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Contribution to The Study of Vitamin D Deficiency in Chronic Hemodialysis Patients in Senegal

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Abstract

Introduction: Vitamin D deficiency and relative vitamin D deficiency is frequently observed in patients with chronic kidney disease and chronic dialysis patients. In sub-Saharan Africa, there are not many studies based on the prevalence of vitamin D deficiency. In Senegal, two pilot studies on the prevalence of the decline in vitamin D reserves were conducted in 2011 and in 2013 showed respectively a decrease in vitamin D reserves in 32.6% and 62.2% compared to general population. Thus, we conducted this third study to complete these studies to determine the prevalence of vitamin D depletion in chronic hemodialysis patients in Senegal and to evaluate related complications.

Material and Method: This was a multicenter, retrospective and analytical study performed in 3 hemodialysis units in Dakar, covering the files of chronic hemodialysis patients over 67 months (1st June 2011 to 30th November 2017). We included all cases of regularly hemodialysis patients who had benefited from the iPTH, 25 (OH) vitamin D, serum calcium and phosphatemia.

Results: Of 324 files, 111 were retained, representing a prevalence of 33%. The average age was 54.53 +/- 13.85 years old. There were 48 men (43.2%) and 63 women (56.8%), a sex ratio of 0.76. The causative nephropathy was nephroangiosclerosis, chronic glomerulonephritis and indeterminate nephropathy with respectively 47.75% (53 cases); 13.51% (15 cases) and 14.41% (16 cases) of the cases. The mean concentration of 25 (OH) D was 22.87 +/- 12.72 ng/ml. There were 95 patients (85.6%) who had decreased vitamin D 25 D reserves with an average plasma level of 16.1 +/- 7.5 ng/ml. Of these, 57 (51.4%) patients had relative vitamin D insufficiency; 28 patients (25.2%) had a moderate deficit and 10 patients (9%) had a severe deficit. The average concentration of I PTH was 659.36 µg / ml. Hyperparathyroidism was noted in 49 patients (44.1%); 13 patients (11.7%) had osteomalacia. Mean serum calcium was 90.10 +/- 8.61 mg/l. Mean serum calcium was 90.10 +/- 8.61 mg/l. Average phosphatemia was 42.95 +/- 14.4 mg/l. On the therapeutic level, 57 patients (51.35%) with a decrease in vitamin D reserves were supplemented with native vitamin D3; 16.22% had not received any supplementation.

Conclusion: Prevalence of vitamin D deficiency was 85.6% with an average plasma level of 16.1 ng / ml. In our study, there was a significant correlation between decreased vitamin D reserves and dialysis seniority greater than 60 months, diabetes, hypertension and the onset of tricuspid insufficiency. Hence the interest of the annual dosage of 25 OH vitamin D and compliance with KDIGO recommendations.

Keywords: Dialysis; Senegal; Vitamin D 25OH

Abbreviations

iPTH	:	Intact Parathyroïd Hormon
CKD	:	Chronic Kidney Disease
HCV	:	Hepatitis C Virus
HIV	:	Human Immunodeficiency Virus

Introduction

Vitamin D deficiency and relative vitamin D deficiency are defined by levels of hydroxyvitamin D respectively less than 10 ng/ml and 30 ng/ml [1]. This vitamin has been a topic of interest for several years because of its diverse effects in the prevention of osteoporotic fractures. In adults, vitamin D deficiency can cause muscle weakness and increase the risk of fracture and lead to osteopenia, osteoporosis and osteomalacia [1,2]. It is frequently observed in patients with chronic renal disease-causing worsening of secondary hyperparathyroidism [3] and increased bone remodeling (osteoporosis) [4]. Several studies have shown that vitamin D deficiency is associated with risks of cardiovascular calcification, arteriosclerosis and endothelial dysfunction [5]. Deficiency is more common in dialysis patients than in general population, exposing patients to higher mortality [5,6]. In sub-Saharan Africa, there is little data on this issue. In Senegal, two pilot studies on the prevalence of the decline of vitamin D reserves were conducted in 2011 and in 2013 showed respectively a decrease in vitamin D reserves in 32.6% and 62.2% [7]. This is how we conducted this study to complement the two studies already conducted with the objective of determining the prevalence of the decline in vitamin D in chronic hemodialysis patients in Senegal and evaluate the complications related to this decline.

