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Clinical, Etiological and Progressive Aspects of Acute Tubular Necrosis of Toxic Origin at the Brazzaville University Hospital Center

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Abstract

Background and Objectives: Acute tubular necrosis (ATN) is the second cause of acute kidney injury (AKI) in an intra-hospital environment. The toxic origin is avoidable. Our objectives were to determine the toxic substances at the origin of ATN at the Brazzaville University Hospital and determine the evolving aspects and the factors associated with it. **Patients and Methods:** We carried out a 12-month from June 20, 2022 to June 30, 2023. It was a prospective observational study in the Nephrology Department of Brazzaville University Hospital Center. The diagnosis of ATN was done in the presence of AKI occurring in the context of taking nephrotoxic substances with negative albuminuria. Cases of ATN aggravating CKD were excluded. Data analysis was done with Epi-Info 7.2 software. **Results:** We identified 63 cases of AKI on toxic ATN. Their average age was 47 ± 19 years with a male predominance of 60.2%. The 3 main toxicants incriminated were: herbal medicine (49.2%), Gentamycin (17.5%) and non-steroidal anti-inflammatory drugs (14.3%). An indication for hemodialysis was made in 43 patients (68.2%), the evolution was marked by a cure in 29 patients (46.1%), 10 (15.9%) became chronic kidney failure, 19 (30.1%) died, 5 (7.9%) were lost to follow-up. The main factor for non-healing is anuria ($p < 0.001$) and diabetes ($p < 0.001$). **Conclusion:** The main cause of toxic ATN at Brazzaville University Hospital is herbal medicine. The death rate is high there.

Keywords

Brazzaville, Acute Tubular Necrosis, Toxic

1. Introduction

Acute kidney injury (AKI) is defined as an increase in serum creatinine of 50% in 7 days, or 3 mg/L in 2 days, or oliguria [1]. In practice, it is a rapid decline in renal function occurring over several hours or several days, characterized by metabolic disturbances, which, if major, can quickly have lethal consequences [2]. It is staged in 3 stages depending on its severity [3]. Pathophysiologically, we distinguish 3 types of AKI: pre-renal AKI, intrinsic renal AKI and post-renal AKI with various etiologies [4]. In Sub-Saharan Africa, the intra-hospital incidence rate of AKI is estimated at 25.3% [5]. And the acute tubular necrosis (ATN) toxic origin is the second cause of AKI after infections [6]. Indications for dialysis are common [7] [8]. In the Republic of Congo, the intra-hospital incidence of AKI is reported at 13.4% [7], dehydration and ATN of toxic origin are the main causes [7]. Intrinsic renal AKI is a risk factor for chronic kidney disease (CKD) [9]. Dialysis centers are rare in Congo [7] [8], so it is necessary to place an emphasis on prevention. Prevention of ATN involves controlling its etiologies, and therefore toxic substances, in order to avoid them. Our study had two objectives of describing the clinical profile of toxic ATN and determining the toxic substances at the origin of ATN in Brazzaville, the evolutionary aspects and the factors associated with healing.

2. Methodology

We carried out a prospective observational study in the Nephrology Department of Brazzaville University Hospital Center. It was spread over a period of 12 months from June 20, 2022 to June 30, 2023. The diagnosis of ATN toxic origin was retained in front of an AKI occurring as part of a toxic intake with tubular-type urinary sediment (albuminuria negative) and an ultrasound of the urinary tract without obstructive signs. We excluded from our sample toxic acute tubular necrosis superimposed on CKD: and toxic ATN by intratubular precipitation of myoglobin (rhabdomyolysis), hemoglobin (massive hemolysis), bile and light chains of immunoglobulins.

We studied age, gender and socio-economic level and classified into three groups based on professional activities (low; medium and high); co-morbidities: high blood pressure (HBP), diabetes mellitus (DM), heart disease, human immunodeficiency virus (HIV) infection; diuresis; the type of toxicant, the duration between nephrology treatment and exposure to the toxicant, the stage of AKI following the KDIGO (Kidney Disease Improval Global Outcomes) 2012 staging, the indication for dialysis, recovery of renal function. Data were collected from hospitalization medical files and post-hospitalization consultation files.

We treated 256 cases of acute renal failure and 63 met our selection criteria. **Figure 1** shows the different stages of selection of our sample.

