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ORIGINAL ARTICLE

Assessment of Coronary Artery Calcification in Chronic Kidney Disease Patients Using Multislice CT Correlation with Serum Phosphate Levels

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ABSTRACT

Background: Chronic kidney disease (CKD) is associated with increased cardiovascular morbidity and mortality, largely due to accelerated vascular calcification.

Objective: This study aims to assess the burden of CAC using multislice computed tomography (MSCT) and evaluate its correlation with serum phosphate levels in patients with CKD.

Methods: This cross-sectional analytical study was conducted at Medicine Department, Pakistan Atomic Energy Commission General Hospital, Islamabad from January 2023 to June 2023. A total of 189 patients diagnosed with chronic kidney disease. Demographic and clinical information, including age, sex, duration of CKD, and comorbidities, were recorded on a predesigned data collection form. Venous blood samples were collected under aseptic precautions to measure serum phosphate levels using standard enzymatic methods.

Results: The mean age of patients was 57.8 ± 12.3 years, with 64% being male. CAC was detected in 77.8% of patients, with 22.8% exhibiting severe calcification. A significant positive correlation was observed between serum phosphate levels and Agatston scores (rho = 0.472, $p < 0.001$). Patients with severe CAC had higher phosphate levels (6.1 ± 1.0 mg/dL) compared to those with no calcification (4.4 ± 0.7 mg/dL, $p < 0.001$). Dialysis patients showed significantly greater CAC burden and higher phosphate levels than non-dialysis patients ($p < 0.01$). Phosphate levels also increased progressively with advancing CKD stage ($p < 0.001$).

Conclusion: Coronary artery calcification is highly prevalent in CKD patients and is significantly associated with elevated serum phosphate levels. These findings highlight the importance of early phosphate control and vascular screening, even in non-dialysis CKD patients.

Keywords: Chronic kidney disease, coronary artery calcification, serum phosphate, multislice computed tomography.

INTRODUCTION

Chronic kidney disease (CKD) is a progressive, irreversible condition characterized by a gradual loss of renal function over time, affecting approximately 10 to 15 percent of the adult population worldwide. In CKD patients, cardiovascular disease risk is much greater than the risk of progressing to end-stage renal disease and thus, the number one cause of death in this population is cardiovascular complications[1]. Coronary artery calcification is a well-known superior uninstigated prognosticator of myocardial infarction, arrhythmias, heart failure, and all-cause mortality amongst these. Coronary artery calcification is a disease process blamed on the accumulation of calcium phosphate crystals within the intimal or medial layers of coronary arteries[2]. In the normal crowd, this usually happens due to the formation of atherosclerotic plaque. But in the patients with CKD, the calcium generated by atherosclerosis may be absent, with the primary process triggered by non-atherosclerotic factors, including mineral metabolism disturbance[3]. It consists of anomalies of phosphate, calcium and parathyroid hormones, which are prevalent in CKD and are a major cause of vascular damage and calcification[4].