Material and Method

This was a multicenter, retrospective and analytical study in 3 hemodialysis units in Dakar, one hemodialysis in Saint Louis and a Ziguinchor unit for chronic hemodialysis patients during the period from June 1st, 2011 to November 30th, 2017. We included all cases of regularly hemodialysis patients who had benefited from the iPTH, 25 OH vitamin D, serum calcium and phosphatemia. Were excluded all CKD 5 patients, patients younger than 15 years of age, vacationers, acute renal failure records and incomplete records. The data was collected through an individual survey card. The studied parameters were epidemiological (age, sex, clinical (initial nephropathy, history, osteo-articular signs and associated signs), paraclinical (25 OH vitamin D, iPTH, calcemia, phosphatemia hemogram, echocardiography, electrocardiogram, Hbs Antigen, antibodies against HCV and HIV) and therapeutic (number of sessions per week, duration of sessions, seniority of dialysis and dialysate calcium). Data analysis was done on SPHINX version 3.3.2. The Chi² test was used for the analysis of qualitative variables. A difference is considered significant if the value of p that corresponds to these tests is <0.05. Concerning the operational variables: [46]

- Vitamin insufficiency: 25 (OH) live rate D including 50 - 75 nmol/l (20 to 30 ng/ml)
- Moderate deficiency: 25 (OH) D content between 30 to 50 nmol/l (12 to 20 ng/ml)
- Severe deficiency (deficiency): 25 (OH) D < 30 nmol/l (< 12 ng/ml)
- In case of chronic renal failure, the rate of iPTH is considered normal if it was between 150 and 450 pg/ml as 3 to 9 times normal.
- Normal serum calcium was 84-102 mg/l; normal phosphatemia was 25-45mg/l and hemoglobin level > 11g/dl was normal [49].

Results

One hundred and eleven files were selected from a total of 342 patients, as a prevalence of 33%. The average age was 54.53 +/- 13.85 years old with [17 to 83 years old]. The 50 to 70 age group accounted for 56.4%. There were 48 men (43.2%) and 63 women (56.8%), as a sex ratio of 0.76. Causal nephropathy was nephroangiosclerosis, chronic glomerulonephritis and indeterminate nephropathy with 47.75% (53 cases); 13.51% (15 cases) and 14.41% (16 cases) of the cases. For comorbidities, 73% (81) of patients had a history of isolated hypertension and 13.5% (15) of diabetes-associated hypertension. Clinically, 16.2% (18) of patients had osteoarticular pain. It was diffuse pain in 66.7% of cases, sometimes localized in the hip 11.1%, fingers and knees respectively in 8.2% and 5.6% of cases associated with functional impotence relative to 7.2% of the population. Spontaneous fractures were observed in 4 patients (3.6%).

Paraclinically, the average concentration of 25 (OH) D was 22.87 +/- 12.72 ng/ml [8 and 125 ng/ml]. Ninety-five patients (85.6%) had a decrease in vitamin D (25 (OH) vitamin D) with an average plasma level of 16.1 +/- 7.5 ng/ml. Of these, 57 (51.4%) patients had relative vitamin D insufficiency; 28 patients (25.2%), moderate deficiency and 10 patients (9%), severe deficiency. In the group of patients with normal vitamin D, the mean plasma vitamin D level was 41.31 ng / ml as shown in (Figure 1). The average concentration of iPTH was 659.36 ± 542.85 µg/ml. Forty-nine patients (44.1%) had normal iPTH levels. Hyperparathyroidism was noted in 49 patients (44.1%); 13 patients (11.7%) had osteomalacia. In the group of patients with normal vitamin D levels, the average rate of iPTH was 880.3 pg/ml. It was 576.8 pg / ml in patients with a decrease in vitamin D reserves with an average of

614.47pg/ml, 717.71 pg/ml and 398.3 pg/ml for patients with relative insufficiency, in moderate deficit and severe deficit. Mean serum calcium was 90.10 +/- 8.61 mg/l with [61 to 108 mg/l]. Ninety patients (81.1%) had normal calcemia and nineteen patients (17.1%) had hypocalcaemia with an average of 72.6 mg/l. In the group of patients with normal 25 (OH) D, mean serum calcium was 89.69 mg/l.

