

A Comparative Study of Serum Calcium, Phosphorus and Amylase in Chronic Kidney Disease Patients at SMS Medical College & Attached Hospital, Jaipur, Rajasthan

Mukesh Kumar Bunkar¹, Mahendra Sharma², Kritesh Sharma³, Gigaram Verma⁴, Neelima Hemkar⁵

^{1,2,3}Resident (Jr3), Department of Biochemistry, SMS Medical College, Jaipur

⁴Resident (Jr1), Department of Biochemistry, SMS Medical College, Jaipur

⁵Senior Professor, Department of Biochemistry, SMS Medical College, Jaipur

Received: 25-03-2023 / Revised: 25-04-2023 / Accepted: 30-05-2023

Corresponding author: Gigaram Verma

Conflict of interest: Nil

Abstract

Background: Chronic Kidney Disease (CKD) is a progressive loss in renal function over period of many months or years. As compared to the past decades, the number of kidney diseases leading to end CKD is increasing in India. The disease is associated with the decreased glomerular filtration rate (GFR). As the GFR declines, there is accumulation of metabolic end products excreted by Kidney. Serum Calcium, Phosphorus and serum amylase levels may be disturbed in CKD. So we aimed to evaluate serum Calcium, Phosphorus and Amylase levels in Chronic Kidney Disease patients with healthy controls.

Methodology: After taking necessary permission study conducted in Department of Biochemistry and Urology & Nephrology Clinic and Medical Outdoor of S.M.S. Hospital, Jaipur. 95 cases of CKD compared with healthy controls for Serum calcium, Phosphorus and amylase.

Observation: Results were analysed statistically by student's t test and pearson correlation coefficient test. Mean Calcium, Phosphorus and amylase level in CKD patients was 6.44 ± 0.78 mg/dl, 10.31 ± 1.50 mg/dl, 104.43 ± 20.89 U/L respectively and in controls 9.54 ± 0.58 mg/dl, 3.57 ± 0.48 mg/dl and 52.27 ± 13.89 U/L respectively. This difference was statistically significant ($p < 0.01$).

Conclusion: Due to derangement of serum calcium, phosphorus and amylase levels level in patients with CKD estimation of serum level of serum calcium, phosphorus and amylase even in the early stage CKD is recommended.

Keywords: Chronic kidney disease (CKD), Estimated glomerular filtration rate (eGFR), Serum Amylase.

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

Chronic kidney disease (CKD) affects between 8% and 16% of the population worldwide and is often under recognized by patients and clinicians. [1–4] Chronic kidney disease (CKD) is defined as the presence of kidney damage or an estimated

glomerular filtration rate (eGFR) less than 60 ml/min/1.73 mt², persisting for 3 months or more, irrespective of the cause. [5] As kidney function declines, there is a progressive deterioration in mineral homeostasis with disruption of normal

serum concentrations of phosphorus, calcium levels. It is vital for physician to know the relation among them to treat chronic kidney disease patients.

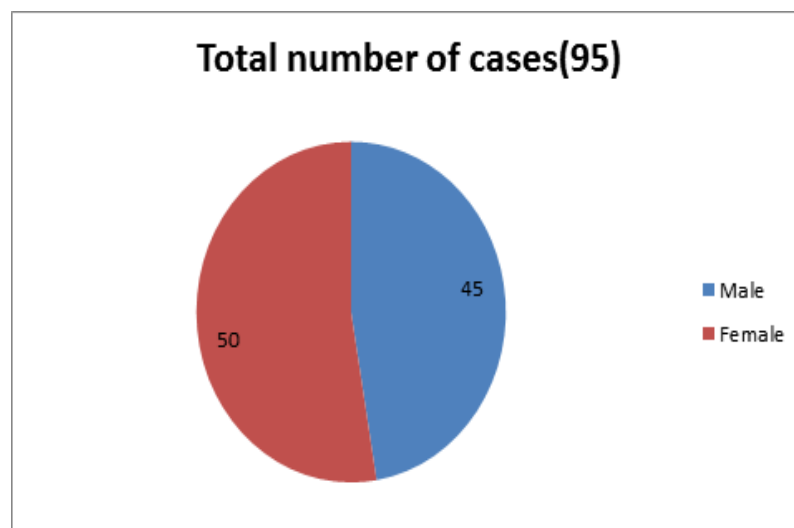
Amylase is a digestive enzyme that normally acts extracellular to cleave starch into smaller carbohydrate groups and, finally, into monosaccharides. Amylase has a molecular weight of 50,000 Kilo Dalton and mostly 40-45% reabsorbed by tubular cells. Twenty percent of pancreatic enzymes are excreted by the kidney. Thus patients with end stage renal disease have change in levels of serum pancreatic enzymes. A various studies done in various parts of the world showed varied studies but there is very few studies found in India. So the main objective of the study is to gather and analyze the data from chronic kidney disease patients and relation between level of serum calcium, serum phosphorus, and amylase levels in SMS hospital Jaipur Rajasthan. Aim of this study was to evaluate serum calcium, phosphorus and amylase levels in Chronic Kidney Disease patients with healthy controls.

