Acute kidney injury in hospitalized HIV-infected patients: a cohort analysis

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Abstract

Background. Acute kidney injury (AKI) in hospitalized human immunodeficiency virus (HIV)-infected patients in the highly active antiretroviral therapy (HAART) era has not been extensively addressed. The aim of the present study was to analyze the incidence, etiology, risk factors and the impact of AKI on in-hospital mortality in this population.

Methods. A total of 489 HIV-infected patients hospitalized in the Department of Infectious Diseases of the Hospital de Santa Maria (Lisbon, Portugal) between January 2005 and December 2007 were retrospectively studied. AKI was defined by ’Risk Injury Failure Loss of kidney function End-stage kidney disease’ (RIFLE) criteria based on serum creatinine. Comparisons between patients with and without AKI were performed using the Student’s t-test or the χ2 test. Logistic regression method was used to determine predictors of AKI and in-hospital mortality. A two-tailed P-value <0.05 was considered significant.

Results. Eighty-eight patients (18%) had AKI within the hospitalization period. The most common etiologies of AKI were sepsis (59%), nephrotoxic drug administration (37.5%), volume depletion (21.6%) and radiocontrast use (20.5%). Preexisting hypertension [adjusted odds ratio (OR) 2.4, 95% confidence interval (CI) 1.04–5.6, P = 0.04], acquired immunodeficiency syndrome (adjusted OR 2.7, 95% CI 1.2–6, P = 0.02), sepsis (adjusted OR 23, 95% CI 11–45.3, P < 0.001) and nephrotoxic drug administration (adjusted OR 2.8, 95% CI 1.4–5.8, P = 0.004) were risk factors of AKI. Patients with AKI had higher in-hospital mortality than patients without AKI (27.3 versus 8%, P < 0.001). In multivariate analysis, AKI was a risk factor of in-hospital mortality (adjusted OR 2.7, 95% CI 1.3–5.6, P = 0.008).

Conclusion. AKI occurred in 18% of hospitalized HIV-infected patients and it was independently associated with increased in-hospital mortality.

Keywords: acute kidney injury; HIV; in-hospital mortality

Introduction

Over the last two decades, the number of individuals infected with human immunodeficiency virus (HIV) has markedly increased, and, actually, >30 million people are affected with HIV infection worldwide [1]. Since the introduction of the highly active antiretroviral therapy (HAART) at the end of 1995, the annual number of deaths reported with HIV infection decreased dramatically as well as the number of deaths caused by HIV infection or by an acquired immunodeficiency syndrome (AIDS)-defining disease. Conversely, comorbidities such as kidney disease, liver disease, heart disease and non-AIDS-defining cancers have proportionally increased and have become significant contributors to morbidity in HIV-infected patients [2–4].

Renal disorders in HIV-infected patients can present as an acute or chronic condition, and they are associated with increased morbidity and mortality in this population [5–9].
Acute kidney injury (AKI) is a common complication in ambulatory HIV-infected patients treated with HAART and has been associated with prior renal impairment, lower CD4 levels, AIDS, hepatitis C virus infection and liver disease [10, 11]. HIV-infected patients are also at increased risk for AKI development within hospitalization, related to volume depletion, sepsis and the acute administration of nephrotoxic medications or radiocontrast. Before the advent of HAART, studies addressing AKI on HIV-infected patients typically included only severe cases of AKI which were identified through hospital records or biopsy databases [12–14]. The epidemiology of AKI in hospitalized HIV-infected patients in the HAART era has also not been extensively analyzed. In fact, few studies have focused on the clinical characteristics of AKI in hospitalized HIV-infected patients in the HAART era [15–17]. The aim of the present study was therefore to further evaluate the incidence, etiology, risk factors as well as the impact on outcome of AKI in this specific population.