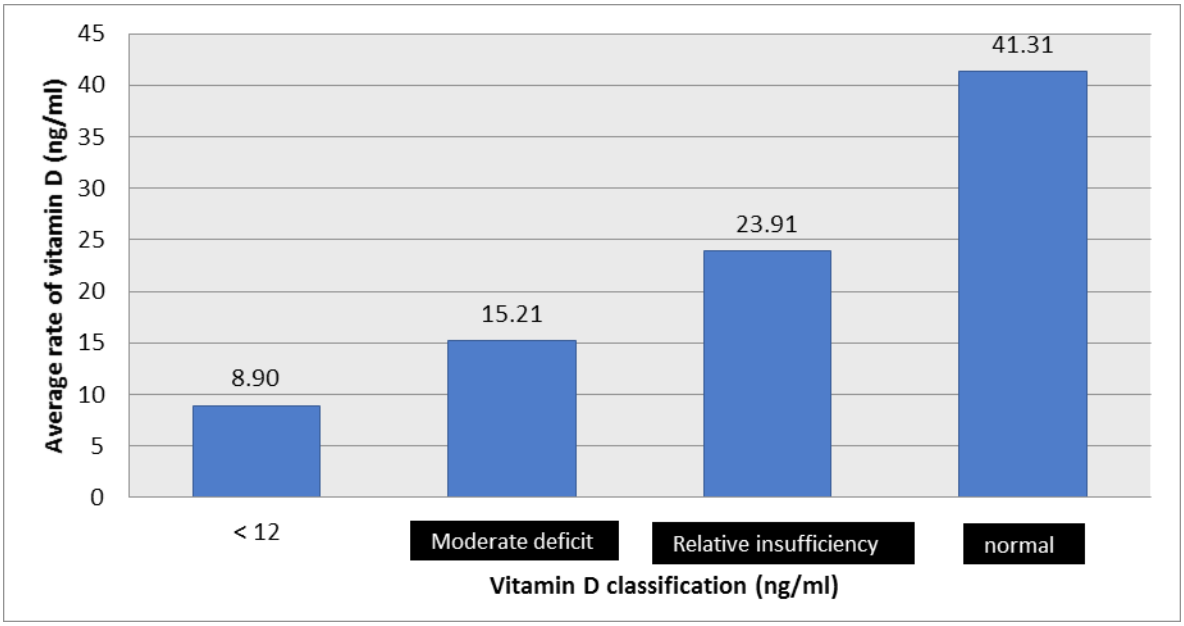

Figure 1: Average concentration of vitamin D.

It was 90.53 mg / l in patients with decreased vitamin D reserves. Average phosphatemia was 42.95 +/- 14.4 mg/l with [19 to 90 mg/l]. Hyperphosphatemia was noted in 46 patients (41.4%). In the group of patients with a normal 25 (OH) D level, the average phosphatemia was 41.19 mg/l. It was 43.25 mg/l in patients with a decrease in vitamin D reserves. The distribution of phosphatemia in patients with relative, moderate and severe vitamin D deficiency was 42.53; 45.14 and 42.1 mg/l. Average hemoglobin level was 9.41 +/- 1.82g/dl with [6.8 to 16.3 g/dl]. Eighty-one patients (72.9%) had anemia and 33 patients (27.1%) had normal hemoglobin.

Sixty-four patients (57.70%) had an electrocardiogram. Left ventricular hypertrophy was noted in 36 patients (56.25%) and left atrial hypertrophy in 17 patients (26.56%), epicardial ischemia in 10 patients (15.6%) and repolarization disorders in 7 patients (10.9%). Seventy-three patients (65.80%) had undergone transthoracic echocardiography. Arterial pulmonary hypertension in 45 patients (61.64%); concentric Left ventricular hypertrophy in 44 patients (60.27%), valvulopathies in 35.51% and septal hypertrophy in 17.81% of cases. Regarding the parameters of hemodialysis, the average duration of hemodialysis was 59.91 months with [6 to 204 months]. One hundred patients (91.7%) had 3 sessions of 4 hours per week and 9 patients (8.3%) had 2 sessions of 5 hours per week. Ninety-five patients (91.3%) underwent dialysis with a standard calcium bath at 1.5mmol/l and 9 patients (8.7%) had a calcium bath at 1.75mmol / l. On the therapeutic level, 57 patients (51.35%) with a decrease in vitamin D reserves were supplemented with native vitamin D3; 16.22% had not received any supplementation. After supplementation, thirty-two patients received a control dose with a return to normal of 25 (OH) D in 17 patients (53.1%) (Figure 2). Fourteen patients (12.6%) had parathyroidectomy, 85.7% of whom had the 7 / 8th method (subtotal parathyroidectomy).

