Prevalence and Risk Factors of Osteoporosis in Saudi End-stage Renal Disease Patients on Hemodialysis

Moeber M. Mahzari[1,2,3], Ahmed R. Alibrahim[2,3], Nawaf A. Alghamdi[1,2,3], Muatassem A. Alsadhan[1,2,3], Saad M. Almoamary[1,2,3], Emad M. Masuadi[1,2], Awad S. Al Shahrani[1,2,3]

[1]College of Medicine, King Saud Bin Abdulaziz University for Health Sciences, [2]King Abdullah International Medical Research Center, [3]Department of Medicine, Ministry of the National Guard - Health Affairs, Riyadh, Saudi Arabia

Abstract

Background: Osteoporosis is characterized by a decrease in bone mineral density, thereby increasing the risk of pathological fractures. It is a common complication of chronic kidney disease. However, there is limited local data on the prevalence of osteoporosis in end-stage renal disease.

Objective: The current study evaluated the epidemiology of osteoporosis in end-stage rental disease patients at a Saudi Arabian tertiary care center.

Methods: This cross-sectional retrospective study was conducted using data obtained between 1 January 2016 and 31 December 2019 at the Dialysis Center at King Abdulaziz Medical City, Riyadh, Saudi Arabia. End-stage rental disease patients who were aged ≥50 years and underwent hemodialysis for at least 1 year were included, while those with documented metabolic bone disease and absence of bone mineral density data were excluded.

Results: Sixty-four end-stage rental disease patients undergoing hemodialysis met the inclusion criteria. The patients underwent bone mineral density measurement at the discretion of the treating physician. The mean patients' age was 73 ± 11.5 years and 76% were women. The overall prevalence of osteoporosis was 37.5%, and it was similarly distributed among women and men (38.8% and 33.3%, respectively). Nine of the 15 male patients (60%) and 24 of the 49 female patients (49%) had fractures. Twenty-five (39%) patients used glucocorticoids. Osteoporosis was most commonly identified in the femoral neck (26.2%), followed by proximal femur (19.4%), and lumbar spine (18.8%). A high rate of osteoporosis was significantly associated with older age and being underweight.

Conclusion: A high rate of low bone mineral density was demonstrated in end-stage renal disease patients. The femoral neck was the most common osteoporosis site in this patient population, and advanced age and underweight were possible risk factors for low bone mass.

Keywords: Bone mineral density, end-stage renal disease, osteopenia, osteoporosis, prevalence, Saudi Arabia

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INTRODUCTION

Osteoporosis is the decrease in bone mineral density (BMD), which, in turn, leads to an increased risk of fractures.[1] Osteoporosis is a significant complication of chronic kidney disease (CKD), defined as a structural or functional kidney abnormality leading to decline in the glomerular filtration rate (≤60 mL/min).[2] Abnormalities in the bone structure and mineral metabolism develop early in the course of CKD and are directly proportional to the gradual loss of kidney function.[2] The pathophysiology behind osteoporosis in CKD is primarily attributed to the decreased excretion of phosphorus and reduced active form of vitamin D, which results in hypocalcemia and an increase in parathyroid hormone (PTH) secretion. Excess PTH causes the release of calcium in the blood, which leads to low bone mass and a predisposition to fractures.[3]

End-stage renal disease (ESRD) is an advanced form of CKD. Patients with ESRD require renal replacement therapy, such as hemodialysis and kidney transplantation. Many studies have demonstrated that ESRD is associated with a high risk of fragility fractures. Hence, it is believed that fracture-related mortality risk correlates with CKD severity.[3]

Globally, few studies have assessed the extent of BMD alterations in patients with CKD. The prevalence of osteoporosis in patients with CKD has been reported to vary from 2–31%.[4] In Palestine, in a study conducted on 194 patients to assess the prevalence of osteoporosis in ESRD patients, the overall prevalence of osteoporosis was 43%; its prevalence was 32% and 34% in the hip and lumbar spine (LS), respectively.[5] In Saudi Arabia, a cross-sectional analysis of healthy individuals aged 50–79 years demonstrated that 34% and 31% of Saudi women and men were osteoporotic.[6] However, limited data are available from Saudi Arabia on the prevalence of osteoporosis in Saudi patients with ESRD.

