MED-PHOENIX: JOURNAL OF NATIONAL MEDICAL COLLEGE

ORIGINAL ARTICLE

# STUDY OF HEMOGLOBIN AND CALCIUM PHOSPHORUS PRODUCT IN PATIENTS WITH CHRONIC KIDNEY DISEASE

**Suprita Gupta,[1]Sunita Kumari Gupta,[2] SurendraMarasini,[1]Sanjay Kumar Sah,[1] Amit ChandraJha,[1]NirdhanYadav [1]**

[1] 1Department of Biochemistry, National Medical College and Teaching Hospital, Brigunj, Parsa, Nepal.
[2] Department of Emergency Medicine, National Medical College and Teaching Hospital, Brigunj, Parsa, Nepal.

***Date of Submission*** : Jan 13, 2023
***Date of Acceptance*** : June 30, 2023
***Date of Publication*** : July 28, 2023

***Correspondence to:***
Suprita Gupta, Department of Biochemistry, National Medical College and Teaching Hospital, Birgunj, Parsa, Nepal.
Phone No: +977-9845035181
Email: drsuprita40@gmail.com

***Citation:***
Gupta S, Gupta SK, Marasini S, Sah SK, Jha AC, Yadav N.Study of Hemoglobin and Calcium Phosphorus Product in Patients with Chronic Kidney Disease. Medphoenix. 2023;8(1):74-78
***DOI:https://doi.org/10.3126/medphoenix.v8i1.56928***
***Conflict of interest:*** None, ***Funding:*** None

***Publisher:*** *National Medical College Pvt. Ltd.*
***MedPhoenix - Journal of National Medical College (JNMC); 2023,8(1), available at www.jnmc.com.np***
ISSN:2631-1992 (Online); ISSN:2392-425X (Print)



## ABSTRACT

***Introduction:*** *Kidneys play a vital role in the metabolism of minerals such as calcium and phosphorous. Moreover, kidney is involved in the production of erythropoietin hormone. The bone marrow suppression may occur in Chronic Kidney Disease (CKD) patients. Reduced hemoglobin and increased calcium phosphorous product concentration is also common in CKD patients.The current study is aimed to find out the impact of CKD in calcium phosphorous product and hemoglobin level in Nepalese population.*

***Methods:*** *One hundred consecutive diagnosed cases of CKDpatients were enrolled retrospectively for the study. Calcium, phosphorous, urea, creatinine and other biochemical parameters were measured in fully automated biochemistry analyzer and hemoglobin was measured using hematology analyzer (Beckman Coulter DxH500 Automated Hematology analyzer).*

***Results:*** *The current study revealed the hemoglobin and calcium phosphorous product in CKD patients.The Calcium Phosphorous Product (CaP) of 69 subjects were having less than <40mg2/dL2 and remaining 31 were having ≥ 40mg2/dL2. The negative correlation of calcium phosphorous product was seen with calcium (r= -0.478, p-value = 0.000) and sodium (r=-0.309, p-value=0.002) whereas positive correlation of calcium phosphorous product was seen with urea (r= 0.559, p-value=0.000) andCreatinine (r=0.353, p-value = 0.000). The creatinine was negatively correlated with the hemoglobin concentration (r= -0.320, p-value = 0.001).*

***Conclusions:*** *Calcium phosphate product can be fluctuated in chronic kidney disease patients along with the decrement of hemoglobin concentration. The serum calcium phosphorous product measurement can assist to rule out the severity of chronic kidney disease.*

***Keywords:*** *Calcium, Chronic Kidney Disease, Hemoglobin, Phosphorous*

## INTRODUCTION

Calcium and phosphorous are two essential minerals involved in various biochemical processes in human body. Calcium plays role in muscle contraction, blood coagulation pathway, role as a second messenger for hormonal action etc.[1,2]Secondly, phosphorous also plays vital role in plethora of cellular processes such as growth and maintenance, repair of tissues and formation of different phosphorylated intermediates like 2,3 bisphosphoglycerate.[3]

The morbidity and mortality of the Chronic Kidney Disease (CKD) patients is high when the serum level of calcium phosphorous product is elevated. It may occur via several mechanisms including hypercalcemia related kidney injury andacute phosphate nephropathy.[4]