Materials and methods

The present study is retrospective, including HIV-infected patients admitted to the Department of Infectious Diseases of the Hospital de Santa Maria (Lisbon, Portugal) between January 2005 and December 2007. Hospital de Santa Maria is a tertiary and teaching hospital providing medical assistance to an area with almost 3 000 000 inhabitants. Since this was a retrospective and observational study that did not evaluate a specific therapeutic or prophylactic intervention, study approval was waived by the Ethical Committee of our Hospital according to Institutional guidelines.

Study population

During the study period, 547 HIV-infected patients were admitted to the Department of Infectious Diseases of our hospital; 13 of them were chronic kidney disease (CKD) patients on dialysis and were not included in this study. None of the patients had received a renal transplant. From the 534 remaining patients, 45 patients were hospitalized <24 h and/or had no serum creatinine determination within hospitalization and were excluded from the analysis. Therefore, in this study, we focused on 489 HIV-infected patients (mean age: 42 years; 168 Male; 353 Caucasian; 464 infected with HIV-1, 21 with HIV-2 and 4 with both HIV-1 and HIV-2) and analyzed them as a cohort.

Definitions

AKI was defined and categorized according to “Risk Injury Failure Loss of kidney function End-stage kidney disease” (RIFLE) classification [18] based on all serum creatinine values determined within the hospitalization. Class R (Risk) was considered if there was an increase of baseline serum creatinine $\times 1.5$; Class I (Injury) was considered if there was an increase of baseline serum creatinine $\times 2$ and Class F (Failure) was considered if there was an increase of baseline serum creatinine $\times 3$, or in patients with baseline serum creatinine $>4$ mg/dL if there was an acute rise in serum creatinine of at least 0.5 mg/dL. The maximum RIFLE score within hospitalization was reported. The most recent serum creatinine value registered within 1–6 months prior to admission was considered the baseline serum creatinine and was available in 472 patients; when it was unavailable ($n = 17$) baseline serum creatinine was estimated by the Modification of Diet in Renal Disease (MDRD) equation [19], as recommended (assuming a lower limit of the normal baseline glomerular filtration rate of 75 mL/min/1.73m$^2$) and previously applied [20–22]. Complete renal function recovery was considered if the serum creatinine at hospital discharge with reference to baseline serum creatinine was lower than $\times 1.5$, and in patients with baseline serum creatinine $>4$ mg/dL, complete renal function recovery was also considered if serum creatinine at hospital discharge was also $<0.5$ mg/dL with reference to baseline serum creatinine [18].

HIV infection was staged according to the Centers for Disease Control and Prevention (CDC) classification [23].

Diabetes mellitus was diagnosed according to the World Health Organization criteria [24], and hypertension was diagnosed based on the seventh report of the Joint National Committee (JNC 7) [25].

Cardiovascular disease included chronic heart failure defined by specific symptoms (i.e. fatigue, dyspnea, orthopnea, paroxysmal nocturnal dyspnea) and signs (i.e. crepitant rales, pleural effusion, peripheral edema), coronary artery disease which was considered whenever previous acute myocardial infarction, stable and unstable angina and/or evidence of cardiac ischemia by electrocardiogram, scintigraphy or coronary angiography, cerebrovascular disease which was considered whenever previous transient ischemic attack and/or stroke and peripheral arterial disease defined by the presence of claudication, ischemic rest pain or ulceration/gangrene of the lower limbs and/or whenever disease was evidenced by Doppler ultrasound or arteriography.

CKD was considered whenever baseline glomerular filtration rate was $<60$ mL/min/1.73m$^2$ [26].

Chronic lung disease included emphysema, chronic bronchitis and asthma.

Cirrhosis diagnosis was based on clinical signs (i.e. spider angioma, palmar erythema, gynecomastia, testicular atrophy, hepatomegaly, splenomegaly, ascites, dilated abdominal veins, feto hepaticus, jaundice and asterixis), laboratory findings (elevation of aminotransferases, alkaline phosphatase, gamma-glutamyl tranpeptidase, bilirubin, prothrombin time and globulins, low serum albumin, hyponatremia, anemia, low platelets and leukopenia and/or neutropenia), echographic signs (i.e. surface nodularity and increased echogenicity with irregular appearing areas), increasing stiffness of the tissue evidenced by sonography and/or on histologic findings.

