

Relation between Calcium, Phosphorus, Calcium-Phosphorus Index and iPTH in Chronic Kidney Disease Patients

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ABSTRACT

Background: The disturbance in homeostasis of calcium, phosphorus, vitamin D, and parathyroid hormone are frequently seen in chronic kidney disease patients. It is vital for physician to know the relation among them to treat chronic kidney disease patients. The main objective of the study is to 1) gather and analyze the data from chronic kidney disease patients undergoing dialysis to find out intact parathyroid hormone status 2) the relation between level of serum calcium, serum phosphorus, calcium-phosphorus index and serum intact parathyroid hormone in Nepalese population.

Methods: Verbal consent was taken from all the participants. Eighty participants between the age of 29 and 70 years with chronic kidney disease having indication of emergency hemodialysis were included in this study. Serum calcium, and phosphorus were measured by Fully Automatic Biochemistry Analyzer, and serum intact parathyroid hormone (iPTH) was measured using Chemi Luminescence Immuno Assay (CLIA) method.

Results: There is positive correlation between high calcium – phosphorus index and raised serum intact parathyroid hormone ($r= 0.30$). The relation is also true for serum calcium level and serum intact parathyroid hormone ($r= 0.38$). There is weak negative correlation between serum phosphorus and serum intact parathyroid hormone ($r= -0.03$).

Conclusions: In Chronic kidney disease patients, high serum calcium or calcium – phosphorus index associated with raised level of serum intact parathyroid hormone and reverse is true for increased serum phosphate level. The relation may guide physician to suspect hyperparathyroidism in chronic kidney disease patients and manage the complications related to hyperparathyroidism like renal mineral bone disease, anemia resistant to erythropoietin.

Keywords: Calcium; calcium phosphorus index; intact parathyroid hormone; Nepalese population; phosphorus.

INTRODUCTION

Disturbance in mineral and bone metabolism are common in patients with chronic kidney disease (CKD).^{1,2} Beginning in CKD stage 3, the ability of the kidneys to appropriately excrete a phosphate load is diminished, leading to hyperphosphatemia, decreased 1,25(OH)₂D with associated elevations in the levels of fibroblast growth factor -23 (FGF-23).³ Impaired renal hydroxylation of 25(OH)D to 1,25(OH)₂D, reduced distal renal tubular calcium

(Ca) reabsorption, phosphate (PO₄) retention, resistance to the calcemic actions of parathyroid hormone (PTH) on bone, decreased expression of the calcium sensing receptors (CaSRs), and down regulation of 1,25(OH)₂D₃ receptor at the tissue level leading to hypocalcemia. Hyperphosphatemia, hypocalcemia, diminished level of 1,25(OH)₂D and increased concentration of FGF- 23 are responsible for raised PTH level in CKD patient.^{3,4}

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The disturbance in homeostasis of calcium, phosphorus, vitamin D, and intact parathyroid hormone (iPTH) in CKD patients also increases the risk of CKD mineral bone diseases (MBD), coronary artery disease (CAD), and extraskeletal calcification.^{1,3} There is a strong relationship between elevated serum PO₄, Ca, Ca - PO₄ index, and PTH and cardiac causes of death in hemodialysis (HD) patients, especially deaths resulting from CAD and sudden death^{5,6} Patients with Ca-PO₄ index above 72 had a 34% higher relative risk of death compared to patients with Ca-PO₄ index in the range of 42 to 52.⁷

In this study, we have assessed serum level of iPTH and its correlation with Ca, Po₄, and Ca-Po₄ index, if there is any, in HD patients. Confirmation of this association may have clinical relevance in assessing the serum iPTH level in CKD patients which is associated with high risk mortality, especially due to CAD.

METHODS

This is a hospital-based cross sectional study carried out at Division of Nephrology, Department of Internal Medicine, Kathmandu Medical College Teaching Hospital, Kathmandu, Nepal. A total of 80 CKD patients attending Kathmandu Medical college teaching hospital, the division of Nephrology between June 2013 to May 2014 for dialysis were enrolled in this cross sectional study after ethical clearance was obtained from the Research and Ethical committee, Kathmandu Medical Collage. Participants having a history of parathroidectomy or throidectomy were excluded. Weight in kilogram, height in centimeter, Body Mass Index in kg/m², and Body Surface Area in square meter were recorded. Serum calcium and phosphorus in milligram per deciliter were measured by fully automatic biochemistry analyzer. Serum intact parathyroid hormone in picogram per milliliter was measured using Chemi Luminescence Immuno Assay (CLIA) method. Calcium - Phosphorus index in square milligram per square deciliter was calculated by multiplying serum calcium and phosphorus.

