

Association between Parathyroid Hormone and Phosphorus Levels with Catheter-Related Bloodstream Infections in Hemodialysis Patients: A Cross-Sectional Study

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Received:
Aug 8, 2025

Revised:
Mar 30, 2026

Accepted:
Apr 24, 2026

Published:
Apr 27, 2026

Abstract

Background and Objectives: Catheter-related bloodstream infection (CRBSI) is a major cause of morbidity and mortality among hemodialysis (HD) patients. Disturbances in mineral metabolism, including abnormalities in parathyroid hormone (PTH), phosphorus, and calcium levels, may contribute to immune dysfunction; however, their association with CRBSI remains unclear. This study aimed to investigate the association between serum phosphorus, PTH, and calcium levels and the occurrence of CRBSI in hemodialysis patients.

Methods: In this cross-sectional study, 100 adult patients undergoing maintenance hemodialysis with permanent tunneled catheters were evaluated between April 2021 and September 2022. Demographic data and laboratory parameters were collected, and average laboratory values during follow-up were used for analysis. CRBSI was defined according to CDC criteria. Multivariable logistic regression was performed to identify factors associated with CRBSI.

Results: CRBSI occurred in 19 patients (19%), with an incidence density of 1.3 episodes per 1,000 catheter-days. Patients with CRBSI were significantly older ($P = 0.020$) and had higher mean PTH levels ($P = 0.012$) and lower calcium levels ($P = 0.014$). Serum phosphorus levels were higher in infected patients but did not reach statistical significance. In multivariable analysis, advanced age was independently associated with CRBSI (OR 1.07; 95% CI 1.02–1.12; $P = 0.006$).

Conclusion: Advanced age was independently associated with CRBSI in hemodialysis patients with permanent catheters. Higher PTH and lower calcium levels were observed among infected patients, suggesting a potential association between mineral metabolism disturbances and infection risk. Further prospective studies are needed to clarify causality and underlying mechanisms.

Keywords: Parathyroid Hormone, Phosphor, Catheter-Related Bloodstream Infection, Hemodialysis

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Cite this article as: Bagherinejad M, Shamspour N, Ahmadipour H, Askari H. Association between Parathyroid Hormone and Phosphorus Levels with Catheter-Related Bloodstream Infections in Hemodialysis Patients: A Cross-Sectional Study. *Iran Red Crescent Med J.* 2026;40.1-6.

1. Introduction

End-stage renal disease (ESRD) is increasing globally, with a projected 18% rise in incidence by 2030 (1, 2). Among the modalities of renal replacement therapy (RRT), hemodialysis (HD) is the

most widely used modality in Iran and the world (1, 2). While arteriovenous fistulas (AVFs) are the preferred vascular access, the use of permanent catheters is rising due to late referrals and vascular complications (3).

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Key Messages:

↑**Question** Are PTH, phosphorus, calcium levels, and age associated with CRBSI in hemodialysis patients with permanent catheters?

↯**Findings** Advanced age was independently associated with CRBSI; higher PTH and lower calcium were observed in infected patients.

→**Meaning** Older patients with CKD-MBD disturbances may require closer monitoring and earlier preventive strategies.

Catheter-related bloodstream infection (CRBSI) is a major complication of permanent hemodialysis catheters, contributing substantially to mortality, healthcare costs, and hospitalization, and representing the second leading cause of death in hemodialysis patients (4). Reported CRBSI incidence in tunneled catheters ranges from 0.5 to 5.5 episodes per 1,000 catheter-days, with the highest risk occurring within the first three months after catheter insertion (5-7).

Identifying the risk factors that increase the risk of CRBSI is important because, by identifying these risk factors, preventive policies can be established and cost wastage can be avoided. In previous studies, the duration of catheter use, diabetes, old age, low hemoglobin level, and low serum albumin level were identified as risk factors for increasing the risk of CRBSI in patients undergoing HD (8-10). Secondary hyperparathyroidism and hyperphosphatemia, key components of chronic kidney disease, mineral and bone disorder (CKD-MBD), have traditionally been linked to skeletal and cardiovascular complications; however, increasing evidence suggests that they may also influence inflammatory pathways and host immune responses (11).