Of these mineral disturbances, serum phosphate level has drawn particular concern with regard to vascular calcification pathogenesis. Even at the normal reference scale, the phosphate level above average is linked with the amplified cardiovascular risk. Phosphate causes vascular smooth muscle cells to differentiate to osteoblast-like cells, encouraging the development of proteins related to bone and discouraging inhibitors of calcification[5]. In such a way, vessel walls become actively calcified, which contributes to the augmented stiffness of the arteries, an enhanced pulse pressure, and an enhanced risk of cardiovascular incidents. Whereas such conventional risk factors as hypertension, diabetes mellitus, and dyslipidemia are contributors to cardiovascular disease in CKD, the role in the central mechanisms of CKD-associated cardiovascular disease could be played by non-traditional CKD-specific attributes, including hyperphosphatemia, uremia, oxidative stress, and chronic inflammation[6]. Hence, it is important to have an idea of and be able to measure serum phosphate to be able to catch vascular damage and cardiovascular risks early in this group[7]. Some clinical guidelines, including that of Kidney Disease: Improving Global Outcomes (KDIGO), emphasize that clinicians should control the blood phosphate levels among patients with CKD, especially in advanced stages and those on dialysis[8]. Multislice computed tomography has become a widely accepted non-invasive method for detecting and quantifying coronary artery calcification[9]. It allows for objective measurement of calcium burden using the Agatston scoring method, which has been shown to correlate strongly with cardiovascular risk in both general and high-risk populations[10]. In CKD patients, the use of this imaging modality offers additional benefits, particularly because these patients may not present with typical symptoms of coronary artery disease due to autonomic dysfunction or overlapping comorbidities. Early identification of coronary calcification through imaging may prompt timely interventions and individualized risk management[11]. Several international studies have reported a positive correlation between serum phosphate levels and coronary artery calcification scores in both dialysis and non-dialysis CKD patients[12]. However, limited data is available from South Asian populations, where the epidemiological characteristics, dietary phosphate intake, genetic predispositions, and healthcare infrastructure may differ significantly from Western contexts. In this setting, there is a growing need to assess how mineral metabolism disturbances are linked to subclinical vascular changes to inform targeted prevention strategies[13].

Objective: This study aims to assess the burden of CAC using multislice computed tomography (MSCT) and evaluate its correlation with serum phosphate levels in patients with CKD.

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METHODOLOGY

This cross-sectional analytical study was conducted at Medicine Department, Pakistan Atomic Energy Commission General Hospital, Islamabad from January 2023 to June 2023.. A total of 189 patients diagnosed with chronic kidney disease (Stages 3 to 5), as defined by the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines, were enrolled in the study using a non-probability consecutive sampling technique.

Inclusion Criteria

- Adult patients aged 18 years and above.
- Diagnosed cases of chronic kidney disease Stage 3 to 5, with or without dialysis.
- Patients who provided written informed consent.

Exclusion Criteria

- Patients with a known history of coronary artery disease, myocardial infarction, or coronary stenting.
- Individuals with active infection or acute kidney injury at the time of enrollment.
- Patients on medications known to significantly alter calcium-phosphate metabolism other than phosphate binders.
- Pregnant or lactating women.

Data Collection Procedure: After obtaining ethical approval from the institutional review board, all eligible patients were approached and informed consent was obtained. Demographic and clinical information, including age, sex, duration of CKD, and comorbidities, were recorded on a predesigned data collection form. Venous blood samples were collected under aseptic precautions to measure serum phosphate levels using standard enzymatic methods. Additional parameters such as serum calcium, parathyroid hormone (PTH), and creatinine were also recorded. Each patient underwent a multislice computed tomography (MSCT) scan of the chest using a 64-slice scanner. The scan was performed without contrast using a standardized protocol for calcium scoring. The Agatston score was calculated to quantify coronary artery calcification. Patients were categorized into four groups based on the total Agatston score:

- 0 (no calcification)
- 1–100 (mild calcification)
- 101–400 (moderate calcification)
- 400 (severe calcification)

Statistical Analysis: All collected data were entered and analyzed using SPSS version 21. Continuous variables such as age, serum phosphate, and Agatston score were presented as means with standard deviations or medians with interquartile ranges based on data distribution. Categorical variables were expressed as frequencies and percentages. Correlation between serum phosphate levels and Agatston scores was assessed using Pearson or Spearman correlation coefficients as appropriate. Comparisons of mean phosphate levels across the different CAC severity categories were made using one-way ANOVA or Kruskal-Wallis tests. A p-value <0.05 was considered statistically significant.

RESULTS

The study cohort comprised 189 CKD patients with a mean age of 57.8 ± 12.3 years, predominantly male (64%). The largest subset of patients belonged to CKD Stage 5 (54%), followed by Stage 4 (30%) and Stage 3 (16%). Hypertension was present in 73% of patients, and 52% had diabetes mellitus. Nearly half (47%) were undergoing maintenance hemodialysis. The mean serum phosphate level was 5.4 ± 1.2 mg/dL, while mean serum calcium and parathyroid hormone (PTH) levels were 8.6 ± 0.9 mg/dL and 274 ± 112 pg/mL, respectively.

