



E-ISSN: 2706-9575  
P-ISSN: 2706-9567  
IJARM 2021; 3(1): 314-317  
Received: 11-12-2020  
Accepted: 02-01-2021

**Dr. Shreesh Kadur JM**  
Orthopaedic Surgeon, Sky  
Super Speciality Hospital,  
Iritty, Kannur, Kerala, India

**Dr. Sharvani S**  
Senior Resident, Kodagu  
Institute of Medical Sciences,  
Madikeri, Karnataka, India

## Association of serum calcium, phosphorous and parathyroid hormone with cardiac abnormality in CKD patients: A pilot study

**Dr. Shreesh Kadur JM and Dr. Sharvani S**

**DOI:** <https://doi.org/10.22271/27069567.2021.v3.i1f.155>

### Abstract

Chronic kidney disease is commonly associated with increase in blood phosphate levels. In early stages phosphate levels are maintained in normal limits because of the hyperparathyroidism causing phosphaturia. With advancement in renal disease hyperphosphatemia becomes evident. As a consequence of same there will be worsening of hyperparathyroidism and predisposition to develop metastatic calcification. In this study we have analyzed the serum levels of Calcium, Phosphorous and Parathormone levels in chronic kidney disease patients who were evaluated in nephrourology centre over a period of one month. It was then evaluated to see the correlation between aforementioned parameters with cardiovascular disease in those patients. The study showed significant correlation between the serum phosphate levels with cardiovascular morbidity in study population but didn't show significant relation with serum calcium and parathormone levels. From the study it can be concluded that a large percentage of end stage renal disease patients have high phosphate levels and this plays a significant role in cardiovascular morbidity in them.

**Keywords:** Chronic kidney disease, phosphorous, parathyroid hormone, cardiovascular morbidity

### Introduction

Chronic renal failure (CRF) is an irreversible decline of renal function which finally leads to end-stage renal disease (ESRD). This condition is associated with renal replacement therapy including dialysis or transplantation <sup>[1]</sup>. The annual rate of mortality from cardiovascular diseases in hemodialysis patients is around 9%, which is 30 times higher than that in general population <sup>[2]</sup>. Ischemic heart diseases, atherosclerosis, myocardial dysfunction followed by heart failure, left ventricular hypertrophy and calcification of the heart valves are common diseases in haemodialysis patients <sup>[1, 2]</sup>. The progress of chronic kidney disease leads to the development of hyperphosphatemia. Hyperphosphatemia reduces serum levels of calcium via making a connection between calcium and phosphate and chronically inhibiting renal alpha-hydroxylase activity and reducing the synthesis of 1,25-dihydroxyvitamin D. The reduction of 1,25-dihydroxyvitamin D and calcium in the blood will stimulate the parathyroid gland to secrete the parathyroid hormone <sup>[3]</sup>. A link between secondary hyperparathyroidism and cardiovascular disease in dialysis patients has been suspected for a while now <sup>[1, 4]</sup>. High levels of parathyroid hormones as seen in chronic kidney disease patients seem to damage the cardiac myocytes possible mechanism being calcium ionophore effect <sup>[5]</sup>. Few animal studies have demonstrated Parathyroid hormone as a permissive factor in development of uremic cardiomyopathy <sup>[6]</sup>. The aim of our study is to find out the prevalence of cardiac abnormalities in ckd patients and to associate the levels of calcium, phosphorous and PTH with the same.

### Materials and Methods

The study was done in a tertiary nephro-urology care centre in Bangalore. Study was designed on cross sectional basis. Based on retrospective data over a period of three months observed in a month approximately 60 new cases got registered for evaluation of CKD. After considering of inclusion and exclusion criteria 50 was taken as sample size. Age > 18 years with history of CKD were the inclusion criteria. Patients with prior history of cardiac abnormalities were excluded from the study.

**Corresponding Author:**  
**Dr. Sharvani S**  
Senior Resident, Kodagu  
Institute of Medical Sciences,  
Madikeri, Karnataka, India

Two groups 2 groups each for assessing calcium ( $\geq 11$  mg/dl,  $< 11$ mg/dl), phosphorous ( $\geq 5.5$  mg/dl,  $< 5.5$  mg/dl) and PTH ( $\geq 300$  pg/ml,  $< 300$  pg/ml) with respect to prevalence of cardiac abnormalities were made. Results were tabulated and evaluated using SSPS 19 version software. All results are expressed as mean and standard deviation (SD). P value below 0.05 was considered significant.

**Results**

The study involving 50 patients had equal number of male and females. Mean age of the patient was  $46.12 \pm 13.74$  yrs. Diabetic kidney disease was the leading cause (48%) followed by chronic glomerulonephritis (14%). (Table 1) (Figure 1).

**Table 1:** Etiology of CKD in study population

Cause Of Ckd	Number Of Cases	Percentage
Diabetic kidney disease	24	48%
Chronic glomerulonephritis	7	14%
ADPKD	1	12%
IgA nephropathy	6	2%
Others (Lupus nephritis, Interstitial nephritis)	12	24%

Among the cardiac abnormalities in CKD, 22% of patients had changes of hypertensive heart disease and diastolic dysfunction. Twenty percent of cases had Ischemic heart disease with systolic dysfunction. Calcific valves was present in 10 % patients and valvular dysfunction in about 8% patients. (Table 2).

Among the calcium, phosphorous and PTH, serum phosphorous values ( $>5.5$  mg/dl) showed significant relationship with cardiac abnormality ( $p < 0.003$ ). Calcium and PTH values were insignificant but elevated (Table 3, 4, 5).