In Saudi Arabia, guidelines have been developed for medical professionals on osteoporosis screening and management.[7] However, clear local policies for the management and screening of osteoporosis in ESRD patients have not been formulated. Thus, the objective of the current study was to reduce this gap in the literature by providing information on osteoporosis from adults with ESRD in Saudi Arabia who had BMD measurement and identifying possible associated risk factors.

METHODS

Study design, setting, and participants

This retrospective study was conducted using the electronic medical records data of Saudi patients who had undergone hemodialysis between January 1, 2016, and December 31, 2019, at the Dialysis Center at King Abdulaziz Medical City (KAMC), Riyadh, Saudi Arabia. Ethical approval was obtained from the Institutional Review Board of KAMC. The dialysis center at KAMC has a capacity of 120 patients in a 24-hour period (i.e., 40 patients accommodated over three shifts).

The inclusion criteria were ESRD patients of either gender who were aged ≥50 years and underwent hemodialysis for at least 1 year. The exclusion criteria were documented metabolic bone disease (e.g., osteomalacia, osteitis fibrosa cystica, Paget's disease, and adynamic bone disease) and the absence of BMD data. It should be noted that patients underwent BMD measurement at the discretion of the treating physician. Moreover, patients with cancer and metastasis as well as a history of cancer were excluded from the study.

Variables and definitions

The clinical variables recorded were as follows: ages, gender, and diagnosis of osteoporosis based on BMD scan. Data regarding bone health-related variables according to the Fracture Risk Assessment Tool®, such as smoking, a history of chronic illness (i.e., rheumatoid arthritis), previous fractures (history or radiology), and medication history (i.e., the use of steroids and vitamin D analogs), were also collected. Biochemical markers of bone metabolism, such as serial adjusted calcium, alkaline phosphatase (ALP), phosphate, vitamin D, and intact (iPTH) PTH levels were collected. The T-scores, laboratory results, and medications prescribed up to 12 months before and/or after the incident were recorded for patients with fractures; similar data of up to 2 years were obtained for patients with no fracture. Availability of bone biopsy was evaluated.

The World Health Organization's BMD classification was used, wherein osteoporosis was defined as a T-score <−2.5 SD and osteopenia was defined as a T-score between −1.0 and −2.5 SD.[1]

Outcomes

The primary outcomes measured in the current study were the prevalence of osteoporosis and a description of the clinical characteristics in relation to bone health in the study sample. Other outcomes assessed were the management of osteoporosis and the association between osteoporosis and different variables.

Statistical analysis

SPSS version 24.0 (IBM Corp., Armonk, N.Y., USA) was used for the data analysis. The categorical data (e.g., gender) were presented as frequencies and percentages, and the numerical data (e.g., height and weight) were presented as means ± standard deviation. The independent and paired *t*-tests were used to compare the BMD T-scores in the study group. Fisher's exact test was used to assess previous fractures in relation to baseline characteristics. Pearson's correlation coefficient was used to evaluate the relationships between different variables. *P* value ≤0.050 was considered statistically significant.

RESULTS

Characteristics of the subjects

A total of 477 patients with hemodialysis for >1 year presented during the study period, of which 393 patients were aged ≥50 years. However, only 64 subjects met all the other inclusion and exclusion criteria, including having undergone BMD measurements. The mean age of these 64 subjects was 73 (±11.5) years, and the majority were women (*n* = 49, 76%). There were significant differences between male and female in terms of mean body height (164 ± 9 cm vs. 153 ± 7 cm, respectively; *P* < 0.001) and the duration of dialysis (8 ± 7 years vs. 4±3 years, respectively; *P* = 0.002). There were no significant differences in the other variables [Table 1].

For the laboratory data, 25-hydroxy vitamin D levels were available for 40 patients, of which only 11 (28%) had normal levels (50–125 nmol/L). Intact PTH was found to be elevated in 62 (83.8%) patients. The levels of other biomarkers, such as ALP, phosphate, and adjusted calcium, were high in 18.8%, 28.1%, and 6.3% of the participants, respectively, and these levels were wide ranging. Thirty-three patients (51.5%) had a history of fracture [Figure 1].

