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Acute kidney injury in hospitalized HIV-infected patients living in Cote d'Ivoire

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Abstract

Introduction: Infection with human immunodeficiency virus (HIV) is a common cause of renal dysfunction.

Objectives: We aimed to describe the epidemiological and etiological profile of acute kidney injury (AKI) in HIV infected patients.

Patients and Methods: This is a descriptive cohort study which was carried out during the period of January 2009 to December 2014 in department of nephrology-internal medicine of university hospital of Treichville. The highest value of serum creatinine (sCr) was used to stage AKI using the Acute Kidney Injury Network (AKIN) with different stages of AKI. Cox regression analysis was used to identify independent predictors of mortality.

Results: Our study included 146 patients whose mean age was 42±10 years with a female predominance (sex ratio 0.56). The positive retroviral status was unknown at admission in most cases (63%). The average CD4 cell count was 125±8 cells/mm^3. The causes were dominated by infections (67.8%) and water loss (24%). The outcome was favorable in 67% of cases. Factors such as clinical AIDS stage (odds ratio [OR] = 2.94; 95% CI = 1.47-5.90; P=0.002), coma (OR = 9.65; 95% CI=7.29-11.88; P=0.001), severity of immunosuppression (P = 0.02), septic shock (OR = 3.70; 95% CI=1.61-8.49; P=0.002) and acute pyelonephritis (OR = 9.61; 95% CI=2.45-37.65; P = 0.001) were associated with mortality in our patients.

Conclusion: AKI occurs at a late stage of HIV/AIDS infection and is in most cases the circumstance of discovery of retroviral infection. The causes are dominated by infections and digestive disorders responsible for water loss.

Keywords: Acute kidney injury, HIV infection, Water loss, Digestive mycosis, Cervical cancer, Human immunodeficiency virus (HIV)

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Introduction

Human immunodeficiency virus (HIV), the causative agent of acquired immunodeficiency syndrome (AIDS), is a public health problem worldwide. An estimated 24.7 million people are living with HIV in sub-Saharan Africa, nearly 71% of the global total. Despite progress in preventing new HIV infections, sub-Saharan Africa remains the most affected region, with nearly 1 in 25 (4.4%) adults living with HIV (1). The burden of the disease is more severe in Africa where poverty, ignorance and illiteracy are the most important part of the population (2).

In Côte d'Ivoire, the prevalence of HIV infection was 2% in 2013 (1). In addition, this infection is the second leading cause of chronic kidney disease (CKD) in this country with a significant proportion up to 17% in an internal medicine department (3). Renal impairment during HIV infection is sometimes nonspecific and may be the cause of acute kidney injury (AKI). AKI is a sharp drop in glomerular filtration rate (GFR). Its incidence during HIV infection varies between 10% and 18% depending on the series (4-6). HIV infection at the AIDS stage is a risk factor for AKI, in the same way as diabetes, cancer and cardiac surgery (7).

AKI in the person living with HIV (AKI-HIV) is a reality in our daily practice. However, if data on CKD in the course of HIV infection exist in our country, no data, to our knowledge, are available on AKI-HIV in West Africa in general and in Côte d'Ivoire in particular.

Objectives

This study aims to describe the epidemiological, clinical and evolutionary aspects of AKI in people living with HIV who are hospitalized in our department.

Patients and Methods

Population and period study

We analyzed the cohort of patients hospitalized from 1 January 2009 to 31 December 2014 for AKI and associated HIV infection. All patients aged >15 years, hospitalized

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Implication for health policy/practice/research/ medical education

Acute kidney injury (AKI) occurs in advanced stages of HIV/ AIDS infection. It is the circumstance of retroviral infection discovery in the majority of cases. The causes are dominated by infections and water loss. Moreover, cervical cancer is the leading cause of obstructive AKI. Prevention is necessary. This is modality achieved through access to primary health care and regular monitoring of renal function in patients undergoing potentially nephrotoxic treatment.

during the study period were included. These patients were gradually included at the time of their admission into the service. Recruitment of subjects was voluntary. This study was carried out in the department of nephrology-internal medicine of the teaching hospital of Treichville. This department consists of a unit of consultation, a unit of care for HIV infected patients and a conventional hospitalization unit. The HIV screening test is proposed to each patient and performed after consent. For patients whose clinical condition does not allow for consent, we do the screening by using the "Opt Out" technique (7). This indicates that the screening is done in all cases, unless a patient explicitly specifies that he does not interested the screening. Highly active antiretroviral therapy project is executed after initial biological tests (including HIV typing, blood count, the CD4 count, serum creatinine [sCr], transaminase and blood sugar) with the patient's consent, and whatever the screening technique.

