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ORIGINAL ARTICLE

Impact of Hemodialysis Duration and Clinical Factors on Bone Mineral Density

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ABSTRACT

Background: *Patients with end-stage renal disease (ESRD) on maintenance hemodialysis face increased risk of bone mineral density loss due to disrupted mineral metabolism and chronic inflammation. Identifying key determinants of low BMD is crucial for effective prevention and management.* ***Aim of the study:*** *To evaluate the impact of hemodialysis duration and associated clinical factors on bone mineral density at different anatomical sites in patients with end-stage renal disease (ESRD).* ***Methods & Materials:*** *This cross-sectional study included 60 hemodialysis patients. BMD and T-scores at the spine, hip, and forearm were measured using DEXA. Clinical, biochemical, and inflammatory factors were analyzed using correlation and regression to identify predictors of low BMD.* ***Result:*** *The mean age was 52.4 ± 10.3 years, with a mean dialysis duration of 48.6 ± 22.8 months. BMD was lower in patients with longer dialysis duration, with correlations of −0.412 (spine), −0.389 (hip), and −0.498 (forearm) ($p < 0.01$). Male gender and absence of diabetes were linked to higher BMD ($p < 0.05$). Elevated phosphate and PTH, and reduced vitamin D correlated with lower BMD ($p < 0.05$). Regression identified dialysis duration ($\beta = -0.362$, $p = 0.003$), PTH ($\beta = -0.298$, $p = 0.007$), phosphate ($\beta = -0.251$, $p = 0.016$), and CRP ($\beta = -0.209$, $p = 0.030$) as key predictors.* ***Conclusion:*** *Our findings indicate that longer dialysis duration, high PTH, phosphate, and inflammation predict low BMD in ESRD patients, highlighting the need for early bone health management.*

Keywords: *Bone mineral density, hemodialysis duration, serum phosphate, parathyroid hormone*

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INTRODUCTION

Chronic kidney disease (CKD) is a global public health issue affecting over 10% of the population, and its progression to end-stage renal disease (ESRD) necessitates renal replacement therapy, most commonly hemodialysis (HD).[1] A significant complication of CKD is the disruption of bone and mineral metabolism, leading to conditions such as renal osteodystrophy and increased fracture risk.[2] Patients undergoing hemodialysis are particularly susceptible to alterations in bone mineral density (BMD), which can result in substantial morbidity and mortality.[3] Understanding the impact of hemodialysis duration and associated clinical factors on BMD is crucial for developing effective management strategies. Renal osteodystrophy encompasses a spectrum of bone disorders resulting from CKD-related mineral metabolism abnormalities. [4] These disorders are characterized by alterations in bone turnover, mineralization, volume, and strength, collectively referred to as CKD–mineral and bone disorder (CKD–MBD). [5] The pathogenesis of CKD–MBD involves complex interactions between disrupted calcium and phosphorus homeostasis, secondary hyperparathyroidism, and deficiencies in active vitamin D synthesis. These disturbances contribute to decreased BMD and an elevated risk of fractures among CKD patients. [6] Hemodialysis, a life-sustaining therapy for ESRD, plays a pivotal role in managing CKD–MBD, with its duration implicated in influencing BMD. Prolonged hemodialysis may exacerbate bone loss due to factors such as chronic inflammation, acidosis, and the accumulation of uremic toxins. [7] Conversely, some studies suggest that extended dialysis

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duration could stabilize or even improve BMD by enhancing the removal of phosphate and mitigating secondary hyperparathyroidism. The complex relationship between hemodialysis duration and BMD warrants further investigation, as several clinical factors, including secondary hyperparathyroidism from impaired phosphate excretion and hypocalcemia, contribute to increased bone resorption and decreased BMD.[8] Vitamin D deficiency, prevalent in CKD patients, exacerbates bone demineralization by impairing calcium absorption and promoting PTH secretion, while metabolic acidosis in ESRD stimulates bone buffering mechanisms, leading to mineral loss.[9] Inflammatory cytokines and oxidative stress from uremia contribute to bone remodeling disturbances, while nutritional status and body composition, including malnutrition and low BMI, are critical determinants of BMD and fracture risk in hemodialysis patients.[10] Conversely, obesity may protect BMD due to higher mechanical loading and increased estrogen production, though the relationship between BMI and BMD is not linear, as excessive adiposity can negatively affect bone quality, making it essential to maintain optimal nutritional status for bone health in this population.[11] Pharmacological interventions, including phosphate binders, active vitamin D analogs, and calcimimetics, are essential for managing CKD–MBD by correcting mineral imbalances, suppressing PTH secretion, and mitigating bone turnover abnormalities.[12] However, their effects on BMD are variable, and potential adverse effects, such as vascular calcification, must be carefully considered.[13] Individualized treatment strategies, guided by regular monitoring of biochemical parameters and bone density assessments, are recommended to optimize outcomes.[14] This study aims to evaluate the impact of hemodialysis duration and clinical factors on bone mineral density.

