ORIGINAL RESEARCH PAPER

General Medicine

OUTCOME IN PATIENTS OF ESRD WITH VARYING LEVELS OF SERUM CALCIUM, PHOSPHORUS AND PTH

KEY WORDS: ESRD; Hemodialysis; Calcium; Phosphorus; Parathyroid Hormone; CKD-MBD; Mortality

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ABSTRACT

Background: End-stage renal disease (ESRD) is associated with profound disturbances in mineral and bone metabolism, collectively termed Chronic Kidney Disease–Mineral and Bone Disorder (CKD-MBD). Abnormal serum calcium, phosphorus, and parathyroid hormone (PTH) levels contribute significantly to vascular calcification, cardiovascular morbidity, skeletal complications, and mortality. Limited data exist regarding the optimal biochemical targets associated with the best clinical outcomes in ESRD patients on maintenance hemodialysis. **Aim:** To assess morbidity and mortality risk in patients with ESRD in relation to serum calcium, phosphorus, and PTH levels.**Methods:** A prospective cohort study was conducted among 150 ESRD patients undergoing maintenance hemodialysis. Baseline serum calcium, albumin-corrected calcium, phosphorus, and intact PTH levels were measured. Patients were followed for 12 months for hospitalization, cardiovascular events, fractures, and mortality.**Results:** Hyperphosphatemia (>5.5 mg/dL) was observed in 42% of patients; elevated PTH (>600 pg/mL) was noted in 34%. A significant positive correlation was observed between serum phosphorus and PTH ($r = 0.58$, $p < 0.001$). Patients with hyperphosphatemia had significantly higher hospitalization rates (46.0% vs. 21.8%, $p = 0.003$). Mortality was highest among patients with serum phosphorus >6.5 mg/dL (18.7%) and PTH >600 pg/mL (21.6%). Multivariate analysis demonstrated that elevated phosphorus and PTH were independent predictors of mortality.**Conclusion:** Abnormal serum phosphorus and PTH levels are strongly associated with increased morbidity and mortality in ESRD patients on maintenance hemodialysis. Maintaining mineral metabolism parameters within recommended targets may improve clinical outcomes.

.INTRODUCTION

Chronic kidney disease (CKD) represents a major global health burden, with progression to end-stage renal disease (ESRD) necessitating renal replacement therapy in the form of dialysis or kidney transplantation. Mineral metabolism disturbances begin early in CKD progression and become increasingly severe in ESRD, affecting virtually all patients receiving maintenance hemodialysis.

Reduced phosphate excretion leads to hyperphosphatemia, while impaired renal activation of vitamin D results in hypocalcemia and compensatory secondary hyperparathyroidism. These biochemical abnormalities collectively define CKD–Mineral and Bone Disorder (CKD-MBD), characterized by alterations in bone turnover, mineralization defects, and extra-skeletal calcification—particularly vascular and soft-tissue deposits. Elevated serum phosphorus and PTH have been independently associated with vascular calcification, left ventricular hypertrophy, cardiovascular events, bone fractures, and all-cause mortality in dialysis patients. Despite substantial evidence linking these biochemical derangements to adverse outcomes, the exact threshold levels associated with the lowest risk remain controversial, particularly in diverse ethnic and geographic populations, including South Asian patients.

Guidelines from the Kidney Disease Improving Global Outcomes (KDIGO) and the Kidney Disease Outcomes Quality Initiative (KDOQI) provide recommended target ranges for serum calcium, phosphorus, and PTH; however, adherence remains suboptimal in clinical practice. There is a need for prospective observational data from tertiary dialysis centers to validate these targets and assess their prognostic significance.

This study was conducted to evaluate the relationship between serum calcium, phosphorus, and PTH levels and clinical outcomes among ESRD patients receiving maintenance hemodialysis at a tertiary care teaching hospital.

AIMS AND OBJECTIVES

Aim

To assess morbidity and mortality risk in patients with ESRD in relation to serum calcium, phosphorus, and PTH levels.

