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Original Research Article

A study on prevalence of cardiac valvular calcification and its correlation with serum phosphate levels in chronic kidney disease

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ABSTRACT

Background: Higher cardiovascular morbidity found to be more in early stages of chronic kidney disease patients. Present study was done to study the prevalence of cardiac valvular calcification correlated with serum phosphate levels in chronic kidney disease.
Methods: A total of 153 (78 chronic kidney disease patients, 75 controls with age and sex matched) coming to ESIC Hospital, Chennai were utilized to conduct the present study. Patients of stages 3 to 5 with matched controls of age and sex were considered for this study. Cases were classified in to different stages of chronic kidney disease based on estimated Glomerular Filtration Rate which was calculated using Cockcroft-Gault equation using age, body weight, and serum creatinine. The blood samples of patients belonging to both the groups were tested for serum creatinine and serum phosphate. The Echocardiogram was done for the patient with chronic kidney disease to assess cardiac valvular calcification.
Results: 51% of the subjects in the study group were detected as having chronic kidney disease in ultrasonogram. 20% of the patients in the study group were having coronary artery disease compared to 4% in the control group. Mean serum phosphate levels between subjects with Valvular calcification in chronic kidney disease and without calcification was statistically significant among the study group was noted in the present study.
Conclusions: Elevated levels of serum phosphate correlated with cardiac valvular calcification showed significant role in chronic kidney disease.

Keywords: Calcification, Cardiac, Kidney, Serum phosphate, Valvular

INTRODUCTION

Chronic kidney disease (CKD) is associated with a higher incidence of cardiovascular events. It is the leading cause of morbidity and mortality in every stage of chronic kidney disease.[1] Most of the patients with CKD succumb to cardiovascular disease before reaching End stage renal disease (ESRD).The CKD registry of India has shown 28.7% of patients in chronic kidney disease stage 4 have cardiovascular complications.[2] Cardio vascular profile in chronic kidney disease includes Ischemic vascular occlusive disease, myocardial ischemia, left ventricular hypertrophy and dilated cardiomyopathy.[3] Phosphate being the novel risk factor for the valvular calcification in CKD patients. Elevated serum phosphate activates vascular smooth muscle to acquire an osteoblast like phenotype allowing the deposition of more calcium in the arteries.[4] Mortality in ESRD patients strongly correlates with elevated serum phosphate levels (>5.5 mg/dl). In early CKD, renal insufficiency leads to impaired

phosphate excretion but serum phosphate levels are maintained in the normal range by upregulation of FGF 23 and PTH.[5] Phosphate metabolism is altered in CKD and it results vascular calcification. Excess phosphorus gets deposited in the heterotopic sites leading to vascular calcification.[6] Calcification results in valvular calcification, left ventricular failure and myocardial infarction leading to increased mortality.[7] The present study is undertaken to study the prevalence of cardiac valvular calcification correlated with serum phosphate levels in chronic kidney disease.

METHODS

A total of 153 (78 chronic kidney disease patients,75 controls with age and sex matched) coming to ESIC Hospital, Chennai were utilized to conduct the present study. Patients of stages 3 to 5 with matched controls of age and sex were considered for this study. Cases were classified in to different stages of chronic kidney disease based on estimated Glomerular Filtration Rate (eGFR) which was calculated using Cockcroft-Gault equation using age, body weight, and serum creatinine. Documented elevated renal parameters for more than 3 months, ultrasonography suggestive of chronic kidney disease and Patients on dialysis for chronic kidney disease were included in the present study whereas Patients with past history of coronary heart disease, unstable angina, myocardial infarction, rheumatic valvular heart disease and congenital heart disease were excluded in our study. Detailed history with clinical examination was done for the individuals with chronic kidney disease and also the control subjects. The blood samples of patients belonging to both the groups were tested for serum creatinine and serum phosphate. Echocardiogram was done for the patient with chronic kidney disease to assess cardiac valvular calcification. The present study was in clearance with human ethical committee, ESIC Hospital, Chennai, India.

RESULTS

The study was conducted in 153 patients of which 78 patients with CKD and 75 subjects with normal kidney function. About 61% of study subjects were in the age group of 41-60 years while 19% were aged 61-70 years (Table 1).

Table 1: Age distribution of the study population (n=153).

Age group	Study group N (%)	Control group N (%)	Total N (%)
21-30 years	0 (0)	5 (6.7)	5 (3.3)
31-40 years	16 (20.5)	9 (12)	25 (16.3)
41-50 years	30 (38.5)	28 (37.3)	58 (37.9)
51-60 years	17 (21.8)	19 (25.3)	36 (23.5)
61-70 years	15 (19.2)	14 (18.7)	29 (19)
Total	78 (51)	75 (49)	153 (100)

Table 2: Gender distribution of the study population (n=153).

Gender	Study group N (%)	Control group N (%)	Total N (%)
Female	29 (37.2)	26 (34.7)	55 (35.9)
Male	49 (62.8)	49 (65.3)	98 (64.1)
Total	78 (51)	75 (49)	153 (100)

The mean age of the study population was 48 years, minimum age was 26 years and maximum was 65 years. Majority of the study subjects were males (64%) while the remaining 36% were females (Table 2). We have not observed any abnormalities in study group.

Table 3: Distribution of the study population according to USG findings (n=153).