In recent studies, parathyroid hormone (PTH) has been identified as an important factor in immunological dysfunction. Parathyroid hormone (PTH) receptors have been identified on circulating lymphocytes, and elevated PTH levels have been associated with impaired lymphocyte proliferation, altered cytokine production, and reduced neutrophil function (12). Observational studies have further demonstrated associations between higher PTH concentrations and markers of systemic inflammation, suggesting a potential link between secondary hyperparathyroidism and impaired host defense mechanisms in advanced chronic kidney disease (12, 13).

In parallel, hyperphosphatemia has been implicated in immune dysfunction among patients receiving hemodialysis. Experimental and clinical studies have reported associations between elevated serum phosphorus levels and reduced T-lymphocyte counts, endothelial dysfunction, and increased inflammatory activity (14). Moreover, abnormalities in serum phosphate levels have been associated with infection-related outcomes and mortality in dialysis populations, although findings across studies remain heterogeneous and sometimes conflicting (15). These inconsistencies highlight the complexity of the relationship between phosphate metabolism and immune response and underscore the need for further investigation.

Despite these observations, the relationship between serum PTH and phosphorus levels and the risk of catheter-related bloodstream infection has not been adequately investigated. Given the high burden of CRBSI and the biological plausibility linking CKD-MBD to immune dysfunction, further clarification of this association is warranted.

Therefore, the present study aimed to investigate the association between serum phosphorus and parathyroid hormone levels and the incidence of catheter-related bloodstream infections in patients.

2. Materials and Methods

2.1. Study Design and Study Population

This cross-sectional study was conducted between April 2021 and September 2022 in hemodialysis centers in Kerman, Iran. Sampling was performed as a census, and all patients referred to start hemodialysis with a permanent catheter were evaluated during the period mentioned for entry. Given the observational cross-sectional design, temporal relationships and causality between exposures and outcomes could not be assessed.

2.2. Inclusion and Exclusion Criteria

Hemodialysis patients aged 18 years and older undergoing maintenance hemodialysis who had a permanent catheter and provided informed consent were included in the study. Exclusion

Criteria were a history of parathyroidectomy, treatment with antibiotics for other reasons, Prophylaxis with TaurLock™, vascular problems, and a history of previous catheter infections.

2.3. Data Collection

Demographic data and laboratory parameters (calcium, phosphorus, PTH, hemoglobin, alkaline phosphatase, urea, creatinine, KT/V, URR, and ferritin) were recorded. To reduce intra-individual variability, average monthly laboratory values were calculated for each patient over the observation period and used in all statistical analyses, rather than single baseline measurements.

Five cubic centimeters of venous blood was collected from each hemodialysis patient following a 10-h fast during their visit. Blood samples were promptly transported to the same laboratory. Hemoglobin (Hb) levels were assessed using a Sysmex KX-21N hematology auto-analyzer (Sysmex Corporation, Kobe, Japan). Serum ferritin levels were determined using the ELISA method (Monoband, CA, USA). Creatinine, calcium, and phosphorus levels were measured using a commercial kit (Pars Azmoon Co., Iran). To adjust patients' total calcium levels based on albumin levels, the corrected total calcium was calculated as measured serum calcium (mg/dL) + (4 - ALB serum [g/dL]) × 0.8. PTH levels were analyzed using a new PTH (1-84) kit (Fardavar Co., Iran). The dialysis adequacy of patients was evaluated using a Kt/V calculator and URR formula for patients undergoing hemodialysis (16).

Catheter-related bloodstream infection (CRBSI) was defined as the presence of fever (>38°C) or chills in patients with an indwelling hemodialysis catheter, with no alternative source of infection. Simultaneous blood cultures were obtained from the catheter hub and a peripheral vein. CRBSI was classified as definite when the same organism was isolated from blood and catheter tip cultures, and as probable when symptoms resolved with antibiotic therapy in the presence of positive blood cultures but unavailable or negative catheter tip cultures (4).

