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Vitamin D Status in Supplemented Hemodialysis Patients

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Introduction: Chronic kidney disease (CKD) causes decreased activity of the enzyme 1-alpha-hydroxylase and calcitriol deficiency with mineral and bone metabolism disorders or secondary hyperparathyroidism. Anticipation of the occurrence of these complications implies the systematic supplementation of all hemodialysis patients, with monitoring of biological parameters. It is in this context that this study was carried out, the general objective of which was to establish the profile of vitamin D concentration in hemodialysis and Ivorian public sector supplemented patients in Abidjan.
Patients and Methods: In a cross-sectional study conducted from September to December 2022, we included 89 patients with end-stage CKD treated with hemodialysis at the CNPTIR in Cocody.

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The collection of epidemio-clinical data was done on the basis of a questionnaire on the one hand and the patients' medical records on the other. The vitamin D concentration was determined by the ELFA immunoassay method on mini Vidas (BIOMERIEUX).
Results: The mean age of the patients was 45 ± 13 and 65.17% of them were men. 55.06% of the patients had been treated with dialysis for at least 5 years. 48.31% of the patients had regular supplementation treatment. Of the two types of vitamin D supplementation, 94.38% of the study population was supplemented with cholecalciferol compared to 18% for alfacalcidol with 12% of patients included, using both types. From a biological point of view, it appears that the average concentration of vitamin D in the patients was 26.9 ng/mL, and only 16% have a concentration of less than 20 mg/mL, corresponding to an deficiency vitamin D status.
Conclusion: At the end of this cross-sectional study, it emerged that the average in adult hemodialysis subjects followed at the CNPTIR in Cocody had an insufficient vitamin D status. And 37% of the study population with normal vitamin D status. However, these results could be improved by better accessibility to the products, and regular compliance with supplementation.

Keywords: Vitamin D; African; hemodialysis; chronic kidney disease.

1. INTRODUCTION

In humans, cholecalciferol or vitamin D3 (VitD3) has a dual origin: an endogenous origin occurring in the epidermis and an exogenous origin (food and drug intake). Its main biological role (the regulation of phosphocalcic metabolism) requires activation by two successive hydroxylations: the first, at the level of the liver and the second at the level of the kidney (by the enzyme 1-alpha-hydroxylase) to obtain calcitriol or active vitamin D3: $1,25(OH)_2D$ [1,2].

Also, chronic kidney disease (CKD), by causing the decrease or even suppression of the activity of the enzyme 1-alpha-hydroxylase, leads to calcitriol deficiency at the origin and to mineral and bone metabolism disorders such as osteoporosis and secondary hyperparathyroidism constituting a serious complication in dialysis patients.

Also, calcitriol deficiency leads to hypocalcemia due to a decrease in intestinal absorption and stimulates the synthesis of parathyroid hormone (PTH), which allows the hydroxylation of 25 hydroxy vitamin D (25(OH)D) to 1,25(OH)2D, active. This parathyroid regulation allows the stability of 1.25(OH)2D levels at the expense of 25(OH)D, regardless of the amount of sunlight. This deficiency therefore induces secondary hyperparathyroidism (HPT) responsible for osteoporosis or osteomalacia in adults.

A meta-analysis by Bischoff-Ferrari (18) shows a reduction in the risk of non-vertebral fracture in patients receiving vitamin D supplementation > 800 IU/day (effect more pronounced in patients deficient at the start of the study and those over 70 years of age). There is a lower response to anti-osteoporotic treatments when vitamin D stocks are insufficient, the necessary level being 30 to 40 ng/mL.

Thus, the measurement of vitamin D concentration in CKD patients can prevent or improve the management of complications related to vitamin D deficiency [3].

Thus, our study aims to establish the status of chronic kidney failure patients on dialysis in public centers in Abidjan (Côte d'Ivoire) receiving vitD supplementation.

2. PATIENTS AND METHODS

2.1 Study Design and Patients

This is a pilot cross-sectional study, with a descriptive aim that took place over a period of 3 months. It was carried out at the biology laboratory of the SAMU (Emergency Medical Assistance Service) in Abidjan.

The study involved African black adult pateints with end-stage chronic kidney disease. These patients are treated and monitored at the Abidjan Public Dialysis Center (CNPTIR: National Center for the Prevention and Treatment of Renal Failure) where they receive 8 hours of hemodialysis per week divided into two four-hour sessions. In addition, faced with the risk of complications of the disease, in particular bone metabolism disorders, they are systematically supplemented with vitamin D during their treatment. This supplementation is done with both cholecalciferol and alfacalcidol.

Patient recruitment was done according to the inclusion criteria below:

Subjects of both sexes aged 18 years or older, with chronic kidney disease and vitamin D supplementation, who have given consent to participate in the study with an available medical record.

