Evaluation of Serum α-Amylase Activity in Sudanese Patients with Chronic Renal Failure

Khalid S. Elnour[1], Adil Mahgoub[2], Salah Bahroun[3], and Altayeb Elazomi[1].
[1]DEPARTMENT OF Medical Laboratories, Faculty of Medical Technology, Zawia Univeristy,
[2]Sudan University of Science and Tecnology, [3]National Medical Research Centre, Zawia, Libya.

Abstract

The serum enzymes of patients with end-stage renal disease (ESRD) are commonly abnormal. This is due in part to the absence of renal excretion and to the frequent presence of multiple comorbid conditions. Since the diagnosis of many diseases is based upon the detection of elevated levels of these enzymes, the accurate clinical assessment of the patient with ESRD is hampered by a paucity of knowledge concerning the serum concentrations of different enzymes in various disease states. This study was conducted to essentially investigate status of serum α-amylase in Sudanese patients of chronic renal failure (CRF) with special reference to the effects of diabetes mellitus. A non randomly selected group of 50 patients with chronic renal failure (31 male, 19 female) with mean age of 46 ±1.6 year, undergoing regular haemodialysis, visiting Khartoum Renal Dialysis centre (KRDC), an Sudanese Transplanted Kidney Association Medical center (STKA). A total number of 25 healthy volunteered individuals as a control group (16 male, 9 female) with mean age of 37.4 ±2.5 year. Blood specimens were collected from all groups (n, 75), and level of serum α –amylase, creatinine, urea whereas glucose were determined. Statistical analysis was done, using SPSS package descriptive and comparing different parameters between groups of patients and control. The study indicates a significant increase (P= 0.00) in α-amylase levels of chronic renal failure patients when compared with control group, as a significant difference in serum α-amylase level was similarly confirmed within subgroups of patients(diabetics & non-diabetics) and control group; the level of α-amylase in group of diabetics was less than non-diabetics group (P= 0.008). Serum α-amylase is significantly correlated with creatinine and duration of diabetes mellitus (P= 0.31), (P= 0.008), respectively unlike blood glucose level, age, and duration o f chronic renal failure.

***Keywords*—**CRF, Diabetes mellitus, α-amylase

Introduction

End stage renal failure (ESRF) has become a major health problem in Sub Saharan Africa (SSA). There were limited data about causes of ESRF in the Sudan.Chronic renal failure is defined as the clinical condition resulting from chronic derangement and insufficiency of renal excretory and regulatory function (uremia).[1,] [2]It can range from mild dysfunction to severe kidney failure; progression may continue to an end-stage renal disease (ESRD).[3] In United States about 50000 cases of ESRD per year as hypertension cause about 23% of ESRD cases. Diabetes is therefore considered as the most common contributor to ESRD (relative risk~13 fold).[4]The causes of CRF in Sudan are chronic glomerulonephritis, obstructive nephropathy (stone disease), hypertension and diabetes mellitus in that order.[5] Recent study in Sudan reported that hypertension is a leading cause of ESRD in

