

Original article

# Assessment of Calcium, Phosphorous Parathyroid Hormone in End Stage Renal Disease in Ibn Sina Teaching Hospital, Sirt

Khadega Alazoumi<sup>1</sup>, Mahmud Abushhewa\*<sup>2</sup>, Abdulati Salem<sup>3</sup>, Laila Shaglouf<sup>4</sup>, Ramzi Mohsen<sup>5</sup>

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<sup>1</sup>Department of Diagnostic and Therapeutic Radiology, Faculty of Health Science, Sirt University, Libya

<sup>2</sup>Department of Biochemistry, Faculty of Medicine, Azzaytuna University, Libya

<sup>3</sup>Department of Biochemistry, Faculty of Medicine, University of Misrata, Libya

<sup>4</sup>Department of Medical Laboratory, Faculty of Medical Technology, Elmergib University, Libya

<sup>5</sup>Department of Pharmacology, Faculty of Medicine, Azzaytuna University, Libya

\* **Correspondence:** [alhmroni832004@yahoo.com.au](mailto:alhmroni832004@yahoo.com.au)

## Abstract

Dialysis is essential for patients with end-stage renal disease (ESRD), a potentially fatal illness. Nevertheless, Patients continue encountering significant metabolic issues, such as calcium and phosphate imbalances, even with dialysis. These disorders raise the risk of cardiovascular disease, bone fragility, and death. Examples of these disorders include hypocalcemia, hyperphosphatemia, and secondary hyperparathyroidism. Although many patients are aware of these problems, less focus has been placed on aspects that may be changed, like dietary choices, the use of supplements, and the way comorbid conditions like hypertension and diabetes mellitus (DM) exacerbate these imbalances. This study investigates the prevalence and factors contributing to calcium-phosphate imbalances in ESRD patients on dialysis. It examines how demographic, clinical, and lifestyle factors influence these metabolic disturbances, aiming to inform more individualized care. This cross-sectional study was conducted at Ibn Sina Teaching Hospital, Sirt, Libya from November 2023 to June 2024. A total of 99 ESRD patients undergoing dialysis. The measures obtained were Serum calcium, phosphate, and parathyroid hormone (PTH) levels. The study also collected data on age, gender, DM and hypertension, supplement use, and dairy consumption. Correlation analyses were performed to explore the relationships between these variables and mineral disturbances. The study found that 78.8% of patients had low calcium levels, and 70.7% had elevated phosphate levels despite dialysis. 57.6% of patients exhibited elevated PTH, indicating secondary hyperparathyroidism. DM was present in 39.4% of patients, and 80.8% of patients had hypertension. Notably, 56.6% of patients used supplements, and 53.5% consumed dairy products, but hypocalcemia persisted in the majority. The findings emphasize the difficulty of maintaining calcium and phosphate imbalances in ESRD patients receiving dialysis. These results highlight the necessity of patient-specific, customized approaches to regulating mineral metabolism, particularly in individuals with co-occurring diseases such as diabetes mellitus and hypertension. Reducing problems and raising ESRD patients' quality of life requires addressing these imbalances.

**Keywords:** ESRD, PTH, Calcium, Phosphate, Diseases, DM.

## Introduction

The final stage of chronic kidney disease (CKD), known as end-stage renal disease (ESRD), is marked by a near-total or complete loss of kidney function. This means that the kidneys cannot carry out vital functions like waste filtering, electrolyte and fluid balance maintenance, and important hormone regulation. The frequency of end-stage renal disease (ESRD) is increasing worldwide, and individuals with ESRD need kidney transplantation or renal replacement treatment (dialysis) to survive. The Global Burden of Disease study indicates that chronic kidney disease (CKD) and its consequences rank among the leading causes of death globally, carrying substantial socioeconomic and healthcare costs [1].

