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Interpretation of Total Serum Amylase in Renal Dysfunction: A Diagnostic Challenge

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Abstract: *Serum Total Amylase (TA) is a biomarker routinely used for the diagnosis of acute pancreatitis. In ChronicKidney Disease (CKD), due to the gradual loss of renal function, there may be increased serum Total Amylase, thus making the interpretation difficult.Our aim wasto compare serum total amylase levels in CKD patients with healthy controls and to assess the serum total amylase levels in different stages of CKD. A cross-sectional observational studywas planned to estimate the serum Total Amylase obtained by IFCC recommended enzymatic colorimetric method in samples received from known cases of CKD. e-GFR for each patient was calculated using 4 parameter MDRD formula from serum creatinine values. Results were compared between different groups using ANOVA followed by post hoc Bonferroni test and Pearson's correlation. The mean age of the 181 CKD patients was 40.12 ± 9.20 years consisting 124 (68.5%) males. The median serum TA was significantly higher than healthy controls (p <0.001. The serum TA was highest in stage 5 CKD [157(25-938) IU/L] followed by stage 4 [134 (41-506) IU/L (p =0.05). Higher levels of serum TA in CKD patients was observed however without any significant correlationwith the stages of CKD. Awareness regarding the analysis of serum TA amongst treating physician is a necessity in view of high frequency of acute pancreatitis in CKD patients.*

Keywords:*CKD, e-GFR, MDRD,Pancreatitis,Total Amylase*

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I. Introduction

Chronic kidney disease (CKD) is characterized by a gradual deterioration of renal function that leads to decrease in glomerular filtration rate (GFR). Globally with the rising incidence of CKD, itis beginning to pose a major healthcare problem and a burden on the economy. In India alone, it is estimated that incidence rate of end stage renal disease (ESRD) is 229 per million population, and more than 100,000 newly diagnosed patients enter renal replacement programs annually.(1) Hence, it becomes relevant to look into different biomarkers in the light of concurrent CKD as they often tend to pose a diagnostic dilemma.

Serum Total Amylase (TA) is one such biomarker routinely used for the diagnosis of acute pancreatitis.(2–4) Major sources of amylase are the exocrine part of pancreas (p-AMY) and salivary glands (s-AMY) and minor being the fallopian tube, lung tissue, tonsils and ovary (5). Thus, the differential diagnosis of hyperamylasemia could be many, namely, parotitis, enlarged parotid glands(6), pseudo-cyst of pancreas(7), intestinal obstruction(8), tramadol overdose(9), organophosphate poisoning(10), lung cancer(11), macroamylasemia(12), and familial(13).

There is evidence that a portion of circulating serum TA is eliminated through kidneys, which accounts for the physiological presence of amylase in urine. (14,15) We hypothesised that in CKD, due to the gradual loss of renal functionthere may be increased serum TA, thus making the interpretation of serum amylase difficult. In the absence of a clear evidence on the correlation of serum TA levels in chronic renal dysfunction, this study was conducted to compare serum TA levels in various stages of renal impairment.

II. Aims and Objectives

To compare the serum total amylase level in patients with chronic kidney disease (CKD) with healthy controls and to assess the serum total amylase levels in different stages of CKD.

III. Methodology

The present cross-sectional observational study was carried out in the clinical biochemistry laboratory of AIIMS, Delhi over a period of three months (May -July 2016). Based on the medical records available on the Hospital Information System, serum samples received for routine biochemical tests from known cases of CKD having no obvious cause of hyperamylasemiaadmitted in the hospital were included in the study. Patients with

acute kidney injury (AKI), malnutrition, major limb amputation, cirrhosis, severe obesity, hypercatabolic states or muscle injury and those patients with a request for estimation of serum amylase levels for any clinical suspicion for elevated levels (pancreatitis, parotitis, intestinal obstruction, etc.) were excluded. e-GFR for each patient was calculated using 4 parameter MDRD formula from serum creatinine values obtained by rate blanked Kinetic Jaffe's method [eGFR (mL/min/1.73 m2) = 175 × (Serum creatinine)-1.154 × (Age)-0.203 × (0.742 if female) × (1.212)] (16). CKD was re confirmed by the eGFR value <60 mL/min/1.73 m^2 persistent for more than 3 months with or without proteinuria. Patients were further subcategorised into CKD stage 3, 4 and 5 based oneGFR values of 30-59, 15-29 and <15 respectively. After performing the requested routine biochemical tests, the left over serum samples were used for the total amylase estimation. IFCC recommended enzymatic colorimetric method on Hitachi Modular P800 biochemistry autoanalyzer (Roche Diagnostics, USA) was used for the same. Age and sex matched 46 healthy controls were also included in the study for comparison.

