

RESEARCH ARTICLE

Bone mineral density and related clinical and laboratory factors in peritoneal dialysis patients: Implications for bone health management

Rami Tamimi¹✉, Amjad Bdair¹✉, Ahmad Shratih¹✉, Mazen Abdalla^{1,2}, Alaa Sarsour³, Zakaria Hamdan^{1,4*}, Zaher Nazzal^{1*}

1 Department of Medicine, Faculty of Medicine and Health Sciences, An-Najah National University, Nablus, Palestine, **2** Department of Orthopedics, An-Najah National University Hospital, Nablus, Palestine, **3** Kidney and Dialysis Section, An-Najah National University Hospital, Nablus, Palestine, **4** Department of Internal Medicine, An-Najah National University Hospital, Nablus, Palestine

✉ These authors contributed equally to this work.

* znazzal@najah.edu (ZN); z.hamdan@najah.edu (ZH)



OPEN ACCESS

Citation: Tamimi R, Bdair A, Shratih A, Abdalla M, Sarsour A, Hamdan Z, et al. (2024) Bone mineral density and related clinical and laboratory factors in peritoneal dialysis patients: Implications for bone health management. *PLoS ONE* 19(5): e0301814. <https://doi.org/10.1371/journal.pone.0301814>

Editor: Patricia Khashayar, Gent University, BELGIUM

Received: September 18, 2023

Accepted: March 24, 2024

Published: May 16, 2024

Peer Review History: PLOS recognizes the benefits of transparency in the peer review process; therefore, we enable the publication of all of the content of peer review and author responses alongside final, published articles. The editorial history of this article is available here: <https://doi.org/10.1371/journal.pone.0301814>

Copyright: © 2024 Tamimi et al. This is an open access article distributed under the terms of the [Creative Commons Attribution License](https://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Data Availability Statement: All relevant data are within the manuscript and its [Supporting Information](#) files.

Abstract

Background

End-stage renal disease (ESRD) patients often experience accelerated bone turnover, leading to osteoporosis and osteopenia. This study aimed to determine the prevalence of osteoporosis in Peritoneal Dialysis (PD) patients using bone mineral density (BMD) measurements obtained through dual-energy X-ray absorptiometry (DEXA) scan and to explore any possible associations with clinical and biochemical factors.

Methods

In this cross-sectional study, we enrolled 76 peritoneal dialysis patients from the dialysis center at An-Najah National University Hospital in Nablus, Palestine. We used the DEXA scan to measure BMD at the lumbar spine and hip, with values expressed as T-scores. We conducted a multivariate analysis to explore the relationship between BMD and clinical and biochemical parameters.

Results

Over half (52.6%) of the PD patients had osteoporosis, with a higher prevalence observed among patients with lower BMI ($p < 0.001$). Higher alkaline phosphatase levels were found among osteoporotic patients compared to non-osteoporotic patients ($p = 0.045$). Vitamin D deficiency was also prevalent in this population, affecting 86.6% of patients. No significant correlation was found between 25 vitamin D levels and BMD. No significant correlation was found between Parathyroid hormone (PTH) levels and BMD.

Funding: The authors received no specific funding for this work.

Competing interests: The authors have declared that no competing interests exist.

Conclusion

A notable proportion of PD patients experience reduced BMD. Our study found no correlation between vitamin D levels and BMD, but it highlighted the significant vitamin D deficiency in this population. Furthermore, our analysis indicated a positive correlation between BMI and BMD, especially in the femoral neck area. This underscores the significance of addressing bone health in PD patients to mitigate the risk of fractures and improve their overall well-being.

Introduction

Chronic kidney disease (CKD) is a significant public health concern and a major cause of premature death. End-Stage–Renal Disease (ESRD) is the result of CKD and is defined as GFR less than 15 ml/min, which ultimately needs kidney replacement therapy (KRF), dialysis, or transplantation [1]. In 2016, Peritoneal Dialysis (PD), a type of kidney replacement therapy [2], was established in Palestine despite many challenges and limitations. It has been successfully developed over the years to meet the demand of the growing number of ESRD patients in need of kidney replacement therapy [3].

CKD patients suffered from accelerated bone turnover and decreased bone density, for which a broad range of pathophysiological states could be responsible, such as secondary hyperparathyroidism [4], hyperphosphatemia [5], decreased vitamin D synthesis [6], hypocalcemia [5], and advancing age. This makes ESRD patients more vulnerable to bone fractures than the general population [7, 8].

Bone mineral density (BMD) serves as an indicator of bone mass and mineralization [9]. According to the International Society for Clinical Densitometry (ISCD), BMD can be assessed by Dual-Energy X-ray Absorptiometry (DEXA) scan at both the postero-anterior lumbar spine (L1-L4) and the hip (femoral neck or total proximal femur) [10]. The DEXA scan results can be expressed as BMD (g/cm²), Z-score, or T-score, with the T-score representing the number of standard deviations (SD) from the mean of a healthy young adult.

The 2017 KDIGO Chronic Kidney Disease–Mineral and Bone Disorder (CKD-MBD) guideline update recommends BMD testing for patients with CKD who show evidence of CKD-MBD and/or have risk factors for osteoporosis [11]. A meta-analysis of studies in CKD patients revealed a significant relationship between a low BMD and the risk of bone fracture [12], confirming the importance of BMD measurement and fracture risk prevention. Identifying low BMD in CKD patients early is crucial, particularly in candidates for kidney transplants, as treatment becomes more challenging post-transplantation [13].