One of the most urgent problems in the treatment of end-stage renal disease (ESRD) is the disruption of mineral metabolism, particularly calcium, phosphate, and parathyroid hormone (PTH). By filtering excess phosphate and helping to activate 1,25-dihydroxy vitamin D, the active form of vitamin D, which improves calcium absorption in the intestines, the kidneys in healthy people maintain calcium and phosphate homeostasis [2]. In ESRD, however, these processes are severely impaired, leading to hyperphosphatemia, hypocalcemia,

and compensatory secondary hyperparathyroidism (SHPT). Hyperphosphatemia arises due to the kidneys' reduced ability to excrete phosphate, while hypocalcemia results from impaired vitamin D activation and reduced calcium absorption [3]. The release of elevated levels of PTH in response to these disturbances leads to increased calcium mobilization from bones, causing bone demineralization and a range of skeletal disorders, such as renal osteodystrophy and osteomalacia [4].

The illness known as CKD-Mineral and Bone Disorder (CKD-MBD) encompasses several anomalies in mineral metabolism. One of the main causes of the increased cardiovascular risk seen in individuals with CKD and ESRD is vascular calcification, which is one of the many problems that are brought on by CKD-MBD. Vascular calcification has been demonstrated in studies to dramatically raise mortality rates among dialysis patients. According to Goodman et al. (2000), coronary artery calcification is common even in younger dialysis patients, highlighting how serious this issue is. [5]. Cardiovascular disease remains the leading cause of death in ESRD patients, driven in part by the combination of phosphate retention, hypercalcemia, and SHPT.

Dialysis, though life-sustaining, is inadequate in fully correcting the endocrine functions of the kidneys, particularly in terms of mineral metabolism. While dialysis effectively removes excess fluid and waste products, it does not sufficiently restore phosphate homeostasis or adequately correct hypocalcemia. As a result, even with regular dialysis sessions, patients continue to experience significant hyperphosphatemia and hypocalcemia, necessitating the use of phosphate binders, vitamin D analogs, and calcimimetics [6].

Previous studies, such as Block et al. (2004) and Tentori et al. (2008), have demonstrated that despite the use of these pharmacological interventions, abnormalities in calcium and phosphate levels persist in a substantial proportion of dialysis patients [7, 8]. Moreover, little research has been done on how modifiable lifestyle factors—such as dietary practices, supplement use, and comorbidities including diabetes mellitus (DM) and hypertension—affect the metabolism of minerals in patients with end-stage renal disease (ESRD).

This study investigates the frequency of and underlying causes of chronic calcium-phosphate imbalances in dialysis patients with end-stage renal disease (ESRD). We concentrate on the interaction of comorbidities like diabetes and hypertension, lifestyle changes like nutritional consumption and supplement use, and demographic characteristics like age and gender. We hope this thorough research will shed light on the management of CKD-MBD and emphasize the need for more tailored treatment plans for this particular population.

## **Methods**

### ***Study design and data collection***

This cross-sectional study was conducted at Ibn Sina Teaching Hospital, Sirt, Libya from November 2023 to June 2024. A total of 99 patients were diagnosed with end-stage renal disease (ESRD) who were receiving regular dialysis. Serum calcium, phosphate, and parathyroid hormone (PTH) were measured using standard laboratory techniques. Demographic data (age, gender), clinical history (diabetes and hypertension), and lifestyle data (dairy consumption and supplement use) were obtained through patient questionnaires and medical records.

The relationship between diverse clinical, lifestyle, and demographic factors and serum calcium and phosphate levels was examined by statistical analysis.

### ***Statistical Analysis***

The statistical analysis of the data was done using SPSS version 24. Student t-test and correlation analysis were done for the secondary statistical analysis. A p-value of less than 0.05 was accepted as significant in all types of statistical tests.

## **Results**

The male-to-female ratio was 1.3:1, and the mean age of the 99 patients was  $53.4 \pm 15.2$  years. Hypocalcemia was present in 78.8% of the subjects, with serum calcium levels below the usual reference range. One patient had increased calcium levels, whereas only 20.2% had normal levels. The mean serum phosphate level was  $6.36 \pm 2.05$  mg/dL, higher than normal in 70.7% of the patients.

