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RESEARCH ARTICLE

Aspects of Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD) in Chronic Hemodialysis Patients in Resource-Limited Countries: An Example of the Aristide Le Dantec University Hospital in Dakar (Senegal)

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Abstract

Introduction: Chronic kidney disease–mineral and bone disorder (CKD-MBD) are frequently encountered in chronic dialysis patients and are responsible for heavy morbidity and mortality with an impairment of their quality of life. Few studies are available in sub-Saharan Africa. The objectives of this study were to determine its prevalence in our resource-limited context, and to study its types, biological and therapeutic aspects.

Patients and methods: This is a single-center descriptive and analytical cross-sectional study over 15 months carried out in the dialysis units (hemodialysis and peritoneal dialysis) of the nephrology department at the Aristide Le Dantec University Hospital in Dakar. Patients on chronic dialysis for more than 3 months who had completed a complete phospho-calcium assessment during the study period were included.

Results: Eighty-three chronic dialysis patients were studied, among whom 76 patients (91.5%) had MBD. The average age of the patients was 47.94±13.41 years with a sex ratio of 0.9. The first causal nephropathy was hypertensive nephropathy found in 40.8% of cases. Length of time on dialysis was 7.46±3.71 years. Fifty-nine patients (i.e., 93.6% of cases) benefited from 3 hemodialysis sessions per week and 13 patients benefited from PD. Fifty patients (65.78%) had secondary hyperparathyroidism, 22 patients (28.94%) had tertiary hyperparathyroidism, 3 patients (3.94%) had adynamic bone disease, 1 patient (1.31%) had osteomalacia. For hyperparathyroidism, the average PTHi was 1555.55±1223.94 ng/ml (or 23.94 times of the upper limit of normal (ULN)). Insufficiency and deficiency of 25-OH Vitamin D were noted respectively in 68.42% and 1.32% of patients. Therapeutically, 48.68% of patients had received treatment based on calcium carbonate, 5.26% of patients had received treatment based on non calcium-based phosphate binders, 68.42% of patients had received vitamin D and 6.5% of cases had benefited from treatment with calcimimetics. Parathyroidectomy was performed in 21% of cases. Three patients had adynamic bone disease, the average age was 46.33±13.6 years. The average PTH was 56.33 ng/ml, the average serum calcium was 82.73 mg/l, the average serum phosphate was 45.23 mg/l and the average vitamin D was 32.13 ng/ml, only one patient had osteomalacia. Seven patients (11.5% of cases) had vascular calcifications.

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Conclusion: CKD-MBD are common among our hemodialysis patients, hence the need to implement a diagnostic and therapeutic strategy to better prevent them and, if necessary, manage them.

Keywords: CKD-MBD, Hyperparathyroidism, Adynamic bone disease, Osteomalacia, Chronic dialysis.

1. Introduction

The progressive decrease in glomerular filtration rate as observed during chronic kidney disease (CKD) is accompanied by significant mineral and metabolic disorders grouped under the term CKD-MBD for "chronic kidney disease - mineral and bone disorders". These disorders are characterized by biochemical abnormalities of phosphocalcic metabolism, bone remodelling and mineralization and by the development of vascular calcifications [1].

These disorders include osteitis fibrosa, adynamic bone disease (ABD), osteomalacia (OM) and vascular calcifications (VC). These abnormalities occur early in stage 3 of CKD and worsen progressively and more intensely at the dialysis stage [2].

Numerous observational studies have highlighted the epidemiological correlation between CKD-MBD and morbidity and mortality, mainly cardiovascular, in dialysis patients with an increase in mortality risk of 40 to 60%. These uncontrolled CKD-MBD seriously affect the quality of life of these patients in relation to gait disorders and pathological fractures [3].

International recommendations are regularly issued by the KDIGO (kidney disease: improving global outcomes), the most recent of which was published in 2017 [4]. It aims to prevent and control complications related to these CKD-MBD by recommending strict biological monitoring and therapies adapted according to the disorders identified. In Senegal, a previous study found a prevalence of 82.5% of CKD-MBD in chronic hemodialysis patients [5].

With a view to continuously improving the quality of life of hemodialysis patients in our hospital, we carried out this work which aims to determine the prevalence of CKD-MBD in our chronic hemodialysis patients, to study the clinical and biological aspects, radiological, therapeutic of these CKD-MBD and to identify the complications and risk factors associated with these CKD-MBD.