USG findings	Study group N (%)	Control group N (%)	Total N (%)
Chronic kidney disease	78 (100)	0 (0)	78 (51)
No abnormality	0 (0)	75 (100)	75 (49)
Total	78 (51)	75 (49)	153 (100)

About 51% of the subjects in the study group were detected as having chronic kidney disease in ultrasonogram (Table 3).

Table 4: Distribution of the study population according to coronary artery disease (n=153).

Coronary artery disease	Study group N (%)	Control group N (%)	Total N (%)
Present	20 (25.6)	4 (5.3)	24 (15.7)
Absent	58 (74.4)	71 (94.7)	129 (84.3)
Total	78 (51)	75 (49)	153 (100)

A total of 24 patients in both control and study group were having coronary artery disease in the present study. 20 patients with an incidence of 25.6% in the study group were having coronary artery disease compared to 4 patients (5.3%) in the control group (Table 4).

Table 5: Distribution of calcification in echocardiogram among population (n=153).

Echocardiogram	Frequency	Percent
Aortic calcification	3	2.0
Mitral annular calcification	11	7.2
No calcification	139	90.8
Total	153	100.0

A total of 13 patients with calcification and 65 patients without calcification were noted in the study group whereas 1 patient with calcification in control group was

observed in echo cardiogram. The proportion of calcification between study group and control group by echo cardiogram was statistically significant (Table 5). 3 patients with an incidence of 11.1% were noted in eGFR 15-29 group in the present study. Most of the valve calcifications in study group were seen with eGFR less than 15 (Table 6).

Table 6: Cardiac valvular calcification and e GFR levels in the study group (n=78).

GFR group	Calcification	No calcification	Total
30-59	0 (0%)	3 (100%)	3 (100%)
15-29	3 (11.1%)	24 (88.9%)	27 (100%)
<15	10 (20.8%)	38 (79.2%)	48 (100%)
Total	13 (16.7%)	65 (83.3%)	78 (100%)

15 out of 78 patients in study group (8 patients with cardiac calcification) associated with diabetes and (7 patients without calcification) was noted. Calcification between patients on dialysis and patients not on dialysis was statistically significant (Table 7).

Table 7: Cardiac valvular calcification and dialysis association in the study group (n=78).

Dialysis	Calcification	No calcification	Total
Dialysis	8 (53.3%)	7 (46.7%)	15 (100%)
No dialysis	5 (7.9%)	58 (92.1%)	63 (100%)
Total	13 (16.7%)	65 (83.3%)	78 (100%)

The mean serum phosphorus level in patients with valvular calcifications was 6.7mg/dl. The mean serum calcium-phosphate product in CKD patients with valvular calcification was 59.03mg^2/dl^2.The serum phosphate levels between subjects with valvular calcification and without calcification were statistically significant among the study group. Serum calcium levels between subjects with calcification and without calcification were not statistically significant among the study group. Calcium phosphate product between subjects with calcification and without calcification was statistically significant among the study group (Table 8).

Table 8: Comparison of mean serum levels of various parameters between subjects with and without cardiac valvular calcification in the study group (n=78).

Serum levels		N	Mean	Std. Deviation	Mean difference
PO4	Calcification	13	6.708	0.5377	1.42
	No calcification	65	5.288	1.4972	
Ca	Calcification	13	8.877	0.8974	0.333
	No calcification	65	8.543	1.0899	
Ca x P	Calcification	13	59.303	5.619	14.69
	No calcification	65	44.604	11.478	

Table 9: Student 't' test.

Calcification versus No calcification	Mean difference	p value	95% confidence interval
Serum phosphate levels	1.42	<0.001	0.94 to 1.89
Serum calcium levels	0.333	0.304	-0.308 to 0.976
Calcium phosphate product	14.69	<0.001	8.184 to 21.215

DISCUSSION

Serum phosphorus levels were elevated in CKD patients with valvular calcification. In patients with calcification the mean serum phosphorus level was 6.7mg/dl and in patients without calcification the mean value was 5.3mg/dl. The difference in mean serum phosphate levels between patients with calcification and without calcification was statistically significant. Chronic kidney disease patients with valvular calcifications were having elevated serum phosphorus levels suggesting that hyperphosphatemia may be a novel risk factor for valvular calcifications.[4] Elevated serum phosphate levels were associated with aortic and mitral annular calcification.[9] Higher serum phosphate levels were associated with increased mortality in late stages of CKD and also noted that cardiovascular mortality risk increases as serum phosphate level increases in CKD patients.[10] Increased serum phosphate was associated with aortic and mitral annular calcification, thereby increasing the cardiovascular mortality in 7021 patients with CKD and found that mortality increases significantly with each 0.5mg/dl increase in serum phosphate.[4,11,12] Serum phosphate as a cardiovascular risk factor for increased mortality in CKD patients particularly in dialysis patients.[13] For every 0.5mg/dl increase in serum phosphate, the risk of cardiac valvular calcification increases by 3.6 times in the present study suggesting that there is a significant role of serum phosphate correlation

with cardiac valvular calcification in chronic kidney disease in agreement with previous literatures.[4,11]

CONCLUSION

Present study suggests that there is a strong positive correlation between the elevated levels of serum phosphate and cardiac valvular calcification in chronic kidney disease.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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