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Original Article

Correlation Between Metabolic Acidosis and Bone Mineral Density in Pre-Dialysis Chronic Kidney Disease

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ABSTRACT

Background: Chronic kidney disease is associated with metabolic acidosis and disturbances in bone mineral metabolism that contribute to skeletal fragility. Objective: To evaluate the correlation between serum bicarbonate levels and bone mineral density in patients with pre-dialysis chronic kidney disease. Methods: This cross-sectional analytical study was conducted at a tertiary care hospital and included 103 adult patients with CKD stages 1–5. Biochemical parameters including serum bicarbonate, phosphate, calcium, and intact parathyroid hormone were measured. Bone mineral density at the lumbar spine and femoral neck was assessed using dual-energy X-ray absorptiometry. Correlation analysis was performed to determine associations between biochemical markers and BMD indices. Results: Serum bicarbonate demonstrated significant positive correlations with lumbar spine T-score (r=0.315, p=0.001), lumbar spine Z-score (r=0.267, p=0.006), femoral neck T-score (r=0.199, p=0.044), and femoral neck Z-score (r=0.233, p=0.018). Serum phosphate showed a moderate positive correlation only with femoral neck T-score (r=0.304, p=0.002). Serum calcium and iPTH showed weak, non-significant associations with BMD. Conclusion: Higher serum bicarbonate levels are associated with better bone mineral density in pre-dialysis CKD, suggesting a clinically relevant link between metabolic acidosis and skeletal health. Keywords: Chronic kidney disease, metabolic acidosis, bone mineral density, bicarbonate, CKD-MBD.

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INTRODUCTION

Chronic kidney disease (CKD) is accompanied by progressive disturbances in acid-base homeostasis and mineral metabolism, both of which contribute substantially to skeletal deterioration before the onset of dialysis dependence. The kidneys play a central role in net acid excretion, and declining renal function reduces the ability to maintain physiologic acid-base balance, predisposing patients to metabolic acidosis. In CKD, chronic acid retention promotes buffering through bone, stimulates osteoclastic activity, and may accelerate the loss of bone mineral content, thereby contributing to osteoporosis, renal osteodystrophy, and broader CKD-mineral and bone disorder (CKD-MBD) pathology (1,2). CKD-MBD represents a systemic disorder characterized by abnormalities of calcium, phosphate, parathyroid hormone regulation, vitamin D metabolism, bone turnover, bone mineralization, and extra skeletal calcification, with clinically important implications for fracture risk, cardiovascular morbidity, and mortality (3-8).

Assessment of bone health in CKD remains challenging because the pathophysiology is multifactorial and conventional biochemical markers do not always correlate consistently with skeletal integrity across disease stages. Bone biopsy remains the reference standard for characterization of renal bone disease, but its invasive nature, cost, and limited availability restrict routine application in clinical practice. Consequently, noninvasive tools such as dual-energy X-ray absorptiometry (DEXA) have become important for evaluating bone mineral density (BMD), particularly at clinically relevant skeletal sites such as the lumbar spine and femoral neck. DEXA is widely used because of its reproducibility, low radiation burden, and practical clinical utility, and it has been increasingly recognized as a useful adjunct

in the evaluation of CKD-associated bone fragility (3,7-10). However, BMD in CKD is not determined by a single pathway; rather, it reflects the combined influence of metabolic acidosis, phosphate retention, secondary hyperparathyroidism, altered calcium handling, and CKD stage progression, which makes site-specific interpretation especially important (4,5,8,10).

Although previous studies have linked lower bicarbonate levels with poorer bone outcomes and accelerated bone loss, the available evidence remains limited in pre-dialysis CKD populations, particularly regarding the correlation between serum bicarbonate and site-specific BMD indices at the lumbar spine and neck of femur. Existing literature also suggests that biochemical markers such as phosphate and intact parathyroid hormone (iPTH) may show variable and sometimes paradoxical associations with BMD depending on disease severity, bone compartment, and skeletal site examined (14-18). This creates an important knowledge gap in the early CKD setting, where identifying modifiable biochemical correlates of bone loss may improve risk stratification before dialysis initiation. In particular, the relationship between metabolic acidosis and BMD in pre-dialysis CKD has not been sufficiently characterized in local clinical populations using concurrently measured arterial blood gas parameters and DEXA-derived T- and Z-scores.

