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Factors Associated with Poor Control of Hypertension in Patients with Non-Dialysis Chronic Renal Failure

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Abstract

Introduction: Arterial hypertension is frequently encountered in patients with chronic renal failure. Whether primary or secondary to kidney disease, hypertension remains an important risk factor not only for the progression of kidney disease but also for the occurrence of cardiovascular events. Currently, there is no data on the control of hypertension in CKD patients in Chad. The main objective of this study was to determine the factors of poor control of hypertension during CKD and their therapeutic modalities. **Methodology:** This is a cross-sectional, descriptive and analytical study carried out over a period of 8 months from September 1, 2021 to May 31, 2022 in the Nephrology Department of the Renaissance University Hospital Center in N'Djamena, Chad. During the study period, patients aged 18 years and above, which were hospitalized and/or followed for CKD with uncontrolled hypertension were included. **Results:** A total of 1013 patients were consulted during the study period, however, 36 cases were included, with a hospital prevalence of 3.5%. The mean age of the patients was 60 ± 9.68 years [22 and 75 years]. The patient's history was dominated by hypertension (94.4%) and diabetes (41.7%). The main risk factors of hypertension found were diabetes (38.9%), physical inactivity (19.4%) and obesity (36.1%). Type 2 diabetes was present in 38.9% (n = 14) of the patients. There was a statistical relationship between unbalanced diabetes and poor blood pressure control ($p < 0.001$). Grade 1, 2 and 3 hypertension accounted for 47.2% (n = 17), 25% (n = 9) and 27.8% (n = 10), respectively. According to the GFR estimate, 12 patients (33.3%) had stage 3 chronic kidney disease, 13 patients (36.1%) had stage 4 chronic kidney disease and 11 patients (30.6%) had stage 5 chronic kidney disease. 18 patients (50%) were treated with monotherapy, 15 patients (41.7%) were treated with

dual therapy with at least one included an angiotensin II receptor blocker, at least one molecule was a blocker of the renin-angiotensin system and 3 patients (8.3%) were treated using a triple antihypertensive therapy. The factors involved with poor control of hypertension were the grade of hypertension ($p = 0.036$), monotherapy ($p = 0.042$), stages 4 and 5 of CKD ($p = 0.011$) and dilation of the heart chambers ($p < 0.001$). **Conclusion:** Patients with chronic renal failure are at a risk of developing hypertension. Good control of blood pressure prevents deterioration of kidney function.

Keywords

Hypertension, Chronic Kidney Disease, Chad

1. Introduction

Chronic renal disease (CKD) is defined as the presence of kidney damage with an estimated glomerular filtration rate (GFR) of <60 ml/min/1.73m^2 [1] [2]. Hypertension is frequently encountered in CKD patients. Whether primary or secondary to kidney disease, it remains an important risk factor for the progression of kidney failure. In 2017, there were 1.13 billion hypertensive people worldwide, with more than 100 million hypertensive people in Africa [3] [4]. It affects approximately 31% of adults (WHO 2017), compared to a global average of 22% (WHO 2014) [5]. In France, hypertension and diabetes represented in 2018 nearly, half of the causes of chronic end-stage renal failure [6]. However, declining kidney function associates with a higher risk of occurrence of cardiovascular events. It has been demonstrated the occurrence of carotid atherosclerosis early in CKD patients with cardiovascular risk factors including hypertension and diabetes [7]. The cardiovascular risk becomes greater as soon as the GFR is <45 ml/min/1.73m^2 [8]. This association is partly explained by an increase in the prevalence of hypertension as renal function decreases [9]. In Madagascar, out of 210 CKD patients included, hypertension was found in 41.3% [10]. In Chad, in a study carried out in 2016 which collected 195 patients at the General Hospital, hypertension was noted in 66.2% of CKD cases including 1/4 of the patients were in chronic dialysis [11]. This is why the control of blood pressure in hypertensive patients with CKD slows down the deterioration of renal function and also reduces the occurrence of cardiovascular events [12] [13]. There is no available data in Chad on the control of hypertension in CKD patients, which justifies the present study in aiming to improve the management of arterial hypertension during chronic renal failure, but more specifically to determine the factors of poor control of hypertension during CKD and their therapeutic modalities.

