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Acute Renal Failure in Hospitals in Togo: Comparative Analysis of HIV Positive Patients and HIV Negative Patients

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Abstract

Introduction: Human Immunodeficiency (HIV) is a risk factor often associated with the occurrence of Acute Renal Failure (ARF). **Objectives**: To describe the profile of Acute Renal Failure (ARF) in HIV-infected patients and compare them to non-infected patients. **Patients and Methods:** It was a prospective study from January 2018 to February 2019 that took place in the nephrology, infectious diseases and internal medicine departments of the Sylvanus Olympio University Hospital Center in Lomé (Togo). **Results:** The prevalence of ARF in HIV-infected patients was 48.07%. HIV-infected patients had an average age of 46.9 ± 11.6 years ($p = 0.36$) compared to 44.0 ± 20.4 years for non-HIV infected patients. Female sex was predominant in the HIV-infected population with a sex ratio H/F of 0.6 ($p < 0.0001$) versus 2.9 for the non-infected. The reasons for admission were such as fever (28%), digestive disorders (56%) were more common in HIV-infected patients than non-infected patients (11.1%, 37%). Infected patients had more diarrhea than non-infected patients (24% versus 7.4%) with $p = 0.01$. They showed more signs of infections than uninfected patients (40% versus 18.5%) with $P = 0.02$. HIV infection was known before admission in 96% of cases. Patients whose HIV was known before admission had hypertension (16.7%), diabetes (12.5%) and CD4 count < 200 (/mm^3) in 50% of cases. HIV infected patients had more anemia (52.0% versus 22.2%) with $p = 0.002$. **Conclusion:** No deaths were recorded in the HIV-infected group.

Keywords

ARF, HIV, Togo

1. Introduction

Acute Renal Failure (ARF) is a generic term characterized by a sudden decrease in glomerular filtration rate resulting in the retention of nitrogenous waste [1]. In Africa, the causes of ARF are dominated by infections, toxic causes and gyneco-obstetrical causes [2]. Since the advent of HIV infection over the past two decades, several studies have described the incidence and causes of ARF in infected patients [2]. Indeed, before the introduction of HAART, opportunistic infections and deep immunosuppression were the most common conditions associated with episodes of acute renal failure (ARF) [3]. Currently, less than 10% of ARFs are due to problems with nephrotoxicity of antiretrovirals [3].

In Togo, no studies on the prevalence of ARF in HIV-infected patients have yet been conducted. For us, it is therefore a question of looking for the particularities of ARF in HIV-infected patients and comparing them to non-infected patients.

2. Materials and Methods

2.1. Case of Study

Our study was carried out in the nephrology, internal medicine and infectious diseases departments of the Sylvanus Olympio University Hospital in Lomé. In addition to the care activities, these various services also carry out training and research activities.

2.2. Type and Period of Study

This was a prospective study from January 2018 to February 2019 that compared infected patients to HIV non-infected patients.

2.3. Study Population

It is based on an exhaustive sampling by reasoned choice of patients hospitalized in the Nephrology, Internal Medicine and Infectiology Department of the Sylvanus Olympio University Hospital of Lomé in Togo.

2.4. Inclusion Criteria

Included in our study were subjects of both sexes, all age included, and hospitalized for ARF. The HIV test was performed after informed consent of the patients. HAART was initiated after an initial biological checkup including (HIV typing, blood count-formula, CD4 count, serum creatinine, uremia, serum calcium and phosphoremia) and in agreement with the patient. Informed consent was obtained of all participants prior to data collection. The collection of information gathered as part of this study complied with the medical code of ethics.

2.5. Criteria of Non-Inclusion

Patients who were not hospitalized or who refused to participate in the study were not included.

2.6. Data Collection Technique

The data were collected using a pre-established survey form with the following main variables: serum creatinine and plasma urea; demographic data (age, sex); comorbidities (diabetes mellitus, hypertension). Clinical data (reason for admission, blood pressure at admission, temperature, state of consciousness, state of hydration, diuresis and CDC classification of HIV infection), laboratory data (serum creatinine, plasma urea, calcium, phosphoremia, hemoglobin level, leukocyte count, platelets, cytobacterioligical urine exam, blood culture, HIV serology, CD4 cell count) and imaging data (renal echostructure) were also analyzed. A serum creatinine assay at D0, D3, D7 and at 3 months made it possible to evaluate the evolution of the ARF. This evolution was considered favorable if serum creatinine decreased by at least 50% compared to baseline creatinine. The causes of ARF such as sepsis, water loss, bleeding and administration of nephrotoxic drugs have been analyzed.

