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Pathological Fractures in Chronic Hemodialysis Patients in a Teaching Hospital in Senegal: Prevalence and Associated Risk Factors

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Abstract

Introduction: The lack of follow-up and adequate management of chronic kidney disease-mineral and bone disorder (CKD-MBD) in chronic hemodialysis patients is associated with pathological fractures. Few studies are available on the subject in sub-Saharan Africa. The objective of this work was to evaluate the prevalence of pathological fractures in our chronic hemodialysis patients, to analyze their clinical aspects and to determine the factors associated with their occurrence. **Patients and Methods:** We conducted a retrospective, descriptive and analytical study over 9 years (January 1, 2011, to December 31, 2020) based on the medical records of chronic hemodialysis patients at the CHU Aristide Le Dantec. The diagnosis of pathological fracture was retained in front of any fracture occurring spontaneously or following minimal trauma and confirmed by X-ray. **Results:** Nineteen cases of pathological fractures were collected with a hospital prevalence of 19.39%. The mean age was 53.32 ± 13.94 years with a sex ratio of 0.36. The average seniority in dialysis was 84.16 ± 29.88 months. Among these patients, one had had 3 episodes of fractures and another 6 episodes. The circumstances of occurrence of the fractures were the fall in 63% of the cases, spontaneously in 37% of the cases. The predominant site of fractures was the femoral neck (47.38% cases). Female gender ($p < 0.045$), seniority in hemodialysis > 5 years ($p = 0.049$), gait disturbances prior to the fracture ($p = 0.001$), positive CRP ($p = 0.028$) and the presence of vascular calcifications ($p = 0.002$) were significantly associated with the occurrence of pathological fractures. **Conclusion:** This study has identified the factors associated with the occurrence of pathological invoices in hemodialysis patients in our context. These fractures are often associated with the lack of regular biological follow-up due to the low

socioeconomic level of our patients.

Keywords

Pathological Fractures, CKD-MBD, Hyperparathyroidism, Osteomalacia, Adynamic Bone Disease, Chronic Hemodialysis

1. Introduction

Disturbances in bone-mineral metabolism occur early in chronic kidney disease (CKD). They have been grouped since the Kidney Disease Improving Global Outcome (KDIGO) conference published in 2006 [1] under the term Chronic Kidney-Disease Mineral and Bone Disorder (CKD-MBD). The latter describes all disorders of the metabolism of calcium, phosphorus, intact parathyroid hormone (PTHi) or vitamin D, anomalies of turnover, mineralization, and bone volume and extraskeletal calcifications (vascular and soft tissue). These metabolic changes are associated with increased mortality and morbidity, including fracture risk [2] [3].

A pathological fracture is defined as any fracture occurring spontaneously or following minimal trauma [4] [5]. In the analysis of the Dialysis Outcomes and Practice Patterns Study (DOPPS) in 2014, the incidence of hip fracture was 4 times higher in hemodialysis patients than in the general population [6]. Its prevalence in the world is variously appreciated. Brunerov *et al.* found a prevalence of 11.9% [7]. In Africa, a Moroccan study by Lazrak *et al.* found a prevalence of 12.5% [8]. Several risk factors have been identified as associated with the increased risk of pathologic fracture in chronic hemodialysis (CHD) patients, including older age, female gender, low Mody Mass Index (BMI), duration of dialysis, opioid treatment, and hypophosphatemia [4] [7] [8].

In Senegal, in our practice context, most of our patients do not have a healthcare coverage to ensure adequate monitoring of complications that may occur in dialysis, in particular CKD-MBD. This partly explains the frequency of pathological fractures observed in our patients, as evidenced by a previous study which found a frequency of 7.27% [9].

The objective of this study was to evaluate the prevalence of pathological fractures in our chronic hemodialysis patients, to analyze their clinical aspects and to determine the factors associated with their occurrence.

2. Patients and Methods

This is a monocentric, retrospective, descriptive and analytical study over a period of 9 years from January 1, 2011, to December 31, 2020, in the two hemodialysis units of the nephrology department at the Aristide Le Dantec University Hospital. We included patients on chronic hemodialysis for at least 3 months and having had at least one pathological fracture confirmed by imaging. Not in-

cluded were chronic hemodialysis patients who developed a fracture following non-minimal trauma. The selection of patients was made from the register and the medical records of patients.