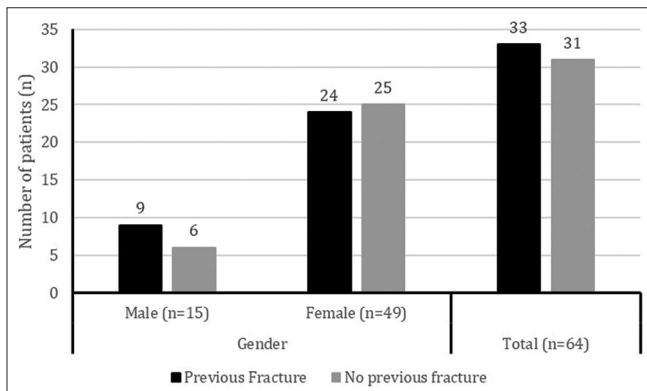The medications and supplements prescribed for the study sample are shown in Figure 2. Twenty-five (39%)

patients used glucocorticoids, of which 11 (33.3%) had fractures.

Bone mineral densitometry and the prevalence of osteopenia and osteoporosis

The baseline BMD values and the rates of osteopenia and osteoporosis at the LS, proximal femur (PF), and femoral neck (FN) sites are provided in Table 2. The percentage of subjects with low BMD (including osteopenia and osteoporosis) at the LS, PF, and FN sites was 54.7%, 58.1%, and 70.5%, respectively. The overall prevalence of osteoporosis (i.e., at any site) was 37.5%, and this was not significantly different in women (38.8%) compared to men (33.3%). The prevalence of osteoporosis was 18.8%, 19.4%, and 26.2%, at the LS, PF, and FN sites, respectively. Only one male had osteoporosis in the LS, three in the PF, and three in the FN; 11 females had osteoporosis in the LS, nine in the PF, and 13 in the FN. The FN was the most common osteoporosis site (27.7% of the women and 21.4% of the men).

Follow-up BMD values were available for 19 patients. Table 3 shows the T-scores obtained at baseline and at

Table 1: Characteristics and clinical variables of the patients, categorized by gender

Variables	Gender (mean±SD)		P
	Male (*n*=15)	Female (*n*=49)	
Age	72.0±13.0	74.0±10.0	0.540
Weight	66.7±15.2	61.7±18.2	0.346
Height	164.0±9.0	153.0±7.0	<0.001
BMI	24.7±4.9	26.3±7.6	0.441
Dialysis duration (years)	8.0±7.0	4.0±3.0	0.002
25-hydroxy vitamin D (nmol/l)	33.8±6.4	46.3±28.5	0.093
iPTH (pmol/l)	59.8±82.0	30.9±38.3	0.205
ALP (u/l)	127.1±94.2	104.9±40.5	0.388
Phosphate (mmol/l)	1.4±0.4	1.3±0.4	0.423
Adjusted calcium level (mmol/l)	2.3±0.3	2.3±0.2	0.471

SD - Standard deviation; ALP - Alkaline phosphatase; BMI - Body mass index; iPTH - Intact parathyroid hormone
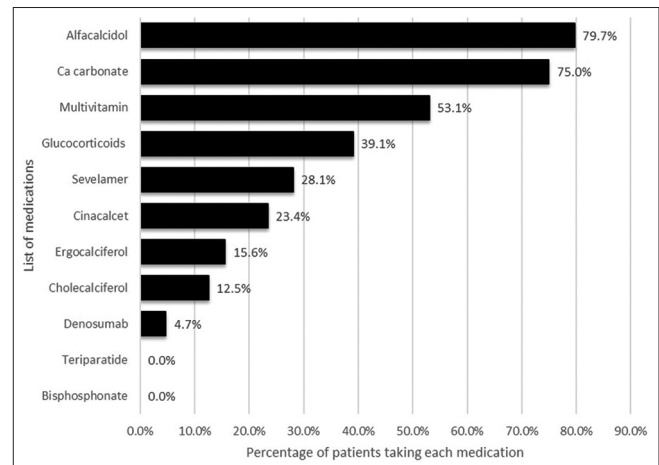