Material Method

A hospital based comparative study was conducted in Central Lab Department of Biochemistry S.M.S. Medical College and Urology & Nephrology Clinic and Medical Outdoor of S.M.S. Hospital, Jaipur. 95 Clinically diagnosed CKD Patients in various stages of CKD (Age above 18years), eGFR is $<60 \text{ mL/min/1.73 m}^2$ and those who were willing to participate were included in this study and compared with age matched healthy controls. Patients on dialysis, Patients with autoimmune disorders, Post parathyroidectomy status patients, patients with other chronic disease, Pancreatitis patients were excluded from the study. CKD patients were compared with normal healthy controls for Serum amylase levels.

Results

In Chronic Kidney Disease patients and controls, Mean and Standard Deviations were calculated for all quantitative variables. Means age in patients of CKD was 58.62 ± 12.79 years and in controls was 59.69 ± 12.20 years. This difference was statistically non-significant ($p=0.2773$). Out of 95 cases and 95 controls males were 45 and 50 were females.



Graph 1: Male female ratio in CKD patients

Table 1 Comparison of Different biochemical parameters between CKD Patients and controls

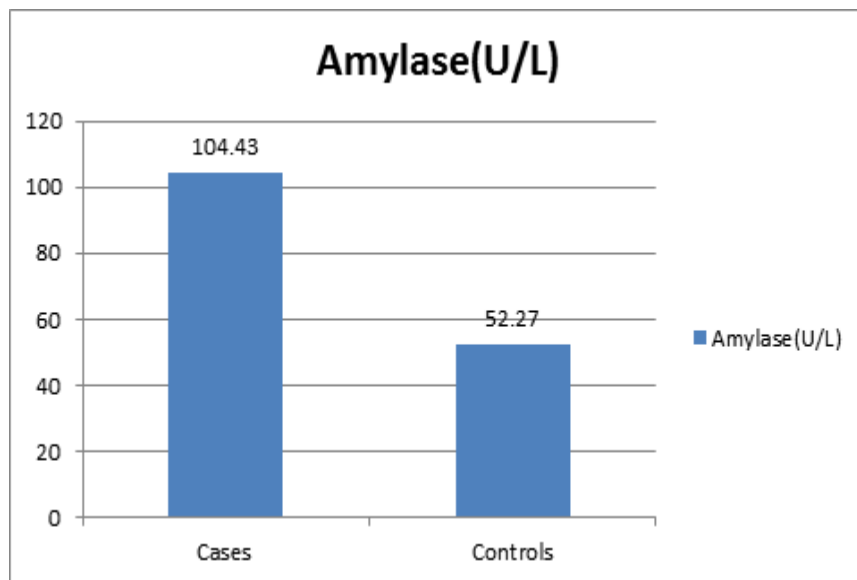
Test/ Parameters	Controls (n=95)	CASES (n=95)	P-value
Urea (mg/dl)	29.60 ± 8.85	119.24 ± 33.95	< 0.01 (S)
Creatinine (mg/dl)	0.84 ± 0.21	4.74 ± 1.29	< 0.01 (S)
Serum Calcium(mg/dl)	9.54±0.58	6.44 ± 0.78	< 0.01 (S)
Serum Phosphorus (mg/dl)	3.57 ± 0.48	10.31 ± 1.50	< 0.01 (S)
Serum Amylase (U/L)	52.27 ± 13.89	104.43 ± 20.89	< 0.01 (S)