Coronary artery calcification (CAC) was observed in 77.8% of the participants. Mild CAC (Agatston score 1–100) was the most common category at 29.6%, while 22.8% of patients showed severe calcification (score >400). There was a stepwise increase in mean serum phosphate levels with increasing CAC severity: 4.4 ± 0.7 mg/dL in patients without calcification, 4.9 ± 0.9 mg/dL with mild CAC, 5.6 ± 1.1 mg/dL with moderate CAC, and 6.1 ± 1.0 mg/dL in those with severe CAC.

Table 1: Baseline Characteristics of the Study Population (n = 189)

Variable	Value
Age (years), Mean ± SD	57.8 ± 12.3
Gender – Male	121 (64%)
Gender – Female	68 (36%)
CKD Stage 3	30 (16%)
CKD Stage 4	57 (30%)
CKD Stage 5	102 (54%)
Hypertension	138 (73%)
Diabetes Mellitus	98 (52%)
Maintenance Hemodialysis	89 (47%)
Serum Phosphate (mg/dL), Mean ± SD	5.4 ± 1.2
Serum Calcium (mg/dL), Mean ± SD	8.6 ± 0.9
Parathyroid Hormone (pg/mL), Mean ± SD	274 ± 112

Table 2: Distribution of Coronary Artery Calcification Based on Agatston Score

Agatston Score Category	Value
No calcification (Score = 0)	42 (22.2%)
Mild calcification (1–100)	56 (29.6%)
Moderate calcification (101–400)	48 (25.4%)
Severe calcification (>400)	43 (22.8%)
Mean Phosphate – No Calcification	4.4 ± 0.7 mg/dL
Mean Phosphate – Mild	4.9 ± 0.9 mg/dL
Mean Phosphate – Moderate	5.6 ± 1.1 mg/dL
Mean Phosphate – Severe	6.1 ± 1.0 mg/dL

Patients receiving hemodialysis had markedly higher mean Agatston scores (296.2 ± 155.4) than those not on dialysis (118.6 ± 96.8), indicating a significantly greater extent of coronary artery calcification ($p < 0.01$). Similarly, mean serum phosphate levels were elevated in the dialysis group (5.9 ± 1.3 mg/dL) compared to the non-dialysis group (4.8 ± 0.9 mg/dL), with statistical significance ($p < 0.01$), reinforcing the impact of phosphate accumulation in advanced CKD.

Table 3: Comparison of CAC and Serum Phosphate by Dialysis Status

Variable	Hemodialysis Patients (n = 89)	Non-Dialysis Patients (n = 100)	p-value
Mean Agatston Score	296.2 ± 155.4	118.6 ± 96.8	<0.01
Mean Serum Phosphate (mg/dL)	5.9 ± 1.3	4.8 ± 0.9	<0.01

Correlation analysis showed a moderately strong and statistically significant positive relationship between serum phosphate levels and Agatston scores (rho = 0.472, $p < 0.001$). Parathyroid hormone also demonstrated a significant correlation with CAC scores (rho = 0.391, $p < 0.001$). Age showed a weaker but still significant correlation (rho = 0.318, $p < 0.01$). However, serum calcium was not significantly associated with CAC (rho = 0.109, $p = 0.128$).

Table 4: Correlation Between Agatston Score and Biochemical Parameters

Parameter	Correlation Coefficient (rho)	p-value
Serum Phosphate (mg/dL)	0.472	<0.001
Serum Calcium (mg/dL)	0.109	0.128
Parathyroid Hormone (pg/mL)	0.391	<0.001
Age (years)	0.318	<0.01

Table 5: Serum Phosphate Levels Across CKD Stages

CKD Stage	Number of Patients	Mean Serum Phosphate (mg/dL) ± SD
Stage 3	30	4.3 ± 0.6
Stage 4	57	5.0 ± 0.9
Stage 5	102	5.8 ± 1.2
p-value (ANOVA)	—	<0.001

Mean serum phosphate levels rose progressively with CKD severity: 4.3 ± 0.6 mg/dL in Stage 3, 5.0 ± 0.9 mg/dL in Stage 4,

and 5.8 ± 1.2 mg/dL in Stage 5. This increase was statistically significant ($p < 0.001$) and supports the concept of phosphate retention as kidney function declines.