For each patient, we collected the following data from hemodialysis notebooks and medical records:

- Epidemiological: age, sex, occupation, and socioeconomic level.
- Comorbidities and history: length of time on dialysis, age at start of dialysis, causal nephropathy, comorbidity, medication intake, history of aluminum toxicity and kidney transplantation, CKD-MBD and their types, parathyroidectomy and its complications.
- Dialysis parameters: duration and frequency of sessions, type of membrane, calcium concentration of the dialysate, type of vascular access and dose of dialysis.
- Clinical: circumstances in which the fracture occurred (minimal/spontaneous trauma), presence of pain, inflammatory swelling, functional impairment (absolute/relative), dry weight, body mass index and gait disturbances.
- Biological: calcemia, phosphatemia, albuminemia, proteinemia, intact parathyroid hormone (PTHi), 25(OH) vitamin D, CRP, hemoglobin level, ferritinemia, transferrin saturation coefficient and aluminum level.
- Radiological: standard radiography (seat and type of fracture, associated lesions), bone CT or MRI, cervical ultrasound and parathyroid scintigraphy, search for vascular calcification.
- Therapeutics: therapeutic abstention, orthopedic treatment or surgical treatment, and treatment of OMT (oral calcium, phosphate binders, native and/or active vitamin D and calcimimetics), parathyroidectomy (PTx).

A pathological fracture was defined as any fracture occurring spontaneously or following minimal trauma [4] [5].

The data collected was entered using Excel and then analyzed using SPSS (Statistical Package for Social Sciences) software. The variables are compared by the KHI 2 or Fischer test according to their applicability condition. Results were considered statistically significant when the p was less than 0.05.

Local ethics committee gave its approval for the study.

3. Results

Sociodemographic data:

During the study period, nineteen (19) patients among the 98 chronic hemodialysis patients presented a pathological fracture. That is a prevalence of 19.39%. Two patients had several fractures of different locations, one patient with 3 different fractures and the other with 6 different fractures. The mean age of the patients was 53.32 ± 13.94 years with a female predominance (5 men for 14 women) *i.e.*, a sex ratio of 0.3. The socioeconomic level was low in 12 patients (63.16%).

The predominant causative nephropathy was hypertensive nephropathy (53%), followed by chronic tubulointerstitial nephropathy (16%). As a cardi-

ovascular risk factor, we noted arterial hypertension in all patients, diabetes in 2 patients, smoking in 3 patients, dyslipidemia, and alcoholism in one patient each. Fifteen patients (78.15%) had cardiomyopathy and 8 women (42.11%) were postmenopausal. Hyperparathyroidism was the most common CKD-MBD (63.16%), followed by adynamic bone disease (21.05%) then osteomalacia (15.79%). Parathyroidectomy was performed in 4 patients (21.05%).

Dialysis parameters:

In our series, the average age of patients at the start of dialysis was 47 ± 14 years. All patients had 4-hour sessions with an average of 11.8 ± 0.88 hours per week. Synthetic polysulfone dialyzers and bicarbonate dialysate containing 1.5 mmol/l calcium were prescribed for all patients. Seventeen patients (89.47%) had an arteriovenous fistula and 2 (10.53%) a tunneled jugular catheter. The fracture occurred after an average duration of dialysis of 84.16 ± 29.88 months.

Clinical data:

The mechanism of fracture occurrence was minimal trauma in 12 patients (63%) and spontaneously in 7 patients (37%). Pain was described in all patients and was associated with absolute functional impotence in 57.9% and relative in 42.1% of cases. Local inflammatory swelling was noted in 8 patients (42.1%) and gait disturbances prior to the fracture in 13 patients (68.48%).

Biological data:

Basal exploration of phosphocalcic metabolism abnormalities noted a mean serum calcium at 90.37 ± 6.88 mg/L, a mean albuminemia at 37.85 ± 5.52 g/L, *i.e.*, a mean corrected serum calcium at 91.81 ± 8.51 mg/L. The mean phosphate level is at 33.21 ± 12.5 mg/L. The average calcium phosphate product was 3082.68 ± 1268.34 mg^2/L^2. The latter was normal in 47.37% of patients. The average intact parathyroid hormone (PTHi) is 1390 ± 1200.67 pg/L and 68.4% of patients had a PTHi level greater than > 9N. The mean value of 25-hydroxy-Vitamin D was 25.94 ± 8.86 ng/ml and 72.22% of patients had hypovitaminosis D at the time of the fracture.