Figure 1: Patients with and without fractures

Figure 2: Medications used in the study sample

Table 2: Bone mineral density values at baseline†

Site	Gender	Mean±SD (minimum-maximum)	Normal bone density, *n* (%)	Osteopenia, *n* (%)	Osteoporosis, *n* (%)	*P**
Lumbar spine	Male	0.3±1.4 (−2.7-3.7)	13 (86.7)	1 (6.7)	1 (6.7)	0.001
T-score	Female	−1.5±1.3 (−4.0-1.9)	16 (32.7)	22 (44.9)	11 (22.4)	
	Total	−1.1±1.5 (−4.0-3.7)	29 (45.3)	23 (35.9)	12 (18.8)	
Proximal	Male	−1.3±1.5 (−4.5-2.1)	5 (33.3)	7 (46.7)	3 (20.0)	0.741
femur *T*-score	Female	−1.3±1.5 (−4.3-1.6)	21 (44.7)	17 (36.2)	9 (19.1)	
	Total	−1.3±1.5 (−4.5-2.1)	26 (41.9)	24 (38.7)	12 (19.4)	
Femoral neck	Male	−1.5±1.2 (−3.0-1.0)	3 (21.4)	8 (57.1)	3 (21.4)	0.587
T-score	Female	−1.7±1.4 (−4.4-1.4)	15 (31.9)	19 (40.4)	13 (27.7)	
	Total	−1.7±1.4 (−4.4-1.4)	18 (29.5)	27 (44.3)	16 (26.2)	

*Calculated using Fisher's exact test, †Total (*n*=64), men (*n*=15), women (*n*=49). *P* value is for statistical test comparing male versus female patients. SD - Standard deviation

Table 3: Comparison of bone mineral density (*T*-scores) at baseline and follow-up‡

Paired sample statistics (*T*-scores)	Mean±SD	Change	*P*
Pair 1			
Lumbar spine (baseline)	−1.52±1.30	0.005	0.965
Lumbar spine (at follow-up)	−1.52±1.23		
Pair 2			
Proximal femur (baseline)	−1.14±1.57	−0.367	0.031
Proximal femur (at follow-up)	−1.51±1.46		
Pair 3			
Femoral neck (baseline)	−1.38±1.34	−0.469	0.054
Femoral neck (at follow-up)	−1.84±1.21		

‡*n*=19. SD - Standard deviation

the BMD follow-up. The mean BMD follow-up duration was 3.4 years (±2.9 years) (range: 1–13 years). The mean T-score at the LS site remained almost unchanged at the follow-up BMD scan. In contrast, the mean PF T-score deteriorated significantly between the baseline and follow-up measurements. Bone biopsy was not performed for any patient.

Risk factors for low bone mineral density

Multivariate analysis of the T-scores at different osteoporosis sites (LS, PF, and FN) were assessed in relation to the baseline characteristics [Table 4]. Gender was found to be a significant factor associated with the LS T-score (*P* < 0.001). Similarly, the duration of dialysis had a significant effect on the LT T-score, wherein patients on dialysis for > 5 years had lower lumber spine T score (*P* = 0.02). FN T-score was significantly lower in older patients (*P* = 0.03). On the contrary, obese patients had better FT T-score than patients with normal weight (*P* = 0.01). No significant differences were found in the other variables. Only two patients had rheumatoid arthritis; one had low testosterone, and none of the participants were smokers.

Associations between different variables

Pearson's correlation coefficient was used to evaluate and describe the relationship between T-scores and the following six variables: age, and vitamin D, iPTH, ALP, phosphate, and adjusted calcium levels [Supplementary Table 1]. A moderate negative correlation was found between age and

iPTH and ALP levels (*r* = −0.47 and *r* = −0.34, respectively; *P* < 0.001). In addition, iPTH was demonstrated to have a strong positive correlation with ALP (*r* = 0.67; *P* < 0.001) but a weak positive correlation with phosphate (*r* = 0.25; *P* < 0.050). For the T-scores, a moderate negative association was observed between age and FN site (*r* = −0.33; *P* < 0.001). The correlation coefficient between the BMD LS and PF values was weakly positive (*r* = 0.28, *P* = 0.050), whereas the association between LS and FN (*r* = 0.39, *P* < 0.001) and PF and FN (*r* = 0.9, *P* < 0.001) had statistical significance.

