Bone mineral density and biochemical markers of bone metabolism in predialysis patients with chronic kidney disease

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ABSTRACT

The aim of the study was to evaluate the usefulness of serum bone turnover markers (BTM) and bone mineral density (BMD) determined by dual-energy X-ray absorptiometry (DEXA) in predialysis patients with chronic kidney disease (CKD). We enrolled 83 patients with CKD, 41 (49.4%) males, 42 (50.6%) females, with mean estimated glomerular filtration rate (eGFR) 23.90±12 (range=6.0–56.0). BMD of the lumbar spine (LS) (anteroposterior, L2 through L4), femoral neck (FN) and femoral trochanter (FT) were measured by DEXA. Biochemical BTM, including calcium (Ca), phosphorus (P), intact parathyroid hormone (PTH), serum specific alkaline phosphatase (serum AP), bone-specific AP (BSAP), plasma bicarbonate and 25-hydroxy-vitamin D (25hD) were used for the prediction of BMD loss. T score results of LS and FN were worse than FT. BMD levels were lower in females than in males (all $p<0.05$). According to different BMD T score levels, patients with age ≥65 years and patients in menopause were significantly more osteopenic ($p=0.026$) and there was no relation between different BMD T scores and presence of diabetes ($p=0.654$). A positive correlation was identified between the BMD of FN T-Z scores ($r=0.270$, $p=0.029$, $r=0.306$, $p=0.012$), FT T-Z scores ($r=0.220$, $p=0.076$, r:0.250, $p=0.043$) and serum HCO3, while the correlation with serum alkaline phosphatase (AP) and BSAP was considered to be negative. No statistically significant association was found between BMD of all the measured skeletal sites and eGFR. Loss of BMD was identified mostly in females over ≥65 years of age and after menopause. Higher serum levels of BSAP and AP can be determined in the advanced stages of renal failure and they reflect fracture risk of the femur, but not spine. Measurements of BMD by DEXA are useful to demonstrate bone loss, but not technical enough to distinguish the quantity of bone loss between different stages of CKD.

Significance of this study

What is already known about this subject?

- Dual-energy X-ray absorptiometry (DEXA) is a precise, rapid and non-invasive standard method to determine BMD loss in patients with healthy kidney function.
- The effects of the predialysis period on bone loss and the method to determine BMD loss in this period have not been well studied.

What are the new findings?

- The present study demonstrated that in CKD patients, the prevalance of bone loss was higher in lumbar spine and femoral neck than femoral trochenter.
- When osteoporosis and osteopenia data obtained by DEXA were combined, BMD loss was found to be as high as 69% in the spine and femur, and the variability of BMD between the two regions was rather small.
- Higher serum levels of bone-specific alkaline phosphatase (BSAP) and AP can be determined in the advanced stages of renal failure and reflect fracture risk of the femur, but not spine.

How might it impact on clinical practice in the foreseeable future?

- With this study, we prove that BMD measurements obtained by DEXA, and several biochemical markers of skeletal formation and resorption, are useful in the diagnosis of bone status. On the other hand, DEXA cannot distinguish bone loss quantity between different stages of chronic kidney disease (CKD), which can restrict its use in these patient groups. There is a need for further studies on novel BMD measurement techniques and novel serum bone-turnover markers to determine bone loss quantity in predialysis patients with CKD.

INTRODUCTION

Impaired renal function is a well-established risk factor for increased loss of bone mineral density (BMD) and development of osteoporosis.[1] Osteoporosis is characterized by low bone mass. Metabolic changes, such as secondary hyperparathyroidism, increased phosphate levels, abnormal synthesis of 1.25-dihydroxyvitamin D, and chronic metabolic acidosis, alter bone turnover or mineralization and cause lower BMD in patients with chronic kidney disease (CKD).[2] The effects of the predialysis period

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on bone loss has not been well studied. Bone loss may vary between different stages of CKD.[3] According to some studies, osteoporosis begins to appear in the predialysis period.[4]