**Table 2:** Types of cardiac abnormalities in study population

Cardiac Dysfunction	Number Of Cases	Percentage
HHD with diastolic dysfunction	12	22%
IHD with systolic dysfunction	10	20%
Calcified valves	5	10%
Valvular heart disease	4	8%

**Table 3:** Phosphorus (Ph) code \* Cardiac dysfunction crosstabulation

		Cardiac dysfunction		Total
		1	2	
Phosphorous (Ph) code	1 Count	21	4	25
	% within the Ph score	84.0%	16.0%	100%
	2 Count	10	15	25
	% within the Ph score	40.0%	68.0%	100%
Total Count		31	19	50
% within the Ph code		62.0%	38.0%	100%
P value= 0.003				
Serum Ph: 1- $\geq 5.5$ mg/dl				
2- $< 5.5$ mg/dl				
Cardiac function: 1-Cardiac dysfunction preset				
2- Cardiac dysfunction absent				

**Table 4:** Calcium (Ca) code \* Cardiac dysfunction crosstabulation

		Cardiac dysfunction		Total
		1	2	
Calcium (Ca) code	1 Count	5	0	5
	% within the Ca score	100.0%	0%	100%
	2 Count	26	19	45
	% within the Ca score	57.8%	42.2%	100%
Total Count		31	19	50
% within the Ca code		62.0%	38.0%	100%
P value= 0.142				
Serum Ca: 1- $\geq 11$ mg/dl				
2- $< 11$ mg/dl				
Cardiac function: 1-Cardiac dysfunction preset				
2- Cardiac dysfunction absent				

**Table 5:** PTH code \* Cardiac dysfunction crosstabulation

		Cardiac dysfunction		Total
		1	2	
PTH code	1 Count % within the PTH score	14 70%	6 30%	20 100%
	2 Count % within the PTH score	16 53.3%	14 46.7%	30 100%
Total Count % within the PTH code P value= 0.238		30 60%	20 40%	50 100%
Serum PTH: 1- $\geq$ 300mg/dl 2- <300 mg/dl Cardiac function: 1- Cardiac dysfunction preset 2- Cardiac dysfunction absent				

## Discussion

Cardiovascular diseases account for 40%-50% of mortality rate among end stage renal disease. Compared to general population, it accounts to 3 to 10 times more than that among healthy counterparts of the same age [7, 8].

In our study diabetic nephropathy (48%) stands out as most common cause of CKD. An US population based study by Yelena *et al* [9] also showed prevalence of Diabetic nephropathy- 31% and glomerulonephritis - 13.7% as etiologies for CKD. Hypertensive heart disease with systolic dysfunction accounted for 22% of cases followed by IHD (20%) and calcified valves(10%).

A study conducted by Nematollahi *et al.* [10] showed aortic valve calcification, mitral valve calcification, and mitral annulus calcification in 20%, 1%, and 4% of hemodialysis patients, respectively. In another study conducted by Jalali *et al.* [11], mitral valve calcification and aortic valve calcification were observed in 3.9% and 1.9% respectively in hemodialysis patients. A study by Avila- Diaz *et al.* [12] showed the prevalence of mitral valve calcification, aortic valve calcification and calcification of both valves in hemodialysis patients as 26.3%, 57.8%, and 15.8% respectively. In other studies, the calcification of the individual valve involvement were described separately, while in the present study we have reported collectively.

The frequent finding of hyperphosphatemia is due partly to the fact that phosphorus clearance by dialysis itself is not the major factor involved in the control of serum phosphorus [13-15]. Phosphate kinetic studies in hemodialysis patients show that there is an initially high phosphate clearance from the extracellular compartment followed by a slow efflux from an intracellular compartment [15-18]. In our study elevated serum phosphorous levels correlated with the cardiac abnormality whereas, calcium and PTH levels didn't. However serum PTH levels were elevated in 70% cases of CKD patients with cardiac abnormalities. Nematollahi *et al.* [10] had found significant positive relationship with the calcification of the heart valves with serum phosphorous. He also found serum phosphorus level had a significant relationship with left ventricular systolic dysfunction. In the study of Mousavi- Movahed *et al.* [19] no significant relationship between serum calcium and phosphorus levels with calcification of the heart valves was detected. However, the prevalence of hyperparathyroidism among hemodialysis patients was 77%, which it had a significant relationship with calcification of the heart valves. Avila-Diaz *et al.* [12] concluded that serum parathyroid hormone level was a major risk factor for the calcification of heart valves and had a direct relationship with valve calcification. The differences can be due to the therapeutic

effects of medications given to the patients in various study groups as a part of CKD treatment.

In our study, we multiplied calcium by phosphorus in hemodialysis patients and the result was 40 mg<sup>2</sup>/dl<sup>2</sup>. In a similar study by Nematollahi [10] it was 44 units. The study of Block *et al.* [20] inferred that every 10 units of Ca $\times$ PO<sub>4</sub> product increase, the mortality rate of hemodialysis patients increased by 7%.

## Conclusion

Cardiac abnormalities are common in end stage renal disease patients. Metabolic abnormalities with calcium and phosphorous along with PTH are seen in these patients. Corelation of metabolic abnormalities with cardiac disorder helps in predicting morbidity and mortality as cardiac disorders are one of causes of mortality in CKD patients. When calcium and PTH levels were non correlating, hyperphosphatemia can be inferred as risk factor for cardiac abnormalities present in CKD patients. Dietary restriction of phosphate can be helpful in reducing cardiovascular morbidity in CKD patient.

## Limitations

It was a single population based study. Duration of dialysis or therapeutic medications were not considered. It was done as a pilot study hence the small sample size too.

**Conflict of Interest:** None

**Acknowledgments:** None

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