SPSS version 20 was used for data entry. Range, mean and standard deviation were computed to describe the characteristics of data. Pearson correlation was used to measure relationship between level of serum calcium, phosphorus, calcium-phosphorus index and serum iPTH. Verbal consent from the study group was taken.

RESULTS

In our study, comprising 80 patients 52(65%) of the subjects were male and 28(35%) were female. The minimum and maximum age of the study group was 29 and 70 years respectively. The mean age was 59.72± 10.56 years (males: 54.96± 10.65, females: 56.82± 10.25).

Ninety-eight percent of patients had raised level of iPTH level above than recommended by KDIGO guideline. There is positive correlation between high calcium - phosphorus index and raised serum iPTH (r= 0.30) as well as for serum calcium level and serum iPTH (r= 0.38) as shown in fig. 1, 2. There is weak negative correlation between serum phosphorus and serum iPTH (r= -0.03) as shown in fig.3. There is no difference between male and female groups in respect to age, serum calcium, phosphorus, calcium-phosphorus index, blood urea, serum creatinine, iPTH and Hemoglobin in CKD patients in our study.

Table 1. Baseline characteristics of patients

Variables		Both sex	Male	Female	P value
Age (years)	Mean ± SD (range)	59.72± 10.56 (29-70)	54.96± 10.65 (29-70)	56.82± 10.25 (29-70)	0.448652
Serum Calcium (mg/dl)	Mean ± SD (range)	7.39±0.62 (5.7 - 8.4)	7.36±0.60 (5.7 - 8.4)	7.36±0.60 (6.2 - 8.4)	0.599044
Serum Phosphorus (mg/dl)	Mean ± SD (range)	6.37±0.43 (5.7 - 7.3)	6.38±0.44 (5.7 - 7.3)	6.38±0.40 (5.7 - 7.1)	0.993353
Blood Urea (mg/dl)	Mean ±SD (range)	274.92±69.15 (100 - 512)	270.69±67.85 (100 - 412)	277.14±75.18 (198 - 512)	0.706643
Serum Creatinine (mg/dl)	Mean ± SD (range)	14.71±3.34 (10.2 - 30)	15.10±3.90 (10.2 - 30)	14.14±1.73 (10.9 - 18)	0.132842
Hemoglobin (g/dl)	Mean ± SD (range)	8.38±0.99 (6.2 - 10.2)	8.34±1.00 (6.3 - 10.2)	8.44±0.97 (6.2 - 10)	0.654253
Calcium Phosphorus Index (mg ² /dl ²)	Mean ± SD (range)	47.07±4.59 (33.63 - 56)	46.99±4.46 (33.63 - 56)	47.58±5.31 (35.96 - 55.61)	0.620085
Intact Parathyroid hormone (Pg/ml)	Mean ±SD (range)	458.12±101.27 (286 - 750)	447.46±98.83 (300 - 750)	475.14±103.99 (286 - 732)	0.253165

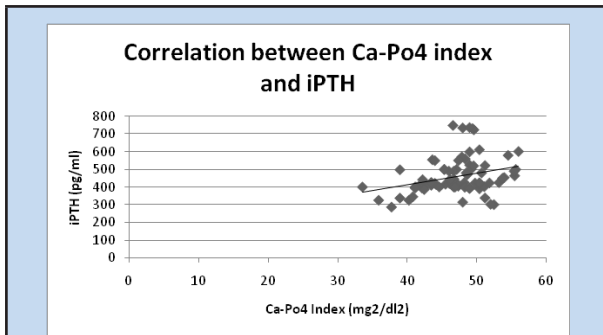


Figure 1. Scatter diagram showing positive correlation between Ca-Po4 Index and serum iPTH level ($r=0.30$).

