

# Hyperuricemia in Patients with Chronic Renal Failure in the General Hospital of National Reference of N'Djamena (Chad)

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## Abstract

**Introduction:** Hyperuricemia is defined as a level of serum uric acid greater than or equal to 70 mg/l (420 µmol/l) in men and 60 mg/l (360 µmol/l) in women. Several studies have shown that it is a risk factor or a factor of progression of chronic kidney disease. Recent experimental and epidemiological data correlate the association of hyperuricemia with chronic kidney disease (CKD), arterial hypertension and cardiovascular diseases, thus raising the question of the usefulness of therapeutics in the prevention of renal diseases. The objective of this study is to seek a link between chronic kidney disease and hyperuricemia. **Materials and Methods:** This is a descriptive and analytical study conducted at hemodialysis unit and cardiology service of General Hospital of National reference of N'Djamena (Chad) from 1<sup>st</sup> January to 1<sup>st</sup> October 2013 (10 months). We included all chronic kidney disease patients hospitalized in hemodialysis unit and cardiology service who presented associated hyperuricemia. **Results:** There were 712 CKD patients who were hospitalized. Among them, there were 108 patients who were included in the study and who had hyperuricemia as a prevalence of 15.20%. The average age of patients was 35.5 years and the sex ratio was 3/1. The age group between 40 to 60 years represented 54.6%. There were 41.7% of traders. Hypertensive patients accounted for 49.1%; association of diabetes and hypertension was noted in 12.90%. Renal insufficiency was moderate in 43.5% of patients. Hyperuricemia was present in more than 90% of patients. Profession, age, hematuria, proteinuria and hypertension were statistically positively related to

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hyperuricemia. Treatment consisted of prescribing allopurinol in 84% of patients. In more than 11% of patients the progression was unfavorable. **Conclusion:** The implication of hyperuricemia in chronic kidney disease has been proved in several recent studies. However, randomized studies at very long scales have to be carried out to conclude from its real impact on the prevention and treatment of chronic kidney disease.

## Keywords

Component, Formatting, Style, Styling

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## 1. Introduction

Chronic kidney disease (CKD) is a major public health problem in the world [1]. Indeed, it is the twelfth cause of death and the seventeenth cause of disability in the world [2]. Its prevalence and incidence have increased significantly in recent years worldwide [3]. In sub-Saharan Africa, the CKD mainly affects young adults in their productive age and is a significant cause of death reducing life expectancy [3] [4] [5]. This epidemic is multifactorial in origin. It is often accompanied by hyperuricemia. Hyperuricemia is defined as a level of serum uric acid greater than or equal to 70 mg/l (420  $\mu$ mol/l) in man and 60 mg/l (360  $\mu$ mol/l) in women. It is a factor of occurrence or progression of chronic kidney disease by several studies. However, it is difficult to know whether hyperuricemia is a risk factor for the development or progression of the CKD. Hyperuricemia may be a consequence of decreasing of glomerular filtration rate (GFR), reflecting tissue hypoxia or cell lysis associated with renal disease [6] [7]. Also the frequent association of hyperuricemia with other risk factors such as high blood pressure, diabetes and cardiovascular diseases makes difficult its causal link between development and progression of the CKD. Recent experimental and epidemiological data correlate the association of hyperuricemia with CKD, arterial hypertension and cardiovascular diseases, thus raising the question of the usefulness of therapeutics in reducing of hyperuricemia for prevention of renal disease [8]. A recent study in Australia of 21.475 healthy volunteers followed prospectively for 7 years suggests that hyperuricemia is an independent risk factor for the onset of chronic kidney disease [9]. However, there are few studies on the association of hyperuricemia with the development or progression of renal disease in Africa. This work was initiated for the first time in Chad to study the impact of hyperuricemia on the epidemiological, clinical and paraclinical profile of patients with chronic renal insufficiency.