Vitamin D facilitates calcium absorption in the gastrointestinal tract, ensuring sufficient calcium and phosphate levels in the bloodstream. This, in turn, supports the process of normal bone mineralization [14]. Vitamin D deficiency, characterized by a 25-hydroxyvitamin D level below 20 ng/mL, is higher among individuals with CKD than the general population [15]. Multiple factors contribute to vitamin D deficiency, such as progressive hyperparathyroidism [16], hyperphosphatemia, reduced sunlight exposure, and limited dietary intake. Vitamin D deficiency is clinically associated with various medical conditions, including increased cardiovascular morbidity [17], an elevated risk of peritonitis [18], impaired physical performance [19], and decreased bone mineral density [20].

A previous study conducted at An-Najah National University Hospital (NNUH), which included a majority of hemodialysis (HD) patients, found that 42.8% of ESRD patients had

osteoporosis and 40.2% had osteopenia [21]. This study reported no significant difference between patients on hemodialysis or peritoneal dialysis, but it acknowledged that the small sample size of PD patients may limit this result. One regional multicenter study that included 292 PD patients found that 19% of patients had osteoporosis and 36% had osteopenia [22], somewhat similar to what other studies have demonstrated [23–26]. In addition, these studies found an increased risk of reduced BMD with lower Body Mass Index (BMI). However, conflicting results were reported regarding the relation between DEXA scan measurements and biochemical markers. In this study, we aim to assess the prevalence of osteoporosis/osteopenia and evaluate the clinical and biochemical variables associated with BMD in PD patients.

Materials and methods

Design and population

This cross-sectional study was conducted between August 2022 and November 2022 at the dialysis center of NNUH, Palestine, the largest dialysis center offering the option of PD in the region.

The study population consisted of ESRD patients undergoing PD and were regularly followed up by NNUH physicians. A total of 76 patients undergoing PD were recruited, encompassing a significant proportion of the NNUH dialysis center's patient population. Patients on continuous ambulatory peritoneal dialysis above 18 years of age were included. Conversely, patients with a history of parathyroidectomy or malignancy, as well as patients currently taking bisphosphonates or estrogen, were excluded from our study. None of our patients were on any calcimimetic treatment or inactive vitamin D supplementation.

Study measures

After obtaining informed consent from the participants, we extracted baseline demographic and clinical characteristics from patients and their medical records. These variables include age, gender, BMI, duration of PD, smoking status, presence of comorbidities, history of fractures, kidney transplant, history of HD, menopause status, and current medication history (alpha D3 supplements, calcium supplements, phosphate binder use, and steroids use). Laboratory and biochemical markers, including serum level of 25-hydroxyvitamin D, albumin, calcium, phosphate, alkaline phosphatase, parathyroid hormone (PTH), hemoglobin, and ferritin, were obtained via venous blood sampling at the time of their monthly follow-up visits. The blood samples were immediately sent to the laboratory for analysis upon collection and were subsequently tested on the collection day.

DEXA scan is considered one of the best available ways to assess BMD because it is noninvasive and accurate, with a short scanning time and low radiation exposure. The World Health Organization (WHO) defines osteoporosis as a T score on BMD measurement using a DEXA scan at the femoral neck ≤ -2.5 or lower, where a T score between -1.0 and -2.5 is defined as Osteopenia [27]. For this study, patients were classified as osteoporosis and non-osteoporosis groups. The osteoporosis group was defined as any patient with a T score of ≤ -2.5 or lower in at least one site, while the non-osteoporosis group was defined as any patient with a T score of above -2.5 . The BMD assessment was conducted through a Dual-Energy X-ray Absorptiometry (DEXA) scan using the Hologic equipment model Discovery WI with serial number 82189. The imaging process was carried out and evaluated by experienced technicians at Al-Rahma Medical Center, Nablus, within the same month as the blood tests.

The Fracture Risk Assessment Tool (FRAX), developed by the World Health Organization Collaborating Centre in Sheffield, UK, is an online web-based algorithm that estimates the individualized 10-year probability of hip and major osteoporotic fracture (MOF; hip, clinical

spine, distal forearm, and proximal humerus). The algorithm incorporates seven dichotomous clinical risk factors: age, sex, BMI, and, optionally, a BMD measurement [28]. FRAX has been validated for appropriate use in Palestinian patients at high risk of developing osteoporosis.

The Elecsys kit was used to determine the level of 25 vitamin D in the body. Vitamin D deficiency was defined as a 25-hydroxyvitamin D level below 20 ng/mL [29]. The Elecsys kit also measured the Parathyroid hormone (PTH) level. Around 5-10cc of venous blood was drawn by trained nurses at the NNUH dialysis center during patients' monthly follow-up visits, and the samples were sent to the laboratory for analysis.

Analysis plan

We processed the collected data using the Statistical Package for the Social Sciences version 26 (IBM Corp., Armonk, NY, United States). Subsequently, we described the findings as frequency tables and suitable charts for categorical variables, while continuous variables were presented using mean and standard deviation (SD) or median and range values. We used the Shapiro-Wilk test to assess for data normality. For analytical analysis, patients were categorized into osteoporosis and non-osteoporosis groups. Univariate statistical analysis was performed, utilizing relevant significance tests such as Mann-Whitney U, Chi-Square, and independent 2-sample tests. Subsequently, a multivariate analysis was conducted using binary logistic regression, incorporating variables that demonstrated significance in the univariate analysis and additional variables recommended by existing literature. The variables included in the regression model were age, gender, BMI, duration of dialysis, calcitriol supplementation, calcium supplementation, sevelamer supplementation, 25 Vitamin D, alkaline phosphatase, parathyroid hormone, albumin, calcium measured, and phosphate. Multiple linear regression and Spearman's correlation coefficients were used to investigate correlations. The variables deemed significant in the univariate analysis were included in the multiple linear regression (BMI, Sevelamer Dose, Albumin, Phosphate). Statistical significance was set at p-value ≤ 0.05 .