A total of 89 CKD patients were included in the study.

2.2 Methods

Sampling was carried out by successive recruitment of patients meeting the inclusion criteria over the study period. Questioning and consultation of patients' medical records made it possible to collect epidemio-clinical data, in particular the characteristics of vitamin D supplementation treatment (prescribed specialty, dosage and dosage) and patient compliance.

The selected patients were subjected to a venous blood sample at the elbow crease on an empty stomach tube without anticoagulant (with separator gel). On the serum collected after centrifugation at 4000 rpm for 5 minutes, the vitamin D was measured.

The vitamin D assay was done by the ELFA (Enzym Linked Fluorescent Assay) method on Mini VIDAS® (BIOMERIEUX).

The concentration of vitamin D was interpreted according to the following values:

25(OH)D < 20 ng/ mL: Deficiency
25(OH)D between 20 and 25 ng/mL: Impairment
25(OH)D between 25 and 30 ng/mL: Insufficiency
25(OH)D ≥ 30 ng/ mL: Normale

2.3 Statistical Analysis

The data was processed using the Office Excel 2016 software.

Quantitative variables were described using the mean, standard deviation, extremes, median and interquartile range (25th percentile (P25)-75th percentile (P75). Each of the qualitative variable modalities was described in terms of numbers and percentages.

3. RESULTS

The mean age of haemodialysis patients was 45± 7 years. More than half of the study population was under 49 years.

The male/female distribution showed a majority of men (sex ratio (M/F) was 1.87).

Most patients had been on dialysis for more than 5 years. The duration of hemodialysis treatment ranged from 1 to 20 years.

This duration of treatment also corresponded to the duration of vitamin D supplementation.

Characteristics of the study population are presented in Table 1.

Table 1. Patient characteristics

Parameters	Values
Age (years)	
Mean ± sd	45 ± 7
Min - max	18 - 80
Gender: number (%)	
Men	58 (65,17%)
Women	31(34,83%)
Sex-ratio	1,87
Length of time on dialysis (years)	
Mean ± sd	5,78 ± 1,5
Min - max	1 - 20

Regarding the molecules prescribed, two types of supplementation are observed: on the one hand, supplementation with the combination of calcium + cholecalciferol and on the other hand, supplementation with 1-alpha-hydroxycholecalciferol prescribed in combination with calcium only orally.

The majority of patients had a vitamin D concentration greater than or equal to 25 ng/mL. The mean concentration of vitamin D was 26.9 ± 8,8 ng/mL.

Approximately half of the patients in our sample did not regularly follow the supplementation treatment. Regarding supplementation treatment, 69.77% of patients who observed regular compliance had a vitamin D concentration greater than or equal to 25 ng/mL versus 43.48% in non-compliant patients.

Table 2. Distribution of the study population by vitamin D concentration

Plasma concentration of vitamin 25(OH)D (ng/mL)		Values
Mean ± sd		26,9 ± 8,8
Median		26,8
Min - max		8,1 - 52,4
Distribution Number (%)	< 20	14 (16%)
	[20 – 25]	17 (19%)
	[25 – 30]	25 (28%)
	≥ 30	33 (37%)
	Total	89 (100%)

Table 3. Distribution of the study population by vitamin D status and good compliance to supplementation

	Plasma concentration of vitamin 25(OH)D (ng/mL)				
Good compliance	**<20**	**[20-25]**	**[25-30]**	**≥30**	**Total**
No	16	10	7	13	46
Yes	9	4	10	20	43
Total	25	14	17	33	89

4. DISCUSSION

Vitamin D deficiency is common in the general population [4,5] and is associated with many diseases. It is a well-known complication of renal failure, particularly in end-stage renal disease, leading to discorders in bone metabolism, with an increased risk of fractures, bone pain, cardiovascular disease and mortality [6]. In addition, some studies have suggested an association between vitamin D status and metabolic syndrome in haemodialysis patients, given that vitamin D is involved in insulin metabolism, lipid metabolism and blood pressure regulation [7,8].

The prevalence of 25-hydroxy-vitamin D deficiency in end-stage chronic kidney disease depends on the cut-off values chosen to define this deficiency [9]. These vary according to numerous parameters, such as: The population studied (stage of CKD), geographical region (latitude and sunshine, clothing habits) and age. In the general population, it's true that opinions were divided between those in favor of a target level of 20 or 30 ng/mL [5,10]. However, in chronic kidney disease, the data published by the NephroTest cohort provide specific physiological arguments. In this study, after adjustment for age, measured GFR, ionized calcium and ethnicity, a target of over 20 ng/mL appears to be the minimum target [5].