2.7. Data Analysis Technique

Data entry and statistical analysis were carried out using the EPI Info software version 2.4. A univariate analysis (5% significance threshold) was performed using the chi2 test. The tables and figures were created using the EXCEL 2013 software.

2.8. Parameters Definition

- The ARF was defined according to K/DIGO recommendations [4], based on serum creatinine values determined in hospitalization. The ARF was also grouped into 3 stages according to K/DIGO recommendations [4].
- Oliguria is defined by diuresis of less than 500 ml/24 hours.
- Anemia is defined for hemoglobin level below 12 g/dl in women and 13 g/dl in men. It has been described as severe for hemoglobin levels below 8 g/dl in both sexes.
- Diabetes mellitus and high blood pressure have been diagnosed according to the World Health Organization (WHO) criteria.
- Sepsis was diagnosed in accordance with the consensus of the American College of Chest Physicians and the Society of Critical Care Medicine consensus.
- HIV infection has been classified according to the Center for Disease Control and Prevention (CDC) classification.

Data on the viral load of infected patients have not been analyzed. Indeed the viral load is not made at the beginning of antiretroviral treatment in our context in Togo; it is done after 6 months of well conducted treatment.

3. Results

A total of 104 patients were enrolled in this study, 50 of whom were HIV-infected, representing a prevalence of 48.07% of patients. HIV-infected patients had an average age of 46.9 ± 11.6 years with OR of 0.9 [IC = 0.9 - 1] and p = 0.36 versus 44.0 ± 20.4 years for non-HIV-infected patients (**Table 1**). The female sex was

predominant in the HIV-infected population with an M/F sex ratio of 0.6 ($p < 0.0001$) versus 2.9 for the uninfected (Table 1). The reasons for admission were such that fever (28%), digestive disorders (56%) were more common in HIV-infected patients than non-infected patients (11.1%, 37%). Clinically, HIV-infected patients had more infectious stigmas than non-infected patients during ARF with $p = 0.02$ (Table 1 and Table 2). Among the etiologies found, the presence of infection was associated with the occurrence of ARF ($p = 0.02$) (Table 2). The presence of infectious diarrhea in HIV-infected patients was statistically related to the occurrence of ARF ($p = 0.01$) (Table 3). HIV infection was known before admission in 96% of cases. Patients whose HIV was known before admission had hypertension (16.7%), diabetes (12.5%) and CD4 count < 200 (/mm^3) in 50% of cases as shown in Table 4. The general and clinical characteristic remains are grouped in Table 1, Table 4 and Table 5. HIV-infected patients had more anemia (52.0% versus 22.2%) with $p = 0.002$ (Table 6). This anemia was more severe in infected patients whose serological status was not known before admission $p = 0.02$ (Table 4). Regarding the staging of the ARF, no differences were found in the two groups (Table 6).

Table 1. General characteristics of patients with acute renal failure.