Objectives

1. To determine the association between serum calcium, phosphorus, and PTH levels in patients with ESRD.

2. To evaluate dialysis outcomes in relation to these biochemical parameters.

MATERIALS AND METHODS

Study Design

A prospective cohort study was conducted over a 12-month period.

Study Setting
Department of Nephrology and Hemodialysis Unit of a tertiary care teaching hospital.

Study Population
All ESRD patients receiving maintenance hemodialysis who fulfilled the inclusion criteria during the study period.

Inclusion Criteria
(i) ESRD patients on regular maintenance hemodialysis; (ii) Age 18–65 years.

Exclusion Criteria
(i) Diagnosed malignancy; (ii) Post-menopausal women; (iii) Pre-existing cardiovascular disease; (iv) Patients not receiving hemodialysis; (v) Pre-existing bone mineral disease; (vi) Patients presenting with sepsis.

Data Collection
Baseline demographic and clinical characteristics were recorded for all enrolled patients. Laboratory investigations included serum calcium, serum albumin, albumin-corrected calcium, serum phosphorus, and intact PTH. Albumin-corrected calcium was calculated using the Payne formula:

Corrected Calcium (mg/dL) = Measured Calcium + 0.8 × (4.0 − Serum Albumin)

Outcome Measures
Morbidity outcomes included hospitalization, bone pain, pathological fractures, vascular calcification, and cardiovascular events. The primary outcome of interest was all-cause mortality during the 12-month follow-up period.

Statistical Analysis
Data were analyzed using IBM SPSS Statistics version 26.0. Continuous variables were expressed as mean ±standard deviation (SD); categorical variables were expressed as percentages. Pearson's correlation coefficient was used to assess the association between continuous biochemical parameters. Chi-square test was applied for categorical outcomes. A Cox proportional hazards regression model was used to identify independent predictors of mortality. A p-value <0.05 was considered statistically significant.

RESULTS

Baseline Characteristics
A total of 150 ESRD patients receiving maintenance hemodialysis were enrolled. The mean age of the cohort was 48.6 ±10.4 years. Males constituted 62.7% (n = 94) of the study population. The mean duration on dialysis was 4.2 ±2.1 years. Baseline characteristics are presented in Table 1.

Table 1. Baseline Demographic and Clinical Characteristics (N = 150)

Variable	Value
Mean age	48.6 ±10.4 years
Male	94 (62.7%)
Female	56 (37.3%)
Mean dialysis duration	4.2 ±2.1 years

Mineral Metabolism Parameters
The mean serum calcium was 8.6 ±0.9 mg/dL and albumin-corrected calcium was 8.9 ±0.8 mg/dL. Mean serum phosphorus was 5.7 ±1.4 mg/dL, which exceeded the recommended upper limit of 5.5 mg/dL on average. Mean intact PTH was 482 ±278 pg/mL. Detailed values are presented in Table 2.

Table 2. Mineral Metabolism Parameters at Baseline

Parameter	Mean ±SD
Serum Calcium	8.6 ±0.9 mg/dL
Corrected Calcium	8.9 ±0.8 mg/dL
Serum Phosphorus	5.7 ±1.4 mg/dL
Intact PTH	482 ±278 pg/mL

Distribution of Patients by Biochemical Strata
Hyperphosphatemia (serum phosphorus >5.5 mg/dL) was observed in 42% (n = 63) of patients. Only 12% (n = 18) had hypophosphatemia. With respect to PTH, 34% (n = 51) had PTH >600 pg/mL, while 16% (n = 24) had suppressed PTH <150 pg/mL (Table 3 and Table 4).

Table 3. Distribution of Patients According to Serum Phosphorus Level

Serum Phosphorus Group	Number (%)
<3.5 mg/dL (Hypophosphatemia)	18 (12.0%)
3.5–5.5 mg/dL (Target Range)	69 (46.0%)
>5.5 mg/dL (Hyperphosphatemia)	63 (42.0%)

Table 4. Distribution of Patients According to Intact PTH Level

Intact PTH Group	Number (%)
<150 pg/mL (Suppressed)	24 (16.0%)
150–600 pg/mL (Target Range)	75 (50.0%)
>600 pg/mL (Elevated)	51 (34.0%)

Correlation Analysis
A significant positive correlation was observed between serum phosphorus and intact PTH ($r = 0.58$, $p < 0.001$). A negative correlation was noted between serum calcium and PTH ($r = -0.29$, $p = 0.002$), and between corrected calcium and phosphorus ($r = -0.18$, $p = 0.03$) (Table 5).