Definitions

AKI was defined on the basis of sCr values determined in hospitalization. The exclusion criteria were chronic renal failure in HIV positive person and refusal of patient's consent. We have also excluded from the analysis, all patients without normal sCr or with no sCr within 3 months prior to hospitalization.

Serum creatinine was measured using the colorimetric of Jaffe method (Cobas C111 device®). The highest value of sCr was used to stage AKI using the Acute Kidney Injury Network (AKIN) with different stages (1, 2 and 3) of AKI (8). Anemia is defined as a hemoglobin level below 12 g/dL.

HIV infection has been classified as AIDS by the Center for Disease Control and Prevention (CDC) classification (9). Diagnosis of viral hepatitis was made on the basis of the detection of HBs antigen for B virus and antibodies to HCV for C virus.

Diagnostic of diabetes mellitus was made according to criteria of the American Diabetes Association (ADA) (10) and hypertension according to the criteria of the Joint National Committee Eight (JNC8) (11). Cancer patients include those with a solid or hematopoietic malignancy. Sepsis was diagnosed in accordance with the consensus of "the American College of Chest Physicians and the Society of Critical Care Medicine Consensus" (12).

Variables

For each patient enrolled, we collected the following information using a standardized survey form; demographic data (age, gender); co-morbidities (diabetes mellitus, hypertension, hepatitis B virus [HBV], hepatitis C virus [HCV]). The causes of AKI such as sepsis, water loss, cancer, tumors of the urinary tract, and nephrotoxic drug administration were analyzed.

Clinical data (reason for admission, clinical AIDS stage, blood pressure on admission, temperature, level of consciousness, the state of hydration, diuresis), laboratory data (sCr, blood urea, serum calcium, blood glucose, hemoglobin, leukocyte count and formula, platelets urinalysis, blood culture, HIV status, lymphocyte count CD4, HBV status, HCV status,), imaging data (renal ultrasound) were also assessed.

Each patient benefited from a mean follow up of 12 weeks. A regular determination of sCr and in particular to three months was used to assess the outcome of AKI. This outcome is said favorable if sCr was less than 1.5 mg/dL or when we observed a decrease of 50% compared to the baseline creatinine. Data related to the outcome of AKI were the duration of hospitalization, survival (time-to-death) and the vital status until the 90th day. Endpoint primary was death.

Ethical issues

The research followed the tenets of the Declaration of Helsinki. The study protocol was approved by the ethical committee of university hospital of Treichville. Written informed consent was obtained from the study participants. For patients unable to give consent because of severity of illness, the next of kin was identified and gave informed consent.

Statistical analysis

Data were processed in an Excel database and analyzed using SPSS software version 22. We first performed a univariate analysis. The proportions of qualitative variables were compared according to AKI stage and then according to age groups by a chi-square test or Fisher's exact test. Regarding quantitative variables, averages were compared by analysis of variance (ANOVA) test. Cox regression analysis was used to identify independent predictors of mortality. Association measures were calculated with 95% confidence intervals and $P < 0.05$ defined the level of statistical significance.

Results

In the study period, we collected 180 cases of AKI associated HIV infection. Our analysis included 146 cases for which renal function was normal within three months prior to hospitalization.

The mean age was 42.3 ± 10 years with extremes of 26 and 69 years. The majority of patients (69.9%) were between 35 and 64 years of age (Table 1). We observed a female predominance with a sex ratio (53/93) of 0.56.

Before admission, viral infection was not known positive in 92 patients (63%). It was known positive but untreated in 45cases (30.8%) (Table 2). The main comorbidities were hypertension (11.6%), HBV (7.9%) and diabetes (4.1%). The reason for admission was mainly disorders of consciousness in 36 cases (24.6%), diarrhea in 33 cases (22.6%), vomiting in 27 cases (18.4%) and fever in 20 cases (13.7%). Clinical signs were dominated by gastroenteritis in 39 cases (26.7%), coma 44 cases (30.1%), isolated infectious syndrome in 24 cases (16.4%), condensation syndrome in 21 cases (14.4%) and obstructive syndrome of the lower urinary tract in 08 cases (6.6%) (Table 2). In addition, patients were in the clinical AIDS stage in 44.5% of the cases.

AKI was in stage 1 in 32.2% of cases, in stage 2 in 10.3% and in stage 3 in 57.2% of which 46.5% had a SCR >6.0 mg/dL. (Table 1). Anemia was observed in 123 cases (84.2%) and hemoglobin was less than 8 g/dL in 54 cases (37%). The virus of type HIV1 was found in all patients. The CD4 cell count was in average 125 ± 8 cells/mm^3 and below 250 cells/mm^3 in 95.4% (41/43) of tested cases.