Significant statistical differences were not identified between patients with fractures (*n* = 33) and those without in terms of gender, BMI, dialysis duration, glucocorticoid use, age, and laboratory variables, except for phosphate level, which was significantly higher in patients with fractures than those without fractures (mean ± SD: 1.25 ± 0.43 vs. 1.49 ± 0.28, respectively, *P* = 0.011) [Supplementary Tables 2 and 3].

DISCUSSION

BMD variation has multiple determinants, including genetics, ethnicity, and environmental factors. Bone mass (i.e., quality and quantity) in ESRD can deteriorate expeditiously due to multiple factors that have not been well characterized.[8] In the current study, of 477 subjects, BMD measurements were only available for 64 patients (16%), of which BMD assessments were followed-up for only 19 patients. The low screening for osteoporosis in the study is a limitation, as the final study sample is not representative of the wide spectrum of patients with ESRD. Therefore, the study findings cannot be generalized to the overall ESRD population and needs to be confirmed in future studies.

Notably, regular BMD assessments are needed for most ESRD patients.[2] Thus, considerable attention, in the form of BMD scanning, is required to monitor the bone health of dialysis patients, especially since bone loss is asymptomatic, which means that it is simply neglected.

Table 4: Multivariate analysis of baseline bone mineral density *T*-scores and baseline variables

Parameter	*T*-score lumbar spine		*T*-score proximal femur		*T*-score femur neck	
	P	*B* (95% CI)	*P*	*B* (95% CI)	*P*	*B* (95% CI)
Intercept	0.56	−0.755 (−3.31-1.80)	0.99	0.03 (−2.96-3.02)	0.42	1.05 (−1.53-3.64)
Age	0.67	−0.01 (−0.04-0.03)	0.41	−0.02 (−0.05-0.02)	0.03	−0.04 (−0.07-−0.01)
Gender						
Male	<0.001	1.96 (1.18-2.75)	0.67	0.19 (−0.71-1.10)	0.35	0.37 (−0.42-1.16)
Female[a]	.	0	.	0	.	0
BMI[§]						
Underweight	0.24	0.71 (−0.48-1.89)	0.27	−0.76 (−2.13-0.61)	0.36	−0.54 (−1.71-0.64)
Overweight	0.89	−0.06 (−0.87-0.76)	0.38	−0.43 (−1.38-0.53)	0.84	0.09 (−0.75-0.92)
Obese	0.33	0.42 (−0.45-1.29)	0.16	0.75 (−0.30-1.79)	0.01	1.20 (0.33-2.07)
Normal[a]	.	0	.	0	.	0
Duration (years)						
≥5	0.02	−0.84 (−1.49-−0.14)	0.54	−0.25 (−1.06-0.56)	0.32	−0.34 (−1.03-0.34)
≤4[a]	.	0	.	0	.	0
Glucocorticoids use						
Yes	0.84	−0.07 (−0.78-0.64)	0.75	−0.14 (−0.99-0.72)	0.43	−0.29 (−1.03-0.44)
No[a]	.	0	.	0	.	0

§BMI categories: Underweight=<18.5 kg/m², normal weight=18.5-24.9 kg/m², overweight=25.0-29.9 kg/m², obese=≥30 kg/m², [a]Reference group. BMI - Body mass index; CI - Confidence interval

An epidemiological analysis done in 2012 at the regional level showed that 34% and 31% of healthy Saudi women and men aged 50–79 years were osteoporotic.[6] However, there is scarcity of available data on the epidemiology of osteoporosis and osteopenia in patients with ESRD. In this regard, in the current study, the percentage of ESRD subjects with low bone mass (including osteopenia and osteoporosis) at the LS, PF, and FN sites was established to be 55%, 58%, and 71%, respectively. The FN site was impacted the most. In general, osteoporosis based on BMD was seen to equally affect male and female patients; however, female patients had osteoporosis at the LS site more frequently than male patients. Fragility fractures occurred more frequently in male patients, but, likely owing to the small sample size, this finding was not statistically significant. These trends are comparable with those identified in previous reports regarding osteopenia/osteoporosis prevalence. In support of our findings, previous studies demonstrated that the FN was the most common site affected by osteoporosis.[9] FN porosity is common because, in general, CKD affects the cortical bones more than the trabecular bones.[10,11] Conversely, it has been reported elsewhere that the LS (rather than the FN or the hip) is the most affected osteoporosis site in CKD and ESRD patients.[4,5,12]