Apart from the phosphocalcic abnormalities, the patients presented other biological disorders, a normochromic normocytic anemia at 8.89 ± 2.40 [3.6 - 13.6] mg/dL, the mean ferritinemia was 1033.27 ± 957, 64 ng/ml with a transferrin saturation coefficient (TSC) of 35%. The mean CRP was 27.29 ± 14.64 mg/L and it was positive in 8 patients (42.11%).

Radiological data:

Radiologically, the fractures were located mainly at the hip (femoral 47.38%) (**Table 1**). As associated radiological abnormalities, there was bone demineralization in 14 patients (73.70%), osteocondensation lesions in 3 patients (15.79%) and lytic lesions in 2 patients (10.53%). It should be noted that 5 patients (26.32%) had a bone callus already formed. Two patients (10.53%) had used CT for the diagnosis of the fracture. Five cases (26.3%) of vascular calcifications were objectified with a predominance of the aortic valve localization.

Therapeutics data:

Therapeutically, 63.2% received native vitamin D (Cholecalciferol) and 47.7%

Table 1. Distribution of patients according to fractured bone.

Affected bone	Number	Percentage (%)
Femur	9	47.38
Metatarsus	3	15.80
Clavicle	1	5.26
Humerus	1	5.26
Ischium and iliac	1	5.26
Ribs	1	5.26
Radius	1	5.26
Tibia	1	5.26
Tibia and fibula	1	5.26
Vertebrae	0	0.00
Total	19	100.00

Alfacalcidol. Eleven patients (57.89%) were on calcium carbonate. No patient was on non-calcium chelators or calcimimetics. In addition, 36.85% of patients were on Erythropoietin (EPO) and 15.79% on injectable iron. On the orthopedic level, therapeutic abstention was indicated in 6 patients (31.58%), surgical treatment in 6 patients (31.58%) and orthopedic treatment in 7 patients (36.84%).

Associated factors:

Univariate analysis after comparing 2 groups, with and without pathological fractures, showed that the following parameters were associated with the occurrence of pathological fractures in our patients: female gender ($p < 0.045$), duration of hemodialysis greater than 5 years ($p = 0.049$), gait disturbances prior to the fracture ($p = 0.001$), positive CRP ($p = 0.028$), presence of vascular calcifications ($p = 0.002$) and use of alfacalcidol ($p = 0.002$) (**Table 2**).

4. Discussion

It has been clearly established that the fracture risk is more increased as the GFR decreases. Indeed, it is five times higher in patients with a GFR of <15 versus > 60 ml/min per 1.73 m^2 [5] [10]. This lower resistance of the bone to trauma and the increased propensity to falls are the cause of the high fracture risk in dialysis [11]. The prevalence of pathological fractures in our study is 19.39% much higher than what is described in the literature. This can be explained on the one hand by the duration of the study which was longer unlike the other studies. And on the other hand, by the diagnostic and therapeutic delay of CKD-MBDs presented by our African patients, linked to financial difficulties in carrying out biological explorations on a regular basis, unlike European patients.

Our study found that patients who developed a fracture were not older but rather had a long duration of dialysis. As for the normal subject, the advanced age of patients on chronic hemodialysis is accompanied by a slow and steady decline in bone density and therefore in the quantity of bone. This decline begins

Table 2. Correlation between clinical, paraclinical and therapeutic data with the occurrence of pathological fracture.