Ethical consideration

The study and its associated experimental protocols, such as performing DEXA scans and drawing blood, were approved by the Institutional Review Board committee of An-Najah National University [Reference #: Med. Feb. 2022/21]. Appropriate permissions were obtained from the hospital and Rahma Medical Center. The study adhered to the principles outlined in the Declaration of Helsinki and complied with applicable national guidelines and regulations. Patients were given the option to voluntarily participate in the study, with a comprehensive explanation of its purpose, objectives, and potential risks. To ensure confidentiality, no personal information was collected, and codes rather than names identified patients. Access to the collected data was restricted to the research team for research purposes only. All patients provided written informed consent before participating.

Results

Background characteristics of the patients

A total of 76 Peritoneal Dialysis patients were recruited to participate in this study. The mean age of our participants was 49.5 years (SD = 16.5), with 68% (n = 52) under the age of 60. Approximately 54% (n = 41) of the participants were males, 46% (n = 35) had normal BMI, and 83% had been on PD for over a year. Among the participants, 75% (n = 57) had hypertension and 33% (n = 25) had Diabetes mellitus. Around 8% (n = 6) of our patients reported a

Table 1. Clinical and laboratory characteristics of the participants.

	Frequency (%)	Mean \pm SD
Age		49.5 \pm 16.5
Age \geq 60 years	24 (31.6%)	
Age <60 years	52 (68.4%)	
Gender		
Male	41 (53.9%)	
Female	35 (46.1%)	
Body Mass Index		25.4 \pm 5.5
Underweight	6 (7.9%)	
Normal	35 (46.1%)	
Overweight	35 (46.05)	
Duration of Peritoneal Dialysis (Months)		23.0 \pm 15.0
Hypertension (Yes)	57 (75.0%)	
Diabetes Mellitus (Yes)	25 (32.9%)	
Smoking History (Yes)	27 (35.5%)	
History of Hemodialysis (Yes)	57 (75.0%)	
History of Kidney Transplant (Yes)	13 (17.1%)	
History of Fractures (Yes)	6 (7.9%)	
Menopause Status (Yes)	18 (51.4%)	
Steroid Use (Yes)	4 (5.3%)	
1,25 Vit D3 Supplementation (calcitriol) (mcg/day)		0.5 \pm 0.4
Calcium Supplementation (mg/day)		1869.8 \pm 1112.6
Sevelamer Binder Supplementation (mg/day)		3282.8 \pm 1118.1
Alkaline Phosphatase (U/L)		122.3 \pm 67.1
Parathyroid Hormone (pg/ml)		439.4 \pm 323.2
Albumin (g/dl)		3.65 \pm 0.43
Calcium Measured (mg/dl)		9.1 \pm 0.71
Phosphate (mg/dl)		5.46 \pm 1.56
Ferritin (ng/ml)		576.7 \pm 588.8

<https://doi.org/10.1371/journal.pone.0301814.t001>

history of fractures while on dialysis. Table 1 summarizes the patients' baseline demographic, biochemical, and clinical features.

Vitamin D lab results demonstrated that around 86.8% (n = 66) [95%CI: 77.1% - 93.5%] of our patients suffer from 25 vitamin D deficiency, with a median of 8.7 (ng/ml).

Bone mineral density

The overall prevalence of osteoporosis among the participants was 52.6% [n = 40, 95% CI: 40.8%-64.2%]; according to the site, 41% of the patients had osteoporosis in the femoral neck (Median T-score = -2.3) and 38% had osteoporosis in the lumbar spine (Median T-score = -2.1) (Fig 1). According to the FRAX tool, the median 10-year probability of developing a major osteoporotic fracture was 4.1%, with scores ranging up to 52%. In comparison, the median FRAX score for risk of hip fractures was 1.5% (0.1%-49.0%).

A univariate analysis was carried out to examine the relationship between patients' BMD status and their demographic and clinical attributes. BMI was significantly higher in non-osteoporotic patients than in osteoporotic patients (p = 0.001); this relationship remained significant after multivariate analysis, as demonstrated in Table 2.

Multivariate analysis revealed slightly higher alkaline phosphatase levels among osteoporotic patients than non-osteoporotic patients (p = 0.045). Although the age of osteoporotic