Reduction of hemoglobin is common in CKD patients and sometimes it can be correlated to their cardiovascular outcomes. Anemia in CKD may be worsened due to various etiologies including the kidney dysfunction[5], impaired erythropoietin production or resistance, bone marrow suppression from increased levels of proinflammatory cytokines and vitamin deficiencies.[6,7]CKD is one of the major public health problems and is rising day by day. It is also associated with the cardiovascular diseases.[8]

Mineral metabolism is one of the important predictors of morbidity and mortality in CKD patients. The calcium and phosphorous metabolism is positively associated with worse outcome, not only in CKD patients but also in End Stage Renal Disease (ESRD) patients.Calcium phosphorous product derangement can be considered as the marker of renal osteodystrophy.[9]

The aim of this study was to find out the impact of calcium phosphorous product and hemoglobin levels in chronic kidney disease patients.Furthermore, the correlations of hemoglobin and calcium phosphorous product with other renal function test parameters were also found out.

## MATERIALS AND METHODS

This study wasa retrospective study from the data retrieved from the laboratory software at National Medical College and Teaching Hospital (NMCTH), Birgunj, Madhesh Pradesh of Nepal. Study duration wassix months (June2021 to November2021).Ethical clearance was obtained from the Institutional Review Committee (IRC) before starting the research (Ref.F-NMC/533/077-078).

Non probability convenient sampling technique was used to enroll the data of CKD patients. Hundred consecutive CKD patients were enrolled for the study. The parameters urea, creatinine, phosphorous and calcium were measured using fully automated biochemistry analyzer (Beckmann Coulter Inc. AU480, California). Sodium and potassium were measured using electrolyte analyzer. The hemoglobin was measured in the five-part differential analyzer (Beckman Coulter DxH500 Automated Hematology analyzer, California).

Statistical Analyses

All the data were entered in the Microsoft Excel 2010, converted to SPSS version 22 accordingly. Frequency and percentage were calculated for descriptive statistics. Chi square test were applied to compare the categorical variables. Student's t test was used to compare mean between two groups. Continuous data were expressed in the meanSD. Pearson correlation was applied for parametric data and Spearman's correlation was applied for non-parametric data. P value <0.05 was considered as statistically significant.RESULTS

Our study investigated hemoglobin and calcium phosphorous product concentrations in one hundred consecutive CKD patients, out of which59 were male and 41 were female. The variables were expressed as mean and standard deviation as depicted in Table 1.There was significant difference of mean and standard deviation of uric acid between male and female.

Table 1: Mean±SD of study variables based on gender (n=100)

| Variables | Gender | Frequency (N) | Mean SD | P* value |
|---|---|---|---|---|
| Age (years) | Male | 59 | 55.47 ± 17.46 | 0.054 |
| | Female | 41 | 54.63 ± 20.54 | |
| Urea (mg/dL) | Male | 59 | 179.79 ± 67.02 | 0.835 |
| | Female | 41 | 180.70± 65.92 | |
| Creatinine (mg/dL) | Male | 59 | 7.95 ± 4.61 | 0.081 |
| | Female | 41 | 6.96 ± 3.54 | |
| Sodium (mmol/L) | Male | 59 | 134.37± 6.74 | 0.688 |
| | Female | 41 | 132 ±5.89 | |
| Potassium (mmol/L) | Male | 59 | 4.58±1.03 | 0.403 |
| | Female | 41 | 4.46 ±0.89 | |
| Calcium (mg/dL) | Male | 59 | 8.11 ±0.72 | 0.827 |
| | Female | 41 | 8.13 ± 0.67 | |
| Phospho-rous (mg/dL) | Male | 59 | 4.66 ± 1.28 | 0.344 |
| | Female | 41 | 4.58 ± 1.21 | |
| Calcium Phospho-rous prod-uct ($mg^2/dL^2$) | Male | 59 | 37.19 ± 7.95 | 0.773 |
| | Female | 41 | 36.82 ± 7.99 | |
| Uric acid (mg/dL) | Male | 59 | 6.46 ± 1.40 | 0.018* |
| | Female | 41 | 5.26 ± 0.98 | |
| Hemoglobin (g/dL) | Male | 59 | 9.23 ± 2.17 | 0.186 |
| | Female | 41 | 9.48 ± 1.90 | |

The patients were then categorized on the basis of calcium phosphorous product (CaP). The CaP level is categorized into two groups, <40$mg^2/dL^2$ and ≥ 40$mg^2/dL^2$. Out of hundred study subjects, 69 were having less than <40$mg^2/dL^2$ and remaining 31 were having ≥ 40$mg^2/dL^2$. There was statistically significant difference in mean and standard deviation of calcium (P value: 0.01) and potassium(P value: 0.009)with gender as depicted in Table 2.