Given the clinical burden of CKD-related bone disease and the potential reversibility of metabolic acidosis, evaluating serum bicarbonate as a correlate of skeletal health has direct preventive and therapeutic relevance. Clarifying whether lower bicarbonate levels are associated with poorer BMD at trabecular-rich and cortical-rich sites may help refine early management strategies aimed at preserving bone health and reducing future fracture risk. Therefore, this study was designed to evaluate the correlation between biochemical markers of mineral metabolism, particularly serum bicarbonate, and bone mineral density at the lumbar spine and femoral neck in adults with pre-dialysis chronic kidney disease. It was hypothesized that lower bicarbonate levels would be associated with lower BMD indices, supporting a clinically relevant association between metabolic acidosis and skeletal demineralization in CKD before dialysis dependence.

MATERIALS AND METHODS

This cross-sectional analytical study was conducted at the Department of Nephrology, Tertiary Care Hospital, Rawalpindi, from January 2024 to July 2024 after approval from the institutional ethical review body. The study was designed to examine associations between biochemical markers of mineral metabolism and bone mineral density in adults with pre-dialysis chronic kidney disease, rather than to test an intervention. Consecutive eligible patients presenting during the study period were screened for enrollment, and only individuals who provided informed consent were included. The hospital ethical committee approved the study under letter number A/28/ERC/110/24, and the protocol was also registered in the Iranian Clinical Trial Registry under registration number IRCT20240208060941N1 (12,13).

Adult patients aged 18 years or older with established pre-dialysis CKD stages 1 to 5 were considered eligible. CKD staging and diagnosis were based on contemporary guideline definitions. Patients were excluded if they were receiving medications known to alter bone or mineral metabolism, including hormone replacement therapy, immunosuppressive drugs, anticoagulants, corticosteroids, and anticonvulsants. Individuals with clinical or biochemical evidence of alternative metabolic bone disorders, including aluminium-associated bone disease, Paget's disease, osteomalacia, or prior parathyroidectomy, were also excluded. These criteria were applied to reduce major sources of selection heterogeneity and minimize confounding from non-CKD causes of altered bone density (11,14,15).

After enrollment, participants underwent standardized clinical evaluation and demographic profiling by the study team. Information was collected on age, sex, comorbid conditions, and medication exposure, including phosphate binder use. Blood samples were obtained by trained phlebotomy staff and processed according to local laboratory protocols for complete blood count, serum creatinine, blood urea, sodium,

potassium, phosphate, corrected calcium, and intact parathyroid hormone. Acid-base status was assessed using arterial blood gas analysis, with bicarbonate and pH used as the principal biochemical indicators of metabolic acidosis. Bone mineral density was measured by dual-energy X-ray absorptiometry at the lumbar spine (L1-L4) and neck of femur. T-scores and Z-scores from both sites were recorded as the primary skeletal outcome variables. Use of predefined laboratory measurements together with DEXA-derived BMD indices supported standardized outcome ascertainment and improved measurement reproducibility across participants (16,17).

The principal exposure variable was serum bicarbonate level as an indicator of metabolic acidosis. Additional explanatory variables included serum phosphate, corrected calcium, iPTH, creatinine, CKD stage, diabetes status, hypertension status, and phosphate binder exposure. The primary outcome framework was based on the correlation of serum bicarbonate with lumbar spine and femoral neck BMD indices, expressed as T-scores and Z-scores. Site-specific assessment was intentionally retained because trabecular-rich vertebral bone and femoral neck bone may respond differently to metabolic and endocrine disturbances in CKD. Potential confounding by age, CKD severity, and comorbid disease burden was reduced at the design stage through eligibility restrictions and at the analysis stage through structured comparison of biochemical and densitometric variables across CKD stages.

The sample consisted of all eligible consecutive patients recruited during the defined study interval, yielding a final analytical cohort of 103 participants. This sample size was considered adequate for exploratory correlation analysis across major biochemical and densitometric variables within a single-center nephrology cohort. To strengthen data integrity, laboratory values and imaging-derived scores were recorded from source reports, checked before analysis, and entered into the study database in a structured format. Continuous variables were assessed for distributional normality using the Shapiro-Wilk test. Normally distributed variables were summarized as mean with standard deviation, whereas skewed variables were presented as median with interquartile range. Categorical variables were summarized using frequencies and percentages.