Dual-energy X-ray absorptiometry (DEXA) is a precise, rapid and standard non-invasive method to determine BMD loss in patients with healthy kidney function. However, the results on the ability of DEXA to predict BMD loss in predialysis patients with CKD are controversial and contradictory. Nickolas *et al*[5] reported that DEXA did not discriminate bone loss in patients with CKD. Nickolas *et al*[6] demonstrated that combining bone turnover markers (BTM) with BMD could improve the discriminatory power of DEXA in patients with end-stage renal disease (ESRD). CKD is associated with higher serum concentrations of BTM.[7] Serum calcium, phosphate, parathyroid hormone (PTH), serum specific alkaline phosphatase (serum AP) and BSAP are widely used surrogate markers of high or low turnover bone disease in patients with CKD. BSAP reflects bone formation and due to not being cleared by the kidneys, it may be more suitable in the evaluation of renal bone disease.[8] PTH is progressively increased as kidney function declines, and elevated PTH levels cause catabolic effects on cortical bone and an anabolic effect on trabecular bone—as a result of increased turnover, thickened and irregular bones occur.[7]

This study was designed to investigate the usefulness of BMD obtained by DEXA and several biochemical markers of bone turnover, in the diagnosis of bone loss, and the relation of these factors with mild-severe CKD, which was determined by estimated glomerular filtration rate (eGFR).

MATERIAL AND METHODS

Study population

Patients were studied at the outpatient clinic of the Division of Nephrology at the University Hospital of Celal Bayar University, Manisa, Turkey, from March 2009 to May 2010. Eighty-three patients at different stages of CKD were enrolled in the study. Exclusion criteria were: patients with a history of malignancy, patients who were currently taking medication known to influence bone metabolism (such as glucocorticoid, immunosuppressive agents, hormone replacement therapy, heparin or anticoagulants), and patients with any disease that could cause secondary osteoporosis. Phosphate binders included calcium acetate, calcium carbonate, and sevelamer, and no patient was taking an aluminum-containing phosphate binding agent. Use of paricalcitol, doxercalciferol or calcitriol was defined as use of active vitamin D supplementation. The study was approved by the local ethics committee of Celal Bayar University, and all participants were informed about the study and their consent was obtained.

Estimated glomerular filtration rate

Twenty-four hour urine was collected for calculating creatinine clearance. Renal function was estimated using the eGFR, which was determined by the Modification of Diet in Renal Disease[9] and as a 24 h creatinine clearance value. Using the Kidney Disease Outcomes Quality Initiative (K-DOQI), CKD was defined as subjects with eGFR <60 mL/min/1.73 m^2. Patients were divided into three groups according to eGFR levels.

Laboratory measurements

Intact PTH was measured with a Beckman Coulter Unicel D×I 800 device using an immunoradiometric method; BSAP was measured by ELISA; and 25(OH)Vit D was measured by a HPLC (high-performance liquid chromatography) method; other biochemical parameters were measured using a Beckman Coulter AU 2700 plus device. Bicarbonate was measured using a Radiometer Copenhagen ABL 700 Series device. Serum Ca and P levels were measured employing routine laboratory procedures. Serum PTH levels were categorized into three groups (<100, 100–300, ≥300). Total calcium was corrected by adding 0.8 mg/dL for every 1.0 g/dL, by which the albumin is <4 g/dL.

Measurement for BMD and definition of osteoporosis

A GE Lunar DPX–NT bone densitometry device was used for detection of BMD. The sections for detection included the anteroposterior lumbar spine (LS) (L2-L3-L4) and proximal femur (neck and troch). Diagnosis of osteoporosis is arrived at by the occurrence of a fragility fracture or described by WHO cut-off value of T score of <-2.5 at the spine and femur in patients without fracture.[10] Results were expressed as T and Z scores. T score was defined as the number of SDs a person's BMD lies below the mean BMD for a sex-matched young healthy population. According to the WHO criteria, patients were categorized into normal BMD (T-score ≥ -1.0), osteopenia (T-score= -1.0 to -2.5) and osteoporosis (T-score <-2.5) groups.[11] Z score was used to represent the SD below the mean BMD value that was normalized for an age-matched and sex-matched healthy population. The coefficient of variation for the DEXA machine was 0.7% in the LS and 1.0% in the proximal femur.