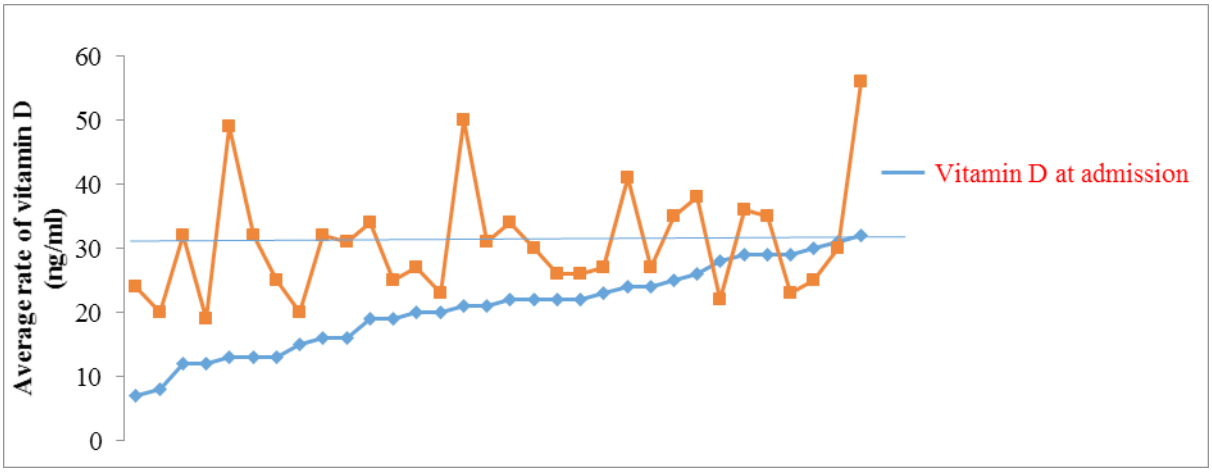

Figure 2: Vitamin D levels before and after supplementation.

Indications were nodules in 57.1% of cases and hyperplasia in 42.9% of cases. Ten cases (9%) of death were observed during our study period; causes were dominated by infections (n = 4), cardiorespiratory arrest (n = 3), and stroke (n = 3). 2) and slip syndrome (n = 1). In multivariate analysis, there was no statistically significant correlation between decreases in vitamin D reserves, age, sex, causative nephropathy, anemia, iPTH, electrical abnormalities, and mortality (p = 0.684). In bivariate analysis, there was a statistically significant correlation between the decrease in vitamin D reserves, diabetes and hypertension (p = 0.035), the onset of tricuspid insufficiency (p = 0.038) and seniority in hemodialysis upper than 60 months (p = 0.031). The main results of the study are summarized in (Table 1).

Features	Results
Population	Population of study: 342
	Population included: 111
Average age (years)	54,53
Sexe ratio	0,76
Initial nephropathy	Common nephroangiosclerosis: 47,75%
	Chronic glomerulonephritis: 13,51%
	Indeterminate nephropathy: 14,41%
Average level of Vitamin D: 22,87 ng/ml	Minimal deficiency: 51,4%
	Moderate deficit: 25,2%
	Severe deficit: 9%
Average rate of iPTH: 659,36 pg/ml	Hyperparathyroidism : 44,1%
	Normoparathyroidism : 44,1%
	Osteomalacia : 11,7%
Average calcium concentration	90,10 mg/l
Average Phosphatemia	42,95 mg/l

Table 1: Summary of the main findings of the study.

Discussion

In our study, 97 patients (85.6%) had vitamin D deficiency. At the dialysis stage, vitamin D deficiency affects 53.5 to 89% of hemodialysis patients [8,9]. Our results corroborate the work of Guillaume J. et al in France who noted a proportion of 78% of hemodialysis patients who were deficient [10]. The same was true in SUVIMAX cohort studies where 78% of chronic hemodialysis patients were found to be deficient [11]. In Senegal, in 2011 [12], prevalence of vitamin D deficiency was 32.6% whereas in Tunisia it was 47.6% [13]. The nutritional status of our patients has not been evaluated. However, a deficiency of intake could be the predominant mechanism. The average age of our work was 54.53 years, thus joining study data in Africa and Europe. An average age of 40.45 years, 50.16 years, 53.6 years, and 52 years were respectively found in Mali [14], Morocco [15], Tunisia [16], and Madagascar [17]. In France, 50% of chronic hemodialysis patients are older than 60 years [18]. This discordance between African countries and Western countries is mainly due to greater access to care for the elderly and a higher standard of living in industrialized countries [17,18].