Statistical analysis was performed using Statistical Package for Social Sciences version 25.0. Bivariate correlation analysis was used to examine associations between biochemical markers and bone mineral density parameters. Comparisons of selected biochemical and densitometric indices across CKD stages were also performed, with p values of 0.05 or less considered statistically significant. The analytical plan emphasized transparent reporting of variable distribution, site-specific BMD interpretation, and biochemical association testing. Because the dataset was analyzed from complete recorded observations available for enrolled participants, results were reported on the basis of observed data. The overall approach was intended to provide a reproducible and clinically interpretable assessment of the relationship between metabolic acidosis and bone mineral density in pre-dialysis CKD (18-24).

RESULTS

A total of 103 patients with pre-dialysis chronic kidney disease were included in the analysis. The mean age was 60.14±13.75 years, and the cohort was predominantly male, with 87 men (84.47%) and 16 women (15.53%). Diabetes was present in 58 patients (56.31%), hypertension in 89 (86.41%), and ischemic heart disease in 16 (15.53%). Most participants were receiving calcium acetate as a phosphate binder, accounting for 81 cases (78.64%), whereas 22 patients (21.36%) were taking sevelamer. Median serum phosphate was 1.37 mmol/L (IQR 1.13-1.71), median serum calcium was 2.23 mmol/L (IQR 2.11-2.41), median serum creatinine was 230.00 µmol/L (IQR 186.00-330.00), and median intact parathyroid hormone level was 14.60 pg/mL (IQR 10.70-16.50). Bone mineral density indices showed reduced skeletal mass overall, with a mean lumbar spine Z-score of -0.14±1.66 and mean lumbar spine T-score of -1.261±1.70, while femoral neck values were lower on median-based assessment, with a Z-score of -0.10 (IQR -1.20 to 0.80) and a T-score of -1.10 (IQR -2.10 to -0.20).

Table 1. Baseline Demographic, Clinical, Biochemical, and Bone Mineral Density Characteristics of the Study Population (n=103)

Variable	Value
Age, years	60.14 ± 13.75
Female sex	16 (15.53%)
Male sex	87 (84.47%)
Diabetes mellitus	58 (56.31%)
Hypertension	89 (86.41%)
Ischemic heart disease	16 (15.53%)
Sevelamer use	22 (21.36%)
Calcium acetate use	81 (78.64%)
Duration of hemodialysis, months*	12.00 (8.00-24.00)
Serum phosphate, mmol/L	1.37 (1.13-1.71)
Serum urea, mmol/L	14.50 (10.80-18.30)
Serum calcium, mmol/L	2.23 (2.11-2.41)
Serum creatinine, µmol/L	230.00 (186.00-330.00)
Serum creatinine, mg/dL	2.60 (2.10-3.73)
Serum iPTH, pg/mL	14.60 (10.70-16.50)
Hemoglobin, g/dL	12.00 (11.20-13.20)
CKD stage 3a	4 (3.88%)
CKD stage 3b	38 (36.89%)
CKD stage 4	41 (39.81%)
CKD stage 5	20 (19.42%)
Lumbar spine Z-score	-0.14 ± 1.66
Femoral neck Z-score	-0.10 (-1.20 to 0.80)
Lumbar spine T-score	-1.261 ± 1.70
Femoral neck T-score	-1.10 (-2.10 to -0.20)

Biochemical parameters and bone mineral density indices varied across CKD stages. Serum calcium did not differ significantly by stage (p=0.224), and serum phosphate also showed no statistically significant stage-wise variation despite a numerical increase from 1.12 mmol/L in stage 3a to 1.36 mmol/L in stage 5 (p=0.181). In contrast, serum iPTH increased significantly with disease progression, rising from a median of 15.17 pg/mL in stage 3a to 19.34 pg/mL in stage 5 (p<0.001).