## 2. Materials and Methods

The study was conducted in the nephrology-hemodialysis unit and cardiology service of General Hospital (GHNR) of National Reference in N'Djamena. This is a descriptive and analytical study conducted at hemodialysis unit and cardiology

service of General Hospital of National reference of N'Djamena (Chad) from 1<sup>st</sup> January to 1<sup>st</sup> October 2013 (10 months). We included all chronic kidney disease patients hospitalized in hemodialysis unit and cardiology service who presented associated hyperuricemia. The information was collected on fact sheets from patients and their families. We have obtained the informed consent of patients. Socio-demographic characteristics of the patients (age, sex, level of education, profession, provenance); Anthropometric measurements (weight, height, waist circumference, body mass index); Eating habits (smoking, alcoholism, excessive consumption of meat or sugary drinks); Clinical data (medical history, duration of development, reason for consultation, clinical signs on physical examination); biologic data (hemogram, serum creatinine, azotemia, uricemia, creatinine clearance, lipid balance, blood ionogram, hematuria, proteinuria (positive if >300 mg)), the management and finally the prognosis of the patients were analyzed.

- Hyperuricemia was defined as a level of serum uric acid greater than or equal to 70 mg/l (420  $\mu$ mol/l) in man and 60 mg/l (360  $\mu$ mol/l) in women.
- The classification of nutritional status according to the WHO and the International Obesity Task Force (1998) was used:
  - Undernutrition is a body mass index (BMI) of less than 18.5 kg/m<sup>2</sup>
  - BMI between 18.5 and 24.9 kg/m<sup>2</sup> is considered normal in an adult;
  - BMI between 25 - 29.9 kg/m<sup>2</sup>, it is overweight (overweight);
  - Moderate obesity was defined as a BMI of 30 - 34.9 kg/m<sup>2</sup>;
  - Severe obesity was defined as a BMI of 35 - 39.9 kg/m<sup>2</sup>
  - Morbid obesity was defined as a BMI > 40 kg/m<sup>2</sup>.
- Arterial hypertension: elevation of blood pressure > 140 and/or 90 mmHg.
- Smoking was defined by the use of smoking tobacco during the last 30 days prior to this consultation.
- Only regular consumption of alcohol, sugary drinks and meat was taken into account without being quantified: yes versus no.

The data obtained were analyzed using Excel and SPSS (Statistical Package for Social Sciences 18.0).

### 3. Results

#### 1) Epidemiology

During our study period, 712 CKD patients were hospitalized and among them, there were 108 patients who were included in the study and who had hyperuricemia as a prevalence of 15.20%. Concerning the profession there were 45 traders (41.6%), 27 housewives (25.7%), 18 civil servants (16.6%), 9 drivers (8.3%) and 9 soldiers (8.3%) as shown in **Table 1**. The mean age was 35.5 years and the extremes were 29 to 85 years. The age group 40-60 years represented 54.6% of the cases and the sex ratio was 3/1. All patients consumed meat per day; 100 patients (92.6%) were taking sweet drinks; 76 (70.3%) took at least 2 cup of alcohol per day; 32 patients smoked tobacco (29.6%).

#### 2) Clinic and paraclinic:

Regarding risk factors there were 53 patients who were hypertensive (49.1%),

14 patients who were diabetic and hypertensive (12.9%) and 8 diabetic patients (7.4%). It was noted that 33 patients had no risk factors (30.6). Regarding BMI, the mean BMI was  $29.5 \pm 12.4$ , there were 39 overweight patients (36.1%), 28 patients (25.9%) with moderate obesity, 19 with severe obesity (17.6%), 8 patients (7.4%) with morbid obesity, 9 normal BMI patients (8.4%) and 5 moderate undernutrition patients (4.6%). For the waist circumference there were 68 (62.9%) patients whose measurement was greater than 102 cm and 38 patients between 88 and 102 cm (35.2%). It was noted that 2 patients had waist circumference less than 88 cm (1.8%). The mean uric acid level was  $65.4 \pm 12.8$  mg/l. It was noted that 64 patients (94%) had uric acid levels up to 90 mg/l and 44 patients had hyperuricemia between 70 and 90 mg/l. The distribution of our patients according to the stage of chronic renal insufficiency was summarized in **Table 2**. Moderate chronic renal insufficiency (CKD 3) was observed in 43.5% of cases. There were 5.6% of patients who were at the terminal stage. Severe anemia with hemoglobin less than 8 g/dl was noted in 69.5% of patients. Ninety-six patients, 88.9% (N = 96), had serum creatinine levels greater than 14 mg/l and 25% had more than 80 mg/l. Univariate analysis showed that there is a statistically positive relationship between hyperuricemia and age of patients (40 to 60 years and 61 to 80 years with respectively  $p = 0.0000$  and  $p = 0.003$ ), high blood pressure and occupation (trader and housewife with  $p = 0.0005$ ). Treatment consisted of prescribing Allopurinol in 83.3% of patients. In 88.9% the trend was favorable.