2. Methodology

This was a cross-sectional, descriptive and analytical study carried out over a pe-

riod of 8 months from September 1, 2021 to May 31, 2022 in the Nephrology Department of the Renaissance University Hospital Center in N'Djamena, Chad. Patients aged 18 years and above, which were hospitalized and/or followed in consultation for stage 3, 4 and 5 of non-dialysis CKD with uncontrolled hypertension were included.

We conducted an exhaustive recruitment of all patients meeting the inclusion criteria. The quantitative survey technique was used for data collection. This collection was carried out using a pre-established survey form for each respondent and filled in from the data of the clinical and paraclinical examinations. Missing information had been completed through a telephone interview of the patients included. Then, we proceeded to the exploitation of therapeutic files.

Each patient included in the study had received a clear and detailed information note on the objectives and purpose of the study with an informed consent. Patients with isolated systolic hypertension, on dialysis and/or on kidney transplant associated with hypertension were not included.

Hypertension is defined by a systolic blood pressure of ≥140 mmHg and/or diastolic blood pressure of ≥90 mmHg associated with or without taking antihypertensive medications [14] [15]. Controlled or optimal hypertension is defined by a PA of ≤140/90 mmHg (patient without proteinuria or diabetes), a BP of ≤130/80 mmHg (patient with diabetes or chronic kidney disease (CKD) with proteinuria < 1 g/24h) and BP ≤ 125/75 mm Hg (patient with proteinuria ≥ 1 g/24h) [10] [11]. CKD is defined by an irreversible decrease in the estimated glomerular filtration rate (GFR) of less than 60 ml/min/1.73m^2 for more than 3 months, which was estimated by the MDRD formula [16]. A low-sodium diet is a diet based on the reduction of sodium intake of <2 g of salt per day according to the KDIGO 2021 recommendations (Kidney disease improving global outcomes). Data collection and analysis were performed using SPSS software version 18.0. Microsoft Excel 2013 software was used to organize the data in the form of tables and figures. Data entry was done by Microsoft Word 2013 software. The quantitative variables were expressed as a mean plus or minus standard deviation, minimum, maximum and percentage. Qualitative variables have been organized into subgroups. The results were presented as a percentage in the form of tables, pie charts and histograms. The statistical correlation tests requested were the T-student test for the comparison of means and the Chi-square test, Fisher's Exact test and linear regression for the comparison of percentages and proportions. For these comparisons, a probability of $p < 0.05$ was considered statistically significant.

3. Results

A total of 1013 patients were consulted during the study period, however, 36 cases were included with a hospital prevalence of 3.5%. The mean age of the patients was 60 ± 9.68 years [22 and 75 years]; there were 47.2% of patients that were at most 58 years old. The male gender was noted in 52.8% (n = 19) with a sex ratio of 1.12. All of the patients lived in urban areas while 52.8% (n = 19) did

not work. The main risk factors for hypertension found were diabetes (38.9%), physical inactivity (19.4%) and obesity (36.1%). Type 2 diabetes was present in 38.9% (n = 14) of patients. In 92.9% of patients, the diabetes duration was more than 36 months. All of the diabetic patients were on medication, 50% (n = 7) of which were on oral antidiabetic medications. There was a statistical relationship between unbalanced diabetes and poor blood pressure control ($p < 0.001$).

The urinary dipstick showed significant proteinuria of 2 to 3 crosses confirmed by quantitative proteinuria greater than 1 g/24 hours in 14 patients (38.8%). The general examination noted systolic hypertension in 55.6% (n = 20) patients, diastolic hypertension in 8.3% (n = 3) patients and systolic-diastolic hypertension in 36.1% (n = 13) patients. Grade 1, 2 and 3 hypertension accounted for 47.2% (n = 17), 25% (n = 9) and 27.8% (n = 10), respectively. The distribution of the different stages of chronic kidney disease with hypertensive patients is summarized in Figure 1, while the clinical and paraclinical characteristics are summarized in Table 1.

According to the GFR estimate, 12 patients (33.3%) had stage 1, 13 patients (36.1%) had stage 4, and 11 patients (30.6%) had stage 5 chronic kidney disease. During the cardiac ultrasound, the cardiac chambers were dilated in 8.3% of cases (n = 3).