Serum bicarbonate declined across advancing CKD stages, from 20.55 mmol/L in stage 3a to 16.00 mmol/L in stage 5, indicating worsening metabolic acidosis with declining renal function (p=0.030). Bone mineral density measures also deteriorated significantly across stages. Lumbar spine T-score declined from 1.35 in stage 3a to -1.90 in stage 4 (p<0.001), while lumbar spine Z-score fell from 2.05 to -0.90 across the same stages (p<0.001). At the femoral neck, T-score differences were also significant (p=0.014), with the lowest median value observed in stage 4 at -1.50, and femoral neck Z-score varied significantly across stages as well (p=0.009). These findings indicate progressive biochemical derangement and skeletal compromise with CKD advancement, particularly from stage 3b onward.

Table 2. Stage-Wise Distribution of Biochemical Markers and Bone Mineral Density Indices Across CKD Severity

Parameter	CKD Stage 3a	CKD Stage 3b	CKD Stage 4	CKD Stage 5	p-value	Statistical Interpretation
Serum calcium, mmol/L	2.32 (2.30-2.35)	2.17 (2.03-2.42)	2.28 (2.16-2.38)	2.24 (2.15-2.47)	0.224	Not significant
Serum phosphate, mmol/L	1.12 (0.99-1.26)	1.52 (1.13-1.85)	1.37 (1.13-1.60)	1.36 (1.16-2.01)	0.181	Not significant
Serum iPTH, pg/mL	15.17 (13.30-17.04)	12.85 (9.17-15.41)	14.30 (10.50-15.60)	19.34 (15.90-24.84)	<0.001	Significant increase across stages
Serum HCO3, mmol/L	20.55 (17.52-23.42)	18.45 (14.95-21.20)	17.70 (15.20-19.45)	16.00 (13.97-18.00)	0.030	Significant decline across stages
Lumbar spine T-score	1.35 (0.52-2.17)	-0.45 (-1.97 to 0.60)	-1.90 (-3.10 to -0.65)	-0.40 (-1.85 to -0.02)	<0.001	Significant deterioration
Lumbar spine Z-score	2.05 (0.82-3.27)	0.25 (-0.65 to 1.65)	-0.90 (-2.30 to 0.10)	0.45 (-1.57 to 1.30)	<0.001	Significant deterioration
Femoral neck T-score	-0.60 (-1.07 to -0.12)	-0.55 (-2.02 to 0.52)	-1.50 (-2.15 to -0.40)	-1.20 (-2.37 to -0.50)	0.014	Significant deterioration
Femoral neck Z-score	0.15 (-0.27 to 0.57)	0.75 (-0.52 to 0.92)	-0.60 (-1.30 to 0.60)	-0.20 (-1.47 to 0.07)	0.009	Significant deterioration

Correlation analysis demonstrated that serum bicarbonate had the most consistent relationship with bone mineral density among the evaluated biochemical markers. A weak but statistically significant positive correlation was observed between bicarbonate and femoral neck T-score (r=0.199, p=0.044), while the association with lumbar spine T-score was moderate and more robust (r=0.315, p=0.001). Similar

positive correlations were observed with Z-scores, including femoral neck Z-score (r=0.233, p=0.018) and lumbar spine Z-score (r=0.267, p=0.006). In contrast, serum calcium showed uniformly weak and statistically non-significant correlations with all BMD indices, with r values ranging from -0.065 to 0.097 and p values from 0.330 to 0.610. Serum phosphate demonstrated a selective association, showing a moderate positive correlation with femoral neck T-score (r=0.304, p=0.002), whereas correlations with lumbar spine T-score (r=0.101, p=0.312), femoral neck Z-score (r=0.157, p=0.114), and lumbar spine Z-score (r=0.051, p=0.610) were not significant. Likewise, serum iPTH showed negligible and statistically non-significant relationships with bone density at all measured sites, with coefficients close to zero. Overall, these results support bicarbonate as the biochemical parameter most consistently associated with skeletal status in this cohort, especially at the lumbar spine, while calcium and iPTH offered limited explanatory value and phosphate showed only a site-specific relationship at the femoral neck.