Table 5. Pearson Correlation Analysis of Biochemical Parameters

Variables	Correlation (r)	p-value
Phosphorus vs. PTH	0.58	<0.001
Calcium vs. PTH	−0.29	0.002
Corrected Calcium vs. Phosphorus	−0.18	0.03

Morbidity Outcomes
Patients with hyperphosphatemia demonstrated significantly higher rates of hospitalization (46.0% vs. 21.8%, $p = 0.003$), fractures (11.1% vs. 2.3%, $p = 0.02$), and bone pain (39.7% vs. 17.2%, $p = 0.001$) compared to those with normal phosphorus levels (Table 6).

Table 6. Morbidity Outcomes by Phosphorus Category

Outcome	Normal Phosphorus	High Phosphorus	p-value
Hospitalization	21.8%	46.0%	0.003
Pathological Fracture	2.3%	11.1%	0.02
Bone Pain	17.2%	39.7%	0.001

Mortality Outcomes
During the 12-month follow-up, 18 deaths (12.0%) occurred. Mortality was lowest in patients with serum phosphorus within the target range (3.5–5.5 mg/dL: 4.3%) and highest in those with elevated phosphorus (>5.5 mg/dL: 18.7%) and low phosphorus (<3.5 mg/dL: 11.1%) ($p = 0.01$). Similarly, mortality was lowest in patients with PTH 150–600 pg/mL (4.0%) and highest in those with PTH >600 pg/mL (21.6%, $p = 0.004$) (Tables 7 and 8).

Table 7. Mortality According to Serum Phosphorus Level (p = 0.01)

Phosphorus Level	Mortality (%)
<3.5 mg/dL	11.1%
3.5–5.5 mg/dL	4.3%
>5.5 mg/dL	18.7%

Table 8. Mortality According to Intact PTH Level (p = 0.004)

PTH Level	Mortality (%)
<150 pg/mL	12.5%
150–600 pg/mL	4.0%

>600 pg/mL	21.6%

Multivariate Cox Regression Analysis

Cox proportional hazards regression identified elevated serum phosphorus (HR 2.72; 95% CI: 1.21–6.09; p = 0.01) and PTH >600 pg/mL (HR 3.18; 95% CI: 1.38–7.31; p = 0.005) as independent predictors of all-cause mortality. Corrected calcium >10.2 mg/dL did not reach statistical significance (HR 1.74; 95% CI: 0.81–3.76; p = 0.12) (Table 9).

Table 9. Multivariate Cox Proportional Hazards Regression for All-Cause Mortality

Variable	Hazard Ratio	95% CI	p-value
High Phosphorus (>5.5 mg/dL)	2.72	1.21–6.09	0.01
PTH >600 pg/mL	3.18	1.38–7.31	0.005
Corrected Calcium >10.2 mg/dL	1.74	0.81–3.76	0.12

DISCUSSION

The present study demonstrates a strong and significant association between abnormalities in mineral metabolism and adverse clinical outcomes among ESRD patients undergoing maintenance hemodialysis. Both hyperphosphatemia and elevated PTH emerged as independent predictors of morbidity and all-cause mortality. Hyperphosphatemia was present in 42% of the study cohort, consistent with reports from large international registries such as the Dialysis Outcomes and Practice Patterns Study (DOPPS), which have consistently documented suboptimal phosphorus control across diverse dialysis populations. In our cohort, patients with serum phosphorus >5.5 mg/dL experienced significantly higher rates of hospitalization, fractures, and bone pain compared to those with target-range phosphorus levels. The pathophysiological basis for these observations is well established: elevated phosphorus promotes vascular smooth muscle calcification, activates inflammatory pathways, induces endothelial dysfunction, and stimulates PTH secretion—collectively accelerating cardiovascular disease progression.

