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Original Research Article

Risk Factors for Osteoporosis in Chronic Hemodialysis Patients

Majdouline Errihani[1*], Aya Sobhi[1], Kawtar Hassani[1], Sanaa Benbria[1], Driss ElKabbaj[2]

[1,2]Department of Nephrology Hemodialysis and Renal Transplantation, Mohammed V Military Hospital, Faculty of Medicine and Pharmacy University Mohammed V-Souissi, Rabat, Morocco

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***Corresponding Author:** Majdouline Errihani
Department of Nephrology Hemodialysis and Renal Transplantation, Mohammed V Military Hospital, Faculty of Medicine and Pharmacy University Mohammed V-Souissi, Rabat, Morocco

Abstract

Introduction: in hemodialysis patients. Osteoporosis associated with kidney disease chronic is a complex entity with significant morbidity and mortality relative to risk of fracture. Its prevalence is high, but the incrimination of clinical and biological factors remains poorly identified. The purpose of our study is to determine the prevalence and factors associated with osteoporosis. ***Methods:*** A cross-sectional study included 40 chronic hemodialysis patients for at least 6 months. All subjects underwent a bone mineral density (BMD) assay with dual-energy x-rays absorptiometry (DXA) at the lumbar spine (LS) and femoral neck (FN). Data were statistically analyzed by means of descriptive analysis. Patients were divided into 2 groups based on the T-score to define the osteoporotic (t score≤-2.5) and the no-osteoporotic (t score>-2.5). The search for the risk factors studied [age, duration of hemodialysis, parathyroid hormone (PTH), alkaline phosphatases (ALP), and calcification of the abdominal aorta (AAC)] has been carried out by logistic regression. ***Results:*** The average age was 59 ± 16 years, 47% were women, and the median of hemodialysis duration was 54 months. The prevalence of osteoporosis at the lumbar spine was 27.5% and at the femoral neck was 32.5%. Regarding risk factors, at the LS, the factors associated with osteoporosis retained in the univariate analysis were age (p=0.034), PTH (p=0.024), AAC (p=0.024), ALP (p=0.027) and in the multivariate analysis, only PTH was significantly associated (p=0.019). At the FN; The factors associated with osteoporosis retained in analysis univariate were age (p = 0.03), AAC (p = 0.01), ALP (p=0.04) and in analysis multivariate was the APL (p= 0.035). ***Conclusion:*** Osteoporosis is associated with turnover abnormalities. We suggest that regular screening for fracture risk using DXA and early correction of the disorders.

Keywords: Osteoporosis, DXA, Hemodialysis.

INTRODUCTION

The chronic kidney disease–mineral bone disorder (CKD-MBD) captures a broader systemic disorder, including both bone and vascular disease, within which osteoporosis resides as one of the bone components of the CKD-MBD [1].

Osteoporosis is a disease that is characterized by poor bone quality and low bone mineral density (BMD) and strength leading to risk of fractures. The World Health Organization defines osteoporosis based on a decreased BMD T score ≤ −2.5[2].

Large systematic reviews document that persons with advanced chronic kidney disease are fold increased risk of osteoporosis and fractures compared with the general population [3].

The overall relative risk for hip fracture was 4.4 for dialysis patients compared with general population [4].

It's important to periodically evaluate the BMD in these patients. Although the diagnosis of osteoporosis in this population can be difficult, imaging, especially with DXA, is the most recommended method because of its high precision and accuracy [5] in addition to other important risk factors. Although blood biomarkers including parathyroid hormone and Bone-specific alkaline phosphatases concentrations can aid in assessing bone turnover state, bone biopsy remains the gold standard in determining bone turnover in persons with advanced kidney disease and osteoporosis [6].

This study aims to investigate the status of BMD among hemodialysis patients and to explore the associated factors related to loss of bone mass.

METHODS

This is a transverse monocentric descriptive and analytical screening study, carried out over a period of 30 days from January 2024 to February 2024 at the Department of Nephrology Dialysis and kidney Transplantation at Mohammed V Military Teaching Hospital, including the 40 chronic hemodialysis patients in the hemodialysis unit who benefited from a bone mineral density assay with dual-energy x-ray absorptiometry.

the Inclusion criteria were: Age ≥ 18 years and duration of dialysis ≥ 6 months without liver damage.

