

ORIGINAL RESEARCH

25 [OH] Vitamin D and Intact Parathyroid Hormone in Congolese Hemodialysis Patients: Evaluation of **KDIGO Targets**

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Background: Data on 25 [OH] vitamin D and intact parathyroid hormone [iPTH] in hemodialysis patients are very limited in sub-Saharan African countries. The present study aimed to assess the magnitude of hypovitaminosis D, and to evaluate the achievement of iPTH KDIGO 2017 targets among chronic hemodialysis patients followed in Kinshasa.

Methods: We conducted a multicenter cross-sectional study in 6 hospitals in Kinshasa. All patients followed on hemodialysis for more than 3 months were included. Hypovitaminosis D was defined as <30 ng/mL (insufficiency = 20-29 ng/mL; deficiency if <20 ng/mL mL) and the targets for iPTH values were based on the 2017 KDIGO guidelines. The determinants for hypovitaminosis D were evaluated by logistic regression.

Results: 251 patients [mean age 56 ± 14 years, 72.5% men, 63% hypertensive, 31% diabetic, 100% supplemented with native 25 [OH] vitamin D + CaCO3 were included. Hypovitaminosis D was found in 79.7% (deficiency 47.4%) and was associated with the male gender aOR 2.7 [1.4–5.2], p = 0.004, the low-permeability dialyzer 2.2 [1.1–4.2], p = 0.025 and anemia 3.9 [1.2–12.7], p = 0.022. Only 40% of patients with 25 [OH] vitamin D deficiency had iPTH according to KDIGO targets vs 6% of patients with severe hyperparathyroidism (iPTH > 600 pg/mL), 45% with levels between 16 and 150 pg/mL and 9% a iPTH \leq 15 pg/mL.

Conclusion: Despite a sunny environment, a large proportion of Congolese hemodialysis patients have hypovitaminosis D, in particular a deficiency. Among them, less than half have target iPTH values. These results show the benefit of regular monitoring of these parameters in order to optimize treatment.

Keywords: KDIGO targets, hemodialysis, hypovitaminosis D, iPTH

Introduction

Several studies show that hypovitaminosis D is common in black populations, both those living in cold and warm regions. ^{1,2} This difference can be explained by the fact that ultraviolet rays, which are essential for vitamin D synthesis, penetrate black skin less [7.4% UVB] than white skin [24%].^{3,4} People with black skin may therefore be deficient in vitamin D if they receive minimal sunlight.^{4,5}

The role of the kidney in the synthesis of the active form of vitamin D, 1.25 [OH] D3, is crucial. Loss of renal 1-αhydroxylase activity promotes secondary hyperparathyroidism and mineral-bone disorders [MBD].⁶ Fibroblast growth factor 23 [FGF-23], hormone synthesized by osteocytes, has two main actions in the renal proximal tubular cell: inhibition of 1-alpha-hydroxylase and of apical membrane, the expression of Npt2a/Npt2c co-transporters. This leads to a decrease in 1.25 [OH] D and a phosphaturic effect.^{7,8} FGF-23 also acts at the level of the parathyroid by inhibiting

the synthesis of parathyroid hormone [PTH]. Another transmembrane protein that exists in soluble form and is mainly synthesized at the distal tubular level, Klotho, has been shown to be an essential co-factor of FGF-23 activity. Recent studies in mice implicate Wnt inhibitors (portmanteau of wingless and int) in the pathogenesis of CKD-MBD. These Wnt inhibitors, including Dickkopf-1 (Dkk1) and sclerotin, are secreted in kidney disease. Using a monoclonal antibody to reduce their levels improves bone abnormalities. Apart from disorders of the metabolism of calcium, phosphorus, iPTH or vitamin D, abnormalities of bone renewal, mineralization and volume and extraskeletal calcifications (vascular and soft tissues) are among the complications grouped together under the term CKD-MBD. These abnormalities are associated with increased mortality and morbidity, including fracture risk. Apart from CKD-MBD.