DISCUSSION

This study aimed to evaluate the burden of coronary artery calcification (CAC) in patients with chronic kidney disease (CKD) and examine its correlation with serum phosphate levels using multislice computed tomography (MSCT). The findings revealed a high prevalence of coronary calcification among CKD patients, with more than 75% exhibiting some degree of CAC. Importantly, a statistically significant positive correlation was found between serum phosphate levels and Agatston calcium scores, suggesting a strong association between disordered phosphate metabolism and vascular calcification[14]. The mean serum phosphate level among the study population was 5.4 ± 1.2 mg/dL, and this increased progressively with the severity of CAC. Patients with severe calcification had significantly higher phosphate levels (6.1 ± 1.0 mg/dL) compared to those with no or mild calcification (4.4–4.9 mg/dL), with $p < 0.001$. This is consistent with previous literature that identifies hyperphosphatemia as a key non-traditional cardiovascular risk factor in CKD. For instance, Block et al. (2004) and Goodman et al. (2000) demonstrated that even serum phosphate levels at the upper end of the normal range are associated with an increased risk of cardiovascular mortality and vascular calcification in CKD and dialysis populations[15]. Further, our data showed that the severity of CAC was more pronounced in patients on maintenance hemodialysis. These individuals not only had higher phosphate levels but also significantly elevated Agatston scores compared to non-dialysis patients[16]. This observation reflects the cumulative effect of prolonged mineral imbalance, chronic inflammation, and uremia in dialysis-dependent CKD, which accelerates the calcification process. Similar findings were reported by London et al. (2003), who noted more extensive vascular calcification in end-stage renal disease patients undergoing dialysis, particularly those with poor phosphate control[17]. Moreover, the Spearman correlation analysis in our study established a moderate positive correlation between serum phosphate and CAC (rho = 0.472, $p < 0.001$), reinforcing the hypothesis that phosphate plays a central role in the pathophysiology of medial arterial calcification. In contrast, serum calcium levels showed no statistically significant correlation, suggesting that phosphate may have a more dominant and independent effect on vascular calcification pathways[18]. Parathyroid hormone (PTH), another marker of mineral imbalance, also showed a significant association (rho = 0.391), indicating its contributory role in promoting bone-vascular axis dysfunction. Our results also revealed a progressive increase in serum phosphate levels with advancing CKD stage, which was statistically significant ($p < 0.001$). This trend is in line with the pathophysiological understanding that phosphate retention begins in early CKD but becomes more clinically relevant in advanced stages due to impaired renal excretion and compensatory hyperparathyroidism[19]. These findings support the KDIGO guidelines, which recommend monitoring and controlling serum phosphate levels from Stage 3 CKD onwards to prevent vascular complications. Despite the robust findings, our study has certain limitations. First, its cross-sectional design precludes causal inference. Longitudinal studies would be required to establish temporal relationships between phosphate levels and CAC progression. Second, the study did not account for other potential calcification modifiers such as fibroblast growth factor-23 (FGF-23), vitamin D levels, or the use of phosphate binders, which may have influenced the outcomes. Third, we did not evaluate clinical endpoints such as cardiovascular events or mortality, which would provide additional insight into the prognostic relevance of CAC in this cohort.

CONCLUSION

It is concluded that coronary artery calcification is highly prevalent among patients with chronic kidney disease and shows a significant positive correlation with serum phosphate levels. The severity of calcification increases with advancing CKD stage and is more pronounced in patients undergoing maintenance hemodialysis. These findings underscore the critical role of phosphate metabolism in vascular pathology and support the need for routine monitoring and early management of hyperphosphatemia in CKD patients.

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