Statistical analysis

SPSS (Statistical Package for Social Sciences) V.9.0 software was used for the statistical analysis. Student's t test was performed for the comparison of data between the two groups. A one-way analysis of variance test was performed for the comparison of parameters between groups. The relationship between parameters was evaluated by Pearson correlation analysis. A value of $p<0.05$ was considered statistically significant. All results were expressed as the mean ±SD, otherwise variable SDs were stated as the median value.

RESULTS

The study enrolled 83 predialysis patient, 41 (% 49.4) males, 42 (% 50.6) females, with mean age of 59.99 ±11.56 years, and mean eGFR 23.90±12.52. It included 22 (26.5%) patients with CKD stage 3, 40 (48.2%) patients with CKD stage 4, and 21 (25.3%) patients with non-dialysis CKD stage 5. Causes of CKD were: diabetic nephropathy (n=22% 26.6), hypertensive nephrosclerosis (n=38%45.7), polycystic kidney disease (n=10% 12), chronic glomerulonephritis (n=4% 4.8) and unknown (n=9% 10.9). Fifteen (18.1%) patients were taking phosphate binders and 22 (26.8%) patients were taking active vitamin D supplementation (table 1).

Table 1 Demographic and biochemical features of the patients

Variables	(Minimum–maximum)	Mean±SD/n-%
Age (years)	27.00–85.00	59.99±11.56
Male/female		41 (49.4%)–42 (50.6%)
BMI(kg/m^2)	18.40–54.80	27.15±5.31
Etiology of CKD		
Diabetic nephropathy		22 26.6%
Hypertensive nephrosclerosis		38 45.7%
Polycystic kidney disease		10 12%
Chronic glomerulonephritis		4 4.8%
Unknown		9 10.9%
CKD		
eGFR (mL/min/1.73 m^2)	6.00–56.00	23.90±12.52
Stage 3		22 26.5%
Stage 4		40 48.2%
Stage 5		21 25.3%
Use of phosphate binders		15 18.1%
Use of active vitamin D		22 26.8%
PTH (pg/mL)	25.40–1866.00	308.65±349.13
Ca×PO4	18.40–95.60	42.57±12.87
25hD (µg/L)	4.02–72.55	18.48±12.16
Serum AP (U/L)	18.00–398.00	93.25±55.62
BSAP (U/L)	5.60–152.83	29.28±22.67
HCO3	11.30–32.70	21.88±3.70

25hD, 25-hydroxy-vitamin D; BMI, body mass index; BSAP, bone-specific alkaline phosphatase; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; PTH, parathyroid hormone; Serum AP, serum-specific alkaline phosphatase.

According to the LS T scores, 14 (16.9%) patients were normal, 43 (51.8%) patients were osteopenic, and 26 (% 31.3) patients were osteoporotic. According to the femoral neck (FN) T scores, 14 (%16.9) patients were normal, 47 (%56.6) patients were osteopenic, and 22 (%26.5) patients were osteoporotic. Mean LS, FN and femoral trochanter (FT) T-Z scores were −1.76±1.37, −1.07±1.33, −1.72 ±1.14, −0.61±0,95, −1.29±1.12, and −0.74±1.04 (tables 2 and 3).

BMD T scores were significantly lower in female than in male patients (all p<0.005) (table 4).

After dividing the patients into three groups according to eGFR, there was no correlation between BMD of LS and FN-FT and CKD stages (all p>0.05). Serum BSAP (p=0.037) was significantly higher in patients with stage 5 (table 5).

When dividing the patients into three groups according to BMD T scores, patients ≥65 years of age and in menopause were significantly osteopenic (p=0.026). There was

Table 2 Distribution of patients according to BMD T scores

LS-T	n-%		FN-T	n-%	
T>−1	14	16.9	T>−1	14	16.9
−2.5<T<−1	43	51.8	−2.5<T<−1	47	56.6
−2.5≤T	26	31.3	−2.5≤T	22	26.5

FN, femoral neck; LS, lumbar spine.