METHODS & MATERIALS

This cross-sectional observational study was conducted at the Department of Nephrology, Dhaka Medical College and Hospital, Dhaka, from October 2020 to September 2021. Ethical approval was obtained from the Research Review Committee (RRC) of the Department of Nephrology, followed by approval from the Ethical Review Committee (ERC) of Dhaka Medical College, Dhaka. A total of 60 adult ESRD patients undergoing maintenance hemodialysis for at least six months were recruited based on predefined inclusion and exclusion criteria. Purposive sampling was employed to select participants who met the criteria.

Inclusion Criteria

- ESRD patients aged ≥18 years undergoing maintenance hemodialysis for at least six months.
- Stable hemodialysis patients with no recent fractures or acute illness.

Exclusion Criteria

- ESRD patients with a history of chronic corticosteroid use, malignancy, or metabolic bone diseases other than renal osteodystrophy.
- ESRD patients with severe hepatic disease, recent fractures (within 6 months), or pregnancy.

Data Collection and Laboratory Analysis

Demographic and clinical data—including age, sex, body mass index (BMI), hemodialysis duration, and comorbidities (diabetes and hypertension)—were collected from patient records and interviews because of their known influence on bone health in hemodialysis patients. Bone mineral density (BMD) was assessed using Hologic Discovery Dual-Energy X-ray Absorptiometry (DEXA). Patients were advised to avoid calcium supplements 24 hours before the test and to remove jewelry and other metallic items on the day of the exam to prevent interference with the X-ray. During the procedure, which lasted 15 to 30 minutes, patients lay fully clothed on a padded platform while a low-dose X-ray beam scanned the bones. The DEXA system's software computed BMD, expressed in grams per square centimeter (g/cm^2) and as T-scores (comparing patients' values to those of a young, healthy reference population). Height and weight were measured using a stadiometer and a calibrated weight scale, respectively. Fasting blood samples were drawn prior to scheduled dialysis sessions to analyze biochemical markers pertinent to bone metabolism. These included serum calcium (8.5–10.2 mg/dL), phosphate (2.5–4.5 mg/dL), intact parathyroid hormone (iPTH; 10–65 pg/mL), 25-hydroxyvitamin D (with sufficiency defined as ≥30 ng/mL), serum albumin, and C-reactive protein (CRP). All assays were performed using standardized enzymatic and immunoassay techniques in a certified laboratory to ensure accuracy and reproducibility.

Statistical Analysis

Data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 26. Continuous variables were expressed as mean ± standard deviation (SD), and categorical variables as frequencies and percentages. Pearson's correlation coefficients were computed to assess associations between duration of hemodialysis, laboratory parameters, and BMD at different sites. A multivariate linear regression model was constructed to identify independent predictors of BMD, adjusting for potential confounders. Statistical significance was determined with a p-value threshold of <0.05.

RESULT

A total of 60 ESRD patients undergoing maintenance hemodialysis were included in this study. The mean age was 52.4 ± 10.3 years, with 53.33% of participants under 60 years. The cohort comprised 35 males (58.33%) and 25 females (41.67%). The average body mass index (BMI) was 24.8 ± 4.2 kg/m^2, and the mean duration of hemodialysis was 48.6 ± 22.8 months. Common comorbidities included hypertension (50.00%) and diabetes mellitus (36.67%) (Table I). Table 2 represented that the mean BMD at the lumbar spine was 0.92±0.18 g/cm^2 with a T-score of -1.95±1.14. Osteoporosis was observed in 16.67% of patients, osteopenia in 36.67%, and normal BMD in 46.67%. At the left hip, the mean BMD was 0.87±0.15 g/cm^2, and similar patterns of osteoporosis (16.67%), osteopenia (36.67%), and normal BMD (46.67%) were found. The left forearm showed the lowest mean BMD of 0.74±0.16 g/cm^2 and the highest prevalence of osteoporosis