2. Patients and Methods

This is a single-center descriptive and analytical cross-sectional study carried out at the dialysis units (hemodialysis and peritoneal dialysis) of the nephrology, dialysis, and kidney transplantation department at the Aristide Le Dantec University Hospital in Dakar over a period of 15 months (1st January 2020 to March 30, 2021). The study population consisted of all chronic hemodialysis patients.

We included all patients on chronic dialysis for more than 3 months who had completed a complete phospho-calcium assessment during the study, namely: serum calcium; phosphoremia; 25 (OH) Vitamin D; iPTH and total alkaline phosphatase (ALP). Not included in the study: chronic dialysis patients on vacation in Senegal and patients dialyzed in another dialysis center in Senegal and treated for a temporary stay in our hospital.

The data were collected from the results of the CKD-MBD explorations and from the patients' medical files using a pre-established operating sheet which included: epidemiological data, dialysis parameters (duration on dialysis, number of sessions per week, number of hours of dialysis per week, type of vascular access, dialysis bath, Kt/V) clinical data, paraclinical data, type of CKD-MBD, and therapeutic data. The different types of CKD-MBD were selected based on the KDIGO 2017 criteria [4].

The data was collected on a pre-established form. They were entered using the "Excel 2016" software and analysed with SPSS software version 18. The data collected were expressed as a proportion (percentage) for the qualitative variables and as an average with their standard deviation for the quantitative variables.

The local ethics committee gave its approval for carrying out the study.

3. Results

Eighty-three chronic hemodialysis patients were studied, among whom 76 patients had mineral and bone disorders (i.e., 91.5%) (figure 1). The average age of the patients was 47.94±13.41 years, with extremes of 13 and 83 years. There were 40 women to 36 men, a sex ratio of 0.9. The first causal nephropathy was hypertensive nephropathy found in 40.8% of cases (figure 2). The average length of time on dialysis was 7.46 ± 3.71 years, with extremes of 6 months and 16 years. Fifty-nine patients (93.6% of cases) received 3 hemodialysis (HD) sessions per week, 4 patients (6.4% of cases) were only hemodialyzed twice per week. The average duration of the sessions was 3.93