Table 3. Correlation of Biochemical Markers with Bone Mineral Density at Lumbar Spine and Femoral Neck

Biochemical marker	BMD site and index	Correlation coefficient (r)	p-value	Effect size interpretation
Serum calcium	Lumbar spine T-score	0.097	0.330	Very weak positive, not significant
Serum calcium	Lumbar spine Z-score	0.100	0.286	Very weak positive, not significant
Serum calcium	Femoral neck T-score	-0.065	0.513	Very weak negative, not significant
Serum calcium	Femoral neck Z-score	-0.051	0.610	Very weak negative, not significant
Serum phosphate	Lumbar spine T-score	0.101	0.312	Very weak positive, not significant
Serum phosphate	Lumbar spine Z-score	0.051	0.610	Very weak positive, not significant
Serum phosphate	Femoral neck T-score	0.304	0.002	Moderate positive, significant
Serum phosphate	Femoral neck Z-score	0.157	0.114	Weak positive, not significant
Serum iPTH	Lumbar spine T-score	0.090	0.367	Very weak positive, not significant
Serum iPTH	Lumbar spine Z-score	-0.021	0.833	Negligible negative, not significant
Serum iPTH	Femoral neck T-score	0.025	0.799	Negligible positive, not significant
Serum iPTH	Femoral neck Z-score	-0.029	0.770	Negligible negative, not significant
Serum bicarbonate	Lumbar spine T-score	0.315	0.001	Moderate positive, significant
Serum bicarbonate	Lumbar spine Z-score	0.267	0.006	Weak-to-moderate positive, significant
Serum bicarbonate	Femoral neck T-score	0.199	0.044	Weak positive, significant
Serum bicarbonate	Femoral neck Z-score	0.233	0.018	Weak positive, significant

From a clinical interpretation perspective, the stage-wise analysis and the correlation matrix point in the same direction. As CKD advanced from stage 3a to stage 5, bicarbonate levels declined by 4.55 mmol/L, from 20.55 to 16.00, while lumbar spine T-score shifted from a positive median of 1.35 to negative values, reaching -1.90 by stage 4. This parallel worsening supports the biological plausibility of an acidosis-related adverse skeletal effect. The most clinically relevant association was observed between bicarbonate and lumbar spine T-score (r=0.315, p=0.001), suggesting that vertebral bone density may be more sensitive to acid-base disturbance than femoral measures in this population. Meanwhile, the isolated phosphate association with femoral neck T-score (r=0.304, p=0.002) should be interpreted cautiously, as it was not replicated across the other densitometric indices and may represent a site-specific or stage-dependent phenomenon rather than a generalized skeletal effect.

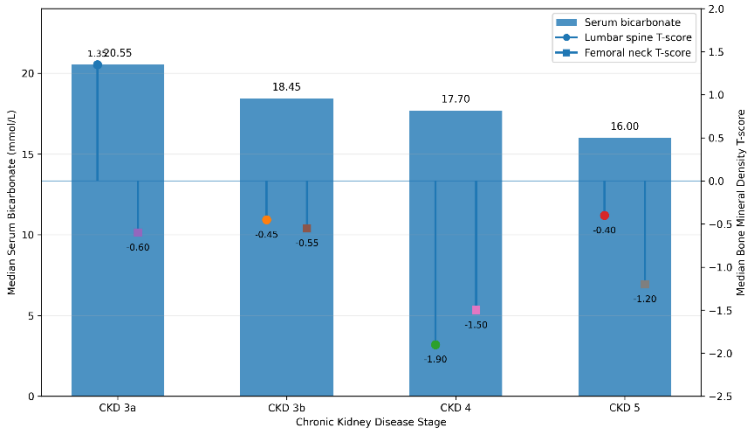

Figure 1 Progressive Metabolic Acidosis Tracks with Declining Site-Specific Bone Density Across CKD Stages

This layered dual-axis figure shows that median serum bicarbonate declined steadily by 22.1% across CKD progression, from 20.55 mmol/L in stage 3a to 16.00 mmol/L in stage 5, while bone density

deteriorated in parallel, most prominently at the lumbar spine where the median T-score fell from 1.35 in stage 3a to -1.90 in stage 4 before a partial recovery to -0.40 in stage 5; femoral neck T-score showed a more consistently negative profile, declining from -0.60 to -1.50 by stage 4 and remaining low at -1.20 in stage 5. The figure adds clinically useful interpretation beyond the existing scatter plots by revealing a stage-gradient pattern rather than isolated pairwise correlations, showing that worsening metabolic acidosis coexists with progressively poorer skeletal status, with the strongest stage-related deterioration occurring in vertebral bone. This visualization is consistent with the reported overall statistical significance for bicarbonate (p=0.030), lumbar spine T-score (p<0.001), and femoral neck T-score (p=0.014), and highlights that lumbar bone appears more dynamically affected across CKD stages than femoral bone.