Hypovitaminosis D is very common in chronic kidney disease [CKD], especially in hemodialysis patients. Apart from the more pronounced deterioration of renal function recognized at this stage of the disease, other factors contribute to its occurrence. These include the age of patients, which is often higher than the average for the general population, the exposure to the sun due to their reduced mobility, nutritional deficiencies, insufficient vitamin D supplementation. ^{10,11}

A few rare studies conducted in sub-Saharan Africa [SSA] have reported a frequency of hypovitaminosis D varying between 60 and 80% among chronic hemodialysis patients, often associated with normal or elevated PTH levels. ^{12–15} The factors associated with this decrease and the concordance between 25 [OH] D levels and expected iPTH values have not yet been studied in our setting.

In order to contribute to the improvement of the management of abnormalities of phosphocalcium metabolism in patients undergoing chronic hemodialysis [HD] in Kinshasa, the objectives of this study were to determine the frequency and determinants of hypovitaminosis D in this population, and to establish the concordance between the results of 25 [OH] D and iPTH levels.

Methods

Study Design, Setting and Population

We conducted a cross-sectional study from August 2018 to December 2019 in 6 HD centers in Kinshasa: the HD center of the University of Kinshasa Hospital [UKH], the HD center of Ngaliema Medical Center [NMC], Afia Medical Center [AMC], HJ Hospital, the dialysis center of Kinshasa at the provincial general hospital of Kinshasa [CDK], the HD center of the Congolese National Police Hospital [CNP]. In all these hospitals, 25 [OH] D and PTH were rarely measured and patients followed in chronic HD were systematically supplemented with native vitamin D and CaCO3 at doses of 400 IU and 500 mg twice daily, respectively. The sample consisted of patients undergoing chronic HD [HD ≥ 3 months] aged over 18 years.

A minimal sample size of 245 participants was calculated according to the formula $n = Z^2PQ/d^2$ assuming a confidence coefficient (z) of 1.96 for a confidence interval (CI) of 95%, a degree of precision (d) of 5%, Q=1-P and an expected proportion (p) of patients presenting abnormalities in phospho-calcium metabolism is 0.8, referring to the result found by Bala W et al in South Africa.¹³ The active queue of patients followed for hemodialysis in these 6 hospitals being 251, we opted for exhaustive sampling.

Data Section

Sociodemographic data [age, sex, educational level] and medical history were collected, including the search for pathological fractures documented in the medical file. Apart from 25[OH] D, the other parameters of interest were: ionized calcium, phosphorus, intact parathyroid hormone [iPTH], blood count, lipid profile and HD treatment modalities. The specific parameters during the HD sessions were: the patient's estimated dry weight, height and body mass index [BMI], the number of HD sessions per week, the calcium concentration of the dialysis bath prescribed to the patient [Ca++1 mmol/L, Ca++1.25 mmol/L, Ca++1.5 mmol/L or Ca++1.75 mmol/L], the type of dialysis bath acid prescribed to the patient [bicarbonate with acetic acid, bicarbonate with hydrochloric acid, bicarbonate with citric acid, bicarbonate without acid, acetate], the type of machine used during the dialysis session [conventional hemodialysis machine = HD, hemodiafiltration machine = HDF], the type of dialyzer used during the HD session [low permeability dialysis, high permeability dialysis].

The patient's blood samples were collected fasting before the HD session in dry tubes (just before the first dialysis session of the week). They were kept cold and sent the same day to the HJ Hospital laboratory for analysis. Ionized blood

calcium was determined by the direct potentiometric method using a Cobas 6000 device. The determination of phosphatemia was carried out by the spectrophotometric method using a Cobas c 311[®]. The determination of 25 [OH] D and iPTH was performed by the chemiluminescence method using a Cobas c 411[®] device. The lipid profile and the hemogram were carried out using the usual methods.