Secondary hyperparathyroidism, defined by PTH >600 pg/mL in our analysis, was present in 34% of patients and was associated with the highest mortality risk (HR 3.18, p = 0.005). Markedly elevated PTH drives high-turnover bone disease, increases cortical bone resorption, and exacerbates vascular and soft-tissue calcification through fibroblast growth factor-23 (FGF-23)-mediated pathways. These mechanisms translate directly into the clinical outcomes observed in our cohort.

Notably, both very high PTH (>600 pg/mL) and suppressed PTH (<150 pg/mL) were associated with higher mortality compared to the target range of 150–600 pg/mL, corroborating the U-shaped relationship previously described in the literature. This finding underscores the importance of avoiding over-suppression of PTH, which may reflect adynamic bone disease and is associated with vascular calcification and fracture risk.

Corrected serum calcium showed only a trend toward association with mortality (HR 1.74, p = 0.12), suggesting it may be a weaker prognostic biomarker compared to phosphorus and PTH in this population. This is consistent with prior observational studies that have reported phosphorus and PTH as stronger predictors of cardiovascular events and survival in ESRD.

The strong positive correlation between serum phosphorus and PTH (r = 0.58, p <0.001) reflects the well-established physiological loop: phosphate retention stimulates PTH secretion both directly and indirectly through suppression of calcitriol synthesis. Addressing hyperphosphatemia with dietary restriction, appropriate phosphate binders, and optimization of dialysis adequacy therefore represents a dual strategy to control both phosphorus and PTH levels.

The findings of this study are in accordance with recommendations from the 2017 KDIGO CKD-MBD Guideline Update and KDOQI guidelines, which advise targeting serum phosphorus in the normal range and maintaining PTH between two and nine times the upper limit of normal (approximately 150–600 pg/mL) in dialysis patients. Achieving these targets in practice requires regular biochemical monitoring, patient education regarding dietary phosphorus, and individualized use of active vitamin D analogues, calcimimetics, and phosphate binders.

This study has several strengths, including its prospective design, complete 12-month follow-up, and standardized biochemical measurements. Limitations include the single-center design, a relatively modest sample size of 150 patients, and the exclusion of patients with pre-existing cardiovascular disease, which may limit generalizability. Larger multicenter studies are warranted to establish population-specific optimal biochemical targets for Indian ESRD patients.

CONCLUSION

Abnormal serum phosphorus and PTH levels are significantly and independently associated with increased morbidity and all-cause mortality among ESRD patients receiving maintenance hemodialysis. Patients with serum phosphorus >5.5 mg/dL or PTH >600 pg/mL face substantially poorer clinical outcomes and higher mortality risk. Strict monitoring and targeted management of CKD-MBD biochemical parameters—aligned with KDIGO guidelines—are essential to improve survival and reduce complications in this vulnerable patient population.

RECOMMENDATIONS

1. Regular monitoring of serum calcium, phosphorus, and PTH at least every one to three months in all ESRD patients on maintenance hemodialysis.

2. Early and aggressive treatment of secondary hyperparathyroidism using active vitamin D analogues and/or calcimimetics before PTH exceeds 600 pg/mL.

3. Appropriate use of calcium-based and non-calcium-based phosphate binders tailored to individual patient profiles to achieve target serum phosphorus levels.

4. Maintaining phosphorus and PTH within KDIGO-recommended target ranges as a quality benchmark for dialysis units.

5. Larger multicenter prospective studies across diverse Indian dialysis centers to establish population-specific optimal biochemical targets and validate prognostic thresholds.

DECLARATIONS

Conflict of Interest: The authors declare no conflicts of interest.

Funding: This study received no external funding.

Ethical Approval: The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Ethics Committee. Written informed consent was obtained from all participants.

Data Availability: The dataset supporting the conclusions of this article is available from the corresponding author upon reasonable request.

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