Results were compared between different groups using ANOVA followed by post hoc Bonferroni test and Pearson's correlation. A p-value of <0.05 was considered as statistically significant.

IV. Results

The mean age of the 181 CKD patients was 40.12 ± 9.20 years consisting 124 (68.5%) males. Table 1 shows the results of demographic and biochemical parameters of the study population and controls. The median serum TA was significantly higher than healthy controls (p <0.001). Out of the total patients enrolled 66.8% (n=121) had a value more than 110 IU/L and 1.6% (n=3) patients had values more than five times the upper reference limit of amylase. All these three patients had ESRD (stage 5 CKD).

On further sub classification on the basis of stages of CKD, 117 (65%) belonged to stage 5, 41 (22.6%) to stage 4 and 23 (12.7%) to stage 3 CKD. The serum TA was highest in stage 5 CKD [157(25-938) IU/L] followed by stage 4 [134 (41-506) IU/L] and stage 3[100(42-398) IU/L] (p =0.05) illustrated in Figure 1. No significant correlation was observed for amylase levels with e-GFR (r = -0.1099), shown in Figure 2 (p=0.14).

V. Discussion

Although the synthesis of amylase and its diagnostic importance in various diseases are described extensively in literature, the route of elimination of amylase from the body is not yet clear. However, few studies suggest that the renal route plays a role in its elimination. (12,14,17) This study is an attempt to find the correlation between levels of serum TA with the stages of renal failure depicted by e-GFR.

Serum TAwas higher in CKD patients than in healthy controls and values highest in CKD stage 5 (ESRD). However, the levels did not correlate with values of e-GFR or any of the stages of CKD. Increased serum pancreatic enzymes in patients with CRF have been previously reported.(18,19) Studies suggest that the elevation in serum total amylase found in patients with chronic kidney disease is probably due to impaired renal clearance.(12,20)

A study suggests that hyperamylasemia associated with renal failure is usually mild to moderate and this corroborates with our findings and serum amylase activity rarely exceeds 5 times the upper limit of normal, a value that is diagnostic of primary acute pancreatitis.(21)The renal clearance of amylase is about 1-2 ml/min in normal individuals and increases to 5-15 ml/min among patients with acute pancreatitis.(21) However, we found three patients with a value 5 times higher than the upper reference limit.

Also, considering the higher risk of occurrence of pancreatitis in CKD patients than in the general population, clinicians may often face difficulty in the interpretation of serum TA.(22–25) In those cases, the elevation of serum TA observed is actually caused due to acute pancreatitis rather than insufficient renal clearance. Further evaluation that includes more specific serum markers of pancreatitis, urine amylase levels and radiological evaluation along with clinical correlation may hold significance.

Similar difficulty in the interpretation of laboratory results has been suggested in studies on cardiac markers in patients of acute myocardial infarction and heart failure with CKD. Interpretation of inflammatory markers like C-reactive proteins, hormones, tumour markers and markers of bone turn over in the settings of ESRD have also been described. (26–29)

We suggest that the awareness on this existing diagnostic challenge in the setting of CKD along with the promptness of the treating physician to diagnose the cause of hyperamylasemia, can surely improve patient outcome.

VI. Conclusions

Higher levels of serum TA in CKD patients was observed however without any significant correlationwith the stages of CKD. Awareness regarding the analysis of serum TA amongst treating physician is a necessity in view of high frequency of acute pancreatitis in CKD patients. The role of other specific laboratory and radiological tests for the diagnosis of pancreatitis in CKD patients along with optimum clinical correlation cannot be undermined.