Hepatitis C virus and hepatitis B virus coinfections were diagnosed by the identification of antibody to hepatitis C virus and hepatitis B surface antigen, respectively.

Patients with cancer included those patients with malignant solid or hematopoietic neoplasm.

Sepsis was diagnosed in accordance with the American College of Chest Physicians and the Society of Critical Care Medicine consensus [27].

Variables

Demographic data (age, gender, race), comorbidity (diabetes mellitus, hypertension, cardiovascular disease, CKD, chronic lung disease, cirrhosis, hepatitis C virus and hepatitis B virus coinfections and cancer), HIV-related characteristics (type of HIV, antiretroviral therapy, CD4 cell count, HIV viral load, stage of HIV infection according to the CDC classification), causes of AKI such as sepsis, volume depletion, hemorrhage, administration of nephrotoxic drugs (aminoglycosides, amphotericin B, vancomycin, acyclovir, gancyclovir and foscarnet), radiocontrast use and the occurrence of rhabdomyolysis or tumor lysis syndrome as well as serum creatinine values, need for renal replacement therapy (RRT), intensive care unit (ICU) admission and outcome were analyzed.

Statistical analysis

Continuous variables are expressed as mean (SD) and categorical variables as percentage of number of cases. Comparisons between patients with and without AKI were performed using the Student’s $t$-test and the $\chi^2$ test, respectively, for continuous and categorical variables. Logistic regression method was used to determine independent predictors of AKI and inhospital mortality. Risk factors were assessed with univariate analysis, and variables that were statistically significant (P $<0.05$) in the univariate analysis were included in the multivariate analysis. Data are presented as
odds ratios (ORs) with 95% confidence intervals (CIs). A two-tailed P-value < 0.05 was considered significant. We performed a separate analysis excluding those patients (n = 17) in whom baseline serum creatinine was calculated using the MDRD formula. Kaplan-Meier method was used to determine survival curves and log-rank test was employed to evaluate statistical differences between the survival curves. Analysis was performed with the statistical software package SPSS 18.0 for Windows (Produtos e Servicos de Estatisticas, Lisboa, Portugal).

Results

Eighty-eight patients (18%) had AKI, as follows: 32 patients (6.5%) were categorized as Risk, 30 patients (6.1%) as Injury and 26 patients (5.3%) as Failure. Twelve patients were actually admitted with AKI and the remaining developed AKI during the hospital stay. Median time to the occurrence of AKI was 8 days (0–59 days). Of interest, 10 of the 17 patients (58.8%) in whom baseline serum creatinine was calculated using the MDRD formula had AKI. After excluding those patients (n = 17) in whom baseline serum creatinine was calculated using the MDRD formula, the incidence of AKI still persisted to be similar (16.5 versus 18%, P = 0.202).

Baseline serum creatinine was similar between patients with no AKI and in those patients who had AKI (P = 0.670) (Table 1), and in AKI patients, it did not differ according to severity of AKI [Risk, 0.9 (0.3); Injury, 1 (0.6) and Failure, 1 (0.3); P = 0.724]. Conversely, serum creatinine at maximum RIFLE score was higher as severity of AKI increased [Risk, 1.2 (0.5); Injury, 2.1 (1.6) and Failure, 5 (3.5); P < 0.001].

Patients who developed AKI were more likely to have preexisting hypertension (P = 0.03), cirrhosis (P = 0.007) and cancer (P = 0.03) as well as AIDS (P < 0.001). Furthermore, sepsis was more prevalent in patients with AKI and these patients had lengthened time of hospitalization (P < 0.001), as compared with patients with no acute renal impairment. Individuals who were treated in the ICU were also more likely to experience AKI (P < 0.001) (Table 1).