As for etiologies, functional AKI was related water loss (24%). Organic AKI was due to infections (65.8%) and drugs (3.4%). The main infections were septic shock (21.9%), pleuro-pneumopathies (11%), acute pyelonephritis (8.9%), infectious diarrhea (7.5%) and malaria (4.1%) (Table 3). Obstructive AKI was primarily related to cervical cancer (4.1%); other causes of obstacle were neurogenic bladder (two cases) and Hodgkin disease (one case).

The outcome was favorable in 92 cases (63%). It is noted however, a persistent alteration of the renal function in four patients with cancer of the cervix and three cases of renal failure due to drug. Hospital mortality was 37%. The median survival was three days (95% CI = 2.28-3.71). The patients who died had a mean age of 46 ± 12 years against 40 ± 8.9 years for patients with a favorable outcome (P = 0.001). In addition, all patients aged ≥ 65 years died (OR = 2.84, 95% CI = 2.27-3.55, P = 0.01). We did not observe any difference in gender. All diabetic patients were also died (OR = 2.91, 95% CI = 2.31-3.66, P = 0.002). Clinically, the clinical AIDS stage (OR = 1.50, 95% CI = 1.13-1.98, P = 0.002) and coma (OR = 3.37; 95% CI = 2.23-5.09; P = 0.0001) were significantly more observed in the group of the deceased.

We found no difference in AKI stage between the two groups. Further, sCr was above 60 mg/L in 50% of cases in patients with a favorable outcome against 40.7% in the

Table 1. Comparison of patients according to the outcome

Characteristics	Total (n = 146)	Dead (n = 54)	Favorable (n = 92)	*P* value	OR (95%CI)
Gender					
Male	36.3% (53/146)	38.9% (21/54)	34.8% (32/60)		
Female	65.2% (93/146)	61.6% (33/54)	65.2% (60/92)	0.37	0.89 (0.58-1.37)
Age (y)					
Average	42±10	46±12	40±8.9	0.001	
<35	27.4% (40/146)	22.2% (12/54)	30.4% (28/92)	0.18	0.75 (0.44-1.28)
35-64	69.9% (102/146)	70.4% (38/54)	69.6% (64/92)	0.53	1.02 (0.64-1.63)
≥65	2.7% (4/146)	7.4% (4/54)	-	0.01	2.84 (2.27-3.55)
Co-morbidities					
Hypertension	11.6% (17/146)	7.4% (4/54)	14.1% (13/92)	0.17	0.80 (0.54-1.07)
Diabetes	4.1% (6/146)	11.1% (6/54)	-	0.002	2.91 (2.31-3.66)
HBV	7.9% (6/76)	10.30% (3/29)	6.3% (3/47)	0.78	
HCV	1.31% (1/76)	-	2.1% (1/47)	0.58	
Clinical					
Clinical AIDS stage	44.5% (65/146)	61.1% (33/54)	34.8% (32/92)	0.002	1.50 (1.13-1.98)
Coma	30.1% (44/146)	59.3% (32/54)	13% (12/92)	0.0001	3.37 (2.23-5.09)
Stage AKI					
AKI 1	32.2% (47/146)	37% (20/54)	29.3% (27/92)	0.21	1.23 (0.80-1.90)
AKI 2	10.3% (15/146)	5.6% (3/54)	13% (12/92)	0.12	0.51 (0.18-1.44)
AKI 3	57.2% (84/146)	57.4% (31/54)	57.6% (53/92)	0.55	0.99 (0.64-1.52)
Creatinine >6.0 mg/dL	46.5% (68/146)	40.7% (22/54)	50% (46/92)	0.18	0.78 (0.51-1.21)
Hemoglobin (g/dL)					
>12	15.8% (23/146)	11.1% (6/54)	18.5% (17/92)	0.17	0.66 (0.32-1.37)
8-12	47.3% (69/146)	44.4% (24/54)	48.9% (45/92)	0.36	0.89 (0.58-1.36)
<8	37% (54/146)	44.4% (24/54)	32.6% (30/92)	0.10	1.36 (0.89-2.07)
Etiologies					
Water loss	24% (35/146)	16.7% (9/54)	28.3% (26/92)	0.08	0.63 (0.34-1.16)
Infections	65.8% (96/146)	75.9% (41/54)	59.8% (55/92)	0.034	1.64 (0.97-2.76)
Drugs	3.4% (5/146)	3.7% (2/54)	3.3% (3/92)	0.61	0.92 (0.30-2.75)
Cancers	4.1% (6/146)	1.9% (1/54)	5.4% (5/92)	0.27	0.44 (0.07-2.66)
Others	2.1% (3/146)	-	3.3% (3/92)	0.24	0.6 (0.41-1.82)