Exclusion criteria: taking corticosteroids, fracture of the lumbar spine or hip, inability to perform the radiological examination and patient's refusal.

Clinical, biological and therapeutic data were collected, based on the review of medical records and dialysis data as well as on the history in order to complete a digitized Information Sheet.

Clinical and biological and radiological data

The clinical data collected were: age; gender; primary cause of end-stage renal disease (ESRD); duration of dialysis; physical activity; cardiovascular risk factors: diabetes, hypertension, smoking; Also, a balance sheet including the determination of calcemia, phosphoremia, alkaline phosphatases, intact parathormone 1-84, albumin and 25 OH vitamin D.

Biochemistry data was collected the same month as BMD measurement.

The existence of vascular calcifications was assessed by the abdominal profile radiography.

Therapeutic modalities

Our patients were dialyzed three times a week at a rate of 4 hours per session. The dialysate bath contained 3 mmol/l potassium and 1.50 mmol/l calcium. High-permeability polysulfone membranes were used in all patients.

Regarding oral treatment, the phosphate binders calcium carbonate and vitamin D and calcimimetics were given to the patients to maintain phosphocalcic balances.

Bone mineral density assay with dual-energy x-ray

All subjects underwent DXA assays at the LS and FN BMD by the same technologist.

Based on the World Health Organization definition [2], patients were divided into 2 groups based on the BMD T-score to define osteoporotic (t score≤-2.5) and no osteoporotic (t score > -2.5).

Statistical analysis:

First, we performed a descriptive analysis using means and medians for quantitative variables and frequencies for qualitative variables. In a second step, the patients were divided into 2 groups according to: osteoporotic (T score≤-2.5) and no osteoporotic (ScK> -2.5). The search for the risk factors studied [age, duration of hemodialysis, parathyroid hormone (PTH), alkaline phosphatases (ALP), calcification of the abdominal aorta (AAC)] and osteoporosis has been carried out by logistic regression

The factors correlated with low bone mass were estimated by regression models: Initially, analysis by univariate logistic regression was carried out to independently obtain a crude association between risk factors and osteoporosis. Then the variables that emerged as significant in the univariate analysis were inserted into the multivariate analysis model, which allowed us to define a model for predicting osteoporosis.

Statistical significance is defined as $p < 0.05$. All analyzes were performed with SPSS version 21 software.

RESULTS

The study involved 40 chronic hemodialysis patients, who had an average age of 59 ± 16 years, 47% were women, of whom 40% were post-menopausal or permanently amenorrheic. The median duration of hemodialysis was 59 [31,108] months, Diabetic nephropathy predominated in the etiologies of end-stage renal disease (35%).

65% of our patients were hypertensive, 17.5% were smoking. The average BMI was 25±5, AAC were observed in 57% of cases. The prevalence of osteoporosis at the lumbar spine was 27.5% and at the femoral neck was 32.5 % (Table 1).

At the lumbar spine, the univariate analysis showed that osteoporosis was significantly associated with age ($p = 0.034$), PTH ($p = 0.024$), AAC ($p = 0.024$), and APL ($p = 0.027$), and there was no significant association between osteoporosis and duration of hemodialysis. In multivariate analysis, after adjustment for confounding factors, only PTH [OR = 1.003, 95% CI (1.001, 1.006), $p = 0.019$] was independently associated with severe AAC (Table 2).

At the femoral neck, the factors associated with osteoporosis retained in the analysis univariate were age ($p = 0.03$), AAC ($p = 0.01$), and PAL ($p = 0.04$). In multivariate analysis, after adjustment for confounding factors, only APL [OR = 1.062, 95% CI (1.002, 1.040), $p = 0.035$] was independently associated with osteoporosis (Table 3).

Table 1: Characteristics of the study population

Data	Results
Gender*	
Women	21 (52)
Man	19(48)
Age (years) **	59±16
Duration of dialysis (months) ***	54(31-108)
Initial nephropathy *	
diabetic nephropathy	14(35)
chronic interstitial tubulo nephropathy	8(20)
vascular nephropathy	6(15)
glomerular nephropathy	6(15)
indeterminate nephropathy	6(15)
Hypertension	35(65)
BMI*	25±5
Smoking*	6(15)
Physical activity*	22(54)
APL (UI /l) ***	120(89-167)
Ca (mg/l) **	87±11
Ph (mg/l)**	43±16
PTH (pg/ml)	700(50-1100)
Vit D (µg/l)**	31±14
C Reactive protein (mg/l)***	3.9 (2-7)
KT/V**	1.6±0,15
Tscore LS***	-1.31 (-3.70,2.50)
Tscore FN***	-1.61(-6.60,2.70)
AAC*	23(57)
Osteoporosis LS*	11(27.5)
Osteoporosis FN*	14(33)