18 patients (50%) were treated with monotherapy, 15 patients (41.7%) were treated with dual therapy with at least one included an angiotensin II receptor blocker and 3 patients (8.3%) with triple antihypertensive therapy.

On the therapeutic level, 36.1% (n = 13) did not respect the low sodium diet. The antihypertensives prescribed were antagonists of the renin-angiotensin-aldosterone system (63.9%), calcium channel blockers were prescribed in 38.9% of patients (Table 2). Poor compliance with antihypertensive treatments was noted in 36.1% of patients (n = 13). While poorly controlled hypertension was present in 41.7% (n = 15). In multivariate analysis, the factors involved in the poor control

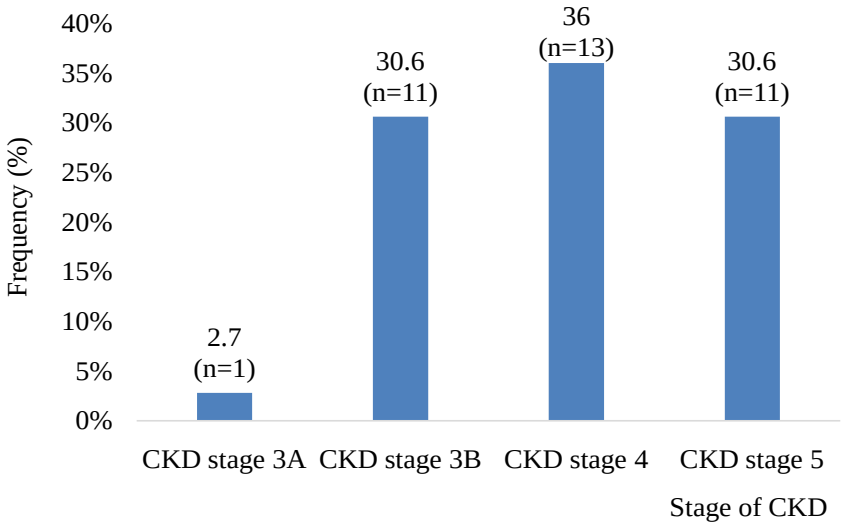

Figure 1. Distribution of hypertensive patients according to the stage of chronic kidney disease.

Table 1. Clinical and paraclinical characteristics of patients.

Data	Effective	Frequency (%)
Age (year)		
18 - 49	3	8.3
50 - 57	8	22.2
58 - 65	17	47.2
>65	8	22.
Male	19	52.8
Female	17	47.2
Cardiovascular risk factors		
Diabetes	14	38.9
Sedentary lifestyle	7	19.4
Overweight	13	36.1
Clinical data		
Uremic syndrome (nausea, asthenia)	6	16.7
Headaches, visual disturbances	18	50
Lower limb edema	4	19.4
Dipstick		
Proteinuria	14	38.8
Hematuria	3	8.3
Arterial pressure		
Systolic hypertension	20	56.6
Diastolic hypertension	3	8.3
Systolic-diastolic hypertension	13	36.1
Grade 1	17	47.2
Grade 2	9	25
Grade 3	10	27.8
Electrocardiogram		
Myocardial ischemia	1	2.8
Arrhythmias and conduction disturbances	2	5.5
Ventricular hypertrophy	1	2.8

Table 2. Therapeutic data.

Data	Effective	Frequency (%)
Low sodium diet	23	63.1
Normal diet	13	36.9
Antihypertensive treatment		
Monotherapy	18	50
Dual therapy	15	41.7
Tritherapy	3	8.3

Continued

Therapeutic classes		
Renin angiotensin system blockers	23	63.9
Calcium channel blockers	14	38.9
Beta-blockers	2	5.6
Diuretics	17	47.5
Therapeutic compliance		
Good	23	63.9
Bad	13	36.1

of hypertension were poor therapeutic compliance (Khi2 = 12,166[a]; ddl = 1; p < 0.04), grade of hypertension (Khi2 = 11,142[a]; ddl = 3; p = 0.036), proteinuria (Khi = 4905[a]; ddl = 2; p = 0.02), monotherapy (Khi2 = 6643[a]; ddl = 3; p = 0.042), stages 4 and 5 of CKD (Khi2 = 6331[a]; ddl = 3; p = 0.011) and dilatation of the heart chambers (Khi2 = 8445[a]; ddl = 2; p = 0.011; P < 0.001).