*P-value as obtained on applying students' t-test

Mean Urea and creatinine level in CKD patients was significantly high in cases (119.24 ± 33.95 mg/dl and 4.74 ± 1.29 mg/dl) respectively and in comparison to controls (29.60±8.85mg/dl and 0.84 ± 0.21 mg/dl respectively). This difference in urea, creatinine between cases and controls was statistically significant (p<0.01).

Mean Calcium level in CKD patients 6.44 ± 0.78 mg/dl and in controls 9.54±0.58

mg/dl. This difference was statistically significant (p<0.01). Mean Phosphorus level in CKD patients 10.31 ± 1.50 mg/dl and in controls 3.57 ± 0.48 mg/dl. This difference was statistically significant (p<0.01). Mean serum amylase level in CKD patients 104.43 ± 20.89 U/L and in controls 52.27 ± 13.89 U/L. This difference was statistically significant (p<0.01).



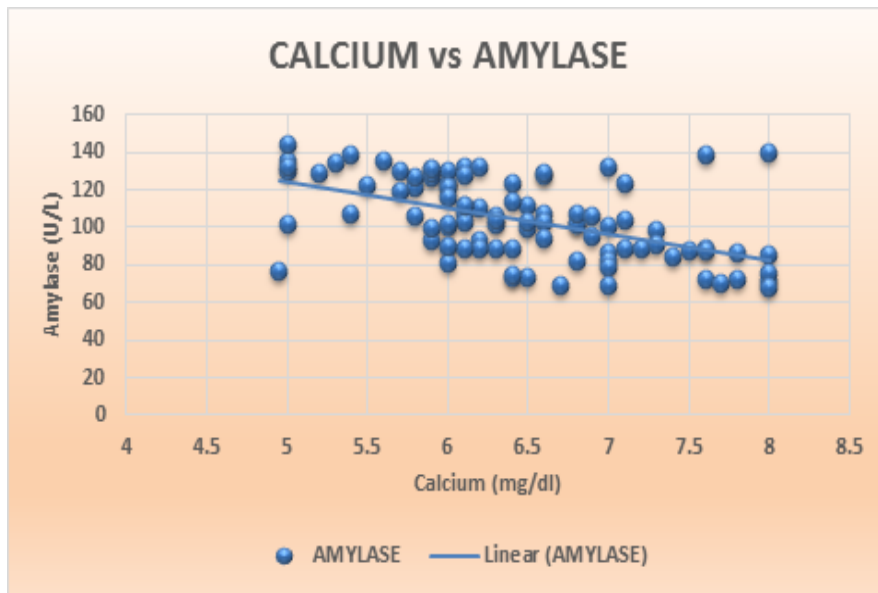
Graph 2: Comparison of Mean Amylase Levels between CKD Patients and controls

Table 2: Correlation between Serum Calcium and Serum Amylase in CKD Patients

Parameter	P value	R Score	R ²	Significance
Serum Calcium vs. Serum Amylase	<0.0001	0.5273	0.278	S

*Data analysis using Pearson correlation analysis

Serum calcium level in patients of CKD had positive(R=0.5273) and statistically significant(p<0.0001) correlation with amylase.