As there is also a relatively high extrarenal production of 1,25(OH)2D, supplementation with native vitamin D or 25(OH)D in dialysis patients seems justified. This correction is not yet well codified, due to a lack of prospective studies. Guidelines, in particular KDIGO, recommend that all dialysis patients have their total serum 25(OH)D (25[OH]D2 + D3) measured at least once a year [9].

However, in developing countries such as Côte d'Ivoire, compliance with these recommendations is not always easy, especially as vitamin D supplementation and measurements are entirely at the patient's expense, and the status of patients is not clearly known. It therefore seemed appropriate to examine the vitamin D profile of dialysis patients in public facilities in Abidjan, through a cross-sectional pilot study.

This is a relatively young population with an mean age of 45 ± 7 years, ranging from 18 to 80 years. The distribution by age group showed that more than half of the study population is under 49 years of age; The relative youth of CKD patients highlighted in our study is also observed in other studies in Africa, particularly in Burkina Faso [11] with an average age of 45 years. On the other hand, in Caucasian populations with CKD, the average reported ages remain above 60 years [5,6,12,13]. These observed differences are widely documented, involving in particular the youth of the general population in Africa as well

as self-medication [14] the frequent and endemic nature of certain diseases such as schistosomiasis, HIV-AIDS [15].

The male predominance observed in our population has also been reported in numerous studies both in Africa and elsewhere in the world [16–18]. Generally speaking, many authors agree that men are more affected by CKD than women due to the higher frequency of kidney disease in men [2] and the notion of smoking that could have a detrimental effect on the rate of progression of chronic kidney disease.

Regarding the length of time spent on hemodialysis treatment, the average of 6 years we found is similar to those reported by El harraqui et al. [3] in Morocco (7 years) and Dammack et al. [19] in Tunisia (9 years). This duration can be superimposed on that of vitamin D supplementation.

The median concentration of vitamin D found in our study is 26.8 ng/mL. It is significantly lower than that reported by Cavalier et al. [20] in 2018 in CKD patients in the same city of Abidjan (40.2 ng/mL).

Similarly, the proportions of patients with 25(OH)D levels greater than 30 ng/mL differ significantly (37% in our study vs. 80% in the Cavalier study). These differences can be explained by the platforms used for the determination of 25(OH)D in the 2 studies: VIDAS bioMerieux vs Fujirebio Lumipulse. Indeed, several authors have noted the tendency of certain equipment (notably VIDAS) to under-recover 25(OH)D compared to other equipment such as Fujirebio Lumipulse [20,21].

Compared to other populations of chronic kidney disease, particularly in Morocco, our results remain relatively low, especially compared to those reported by Benabdellah et al. [22] (mean vitamin D concentration equal to 34.8 ng/mL) without specifying the assay platform used.

Moreover, in the same city of Abidjan and for the same assay technique (Vidas bioMerieux), the proportion of 25(OH)D deficiency reported by Boyvin [23] in a healthy population is 33% compared to 16% in our dialysis population. This result suggests that systematic supplementation of these at-risk patients helps maintain an acceptable vitamin D stock. Of the different types of vitamin D supplementation, 94.38% of the study population was supplemented with cholecalciferol, 18% with alfacalcidol, and 12% used both types.

The low prescription rate of alfacalcidol could be explained by its high cost and low availability on the Ivorian market. Also, its prescription is generally used as a curative treatment after the onset of hyperparathyroidism or bone complications.

For cholecalciferol, the daily doses used varied from 400 IU to 6000 IU depending on the patient's blood calcium level and the pharmaceutical specialty prescribed.

Although relatively low, the proportion of dialysis patients with vitamin D deficiency could have been lower if compliance with supplementation was correct in all patients.

Indeed, the analysis of the average vitamin D concentration value as a function of the regularity of supplementation shows that 65% of deficient patients are non-compliant. This poor compliance is mainly linked to financial difficulties in honoring prescribed prescriptions, as vitamin D is not covered by the Ivorian state subsidy or reimbursed by insurance companies.

5. CONCLUSION

At the end of our cross-sectional study to establish the profile of vitamin D concentration in patients on hemodialysis and supplementation in public centers in Abidjan (Côte d'Ivoire), it appears that the proportion of patients who are deficient is low, and could be improved by greater accessibility to products leading to better compliance. These results highlight the interest of regular systematic supplementation in Ivorian hemodialysis subjects.

6. LIMITATIONS OF OUR STUDY

It would have been interesting to work on a larger squad. In addition, considering a case-control study would make it possible to compare the profiles of dialysis patients with healthy subjects in the same context, and to establish cause-and-effect relationships with factors that appear to be confounding in a cross-sectional study.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image

generators have been used during the writing or editing of this manuscript.

ETHICAL APPROVAL

The study was approved by the local ethical committee of the Ministry of Health. A free and informed consent form was obtained from all participants.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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