Definitions

Hypovitaminosis D was defined as insufficiency if 25 [OH] D level between 20–29 ng/mL and deficiency if < 20 ng/mL. ¹⁶ Ionized hypocalcemia: calcium < 1.05 mmol/L. ¹⁶ Hyperphosphatemia: > 1.5 mmol/L. ¹⁶ Hypophosphatemia: < 0, 8 mmol/L. ¹⁶ iPTH values exposing the HD patient to low bone remodelling: < 150 pg /mL. ¹⁷ iPTH values exposing to rapid bone remodelling: > 600 pg /mL. ¹⁷ Recommended iPTH values in HD patients: iPTH between 151–600 pg /mL (values ranging from 2 to 9 times the upper normal limit). ¹⁷ Low iPTH: ≤ 15 pg /mL. ¹⁸ High phospho-calcium product [PxCa]: value ≥ 4.51 mmol2 /L2. ¹⁹ Anemia: Hb < 13 g/dL in men and < 12 g/dL in women. ²⁰ Total hypercholesterolemia: ≥ 150 mg/dL, ²¹ Hypertriglyceridemia: ≥ 150 mg/dL; ²¹ high LDL-c: ≥ 100 mg/dL, ²¹ low HDL-c: < 40 mg/dL in men and < 50 mg/dL in women. ²¹

Statistical Analyses

Validated data were compiled into Excel and analyzed using SPSS software version Windows 21.0. The qualitative variables are described in terms of proportions or percentages and the quantitative variables in terms of means \pm standard deviation. The Pearson chi-square test or Fisher's exact test [for small numbers] was used to compare proportions. The Student t test was used to compare the means of the variables when the distributions were Gaussian. The Pearson's correlation coefficient was calculated to assess the relationship between two continuous variables. The relative contribution of each risk factor for hypovitaminosis D was studied by multivariate logistic regression, using the stepwise descending method. The coefficients obtained by the logistic regression were used to calculate the Odds ratio [OR] and the 95% confidence interval [CI]. For the selection of variables in the logistic regression model, the minimum threshold of significance to enter the model was 0.05 and a variable whose significance level reached 0.10 had to be removed from the model. The value p < 0.05 defined the statistical significance level.

Ethical Considerations

The ethical principles applicable to medical research involving human beings have been in accordance with the Declaration of Helsinki developed by the World Medical Association. Patients were recruited on the basis of free and informed consent, and the confidentiality of all personal information of the patients was respected. The study protocol was submitted to the ethics committee of the Kinshasa School of Public Health for review and Kinshasa for analysis and received approval registered at number ESP/CE/053/2016.

Results

The present study included 251 patients, 182 of whom were male [72.5%]. The patients were relatively young [mean age = 56±14 years]; 63% were hypertensive 31% were diabetic. Apart from the level of education, financing of care, alcohol and tobacco, no difference was observed between men and women [Table 1].

Concerning data on HD technique, 71% of the patients were under HD and 29% alternated conventional HD and HDF. The Ca++ 1.75 bath was used in 29% of patients vs 71% with a 1.5 Ca++ bath. More than two thirds of patients [71%] used a low-permeability filter while 29% of patients used a high-permeability filter. Anemia was present in 94% of patients and HDL hypocholesterolemia [75%] was the most common lipid disorder. HIV [2%], HCV [4%] and HBV [2%] infections were uncommon. Mean ionized calcium, phosphorus, and iPTH were not elevated, with no statistically significant difference between men and women [p < 0.05]. The mean 25 [OH] vitamin D level was 22.6±15.1 ng/mL, with lower values in men, 21.1±14.5 ng/mL vs 26.6±16.5 ng/mL in women [p=0.017] [Table 2].

The 25 [OH] vitamin D was negatively correlated with iPTH [r = -0.166, p = 0.008] and phosphatemia [r = -0.267, p < 0.001] vs a positive correlation with PxCa [r = 0.252, p < 0.001]. Hypovitaminosis D was found in 79.7% of patients, with 32.3% having insufficiency and 47.4% having deficiency.