2.4. Sample Size and Power Considerations

This study was census-based and included all eligible patients during the study period (n = 100). A post hoc power consideration was performed based on the observed

CRBSI incidence (19%). Given this event rate, the sample size allowed inclusion of a limited number of clinically relevant predictors in multivariable logistic regression, while acknowledging reduced power to detect small effect sizes.

2.5. Statistical Analysis

Continuous variables were reported as mean $\pm$ standard deviation, and categorical variables as frequencies and percentages. Group comparisons were performed using independent t-tests or ANOVA for continuous variables and chi-square tests for categorical variables. Multivariable logistic regression analysis was conducted to identify factors associated with CRBSI. Variables entered into the model were selected based on clinical relevance and prior literature and included age, sex, serum phosphorus, PTH, calcium, and total iron-binding capacity (TIBC).

Multicollinearity was assessed using variance inflation factors (VIF), with values <5 considered acceptable. Linearity of continuous variables with the logit of the outcome was evaluated using the Box-Tidwell test and graphical assessment. Odds ratios (ORs) with 95% confidence intervals (CI) were reported. Statistical analyses were performed using SPSS version 23, with a significance level set at $P < 0.05$.

3. Results

3.1. Patient Characteristics

A total of 100 patients undergoing maintenance hemodialysis with permanent tunneled catheters were included in the study. The mean age of the study population was 54.1 ± 16.9 years, and 56% of participants were male. During the study period, 19 patients (19%) developed catheter-related bloodstream infection (CRBSI). Baseline demographic and clinical characteristics of patients with and without CRBSI are presented in Table 1. Patients who developed CRBSI were significantly older than those without infection (62.6 ± 16.5 vs. 52.3 ± 16.6 years; $P = 0.020$). There were no significant differences between the

two groups with respect to sex distribution, duration of hemodialysis, prevalence of diabetes mellitus, or dialysis adequacy indices, including Kt/V and urea reduction ratio (URR).

3.2. Laboratory Findings

Laboratory parameters of patients with and without CRBSI are summarized in Table 2. Mean serum parathyroid hormone (PTH) levels were significantly higher in patients with CRBSI compared with those without infection (406.6 ± 264.0 vs. 306.7 ± 389.2 pg/mL; $P = 0.012$) (Figure 1). In contrast, mean corrected serum calcium levels were significantly lower in the CRBSI group (8.56 ± 0.77 vs. 8.85 ± 0.84 mg/dL; $P = 0.014$).

Serum phosphorus levels tended to be higher among patients with CRBSI; however, this difference did not reach statistical significance (5.43 ± 1.47 vs. 4.88 ± 1.08 mg/dL; $P = 0.089$) (Figure 2). No statistically significant differences were observed between the two groups regarding hemoglobin concentration, serum albumin, alkaline phosphatase, iron indices (serum iron, total iron-binding capacity, ferritin), or other laboratory parameters.

3.3. Incidence Density of CRBSI

During the observation period, the total catheter exposure time was approximately 14,600 catheter-days, yielding an incidence density of 1.3 CRBSI episodes per 1,000 catheter-days, corresponding to an annual infection rate of approximately 0.47 episodes per catheter-year. Multivariable Logistic Regression Analysis

Multivariable logistic regression analysis was performed to identify factors independently associated with CRBSI. Variables entered into the model included age, serum phosphorus, PTH, calcium, and total iron-binding capacity (TIBC). Increasing age was independently associated with higher odds of CRBSI (OR 1.07; 95% CI 1.02–1.12; $P = 0.006$). Serum phosphorus and PTH levels were not independently associated with CRBSI after adjustment. Lower serum calcium showed a borderline asso-

Table 1. Demographic and clinical characteristics of hemodialysis patients according to CRBSI status