Table 2. General characteristics of patients

Characteristics	Number	Percent
Retroviral status before admission	(n=146)	
Not known positive	92	63.01
Known positive untreated	45	30.82
Known positive treated	09	6.16
Clinical signs	(n=146)	
Oral candidiasis	18	12.3
Gastroenteritis	39	26.7
Febrile coma	35	24
Febrile meningoencephalitis	13	8.9
Condensation syndrome	21	14.4
Obstructive syndrome of lower urinary tract	07	4.8
Edematous syndrome	12	4.8
Isolated infectious syndrome	24	16.4
CD4 cell counts (cells/mm³)	(n=43)	
<250	41	95.4
≥250	02	5.6

patients who died with no statistical difference ($P=0.18$). The proportion of severe anemia was 32.6% among patients with a favorable outcome against 44.4% among patients who died ($P=0.10$). The average CD4 cell count was 145 ± 87 mm³ for patients with favorable outcome against 82 ± 33/mm³ for patients who died ($P=0.02$).

In etiological terms, the proportion of patients with infection in the group with a favorable outcome was 59.8% against 75.9% in the group of patients who died with a statistically significant difference (OR = 1.64; 95% CI = 0.97-2.76; $P=0.034$). Among these infections, septic shock (OR = 1.56; 95% CI = 1.03-2.35; $P=0.01$) and acute pyelonephritis (OR = 2.9; 95% CI = 1.06-7.87; $P=0.003$) were significantly associated with mortality in our patients. All patients with pleuro-pneumopathy -AKI had a favorable outcome (OR = 0.57; 95% CI = 0.50-0.67; $P=0.0001$).

In multivariate analysis, the clinical AIDS stage (OR = 2.94; 95% CI = 1.47-5.90; $P=0.002$), coma (OR = 9.65; 95% CI=7.29-11.88; $P=0.001$), infections such as septic shock (OR = 3.70; 95% CI = 1.61-8.49; $P=0.002$), and acute pyelonephritis (OR = 9.61; 95% CI = 2.45-37.65; $P=0.001$ were associated with death in our patients (Table 4).

Discussion

We carried out this study including 146 patients to analyze the profile of AKI in patients with HIV infection.

Our patients were mostly young females. HIV infection mainly affects the young segment of the population (13,14). In sub-Saharan Africa, about 60% of HIV infected patients are females (15). In this area, the prevalence of HIV infection among women was higher than that of the male population (15,16). This female vulnerability is related to not only susceptibility to heterosexual transmission, but also difficult socio-economic conditions of women (15). This important proportion of females in our study could be related to the female preponderance in the population of people living with HIV in our country.

More than half (60%) of the patients do not know that they were infected with HIV prior to admission. This raises the issue of adherence to voluntary screening for early adequate care before AIDS stage.

The clinical features observed in our patients were in favor of the advanced stage of the viral infection (AIDS). We were unable to systematically achieve the CD4 count for all patients. Of the 43 tested, the rate of CD4 low in almost all cases. In addition, nearly half of them have already had an AIDS-like illness such as tuberculosis, cerebral toxoplasmosis and cervical cancer. This condition happened during HIV infection when the immunosuppression is profound, particularly at the late stage of disease. AKI is a common complication in HIV infected patients. It is associated with a low CD4 cell counts, at the stage of AIDS, a co-infection with hepatitis C and a hypoalbuminemia (17-19).

Functional AKI was related to water loss. Prakash et al have shown that HIV contributed to 1.65% of functional AKI, out of a total of 2405 cases of AKI in India during the period 1996- 2008 (20). The organ involvement was by far dominated by infections and drugs accounted for only 3.4%. Infections, drugs, obstetric and surgical complications are the main causes of AKI in Africa (19). The main causes of the AKI during HIV infection in Western countries are infections (59%), drugs (37.5%), water loss (21.6%) and contrast products (20.5%) (2). Other etiologies of AKI included acute tubular necrosis (ATN) from shock or sepsis (21). Regarding drugs, tenofovir and cotrimoxazole prophylaxis are regularly mentioned (22,23). In our study, we observed three cases of AKI related to the use of tenofovir. Obstructive AKI was mainly due to cervical cancer (3.4%). A joint study carried out in Côte d'Ivoire and Benin showed that cancers occurring during HIV infection such as invasive cancer of the cervix were associated with HIV infection in 25% of cases, behind Kaposi's sarcoma (74.2%) (24). The absence of early treatment leads to a loco-regional invasion and