Table I Sociodemographic Characteristics of Patients

| Variables | Whole Group n=251 | Men n=182 | Women n=69 | р |
|-------------------------|----------------------|--------------|---------------|---------|
| Age years old | 56 ±14 | 57 ±14 | 53 ±14 | 0.053 |
| Age < 40 | 37 [15] | 24 [13] | 13 [19] | 0.435 |
| 40–59 | 103 [41] | 74 [41] | 29[42] | |
| ≥ 60 | 111 [44] | 84 [46] | 27 [39] | |
| Financing of care | 80 [32] | 66 [36] | 14[20] | 0.010 |
| Higher and universities | 133 [53] | 113 [62] | 20[29] | < 0.001 |
| studies | | | | |
| Hypertension | 157 [63] | 115 [63] | 42 [61] | 0.422 |
| Diabetes mellitus | 78 [31] | 56 [31] | 22[32] | 0.489 |
| Tobacco | 51 [20] | 49 [27] | 2[3] | < 0.001 |
| Alcohol | 118 [47] | 102 [56] | 16 [23] | < 0.001 |
| Obstructive uropathy | 5 [2] | 3 [2] | 2 [3] | 0.420 |
| BMI Thinness | 25 [10] | 13 [7] | 12 [17] | 0.094 |
| Normal weight | 144 [57] | 109 [60] | 35[51] | |
| Overweight | 60 [24] | 45 [25] | 15[21] | |
| Obesity | 22 [9] | 15 [8] | 7 [10] | |

Notes: Results expressed either as mean \pm standard deviation or as absolute frequency (percentage). **Abbreviation:** BMI: body mass index.

Table 2 Biological Characteristics and Dialysis Parameters of Patients

| Variables | Whole Group n=25 l | Men n=182 | Women n=69 | р |
|--|-----------------------|--------------|---------------|-------|
| Hb, g/dl | 8.5 ±1,9 | 8.6 ± 2.0 | 8.4 ± 1.7 | 0.522 |
| Anemia | 237 [94] | 173 [95] | 64[93] | 0.332 |
| Hct, % | 25.8 ± 6.2 | 26.2 ± 6.3 | 24.7 ± 6.0 | 0.144 |
| WBC/mm ³ | 7753± 4353 | 7800 ±4513 | 7637 ±3972 | 0.824 |
| WBC < 4000/mm ³ | 24 [10] | 16 [9] | 8 [12] | 0.694 |
| WBC 4000-10,000/mm ³ | 174 [69] | 125 [69] | 49 [71] | |
| WBC > 10,000 /mm ³ | 53 [21] | 41 [23] | 12 [17] | |
| Platelets < 1.5×10 ³ /mm ³ | 229 ± 87 | 220 ± 84 | 247 ± 90 | 0.162 |
| Total cholesterol ≥ 150 mg/dL | 38 [15] | 29[16] | 9 [13] | 0.362 |
| LDLc ≥ 100 mg/dL | 83 [33] | 68 [37] | 15 [22] | 0.013 |
| HDLc < 40 mg/dL [man], < 50 mg/dL [woman] | 187[75] | 140 [77] | 47 [68] | 0.104 |
| TG ≥ I50 mg/dL | 73 [29] | 47 [26] | 26[38] | 0.047 |
| HIV antibodies | 6 [2] | 4 [2] | 2 [3] | 0.529 |
| HCV antibodies | 11[4] | 8 [4] | 3 [4] | 0.641 |
| HbS antigen | 6 [2] | 4 [2] | 2 [3] | 0.529 |
| Ionized calcium | 0.98±0.38 | 0.97±0.31 | 0.99±0.52 | 0.801 |
| Phosphatemia | 2.57±1.79 | 2.58±1.85 | 2.56±1.63 | 0.950 |
| 25 [OH] D | 22.6±15.1 | 21.1±14.5 | 26.6±16.5 | 0.017 |
| iPTH | 192±251 | 203±252 | 163±249 | 0.258 |
| HD | 178 [71] | 131 [72] | 47 [68] | 0.325 |
| HD + HDF | 73 [29] | 51 [28] | 22 [32] | |
| Bath Mg ⁺⁺ 0.5 | 73 [29] | 51 [28] | 22 [32] | 0.325 |
| Bath, Mg ⁺⁺ I | 178 [71] | 131 [72] | 47 [68] | |
| Bath, Ca ⁺⁺ 1.75 | 73 [29] | 51 [28] | 22 [32] | 0.325 |
| Bath, Ca ⁺⁺ 1,5 | 178 [71] | 131 [72] | 47 [68] | |
| Bath, CI ⁻ 107 | 73 [29] | 51 [28] | 22 [32] | 0.325 |

(Continued)