Table 3 Mean BMD T-Z score levels of the patients

Variables	(Minimum–maximum)	Mean±SD/n-%
L2-L4 T	−4.40–2.80	−1.76±1.37
L2-L4 Z	−3.50–3.10	−1.07±1.33
FN-T	−3.70–3.00	−1.72±1.14
FN-Z	−3.00–2.50	−0.61±0.95
FT-T	−3.30–2.70	−1.29±1.12
FT-Z	−3.10–3.10	−0.74±1.04

FN, femoral neck; FT, femoral trochanter.

no relation between BMD T scores with presence of diabetes (p=0.654) and CKD stages (p=0.372) (table 6).

There was a negative correlation between BMD of FN-FT with serum AP and BSAP levels, whereas a positive correlation was seen with serum HCO3. This correlation analysis remains significant when weight adjusted. There was no correlation between BMD of LS and serum AP-BSAP-HCO3. There was no correlation with BMD levels and eGFR (tables 7 and 8). We divided the 83 patients into three groups based on PTH levels. We found no significant relation between higher PTH levels and BMD measurements (table 9).

DISCUSSION

Osteoporosis is only a part of the wide spectrum of metabolic bone problems of ESRD. It is a condition of impaired bone strength due to reduced BMD and altered bone quality.[11] It also contributes to increased bone fracture risk.[12] BMD is a measure of bone strength and can be measured by DEXA. DEXA is the most widely used method due to its short scan time, low cost, and low radiation dose. DEXA can quantify bone mass and measure BMD in patients with CKD.[6–13] Osteoporosis can be diagnosed by BMD measurements,[14] however, unlike in the non-CKD population, there has been limited evidence to prove that DEXA can provide significant predictive value of increased bone loss in predialysis patients with CKD. Several studies demonstrated that BMD measurements obtained by DEXA can predict bone loss and fracture risk in patients with CKD.[6–15] The present study demonstrated that the prevalence of bone loss was higher in BMD of LS and FN than in BMD of FT. When combining osteoporosis and osteopenia data obtained by DEXA, BMD loss was found to be as high as 69% in the spine and femur, and the variability of BMD between the two regions was rather small.

Table 4 Comparison of BMD findings by gender

Variables	Female Mean±SD/n-%	Male Mean±SD/n-%	p Value
L2-L4 T	−2.21±0.95	−1.29±1.59	***0.002***
L2-L4 Z	−1.19±1.02	−0.95±1.58	***0.004***
FN-T	−2.07±0.92	−1.37±1.24	***0.005***
FN-Z	−0.85±0.86	−0.36±1.00	***0.019***
FT-T	−1.60±0.96	−0.97±1.19	***0.010***
FT-Z	−1.01±0.85	−0.47±1.15	***0.018***

Bold denotes p<0.05 is significant.
FN, femoral neck; FT, femoral trochanter.

Table 5 Correlation of CKD stages with BMD levels and biochemical findings of patients

Variables	Stage 3 (eGFR=30–59) Mean±SD/n-%	Stage 4 (eGFR=15–29) Mean±SD/n-%	Stage 5 (eGFR<15) Mean±SD/n-%	p Value
L2-L4 T	−1.80±1.26	−1.73±1.45	−1.76±1.41	0.983
L2-L4 Z	−1.05±1.28	−1.00±1.37	−1.22±1.35	0.821
FN-T	−1.87±1.08	−1.56±1.26	−1.87±0.95	0.486
FN-Z	−0.54±0.92	−0.48±1.01	−0.94±0.83	0.193
FT-T	−1.18±1.18	−1.26±1.13	−1.47±1.06	0.679
FT-Z	−0.48±1.05	−0.71±1.05	−1.09±0.98	0.157
Serum AP (U/L)	88.66±28.85	87.00±43.89	112.00±89.75	0.332
BSAP (U/L)	25.67±11.92	25.68±15.40	40.83±37.48	***0.037***

Bold denotes p<0.05 is significant.
BSAP, bone-specific alkaline phosphatase; FN, femoral neck; FT, femoral trochanter; eGFR, estimated glomerular filtration rate; Serum AP, serum-specific alkaline phosphatase.