Table 3. Distribution of patients according to the type of infection

Type of infection	Total (n = 99)	Dead (n = 45)	Favorable (n = 54)	*P* value	OR (CI 95%)
Acute pyelonephritis	8.9% (13/146)	22.2% (10/45)	5.5% (3/ (54)	0.003	2.9 (1.06-7.87)
Infectious diarrhea	7.5% (11/146)	13.3% (6/45)	9.2% (5/54)	0.17	1.41 (0.73-2.74)
Pleuropneumopathy	11% (16/146)	-	29.6% (16/54)	0.0001	0.57 (0.50-0.67)
Malaria	4.1% (6/146)	6.6% (3/45)	5.5% (3/54)	0.39	1.27 (0.56-2.85)
Septic shock	21.9% (32/146)	40% (18/45)	25.9% (14./54)	0.01	1.56 (1,03-2.35)
Other infections	14.3% (21/146)	17.7% (8/45)	24.07% (13/54)	0.47	1.09 (0.64-1.38)

Table 4. Multivariate analysis with Cox regression

Variables	*P* value	OR	95% CI	
			Inferior	Superior
Age ≥65 years	0.165			
Diabetes mellitus	0.999	-	-	-
Clinical AIDS stage	0.002	2.94	1.47	5.90
Coma	0.0001	9.65	7.29	11.88
SCr >6.0 mg/dL	0.28	0.68	0.34	1.35
Hemoglobin <8 g/dL	0.15	1.65	0.82	3.30
Infections	0.161	1.76	0.768	4.89
Septic shock	0.002	3.709	1.61	8.49
Acute pyelonephritis	0.001	9.61	2.45	37.65

a sheathing of ureters that may lead to obstructive renal failure. In addition, we also observed a case of obstructive AKI by bilateral compression of ureters by voluminous celiomesenteric lymphadenopathies during a Hodgkin disease, and two other cases that occurred after a neurogenic bladder. In one case, AKI occurred following a cerebral toxoplasmosis responsible for a pyramidal syndrome in a subject carrier of a bifurcated kidney with a normal initial renal function. The other case was related to an ascending sensorimotor polyneuropathy responsible for urinary retention.

More than two-thirds of our patients had anemia. This was due to inflammatory syndrome related to the infection responsible for AKI, and on the other hand to HIV infection. The prevalence of anemia is high during HIV infection, in the order of 41.5% to 62.9% prior to the highly active antiretroviral therapy. The associated factors are female gender, low CD4 lymphocyte (<200/mm^3) and high viral load (25,26).

The outcome was favorable in more than half (67%) of cases. Obstructive renal involvement can become irreversible when the obstacle is later lifted as shown in our results. The death rate is high and can reach to 72.2% when the AKI is associated with HIV infection (27,28). The proportion of patients with severe AKI was lower in patients who died. Mortality is therefore not only related to the severity of AKI, but probably is related to the state of deep immunosuppression of our patients. Severe immunosuppression and opportunistic diseases are factors of mortality during AKI associated with HIV infection (29). Neither the presence of anemia nor its severity appears as factors associated with death among our patients. According to other authors, the factors associated with hospital mortality are severe acute renal failure, heart failure, cardiovascular disease, end-stage of renal failure and anemia (30).

According to etiology, infections were the most cause of AKI in our study. Sepsis has long been recognized as a foremost precipitant of AKI. Sepsis-associated AKI portends a high burden of morbidity and mortality in both children and adults with critical illness (31,32). Septic AKI patients are clinically distinct compared to non-septic AKI patients with different prognostic factors and poorer renal function outcome (33).

Conclusion

AKI occurs in advanced stages of HIV/AIDS infection. It is the circumstance of retroviral infection discovery in the majority of cases. The causes are dominated by infections and water loss. Moreover, cervical cancer is the leading cause of obstructive AKI. Mortality is high.

Prevention is necessary. This is modality achieved through access to primary health care and regular monitoring of renal function in patients undergoing potentially nephrotoxic treatment.

Limitations of the study

Our study has some limitations that must be considered in interpreting the results. The single-center nature and sCr by Jaffe method are the limitations of our study.

Furthermore we were unable to assess the long-term survival of patients.

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Authors' contribution

YKH have made substantial contributions to conception and design, analysis and interpretation of data, as well as has been involved in drafting the manuscript and revising it critically for important intellectual content. KSD, NKS and DA have collected data. DAD and SS have revised the manuscript critically for important intellectual content. All authors have given final approval of the version to be published. All authors read and approved the final manuscript.

Conflicts of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this paper.

Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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