Sudan followed by chronic glomerulonephritis. Hypertension and diabetes mellitus are the leading causes of ESRF among patients over 40 year's old.[1]The serum enzymes of patients with end-stage renal disease (ESRD) are commonly abnormal. This is due in part to the absence of renal excretion and to the frequent presence of multiple co morbid conditions. Since the diagnosis of many diseases is based upon the detection of elevated levels of these enzymes, the accurate clinical assessment of the patient with ESRD is hampered by a paucity of knowledge concerning the serum concentrations of different enzymes in various disease states.[6] small amounts of pancreatic digestive enzymes normally leak into the circulation, but in acute pancreatitis, the circulating levels rise markedly. Measurement of plasma amylase or lipase concentration is therefore of value in diagnosing the disease[7]. Twenty percent of pancreatic enzymes are excreted by the kidneys. Thus, patients with end stage renal disease (ESRD) has elevated levels of serum pancreatic enzymes.[8] Amylase is filter through the glomerular membrane and reabsorbed in the proximal tubule. In healthy individuals, the amylase clearance parallels creatinine clearance. During acute pancreatitis, there is an increase in amylase clearance opposed to creatinine clearance. Although this ratio was one thought to be specific to acute pancreatitis, other condition that produced hyperamylasemia (such as diabetic ketoacidosis, burns, renal failure, and perforated duodenal ulcer) may demonstrate a similar elevation.[9] In macroamylasemia amylase molecules form large polymers they cannot pass thorough the glomerular membrane. This harmless condition may be confused with other causes of hyperamylasemia whereas high plasma amylase is due to a low renal excretion of enzyme, despite normal glomerular function.[10] Hyperamylasemia is common finding in chronic renal failure (CRF) patients. It has been suggested that the diagnosis of acute pancreatitis in these patients is confirmed when serum amylase activities are greater than three times the upper limits or the presence of pancreatic enzymes in peritoneal fluid may suggest coexistent pancreatitis.[11. 12, 13]Diabetes mellitus is a group of chronic metabolic disorder which is associated with hyperglycemia.[14, 15] More than 150 million worldwide suffers diabetes according to recent WHO estimates.[16] The incidence of diabetes mellitus is increasing rapidly, and it estimated that by the year 2025 this number will double in the more developed countries. In Sudan, diabetes mellitus is common medical problem with considerable morbidity and mortality, according to Federal Ministry of Health, the diabetes patients seeking treatments constituted 1-2.5% of the total population.[17`] It is caused by a derangement in the secretion or function of the endocrinal portion of the pancreas. There is a close anatomical and functional relationship between its exocrine and endocrine portions. Previous study, reported that in type 2 Diabetes mellitus, wherever the blood glucose level was higher, the serum amylase activity was found to be significantly lower.[14]For the last decade, low serum amylase (hypoamylasemia) has been reported in certain common cardiometabolic conditions such as obesity, diabetes (regardless of type), and metabolic syndrome, all of which appear to have a common etiology of insufficient insulin

action due to insulin resistance and/or diminished insulin secretion.[18]

Materials and Methods

A total of 50 patients with chronic renal failure (31 male, 19 female) with mean age of 46 ±1.6 year, undergoing regular haemodialysis, visiting Khartoum Renal Dialysis centre (KRDC), an Sudanese Transplanted Kidney Association Medical center (STK), were randomly selected. A total number of 25 healthy volunteered individuals as a control group (16 male, 9 female) with mean age of 37.4 ±2.5 year was involved to this study for comparison. Group of patients divided to two groups: one is non-diabetic group (n, 36) and other is diabetic group (n, 14). Patients with any symptoms of pancreatitis, or abdominal pain were excluding from the study. The objectives and procedures were verified to all subjects and patients as they express their consent willingness to contribute to this study. Venous blood samples were collected for the patients before dialysis, and also for control subjects. α- amylase activities were determined by commercial kit by using (CNP-G3 substrate) from Linear Chemicals Ltd Barcelona- Spain, using spectrophotometer (Jenway 6305 U/V-vis-German). Glucose level s was determined by commercial kit by using (GOD-PAP Method) from Crescent Diagnostics, Jeddah- Saudi Arabia, using spectrophotometer (Jenway 6305 U/V-vis-German). Urea level s was determined by commercial kit by using (Berthelot Method) from Crescent Diagnostics, Jeddah- Saudi Arabia, using spectrophotometer (Jenway 6305 U/V-vis-German). Creatinine level s was determined by commercial kit by using (Jaffe Reaction) from Crescent Diagnostics, Jeddah- Saudi Arabia, using spectrophotometer (Jenway 6305 U/V-vis-German). Statistic analysis was carried out using SPSS, Ver. 10.5 (SPSS Inc. Chicago, IL, USA). The as data obtained was expressed as mean± SD. Analysis of Variance (Tukey HSD) and Pearson test was used to correlation determine whether difference between the means were significant, with $P<0.05$ and $P<0.01$ respectively taken as the significant level.