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(60%) (Table II). Significant negative correlations were observed between hemodialysis duration and BMD at the lumbar spine (r = -0.412, p = 0.003), left hip (r = -0.389, p = 0.007), and left forearm (r = -0.498, p < 0.001) (Table III). Table IV showed that males exhibited the highest BMD values across all measurement sites, with a mean BMD of 0.94±0.17 g/cm^2 at the lumbar spine, 0.89±0.14 g/cm^2 at the left hip, and 0.76±0.18 g/cm^2 at the left forearm, significantly higher than females (p =0.037). Parathyroid hormone exhibited the strongest negative correlation with BMD across all sites, with the highest correlation magnitude at the left hip (r = -0.438, p = 0.002), followed by the forearm (r = -0.415, p = 0.003) and lumbar spine (r = -0.402, p = 0.004). Serum phosphate also showed significant negative correlations, with the strongest association at the left forearm (r = -0.312, p = 0.015). In contrast, vitamin D demonstrated the highest positive correlation with BMD at the lumbar spine (r = 0.378, p = 0.007), followed by the left hip (r = 0.341, p = 0.012) and left forearm (r = 0.332, p = 0.018) (Table V). Multivariate regression analysis identified hemodialysis duration as the strongest predictor of lower BMD, with a beta coefficient of -0.362 (p = 0.003) and a 95% confidence interval of (-0.21, -0.05) (Table VI).

Table – I: Baseline Characteristics of Study populations (*n*=60)

Variables	Number (n)	Percentage (%)
Age in years		
<60	32	53.33
≥60	28	46.67
Mean± SD	52.4 ± 10.3	
Gender		
Male	35	58.33
Female	25	41.67
BMI (kg/m^2)		
Mean± SD	24.8 ± 4.2	
Duration of Dialysis (months)		
Mean± SD	48.6 ± 22.8	
Comorbidities		
Diabetes Mellitus	22	36.67
Hypertension	30	50.00

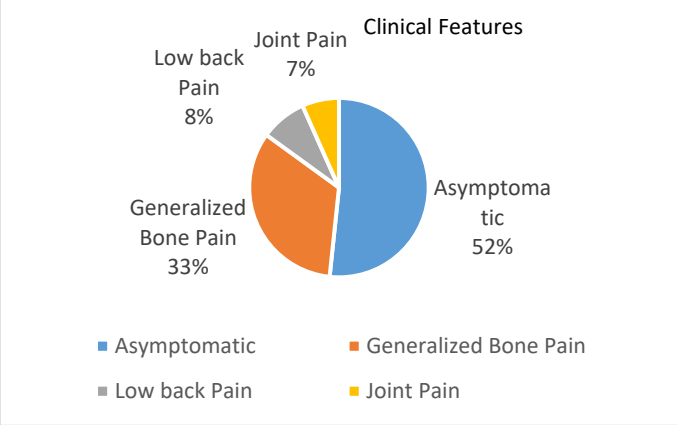

Figure – 1: clinical features of bone disease among study populations

Table – II: Bone Mineral Density (BMD) and T-scores at Different Sites

Measurement Site	BMD (g/cm^2) (Mean ± SD)	T-score (Mean ± SD)	Osteoporosis		Osteopenia		Normal	
			n	%	n	%	n	%
Lumbar Spine	0.92 ± 0.18	-1.95 ± 1.14	10	16.67	22	36.67	28	46.67
Left Hip	0.87 ± 0.15	-1.68 ± 1.07	10	16.67	22	36.67	28	46.67
Left Forearm	0.74 ± 0.16	-2.30 ± 1.20	36	60.00	16	26.67	8	13.33

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Table – III: Correlation Between Hemodialysis Duration and BMD

Measurement Site	Pearson's Correlation Coefficient (r)	p-value
Lumbar Spine BMD	-0.412	0.003**
Left Hip BMD	-0.389	0.007**
Left Forearm BMD	-0.498	<0.001**