In all cases, there was at least an obvious cause for the development of AKI which was multifactorial in 43 patients (48.9%). The most common etiologies of AKI in this cohort were sepsis (n = 52; 59%), nephrotoxic drugs administration (n = 33, 37.5%), volume depletion (n = 19, 21.6%) and use of radiocontrast (n = 18, 20.5%). Other less common causes of AKI were tumor lysis syndrome (n = 2), hemorrhage (n = 1), acute urinary tract obstruction (n = 1) and thrombotic microangiopathy (n = 1).

In multivariate analysis, preexisting hypertension (adjusted OR 2.4, 95% CI 1.04–5.6, P = 0.04), AIDS (adjusted OR 2.7, 95% CI 1.2–6, P = 0.02), sepsis (adjusted OR 23, 95% CI 11–45.3, P < 0.001) and nephrotoxic drug administration (adjusted OR 2.8, 95% CI 1.4–5.8, P = 0.004) were independent risk factors of AKI (Table 2).

Of interest, the percentage of patients who were receiving HAART or a tenofovir-containing regimen was similar between patients with AKI and without AKI (95.5 versus 94.8%).

Table 1. Baseline characteristics of 489 hospitalized HIV-infected patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>No AKI (N = 401)</th>
<th>AKI, (N = 88)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>42 (12)</td>
<td>43 (12)</td>
<td>0.25</td>
</tr>
<tr>
<td>Gender (Male)</td>
<td>137 (34.2%)</td>
<td>31 (35.3%)</td>
<td>0.85</td>
</tr>
<tr>
<td>Race (Caucasian)</td>
<td>290 (72.3%)</td>
<td>63 (71.6%)</td>
<td>0.89</td>
</tr>
<tr>
<td>Comorbidity</td>
<td>22 (5.4%)</td>
<td>5 (5.7%)</td>
<td>0.9</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>37 (9.2%)</td>
<td>15 (17%)</td>
<td>0.03</td>
</tr>
<tr>
<td>Hypertension</td>
<td>21 (5.2%)</td>
<td>5 (5.7%)</td>
<td>0.87</td>
</tr>
<tr>
<td>CVD</td>
<td>53 (13.2%)</td>
<td>15 (17%)</td>
<td>0.51</td>
</tr>
<tr>
<td>CKD</td>
<td>11 (2.7%)</td>
<td>2 (2.3%)</td>
<td>0.8</td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>34 (8.4%)</td>
<td>16 (18.2%)</td>
<td>0.007</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>136 (33.9%)</td>
<td>31 (35.3%)</td>
<td>0.81</td>
</tr>
<tr>
<td>HCV coinfection</td>
<td>26 (6.5%)</td>
<td>10 (11.4%)</td>
<td>0.11</td>
</tr>
<tr>
<td>HBV coinfection</td>
<td>8 (2%)</td>
<td>2 (2.3%)</td>
<td>0.8</td>
</tr>
<tr>
<td>Cancer</td>
<td>33 (8.2%)</td>
<td>14 (15.9%)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Table 2. Univariate and multivariate analysis to determine risk factors for AKI