The representation of tables and graphs was enriched with Microsoft Excel 2019 software. Qualitative variables were presented in numbers and percentages in parentheses with their confidence intervals. The mean and its standard deviation, the

maximum and the minimum were used to present the continuous quantitative variables. Discrete quantitative variables were presented by the mean and its standard deviation. For comparisons, the chi-square test was used for percentages, and the Student t test for means. The significance threshold was set at $p < 0.05$. The data were analyzed with Epi-Info software 7.2.4 version.

3. Results

3.1. Sociodemographic Characteristics

Patients with AKI caused by toxic ATN were 63 representing a frequency of 24.6 % of causes of AKI in the Nephrology Department of Brazzaville University Hospital. The average age of patients with toxic ATN was 47 ± 19 years (min = 21 years max = 63 years. Their distribution according to age intervals is shown in Figure 2. We counted 38 men (60.3%) and 25 women (39.7%), *i.e.* a sex ratio of 1.5. When evaluating the socio-economic level, 27 patients (42.8%) had a low socio-economic level, 29 (46.0%) had a medium socio-economic level and 7 (11.1%) high socio-economic level.

3.2. Clinical Characteristics

The duration between exposure to the toxicant and admission to nephrology was on average 14 ± 7.5 days. We found hypertension due to water and sodium retention in 9 patients (14.3%). 57 patients (90.5%) had a normal BMI; 5 were overweight 1 patient was obese (1.6%). Oliguria or anuria was found in 28 patients (44.4%). 31 patients had no associated comorbidity. Figure 3 shows the representation of our sample according to comorbid-dities. The mean serum creatinine at 86.3 ± 53.6 mg/L. 43 patients (68.3%) had KDIGO stage 3 AKI and 20 (31.7%) at stage 2.

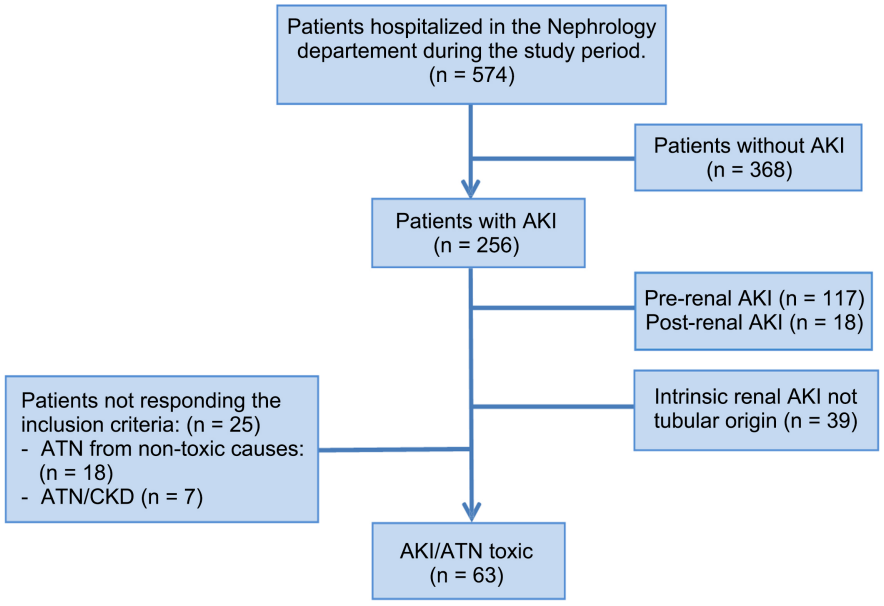

Figure 1. Flow diagram.

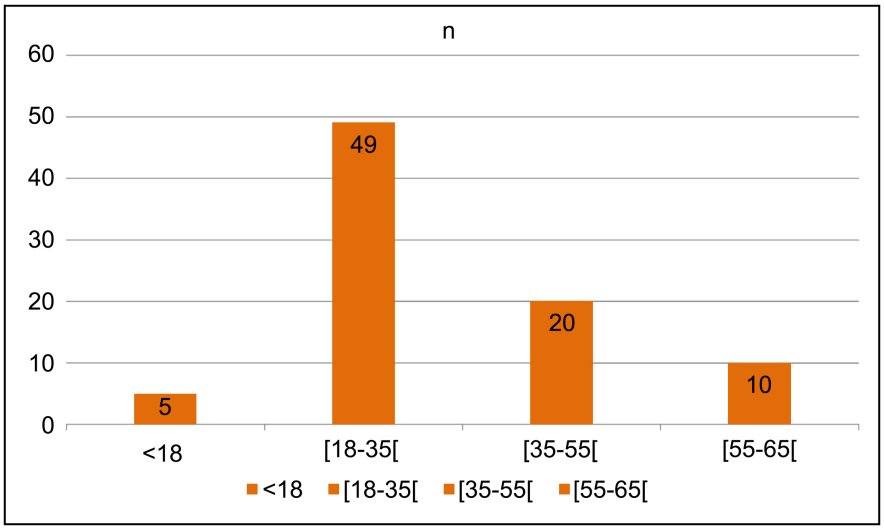

Figure 2. Distribution of patients with ATN of toxic origin according to age.