Graph 3: Correlation between Serum Calcium and Serum Phosphorus in CKD Patients

Discussion

Chronic kidney disease leads to many long-term complications in different organs like iron deficiency anaemia, hypertension, pulmonary oedema due to fluid overload, electrolyte abnormalities, sexual dysfunction, dyslipidemia, nutritional disorders, metabolic acidosis, bone disorders and cardiovascular disease (CVD). CKD increases the risk of CVD, which itself is one of the main reasons of mortality in CKD. These complications can gradually result in progressive decline in kidney function, cardiovascular disease and death. Among these complications, bone complications in the form of deregulated metabolism of bone minerals like calcium, phosphorus and alteration in synthesis are very common. This renal osteodystrophy is attributed to be one of the main reasons for morbidity and decline in quality of life. Enzyme Amylase is produced by exocrine pancreas and salivary gland that hydrolyses starch. It normally occurs in human plasma with molecular weights varying from 54,000 to 62,000 Da. The enzyme is thus small enough to pass through the glomeruli of the kidneys, and amylase is the only plasma enzyme normally found in urine.⁶ Elevated levels of serum Amylase is one

of diagnostic indicators of Acute Pancreatitis. But amylase is elevated in many non-pancreatic conditions also. It is known that 24% of circulating amylase is excreted in urine. [7] Since the diagnosis, assessment, monitoring and follow up of many hepatic and pancreatic diseases is based upon the levels of these enzymes, the accurate clinical assessment of the patient with CKD is hampered by a paucity of knowledge concerning the serum concentrations of these enzymes in various stages of CKD. There are not many studies from India about the hepatic and pancreatic enzyme levels in various stages of CKD.

So in this study we attempted to evaluate serum calcium, phosphorus and amylase levels in Chronic Kidney Disease patients and compare them with healthy controls.

95 patients with CKD and 95 healthy controls were included in this study. Out of 95 patients 45 were males while 50 were females. In control group out of 95 subjects 45 were males and 50 were females. This defines male female ratio of our study was 47:53. In this study mean age of cases was 58.62 ± 12.79 years and for controls mean age was 59.69 ± 12.2 years. This difference between cases and controls group in mean age was

statistically non-significant. ($p=0.28$). This shows our study was age and sex matched in respect of cases and controls. In this study we found slightly high incidence of CKD in women in comparison to male. These results were consistent with results of previous studies by Levine et al [8] 1989 and Carrero et al [9] 2017. They show Women had a slightly higher risk of kidney dysfunction than men. In our study mean urea, creatinine levels were 119.24 ± 33.95 mg/dl, 4.74 ± 1.29 mg/dl respectively while in controls mean level was 29.6 ± 8.85 mg/dl and 0.84 ± 0.21 mg/dl respectively. This difference was statistically significant ($p < 0.001$). This difference was in accordance to biochemical analysis of CKD. In this study mean calcium level in cases was 6.44 ± 0.78 mg/dl and in controls it was 9.54 ± 0.58 mg/dl. It shows significantly low ($p < 0.001$) values of calcium in CKD patients in comparison to healthy controls. Our results were in concordance with study conducted by Thomas R et al [10] in 2008 and a study by Patel et al [11] in 2016. These results of our study correlate with study conducted by Freethi R et al [12] in 2016 which shows significantly low ($p < 0.001$) levels of calcium in CKD patients. One study conducted by Cynthia J. Janmaat et al [13] in 2018 found that the other way around, lower baseline serum calcium is associated with a faster subsequent kidney function decline. The adjusted associations in these stages are substantial, ranging from an increase of 24% to 70% of the mean annual decline rate for every unit lower in serum calcium.

In this study we found mean phosphorus levels in CKD patients were 10.31 ± 1.50 mg/dl while in controls it was 3.57 ± 0.48 mg/dl. It shows very high levels of Phosphorus in CKD patients in comparison to controls. Similar results were obtained by Nirmala Devi et al [14] in 2017 which shows statistically significant elevated phosphorous levels in stage 4 and 5 of CKD patients compared to

the controls. Phosphorus is one of the main requisites for mineralization and proper formation of bone. Hyperphosphatemia plays a major role in the causation of vascular calcification and cardiovascular events in CKD. Hyperphosphatemia in CKD occurs due to failure of phosphorus excretion by kidneys. Due to impaired and defective bone remodeling in CKD, phosphorus moves from the bones to the blood causing hyperphosphatemia. Studies have shown that in CKD, osteoclastic activity is more than osteoblastic activity resulting in bone resorption. In CKD, the formation of 1,25 dihydroxycholecalciferol (active form of Vitamin D) is impaired due to defective activity of 1 alpha hydroxylase enzyme in the kidney. This in turn decreases calbindin formation resulting in decreased absorption of calcium from intestine, hypocalcemia and stimulation of parathyroid hormone (PTH) secretion. The increase in PTH levels result in increased release of phosphate from bone into blood. The decrease in calcitriol synthesis causes decrease stimulation to the osteocytes and osteoblasts for the secretion of fibroblast growth factor 23 (FGF23) [15,16]. PTH exerts its action on both renal tubules and bone. In the kidneys, it increases the excretion of phosphate. In the bone, PTH stimulates calcium release from the bone. But the fact that the net effect is increase in phosphate levels shows the predominant effect of bone.