Characteristics	HIV Positive	Non-Positive HIV	Value p	OR (IC 95%)
	(n = 50)	(n = 54)		
Average Age	46.9 ± 11.6	44.0 ± 20.4	0.36	0.9 (0.9 - 1.0)
Sex-Ratio (M/F)	**0.6 (18/32)**	**2.9 (40/14)**	**0.0001**	-
MR Risk Factors				
High Blood Pressure	16.0% (8/50)	14.8% (8/54)	0.86	1.1 (0.3 - 3.2)
Diabetes	12.0% (6/50)	7.4% (4/54)	0.42	1.7 (0.5 -6.4)
Reason for admission				
Fever	28.0% (14/50)	11.1% (6/54)	0.02	3.1 (1.1 - 8.9)
Loss of Consciousness	-	7.4% (4/54)	0.05	2.0 (1.6 - 2.4)
Dyspnea	**24.0% (12/50)**	**-**	**0.0001**	**2.4 (1.9 - 3.1)**
Digestive disorders	**56.0% (28/50)**	**37.0% (20/54)**	**0.05**	**2.0 (1.6 - 2.4)**
Convulsion	-	7.4% (4/54)	0.05	2.0 (1.6 - 2.4)
Dysuria	8.0% (4/50)	14.8% (8/54)	0.27	0.5 (0.01 - 1.7)
Oedema	8.0% (4/50)	7.4% (4/54)	0.91	1.1 (0.3 - 4.6)
Renal failure	56.0% (28/50)	48.1% (26/54)	0.42	2.0 (1.6 - 2.4)
Coma	-	3.7% (2/54)	0.17	1.9 (1.6 - 2.4)
Other Reasons	12.0% (6/50)	11.1% (6/54)	0.89	1.1 (0.3 - 3.7)
Clinical Signs				
Non Feverish Icterus	5.0% (2/50)	8.3% (4/54)	0.53	1.8 (1.5 - 2.3)
Feverish Icterus	-	8.3% (4/54)	0.06	1.9 (1.6 - 2.3)
Non Febrile Coma	-	100% (2/54)	0.17	0.5 (0.4 - 0.6)
Gastroenteritis	20.0% (8/50)	20.8% (10/54)	0.92	0.9 (0.3 - 2.6)
Pyelonephritis	15.0% (6/50)	8.3% (4/54)	0.32	1.9 (0.5 - 7.4)

Table 2. Comparison of Patients by ARF etiologies.

Etiologies	HIV Positive	Non Positive HIV	Value p	OR (IC 95%)
	(n = 50)	(n = 54)		
Water Loss	28.0% (14/50)	40.7% (22/54)	0.17	0.06 (0.2 - 1.3)
Haemorrhage	-	3.7% (2/54)	0.17	1.9 (1.6 - 2.4)
Nephrotoxic drugs	40.0% (20/50)	25.9% (14/54)	0.12	1.9 (0.8 - 4.3)
Benign Tumor VU	-	-	-	-
Cancer	8.0% (4/50)	3.7% (2/54)	0.34	2.6 (0.4 - 12.9)
Infections	**40.0% (20/50)**	**18.5% (10/54)**	**0.02**	**2.9 (1.2 - 7.1)**
Other	8.0% (4/50)	3.7% (2/54)	0.34	2.3 (0.4 - 12.9)

UT: Urinary Tract.

Table 3. Distribution of patients by types of infection.

Types of Infections	HIV Positive	Non Positive HIV	Value p	OR (IC 95%)
	(n = 20)	(n = 10)		
Acute Pyelonephritis	8.0% (4/50)	3.7% (2/54)	0.34	2.3 (0.4 - 12.9)
Infectious Diarrhea	**24.0% (12/50)**	**7.4% (4/54)**	**0.01**	**3.9 (1.2 - 13.2)**
Pleuro-Pneumopathy	4.0% (2/50)	3.7% (2/54)	0.9	1.1 (0.1 - 7.9)
Malaria	4.0% (2/50)	3.7% (2/54)	0.9	1.1 (0.1 - 7.9)

Table 4. Characteristics of HIV positive patients known or unknown before admission.

Parameters	HIV Known before Admission			
	Yes (n = 48)	No (n = 2)	Value p	OR (IC 95%)
Male Sex	37.5% (18/48)	-	0.97	1.1 (1.0 - 1.2)
High Blood Pressure	16.7% (5/48)	-	0.52	1.1 (0.9 - 1.1)
Diabetes	12.5% (6/48)	-	0.59	1.0 (0.9 - 1.1)
Water Loss	29.2% (14/48)	-	0.36	1.1 (0.9 - 1.1)
Nephrotoxic Drugs	41.7% (20/48)	-	0.23	1.1 (0.9 - 1.1)
Infections	37.5% (18/48)	100% (2/2)	0.07	0.9 (0.8 - 1.0)
CD4 Count < 200 (/mm^3)	50.0% (24/48)	100% (2/2)	0.16	0.9 (0.8 - 1.0)
Cancer	8.3% (4/48)	-	0.67	1.0 (0.6 - 1.1)
AIDS Stage	45.8% (22/48)	-	0.2	1.1 (0.9 - 1.2)
ARF Stage 3	58.3% (28/48)	100% (2/2)	0.23	0.9 (0.8 - 1.0)
Anemia	54.2% (26/48)	-	0.13	1.1 (0.9 - 1.2)
Severe Anemia	**25% (12/48)**	**100% (2/2)**	**0.02**	**0.8 (0.7 - 1.1)**
Other	8.3% (4/48)	-	0.67	1.0 (0.9 - 1.1)