#### 4. Discussion

During our study period, 108 hyperuricemic patients were included. The total

**Table 1.** Distribution of patients according to occupation.

Occupation	n	%	Uricemia (mg/l)			p
			<70	70 - 90	>90	
Driver	9	8.3	1	3	5	0.839
Trader	45	41.7	4	6	35	0.0005
Fonctionnaire	18	16.7	0	6	12	0.448
Housewife	27	25.0	2	15	10	0.0005
Military	9	8.3	0	7	2	0.015
Total	108	100	7	37	64	

**Table 2.** Distribution of patients according to GFR.

GFR (ml/mn)	Patients	Percentage
>90	12	11.1
60 -89	9	08.3
<b>30 - 59</b>	<b>47</b>	<b>43.5</b>
15 - 29	34	31.5
<15	6	05.6
Total	108	100.0

population was 712 patients, as a prevalence of hyperuricemia of 15.20%. It was superior to other studies carried out in the Indian population of the Amazon region of Brazil with 5.6% [12], and 5.1% in healthy Spanish male subjects, a study conducted in Valencia (54), but lower than results in Russian and hypertensive patients' study (31%) [10] [11] [13].

The most affected age group was 50 - 60 years (54.6%) with a male predominance (sex ratio = 3). The male sex confers a double univariate risk but a quadruple multivariate risk of hyperuricemia [14]. These results confirm the data from the Framingham study showing higher values of uric acid in men compared to women [15]. Estrogens in women have a depressing effect on urates [16]. The male sex aged over 55 years and the female sex aged over 65 were cited as cardiovascular risk factors [17]. Associated with hyperuricemia, age increases the likelihood of stroke in both sexes, and myocardial infarction in men [18].

Of the 108 patients, 70.3% consumed alcohol. Our result was superior to that of LON-GO *et al.*, who reported 20% excess univariate risk of hyperuricemia due to alcoholism [14]. The abuse of alcohol consumption is the basis of gout attacks [19] [20] [21]. Obesity has been identified as a multivariate risk factor for hyperuricemia. Obesity, an independent variable, confers a double risk of hyperuricemia to Congolese hypertensive patients [14]. Our result is lower than that of Jean *et al.* who reported 30% excess risk of hyperuricemia in Congolese Kinshasa patients linked to obesity [14]. Longo-Mbenza *et al.* found a positive and very significant correlation between body weight and uric acid in a population where hyperuricemia was isolated as a significant risk factor for stroke and coronary heart disease [18]. The role of insulin resistance in the pathogenesis of cardiovascular diseases in African black, as emphasized by Longo-Mbenza [22] [23], will be the challenge to be overcome by African researchers in eradicating the epidemic of chronic non communicable diseases. Its reflection blood biology is hyperuricemia and hypertriglyceridemia as suggested by the work of Clausen [24].

In our study, 32 hyperuricemic patients were active smokers, as 29.6%. Our result was lower than that of Jean *et al.*, who reported 67.4% of patients with hyperuricemia among tobacco users [14]. Smokers have a univariate risk of hyperuricemia twice as high as their non-smoking colleagues. Longo-Mbenza *et al.* had already demonstrated a significant association between cigarette smoking and high levels of uric acid [18]. Other studies in the literature confirm this significant relationship between smoking and hyperuricemia [25] [26]. Majority of our patients had a high waist circumference. High waist circumference values define insulin resistance. This positive and significant relationship between waist circumference and hyperuricemia confirms data from the literature that considers hyperuricemia as a component of insulin resistance/metabolic syndrome [18] [19] [24] [25] [26] [27].