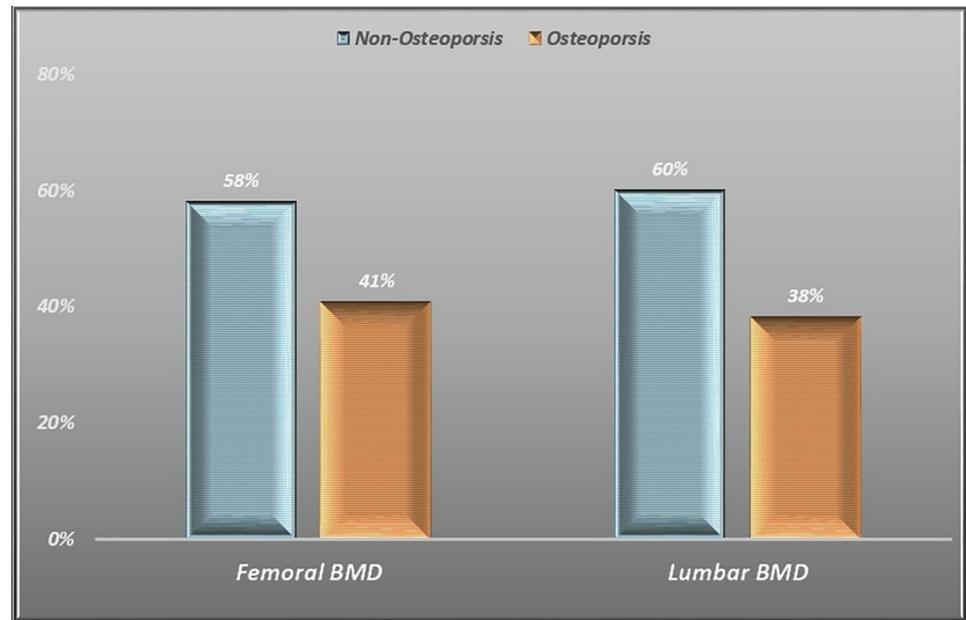


Fig 1. Bone mineral density distribution.

<https://doi.org/10.1371/journal.pone.0301814.g001>

patients tended to be less than that of non-osteoporotic patients, this difference was not statistically significant even after adjusting for confounders ($p = 0.108$). Regarding gender, males exhibited higher levels of osteoporosis than females, but this relationship did not reach statistical significance even after multivariate analysis ($p = 0.977$). The duration of PD was longer among osteoporotic patients, but this association did not reach statistical significance even after multivariate analysis ($p = 0.921$) (Table 3).

No statistically significant differences were observed between the two groups regarding biochemical parameters, including serum vitamin D, parathyroid hormone, albumin, and calcium. According to Spearman correlation, there was a significant positive correlation ($p < 0.01$) between BMI and lumbar spine BMD and femoral neck BMD; higher patient BMI was associated with higher bone mineral density. A significant positive correlation was also identified between binder sevelamer supplementation and femoral neck BMD. Albumin and phosphate laboratory levels significantly correlated with BMD at the femoral neck (Table 4).

However, upon conducting multivariate analysis, only albumin demonstrated a significant correlation with BMD at the femoral neck ($p < 0.01$) (Table 5).

Discussion

In our study of 76 Peritoneal Dialysis patients, we observed osteoporosis prevalence of 41% and 38% based on femoral neck and lumbar spine T-scores, respectively. These figures diverge from findings in other studies; one study reported a lower prevalence of osteoporosis in PD patients, with 26% and 19% based on femoral neck and lumbar spine T-scores, respectively [22]. In contrast, another study found a higher prevalence of osteoporosis, with 78% at the femoral neck and 58% at the lumbar spine [30]. However, when considering the combined prevalence of osteoporosis and osteopenia in our study, the overall bone mineral loss in PD patients was as high as 52%, similar to what other studies have found [22]. Notably, we observed a significantly higher rate of osteoporosis and osteopenia in the femoral neck compared to the spine. This difference may be attributed to potential aortic calcifications, which

Table 2. Univariate analysis of clinical and laboratory characteristics with BMD status.

	Osteoporosis (n = 76)		P Value*
	Yes (n = 40)	No (n = 36)	
Age Total	51 (18–79)	52 (19–82)	0.778
Gender			0.598
Male	23 (57.5%)	18 (51.4%)	
Female	17 (42.5%)	17 (48.6%)	
Body Mass Index Total	22.9 (16.9–29.3)	26.9 (18.0–39.7)	0.001*
Duration of Peritoneal Dialysis	18.9 (5.3–67.2)	17.7 (1.1–66.5)	0.464
Hypertension (Yes)	31 (77.5%)	26 (74.3%)	0.745
Diabetes Mellitus (Yes)	13 (32.5%)	12 (34.3%)	0.870
Smoking History (Yes)	12 (30.0%)	15 (42.9%)	0.247
History of Hemodialysis (Yes)	34 (85.0%)	26 (74.3%)	0.247
History of Transplant (Yes)	7 (17.5%)	5 (14.3%)	0.705
History of Fractures (Yes)	5 (12.5%)	1 (2.9%)	0.125
Menopause Status (Yes)	10 (58.8%)	8 (47.1%)	0.492
Steroid Use (Yes)	3 (7.5%)	1 (2.9%)	0.372
Calcitriol Supplementation (Yes)	30 (75.0%)	27 (77.1%)	0.828
Calcium Supplementation (Yes)	23 (57.5%)	20 (57.5%)	0.975
Sevelamer Supplementation (Yes)	12 (30.0%)	16 (45.7%)	0.160
25 Vitamin D (ng/ml)	8.9 (3.0–34.9)	8.9 (3.0–33.26)	0.907
Alkaline Phosphatase (U/L)	106.0 (59.0–443.0)	104.0 (48.0–204.0)	0.162
Parathyroid Hormone (pg/ml)	297.7 (16.73–1525.0)	388.5 (72.5–1372.0)	0.260
Albumin (g/dl)	3.6 (2.5–4.3)	3.7 (2.6–4.5)	0.086
Calcium Measured (mg/dl)	9.1 (7.1–10.9)	8.9 (7.3–10.4)	0.758
Phosphate (mg/dl)	5.3 (1.6–7.8)	5.8 (2.8–9.9)	0.051
Ferritin (ng/ml)	468.5 (17.0–2547.0)	309.0 (15.0–1988.0)	0.640

*Mann–Whitney U test, Chi-Square test, aP Value: adjusted P value, aOR: adjusted Odds Ratio, CI: Confidence Interval

<https://doi.org/10.1371/journal.pone.0301814.t002>

Table 3. Multivariate analysis of clinical and laboratory characteristics with BMD status.