Mean serum calcium was 90.10mg/l with [61 to 108mg/l]. This was consistent with the results of Rafi and Jebrane who had found respectively mean serum calcium levels of 90.75 and 99.5 mg/l [19,20]. But they were different in Africa with Diallo A.D, who found 60% of hypocalcaemia in Ivory Coast [21]. The average phosphatemia was 42.95 mg/l. Hyperphosphatemia was found in 46 patients or 41.4%. These results were similar to those of Rafi et al as well as Diallo A.D et al. with respectively 36% and 83% hyperphosphatemia in Côte d'Ivoire and Mali [21, 22]. The mean concentration of iPTH was 659.36 pg/ml. Hyperparathyroidism is noted in 44.1% of patients. These data are slightly higher than those found by Traoré, et al. [23], Benabdellah, et al. [24], with respectively an average of iPTH levels of 436.11pg/ml and 508pg/ml.

Regarding dialysis, majority of our patients (91.7%) had 3 sessions of hemodialysis of 4 hours. Rafi et al. [19] noted that 88.7% of patients had 12 hours of hemodialysis per week (3 weekly sessions of 4 hours). An earlier study by Ouattara F in Senegal in 2008 [25] found that 86.70% of patients received only two hemodialysis sessions per week. This difference is easily explained by the improvement of the technical platform with the creation of a new hemodialysis unit, increasing in the number of hemodialysis machines. Insufficient treatment by hemodialysis significantly increases the risk of osteoarticular complications, particularly those related to hyperphosphatemia, hence importance of respecting the 3 recommended hemodialysis sessions.

In our series, majority of patients dialyzed with a 1.5 mmol/l calcium bath (91.3%). The study of a French cohort of hemodialysis patients [26] showed that there was no difference in survival between three types of dialysate calcium (1.25, 1.5 and 1.75 mmol/l), however, a recently published study has shown that the decrease in PTH induced by a calcium-rich dialysis bath was an independent risk factor for cardiovascular mortality in chronic hemodialysis patients [27]. It appears important to be able to individualize the calcium prescription dialysate, which remains an effective way to control and adjust the calcium balance.

Low vitamin D levels are associated with cardiovascular risk factors in both the general population and patients with chronic renal failure [28]. In our study, there was a statistically significant correlation between the decrease in vitamin D reserves and the occurrence of tricuspid insufficiency ($p = 0.038$) as demonstrated by several studies of cardiovascular risk occurrence and low concentrations of 25 (OH) D [29]. Clinical studies in patients with chronic kidney disease have largely demonstrated that poor vitamin D status is an independent risk factor in incidence of cardiovascular disease [104]. Approximately 50% of patients in our series were supplemented with vitamin D. Holick MF, et al. [30] demonstrated that the dose of vitamin D required to correct hypovitaminosis D was 50,000 IU vitamin D2 every week for 8 weeks. To maintain adequate blood levels, continue with the same dose every 2 to 4 weeks. Treatment with vitamin D would reduce all-cause mortality. Thus, for the care of our patients, it would require not only vitamin D supplementation but also a more balanced diet to globally address the risk of other nutritional deficiencies.

Conclusion

Prevalence of vitamin D deficiency in our work was 85.6% with a vitamin D average plasma level of 16.1 ng/ml. Proportion of patients with relative insufficiency, moderate deficit and severe deficit was respectively 51.4%, 25.2% and 9%. Through this work, we prove that the management of vitamin D is a common problem but little studied. We noted that there was a statistically significant correlation between decreased vitamin D reserves, diabetes, hypertension, onset of tricuspid insufficiency and dialysis seniority greater than 60 months. This is a topical issue as more and more it is proven that vitamin D would have a protective effect against several cancers, diabetes, or autoimmune diseases such as multiple sclerosis. Vitamin D deficiency promotes the appearance of chronic kidney disease- mineral bone disorder. Limitations of this work were the weakness of the sample because the study should be extended to all dialysis centers in Senegal to refine the results and conclusions. Alkaline phosphatase and bone biopsy should also be included in further investigations.

Conflict of Interest

The authors do not declare any conflict of interest.

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