4. Discussion

The prevalence in our study was 3.5%. These low figures are partly explained by the limitations of this study. The limits are related to the small sample size whom is explained by the quality of writing of the medical files but also by the quality of the medical follow-up. Many patients disappear during follow-up or are followed in peripheral health centers making it difficult to trace them. Hypertension and CKD maintain close and complex links. With the different causes and consequences, hypertension is definitely a factor in the progression of CKD and one of its main complications. A Paris cohort study carried out in 2016 on the determinants of hypertension control in a population of adult patients with CKD found a prevalence of 94% [17]. In Africa, its exact prevalence is not known, it varies according to the series. Several studies had found a hospital prevalence of 66.6% in the Democratic Republic of Congo, 52.7% in Senegal and 48.7% in Tunisia [18] [19] [20].

The patients are relatively young (mean age 60) with a male predominance (52.8%). This male predominance has been reported generally by most authors [21] [22] [23]. The absence of specialized care hospitals, the high prices of anti-hypertensive medications and the lack of phytotherapy would explain the high proportion of the severity of hypertension and chronic kidney disease. These results are similar to data observed by other authors in developing countries [18] [24]. The personal medical history was dominated by hypertension (94.4%) and diabetes (41.7%). Studies have shown that in Africa, the main risk factor for kidney damage is hypertension [25] [26]. The non-modifiable risk factors of hypertension are represented by age, diabetes and chronic renal disease. Hypertension is frequent and severe in dark-skinned people with rapid development of lesions of cardiac, cerebral and renal target organs [27]. Dark-skinned subjects

have a higher morbidity and mortality in all blood pressure levels [28].

In our study, systolic hypertension is present in half of the cases. This isolated systolic hypertension is accompanied by an increase in pulse pressure. Pulse pressure is itself an independent cardiovascular risk factor. In our study, grade 2 and grade 3 hypertension combined were noted in 52.8% of patients. The electrocardiogram was pathological in 11.1% of the cases (myocardial ischemia, cardiac hypertrophy, arrhythmias and conduction disorders) and the echocardiography pathological in 8.3% of the cases (dilation of the heart chambers). The main cause of these blood pressure abnormalities is the accelerated aging of the arterial system, characterized by abnormal rigidity of the aorta and central arteries, especially in the case of CKD [28]. The management of hypertensive patients was based on lifestyle and dietary measures (86.1%), and pharmacological treatment where the main therapeutic classes of drugs which were prescribed in our study were RAAS inhibitors, diuretics and calcium channel blockers in 63.9%, 47.2% and 38.9% respectively, as found in similar studies but in different proportions [29] [30].

Nevertheless, RAAS inhibitors remain the treatment of choice in the management of proteinuric hypertensive patients with or without CRD and in diabetic patients because of their triple antihypertensive, antiproteinuric and cardioprotective action [29]. Reducing sodium intake reduces proteinuria as well as diurnal and nocternal blood pressure values. A low-sodium diet also increases the effectiveness of RAAS inhibitors, whether or not associated with diuretics. Poor compliance with antihypertensive medications is noted in 1/3 of cases. In Africa, it would be linked to the popular belief that is oriented towards healers in the event of illness and to the economic situation. The dilation of the heart chambers and the severe stage of CKD are factors of poor blood pressure control. This would be largely linked to the increase in blood volume in this context, which is an independent deterrent of resistant hypertension and uncontrolled hypertension during CKD [17]. A good control of hypertension in CKD would take into account these 4 mechanisms including activation of the sympathetic system, water and sodium retention, hyperactivation of the RAAS and endothelial dysfunction.

5. Conclusion

In this study, the prevalence of hypertension in CKD patients is high. Hypertension is one of the major causes of CKD. Factors of poor blood pressure control are parameters to be taken into account in reducing cardiovascular morbidity and mortality related to CKD.

Conflicts of Interest

The authors declare no conflict of interest.

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Abbreviation

GFR: glomerular filtration rate, CKD: chronic kidney disease, RAAS: renin-angiotensin-aldosterone system.