	aP Value	aOR (95% CI)
Age	0.108	1.04 (0.99–1.09)
Gender (Ref: male)	0.977	0.98 (0.25–3.87)
Body Mass Index	0.001*	0.77 (0.66–0.89)
Duration of Peritoneal Dialysis	0.921	0.99 (0.96–1.04)
Calcitriol Supplementation (Ref: No)	0.656	1.39 (0.33–5.88)
Calcium Supplementation (Ref: No)	0.623	1.00 (0.99–1.00)
Sevelamer Supplementation (Ref: No)	0.308	1.00 (0.99–1.00)
25 Vitamin D (ng/ml)	0.619	1.02 (0.94–1.12)
Alkaline Phosphatase (U/L)	0.045*	1.02 (1.00–1.04)
Parathyroid Hormone (pg/ml)	0.383	0.99 (0.99–1.00)
Albumin (g/dl)	0.741	0.76 (0.15–3.96)
Calcium Measured (mg/dl)	0.659	1.25 (0.47–3.33)
Phosphate (mg/dl)	0.240	0.72 (0.41–1.25)

*Ref: Reference group; aP Value: adjusted P value; aOR: adjusted Odds Ratio; CI: Confidence Interval

<https://doi.org/10.1371/journal.pone.0301814.t003>

Table 4. Spearman correlation of clinical and laboratory variables with BMD status.

	BMD Femoral		BMD Lumbar	
	Correlation Coefficient	P-value	Correlation Coefficient	P-value
Age	-0.56	0.635	0.117	0.319
Body Mass Index	0.479	0.01*	0.465	0.01*
Height	-0.041	0.730	0.113	0.335
Weight	0.450	0.01*	0.525	0.01*
Duration of PD	-0.116	0.321	-0.041	0.730
Calcitriol Dose	0.188	0.106	-0.016	0.894
Calcium Dose	0.042	0.718	0.036	0.760
Sevelamer Dose	0.246	0.033*	0.124	0.288
Vitamin D level	0.047	0.689	0.048	0.684
Alkaline Phosphatase	-0.088	0.450	-0.049	0.679
Parathyroid Hormone	0.216	0.063	0.149	0.201
Albumin	0.324	0.01*	0.126	0.280
Calcium	-0.004	0.972	-0.101	0.390
Phosphate	0.357	0.01*	0.180	0.123
Ferritin	-0.101	0.389	-0.181	0.121

PD: Peritoneal Dialysis

<https://doi.org/10.1371/journal.pone.0301814.t004>

could lead to an overestimation of the spine BMD. However, one recent study showed that aortic vascular calcification had a minimal impact on the lumbar spine BMD [31]. Another possible explanation might be that cortical bone appears to be affected more than trabecular bone in renal osteodystrophy. Given the significant presence of cortical bone in the femoral neck and hip, these areas may be more susceptible to bone density alterations.

Table 5. Multiple linear regression analysis of laboratory variables with BMD status.

	BMD Femoral		BMD Lumbar	
	Beta (95%CI)	aP-value	Beta (95%CI)	aP-value
Age				
Body Mass Index	0.428 (0.05–0.13)	0.001*	0.445 (0.06–0.17)	0.001*
Height				
Weight				
Duration of PD				
Calcitriol Dose				
Calcium Dose				
Sevelamer Dose	0.171 (0.00–0.00)	0.096	0.062 (0.00–0.00)	0.585
Vitamin D level				
Alkaline Phosphatase				
Parathyroid Hormone				
Albumin	0.279 (0.21–1.30)	0.007*	0.105 (-0.41–1.12)	0.356
Calcium				
Phosphate	0.166 (-0.04–0.28)	0.138	0.126 (-0.11–0.34)	0.314
Ferritin				

aP-value: adjusted P-value; CI: Confidence interval; PD: Peritoneal Dialysis

<https://doi.org/10.1371/journal.pone.0301814.t005>

Moreover, we identified additional correlations, including albumin, phosphorus, and sevelamer use, specifically with femoral BMD instead of lumbar BMD. This observation may indicate a stronger correlation with cortical bone-rich areas [32]. Additionally, cortical bone has also been linked to mortality, as evidenced by a five-year follow-up study in HD patients, which demonstrated that low BMD at the hip predicted mortality [33, 34].

In our study, 86.8% of our patients were found to have 25 vitamin D deficiency, with a median of 8.7ng/mL. One multicenter study conducted on PD patients reported similar results [15]. However, studies conducted on HD patients found higher levels of 25 vitamin D compared to our findings [35]. This may be explained by the peritoneal losses of the active vitamin D sterols that occur in peritoneal dialysis [15]. Interestingly, we did not observe any significant correlation between 25 vitamin D levels and BMD in the multivariate analysis. However, a recent study evaluating 50 HD patients showed no significant association between vitamin D levels and BMD status [36].

In the general population, the incidence of osteoporosis is typically expected to increase with older age and female sex. Surprisingly, in our study, the prevalence of osteoporosis was higher in male subjects (57.5%) compared to females (42.5%). However, this difference was not statistically significant. We could not establish a significant correlation between age and BMD in our patient population. BMI, however, demonstrated a robust positive correlation with BMD values as measured by DEXA. Similar to a previous study, we observed that patients' weight, rather than height, was responsible for the correlation between BMI and BMD [22]. This finding might be attributed to a certain level of measurement error with DEXA scans in individuals with obesity [37, 38]. Hence, the reliability of BMI-BMD correlations in the lumbar spine region may be questioned.