Clinical data		Fracture Number (%)		p
		Yes	Non	
Age	<65 ans	15 (86.7%)	70 (88.6%)	0.265
	>65 ans	4 (13.3%)	9 (11.4%)	
Gender	F	14 (53.1%)	38 (48.1%)	**0.045**
	M	5 (46.9%)	41 (51.9%)	
Seniority in dialysis	>60 month	16 (80.6%)	16 (20.3%)	**0.049**
BMI < 18.5 kg/m^2		6 (36.7%)	30 (38%)	0.604
Gait disorder		13 (13.26%)	85 (86.73%)	**0.001**
Hb < 12 g/dl		17 (17.34%)	81 (82.66%)	0.604
Serum calcium < 85 mg/L		3 (3.06%)	95 (96.94%)	0.675
Serum phosphorus < 35 mg/L		11 (11.22%)	86 (87.78%)	0.346
25(OH) Vit D < 30 ng/ml		13 (13.20%)	80 (86.80%)	0.578
PTHi	<130 pg/ml	3 (3.06%)	5 (5.10%)	0.427
	>585 pg/ml	13 (13.26%)	59 (60.20%)	0.427
Albuminemia < 40 g/L		9 (19.60%)	37 (80.40%)	0.389
CRP > 6 mg/L		8 (10.09%)	65 (89.04%)	**0.028**
Vascular calcification		5 (5.10%)	93 (94.89%)	**0.002**
Native Vitamin D		12 (60%)	48 (80%)	0.847
Alfacalcidol		9 (42.9%)	12 (57.1%)	**0.002**
Calcimimetic		0 (0%)	7 (100%)	0.178

around the age of 30, the age at which peak adult bone mass is reached, then continues at around 0.5% per year [12].

The female gender was significantly associated with the occurrence of pathological fracture in our series (p = 0.045). These results are like those of Ambrus [13] and Jadoul [14] who objectified female gender as a fracture risk factor. This female prevalence is explained by the fact that bone loss is much more accelerated in women after menopause, which can reach more than 50%, unlike men, where it is around 10% to 15% [12]. This process is even more accelerated with CKD in renal osteodystrophy.

In our series, fractures occurred in a context of minimal trauma in 12 patients (63%). These results were like those of Kouiri [15] and Zenasti [16] who found simple falls (90% and 72.7% respectively) as the main mechanisms for the occurrence of pathological fractures in their studies. This is explained by the bone fragility found in chronic hemodialysis patients.

Gait disorders were significantly associated with fracture occurrence (p = 0.001). In the literature, it has been found that walking difficulties, falls and neurological disorders (uremic neuropathy, or related to causal nephropathy in

particular diabetic) increase the risk of fracture by increasing the risk of falling [13] [17].

Vascular calcifications were significantly associated with the occurrence of pathological fractures. In a Spanish study of 193 patients, Rodriguez *et al.* [18] noted a significant association between fractures and vascular calcifications in medium-caliber arteries. These results indicate that disorders of bone remodeling and mineralization are likely to affect calcium deposition in the arteries and may contribute to the pathogenesis of cardiovascular disease in this population. The pathophysiological mechanism of these calcifications is not yet elucidated but the increase in the serum phosphocalcic product, the secondary hyperparathyroidism, the adynamic osteopathy, the retention of magnesium as well as the intoxication in vitamin D and vitamin K are the factors classically recognized [15].

On the therapeutic level, none of our patients was under Calcimimetics, even if the indication was not lacking. Its low use was noted by Lemrabott *et al.* (15.5%) [11]. The low use of calcimimetics in our countries is linked to its high cost and the unavailability of molecules in our pharmacies, but also to the rebound effect in the event of discontinuation.

The meta-analysis by Bataille *et al.* concluded that calcimimetics bring the concentration of PTH most often within the targets, but their use had no benefit on mortality, cardiovascular death, and the risk of fracture [19]. This was consistent with our results, as we did not find a significant association between its use and the occurrence of fracture. On the other hand, treatment with alfacalcidol was significantly associated with the occurrence of fracture in our cohort. Indeed, alfacalcidol could increase the risk of fracture through hyperphosphatemia and hypercalcemia [20] [21], especially in our context where monitoring of treatment is not regular due to lack of financial means.

In our series, there was a clear predominance of non-surgical treatment (*i.e.* 68.42%), which differed from the results of Kouiri [15] and Tosun [17] on hip fractures, who had reported a predominance surgical treatment by 80% and 77% respectively.

The limit of the surgical indication in our series could be explained by the diagnostic delay of the fracture, the lack of financial means and especially the bone fragility in our patients.

5. Conclusions

Pathological fractures are frequent in our hemodialysis patients. The factors associated with their occurrence have been identified. Prevention occupies an important place in the management and involves the identification and correction of the factors of bone fragility.

The analysis of fracture risk factors has made it possible to establish management strategies which must essentially be preventive, involving the strengthening of bone resistance to trauma (optimal control of the phosphocalcic balance,

by aiming for the targets of the recommendations of good clinical practice) and the identification and reduction of the risk of falls.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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