Table 2 (Continued).

| Variables | Whole Group n=251 | Men n=182 | Women n=69 | Р |
|----------------------------|----------------------|--------------|---------------|-------|
| Bath, Cl ⁻ 91 | 178 [71] | 131 [72] | 47 [68] | |
| Bath, Na ⁺ 138 | 73 [29] | 51 [28] | 22 [32] | 0.325 |
| Bath, Na ⁺ 140 | 178 [71] | 131 [72] | 47 [68] | |
| Bath, bicarbonate 32 | 73 [29] | 51 [28] | 22 [32] | 0.325 |
| Bath, Bicarbonate 35 | 178 [71] | 131 [72] | 47 [68] | |
| High permeability dialyzer | 76 [29] | 53 [29] | 23 [33] | 0.308 |
| Low permeability dialyzer | 175 [71] | 129 [71] | 46 [67] | |
| ≤ I session per week | 63 [25] | 42 [23] | 20 [29] | 0.589 |
| 2 sessions per week | 23 [9] | 18 [10] | 5 [7] | |
| ≥ 3 sessions per week | 165 [66] | 122 [67] | 44 [64] | |

Notes: Results expressed either as mean ± standard deviation or as absolute frequency [percentage].

Abbreviations: Hb, hemoglobin; HbS, hepatitis B surface; Hct, hematocrit; HD, hemodialysis; HDF, hemodiafiltration; WBC, white blood cells; LDL, low density lipoprotein; HDL, high density lipoprotein; TG, triglycerides; HIV, human immunodeficiency virus; HCV, hepatitis C virus; iPTH, intact parathyroid hormone; 25 [OH] D, 25 hydroxy vitamin D.

Table 3 shows that 11 patients [9%] with 25[OH]D deficiency had low iPTH level vs 53 patients [45%] a iPTH between 16 and 150 pg/mL vs 48 patients [40%] a iPTH 151–600 pg/mL, and only 7 patients [6%] had iPTH > 600 pg/mL. Among patients with 25(OH)D insufficiency, 4 [5%] had low PTHi level vs 13 patients [16%] a iPTH between 16 and 150 pg/mL and 62 patients [77%] a iPTH between 151–600 pg/mL, and only 2 patients [2%] had a iPTH > 600 pg/mL. Among patients with normal 25 [OH] D levels, 6 patients [12%] had low iPTH levels, 2 patients [4%] had iPTH > 600 pg/mL and 30 patients [59%] had iPTH levels between 16 and 150 pg/mL.

In the multivariate logistic regression model, male sex [aOR 2.7 [1.4–5.2], p = 0.004], low-permeability dialyzer [aOR 2.2 [1.1–4.2], p = 0.025] and anemia [aOR 3.9 [1.2–12.7], p = 0.022] were associated with hypovitaminosis D [insufficiency and deficiency]. Table 4 shows that hyperphosphatemia was near to statistical significance [aOR 2.0; 95% CI [1.0–5.0], p = 0.053].

Table 3 Number of Patients Achieving 2017 KDIGO Targets and Vitamin D Status

| | iPTH | | | | |
|-----------------------|------------|--------------|---------------|-------------|--|
| | ≤ I5 pg/mL | 16-150 pg/mL | 151-600 pg/mL | > 600 pg/mL | |
| 25 [OH] D, deficiency | П | 53 | 48 | 7 | |
| Insufficiency | 4 | 13 | 62 | 2 | |
| Normal value | 6 | 30 | 13 | 2 | |
| Total | 21 | 96 | 123 | П | |

Abbreviation: 25 [OH] D, 25 hydroxy vitamin D.