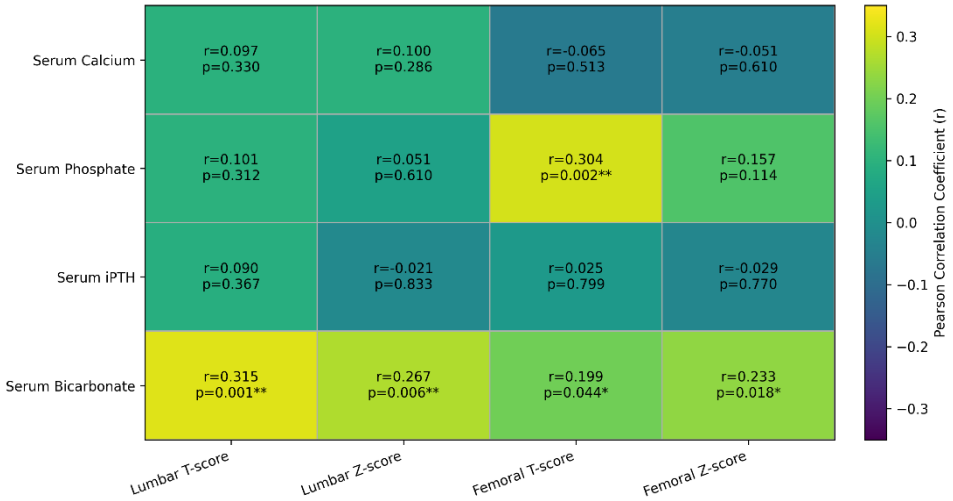

Figure 2 Compact correlation matrix showing the relationship of biochemical markers with bone mineral density indices at the lumbar spine and femoral neck.

Cells display Pearson correlation coefficients and corresponding p-values. Serum bicarbonate demonstrated consistent positive correlations with all BMD indices, with strongest association at the lumbar spine T-score (r=0.315, p=0.001). Serum phosphate showed a significant positive correlation only with femoral neck T-score (r=0.304, p=0.002), whereas serum calcium and iPTH showed weak, non-significant associations throughout.

DISCUSSION

The present study evaluated the association between metabolic acidosis, reflected by serum bicarbonate levels, and bone mineral density in patients with pre-dialysis chronic kidney disease, while also examining the role of other biochemical markers including phosphate, calcium, and intact parathyroid hormone. The findings demonstrate that serum bicarbonate exhibits the most consistent and statistically significant relationship with bone mineral density across both lumbar spine and femoral neck, whereas other biochemical parameters showed either weak or site-specific associations. These results reinforce the emerging concept that metabolic acidosis plays a clinically meaningful role in skeletal deterioration in CKD even prior to dialysis initiation.

A progressive decline in serum bicarbonate levels was observed with advancing CKD stage, accompanied by worsening bone mineral density indices, particularly at the lumbar spine. The correlation between bicarbonate and lumbar spine T-score (r=0.315, p=0.001) was moderate and stronger than that observed at the femoral neck, suggesting that trabecular-rich vertebral bone may be more sensitive to acid-base disturbances than cortical bone. This finding is biologically plausible, as metabolic acidosis promotes bone buffering through dissolution of hydroxyapatite, stimulates osteoclastic bone resorption, and inhibits osteoblastic activity, ultimately leading to net bone loss (1,13). Previous studies have similarly reported that lower bicarbonate levels are associated with reduced bone mineral density and accelerated

bone loss, supporting the pathophysiological basis of these observations (14,15). The consistency of bicarbonate associations across multiple BMD indices in the present study strengthens its potential role as a modifiable biochemical marker for early skeletal risk stratification in CKD.