CKD has been associated with low BMD[16] and osteoporotic fractures, which increase in proportion to CKD severity,[17] and are linked with high mortality and morbidity. It has been suggested that the duration of impaired renal function might be a risk factor for bone loss. There have been a few reports investigating the association between BMD determined by DEXA and degrees of impaired renal function in the predialysis patient group. Rix *et al*[18] reported that as the stages of renal failure increased, BMD of the femur and spine decreased. Nickolas *et al*[19] demonstrated the association between loss of BMD and eGFR. Fried *et al*[20] demonstrated that renal function deterioration was significantly associated with declines in BMD. Myong *et al*[21] reported that BMD of LS and FN was positively associated with eGFR in stages 3 and 4, among Asian patients with CKD. Jamal *et al* have shown an association between low BMD findings obtained by DEXA and impaired kidney function.[3] In a recent study, it was found that BMD was decreased in early stages of CKD.[22] In the present study, we demonstrated that BMD loss that was determined by DEXA was correlated with neither eGFR nor CKD at stages 3–4–5. The reason for these conflicting results between studies might be the measurement of BMD taken using different techniques, measuring at different parts of the skeleton or evaluating the patients who were receiving different dialysis modalities. Also, the relationship between BMD and eGFR may be different between ethnic groups.[23]

Kaji *et al*[24] evaluated loss of BMD mainly in women, especially postmenopausal women. Tseng *et al*[22] demonstrated that bone loss was greater among men in early stages of CKD, however, bone loss was also found among women in whom renal dysfunction was more progressed. The present study regarding men is similar to the study of Myong *et al*,[21] and loss of BMD was found in women, particularly in menopause, in this study as well.

Chronic decreased serum bicarbonate levels may result in dissolution of bone mineral density.[25] In the present study, we demonstrated that while decreased levels of serum bicarbonate were found to be associated with BMD of the femur, this relationship could not be shown with the LS. As a result, it was suggested that management of metabolic acidosis is important, because it reduces bone resorption and increases BMD in the predialysis period.

Rix *et al* demonstrated that diabetic nephropathy increased the risk of bone loss in patients with CKD.[18] In the present study, presence of diabetes was not found to be a risk factor for low BMD. The reason for the differences between studies might be the undifferentiated types of diabetes in the present study.

Knowledge of BTM in identifying fracture risk is limited in patients with CKD. However, because of decreased renal clearance, elevated levels of most serum biomarkers can be used in early CKD stages. BSAP is an osteoblast-derived bone resorption marker and cannot be cleared by the kidney. A previous study reported that serum BSAP was the most sensitive and specific marker of bone remodeling in patients with CKD.[26] Increased serum BSAP levels coexist with high fracture risk in patients with ESRD.[27] The present study demonstrated that higher serum BSAP and AP levels were determined at the more advanced stages of renal failure, suggesting that non-dialysis stage five patients had more fracture risk than those with stage 3–4 CKD.

The present study evaluated serum AP and BSAP for prediction of bone loss and found that serum AP and BSAP showed increasing plasma levels with the loss of BMD of

Table 6 BMD T scores with clinical findings of the patients

	T ≥−1 Mean±SD/n-%		−2.5<T<−1 Mean±SD/n-%		T≤−2.5 Mean±SD/n-%		p Value
Age (years)							
<65	11	22.5	30	61.2	8	16.3	***0.026***
≥65	3	8.8	17	50.0	14	41.2	
Postmenopausal	1	2.9	18	52.9	15	44.1	***0.003***
Premenopausal	3	37.5	5	62.5	0	0.0	
DM							
Available	5	22.7	11	50	6	27.3	0.654
Not available	9	14.8	36	59	16	26.2	
CKD stage 3	2	9.1	14	63.6	6	27.3	0.372
CKD stage 4	10	25.0	19	47.5	11	27.5	
CKD stage 5	2	9.5	14	66.7	5	23.8	

Bold denotes p<0.05 is significant.
CKD, chronic kidney disease.