***Expressed in staff (%); ** Expressed as Average ± Standard Deviation; *** Expressed in Median (quartiles)**

Table 2: Risk factors independent of Lumbar spine BMD

Associated factors		**Univariate**			**Multivariate**	
	OR brut	**CI 95%**	***p***	**OR adjusted**	**CI 95%**	***p***
Age (years)	1.061	(1,005; 1.120)	**0.034**	1.078	(0.977; 1.183)	0.173
Duration of dialysis (months)	1.002	(0,999; 1.020)	0.090	1.003		
APL (UI/l)	1,010	(1.001; 1.019)	**0.027**	1.001	(0.986; 1.010)	0,740
AAC	12	(1.380; 19.10)	**0.024**	1.048	(0.232; 1.207)	0.292
PTH(pg/l)	1.009	(1.001; 1.004)	**0.024**	1.003	1.001.1006	**0.019**

Table 3: Risk factors independent of femoral neck BMD

Associated factors		**Univariate**			**Multivariate**	
	OR brut	**CI 95%**	***p***	**OR adjusted**	**CI 95%**	***p***
Age (years)	1.116	(1,116; 1.038)	**0.03**	1.198	(0.969; 1.165)	0.198
Duration of dialysis (months)	1.010	(0,999; 1.021)	0.072			
APL (UI /l)	1.025	(1.008; 1.043)	**0.04**	1.062	(1.002; 1.040)	**0.035**
PTH (pg/l)	1.001	(1.000; 1.003)	0.132			
AAC	0.010	(1.974; 15.355)	0.356			

DISCUSSION

Osteoporosis is defined by the National Institutes of Health as a skeletal disorder characterized by compromised bone strength, predisposing a person to an increased risk of fracture. Bone strength is determined by bone quantity and bone quality.

Bone quantity can be assessed by BMD with DXA or by volumetric BMD of cortical and trabecular bone by quantitative computed tomography. Bone quality pertains to bone material properties and includes bone turnover, mineralization, microdamage, collagen properties, and cortical and trabecular microarchitecture.

CKD is associated with global impairments in bone strength; therefore, bone disease in patients with CKD may be classified as CKD-associated osteoporosis [7].

Cortical bone comprises around 80% of the skeleton and contributes largely to bone strength. Hyperparathyroidism, a kidney disease, leads to increased cortical porosity and decreased cortical thickness [8]. Cortical bone loss subsequently results in the loss of areal BMD. Trabecular bone also contributes to bone strength [9].

In patients with CKD, older age, hypogonadism, and medications used to treat kidney diseases (i.e., glucocorticoids and calcineurin inhibitors) may result in the loss of trabeculae. Mineralization defects (i.e., osteomalacia) are not uncommon in CKD, though widespread use of vitamin D analogues seems to have decreased the prevalence of mineralization defects in recent years. Bone quality in CKD is further impaired as advanced glycation products accumulate and weaken the collagen network, as damaged bone and microcracks are not adequately repaired, and as oxidative stress levels are heightened [9–10].

In health, bone remodeling is balanced between bone formation by osteoblasts and bone resorption by osteoclasts; mineralization of bone is also necessary to form mature bone. The metabolic derangements present in CKD alter both remodeling and mineralization and are increasingly recognized as occurring in early kidney disease when function is considered normal, even before the development of biochemical evidence of CKD-MBD [11–1].

Klotho deficiency occurs in CKD and is one of the first derangements of CKD-MBD [13]. Low expression of Klotho induces fibroblast growth factor (FGF23) resistance, resulting in increased FGF23 levels. Both FGF23 and Klotho are expressed in osteocytes with a complex inter-relationship; their effects on bone are both dependent and independent of each other [14-15]. The decline in Klotho and the rise in FGF23 is followed by a rise in PTH levels, a decline in vitamin D levels and abnormalities in calcium and phosphorus homeostasis. Moreover, metabolic acidosis alters the balance between resorption and formation. CKD is additionally accompanied by chronic inflammation that can be deleterious to bone health [16].