RESULT

Demographic features of chronic renal failure patients and control with duration of CRF and diabetes are summarized in Table I. Biochemical Findings for Test group and Control group are given in Table II. Serum α-amylase in study groups are given in Table III. Correlation of serum α-amylase level, with duration of CRF, and duration of diabetes was given in Table IV. Table II indicate that α-amylase, creatinine, urea, and glucose level has significantly increase in test group (n, 50) when compared with control group (n, 25) (P=0.00, 0.00, 0.00, and 0.002) respectively. Mean ± SD: (101.10±9.96) U/L versus (37.40±3.37) U/L. Interestingly, in Table III the analysis of variance (ANOVA), verified that α-amylase had been significantly reduced in subgroup of DM CRF when compared

with NDM CRF subgroup (P=0.008). According to correlation analysis, α-amylase level appeared to be affected neither by age nor the duration of chronic renal failure as shown in Table IV. However, α-amylase level appeared to be affected significantly by duration of diabetes mellitus (2-tailed=0.008).

Variable	test group n=50	Control group n=25
Age(years)	46±1.6 (20.00-60.00)	37.4±2.5 (22.00-62.00)
sex	(31 male, 19 female)	(16 male, 9 female)
Duration of CRF(months)	20.74±3.16. (1.00-144.00)	0
Duration of diabetes (years)	6.6±00 (1.00-15.00)	0

Table I: Demographics Features of Test group and the Control group

Study groups	**test group (N, 50)**			**Control (N, 25)**			P value
Biochemical variable	**Mean**	**±S.E**	**Range**	**Mean**	**±S.E**	**Range**	
α-amylase (U/L)	101.10	9.96	27.00-502.00	37.40	3.37	13.00-81.00	0.00
Creatinine (mg/dl)	9.81	0.47	2.40-18.00	0.71	2.3E-02	0.60-0.97	0.00
Urea(mg/dl)	125.1	6.26	74.00-298.00	18.48	1.450	10.00-37.00	0.00
Glucose (mg/dl)	153.18	12.15	70.00-411.00	96.36	4.30	62.0-162.00	0.002

Table II: Comparison of Biochemical Findings for Test group and Control group

Study groups		Sig.	95% Confidence Interval	
			Lower bound	Upper bound
DM CRF	NDM CRF	0.008*	-98.0793	-12.3780
	NDM Control	0.456	-22.6152	68.2767
NDM CRF	DM CRF	0.008*	12.3780	98.0793
	NDM Control	0.000*	43.6506	112.4683
NDM Control	DM CRF	0.456	-48.2767	22.6152
	NDM CRF	0.000*	-112.4683	-43.6506

Table III : Analysis of Variance (Tukey HSD) of serum α-amylase in study groups

***The mean difference is significant at the 0.05 level**

Variable	**Pearson correlation**	**Sig. (2-tailed)**

CRF duration	0.080	0.489
DM duration	0.416	0.008*
Age	0.641	0.055
S.creatinine	0.305	0.031*

Table IV: Correlation of serum α-amylase level, with duration of CRF, duration of diabetes, S.creatinine, and age. **Correlation is significant at the 0.01 & 0.05 level (2-tailed)

Discussion

Chronic renal failure is common health problem in Sudan. The disease is mostly caused as result to long-standing diabetes or hypertension. Other minor causes are glomerulonephritis, kidney stones, polycystic kidney disease, Alport syndrome, reflux nephropathy, infections, obstructive uropathy, and analgesic nephropathy.[1]Brancati et al[19]reported that diabetes mellitus and hypertension account for approximately two third of the cases of chronic renal failure and end stage of renal disease (ESRD). In previous study, Abboud[20] noted that renal calculi was being the second commonest cause of CRF in the Sudan, but were rare in European countries. Also diabetes mellitus was a much commoner cause of CRF in Sudan than Europe. In present study, about 76% of the patients were hypertensive, and about 26% were diabetics. In present study, majority of the patients had an age over 40 years (75%), but only 10% had an age less than 30 year. Anderson and Brenner[21]noted that after age 30 year progressive physiological glomerulosclerosis, with glomerular filtration rate (GFR) and creatinine clearance falling linearly at rate of approximately 8m/min/1.73mm/year. This study showed a significant increase of the level of α- amylase, despite absence of signs of acute pancreatitis or any abdominal pain, so the hyperamylasemia resulted from impairment of renal function, where 20% of α- amylase is filtered through the glomerular membrane. In healthy individuals, the amylase clearance parallels creatinine clearance.[8, 9]many studies observed this trend.[11,12,13,14] According to this study, highest level of creatinine was recorded in non diabetic patients, but there was no difference in the level of blood urea between the patients groups. Analysis of serum α- amylase (in present study), revealed that 46% of patients (23 of 50) had hyperamylasemia (α- amylase>90U/l). In previous study, Thierry et al [22]noted that serum α- amylase activity was significantly increased in 68% of the patients of the study. Of special interest this study emphasized that α-amylase affected by the combination of two factors (CRF & DM), the highest level was recorded in non-diabetics with chronic renal failure patients (114±13U/L), as a diabetics with chronic renal failure had a mean of 62.8±7.4U/L (P= 0.008). No significant difference (P=0.233) between diabetic group and control group (42±5 U/L), (37.40±3.37) respectively. Combination of two factors (CRF & DM) keeps serum α- amylase level in its normal values, where in diabetes level of α-