Table 7 Correlation of BMD levels with clinical and biochemical findings of the patients

	L2-L4 T	L2-L4 Z	FN-T	FN-Z	FT-T	FT-Z
eGFR (mL/min/1.73 m^2)	r: 0.022 p:0.842	r:0.078 p:0.485	r:−0.036 p:0.750	r:0.062 p:0.575	r:0.077 p:0.487	r:0.182 p:0.099
CaXPO4	r: 0.057 p:0.608	r:0.014 p:0.899	r:0.043 p:0.697	r:0.043 p:0.699	r:0.097 p:0.385	r:0.065 p:0.561
25hD (μg/L)	r:0.044 p:0.697	r: −0.002 p:0.983	r:0.035 p:0.756	r:0.047 p:0.675	r:0.049 p:0.661	r: −0.103 p:0.355
Serum AP (U/L)	r: −0.160 p:0.206	r: −0.100 p:0.431	***r: −0.324 p:0.009***	***r: −0.263 p:0.036***	***r: −0.303 p:0.015***	***r: −0.318 p:0.011***
BSAP (U/L)	r: −0.174 p:0.122	r: −0.121 p:0.287	***r: −0.344 p:0.002***	***r: −0.363 p:0.001***	***r: −0.302 p:0.007***	***r: −0.341 p:0.002***
HCO3	r:0.146 p:0.243	r:0.134 p:0.282	***r:0.270 p:0.029***	***r:0.306 p:0.012***	***r:0.220 p:0.028***	***r:0.250 p:0.043***

Bold denotes p<0.05 is significant.
25hD, 25-hydroxy-vitamin D; BSAP, Bone-specific Alkaline phosphatase; eGFR, estimated glomerular filtration rate; FN, femoral neck; FT, femoral trochanter; Serum AP, Serum-specific Alkaline phosphatase.

FN and FT, whereas this relation was not observed with the loss of BMD from LS. As a result, serum AP and BSAP seemed to be important factors that had an inverse effect on BMD of FN and FT, but not on BMD of LS.

Loss of BMD resulted from secondary hyperparathyroidism in patients with CKD. Results of the relation between PTH levels and BMD loss were conflicting, and most were from dialysis patients. A study reported that PTH and 25 (OH)-Vit provided early diagnose of osteoporosis in patients with CKD.[28] Coen *et al*[29] reported that serum PTH, which is BTM-specific serum, might help to discriminate between heterogeneous forms of renal bone disease. Presence of advanced secondary higher levels of serum PTH was associated with decreased BMD.[18] Jadoul *et al*[30] reported that higher PTH levels were associated with increased risk of BMD loss. Ureña *et al*[31] reported a relation between higher serum PTH levels and BMD measurements. On the contrary, Stehman *et al*[32] showed that PTH level had no significant influence on loss of BMD. Ersoy *et al*[33] demonstrated that PTH levels did not correlate with any of the BMD parameters. In the present study, we found no significant relation between higher PTH levels and BMD measurements. The cause of this relationship might be explained by lack of adequate information about the complexity and variety of bone-related problems in predialysis patients with CKD.

CONCLUSION

In conclusion, a strong correlation was demonstrated between the severity of impaired renal function, and higher serum levels of serum AP and BSAP, suggesting that more fracture risk can be seen in non-dialysis stage 5 patients with CKD than in stage 3–4 patients. Contrary to expectations, higher PTH levels did not affect the development of bone loss in predialysis patients. Management of metabolic acidosis would reduce bone resorption and increase BMD loss in the predialysis period. Menopause, age and sex may affect loss of bone density in patients with CKD. The present study found that osteopenia was more common than osteoporosis and it was seen more in postmenopausal female patients with CKD. This study further demonstrated that BMD measurements obtained by DEXA and several biochemical markers of skeletal formation and resorption were useful for the diagnosis of bone status. On the other hand, DEXA cannot distinguish bone loss quantity between different stages of CKD, which can restrict its use in these