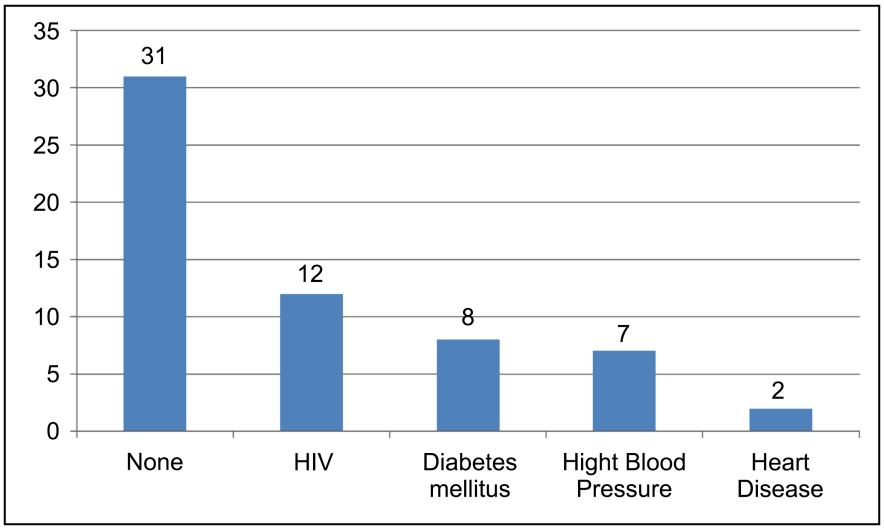

Figure 3. Distribution of patients with ATN of toxic origin according to t co-morbidities.

3.3. Types of Nephrotoxic Substances

Herbal medicine was the leading cause of ATN with 31 patients affected (49.2%). It was consumed in the form:

- Tysanne made from plant leaves purchased in a market;
- Tree bark purchased at the market.

However, the nature of the plants and trees used were not known to the patients. Table 1 represents the different types of toxic substances found and their proportions.

Nephrotoxic drugs were implicated in 31 patients (49.2%). The different molecules found are also cited in Table 1. 64% of nephrotoxic medications were recommended by medical prescription in a hospital under prescription. The places of recommendation of the drug which caused the ATN are reported in Figure 4.

3.4. Treatment and Evolution

Dialysis was indicated in 43 patients (68.3%); 19 patients had access to hemo-dialysis (30.1%). The other patients (24 patients) with an indication for dialysis did not do so due to lack of finances. The evolution was marked by a cure in 29 patients (46.1%); 10 (15.9%) became chronic, 19 (30.1%) died; 5 (7.9%) were lost to follow-up. The results of the comparative analysis between patients who recovered renal function and those who did not are shown in Table 2.

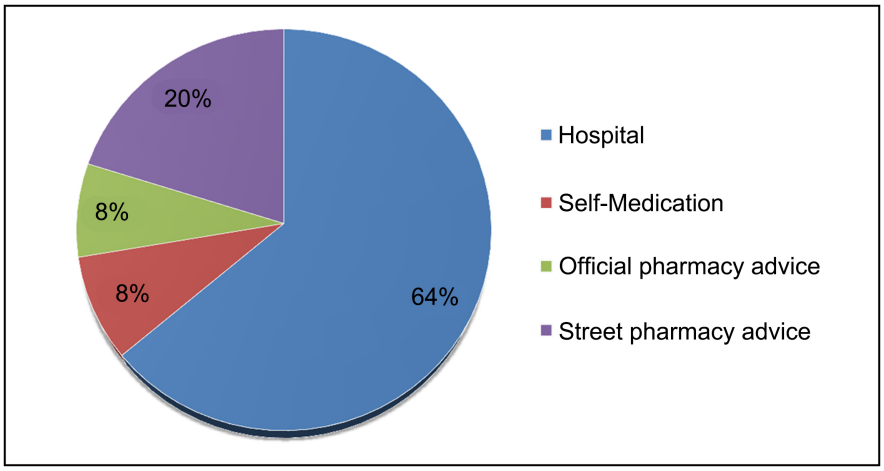

Figure 4. Recommendations drugs places.