In our study, 67 patients (62%) were hypertensive with statistically positive relationship between hyperuricemia and hypertension. The positive and significant relationship between hyperuricemia and blood pressure has been observed

in Congolese patients in Kinshasa [18] and in other literature [10] [11] [19] [25] [28] [29]. Interpret as blood pressure may be a consequence of hyperuricemia. The present study considers the implications of the discovery of hyperuricemia in patients with essential arterial hypertension [29]. Indeed, no patient had a gout attack despite hyperuricemia [18]. But some attacks of gout settle with a normal blood level of uric acid [30]. This prevalence of asymptomatic hyperuricemia has already been estimated to be very high in Polynesian women [31].

Some studies have shown that hyperuricemia is associated with a high risk of kidney disease incidence [32] [33], but this association may be confused by factors not included in these previous studies [34]. Hypertension was considered a confounding factor. However, studies have shown that hyperuricemia is an independent risk factor for hypertension [35]. In our study, normotensive patients with hyperuricemia had developed renal disease. Our result is similar to that of Bellomo *et al.*, which reported that each increase of 10 mg/l (59  $\mu$ mol/l) was associated with 23% risk of decreased GFR greater than 2 ml/min/year (after adjustment of confounding factors) in healthy normotensive adults [12]. A randomized clinical trial in hyperuricemic adolescents with hypertension (the decrease in uricemia under allopurinol was related to a decrease in blood pressure) changed the classic design where the cardiovascular drop-risk association in some studies was due to 1 Gout belongs to the metabolic syndrome [36].

The decrease in GFR was considered to be a key confounding variable, as serum uric acid elevation is generally associated with transport defects in nephrons when renal function deteriorates [37]. This study did not record the pre-existing nephropathy in patients who may explain the occurrence of hyperuricemia. Also in a study including 117 non diabetic patients with CKD (mean GFR  $64 \pm 39$  ml/min/1.73m<sup>2</sup>) with doubling of creatinine or terminal renal failure requiring dialysis did not have a higher uric acid level than other patients [38]. Similarly, in a retrospective study analyzing 223 patients with Ig A nephropathy, hyperuricemia was observed in association with an increased risk of progression of the chronic kidney disease [39] but was no longer statistically significant after adjustment for Confounding factors. Nevertheless, uric acid may have an independent role in the development of tubulo-interstitial lesions and contribute to inflammation in the renal parenchyma observed in these patients [40] as in other chronic glomerulopathies [41]. Thus, although hyperuricemia may be a consequence of a pre-existing kidney disease, these results show the involvement of uric acid in renal diseases.

In our study, 65 patients, as 59.7%, did not have a pathological history that could explain the occurrence of a kidney disease other than the hyperuricemia they presented. But compared with the large international cohorts in this field, our study was limited by the weakness of the sample. Thus, in a study involving 21,475 healthy volunteers in Australia followed on average for 7 years, the risk of developing a CKD 3 stage was 26% higher in individuals with slightly higher than normal uric acid levels (416 - 526  $\mu$ mol/l or 70 to 90 mg/l). This result would prove the implication of uric acid in renal disease. Thus, an improvement

in renal function under allopurinol 100 mg/d in a randomized study involving 113 patients was observed [42].

## 5. Conclusion

Hyperuricemia has long been associated with chronic kidney disease. In our study, 108 hyperuricemic patients suffering from chronic kidney disease had no other factors that could explain the occurrence of their disease. It is common in the majority of hypertensive patients. Factors such as male sex, age, obesity, smoking, abuse of alcohol and sugary drinks, waist circumference, blood glucose and blood pressure are risk factors for hyperuricemia. A statistically significant relationship has been found between hyperuricemia, hypertension and the profession. The implication of hyperuricemia in renal disease is proved by several recent studies. However, large-scale randomized studies seem necessary to determine whether the reduction in uric acid has a beneficial effect on the prevention or treatment of this condition.

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## Abbreviations

GFR: glomerular filtration rate;  
CKD: chronic kidney disease;  
BMI: body mass index.



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