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SERUM AMYLASE IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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ABSTRACT

Introduction: Chronic kidney disease is a progressive loss in renal function over period of many months or years. There is decline in nephron function and number generally quantitated as reduction in glomerular filtration rate. As the GFR declines there is accumulation of metabolic end products excreted by Kidney. Amylase is one of enzyme that is rapidly excreted by kidney, thus patients in chronic kidney disease have elevated serum pancreatic enzymes.

Aims and Objectives: The aim of present study was to determine changes in serum total amylase levels in patients with end stage renal disease on hemodialysis and non dialysed chronic kidney disease patients.

Material and Method: Fifty patients with end stage renal disease coming for hemodialysis and fifty non dialysed chronic kidney diseases on outpatient follow up were included in this study. Fifty age and gender matched healthy individuals were included as control group. Blood samples were collected from patients as well as controls and were analysed for amylase, urea and creatinine using a fully automated analyzer. The results were analyzed statistically using student "t" test.

Result: Present study has showed that serum total amylase levels were significantly higher in end stage renal disease and chronic kidney disease patients as compared to healthy controls (p value <0.001). Serum total amylase levels was above the upper limit in sixty percent of patient and more than twice of upper limit in ten percent of patients.

Conclusion: From our study it was concluded that in end stage renal disease and chronic disease patients, serum total amylase levels was found to be elevated. Serum amylase alone as a diagnostic tool in recognising acute pancreatitis leads to false positive results. Hence interpretation of elevated amylase in chronic kidney patients has to be supported by other laboratory and clinical evidence.

Keywords: End stage renal disease, chronic kidney disease, serum amylase

INTRODUCTION

Chronic kidney disease (CKD) is associated with the decreased glomerular filtration rate over period of months to years. In the later stages of CKD, the glomerular filtration falls drastically eliding to the accumulation of metabolic end products. There is decline in nephron function and number generally

quantitated as reduction in glomerular filtration rate ⁽¹⁾

Chronic kidney disease is identified by blood tests, creatinine and urea are two such substances routinely measured.

The National kidney foundation proposed a new classification system to classify chronic kidney disease in five stages, this system is known as

Kidney disease outcome quality initiative (KDOQI)

Stage I being mildest with GFR 60 to 90 ml/min, Stage II is with GFR between 45 to 59 ml/min, Stage III patients having GFR of 30 to 44 ml/min, Stage IV are patients with GFR of 15 to 29 ml/min and stage 5 are patients with GFR of less than 15 ml/min. Patients with advanced CKD (Stage III, IV and V) have profound impaired GFR and accumulation of metabolic end products. End stage renal disease (ESRD) is group of patients on maintenance hemodialysis for CKD and requires dialysis to sustain life⁽²⁾

Amylase is one of the enzyme that is produced by exocrine pancreas and salivary gland that hydrolyses starch is rapidly cleared by kidney. Twenty percent of pancreatic enzymes is excreted by the kidney thus patients with end stage renal disease have elevated levels of serum pancreatic enzymes. The serum amylase and lipase are elevated in patients with end stage renal disease in absence of pancreatitis^(3,4,5). The highest levels of amylase and lipase are noted in advanced CKD patients but marked elevations can also be seen in patients undergoing peritoneal dialysis^(6,7). In one of study by Montalto et al found increase in serum pancreatic enzyme during chronic renal pathology is slight but frequently occurs⁽⁸⁾.

The purpose of this study was to evaluate the changes of serum amylase levels in patients with end stage disease on hemodialysis and non dialysed chronic kidney disease patients in the Indian subcontinent.

METHODS

Study subjects

100 patients of age group between 18 to 70 years of either gender were enrolled in the study.

They were divided in to two groups as follows

(1) 50 patients with ESRD coming for maintenance hemodialysis to the department of nephrology.

(2) 50 nondialysed Chronic Kidney Disease patients on outpatient follow up.

Study controls

Control group comprised of 50 healthy voluntary adults in the Rajarajeswari medical college.

All patients and subjects showed no evidence of pancreatitis, alcoholic liver disease, acute infections and patients with HbsAg/Hcv positive and they were not on medications which may lead to pancreatitis.

Informed consent was obtained from these subjects. The study was approved by the institutional human ethical committee

SAMPLING

Blood samples (4ml) were drawn with proper aseptic precautions from these subjects using vacutainers containing clot activators. The blood was allowed to clot, centrifuged and serum was used to perform biochemical analysis on the same day.

ANALYSIS

I. Serum creatinine levels were estimated using modified Jaffes method.

II. Blood urea was estimated using Urease – GLDH (Glutamate Dehydrogenase) method.

Above parameters were estimated in hospital laboratory using fully automated analyser.