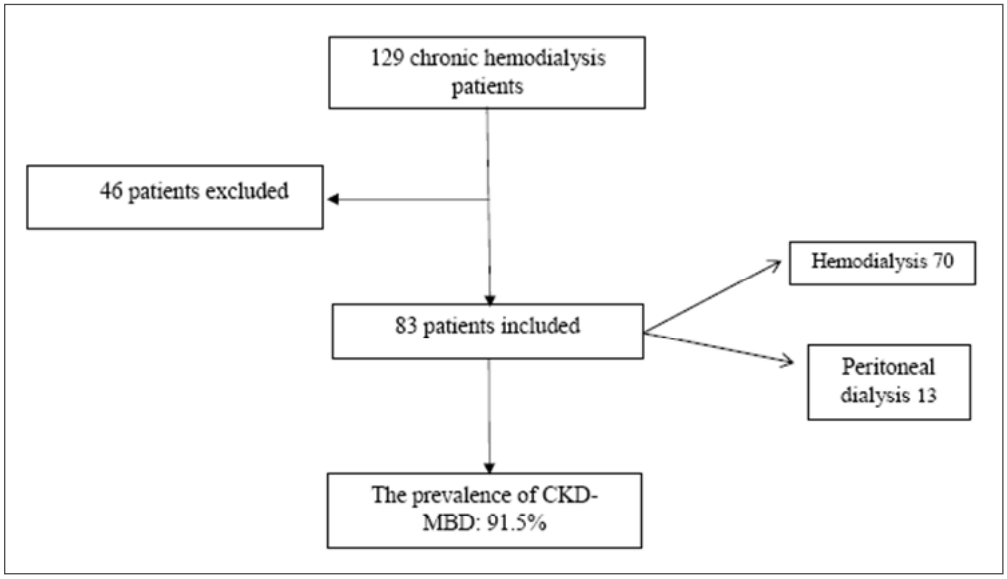

Figure 1. *Patient Flow Diagram*

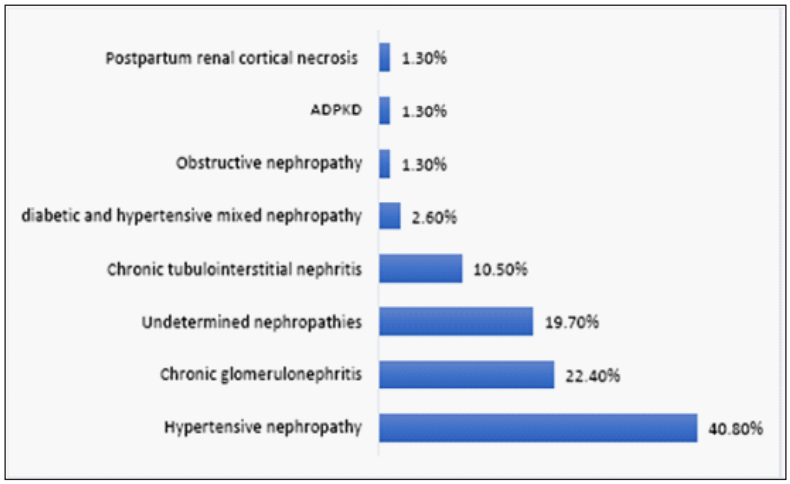

Figure 2. *Distribution of patients according to different causal nephropathies.*

± 0.39 hours. The weekly duration of HD sessions was 11.51 ± 0.63 h. Fifty-nine patients (93.6% of cases) had 12 hours of hemodialysis per week, while 3 patients (4.73% of cases) had 8 hours and one patient had 2 hours of dialysis per week.

Thirteen patients benefit from peritoneal dialysis (PD) including 9 continuous ambulatory peritoneal dialysis (CAPD) patients, and 4 automated peritoneal dialysis (APD) patients.

Forty-nine patients (44.1%) had AVF, while 14 patients (25%) were dialyzing on a temporary venous catheter and 13 patients (17.10%) were on peritoneal dialysis. The dialysis composition was identical during all hemodialysis sessions: Sodium: 138 mmol/l, Potassium: 2 mmol/l, Calcium: 1.5mmol/l and bicarbonate: 32mmol/l.

However, after each parathyroidectomy, a dialysate with calcium at 1.75 mmol/l was used until the serum calcium level was corrected. The average KT/V was 1.46±0.19 with extremes of 0.8 and 1.9.

Concerning the type of CKD-MBD, fifty patients (or 65.78%) had Secondary hyperparathyroidism (SHPT). Twenty-two patients (28.94%) of the cases had tertiary hyperparathyroidism (THPT). Three patients (3.94%) had ABD. Only one patient (i.e., 1.31%) of the hemodialysis patients had osteomalacia (figure3).

As regards the secondary hyperparathyroidism, there were 27 women and 23 men, i.e., a sex ratio of 0.85, and the average age was 50.44±12.3 years. For tertiary hyperparathyroidism, there were 14 women and 8 men, i.e., a sex ratio of 0.57 with a mean age of 43.42±11.5 years.

On the biological level for the 2 types of hyperparathyroidism, the average serum calcium was 86.33 ± 11.14 mg/l with extremes of 38 mg/l and 115 mg/l, 33.33% of patients had a hypocalcemia and one had hypercalcemia. The mean phosphate level was 35.67 ± 14.07 mg/l, with extremes of 7 mg/l and 87 mg/l, 52.77% of patients had hypophosphatemia and 6.9% had hyperphosphatemia.

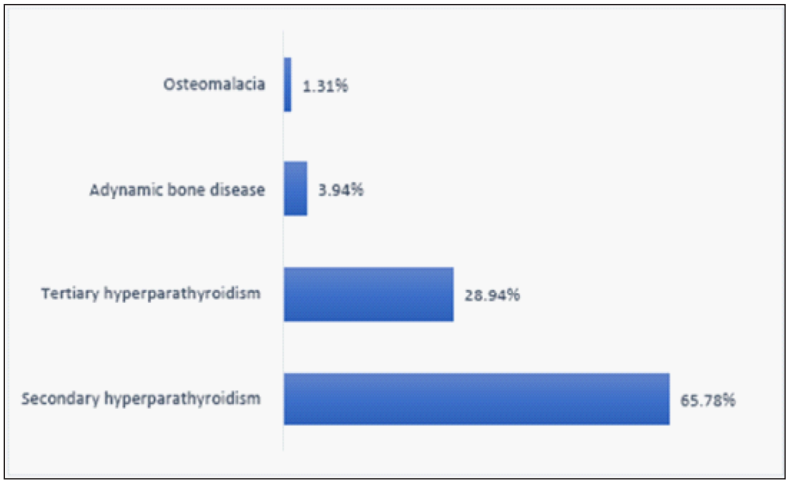

Figure 3. *Distribution of patients according to type of mineral and bone disorder.*

The average PTH was 1555.55±1223.94 ng/ml (or 23.94 times of the upper limit of normal (ULN)). The average value of 25-OH-vitamin D was 26.46±10.96 ng/ml, 68.42% of patients had Vitamin D insufficiency, one patient was deficient, and 30.26% had normal vitamin D. The average total ALP was 364.9 IU/l (or 2.7 N). Seven patients (i.e., 11.5% of cases) had vascular calcifications.