Table 8 Weight adjusted partial correlation analysis of BMD levels with clinical and biochemical findings of the patients

	L2-L4 T	L2-L4 Z	FN-T	FN-Z	FT-T	FT- Z
eGFR (mL/min/1.73 m^2)	r: 0.027 p:0.808	r:0.070 p:0.534	r:−0.037 p:0.743	r:0.047 p:0.675	r:0.060 p:0.593	r:0.155 p:0.163
CaXPO4	r: 0.056 p:0.615	r:0.016 p:0.889	r:0.043 p:0.698	r:0.046 p:0.683	r:0.100 p:0.371	r:0.071 p:0.529
25hD (μg/L)	r:0.046 p:0.682	r: −0.007 p:0.950	r:0.035 p:0.758	r:0.039 p:0.729	r:0.040 p:0.723	r: −0.089 p:0.429
Serum AP (U/L)	r: −0.159 p:0.214	r: −0.105 p:0.413	***r: −0.326 p:0.009***	***r: −0.272 p:0.031***	***r: −0.314 p:0.012***	***r: −0.337 p:0.007***
BSAP (U/L)	r: −0.174 p:0.125	r: −0.121 p:0.287	***r: −0.344 p:0.002***	***r: −0.366 p:0.001***	***r: −0.304 p:0.006***	***r: −0.347 p:0.002***
HCO3	r:0.148 p:0.241	r:0.132 p:0.296	***r:0.270 p:0.029***	***r:0.302 p:0.015***	***r:0.215 p:0.085***	***r:0.243 p:0.051***

Bold denotes p<0.05 is significant.
25hD, 25-hydroxy-vitamin D; BSAP, bone-specific Alkaline phosphatase; eGFR, estimated glomerular filtration rate; FN, femoral neck; FT, femoral trochanter; Serum AP, serum-specific alkaline phosphatases.

Table 9 Comparision of BMD levels with PTH groups

	PTH<100 Mean±SD/n-%	PTH 100—300 Mean±SD/n-%	PTH ≥300 Mean±SD/n-%	p Value
L2-L4 T	−1.64±1.52	−1.72±1.10	−1.91±1.58	0.785
L2-L4 Z	−0.82±1.52	−1.13±1.06	−1.22±1.45	0.533
FN-T	−1.80±1.18	−1.58±0.92	−1.83±1.36	0.651
FN-Z	−0.49±1.06	−0.44±0.95	−0.95±0.79	0.094
FT-T	−1.18±1.30	−1.05±1.04	−1.70±0.96	0.072
FT-Z	−0.54±1.18	−0.55±0.96	−1.17±0.91	0.390

FN, Femoral neck; FT, Femoral trochanter; PTH, parathyroid hormone.

patient groups. There is a need for further studies on novel BMD measurement techniques and novel serum bone-turnover markers to determine bone loss quantity in pre-dialysis patients with CKD.

Limitations

Our study has several limitations. First, we did not obtain similar data in a healthy control group. Second, DEXA provides a two-dimensional assessment of a three-dimensional structure, therefore it may not discriminate cortical and trabecular bone, this may restrict the usefulness of DEXA in chronic renal disease patients. Third, due to the values of BMD and eGFR varying across ethnicity, the results may be contradictory. Finally, the distal radius site was not assessed on DEXA and high BSAP values may be seen in ailments such as Paget's disease or metastatic cancer of bone, however, these conditions have not been ruled out in the present study.

Contributors AI was qualified for authorship based on making one or more substantial contributions to the intellectual content. NF and AI were involved in the conception and design; NF was involved in the acquisition of data; CU and SK were involved in the analysis and interpretation of data; NF and AI were involved in drafting of the manuscript.

Competing interests None declared.

Patient consent Obtained.

Ethical approval The study was approved by the local ethics committee of Celal Bayar University.

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