Variable	Total (n = 100)	CRBSI (n = 19)	No CRBSI (n = 81)	P-value
Age (years), mean $\pm$ SD	54.1 $\pm$ 16.9	62.6 $\pm$ 16.5	52.3 $\pm$ 16.6	0.020
Male sex, n (%)	56 (56.0)	10 (52.6)	46 (56.8)	0.750
Duration of HD (months), mean $\pm$ SD	23.8 $\pm$ 12.1	25.4 $\pm$ 11.8	23.4 $\pm$ 12.2	0.530
Diabetes mellitus, n (%)	40 (40.0)	8 (42.1)	32 (39.5)	0.820
Dialysis adequacy (Kt/V), mean $\pm$ SD	1.31 $\pm$ 0.22	1.29 $\pm$ 0.21	1.32 $\pm$ 0.22	0.610
URR (%), mean $\pm$ SD	66.8 $\pm$ 7.4	65.9 $\pm$ 7.8	67.0 $\pm$ 7.3	0.580

Note: P values represent comparisons between CRBSI and non-CRBSI groups.

Table 2. Laboratory characteristics of hemodialysis patients with and without CRBSI

Variable	Total (n = 100)	CRBSI (n = 19)	No CRBSI (n = 81)	P-value
Hemoglobin (g/dL), mean $\pm$ SD	9.7 $\pm$ 1.5	9.6 $\pm$ 1.4	9.8 $\pm$ 1.5	0.540
Serum albumin (g/dL), mean $\pm$ SD	3.7 $\pm$ 0.4	3.6 $\pm$ 0.4	3.7 $\pm$ 0.4	0.280
PTH (pg/mL), mean $\pm$ SD	325.9 $\pm$ 365.4	406.6 $\pm$ 264.0	306.7 $\pm$ 389.2	0.012
Serum phosphorus (mg/dL), mean $\pm$ SD	5.0 $\pm$ 1.2	5.43 $\pm$ 1.47	4.88 $\pm$ 1.08	0.089
Corrected calcium (mg/dL), mean $\pm$ SD	8.79 $\pm$ 0.83	8.56 $\pm$ 0.77	8.85 $\pm$ 0.84	0.014
Alkaline phosphatase (IU/L), mean $\pm$ SD	265.9 $\pm$ 119.5	282.4 $\pm$ 121.6	261.8 $\pm$ 118.9	0.490
Serum iron (μ g/dL), mean $\pm$ SD	71.3 $\pm$ 26.4	69.8 $\pm$ 25.1	71.7 $\pm$ 26.9	0.780
TIBC (μ g/dL), mean $\pm$ SD	232.5 $\pm$ 41.8	228.4 $\pm$ 39.6	233.4 $\pm$ 42.3	0.620
Ferritin (ng/mL), median (IQR)	248 (180–360)	280 (210–420)	235 (170–330)	0.180

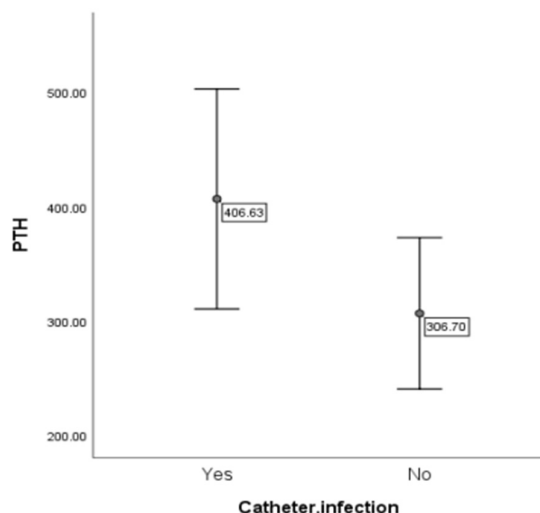


Figure 1. Comparison of mean PTH levels based on the presence or absence of CRBSI

ciation with CRBSI (OR 0.39; 95% CI 0.15–1.01; $P = 0.054$). Detailed regression results, including odds ratios, confidence intervals, and exact p-values, are shown in Table 3.

3.4. Missing Data

Missing data were minimal, with less than 5% missingness across all variables. Analyses were conducted using a complete-case approach, and patients with missing key laboratory or outcome data were excluded from the relevant analyses.