Table 2: Mean±SD of variables based on Calcium Phosphate Product (n=100)

| Variables | Calcium Phos-phate (CaP) product [$mg^2/dL^2$] | Fre-quency (N) | Mean SD | P* value |
|---|---|---|---|---|
| Age (years) | <40 | 69 | 55.85±19.22 | 0.607 |
| | ≥ 40 | 31 | 53.51±17.66 | |
| Urea (mg/dL) | <40 | 69 | 156.49±54.28 | 0.755 |
| | ≥ 40 | 31 | 232.87±60.35 | |
| Creatinine (mg/dL) | <40 | 69 | 6.60±3.71 | 0.186 |
| | ≥ 40 | 31 | 9.66±4.55 | |
| Sodium (mmol/L) | <40 | 69 | 134.55±6.12 | 0.399 |
| | ≥ 40 | 31 | 130.83±6.83 | |
| Potassium (mmol/L) | <40 | 69 | 4.33±0.81 | 0.011* |
| | ≥ 40 | 31 | 4.97±1.15 | |
| Calcium (mg/dL) | <40 | 69 | 8.36±0.65 | 0.009* |
| | ≥ 40 | 31 | 7.58±0.46 | |
| Phospho-rous (mg/dL) | <40 | 69 | 3.92±0.64 | 0.889 |
| | ≥ 40 | 31 | 6.20±0.71 | |
| Calcium Phospho-rous prod-uct ($mg^2/dL^2$) | <40 | 69 | 32.62±4.40 | 0.164 |
| | ≥ 40 | 31 | 46.88±4.29 | |

| | | | | |
|---|---|---|---|---|
| Uric acid (mg/dL) | <40 | 69 | 5.89±1.29 | 0.057 |
| | ≥ 40 | 31 | 6.15±1.55 | |
| Hemoglobin (g/dL) | <40 | 69 | 9.49±2.03 | 0.771 |
| | ≥ 40 | 31 | 8.98±2.11 | |

The hemoglobin level of the patients was then categorized into two groups, <10 g/dL and ≥10 g/dL. There was no any statistically significant difference of variables with the hemoglobin concentration. The mean and standard deviation between two categories of hemoglobin is illustrated in Table 3.

Table 3: Mean ± SD of variables based on hemoglobin levels

| Variables | Hemoglobin level (g/dL) | Frequency (N) | Mean SD | P* value |
|---|---|---|---|---|
| Age (years) | <10 | 30 | 48.54±17.43 | 0.63 |
| | ≥ 10 | 70 | 57.94±18.62 | |
| Urea (mg/dL) | <10 | 30 | 176.56±66.61 | 0.47 |
| | ≥ 10 | 70 | 181.71±66.50 | |
| Creatinine (mg/dL) | <10 | 30 | 7.41±3.72 | 0.29 |
| | ≥ 10 | 70 | 7.61±4.43 | |
| Sodium (mmol/L) | <10 | 30 | 133.53±6.12 | 0.60 |
| | ≥ 10 | 70 | 133.34±6.67 | |
| Potassium (mmol/L) | <10 | 30 | 4.64±0.84 | 0.08 |
| | ≥ 10 | 70 | 4.48±1.03 | |
| Calcium (mg/dL) | <10 | 30 | 8.22±0.65 | 0.29 |
| | ≥ 10 | 70 | 8.08±0.72 | |
| Phosphorous (mg/dL) | <10 | 30 | 4.65±01.43 | 0.08 |
| | ≥ 10 | 70 | 4.62±1.17 | |
| Calcium Phosphorous product ($mg^2/dL^2$) | <10 | 30 | 37.56±9.36 | 0.10 |
| | ≥ 10 | 70 | 36.81±7.21 | |
| Uric acid (mg/dL) | <10 | 30 | 5.79±1.42 | 0.52 |
| | ≥ 10 | 70 | 6.04±1.36 | |
| Hemoglobin (g/dL) | <10 | 30 | 10.58±2.45 | 0.01* |
| | ≥ 10 | 70 | 8.80±1.60 | |

Table 4 depicts the association between the calcium phosphorous products with the hemoglobin concentration. No any statistical significant association was observed between the CaP level and the hemoglobin level.