Table 4 Factors Associated with Hypovitaminosis D in Chronic Hemodialysis Patients

| | Univariate Analysis | | | Multivariate Analysis | | |
|--|---------------------|----------|-------|-----------------------|----------|-------|
| | OR | CI 95% | р | aOR | CI 95% | Р |
| Hyperphosphatemia vs no | 2.0 | 1.0-3.3 | 0.043 | 2.0 | 1.0-5.0 | 0.053 |
| Male vs female sex | 2.8 | 1.4-5.2 | 0.002 | 2.7 | 1.4-5.2 | 0.004 |
| Low permeability dialyzer vs high permeability | 2.3 | 1.2-4.3 | 0.010 | 2.2 | 1.1-4.2 | 0,025 |
| Anemia vs no | 4.4 | 1.5-13.1 | 0.005 | 3.9 | 1.2-12.7 | 0.022 |
| Obesity vs no | 2.5 | 1.0-6.2 | 0.050 | _ | _ | _ |
| Bath, Ca++ 1.5 vs 1.75 | 2.2 | 1.2-4.2 | 0.013 | _ | _ | _ |
| Bath, bicarbonate 32 vs 35 | 0.5 | 0.2-0.9 | 0.013 | _ | _ | _ |
| HD vs HD + HDF | 2.2 | 1.2-4.2 | 0.013 | _ | _ | _ |

Only one case of pathologic fracture was documented by CT scan in a 56 years old woman with hypocalcemia ionized 0.59 mmol/L, phosphatemia 3.6 mmol/L, hypovitaminosis D 21 ng/L, and iPTH 522 pg/mL.

Discussion

The present multicenter study conducted in the HD centers of Kinshasa revealed that 4 out of 5 patients present a hypovitaminosis D and confirmed some determinants already reported in the literature. Other determinants found in present study, such as male and anemia gender, are unusual. Only half of the patients had iPTH values recommended by the 2017 KDIGO guidelines. Notwithstanding suboptimal patient management, only one case of pathologic fracture was reported.

The similarly high incidence of hypovitaminosis D that we describe is within the range of the results reported in the few studies conducted in SSA in hemodialysis patients. Apart from the risk of bone fragility, this complication exposes patients to decreased muscle tone, the occurrence of tetany and seizures [in relation to hypocalcemia], hypocalcemia, an increased risk of cancer, diabetes, depression and autoimmune diseases. 22

Considering the significant extrarenal production of 1, 25 [OH] D even in advanced CKD, the KDIGO experts recommend supplementing dialysis patients with 25 [OH] D.¹⁷ Since the HD centers in Kinshasa comply with these recommendations, a lower frequency of 25 [OH] D deficiency would be expected, which was not the case. It could be that patients are not compliant with compliant or that the doses used were simply low in a setting where health care is not context reimbursed in the DR Congo and native vitamin D supplementation in these HD centers is rarely supported by regular paraclinical examinations. It is advisable to perform an overall serum 25 [OH] D measurement in all dialysis patients prior to initiation of therapy. A second determination is recommended after three to four months and then once a year to adjust doses and to check compliance.¹⁷ The local marketing of highly concentrated oral ampoules or highly concentrated drops of native vitamin D, which can be administered once or twice a month could help to improve compliance and thus reduce the frequency of hypovitaminosis in dialysis patients in our setting.²³

For patients with normal 25 [OH] D levels, excessive supplementation exposes them to overdose of vitamin D, which may be manifested by loss of appetite, nausea, vomiting, weakness and nervousness. ²⁴ In the present study, this group represented 21%. Of these, 12% had an iPTH \leq 15 pg/mL [= hypoparathyroidism] and 59% had a value between 16 and 150 pg/mL [Table 3]. Given the risk of adynamic osteopathy, it is logical to stop supplementation [native vitamin D or 1-alpha derivatives] and schedule a next control of 25 [OH] D. Calcium salts and dialysate calcium content should also be reconsidered. The association between hyperphosphatemia and hypovitaminosis D is classic in CKD.

Indeed, in the early stages of CKD, in response to hyperphosphatemia resulting from glomerular filtration, FGF23 and Klotho are secreted and exert a phosphaturic effect. On the other hand, FGF23 inhibits 1- α -hydroxylase and the secretion of iPTH. Klotho, FGF23, iPTH and 1- α -hydroxylase thus interact in a complex manner to maintain normal blood calcium levels and to limit the rise in plasma phosphate.

It is known that hypovitaminosis D is very frequent in the elderly, particularly in postmenopausal women. Many recent studies report deficiencies that are surprisingly endemic even in apparently healthy populations, including men.²⁵ In the studies conducted in hemodialysis patients, we did not find those that report a greater risk of hypovitaminosis D in men. Given the small sample size [only 182 men and 69 women], it would be appropriate to conduct a study with a conduct a study with a larger sample size to verify our results.