In contrast, serum phosphate demonstrated a moderate and statistically significant correlation only with femoral neck T-score (r=0.304, p=0.002), without corresponding associations at the lumbar spine or with Z-scores. This site-specific relationship suggests that phosphate may exert differential effects on bone compartments or may reflect stage-dependent alterations in mineral metabolism. While phosphate retention is traditionally associated with adverse skeletal and cardiovascular outcomes in CKD, some studies have described transient or compartment-specific associations with bone mineralization, particularly in earlier disease stages (16-18). The lack of consistent correlation across all skeletal indices in this study indicates that the observed association should be interpreted cautiously and may not represent a generalized protective or detrimental effect.

Serum calcium and iPTH did not demonstrate meaningful correlations with bone mineral density in this cohort. Although iPTH levels increased significantly with advancing CKD stage, reflecting progressive secondary hyperparathyroidism, the absence of correlation with BMD suggests that its effect on bone may be more complex and influenced by bone turnover dynamics rather than static density measurements. This finding aligns with previous literature indicating that iPTH is more reflective of bone turnover status than absolute bone mass, and that its relationship with BMD may vary depending on disease stage and skeletal site (19,20). Similarly, the lack of association between serum calcium and BMD may be explained by tight physiological regulation of calcium levels, which limits its sensitivity as a marker of skeletal integrity.

Importantly, the present study emphasizes that metabolic acidosis may represent an early and modifiable contributor to skeletal deterioration in CKD. The observed parallel decline in bicarbonate levels and bone mineral density across CKD stages suggests that correction of acidosis could potentially mitigate bone loss and reduce fracture risk. This is consistent with prior evidence indicating that alkali therapy may improve bone outcomes by reducing acid-mediated bone resorption (23,24). However, given the cross-sectional design of this study, causal relationships cannot be established, and longitudinal studies are required to determine whether correction of metabolic acidosis leads to measurable improvements in bone mineral density and clinical outcomes.

Several limitations should be considered when interpreting these findings. The cross-sectional nature of the study precludes causal inference and limits assessment of temporal relationships between biochemical changes and bone loss. The single-center design and relatively modest sample size may affect generalizability, particularly in advanced CKD stages. Additionally, bone turnover markers and histomorphometric analysis were not performed, which could have provided deeper insights into the mechanisms underlying observed associations. The absence of multivariable adjustment for potential confounders such as age, CKD stage, and comorbid conditions is another limitation that may influence the strength of reported associations. Despite these limitations, the study provides clinically relevant insights into the relationship between metabolic acidosis and bone health in pre-dialysis CKD.

CONCLUSION

Higher serum bicarbonate levels were consistently associated with better bone mineral density at both lumbar spine and femoral neck in patients with pre-dialysis chronic kidney disease, with the strongest relationship observed at the lumbar spine. In contrast, serum phosphate demonstrated a site-specific association limited to the femoral neck, while calcium and iPTH showed no meaningful correlations with bone density. These findings suggest that metabolic acidosis may play a clinically relevant role in early skeletal deterioration in CKD and highlight serum bicarbonate as a potential target for preventive strategies aimed at preserving bone health.