The association between the duration of dialysis and decreased BMD is controversial. In the current study, patients on dialysis for ≥5 years had lower T-scores at all sites compared with those undergoing dialysis for a shorter duration; however, this finding was statistically significant only for the lumbar spine T score after adjusting for other variables. Previous studies have shown a similar trend, with a clear association between decreased BMD and duration of dialysis.[5,9] Thus, the duration of dialysis seems to have an inverse relationship with BMD.

In terms of risk factors and complications, it was established in the current study that age was significantly associated with reduced BMD, primarily at the FN site. These results are similar to the findings of other studies.[5,9] Obese patients had better T-score at FN compared with normal weight individuals, which was consistent with previous findings.[13,14] A third of the study participants with a history of fracture took steroids. The profound effects of glucocorticoids on bone health are well-known and manifest as increased resorption due to osteoclastogenesis, increased RANK ligand expression, and decreased osteoprotegerin receptor expression.[15]

Overall, a correlation between BMD values and laboratory biomarkers was not observed in our study. This finding differs from those of earlier studies that reported a negative association between BMD and intact PTH/calcium.[5,16] The heterogeneity of the studied populations, where variables such as duration of dialysis, transplantation, and/or patients undergoing parathyroidectomy differed significantly between our study and those in the literature, might account for distinctions between findings. Further prospective studies are warranted to evaluate the association between BMD and different bone-related biomarkers.

Regarding the treatment of osteoporosis in patients with CKD, obtaining a bone biopsy prior to the use of osteoporosis-directed therapy is recommended;[2] however, this is a cumbersome process that requires the interpretation of a pathologist. Indeed, in the current study, none of the patients underwent a bone biopsy for those

reasons. Therefore, appropriate management of calcium, phosphorous, PTH, metabolic acidosis, and other aspects of the chronic kidney disease–mineral and bone disorder is the mainstay of bone health management in patients with ESRD. However, it is not rare to use osteoporosis-directed therapies in patients with ESRD who are deemed to be at high risk of fragility fractures.[2] Accordingly, in the current study, bone health management was achieved mainly through adequate calcium, phosphorous, and vitamin D control; only three patients (5%) received denosumab, a safe osteoporosis-directed therapy for patients with ESRD.[2,17]

Globally, multiple small-scale studies have evaluated the effects of different medications on the BMD of patients with ESRD. A significant improvement in bone health parameters was reported in a study that explored the effects of cinacalcet at the bone–tissue level in patients with ESRD and elevated PTH levels.[18] Elsewhere, teriparatide was administered to dialysis patients with hypoparathyroidism and established osteoporosis. Throughout the study, there was evidence of a marked amelioration in the bone formation marker values between baseline (4 weeks) and follow-up (48 weeks); concomitantly, the bone resorption markers remained stable up to 20 weeks, followed by a subsequent steady decrease up to 48 weeks following treatment. In addition, ALP, a bone-specific marker, correlated with a 48-week percentage-based reduction in LS BMD.[19] Further studies are needed to explore the clinical impact of different medications used in ESRD patients and osteoporosis-directed medications on BMD to establish their efficacy in this regard in this patient population.

More than half of the patients had fractures in the current study. Fracture risk increases with low bone mass, often leading to high medical costs and mortality rates. Strategies that can help reduce the burden of fractures in dialysis patients include the optimization of mineral metabolism management, the application of strategies to prevent falls, particularly exercise training, and the use of hip protectors in high-risk patients.[2,8]

Study limitations and strengths
This study had several limitations, and these should be addressed in future research. Firstly, it was a single-center study with a small sample size and many unmeasured confounders. Therefore, the study sample is not fully representative of Saudi patients with ESRD and the generalizability of the study findings is limited until confirmed through comprehensive prospective studies. Nonetheless, this cross-sectional study unveiled several important findings, specifically evidence of a relatively high prevalence of osteoporosis in ESRD patients in the Saudi population. In addition, the risk factors for abnormal bone mass in hemodialysis patients were examined.