Table – IV: Association of Clinical Factors with Bone Mineral Density

Factor	Lumbar Spine BMD (Mean ± SD)	p-value	Left Hip BMD (Mean ± SD)	p-value	Left Forearm BMD (Mean ± SD)	p-value
Gender						
Male	0.94 ± 0.17	0.042*	0.89 ± 0.14	0.028*	0.76 ± 0.18	0.037*
Female	0.89 ± 0.18		0.84 ± 0.15		0.70 ± 0.15	
Diabetes Mellitus						
Present	0.88 ± 0.19	0.015*	0.83 ± 0.14	0.012*	0.72 ± 0.17	0.022*
Absent	0.95 ± 0.17		0.90 ± 0.15		0.76 ± 0.16	
Hypertension						
Present	0.90 ± 0.18	0.064	0.86 ± 0.15	0.075	0.74 ± 0.16	0.095
Absent	0.94 ± 0.17		0.88 ± 0.14		0.76 ± 0.15	

Table – V: Laboratory markers and their association with bone mineral density

Laboratory Parameter	Mean ± SD	Correlation with Lumbar Spine BMD		Correlation with Left Hip BMD		Correlation with Left Forearm BMD	
		r	p	r	p	r	p
Serum Calcium (mg/dL)	8.9 ± 0.7	0.112	0.386	0.135	0.314	0.123	0.356
Serum Phosphate (mg/dL)	5.2 ± 1.1	-0.271	0.032*	-0.295	0.021*	-0.312	0.015*
Parathyroid Hormone (pg/mL)	185.4 ± 78.9	-0.402	0.004**	-0.438	0.002**	-0.415	0.003**
Vitamin D (ng/mL)	22.3 ± 8.6	0.378	0.007**	0.341	0.012*	0.332	0.018*
Serum Albumin (g/dL)	3.8 ± 0.5	0.112	0.312	0.098	0.329	0.115	0.303
C-Reactive Protein (mg/L)	5.7 ± 3.1	-0.26	0.027*	-0.238	0.042*	-0.275	0.018*

Table – VI: Multivariate regression analysis predicting low bone mineral density

Predictor Variable	Beta Coefficient (β)	p-value	95% Confidence Interval
Duration of Hemodialysis	-0.362	0.003**	(-0.21, -0.05)
Parathyroid Hormone Levels	-0.298	0.007**	(-0.15, -0.03)
Serum Phosphate	-0.251	0.016*	(-0.09, -0.01)
Vitamin D Levels	0.21	0.024*	(0.02, 0.18)
Serum Albumin	0.148	0.081 (ns)	(-0.02, 0.31)
C-Reactive Protein	-0.209	0.030*	(-0.38, -0.02)

DISCUSSION

Bone mineral density (BMD) is a critical indicator of bone health, reflecting the strength and density of bones [15]. In patients undergoing hemodialysis, BMD is often compromised due to factors such as mineral metabolism disturbances, hormonal imbalances, and the effects of dialysis itself [16]. These alterations can lead to conditions like osteopenia and osteoporosis, increasing the risk of fractures and adversely affecting the quality of life [17]. The duration of hemodialysis has been identified as a significant factor influencing BMD, with longer dialysis periods associated with greater bone demineralization [18]. Additionally, clinical factors such as serum phosphate levels, parathyroid hormone (PTH) concentrations, and vitamin D status play pivotal roles in modulating bone health in this population [19]. Understanding the interplay between hemodialysis duration and these clinical factors is essential for developing effective strategies to preserve bone health in individuals with end-stage renal disease. In our study, we aimed to investigate the impact of hemodialysis duration and clinical factors on bone mineral density (BMD) in patients with end-stage renal disease (ESRD). The results from our study show significant associations between hemodialysis duration, clinical factors such as gender, diabetes, and hypertension, as well as laboratory markers including serum phosphate, parathyroid hormone (PTH), and vitamin D levels, with BMD at various sites. One of the major findings in the present study is the negative correlation between the duration of hemodialysis and BMD at the lumbar spine, left hip, and left forearm. Specifically, the Pearson's correlation coefficients ranged from -0.389 to -0.498 ($p < 0.01$), highlighting that longer hemodialysis duration is associated with lower BMD at these