In contrast, the femoral neck is predicted to have less fat tissue due to its anatomical location. Our study observed a similarly strong correlation between BMI and BMD measurements in the femoral neck area. Therefore, we also predict that the positive correlation between BMI and BMD is not just a measurement error but a significant clinical correlation. Obesity has been shown to be associated with higher BMD of weight-bearing bones, suggesting that obesity may contribute to preventing bone loss in such bones, pointing to the significance of reduced body weight as the primary risk factor for decreased BMD in individuals undergoing chronic PD.

Previous research has shown that low BMD is linked to prolonged dialysis periods, elevated serum PTH levels, higher serum calcium levels, and a decrease in the consumption of elemental calcium supplements [22, 30]. In a prior study involving 194 dialysis patients, we demonstrated a statistically significant negative correlation between BMD and duration of dialysis. Furthermore, multivariate analysis identified an association between PTH levels and femoral BMD as assessed by DEXA scan [21]. However, in this study, we could not replicate similar results in our patients' population. This might be attributed to our failure to account for the entire duration of dialysis, which includes both PD and HD time. Such inclusion could reveal a significant correlation. We did observe a positive correlation between PTH and BMD at the femoral neck using Spearman's correlation, with a p-value of 0.063. However, it is worth noting that our relatively small sample size may also influence this finding; with a larger sample size, a statistically significant correlation with PTH might have been observed, especially considering that a subset of patients experiences secondary/tertiary hyperparathyroidism, which could potentially explain the low BMD in these individuals.

Nevertheless, osteoporotic individuals exhibited higher alkaline phosphatase levels, a marker indicating bone turnover, consistent with findings from previous research [39, 40]. However, although this observation reached statistical significance, it is essential to clarify that the slight difference in median alkaline phosphatase levels between osteoporotic and non-

osteoporotic groups may not be clinically significant. Spearman's correlation showed a positive correlation between femoral BMD and albumin and phosphorous levels; this was also evident in our prior study involving mainly HD patients. However, after the multivariate analysis, only albumin showed a statistically significant correlation with BMD at the femoral neck. This finding might be related to the nutritional status of the patients, as lower albumin levels may indicate poor nutritional status [41].

There are several potential limitations to this study. Firstly, using a cross-sectional study design indicates a definitive cause-and-effect relationship between variables of interest cannot be established. Secondly, the study was conducted at a solitary clinical center, so we must exercise caution when generalizing the findings. Thirdly, the sample size was limited to only 76 patients, which may need to be increased to draw conclusive relationships between variables of interest. Fourthly, relying solely on DEXA scan results for diagnosing osteoporosis may not be universally applicable, particularly in younger patients. Lastly, we did not account for the entire duration of dialysis, which includes both PD and HD time.

Further studies are needed with a larger sample size and a longer time to study the variables in more detail. However, despite these limitations, this study is the first in the region to explore Bone Mineral Density and its relationship with vitamin D levels and other biochemical factors in peritoneal dialysis patients. This is particularly noteworthy considering the scarcity of research on this subject. Furthermore, our study, with its meticulous data collection, rigorous statistical analyses, comprehensive exploration of various variables, and thoughtful consideration of potential confounders, enhances the reliability and significance of our findings. This contributes to advancing our understanding of Bone Mineral Density and related variables in patients undergoing peritoneal dialysis.

Conclusion

In conclusion, this study provides valuable insights into the prevalence of osteoporosis and osteopenia among the region's Peritoneal Dialysis (PD) patients. A significant proportion of PD patients exhibited reduced Bone Mineral Density (BMD), with osteoporosis rates of 41% in the femoral neck and 38% in the lumbar spine. While our study did not establish a significant correlation between vitamin D levels and BMD in PD patients, it highlighted this group's high prevalence of vitamin D deficiency. Furthermore, our analysis revealed a strong positive correlation between BMI and BMD, particularly in the femoral neck area.

Addressing bone health in PD patients is paramount to mitigating the risk of fractures and improving the overall quality of life. Healthcare providers should consider integrating regular BMD assessments and vitamin D supplementation into the comprehensive care plan for CKD patients undergoing PD. This study serves as a foundation for future investigations in this field, with the ultimate goal of improving the management and outcomes of bone health in PD patients.

Supporting information

S1 Data.
(XLSX)

Acknowledgments

We acknowledge all of the patients who participated in the study. We acknowledge the staff at Al-Rahma Medical Center for performing DEXA scans required for our patients. We also

acknowledge staff in the An-Najah National University Hospital dialysis center for managing patients and keeping follow-ups.

Author Contributions

Conceptualization: Mazen Abdalla, Zakaria Hamdan, Zaher Nazzal.

Data curation: Rami Tamimi, Amjad Bdair, Ahmad Shratih, Alaa Sarsour.

Formal analysis: Rami Tamimi, Amjad Bdair, Ahmad Shratih, Zaher Nazzal.

Investigation: Rami Tamimi.

Methodology: Amjad Bdair, Ahmad Shratih, Mazen Abdalla, Alaa Sarsour, Zakaria Hamdan, Zaher Nazzal.

Project administration: Zaher Nazzal.

Resources: Zaher Nazzal.

Supervision: Mazen Abdalla, Zakaria Hamdan, Zaher Nazzal.

Validation: Alaa Sarsour, Zakaria Hamdan.

Writing – original draft: Rami Tamimi, Amjad Bdair.

Writing – review & editing: Ahmad Shratih, Mazen Abdalla, Alaa Sarsour, Zakaria Hamdan, Zaher Nazzal.