amylase decreased, in contrast to this in CRF level of α- amylase increased. In this study investigations showed a correlation between α- amylase level and serum creatinine concentration (P= 0.035). Montalto et al[23] conducted a study on chronic renal failure patients and concluded that a statistically significant correlation was found between α- amylase vs. creatininemia values in CRF patients, but only up to a certain level (creatininemia <6mg %), above which there was no correlation. Yosif et al[24]noted that serum α- amylase level was increased in diabetics, but adversely other studies documented that a remarkable reduction in serum α- amylase level was recorded in diabetics patients.[18,25,26]In present study we also observed the last trend. Interestingly, serum α- amylase level appeared to be significantly correlated with duration of disease (diabetes mellitus). In this study, a remarkable decrease in enzyme level in patients with long- standing diabetes was shown.

References

[1] Amin S.I, Banga, Elaf B. Mohammed, et al. causes of end stage renal failure among haemodialysis patients in Khartoum State/Sudan. BMC Res Notes. 2015 Sep 29; 8: 502. [PMC free article] [Pub Med] https://doi.org/10.1186/s13104-015-1509-x

[2] Merk et al. The Merk Manual of Diagnosis and Therapy; 1995

[3] De Bore ME, Elseviers MM. Analgesic nephropathy. N Engl J Med. 1998 Feb 12; 338(7):446-452. https//www. DOI:10.1056/NEJM199802123380707

[4] Klag MJ, Whelton PK, Randall BL, Neaton JD, Brancati FL, Stamler J. End-stage renal disease in African- American and white men. 16-year MRFIT findings. JAMA. 1997 Apr 23; 277(16):1293-8. *https://www.ncbi.nlm.nih.gov/pubmed/9109467*

[5] Osman EM, Abboud OI, Danielson BG. Chronic renal failure in Khartoum, Sudan. Ups J Med Sci 1987; 92 (1):65-73. [PubMed] https://www.ncbi.nlm.nih.gov/pubmed/3035772

[6] Neil S Sanghani, Ramesh Soundararajan, Thomas A Golper. Serum enzymes in patients with renal failure. UpToDate [Homepage on the Internet]. Wolter Kluwer; [updated: Jan 15, 2016. cited Feb 2018]. Available from: https/www. Uptodate.com/index

[7] William F. Ganong. Review of Medical Physiology. Exocrine portion of the pancreas. 18th edition .Middle East: 1997: p 464-465.

[8] Jiang CF, Ng KW, Tan SW, Wu CS, Chen HC, Liang CT, Chen YH. Serum level of amylase and lipase in various stages of chronic renal insufficiency. Zhonghua Yi Xue Za Zhi (Taipei). 2002 Feb; 65(2): 49-54. [PubMed]

[9] Thomson A.R.R. first principles of gasteroenterology. Pancreatic function. 8th edition: 1999: p 405-408.

[10] Zilfa J.F, Pannall P.R, Mayne PD. Clinical chemistry in diagnosis and treatment, plasma enzymes in diagnosis. 6th edition. New York: Worth; 1994: p 300-312.

[11] Tsianos EV, Dardawaris MA, Elisa FM, Vaskos S, Siamopoulos KC. The value of alpha- amylase and isoamylase determination in chronic renal failure. Int J Pancreto. 1994; 15(2): 105-11.