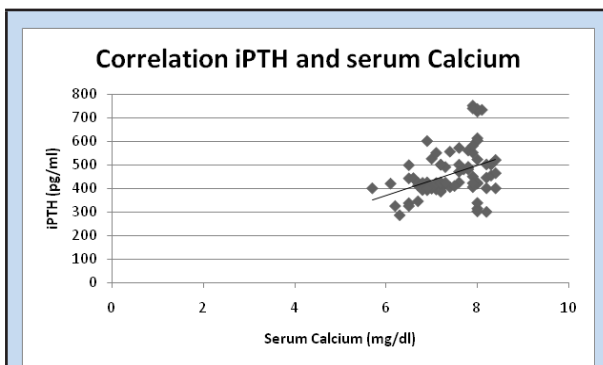


Figure 2. Scatter diagram showing positive correlation between iPTH and Serum Calcium level ($r=0.38$).

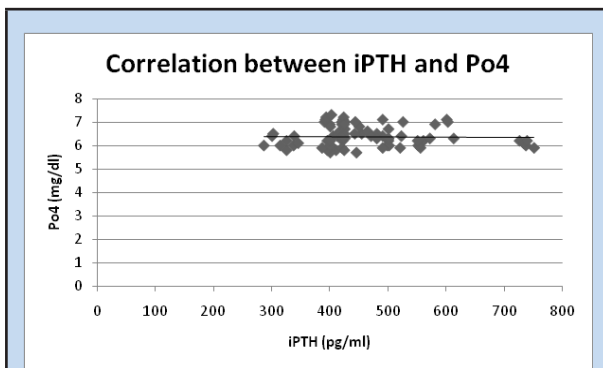


Figure 3. Scatter diagram showing reverse correlation between serum Phosphorus and iPTH level ($r= -0.03$).

function for three or more months, irrespective of the cause. The goal level of Ca-P index should be below 55 and Serum iPTH levels of 35-70 pg/ml for stage 3 CKD, 70-110 pg/ml for stage 4 and 150-300 pg/ml for stage 5 and dialysis.¹

In our study, 1.25% patients had achieved target serum iPTH level and 98.75% patients had had higher serum iPTH level as per KDIGO recommendation for CKD patients on hemodialysis. The DOPPS and Yokoyama and coworkers' study represented similar results; 26% of patients achieved the targets and 26% and 27% had elevated values, respectively.^{10, 11} Al Aly and colleagues showed that 72% of their patients had values greater than target level.¹² There is relation between elevated PTH levels with a higher mortality rate.^{5, 13-16} In this study, the assessment of the mortality or morbidity has not been done.

There is positive correlation between serum iPTH level and Serum Calcium level ($r=0.38$) and weak reverse correlation between serum phosphorus and iPTH level ($r= -0.03$). This result is not consistent with Hamdy Sliem et al study which showed positive correlation of iPTH with serum phosphorus ($r= 0.7$) and reverse relation with serum calcium ($r= -0.6$).¹⁷ Such result can occur if CKD patients are on calcium containing phosphate binder supplementation.

There is positive correlation between Ca-Po4 index and serum iPTH level ($r=0.30$), which implies as Ca-Po4 index increases, serum iPTH level also increase.

Since high serum phosphorus, calcium, ca-po4 product, and iPTH increase the risk of mortality in CKD patients, therapeutic interventions to achieve iPTH targets that compromise targets for calcium, phosphate or the calcium phosphate product may be counterproductive.

DISCUSSION

CKD is accompanied by profound disturbances in calcium, phosphate, vitamin D, and iPTH homeostasis that play a crucial role in the pathophysiology of CKD-MBD, CAD, and extraskeletal calcification.^{1,3,8,9} According to KDOQI and KDIGO guidelines 2013 CKD is defined by the presence of kidney damage or decreased kidney

Supplementation with calcium, phosphorus binder and 1,25(OH)D which alter the serum calcium, phosphorus and intact parathyroid level were not know. Duration of CKD was also not recorded. Whether patients were under hemodialysis or not was unmentioned. If the above things were known we could better correlate.

CONCLUSIONS

In CKD patients, there are definite correlations between iPTH and calcium, phosphorus and calcium - phosphorus index. The relation may guide physician to raise high suspicion of hyperparathyroidism in CKD patients and manage the complications related to hyperparathyroidism like CKD mineral bone disease, anemia resistant to erythropoietin.

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