In our study mean amylase levels for cases were 104.43 ± 20.89 U/L and in controls it was 52.27 ± 13.89 U/L. It shows significantly high ($p < 0.001$) values of amylase in CKD patients in comparison to controls. Similar results were found in the study conducted by M Manju et al [17] in 2019 showed a significant increase in pancreatic enzymes, amylase, and lipase in CKD patients with and without ESRD. ESRD patients had a significant increase in these levels as compared to CKD without ESRD. Another study conducted

by Ray L et al [18] in 2015 showed similar results they found high serum amylase levels in CKD patients in comparison to control group. Jiang CF et al [19] in 2002 showed similar results. Another study by Dr. Arju Saikia et al [20] in 2012 showed similar results they demonstrated that serum amylase levels were elevated in patients with end stage renal disease and chronic kidney disease when compared with healthy controls and this increase was statistically significant ($p < 0.05$). Chronic kidney patients had higher amylase levels (mean 92.5 ± 27.3 SD) than end stage renal disease (mean 86.2 ± 21.4 SD). Serum amylase levels were above the upper limit in 57% of patient and more than twice of upper limit in 12 percent of patients. Elevations in serum amylase among patients with renal failure or ESRD are most likely due to impaired renal clearance. In one study, the serum amylase began to rise only when the creatinine clearance dropped below 50 mL/ minute. [21] The dialysis procedure alone does not appear to alter serum amylase. In one study, for example, no change was observed in serum amylase in samples obtained pre- and post-dialysis. [22] Amylase is one of the enzymes that is produced by the exocrine pancreas and a salivary gland that hydrolyzes starch is rapidly cleared by the kidney. Twenty percent of pancreatic enzymes are 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. [10] 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 .

Conclusion

In conclusion, the present study has revealed severe derangements of calcium, phosphorus and amylase in CKD patients. Among serum electrolyte disorders,

hyperphosphatemia and hypocalcaemia were more prevalent. As the kidney disease progresses there is increase in phosphorus levels and slight fall in calcium levels. This derangement in mineral metabolism not only leads to skeletal calcification but also calcification in extra skeletal tissue like vascular tissue. Hyperamylasia also was the feature of our study in CKD patients. It is worthwhile to check serum calcium, phosphorus and amylase value frequently in CKD patients during the course of the treatment and to treat them accordingly which will decrease their morbidity and mortality.

References

1. Coresh J, Selvin E, Stevens LA, et al. Prevalence of chronic kidney disease in the United States. *JAMA*. 2007; 298 (17):2038–2047.
2. Hsu CY, Vittinghoff E, Lin F, Shlipak MG. The incidence of end-stage renal disease is increasing faster than the prevalence of chronic renal insufficiency. *Ann Intern Med*. 2004; 141(02):95–101.
3. Plantinga LC, Boulware LE, Coresh J, et al. Patient awareness of chronic kidney disease: trends and predictors. *Arch Intern Med*. 2008;168(20): 2268–2275.
4. Jha V, Garcia-Garcia G, Iseki K, et al. chronic kidney disease: global dimension and perspectives. *Lancet*. 2013;382(9888):260–272.
5. Chapter 1: Definition and classification of CKD. *Kidney Int Suppl*, 2011. 2013 Jan;3(1):19-62.
6. Burtis CA, Ashwood ER, Burns DE, editors. *Teitz textbook of Clinical Chemistry and Molecular Diagnostics*. 5th ed. Philadelphia: Elsevier; 2012; 583-585.
7. Bailey GL, Katz AI, Hampers CL, Merrill JP. Alterations in serum enzymes in chronic renal failure. *JAMA*, 1970; 213: 2263-65.
8. Levine, W., Dyer, A. R., Shekelle, R. B., Schoenberger, J. A. & Stamler, J.