[12] Stanescu A, Mayer D, Rosenthal J, Malfer Hewier P, Leber Magen Darm. Effect of chronic renal failure and hemodialysis on the pancreas-specific enzyme pattern in the serum. 1990; 2(2): 83-9.

[13] Royse VL, Jensen DM, Corwin HL. Pancreatic enzymes in chronic renal failure. Arch Intern Med. 1987 Mar; 147(3):537-9.

https://www.ncbi.nlm.nih.gov/pubmed/2435254

[14] Yadav R, BhartiyaJP, Verma SK, Nandkeoliar MK. The evaluation of serum amylase in the patients of type 2vdiabetes mellitus, with possible correlation with pancreatic function. J Clin Diagn Res. 2013 Jul 1; 7(7): 1291-4

https/www.doi:10:78860/JCDR/2013/6016-3120
[15] Michael L. Bishop, Edward P, Larry E. clinical chemistry techniques, principles, correlations. 4th edition. USA: Lippincott Williams; 2000.p215-231.
[16] World Health Organization, Department of Non communicable Disease Surveillance. Diagnosis and classification of Diabetes Mellitus and its complication. [homepage on the Internet]. Geneva: WHO; 1999: 5-36.
[17] Elbagir MN, Eltom MA, Elmahadi EM, Kadam IM, Berne C. A population study of prevalence of diabetes and impaired glucose tolerance in adult in Northern Sudan. Diabetes Care. 1996 Oct; 19(20): 126-128. [PubMed]
[18] Kei Nakajiama. Low serum amylase and obesity in diabetes and metabolic: a novel interpretation. World J Diabetes. 2016 Mar 25; 7(6): 112-121. [PubMed]
https/www.doi:10:4239/wjdv7-i6.112
[19] Brancati FL, Whelton PK, Randal BL, Neaton JD, Stamler J, Klag MJ. Risk of end -stage renal disease in diabetes mellitus: a prospective cohort study of men screened for MRFIT. Multiple Risk Factor Intervention Trial. JAMA. 1997; 278(23): 2069-2074.
http://www.nature.com/hr/journal/v31/n8/full/hr2008200a.html
[20] Abboud OI, Osman EM, Musa AR. The aetiology of chronic renal failure in adult Sudanese patients. Ann Trop Med Parasitol. 1989; 83(4):411-414.
http://www.tandfonline.com/doi/abs/10.1080/00034983.1989.11812365
[21] Anderson S, Brenner BM. Effect of aging on the renal glomerulus. Am J Med. 1986 Mar; 80(3): 435-42. *https://www.ncbi.nlm.nih.gov/pubmed/3513560*
[22] Thiery FX, Dueymes JM, Vernier I, Fauvel J, Meeus F, Meurisse JJ, Pene C, Conte JJ. Serum lipase and amylase levels in chronic renal failure: interpretation of results--effect of external purification. Nephrologie. 1988; (6):263-7.
https://www.ncbi.nlm.nih.gov/pubmed/2467218
[23] Montalto G, Carroccio A, Sparacino V, Lorello D, Di Martino D, Soresi M, Galione A, Notarbartolo A. pancreatic enzymes in chronic renal failure and transpklant patients. Int J Pancreatol. 1992; 12(3): 211-7.
[24] Yousif MA, Ahmad M. heterogeneity of amylase in diabetes mellitus. J Pak Med Assoc. 1997; 27(9): 393-4.
[25] Aughsteen AA, Abu-Umair MS, Mahmoud SA. Biochemical analysis of serum pancreatic amylase and lipase enzymes in patients with type 1 and type 2 diabetes mellitus. Saudi Med J. 2005 Jan; 26(1):73-7. https://www.ncbi.nlm.nih.gov/pubmed/15756357
[26] Rakhee Yadav, Jai Prakash Bhartiya, Sunil Kumar Verma, Manoj Kumar Nandkeoliar. The Evaluation of Serum Amylase in the Patients of Type 2 Diabetes Mellitus, with a Possible Correlation with the Pancreatic Functions. J Clin Diagn Res. 2013 Jul; 7(7): 1291–1294.
https://www. doi: 10.7860/JCDR/2013/6016.3120