Table 5. Characteristics of patients with or without ARV triple therapy at admission.

Parameters	ARV Triple Therapy		Value p	OR (IC 95%)
	Yes (n = 34)	**No (n = 14)**		
Male Sex	29.4% (10/34)	57.1% (8/14)	0.07	0.3 (0.9 - 1.1)
High Blood Pressure	17.6% (6/34)	14.3% (2/14)	0.77	1.3 (0.2 - 7.3)
Diabetes	11.8% (4/34)	14.3% (2/14)	0.81	0.8 (0.1 - 4.9)
AIDS Stage	52.9% (18/34)	28.6% (4/14)	0.12	2.8 (0.7 - 10.7)
ARF Stage 3	64.7% (22/34)	42.9% (6/14)	0.16	2.4 (0.1 - 1.6)
Anemia	58.8% (20/34)	42.9% (6/14)	0.31	1.9 (0.5 - 6.7)
Severe Anemia	29.4% (10/34)	14.3% (2/14)	0.27	2.5 (0.5 - 13.3)
CD4 count < 200 (/mm³)	**58.8% (20/34)**	**28.6% (4/14)**	**0.05**	**3.6 (0.9 - 13.7)**
Water Loss	35.3% (12/34)	14.3% (2/14)	0.14	3.3 (0.6 - 17.1)
Infections	41.2% (14/34)	28.6% (4/14)	0.41	1.7 (0.5 - 6.7)
Cancer	5.9% (2/34)	14.3% (2/14)	0.33	0.3 (0.1 - 2.9)
Other	11.8% (4/34)	-	0.18	1.4 (1.2 - 1.8)

Table 6. Distribution of patients according to biological signs.

Biologiques Signs	HIV Positive	Non Positive HIV	Value p	OR (IC 95%)
	(n = 48)	**(n = 54)**		
ARF Stage				
Stage 1	32.0% (16/50)	33.3% (18/54)	0.88	0.9 (0.4 - 2.1)
Stage 2	8.0% (4/50)	7.4% (4/54)	0.91	1.1 (0.3 - 4.6)
Stage 3	60.0% (30/50)	59.3% (32/54)	0.93	1.0 (0.5 - 2.2)
Plasma Urea				
>30 mmol/L	20.0% (10/50)	40.7% (22/54)	0.02	0.4 (0.2- 09)
Anemia	**52.0% (26/50)**	**22.2% (12/54)**	**0.002**	**3.8 (1.6 - 8.8)**
Severe Anemia	28.0% (14/50)	18.5% (10/54)	0.25	1.7 (0.7 - 4.3)

4. Discussion

To our knowledge, this is the very first study in Togo that compares the characteristics of ARF in HIV-infected patients with those that are not infected. HIV prevalence was 48.07% in the surveyed ARF population. This prevalence was higher than that observed by KH Yao *et al.* [5] in Ivory Coast on a population of 414 patients (35.20%) and even higher than that found in the Vachiat *et al.* [6] series (14.8%) in South Africa, on a total of patients. However, our prevalence was similar to that found by de Ahoui *et al.* [7] in Cotonou (44.19%) in HIV-infected patients newly put on HAART. In the general population, HIV prevalence varies from country to country in sub-Saharan Africa [8]. This contrasting aspect of HIV prevalence in sub-Saharan African studies can be explained by the diverse

and complex combination of socio-cultural, economic and health factors affecting the HIV epidemic in each region of black Africa [9]. It has been shown that each region of Africa has a particular geographic facies of HIV that can explain its prevalence [8]. On the other hand, the selection bias in relation to our study scope would certainly have resulted in an increase in HIV prevalence in our ARF population. Indeed, the highest prevalences were found in studies [7] whose scope included the infectious disease department compared to studies whose scope included only nephrology and/or internal medicine services [5] [6]. Nevertheless, HIV prevalence remains high in the population of sub-Saharan Africa and leads to significant morbidity including acute renal failure. In a New York study of hospitalized HIV-infected patients, the risk of ARF before HAART initiation was 4.62% and that after treatment was 2.82% [10].