Table 1. Nephrotoxic substances.

Nephrotoxic Substances	Herbal Medicine	Aminosides (Gentamycin)	NSAIDs*	Tenofovir	RC**
n (%)	31 (49.2)	11 (17.5)	9 (14.3)	5 (7.9)	7 (11.1)

*Non-steroidal anti-inflammatory drugs; **radiocontrast.

Table 2. Factors for non-recovery renal function and died.

	ATN Toxic Kidney Function Recovered N = 29 n (%)	ATN Toxic Patients Died or Lost Kidney Function N = 29 n (%)	OR [IC 95%]	p-value
Oligo Anurie	7 (24.1)	21 (72.4)	8.25 [2.54; 26.78]	**0.0001**
HBP*	3 (10.3)	2 (20)	2.17 [0.3; 15.3]	0.43
Diabetes Mellitus	3 (10.3)	5 (17.2)	1.8 [0.39; 8.4]	0.42
Overweight/Obesity	2 (6.9)	4 (13.8)	0.46 [0.08; 2.75]	0.35
Heart Diseasei	0 (0%)	2 (7)	-	0.7
HIV	8 (27.6)	4 (13.8)	2.38 [0.63; 9.03]	0.20
Dialysis	16 (55.2)	27 (93.1)	10.97 [2.19; 54.99]	**<0.001**

*Hight blood pressure.

4. Discussion

AKI due to toxic tubular necrosis is common in hospitals [7] [10] [11] [12]. Our work reported a frequency of 24.6% of causes of AKI. In New Jersey (USA), Weisberg *et al.* found 23.8%.

The patients concerned were young, with a male predominance and AKI mainly at KDIGO stage 3. This trend has been found in other studies [7] [13] carried out in intra-hospital settings in Sub-Saharan Africa. This increased vulnerability of the youngest can be explained by the use by this age group, traditional medical plants and nephrotoxic drugs sold without medical prescription by street sellers, reputed to be cheaper and more effective. Thus street pharmacies were found to be the second place of recommendations of nephrotoxic substances in our study. However, the fact that more than 60% of prescriptions for nephrotoxic drugs were made in hospital environment, this raises the question of knowledge of the renal risk of certain medications and precautions to be taken by healthcare personnel. Substances nephrotoxic were mainly plant extracts (44.4%) in the form of oral decoction. Our data on the nephrotoxicity of traditional plants for use medical studies join those of other African authors [13] [14] [15]. Fouda Menye *et al.* in Cameroon reported that traditional plants were responsible for AKI in 44.5% of cases of toxic ATNs. In other studies, the plants were identified [13] [14]. This is not the case in our work. This could be explained by the feeling of guilt felt by our patients and the refusal to direct the investigators towards the places of purchase, for fear of harming the sellers. Drug substances come second, molecules concerned are Gentamycin, NSAIDs and Tenofovir. The majority of patients were at stage 3 of AKI. This can be explained by the untrahospitable nature with as samples from patients hospitalized in nephrology. The second position occupied by medicinal molecules contrasts with the origin of the incriminated drugs, which more than 60% came from official pharmacies while more than 60% received these molecules. This poses the problem of access to certain medications in our pharmacies without a medical prescription. Indications for dialysis are high (68.2%) our results agree with those of Fouda Menye *et al.* in Cameroon who found 62.5% of indications for dialysis in toxic ATN [13]. In USA, Weisberg *et al.* found an indication of 66% dialysis in toxic ATNs [16]. All this is explained by the late diagnosis linked to a recourse late in medical consultation since the average duration between taking the toxicant and the nephrology consultation lasted more than 15 days; associated with this, the evolution of silent renal failure, symptomatic only in cases of severity. The rates of renal non-recovery and deaths are high. The high number of deaths can be explained by the inequity of access to hemodialysis in Brazzaville [17].

The main factors linked to non-recovery of renal function or deaths are the indication for dialysis and anuria.

5. Conclusion

Acute tubular necrosis of toxic origin is common and responsible for several

deaths in our context. The subjects concerned are young. It causes severe AKI, leading to hemodialysis sessions in more than half of cases. The reduction in diuresis is the main factor in poor prognosis. The use of traditional medical plants remains the primary cause and their compositions are unknown. Nephrotoxic drugs are also responsible, notably Gentamycin.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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