References

1. Levey AS, de Jong PE, Coresh J, et al. The definition, classification, and prognosis of chronic kidney disease: a KDIGO Controversies Conference report. *Kidney international* 2011; 80: 17–28.
2. Andreoli MCC, Totoli C. Peritoneal Dialysis. *Rev Assoc Med Bras* 2020; 66Suppl 1: s37–s44. <https://doi.org/10.1590/1806-9282.66.S1.37> PMID: 31939534
3. Taher A, Enaya A, Sarsour A, et al. Growing a peritoneal dialysis program in Palestine from zero to 178 patients in 5 years: a single-center experience. *BMC Nephrol* 2023; 24: 21.
4. Cunningham J, Locatelli F, Rodriguez M. Secondary hyperparathyroidism: pathogenesis, disease progression, and therapeutic options. *Clin J Am Soc Nephrol* 2011; 6: 913–921. <https://doi.org/10.2215/CJN.06040710> PMID: 21454719
5. Felsenfeld AJ, Levine BS, Rodriguez M. Pathophysiology of Calcium, Phosphorus, and Magnesium Dysregulation in Chronic Kidney Disease. *Semin Dial* 2015; 28: 564–577. <https://doi.org/10.1111/sdi.12411> PMID: 26303319
6. Lips P, van Schoor NM. The effect of vitamin D on bone and osteoporosis. *Best Pract Res Clin Endocrinol Metab* 2011; 25: 585–591. <https://doi.org/10.1016/j.beem.2011.05.002> PMID: 21872800
7. Ensrud KE, Lui L-Y, Taylor BC, et al. Renal function and risk of hip and vertebral fractures in older women. *Arch Intern Med* 2007; 167: 133–139. <https://doi.org/10.1001/archinte.167.2.133> PMID: 17242313
8. Bover J, Ureña P, Brandenburg V, et al. Adynamic bone disease: from bone to vessels in chronic kidney disease. *Semin Nephrol* 2014; 34: 626–640. <https://doi.org/10.1016/j.semnephrol.2014.09.008> PMID: 25498381
9. Fonseca H, Moreira-Gonçalves D, Coriolano H-JA, et al. Bone quality: the determinants of bone strength and fragility. *Sports Med* 2014; 44: 37–53. <https://doi.org/10.1007/s40279-013-0100-7> PMID: 24092631
10. Schousboe JT, Shepherd JA, Bilezikian JP, et al. Executive summary of the 2013 International Society for Clinical Densitometry Position Development Conference on bone densitometry. *J Clin Densitom Off J Int Soc Clin Densitom* 2013; 16: 455–466. <https://doi.org/10.1016/j.jocd.2013.08.004> PMID: 24183638
11. Ketteler M, Block GA, Evenepoel P, et al. Executive summary of the 2017 KDIGO Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD) Guideline Update: what's changed and why it matters. *Kidney Int* 2017; 92: 26–36.

12. Bucur RC, Panjwani DD, Turner L, et al. Low bone mineral density and fractures in stages 3–5 CKD: an updated systematic review and meta-analysis. *Osteoporos Int a J Establ as result Coop between Eur Found Osteoporos Natl Osteoporos Found USA* 2015; 26: 449–458. <https://doi.org/10.1007/s00198-014-2813-3> PMID: 25477230
13. Battaglia Y, Bellasi A, Bortoluzzi A, et al. Bone Mineral Density Changes in Long-Term Kidney Transplant Recipients: A Real-Life Cohort Study of Native Vitamin D Supplementation. *Nutrients*; 14. Epub ahead of print January 2022. <https://doi.org/10.3390/nu14020323> PMID: 35057505
14. Khazai N, Judd SE, Tangpricha V. Calcium and vitamin D: skeletal and extraskelatal health. *Curr Rheumatol Rep* 2008; 10: 110–117.
15. Taskapan H, Ersoy FF, Passadakis PS, et al. Severe vitamin D deficiency in chronic renal failure patients on peritoneal dialysis. *Clin Nephrol* 2006; 66: 247–255. <https://doi.org/10.5414/cnp66247> PMID: 17063991
16. Williams S, Malatesta K, Norris K. Vitamin D and chronic kidney disease. *Ethn Dis* 2009; 19: S5–8–11. PMID: 20077598
17. Wang AY-M, Lam CW-K, Sanderson JE, et al. Serum 25-hydroxyvitamin D status and cardiovascular outcomes in chronic peritoneal dialysis patients: a 3-y prospective cohort study. *Am J Clin Nutr* 2008; 87: 1631–1638. <https://doi.org/10.1093/ajcn/87.6.1631> PMID: 18541550
18. Kerschbaum J, Vychytil A, Lhotta K, et al. Treatment with oral active vitamin D is associated with decreased risk of peritonitis and improved survival in patients on peritoneal dialysis. *PLoS One* 2013; 8: e67836. <https://doi.org/10.1371/journal.pone.0067836> PMID: 23844107
19. Taskapan H, Baysal O, Karahan D, et al. Vitamin D and muscle strength, functional ability and balance in peritoneal dialysis patients with vitamin D deficiency. *Clin Nephrol* 2011; 76: 110–116. <https://doi.org/10.5414/cn107160> PMID: 21762642
20. Lips P, Goldsmith D, de Jongh R. Vitamin D and osteoporosis in chronic kidney disease. *J Nephrol* 2017; 30: 671–675. <https://doi.org/10.1007/s40620-017-0430-x> PMID: 28940158
21. Nazzal Z, Khader S, Zawyani H, et al. Bone mineral density in Palestinian patients with end-stage renal disease and the related clinical and biochemical factors: Cross-sectional study. *PLoS One* 2020; 15: e0241201. <https://doi.org/10.1371/journal.pone.0241201> PMID: 33180791
22. Ersoy FF, Passadakis SP, Tam P, et al. Bone mineral density and its correlation with clinical and laboratory factors in chronic peritoneal dialysis patients. *J Bone Miner Metab* 2006; 24: 79–86. <https://doi.org/10.1007/s00774-005-0650-3> PMID: 16369903
23. Lin Y-L, Lai Y-H, Wang C-H, et al. Triceps Skinfold Thickness Is Associated With Lumbar Bone Mineral Density in Peritoneal Dialysis Patients. *Ther Apher Dial Off peer-reviewed J Int Soc Apher Japanese Soc Apher Japanese Soc Dial Ther* 2017; 21: 102–107. <https://doi.org/10.1111/1744-9987.12482> PMID: 27787966
24. Frailty Davenport A., appendicular lean mass, osteoporosis and osteosarcopenia in peritoneal dialysis patients. *J Nephrol* 2022; 35: 2333–2340.
25. Pongchaiyakul C, Pongskul C, Ruengjui S, et al. Bone mineral density among patients undergoing continuous ambulatory peritoneal dialysis (CAPD). *J Med Assoc Thai* 2005; 88 Suppl 5: S40–5. PMID: 16869106
26. Grzegorzewska AE, Mlot-Michalska M. Bone mineral density, its predictors, and outcomes in peritoneal dialysis patients. *Adv Perit Dial* 2011; 27: 140–145. PMID: 22073846
27. Kanis JA, Cooper C, Rizzoli R, et al. European guidance for the diagnosis and management of osteoporosis in postmenopausal women. *Osteoporos Int a J Establ as result Coop between Eur Found Osteoporos Natl Osteoporos Found USA* 2019; 30: 3–44.
28. Whitlock RH, Leslie WD, Shaw J, et al. The Fracture Risk Assessment Tool (FRAX®) predicts fracture risk in patients with chronic kidney disease. *Kidney Int* 2019; 95: 447–454.
29. Levey AS, Eckardt KU, Tsukamoto Y, et al. Definition and classification of chronic kidney disease: A position statement from Kidney Disease: Improving Global Outcomes (KDIGO). *Kidney Int* 2005; 67: 2089–2100.
30. Negri AL, Barone R, Quiroga MA, et al. Bone mineral density: serum markers of bone turnover and their relationships in peritoneal dialysis. *Perit Dial Int J Int Soc Perit Dial* 2004; 24: 163–168. PMID: 15119637
31. Jørgensen HS, Borghs H, Heye S, et al. Vascular calcification of the abdominal aorta has minimal impact on lumbar spine bone density in patients with chronic kidney disease. *Bone* 2022; 162: 116482. <https://doi.org/10.1016/j.bone.2022.116482> PMID: 35787485
32. Adragao T, Herberth J, Monier-Faugere M-C, et al. Femoral bone mineral density reflects histologically determined cortical bone volume in hemodialysis patients. *Osteoporos Int a J Establ as result Coop*