**Table 1. Clinical and biochemical characteristics of the study subjects**

Characteristic	Percentages
Age (mean) y	53.5
Male (%)	56
Female (%)	43
Mean serum calcium	7.8
Mean serum phosphate	6.36
Mean serum PTH	57.6
High blood pressure (%)	80.8
Diabetes Mellitus (%)	39.4

PTH levels were elevated in 57.6% of patients, indicating secondary hyperparathyroidism, whereas PTH levels were normal in 41.4% of patients. Thirty-three patients in the group with DM (39.4%) also had hypocalcemia. Of the patients, 80.8% had comorbid hypertension.

53.5% of patients used dairy products, while 56.6% of patients utilized supplements as lifestyle variables. However, hypocalcemia persisted even after these measures. Significant relationships were shown by correlation studies between high phosphate levels ( $P = 0.752$ ) and low calcium levels and gender ( $P = 0.04$ ), with males being more affected. Age and calcium levels did not correlate in a statistically significant way ( $P = 0.274$ ).

As shown in Table 2. Overall, in our study of 99 cases, 57 had high parathyroid hormone levels. Among them, 44 had lower calcium serum and high parathyroid hormone levels, while 12 had high parathyroid hormone levels and normal calcium serum levels. with  $P = 0.492$ .

**Table 2. The correlation between calcium levels and associated risk factors (Parathyroid) in ESRD patients.**

Calcium	High	Normal	Low	Total
High	1	0	0	1
Normal	12	8	0	20
Low	44	33	1	78

As shown in Table 3. In our study of 99 cases, 70 had high phosphor levels. Among those, 40 had high parathyroid hormone levels, while 29 had normal parathyroid hormone levels with a  $P = 0.723$ .

**Table 3. The correlation between parathyroid hormone levels and associated risk factors (phosphate) in ESRD patients**

Thyroid	High	Normal	Low	Total
High	40	17	0	57
Normal	29	11	1	41
Low	1	0	0	1

As shown in Table 4 Overall, out of the 99 cases in our study, 39 had DM. Among them, 33 had lower calcium serum levels and DM, while 6 had DM and normal calcium serum levels with  $P = 0.214$

**Table 4. The correlation between calcium levels and associated risk factors (DM) in ESRD patients.**

Calcium	Yes	No	Total
High	0	1	1
Normal	6	14	20
Low	33	45	78

As shown in Table 5. Overall, out of the 99 cases in our study, 80 had high blood pressure. Among those, 62 also had lower calcium serum levels, while 17 had normal calcium serum levels. The calculated  $P=0.48$ .

**Table 5. The correlation between calcium levels and associated risk factors (Blood pressure) in ESRD patients.**

Calcium	Yes	No	Total
High	1	0	1
Normal	17	3	20
Low	62	16	78

### Discussion

The findings of the study indicate the ongoing challenge of managing calcium-phosphate imbalances in end-stage renal disease patients undergoing dialysis. Despite improvements in dialysis technology and medication, a significant proportion of patients still experience hypocalcemia and hyperphosphatemia. These findings align with the conclusions of larger research studies such as Tentori et al. (2008) and Block et al. (2004), which also highlighted the widespread occurrence of mineral metabolism abnormalities in end-stage renal disease [7, 8, 9].

It is especially troubling that 70.7% of the patients in our study still had hyperphosphatemia, as elevated phosphate levels have been repeatedly associated with higher rates of cardiovascular morbidity and death. Vascular calcification and serum phosphate levels have been directly linked by Goodman et al. (2000), with coronary artery calcification serving as a major predictor of cardiovascular events in young dialysis patients [5,10]. The precipitation of calcium-phosphate complexes in soft tissues is one of the mechanisms behind vascular calcification, and it can result in arterial stiffness, elevated blood pressure, and increased cardiovascular risk [11,12]. The secondary hyperparathyroidism (SHPT) seen in our cohort—57.6% of patients had increased PTH levels—complicates these issues.

A major cause of bone disease in end-stage renal disease (ESRD) is secondary hyperparathyroidism (SHPT), which increases bone fragility and causes renal osteodystrophy. Increased PTH exacerbates vascular calcification by inducing osteoclastic bone resorption and calcium release from the bone matrix [13,14,15]. Even with the use of calcimimetics and vitamin D analogs, Ketteler et al. (2017) noted that SHPT is still difficult to control in dialysis patients [16,17]. New strategies are therefore required to better regulate PTH levels and avoid long-term problems.