sites. These findings align with previous studies which suggest that prolonged dialysis contributes to bone loss in ESRD patients, possibly through the dysregulation of calcium-phosphate balance and secondary hyperparathyroidism [20-21]. In fact, multivariate regression analysis in our study revealed that hemodialysis duration is a significant predictor of low BMD (β = -0.362, p = 0.003), supporting the evidence that prolonged dialysis duration may exacerbate bone demineralization. A similar study by Nazzal et al. (2020) also reported that a longer duration of dialysis is associated with reduced bone mineral density (BMD) ($p<0.05$) [19]. These findings are consistent with prior research from Japan, which reported that extended dialysis treatment is strongly correlated with hyperparathyroidism and generalized bone loss [22]. In addition, our study observed that gender significantly affected BMD, with males having higher BMD values compared to females at the lumbar spine, left hip, and left forearm. This result is consistent with previous reports which highlight that postmenopausal woman, who are typically at higher risk for osteoporosis, experience more severe bone loss compared to men undergoing hemodialysis [23]. Moreover, diabetes mellitus was found to be associated with lower BMD in our study, particularly in the lumbar spine and left hip ($p < 0.05$). This is consistent with the findings of a meta-analysis by Slouma et al. (2020), which concluded that diabetes is a risk factor for reduced bone density, potentially due to the effects of hyperglycemia and insulin resistance on bone metabolism [15]. Interestingly, while hypertension was common among our study population, it did not show a statistically significant association with BMD at the measured sites. This finding contrasts with some studies that suggest an inverse relationship between hypertension and bone density, possibly due to the effects of antihypertensive medications like thiazide diuretics on calcium metabolism [24]. However, the lack of significance in our cohort may be due to the high prevalence of other factors, such as diabetes, that may mask the potential effect of hypertension on bone density. Further, laboratory markers such as serum phosphate, parathyroid hormone (PTH), and vitamin D were found to be significantly correlated with BMD. In our study, serum phosphate levels showed a negative correlation with BMD at all three sites ($p < 0.05$), suggesting that hyperphosphatemia, which is common in ESRD patients, contributes to bone mineral loss [25]. Similarly, elevated PTH levels were associated with decreased BMD ($p < 0.01$), which aligns with the well-established role of secondary hyperparathyroidism in bone resorption in dialysis patients [25]. On the other hand, higher vitamin D levels were positively correlated with BMD ($p < 0.05$), reinforcing the importance of vitamin D in maintaining bone health in ESRD patients, as suggested by previous studies [26]. Notably, our study identified C-reactive protein (CRP) as a significant negative predictor of BMD (β = -0.209, p = 0.030). This finding suggests that inflammation may contribute to bone loss in dialysis patients, as chronic inflammation is known to impair bone remodeling and increase the risk of fractures [27]. Thus, controlling inflammation in ESRD patients could be an important strategy to prevent further bone demineralization.

LIMITATIONS OF THE STUDY

Despite the significant findings, several limitations of the present study must be acknowledged. Firstly, the cross-sectional design of the study limits our ability to infer causal relationships between hemodialysis duration, clinical factors, and bone mineral density. Longitudinal studies are needed to confirm the temporal effects of these variables on bone health. Additionally, the relatively small sample size of 60 patients may limit the generalizability of the results. Furthermore, factors such as medications, diet, and physical activity, which can also affect bone health, were not systematically controlled for in this study.

CONCLUSION AND RECOMMENDATIONS

In our study, we have demonstrated that both hemodialysis duration and clinical factors significantly influence bone mineral density (BMD) in patients with end-stage renal disease (ESRD). Specifically, prolonged hemodialysis duration was associated with reduced BMD at multiple sites, highlighting the need for ongoing monitoring of bone health in these patients. Moreover, clinical factors such as gender, diabetes, and laboratory markers, including serum phosphate, parathyroid hormone (PTH), and vitamin D levels, also emerged as important contributors to bone demineralization. These findings emphasize the importance of early identification of high-risk patients and suggest that targeted interventions aimed at regulating phosphate levels, optimizing vitamin D status, and controlling inflammation could help prevent further bone loss in ESRD patients. Future research should explore the potential benefits of specific therapeutic strategies to mitigate bone mineral density decline in this vulnerable population.

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