<table>
<thead>
<tr>
<th>Variable</th>
<th>Unadjusted OR (95% CI)</th>
<th>P</th>
<th>Adjusted OR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per decade)</td>
<td>1.1 (0.9–1.3)</td>
<td>0.25</td>
<td>1.05 (0.6–1.7)</td>
<td>0.85</td>
</tr>
<tr>
<td>Gender (Male)</td>
<td>1.05 (0.6–1.7)</td>
<td>0.85</td>
<td>0.9 (0.6–1.6)</td>
<td>0.89</td>
</tr>
<tr>
<td>Comorbidity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1.04 (0.4–2.8)</td>
<td>0.9</td>
<td>1.09 (0.4–3)</td>
<td>0.87</td>
</tr>
<tr>
<td>Hypertension</td>
<td>2 (1.05–3.9)</td>
<td>0.04</td>
<td>2.4 (1.04–5.6)</td>
<td>0.04</td>
</tr>
<tr>
<td>CVD</td>
<td>1.09 (0.4–3)</td>
<td>0.87</td>
<td>1.7 (0.7–4.2)</td>
<td>0.51</td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>0.4 (0.2–3.8)</td>
<td>0.8</td>
<td>2.4 (1.3–4.6)</td>
<td>0.06</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>1.09 (0.4–3)</td>
<td>0.87</td>
<td>1.06 (0.7–1.7)</td>
<td>0.81</td>
</tr>
<tr>
<td>Chronic liver disease</td>
<td>2.1 (1.08–4.1)</td>
<td>0.03</td>
<td>1.2 (0.7–3.9)</td>
<td>0.3</td>
</tr>
<tr>
<td>HIV-related characteristics</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type of HIV (HIV-1)</td>
<td>0.9 (0.4–2.8)</td>
<td>0.87</td>
<td>1.09 (0.4–3)</td>
<td>0.87</td>
</tr>
<tr>
<td>HAART</td>
<td>1.0 (0.6–1.6)</td>
<td>0.9</td>
<td>1.09 (0.4–3)</td>
<td>0.87</td>
</tr>
<tr>
<td>Tenofovir-containing regimen</td>
<td>2.4 (1.3–4.6)</td>
<td>0.06</td>
<td>2.4 (1.3–4.6)</td>
<td>0.06</td>
</tr>
<tr>
<td>CD4 count &lt; 200 cells/mm³</td>
<td>1.0 (0.9–1.3)</td>
<td>0.72</td>
<td>1.0 (0.9–1.3)</td>
<td>0.72</td>
</tr>
<tr>
<td>Viral load detectable</td>
<td>1.09 (0.4–3)</td>
<td>0.04</td>
<td>2.4 (1.04–5.6)</td>
<td>0.04</td>
</tr>
<tr>
<td>AIDS</td>
<td>2 (1.05–3.9)</td>
<td>0.04</td>
<td>2.4 (1.04–5.6)</td>
<td>0.04</td>
</tr>
<tr>
<td>Nephrotoxic drugs</td>
<td>3.3 (1.7–6.3)</td>
<td>&lt;0.001</td>
<td>2.7 (1.2–6)</td>
<td>0.02</td>
</tr>
<tr>
<td>CVD</td>
<td>27.5 (14.8–51)</td>
<td>&lt;0.001</td>
<td>23 (11–45.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Nephrotoxic drugs</td>
<td>4.5 (2.7–7.7)</td>
<td>0.004</td>
<td>2.8 (1.4–5.8)</td>
<td>0.004</td>
</tr>
<tr>
<td>Radiocontrast use</td>
<td>2.1 (1.3–3.8)</td>
<td>0.02</td>
<td>1.3 (0.6–2.9)</td>
<td>0.57</td>
</tr>
</tbody>
</table>

aCKD considered whenever baseline glomerular filtration rate was < 60 ml/min/1.73m²; CVD, cardiovascular disease; HBV, hepatitis B virus; HCV, hepatitis C virus; Scr, serum creatinine.

bCVD, cardiovascular disease; HBV, hepatitis B virus; HCV, hepatitis C virus.
94.8%, \( P = 0.85 \) and 39.7 versus 39.9%, \( P = 0.9 \); respectively), and antiretroviral therapy did not influence the development of AKI (HAART, unadjusted OR 1, 95% CI 0.6–1.6, \( P = 0.9 \) and tenofovir-containing regimen, unadjusted OR 1.1, 95% CI 0.6–2, \( P = 0.72 \)) (Tables 1 and 2). After excluding those patients (\( n = 17 \)) in whom baseline serum creatinine was calculated using MDRD formula, AIDS (adjusted OR 2.7, 95% CI 1.2–6.2, \( P = 0.02 \)), sepsis (adjusted OR 25.9, 95% CI 12.8–52.2, \( P < 0.001 \)) and nephrotoxic drug administration (adjusted OR 2.6, 95% CI 1.3–5.6, \( P = 0.01 \)) still were associated with increased risk of AKI. Preexisting hypertension was also associated with increased risk of AKI, however, it did not reach statistical significance (adjusted OR 2.4, 95% CI 0.98–5.9, \( P = 0.056 \)).