Therapeutically for hyperparathyroidism, thirty-seven patients (or 48.68%) had benefited from treatment with calcium carbonate. Four patients (5.26%) had received treatment with non calcium-based phosphate binders. Fifty-two patients (i.e., 68.42%) had received vitamin D, of which 39 patients (i.e., 75%) had received native vitamin D, 5 patients (i.e., 9.6%) had received alfacalcidol and eight patients (i.e., 15.38%) had received native vitamin D combined with alfacalcidol. Five patients (i.e., 6.5%) had received treatment with calcimimetics (Cinacalcet).

Sixteen patients (i.e., 21.05%) had undergone parathyroidectomy (PTX), the indication for surgical intervention was secondary hyperparathyroidism uncontrollable by medical treatment for 7 patients (i.e., 43.75%), tertiary HPT in 6 patients (i.e., 37.5%) and tertiary HPT on a remaining stump in 3 patients (i.e., 18.75%).

Concerning the adynamic bone disease identified in three (one woman and two men), the average age was 46.33±13.6 years. The mean PTH was 56.33 ng/ml, with extremes of 47 and 61 ng/ml. Mean serum calcium was 82.73 mg/l, mean serum phosphate was 45.23 mg/l, and mean 25-OH vitamin D was 32.13 ng/ml. There was no aluminium toxicity. In one patient, the ABD was secondary to cinacalcet and in the other two patients, the cause was undetermined. Concerning osteomalacia observed in one patient, serum calcium was normal at 87 mg/l, serum phosphate at 26.6 mg/l, her PTH was normal, and hypovitaminosis D at 12 ng/ml. X-rays of the pelvis and hips revealed Looser-Milkman streaks. She was supplemented with native vitamin D.

4. Discussion

In our study, 91.5% of hemodialysis patients had mineral and bone disorders. This prevalence is higher than the literature series [6-9]. It could be explained by insufficient financial resources, but also by the unavailability of certain medications for our patients such as calcimimetics and non calcium-based phosphate binders.

The average age of the patients was 47.94 ±13.41 years. In developed countries, the average age of patients was significantly higher, over 65 years, as evidenced by data from the 2010 REIN registry [10]. The young age of our patients could explain the youth of the general Senegalese population [11].

The average duration on dialysis in our series was 7.46 ± 3.71 years. This is consistent with the results found by Damoune in Morocco [34] and by Yingying in China [12] where the average duration of hemodialysis was 7.13 ± 3 years and 5.1 ± 4.7 years respectively.

In our study, 94.7% of patients had HPT, of which 28.94% were tertiary. The average PTH was 1555.55 ng/ml (i.e., 23.94 times of the upper limit of normal (ULN)). The very high rate of PTHi in our study, higher than those recommended by the KDIGO, could be explained by the absence of regular monitoring of phosphocalcic balance due to lack of financial means but also by the unavailability of a dietician in the center for control the diet of patients. This common HPT in our context can be explained by the frequency of vitamin D deficiency. The first Senegalese study

which aimed to study the prevalence of reduced vitamin D reserves in black-skinned subjects undergoing periodic hemodialysis, conducted by Cissé et al. In 2012, it was found that 62% of hemodialysis patients had a moderate to severe 25-OH-Vitamin D deficiency [13].

Thus, these studies clearly showed that the hemodialysis population is a population particularly affected by vitamin D deficiency, despite the high solar exposure in our patients who live in a country with a high rate of sunshine, this would be due to the skin pigmentation which blocks ultraviolet B rays necessary for the synthesis of vitamin D [14].

For the efficient management of HPT, several constraints exist in our context: the expensive cost of calcimimetics and non-calcium-based phosphate binders and the absence of medical insurance for our patients. The frequent use of PTX in our context would be a good alternative to the prescription of calcimimetics for the reasons explained above. However, this surgery remains expensive because it is not included in the care of hemodialysis patients in Senegal.

Adynamic bone disease and osteomalacia, despite their low frequency in our patients, deserve special monitoring to avoid serious complications, particularly pathological fractures. The latter were found in 7.89% of patients and considerably impaired their quality of life.

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