Table 4: Association of Calcium Phosphorous Product with Hemoglobin

| Calcium phosphate product status($mg^2/dL^2$) | Hemoglobin Status (g/dL) | | Total | P *value |
|---|---|---|---|---|
| | <10 g/dL | ≥10 g/dL | | |
| <40 | 19(63.3%) | 50(71.4%) | 69 | 0.42 |
| ≥40 | 11(36.7%) | 20(28.6%) | 31 | |
| Total | 30 | 70 | 100 | |

Table 5 depicts the correlation of the study variables with the hemoglobin and the CaP levels. The negative correlation of hemoglobin was seen with age, urea and creatinine whereas positive correlation of hemoglobin was seen with sodium. The negative correlation of calcium phosphorous product was seen with calcium and sodium whereas positive correlation of calcium phosphorous product was seen with urea, creatinine, potassium and phosphorous.

Table 5: Pearson correlation of study variables

| Variables | | Calcium Phosphorous Product (CaP) | Hemoglobin (Hb) |
|---|---|---|---|
| Age | Pearson<br>Sig (2 tailed) | -0.079, 0.436 | -0.229, 0.022 |
| Urea | Pearson<br>Sig (2 tailed) | 0.559**,0.000 | -0.168, 0.095 |
| Creatinine | Pearson<br>Sig (2 tailed) | 0.353**,0.000 | -0.320**,.001 |
| Sodium | Pearson<br>Sig (2 tailed) | -0.309**,0.002 | 0.205*,.041 |
| Potassium | Pearson<br>Sig (2 tailed) | 0.247*,0.013 | -0.137, 0.176 |
| Calcium | Pearson<br>Sig (2 tailed) | -0.478**,0.000 | 0.160, 0.111 |
| Phosphorous | Pearson<br>Sig (2 tailed) | 0.960**,0.000 | -0.101,0.317 |
| CaP | Pearson<br>Sig (2 tailed) | 1 | -0.062,0.542 |
| Uric acid | Pearson<br>Sig (2 tailed) | 0.090, 0.375 | -0.196, .051 |
| Hemoglobin | Pearson<br>Sig (2 tailed) | -0.062, 0.542 | 1 |

## DISCUSSION

The current study investigated the hemoglobin and calcium phosphate products in the chronic kidney disease patients. Our study revealed the reduced hemoglobin concentrations, mean hemoglobin concentration (male, 9.23 g/dL & in female, 9.48g/dL) in CKD populations.Androne AS et al., reported reduced hemoglobin and chronic kidney disease are common related factors. Anemia in chronic kidney disease caused

by cardiovascular disease can be pseudoanemia due to hemodilution.[11]Anemia can be worsened by the kidney dysfunction[12], impaired erythropoietin production or resistance, cytokine induced bone marrow suppression, due to increased levels of proinflammatory cytokines,[6,7] iron or vitamin deficiencies,[13]reduced levels of hemoglobin regardless of etiology is associated with the lower exercise tolerance.[14]

In the present study, there is no significant association between hemoglobin and calcium phosphate product ($mg^2/dL^2$) in CKD patients.In a study by Thongprayoon C et al., in Mississippi, United States of America, revealed that elevated Ca×P levels are independently associated with an increased risk for hospital mortality. Admission Ca×P ≥ 45mg2/dL2 is associated with the highest risk in the both CKD and non-CKD patients.They also revealed that the elevated CaP levels (≥ $45mg^2/dL^2$) are also associated with higher in hospital mortality in both CKD as well as non CKD patients.[15] Singh S et al.,reported CaP product less than 55 $mg^2/dL^2$ in 76 patients out of 101 dialysis patients from their retrospective study at Kathmandu Nepal.[18] However, we revealed 31 patients were having more than $40mg^2/dL^2$and 69 patients were having less than 40 $mg^2/dL^2$, when CaP was compared.

In our study significant correlation of urea, creatinine, sodium and potassium was found with the calcium phosphorous product. Serum urea and creatinine levels are raised in kidney diseases along with increment of serum phosphorous levels. Some studies reported a consequence of diminished phosphate filtration and excretion with the progression of CKD. Excess parathormone is released to excrete the phosphate during initial stages of CKD.[16] Among kidney transplant recipients the elevated CaP levels are associated with an increase in the allograft loss.[17]

The limitation of our study was small sample size, no follow up of the patients and the drug history of the patients were not studied. Our study didn't measure the serum level of parathyroid hormone and staging of the chronic kidney disease patients.