The age of occurrence of ARF was similar in the 2 groups of our study. Several authors had reported that HIV-infected patients developed ARF at an early age compared to uninfected patients [6] [11] [12] [13]. For example, Wyatt *et al.* [10], Vichiat *et al.* [6], KH Yao *et al.* [5] all reported that HIV-infected patients were significantly younger than those who were not HIV-infected respectively (44.2 years versus 56.6 years; $P < 0.001$), (37.4 years versus 45.2 years; $p < 0.001$) and (42 years versus 51 years; $p < 0.0001$). The female predominance of HIV-infected patients in our work complies with WHO data showing that there is a feminization of the HIV epidemic, especially in sub-Saharan Africa where women represent 61% of all infected adults [14]. This feminization of HIV infection has been found in some studies [5]. This female vulnerability is not only related to the susceptibility of heterosexual transmission, but also to the difficult socio-economic conditions women face [15]. This large proportion of female sex in our study may also be related to the female predominance in the population of people living with HIV in our country. It should be noted, however, that male predominance has been reported in some studies [6] [10] [16].

Clinically, HIV-infected patients frequently had infectious and related water loss signs during ARF [5] [17]. However, comorbidities such as hypertension and diabetes were more common in uninfected patients. Similar observations had been reported by K. H. Yao *et al.* [5] in Ivory Coast. Severe immunosuppression is one of the main factors in the occurrence of kidney failure in our developing countries [6] [10] [16] [17]. Franceschini *et al.* [17] had shown that, low TCD4 level, high viral replication and AIDS stage were the factors associated with increased incidence of acute renal failure during HIV. As a result, the occurrence of ARF is only the consequence of opportunistic infections occurring during the illness. In our study, fever was more present in infected patients (28.0%) than in non-infected patients (11.1%) with $p = 0.02$; digestive disorders (56.0% versus 37.0%) and $p = 0.05$. It was the same for infections (40.0% versus 18.5%) $p = 0.02$ and infectious diarrhea (24.0% versus 7.4%) $p = 0.01$. It has been reported in several studies [18] [19] [20] that infectious causes were a major etiology of ARF occurrence in HIV-infected patients. Rao and Friedman [19] [20] observed that half of patients with ARF also had sepsis. Similarly, Franceschini *et*

al. [17] showed that the ARF was associated with an infectious cause in 52% of cases. According to Prakash *et al.*, the factors of hypo-infusion and renal ischemia factors are the main causes of ARF in India [21]. Infectious causes and water losses were also the main risk factors for the occurrence of ARF in HIV-infected patients in our Togo series.

Biologically, anemia was predominant in the HIV-infected population also joining the series of Yao *et al.* [5]. Indeed, anemia is common during HIV infection [22] [23]. It may be secondary to isolated mechanisms, but most often entangled combining a context: inflammatory, blood spoliation, deficiency and medullary insufficiency.

No deaths were recorded in the HIV-infected population in our series, while lethality was comparable in both groups according to Yao *et al.* [5]. This confirms literature data that HIV infection does not increase the mortality rate of ARF patients [5]. The death of patients would be related more to the severity of the conditions responsible for ARF [6] [17].

The mordibity of ARF in patients living with HIV could be reduced by making an early diagnosis of the infection, by introducing at the diagnosis of antiretroviral treatment and especially by taking care of all the factors favoring the occurrence of an ARF.

5. Conclusion

The HIV-IRA association is common in hospitals in Lomé. Infectious causes and digestive disorders are the most common risk factors found. Early and effective care would improve the prognosis of these patients.

Conflicts of Interest

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

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