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Table 1: Comparison of study population with control

Variables	CKD (n= 181)	Control (n=46)	P value
Age (years)	40.12 ± 9.20	31.76 ± 8.88	0.99
M: F	124:67	34:12	0.47
Mean e-GFR (mL/min per 1.73 m^2)	15.81 ± 12.49	118.71 ± 19.25	**<0.001**
SerumTotal Amylase (IU/L)	141(25-938)	66.5(34-132)	**<0.001**
Creatinine (mg/dL)	5.8 (1.32-19.6)	0.8(0.6-1)	**<0.001**
Urea (mg/dL)	106.49 ±51.43	22.39±5.29	**<0.001**

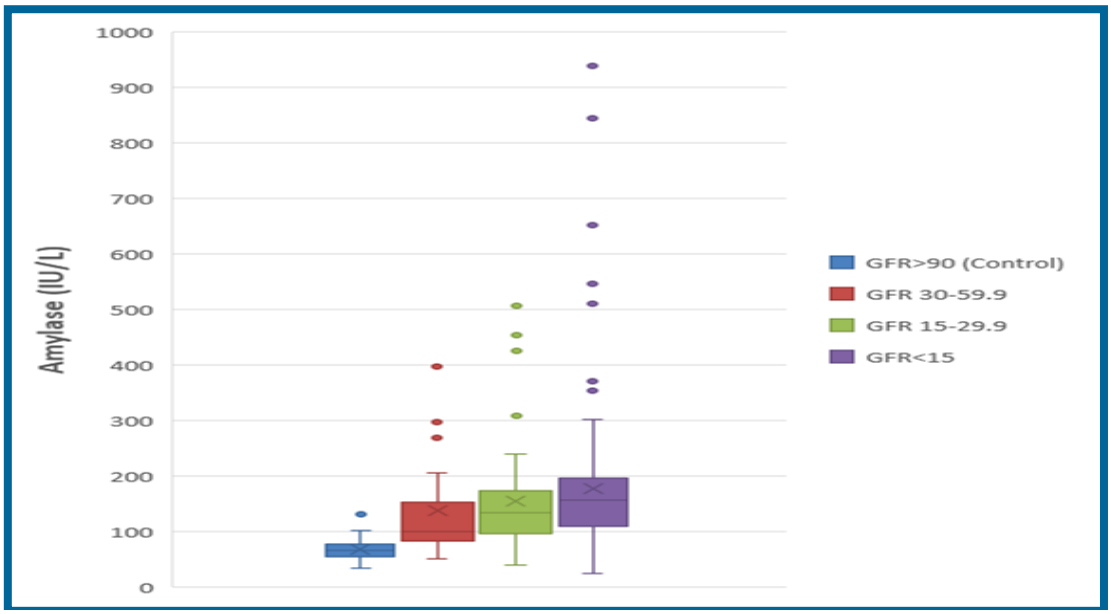
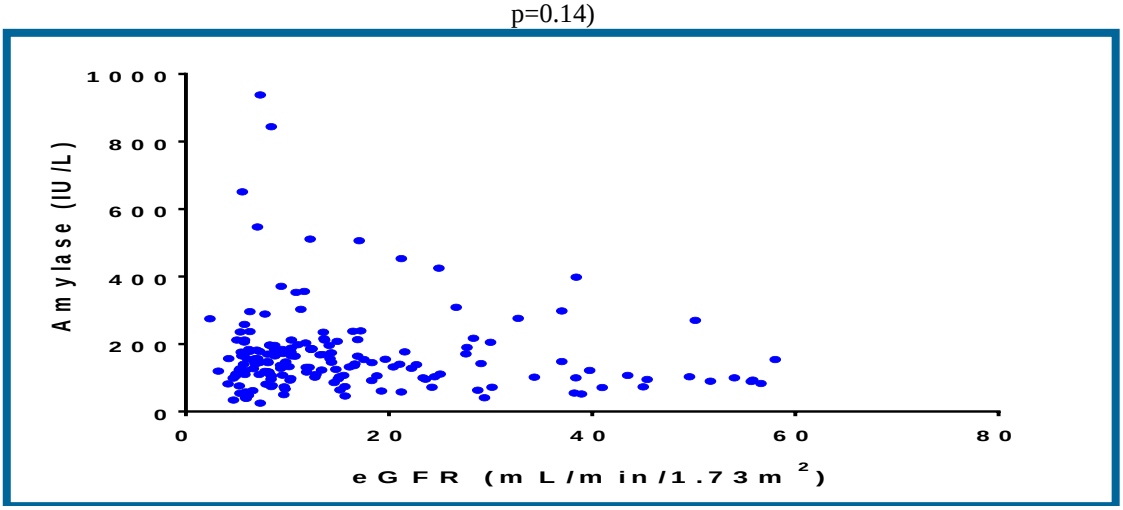


Figure 2: Total serum amylase (TSA) in various stages of chronic kidney disease

Figure 3: Scatter plot demonstrating the correlation between total serum amylase with e-GFR (r = -0.1099, p=0.14)



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