HD membranes [dialyzers] are classified as high or low permeability based on their ability to remove uremic toxins and other molecules according to their molecular weight. Inflammatory cytokines and uremic toxins inhibit 25-hydroxylase, which is essential for the synthesis of 25-OH vitamin D.²⁶ It has been suggested that the removal of medium molecules through high permeability dialyzers may better reflect normal renal function and improve clinical outcomes in dialysis patients. Several of these mechanisms could explain the association found between hypovitaminosis D and the use of the use of low-permeability dialyzers.

Both anemia and hypovitaminosis D are frequently described in the general population and in HD patients. While it is true that in CKD, their co-existence is primarily explained by the alteration of renal functions, many authors also underline the reciprocal interactions between the two complications. Hypovitaminosis D, due to of bone remodelling, can

disrupt erythropoiesis.²⁷ On the other hand, a recent animal model study has shown that correction of anemia by the administration of erythropoietin lowers FGF23 which plays a role in the metabolism of vitamin D.²⁸

The negative correlation found between 25 [OH] D and iPTH accounts for the pathophysiology of CKD. With such high frequencies of hypocalcemia, hyperphosphatemia and hypovitaminosis D, one would expect a greater number of patients with severe iPTH. However, at the threshold defined by the 2017 KDIGO group [iPTH > 9 times the normal value], ¹⁷ only 4.4% of patients had iPTH > 600 pg/mL. In contrast to our results, a study conducted in Ivory Cost reported 30% of cases of iPTH > 600 pg/mL in HD patients. ¹⁵ It cannot be excluded that drug factors may influence the level of iPTH/mL in our patients. Indeed, it is known that calcium-rich dialysis baths, high permeability dialyzers, calcimimetics or vitamin D analogues contribute to decrease the iPTH level. ²⁹ Notwithstanding this hypothesis, it should be recognized that there is no consensus on the ideal level of iPTH. The 2017 KDIGO Working Group considered that modest increases in iPTH may simply represent an adaptive response to declining renal function due to phosphaturic effects and increased bone resistance to PTHi. The only case of pathologic fracture was reported in a patient with hypovitaminosis D, hypocalcemia, hyperphosphatemia, and an iPTH level of 522 pg/mL.

The profile of the patients in this study [relatively young and predominantly male, two-thirds hypertensive and one-third diabetic, almost all anemic, almost two-thirds without funding, many of them not having three HD sessions per week and some treated with low-permeability dialysis machines] corroborates data from previous studies in DRC and some SSA countries.³⁰

The results of this study must be interpreted with some limitations. The markers of phosphocalcic metabolism were measured only once, and it is recommended to perform several examinations [especially for iPTH] before concluding.¹⁷ For a complete focus, measurement of bone alkaline phosphatase, FGF-23, Klotho, and other markers of bone turnover would allow for better interpretation of results. The same is true for the evaluation of vascular calcifications and bone biopsy, which were not part of the subject of this study. The main strength of the study is that it is one of the few to address the subject in a multicenter setting in SSA. The laboratory methods used [chemiluminescence] to determine 25 [OH] D and iPTH are among the most recent and currently recommended. The study was able to demonstrate the extent of the disorders of phosphocalcic metabolism and their Risk factors in hemodialysis patients followed in DR Congo.

Conclusion

Despite a sunny environment, a large proportion of Congolese hemodialysis patients have hypovitaminosis D, in particular a deficiency. Among them, less than half have target iPTH values. These results show the benefit of regular monitoring of these parameters in order to optimize treatment.

Data Sharing Statement

The database is available from the corresponding author on reasonable request.

Ethical Rules

The ethical principles applicable to medical research involving human beings were respected in accordance with the Declaration of Helsinki. Patients were recruited on the basis of free and informed consent, and the confidentiality of all personal information was respected. The protocol was submitted to the ethics committee of the Kinshasa School of Public Health for review and had received approval registered at number ESP/CE/053/2016.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically

reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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