is more common in women.[8] Seventy six percent of diabetes with complication cases were males and 24% were females . This is consistent with the findings of **Ho Y et al[9]** who reported the occurrence of diabetes mellitus more in males (0.95%) than in females (0.20%).

In the present study, the mean FBS levels in diabetes without complications and diabetes with complications were 126.68±15.70 and 166.44±7.99 when compared to controls. These differences were statistically significant (P<0.001) and consistent with the reports given by **Verma M et al[10]** and **Akinloye OA et al**.[11] The PPBS levels in both the study groups were significantly high when compared to control. This finding is consistent with the findings of **Fahmy E et al**.[12]

HbA1c was increased in diabetic compared to control, and further increase in HbA1c was observed in diabetic patients with complication when compared to control, which is a sign of poor glycemic status as described by **Selvin E et al**[13]and **Nakamura K et al**.[14] In diabetic patients, concentration of HbA1c is elevated as much as two fold (**Gabbay KH et al**)[15] and decreases with improvement of glycemic control.

The serum acid phosphatase level was increased significantly (P<0.001) in diabetic when compared to control. This finding is in agreement to the findings of **Agoda** and **Glew**[16] who found elevated activity of acid phosphatase in diabetes mellitus. When comparison was done between diabetes with and without complication group, a statistically significant increase was found in diabetes with complication group . The increased activity of this enzyme in dibetes may be a result of diabetes-induced damage to the tissues.[17] One of the possible explanations for this relation could be that the insufficient influx of glucose into cells owing to the lack of insulin led to the decreased synthesis of adenosine triphosphate (ATP). In laboratory models a transient decrease in ATP was accompanied by the apoptosis of macrophage and fibroblast, i.e., by the release of acidic hydrolases into the serum. It was found that, 44% diabetic cases had serum acid phosphatase level in the range 4.01 – 6IU/L, 40% cases had acid phosphatase level > 8IU/L. 8% diabetic cases had acid phosphatase level < 4IU/L (Table IV).

The serum acid phosphatase level was also increased significantly (P<0.001) in diabetes with complication group when compared to diabetic group without complications. This finding is in agreement to the findings of **Belfoire F et al**[18] who reported that an increase was moderate in uncomplicated diabetics with slightly elevated glycaemia, while it was accentuated in diabetic with either vasculopathies or marked hyperglycaemia.

In diabetes without complication group and diabetes with complication group, there was a significant positive correlation of acid phosphatase with fasting blood sugar and postprandial blood sugar in both the study groups (P<0.001). This finding is in agreement to the findings of **Agoda** and **Glew** [16] who found that elevated activity of acid phosphatase correlated with blood sugar concentration. There was also a significant positive correlation of acid phosphatase with glycosylated haemoglobin in both the study groups (P<0.001).

VII. Conclusion

A statistically significant difference was detected in acid phosphatase levels between control and diabetic without complication (P<0.001) and control and diabetes with complication groups (P<0.001). Also statistically significant increase in acid phosphatase levels were observed in the diabetes with complication

when compared to those without the complication group (P <0.001). Increase levels acid phosphatase results from exocytosis in hyperglycemia leading to the release of these enzymes in the serum from the cells.

On the basis of all the results, it can be concluded that the increase activity acid phosphatase was the consequence of poor metabolic control and increased exocytosis resulting from hyperglycaemia. Therefore, acid phosphatase can be used as an index for the development and prognosis of diabetic complications. Serum acid phosphatase levels along with HbA1c may give earlier and sensitive indication of the success achieved by the patient in controlling their diabetic condition.

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