CONCLUSION

A high percentage of abnormal bone mass was observed in ESRD patients undergoing hemodialysis, and the most affected site was the femur neck. Factors that adversely affected bone mass were advanced age and low bodyweight. Given that bone loss is an asymptomatic process until there is evidence of a fracture, the early detection of low bone mass is vital to ensure a timely intervention and in avoiding bone loss. Further studies are needed to explore the association between different laboratory biomarkers and BMD. In addition, future studies should assess the efficacy of different treatment options in patients with low BMD.

Ethical considerations
The study was approved by the Institutional Review Board of KAMC (Ref. No.: RC20/054/R; dated: March 2020) with a waiver of written consent owing to the study design. The study adhered to the principles of Declaration of Helsinki, 2013.

Data availability statement
The datasets generated during and/or analyzed during the current study are not publicly available but are available from the corresponding author on reasonable request.

Peer review
This article was peer-reviewed by two independent and anonymous reviewers.

Conflicts of interest
There are no conflicts of interest.

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Supplementary Table 1: Assessment of the associations between bone mineral density and related variables (Pearson's correlation coefficient)

Variables	X1	X2	X3	X4	X5	X6	Y1	Y2	Y3
X1	1.000								
X2	0.285	1.000							
X3	−0.469‡‡	−0.291	1.000						
X4	−0.341‡‡	−0.149	0.688‡‡	1.000					
X5	0.010	0.197	0.254§§	0.216	1.000				
X6	0.145	0.123	−0.040	−0.166	−0.214	1.000			
Y1	−0.050	0.175	0.077	0.086	0.218	−0.229	1.000		
Y2	−0.162	0.092	−0.007	0.002	0.009	−0.144	0.284§§	1.000	
Y3	−0.336‡‡	0.056	0.004	0.059	0.045	−0.163	0.397‡‡	0.900‡‡	1.000

§§Correlation is significant at the 0.050 level (two-tailed), ‡‡Correlation is significant at the 0.010 level (two-tailed). X1 - Age; X2 - 25-hydroxy vitamin D; X3 - Intact parathyroid hormone; X4 - Alkaline phosphatase; X5 - Phosphatase; X6 - Corrected calcium levels; Y1 - *T*-score (lumbar spine); Y2 - *T*-score (proximal femur); Y3 - *T*-score (femoral neck)

Supplementary Table 2: Association between fracture history and numerical variables

Variables	Previous fracture		P***
	Mean±SD		
	No	Yes	
Age (years)	72.4±11.0	73.9±10.6	0.591
25-hydroxy vitamin D (nmol/l)	43.8±15.0	46.1±20.3	0.696
Intact parathyroid hormone (pmol/l)	56.5±63.3	50.6±49.4	0.68
ALP (u/l)	129.0±66.0	153.0±92.0	0.246
Phosphate (mmol/l)	1.5±0.3	1.3±0.4	0.011
Adjusted calcium level (mmol/l)	2.3±0.2	2.3±0.2	0.778
Yes	14±56.0	11±44.0	

***Calculated using the independent *t*-test. SD - Standard deviation; ALP - Alkaline phosphatase

Supplementary Table 3: Association between fracture history and categorical variables

Variables	Previous fracture		P†††
	No, *n* (%)	Yes, *n* (%)	
Gender			
Male	6 (40.0)	9 (60.0)	0.560
Female	25 (51.0)	24 (49.0)	
BMI (kg/m²)			
Underweight	3 (50.0)	3 (50.0)	0.192
Normal	14 (50.0)	14 (50.0)	
Overweight	5 (29.4)	12 (70.6)	
Obese	9 (69.2)	4 (30.8)	
Dialysis duration (years)			
≤4	18 (54.5)	15 (45.5)	0.331
5	13 (41.9)	18 (58.1)	
Glucocorticoids			
No	17 (43.6)	22 (56.4)	0.443
Yes	14 (56.0)	11 (44.0)	

†††Calculated using Fishers) racture his. BMI categories: Underweight=<18.5 kg/m², normal weight=18.5-24.9 kg/m², overweight=25.0-29.9 kg/m², obese=≥30.0 kg/m². BMI - Body mass index