4. Discussion

In this cross-sectional study of hemodialysis patients with permanent catheters, catheter-related bloodstream infection (CRBSI) occurred in 19% of participants. The principal findings were that older age was independently associated with increased odds of CRBSI. At the same time, higher serum parathyroid hormone (PTH) levels and lower calcium levels were observed in patients with infection. Although serum phosphorus levels were higher in patients with CRBSI, this association did not remain statistically significant after adjustment for confounding factors. These findings suggest that disturbances in mineral

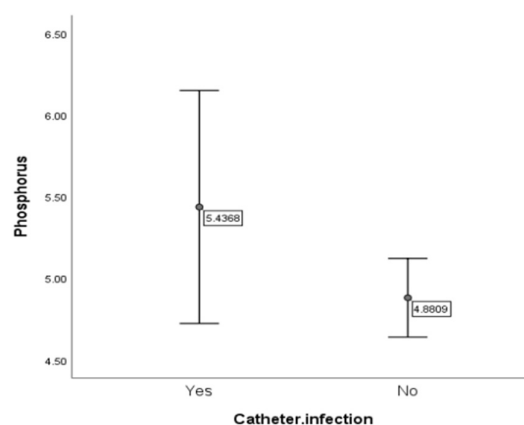


Figure 2. Comparison of mean phosphorus levels based on the presence or absence of CRBSI

metabolism, particularly those related to secondary hyperparathyroidism, may coexist with an increased susceptibility to infection, although causality cannot be inferred.

The observed incidence of CRBSI in our cohort is consistent with previous reports from dialysis populations, which have documented infection rates ranging from 15% to 25% (8, 17).

It appears that increasing age is associated with decreased immunity and self-care factors, increasing the possibility of infection. Advanced age has consistently been identified as a strong risk factor for CRBSI, likely reflecting cumulative comorbidity burden, immunosenescence, and prolonged catheter exposure (9, 10). Our findings are in line with recent meta-analyses demonstrating that older hemodialysis patients experience significantly higher rates of catheter-associated infections (9, 10).

Large population-based studies have also shown associations between CKD-MBD biomarkers and infection-related outcomes. Ishigami et al. reported that higher PTH and corrected calcium levels were independently associated with long-term risk of infection-related hospitalization, even in non-dialysis populations, highlighting the systemic immunomodulatory effects of mineral metabolism disorders (18). Jaqueto et al. demonstrated a significant relationship between higher PTH levels, oxidative stress, and systemic inflammation in hemodialysis patients, support-

Table 3. Multivariable logistic regression analysis of factors associated with CRBSI

Variable	Odds Ratio (OR)	95% CI	P value
Age (per 1-year increase)	1.07	1.02 – 1.12	0.006
PTH (per 100 pg/mL increase)	1.04	0.97 – 1.12	0.260
Serum phosphorus (mg/dL)	1.31	0.89 – 1.92	0.170
Corrected calcium (mg/dL)	0.39	0.15 – 1.01	0.054
TIBC (µg/dL)	0.99	0.97 – 1.01	0.310

Model details:

Variables entered: age, PTH, serum phosphorus, corrected calcium, TIBC

Hosmer–Lemeshow goodness-of-fit: $P = 0.61$

No evidence of multicollinearity ($VIF < 2$)

ing a link between secondary hyperparathyroidism and impaired host defense (11). The observed association between elevated PTH levels and CRBSI is biologically plausible and supported by emerging evidence linking CKD-MBD to immune dysfunction. Recent reviews and experimental studies indicate that PTH receptors are expressed on immune cells, including lymphocytes and monocytes, and excessive PTH may impair immune cell chemotaxis, phagocytosis, and cytokine signaling (11–13). Elevated PTH and phosphate levels contribute to chronic inflammation, oxidative stress, and altered innate and adaptive immune responses through activation of NF- κ B signaling, dysregulation of T-cell function, and macrophage polarization (12, 19). Furthermore, FGF23, often elevated in states of phosphate retention, has been shown to impair neutrophil recruitment and suppress vitamin D-mediated antimicrobial responses (12, 13).

The association between lower calcium levels and CRBSI has not been extensively reported in prior studies. Nonetheless, hypocalcemia has been observed in septic and critically ill patients and may reflect inflammatory cytokine release, altered vitamin D metabolism, and impaired parathyroid-calcium axis regulation during systemic infection (20, 21). Given the cross-sectional design, reverse causality, where inflammation and infection influence calcium homeostasis, cannot be excluded.