REFERENCES

1. Kim HJ. Metabolic acidosis in chronic kidney disease: pathogenesis, clinical consequences, and treatment. Electrolyte Blood Press. 2021;19(2):29-37.
2. Evaggelou E, Lambrou GI. Acid-base disorders and the impact on metabolic bone disease in hemodialysis patients. J Res Pract Musculoskelet Syst. 2021;5(2):65-70.
3. A S, MF H, NR A. Chronic kidney disease-mineral bone disorder (CKD-MBD). Treasure Island (FL): StatPearls Publishing; 2024.
4. Yamada S, Nakano T. Role of chronic kidney disease-mineral and bone disorder (CKD-MBD) in the pathogenesis of cardiovascular disease in CKD. J Atheroscler Thromb. 2023;30(8):835-50.
5. Hu L, Napoletano A, Provenzano M, Garofalo C, Bini C, Comai G, et al. Mineral bone disorders in kidney disease patients: the ever-current topic. Int J Mol Sci. 2022;23(20):12223.
6. Babitt JL, Sitara D. Crosstalk between fibroblast growth factor 23, iron, erythropoietin, and inflammation in kidney disease. Curr Opin Nephrol Hypertens. 2019;28(4):304-10.
7. Magagnoli L, Ciceri P, Cozzolino M. Secondary hyperparathyroidism in chronic kidney disease: pathophysiology, current treatments and investigational drugs. Expert Opin Investig Drugs. 2024;33(8):775-89.
8. Ketteler M, Evenepoel P, Holden RM, Isakova T, Jørgensen HS, Komaba H, et al. Chronic kidney disease-mineral and bone disorder: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) controversies conference. Kidney Int. 2025;107(3):405-23.
9. Iseri K, Dai L, Chen Z, Qureshi AR, Brismar TB, Stenvinkel P, et al. Bone mineral density and mortality in end-stage renal disease patients. Clin Kidney J. 2020;13(3):307-21.
10. Isakova T, Nickolas TL, Denburg M, Yarlagadda S, Weiner DE, Gutiérrez OM, et al. KDOQI US commentary on the 2017 KDIGO clinical practice guideline update for the diagnosis, evaluation, prevention, and treatment of chronic kidney disease-mineral and bone disorder (CKD-MBD). Am J Kidney Dis. 2017;70(6):737-51.
11. KDIGO 2024 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney Int. 2024;105(4 Suppl):S117-S314.
12. Moe SM. Renal osteodystrophy or kidney-induced osteoporosis? Curr Osteoporos Rep. 2017;15(3):194-7.
13. Kraut JA, Madias NE. Metabolic acidosis of CKD: an update. Am J Kidney Dis. 2016;67(2):307-17.
14. Tabatabai LS, Cummings SR, Tylavsky FA, Bauer DC, Cauley JA, Kritchevsky SB, et al. Arterialized venous bicarbonate is associated with lower bone mineral density and an increased rate of bone loss in older men and women. J Clin Endocrinol Metab. 2015;100(4):1343-9.
15. Fidan N, Inci A, Coban M, Ulman C, Kursat S. Bone mineral density and biochemical markers of bone metabolism in predialysis patients with chronic kidney disease. J Investig Med. 2016;64(4):861-6.
16. Hajizadeh N, Mehrkash M, Fahimi D, Qorbani M, Shafa N. Association of bone mineral density with biochemical markers of bone turnover in hemodialysis children. J Ren Inj Prev. 2016;5(4):174-8.
17. Cupisti A, Giannese D, Cozzolino M, Panichi V, D'Alessandro C, Gallieni M. Dietary phosphorus and metabolic health in CKD and ESKD. Clin J Am Soc Nephrol. 2025;20(9):1289-98.

18. Marando M, Tamburello A, Salera D, Di Lullo L, Bellasi A. Phosphorous metabolism and manipulation in chronic kidney disease. Nephrology (Carlton). 2024;29(12):791-800.

19. Kumari S, Singh PP, Kumar D, Kumar N, Kumar S, Shekhar R. Intact parathyroid hormone (iPTH) assay: an early approach for bone health assessment in chronic renal failure. Cureus. 2024;16(10):e72510.

20. Natikar JA, Shailaja A. Secondary hyperparathyroidism in patients with chronic kidney disease: a case control study. Int J Clin Biochem Res. 2020;7(2):291-6.

21. Chen H, Han X, Cui Y, Ye Y, Purrunsing Y, Wang N. Parathyroid hormone fragments: new targets for the diagnosis and treatment of chronic kidney disease-mineral and bone disorder. Biomed Res Int. 2018;2018:9619253.

22. Wang J, Xiao J, Wang R, Wang D. Influencing factors of cardiac valve calcification in patients with chronic kidney disease and the impact of cardiac valve calcification on long-term prognosis: a single-center retrospective study. PeerJ. 2023;11:e15569.

23. Kang DH, Park CH, Kim HW, Park JT, Han SH, Kim J, et al. Kidney function and bone mineral density in chronic kidney disease patients. Clin Kidney J. 2024;17(9):sfae248.

24. Prasad B, Ferguson T, Tangri N, Ng CY, Nickolas TL. Association of bone mineral density with fractures across the spectrum of chronic kidney disease: the Regina CKD-MBD study. Can J Kidney Health Dis. 2019;6:2054358119870539.