## CONCLUSION

We can conclude that calcium phosphate product can be fluctuated inchronic kidney disease patients along with the decrement of hemoglobin concentration. Our study recommends estimatingserum calcium phosphorous product and hemoglobin measurement in chronic kidney disease patients. The serum calcium phosphorous product measurement can assist to rule out the severity of chronic kidney disease.

## ACKNOWLEDGEMENT

All-technical staffs of Central Laboratory, National Medical College, Birgunj, Nepal.

## REFERENCES

1. Michaelsson K, Melhus H, Warensjo Lemming E, Wolk A, Byberg L. Long term calcium intake and rates of all cause and cardiovascularmortality: Community based prospective longitudinal cohort study.BMJ. Clin. Res. 2013; 346: f228.
2. Yan SD, Liu XJ, Peng Y et al. Admission serum calcium levels improve the GRACE risk score prediction of hospital mortality in patients withacute coronary syndrome. Clin. Cardiol. 2016; 39: 516–23.
3. Subramanian R, Khardori R. Severe hypophosphatemia. Pathophysiologic implications, clinical presentations, and treatment. Medicine 2000; 79: 1–8.
4. Markowitz GS, Nasr SH, Klein P et al. Renal failure due to acute nephrocalcinosis following oral sodium phosphate bowel cleansing.Hum. Pathol. 2004; 35: 675–84.
5. Ahmad AA, Rand WM, Manjunath G et al, Reduced Kidney Function and Anemia as Risk Factors for Mortality in Patients With Left Ventricular Dysfunction. J Am Coll Cardiol, 2001;38:955-62.
6. Everson PO, Woldbaek PR, Tonnesen P et al, Decreased Hematopoiesis in Bone Marrow of Mice with Congestive Heart Failure, Am J Phsiol Integr Comp Physiol 2002;282:R166-R172.
7. Weiss G, Pathogenesis and Treatment of Anemia of Chronic Disease, Blood rev, 2002;16:87-96.
8. Weiss JW, Petrik AF, Thorp ML. Identification and management of chronic kidney disease in older adults. Clinical Geriatrics 2011;19:33-7.
9. Block GA, Klassen PS, Lazarus JM et al. Mineral metabolism, mortality and morbidity in maintenance of hemodialysis. J Am Soc Nephrol. 2004;15:2208-18.
10. Colledge NK, Walker BR, Ralston SH.Davidson's Principle and practice of Medicine.21st edition. Churchill Livingstone Elsevier.2010:487-92.
11. Androne AS, Katz SD, Lund L, LaManca J, Hudaihed A, Hryniewicz K, Mancini DM. Hemodilution is common in patients with advanced heart failure. Circulation. 2003; 107:226–9.
12. Ezekowitz JA, McAlister FA, Armstrong PW. Anemia is common inheart failure and is associated with poor outcomes: insights from a cohort of 12,065

patients with new-onset heart failure. Circulation. 2003;107:223–5.

13. Anker SD, Negassa A, Coats AJ, Afzal R, Poole-Wilson PA, Cohn JN, Yusuf S. Prognostic importance of weight loss in chronic heart failure andthe effect of treatment with angiotensin-converting-enzyme inhibitors: an observational study. Lancet.2003;361:1077–83.

14. Kalra PR, Bolger AP, Francis DP, Genth-Zotz S, Sharma R, PonikowskiPP, Poole-Wilson PA, Coats AJ, Anker SD. Effect of anemia on exercise tolerance in chronic heart failure in men. Am J Cardiol. 2003;91:888-91.

15. Thongprayoon C, Cheungpasitporn W, Mao AM et al, Calcium phosphate product and its impact on mortality in hospitalized patients. Nephrology 2019;1-7.

16. Coladonato JA. Control of hyperphosphatemia among patients withESRD. J Am Soc Nephrol 2005; 16:S107-14.

17. Schaeffner ES, Fodinger M, Kramar R et al. Prognostic association of serum calcium, phosphate and calcium phosphate concentration product with outcomes in kidney transplant recipients. Transplant Int. 2007;20:247-55.

18. Singh S, Upadhyay DK, Aryal G. Value of Calcium and Phosphorous in chronic kidney disease patients under hemodialysis: A retrospective study. Journal of Pathology of Nepal. 2012;2:293-6.