Regarding serum phosphorus, previous studies have yielded inconsistent results. While Plantinga et al. reported an increased risk of infection with higher phosphate levels in incident dialysis patients (14), other studies failed to demonstrate a consistent independent association (13, 15). Although serum phosphorus levels were not independently associated with CRBSI in our study, hyperphosphatemia may contribute to infection susceptibility through indirect mechanisms, including FGF23-mediated impairment of innate immunity, altered T lymphocyte function, and promotion of systemic inflammation. These complex and context-dependent pathways may explain the heterogeneous findings reported across previous studies (15–22).

Although causality cannot be inferred, our findings suggest that advanced age and severe secondary hyperparathyroidism may identify patients at higher risk for CRBSI. These results highlight the potential role of optimized CKD-MBD management, timely transition to arteriovenous fistula, and targeted infection surveillance, while underscoring the need for interventional studies to assess whether improved control of PTH or phosphorus reduces infection risk.

Our study has several limitations that should be acknowledged. First, due to the nature of cross-sectional studies, we failed to establish cause-and-effect relationships between the variables examined. Second, the timing of the tests conducted in our study was limited to catheterization at the beginning of the study period and every 3 months during the study period. This limited testing schedule may not have captured the full extent of changes in phosphorus, calcium, and PTH levels. The single-center nature and relatively modest sample size may limit generalizability. Additionally, inflammatory biomarkers and

FGF23 levels were not measured, which could have provided further mechanistic insight.

Future prospective studies with longitudinal assessment of CKD-MBD parameters, inflammatory markers, and vascular access characteristics are warranted to clarify temporal relationships and explore potential therapeutic targets.

5. Conclusion

In this cross-sectional study of patients undergoing hemodialysis with permanent catheters, advanced age was independently associated with a higher likelihood of catheter-related bloodstream infection. Higher parathyroid hormone levels and lower calcium levels were also observed among patients who developed CRBSI, suggesting a potential association between disturbances in mineral metabolism and infection risk.

Given the observational nature of this study, causal relationships cannot be inferred. Nevertheless, these findings suggest that patients with advanced age and poorly controlled CKD-mineral and bone disorder parameters may represent a higher-risk subgroup. Preventive strategies, including optimized management of PTH levels, enhanced infection prevention education, and consideration of earlier transition from catheter-based access to arteriovenous fistula, may be beneficial in reducing infectious complications in this population. Further prospective studies are warranted to confirm these associations and clarify underlying mechanisms.

Acknowledgement

We, the authors, thank the staff and patients of the Kerman University of Medical Sciences dialysis wards. Special thanks to Ms. Rajaii for cooperating in entering the data in SPSS.

Conflict of Interests

The authors declare that they have no competing interests.

Authors' Contributions

Authorship: NS and MB researched the literature and conceived the study. NS, MB, Habibeh A, and Hesam A were involved in protocol development, ethical approval, patient recruitment, and data analysis. NS wrote the first draft of the manuscript. All authors reviewed and edited the manuscript and approved its final version.

Ethical Statement

Data collection forms were anonymous, confidential, and non-disclosure of participants' secrets. Ethical consent was obtained from all patients. This research was approved by the ethical code IR.KMU.AH. The ethics committee of Kerman University of Medical Sciences approved REC.1400.124.

Funding Support

The Kerman University of Medical Sciences funded this study. The data in this article were taken from the General Medicine thesis of Dr Maryam Bagherinejad at

the Kerman University of Medical Sciences. (Reg. No. 400000511).

Data Availability

The data supporting this study are available from the corresponding author upon reasonable request.

AI Use Statement

During the preparation of this manuscript, the authors used ChatGPT (OpenAI) to assist with language editing and the organization of draft text. The AI tool was not used to generate scientific data, perform statistical analyses, interpret findings, or formulate conclusions. All content was critically reviewed, revised, and approved by the authors, who assume full responsibility for the manuscript.

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