Additionally, 78.8% of patients had a significant prevalence of hypocalcemia, according to our findings. This ongoing lack of calcium is directly related to decreased vitamin D metabolism, which lowers the amount of calcium absorbed from the digestive tract. In addition, skeletal diseases like osteopenia, osteoporosis, and osteomalacia are influenced by the ongoing cycle of PTH-driven calcium release from bones. Since diabetes worsens phosphate retention and calcium loss and speeds up kidney deterioration, Moe et al. (2005) observed that these calcium-phosphate abnormalities are frequently more severe in diabetic ESRD patients [18]. Similar findings from our study showed that hypocalcemia is more common in DM patients, which makes treatment even more difficult.

The limited effectiveness of dietary treatments and supplement use in completely addressing these imbalances is another important point brought to light in this study. A considerable proportion of patients continued to have hypocalcemia, even though over half of them reported taking calcium supplements and eating dairy products. The results of Block et al. (2004), who hypothesized that dietary calcium intake might not be enough to overcome the intricate pathophysiology of CKD-MBD, are supported by this observation [7,19]. Furthermore, if vascular calcification is not closely monitored, excessive dependence on calcium-

based phosphate binders may worsen it, as cautioned by Ketteler et al. (2017) [16,20]. Therefore, food management is still a crucial part of treating CKD-MBD, but to get the best outcomes, it needs to be customized for each patient's unique profile and used in conjunction with pharmaceutical therapy.

Gender differences in calcium-phosphate metabolism were also observed, with men being more likely to exhibit hypocalcemia than women. Although the exact mechanisms for this disparity remain unclear, hormonal factors and body composition differences may play a role in altering mineral metabolism. Further research is warranted to elucidate these gender-based variations and to determine whether different therapeutic approaches are required for men and women.

Our study's high prevalence of hypertension (80.8%) highlights the condition's significance as a comorbidity that aggravates mineral imbalances. It is well-recognized that hypertension causes vascular calcification to accelerate, which worsens cardiovascular outcomes for ESRD patients. Furthermore, as diabetes exacerbates phosphate retention and speeds up bone deterioration, managing mineral problems is made more difficult by diabetic nephropathy, which affects 39.4% of our cohort [18]. Effective management of ESRD patients may require a multifaceted strategy due to the interaction between these comorbidities and mineral metabolism.

### Conclusion

The complexity of calcium-phosphate imbalances in ESRD patients undergoing dialysis is underscored by this study. Despite advancements in dialysis technology and pharmaceutical treatments, many patients continue to experience hyperphosphatemia, hypocalcemia, and secondary hyperparathyroidism, which increases the risk of cardiovascular events and bone disease. Our findings underscore the need for personalized treatment strategies that encompass medication adjustments, dietary modifications, and the management of comorbid conditions such as diabetes and hypertension. To improve outcomes and quality of life in this vulnerable population, future research should focus on enhancing these therapeutic approaches.