- Serum uric acid and 11.5-year mortality of middleaged women: findings of the Chicago heart association detection project in industry. *J. Clin. Epidemiol.* 1989; 42: 257–267.
9. Carrero, J.-J., Hecking, M., Ulas, I., Sola, L. & Tomas, B. Chronic kidney disease, gender, and access to care: a global perspective. *Semin. Nephrol.* 2017; 37: 296–308.
 10. Thomas R, Kanso A, Sedor JR. Chronic kidney disease and its complications. Primary care: Clinics in office practice. 2008; 35(2): 329-44.
 11. Patel L, Bernard LM, Elder GJ. Sevelamer versus calcium-based binders for treatment of hyperphosphatemia in CKD: A meta-analysis of randomized controlled trials. *Clinical Journal of the American Society of Nephrology.* 2016;11(2): 23 2-44.
 12. Freethi R, Velayutha Raj A, Kalavathy P, Rasheed Khan M, Sundhararajan A and Venkatesan. Study of serum levels of calcium, phosphorus and alkaline phosphatase in chronic kidney disease. *Int J Med Res Health Sci.* 2016; 5(3):49-56.
 13. Cynthia J. Janmaat¹, Merel van Diepen¹, Alessandro Gasparini² et al Lower serum calcium is independently associated with CKD progression *Scientific Reports.* 2018; 8:5148.
 14. Nirmala Devi K, Arshiya Begum. A, Sathiya. K, Deepa Lakshmi. P. Study of Serum Magnesium, Calcium, Phosphorous and Alkaline Phosphatase in Chronic Kidney Disease *National Journal of Basic Medical Sciences.* 2017; 8:1.
 15. Liu S, Tang W, Zhou J, *et al.* Fibroblast Growth Factor 23 Is a Counter-Regulatory Phosphaturic Hormone for Vitamin D. *J Am Soc Nephrol.* 2006;17:1305–1315.
 16. Tapasyapreeti Mukhopadhyay, Sudhanshu Shekhar, Sudip Kumar Datta Interpretation of Total Serum Amylase in Renal Dysfunction: A Diagnostic Challenge *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS).* 2019; 18(5): Ser. 1: PP 51-54.
 17. M Manju, Suryapriya Rajendran, Sasmita Mishra, Pavithra M4 Serum Liver and Pancreatic Enzymes in Chronic Kidney Disease with and without End-stage Renal Disease: A Comparative Study *Indian Journal of Medical Biochemistry,* January-April 2019; 23:1.
 18. Ray L, Nanda SK, Chatterjee A, et al. A comparative study of serum aminotransferases in chronic kidney disease with and without end-stage renal disease: Need for new reference ranges. *International Journal of Applied and Basic Medical Research.* 2015;5(10):31-35.
 19. Jiang CF, Ng KW, Tan SW, et al. Serum level of amylase and lipase in various stages of chronic renal insufficiency. *Zhonghua Yi Xue Za Zhi(Taipei).* 2002;65:49-54.
 20. Dr. Arju Saikia SR, Dr Syeda Mohsina Rohman. A study of serum amylase in patients with chronic kidney disease *indian journal of research.* July-2018; 7:7.
 21. Collen MJ, Ansher AF, Chapman AB, et al. Serum amylase in patients with renal insufficiency and renal failure. *Am J Gastroenterol.* 1990; 85:1377.
 22. Vaziri ND, Chang D, Malekpour A, et al. Pancreatic enzymes in patients with end-stage renal disease maintained on hemodialysis. *Am J Gastroenterol.* 1988; 83:410.
 23. Chakdoui S., Moumen A., & Guerboub A. Dyslipidemia and Diabetic Retinopathy in Moroccans Type 2 Diabetics Patients: A Cross-Sectional Study. *Journal of Medical Research and Health Sciences,* 2023; 6(3), 2471–2479.