Together, these skeletal abnormalities result in an increased risk of fractures. This risk increases as the estimated glomerular filtration rate (eGFR) decreases and is associated with an eGFR <15 mL/min per 1.73 m2 [17-18]. Fractures in CKD patients are associated with increased economic burden related to hospitalizations, morbidity, and mortality [19].

chronic hemodialysis patients usually have accelerated bone loss that leads to a high prevalence of osteoporosis [20].

Our study found that the percentage of osteoporosis at the LS and FN, sites were 27%, and 33%, respectively. This trend is similar to previous reports [21-22]. Also our study revealed the FN as the region with the highest prevalence of osteoporosis than the LS. Previous studies demonstrated that the amount of bone loss in the FN is greater than that in the vertebra in ESRD patients. Most patients who have a low BMD value in the FN have a higher risk of femoral neck fracture. Thus the FN is the best site for BMD evaluation in dialysis patients [23].

Our study found that the percentage of osteoporosis at the LS and FN sites was 27% and 32.5%, respectively. This trend is similar to previous reports [21–22]. Also, our study revealed the FN as the region with the highest prevalence of osteoporosis compared to the LS. Previous studies demonstrated that the amount of bone loss in the femoral neck (FN) is greater than that in the vertebra in ESRD patients. Most patients who have a low BMD value in the FN have a higher risk of femoral neck fracture. Thus The FN is the best site for BMD evaluation in dialysis patients [23].

In our study, There was a no association between age and BMD at both sites at The multivariate analysis, It was compatible with other previous findings [21, 24-25].

Also, no association was found between the BMD and the duration of dialysis at these two sites, compatible with two other studies [26, 27]. a relationship between bone loss and duration of dialysis that could exist, but wasn't detected by our cross-sectional design may relate to the wide range of duration of dialysis, This also indicated that some other factors could not be determined by BMD measurement, such as architecture and bone turnover in different regions of the skeleton.

The management of osteoporosis in patients with advanced CKD or on dialysis fundamentally revolves around diagnosing and targeting abnormalities of mineralization and turnover with the goal of improving bone density, volume, and quality. Turnover is one of the most important elements of managing the CKD-MBD; both high and low bone turnover can lead to low bone mass and fracture risk [28].

However, our study found an association between markers of bone turnover such as APL, PTH and osteoporosis previous study showed that association [28-29].

The most commonly used bone turnover marker in the clinical setting is iPTH. However, although the iPTH concentrations were directly correlated with bone turnover across the study population, when a dialysis patient has an extremely high iPTH that exceeds the expected range, the specificity for high turnover bone disease is high [23, 24] However, it should be recognized that the specificity of iPTH for low bone turnover is considerably worse than that of high turnover [30 -31].

Alkaline phosphatases and bone-specific alkaline phosphatases are two biomarkers of bone formation that are not affected by GFR [25]. Low concentrations of APL are consistently associated with low bone turnover, depending on the assay and cut points, can be used to help determine the underlying turnover state [32].

In our series, the ACC is not identified as a significant risk factor. but previous studies confirm that the presence of vascular calcification reduces BMD, alters mineral metabolism, and affects several signaling pathways in bone [33].

Targeting abnormalities in bone turnover is one of the most important elements of managing CKD-MBD; both high and low bone turnover can lead to low bone mass and fracture risk [6-32].

Strengths and limitations

Our study presents several points of strength in particular: the prospective nature of the study allowing a considerable reduction of information bias, as well as a representable sample allowing a statistical analysis of quality. However, it also has certain limitations: It was a single center. study with a small patient population, the presence of other potential confounding factors was not measured in our study and therefore not taken into account during the analysis.

CONCLUSION

CKD-associated osteoporosis is a complex disease that confers high morbidity and mortality to patients with kidney disease.

Our study has shown that osteoporosis is highly prevalent in hemodialysis patients. and associated with abnormalities in bone turnover.

Since bone loss is an asymptomatic process, early identification of small reductions in bone mass, It is very important to allow early intervention to prevent bone loss and decrease fracture risk.

In 2017, the Kidney Disease Improving Global Outcomes Committee on Bone Quality updated their guidelines to include screening for osteoporosis and fracture risk by DXA in patients with CKD.

Conflicts of Interest Statement: The authors declare that they have no interest link.

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