### References

1. Global Burden of Disease Study. Chronic kidney disease: Global burden and risk factors. *Lancet*. 2020;395(10225):709-733.
2. Block, G. A., Hulbert-Shearon, T. E., Levin, N. W., Port, F. K., & Goodman, W. G. Association of serum phosphorus and calcium x phosphate product with mortality risk in chronic hemodialysis patients: A national study. *American Journal of Kidney Diseases*.(2004); 43(4), 607-617.
3. Tinter, F., Blayney, M. J., Albert, J. M., Gillespie, B. W., Kerr, P. G., Bommer, J., & Port, F. K. Mortality risk for dialysis patients with different levels of serum calcium, phosphorus, and PTH: The Dialysis Outcomes and Practice Patterns Study (DOPPS). *American Journal of Kidney Diseases*.(2008); 52(3), 519-530.
4. Moe, S. M., & Drüeke, T. B.. Management of secondary hyperparathyroidism: The importance and the challenge of controlling parathyroid hormone levels without elevating calcium, phosphorus, and calcium-phosphorus products. *American Journal of Nephrology*. (2005);25(4), 459-465.
5. Goodman, W. G., Goldin, J., Kuizon, B. D., Yoon, C., Gales, B., Sider, D., & Salusky, I. B. Coronary artery calcification in young adults with end-stage renal disease who are undergoing dialysis. *New England Journal of Medicine*.(2000); 342(20), 1478-1483.
6. Ketteler, M., Block, G. A., Evenepoel, P., Fukagawa, M., Herzog, C. A., McCann, L., & Cunningham, J. Executive summary of the 2017 KDIGO Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD) guideline update: What's changed and why it matters. *Kidney International*.(2017); 92(1), 26-36.
7. Cozzolino, M., Ureña-Torres, P., Vervloet, M. G., Brandenburg, V., Bover, J., Goldsmith, D., & Mazzaferro, S. Is chronic kidney disease-mineral bone disorder (CKD-MBD) a syndrome? *Nephrology Dialysis Transplantation*.(2018); 33(1), 99-105.
8. Isakova, T., Wahl, P., Vargas, G. S., Gutiérrez, O. M., Scialla, J., Xie, H., & Wolf, M.. Fibroblast growth factor 23 is elevated before parathyroid hormone and phosphate in chronic kidney disease. *Kidney International*.(2013); 79(12), 1370-1378.
9. Cernaro, V., Calderone, M., Gembillo, G., Calabrese, V., Casuscelli, C., Lo Re, C., ... & Santoro, D. Phosphate control in peritoneal dialysis patients: issues, solutions, and open questions. *Nutrients*. (2023); 15(14), 3161.
10. Yamada, S., & Nakano, T. Role of Chronic Kidney Disease (CKD)–Mineral and Bone Disorder (MBD) in the Pathogenesis of Cardiovascular Disease in CKD. *Journal of atherosclerosis and thrombosis*.(2023); 30(8), 835-850.

11. London, G. M., & Guérin, A. P. Influence of arterial pulse and calcium load on vascular calcifications in end-stage renal disease. *Hypertension*.(1999); 34(4), 900-906.
12. Feenstra, L. Calciprotein Particles and the Endothelium: A Dynamic Interaction Driving Vascular Calcification.(2024)
13. Cozzolino, M., Gallieni, M., Brancaccio, D., & Slatopolsky, E. Pathogenesis of vascular calcification in chronic kidney disease. *Kidney International*. (2001);60(2), 756-764.
14. Stack, B. C. Secondary Hyperparathyroidism. *Otolaryngologic Clinics of North America*.(2024);57(1), 99-110.
15. Muppidi, V., Meegada, S. R., & Rehman, A. Secondary hyperparathyroidism.(2020)
16. Kovesdy, C. P., & Kalantar-Zadeh, K. Bone and mineral disorders in pre-dialysis CKD. *International Urology and Nephrology*. (2010);42(2), 527-538.
17. Liu, X., Liu, Y., Zheng, P., Xie, X., Li, Z., Yang, R., ... & Zhou, L. Effects of active vitamin D analogs and calcimimetic agents on PTH and bone mineral biomarkers in hemodialysis patients with SHPT: a network meta-analysis. *European Journal of Clinical Pharmacology*.(2024);1-15.
18. Moe, S. M., Chen, N. X., & Newman, C. L. Pathophysiology of vascular calcification in chronic kidney disease. *Circulation Research*. (2004); 95(6), 560-567.
19. Sprague, S. M., Martin, K. J., & Coyne, D. W. Phosphate balance and CKD–mineral bone disease. *Kidney International Reports*. (2021); 6(8), 2049-2058.
20. Evenepoel, P., Jørgensen, H. S., Bover, J., Davenport, A., Bacchetta, J., Haarhaus, M., ... & Shroff, R. Recommended calcium intake in adults and children with chronic kidney disease—a European consensus statement. *Nephrology Dialysis Transplantation*. (2024); 39(2), 341-366.