ESTIMATION OF AMYLASE

The method used to estimate amylase concentration in serum is by CNPG (2-chloro-4-nitrophenol β -1-4 galactopyranosylmaltotrioxide) method. It is a direct substrate for determination of amylase activity. The rate of 2-chloro-4-nitrophenol formation can be monitored at 415 nm and is proportional to amylase activity.

Calculation of Glomerular Filtration Rate

GFR was estimated by CKD EPI (Chronic Kidney Disease Epidemiology Collaboration) equation.

CKD EPI Equation for Estimating GFR Expressed for Specified Race, Sex and Serum Creatinine in mg/dl ⁽⁹⁾

EQUATION

$GFR = 141 \times \min(Scr / \kappa, 1) \alpha \times \max(Scr / \kappa, 1) - 1.209 \times 0.993Age \times 1.018$ [if female] $\times 1.159$ [if black] where Scr is serum creatinine in mg/dl, κ is 0.7 for females and 0.9 for males, α is -0.329 for females and -0.411 for males.

Values for serum creatinine, Age in years were inserted in equation to give values of glomerular filtration rate.

STATISTICAL ANALYSIS

The comparison of mean and SD between two groups was done using students "t" test using Minitab software for windows. A p value of <0.05 was considered to be statistically significant. Pearson correlation coefficient was also calculated.

RESULTS

The patients with Chronic kidney Disease showed positive correlation trends with serum amylase levels and eGFR ($r=.206$) but was not statistically significant.

It was noted that as the GFR declines below 50 ml/min the serum amylase levels showed deviation from the normal cut off values.

Serum total amylase together with serum creatinine and blood urea values for end stage renal disease patients, chronic kidney disease patients and controls are given in Table 1. The age and sex distribution in patients are given in Table 2.

Serum total amylase levels was similar and above the upper limit of normal in both, end stage renal disease patients and chronic kidney disease patients. While it was higher in chronic kidney disease than end stage renal disease, the difference was not statistically significant ($p=2.1$).

Normal range for total amylase is 80 IU/L and there are differences from laboratory to laboratory.

50 control subjects were compared with 50 end stage renal disease it was significantly higher in patients ($p<0.001$) as shown in Figure1.

50 control subjects were compared with chronic kidney disease patients it was significantly higher in patients ($p<0.001$) as shown in Figure 1. Serum total amylase levels was above upper limit of normal in sixty percent of patients and markedly abnormal (more than twice upper limit of normal) in ten percent of patients

The glomerular filtration rates as measured by CKD EPI (Chronic Kidney Disease Epidemiology Collaboration) are given in Table3

In End stage renal disease patients glomerular filtration rate range is 4.1 ml/min to 15.3 ml/min and in chronic kidney disease range is from 9.0ml/min to 50.4 ml/min and there were 32 patients with glomerular filtration rate <30 ml/min and there were 18 patients with >30ml/min.

In 50 chronic kidney disease patients 24 patients had blood urea level between 43 to 100 mg/dl and 26 patients had blood urea level >100mg/dl. Serum creatinine levels in 13 patients were more than 10 mg/dl and 27 Patients serum creatinine ranged from 2.1-10 mg/dl.

In 50 end stage renal disease patients 12 patients had blood urea levels between 43-100mg/dl ,38 patients had blood urea levels >100mg/dl. Serum creatinine levels in 14 patients were more than 10mg/dl and in 26 patients serum creatinine levels ranged from 4-10 mg/dl.

Three patients with end stage renal disease had more than two fold elevations of serum total amylase and in these patients blood urea and serum creatinine were very high.

Three patients with chronic kidney disease had more than three fold increase in serum total amylase levels and their blood urea and serum creatinine levels were also abnormal.

DISCUSSION

The present study has demonstrated that serum total amylase levels were elevated in patients with end stage renal disease and chronic kidney disease

when compared with healthy controls it was statistically significant ($p < 0.001$). Chronic kidney patients had higher total amylase levels (mean 94.3 ± 86.2 SD) than end stage renal disease (mean 84.3 ± 22.7 SD). It would appear that high levels of serum total amylase in patients need not indicate pancreatic disease since our patients had no clinical evidence of exocrine pancreatic disease and were not on drugs which would cause hyperamylasia.