- between Eur Found Osteoporos Natl Osteoporos Found USA 2010; 21: 619–625. <https://doi.org/10.1007/s00198-009-0988-9> PMID: 19554246
33. Yap N, Wong P, McGinn S, et al. Femoral Neck X-Ray Absorptiometry Parameters and Peripheral Quantitative Computer Tomography Tibial Cortical Density Predict Survival in Dialysis Patients. *Nephron* 2017; 136: 183–192. <https://doi.org/10.1159/000460262> PMID: 28319943
 34. Disthabanchong S, Jongjirasiri S, Adirekkit S, et al. Low hip bone mineral density predicts mortality in maintenance hemodialysis patients: a five-year follow-up study. *Blood Purif* 2014; 37: 33–38. <https://doi.org/10.1159/000357639> PMID: 24503711
 35. Ishtawi S, Jomaa D, Nizar A, et al. Vitamin D level, pain severity and quality of life among hemodialysis patients: a cross-sectional study. *Sci Rep* 2023; 13: 1182. <https://doi.org/10.1038/s41598-022-25793-z> PMID: 36681707
 36. Hussain I, Tandir R, Singh G, et al. Correlation of FGF-23 With Biochemical Markers and Bone Density in Chronic Kidney Disease-Bone Mineral Density Disorder. *Cureus* 2023; 15: 1–11. <https://doi.org/10.7759/cureus.33879> PMID: 36812096
 37. Lambert BS, Oliver JM, Katts GR, et al. DEXA or BMI: clinical considerations for evaluating obesity in collegiate division I-A American football athletes. *Clin J Sport Med Off J Can Acad Sport Med* 2012; 22: 436–438.
 38. Mounach A, Mouinga Abayi DA, Ghazi M, et al. Discordance Between Hip and Spine Bone Mineral Density Measurement Using DXA: Prevalence and Risk Factors. *Semin Arthritis Rheum* 2009; 38: 467–471. <https://doi.org/10.1016/j.semarthrit.2008.04.001> PMID: 18571696
 39. Nybo M, Jespersen B, Aarup M, et al. Determinants of bone mineral density in patients on haemodialysis or peritoneal dialysis—a cross-sectional, longitudinal study. *Biochem medica* 2013; 23: 342–350. <https://doi.org/10.11613/bm.2013.042> PMID: 24266305
 40. Park JC, Kovessy CP, Duong U, et al. Association of serum alkaline phosphatase and bone mineral density in maintenance hemodialysis patients. *Hemodial Int* 2010; 14: 182–192. <https://doi.org/10.1111/j.1542-4758.2009.00430.x> PMID: 20345388
 41. Iseri K, Qureshi AR, Dai L, et al. Bone mineral density at different sites and 5 years mortality in end-stage renal disease patients: A cohort study. *Bone* 2020; 130: 115075. <https://doi.org/10.1016/j.bone.2019.115075> PMID: 31669253