Elevations in serum total amylase among patients with chronic kidney disease or end stage renal disease are most likely due to impaired renal clearance⁽¹⁰⁾. In one study serum amylase began to rise only when the creatinine clearance dropped below 50 ml/min⁽¹¹⁾

The highest levels of amylase are noted in hemodialysis patients but marked elevations can also be seen in patients with chronic renal failure and those undergoing peritoneal dialysis. A three fold to five fold increase in amylase levels is most commonly observed but the absolute values do not exceed three times the upper limit of normal. The degree of elevation is roughly proportional to the degree of renal dysfunction^(7,12).

In one study by bastani et al 22 peritoneal dialysis patients were compared with 43 hemodialysis patient and 22 non dialysed chronic renal patients, mean total amylase activity was similar and above the upper limit of normal in all 3 groups it was abnormal in 75% and above twice upper limit of normal in 24% of all patients⁽¹³⁾

We found 60% of patients increase in serum amylase activity and in 10 patients it was more than twice upper limit of normal. The precise mechanism of amylase transfer within the kidney have not yet been clarified. It was earlier

concluded that amylase clearance was essential a function of glomerular filtration without significant tubular reabsorption⁽¹⁴⁾.

In our study it was noted, patients with advanced CKD had higher level of serum amylase (mean 94.4 ± 86.2 SD) in comparison to ESRD patients (Mean 84.2 ± 22.7 SD). It could be due to clearance of amylase during dialysis and malnutrition associated with dialysis.

Recent work by Johnson et al provides strong evidence in favour of tubular absorption of amylase in man⁽¹⁵⁾. This has been shown experimentally in the rat⁽¹⁶⁾. Loss of this preferential clearance of amylase is evident in renal insufficiency and is undoubtedly related to accompanying renal tubular atrophy⁽¹⁷⁾. Acute and chronic renal failure is accompanied by retention of both amylase and lipase⁽¹⁸⁾ hence rise in serum total amylase levels.

CONCLUSION

Serum total amylase was found to be elevated in both end stage renal disease and chronic kidney disease patients when compared to controls. Serum amylase as a diagnostic tool in recognising acute pancreatitis leads to false positive results. Hence interpretation of elevated amylase in chronic kidney disease patients has to be supported by other laboratory and clinical evidence.

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Table 1: Serum Amylase, Creatinine and Blood Urea levels in patients and controls

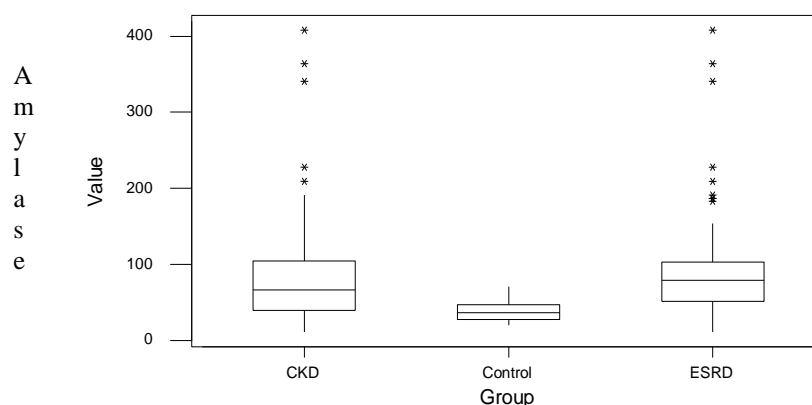
Subjects	Numbers	Serum total amylase (Mean±SD) IU/L	Serum creatinine (Mean± SD) mg/dl	Urea(Mean± SD) mg/dl
Control	50	38.9 ± 13.5	1.05 ± 0.2	23.4 ± 5.8
ESRD	50	84.2 ± 22.7	9.3 ± 3.9	141 ± 60.5
CKD	50	94.4 ± 86.2	3.8 ± 1.9	117 ± 61.7

Table 2: The age and sex distribution in 100 patients

Age group (yrs.)	No. of Patients	Male	Female
18 – 27	17	15	2
28 – 37	17	10	7
38 – 47	17	11	6
48 – 57	12	11	1
58 – 67	18	10	8
67 +	19	15	4

Table 3: Glomerular filtration rate and Serum Amylase levels in patients

Cases	Number	GFR (Mean ± SD) ml/min	Serum total Amylase (Mean ± SD) IU/L
ESRD	50	9.1 ± 3.9	84.2 ± 22.7
CKD	50	25.2 ± 14.3	94.4 ± 86.2
CKD (< 30 ml / min)	31	16.1 ± 6.1	96.31 ± 79.50
CKD (> 30 ml / min)	19	41.3 ± 9.8	90.94 ± 99.45

**Figure 1 Serum Total Amylase levels in ESRD, CKD patients compared with controls****REFERENCES**

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