Eight of the 88 patients with AKI (9%) underwent RRT; 7 patients received intermittent hemodialysis and 1 patient received continuous venovenous hemodiafiltration. All patients with AKI who underwent RRT were in the Failure class.

The majority of patients (\( n = 47, 84 \% \)) died within the first 60 days of hospitalization (Figure 1). Patients who had AKI had higher in-hospital mortality than those patients who did not develop AKI (27.3 versus 8%, \( P < 0.001 \); unadjusted OR 4.3, 95% CI 2.4–7.8, \( P < 0.001 \)). After adjusting for other covariates, AKI still remained associated with increased in-hospital mortality (adjusted OR 2.7, 95% CI 1.3–5.6, \( P = 0.008 \)) (Table 3). After excluding those patients (\( n = 17 \)) in whom baseline serum creatinine was calculated using the MDRD formula, AKI still persisted to be associated with increased in-hospital mortality (29.5 versus 8.1%, \( P < 0.001 \); adjusted OR 3.1, 95% CI 1.4–6.7, \( P = 0.03 \)). Injury class (in-hospital mortality, 30%; adjusted OR, 3.0; 95% CI 1.1–8.1; \( P = 0.026 \)) and Failure class (in-hospital mortality, 38.5%; adjusted OR, 4.1; 95% CI 1.4–12.0; \( P = 0.009 \)) were both associated with increased mortality, while Risk class (in-hospital mortality, 16.5%; unadjusted OR, 1.5; 95% CI 0.5–4.0; \( P = 0.446 \)) was not.

Forty-three patients (67.2%) with AKI had renal function recovery at hospital discharge, and the probability of renal function recovery decreased with increasing severity of AKI (Risk, 85.2%; Injury, 61.9% and Failure, 43.8%; \( P = 0.002 \)). Serum creatinine at hospital discharge was higher in patients who had AKI than in those patients without AKI (\( P < 0.001 \)) (Table 1), and it varied according to severity of AKI [Risk, 0.8 (0.3); Injury, 1.3 (1.4) and Failure, 2.6 (3.2); \( P = 0.01 \)].

**Discussion**

We conducted a cohort study including 489 hospitalized HIV-infected patients to analyze the incidence, etiology...
and risk factors of AKI, as well as its impact on in-hospital mortality. We found that 18% of patients developed AKI within the hospitalization. AKI was multifactorial in approximately one-half of cases, and the most common etiologies were sepsis, nephrotoxic drug administration, volume depletion and radiocontrast use. Preexisting hypertension, AIDS, sepsis and nephrotoxic drug administration were associated with increased risk of AKI. The development of AKI was associated with lengthened time of hospitalization and increased in-hospital mortality of those patients. Furthermore, there was a relationship between more severe AKI and increased in-hospital mortality.

AKI is a common complication of hospitalized patients and it is associated with increased morbidity and in-hospital mortality in several settings [22, 28–36], and its detrimental effect appears to persist also after recovery, since AKI has shown to increase long-term mortality [37–39]. Understanding the epidemiology and etiologies of AKI is a powerful tool in identifying patients at risk. This challenge is magnified when considering the HIV-infected patient with multiple comorbidities, coinfections and nephrotoxic regimens complicating their management. In addition, HIV-infected patients are also at increased risk for AKI development within hospitalization, related to volume depletion, sepsis and the acute administration of nephrotoxic medications or radiocontrast. The epidemiology of AKI in hospitalized HIV-infected patients in the HAART era has not been extensively analyzed. In fact, few studies have focused on the clinical characteristics of AKI in hospitalized HIV-infected patients in the HAART era [15–17]. Wyatt et al. [15] compared the incidence of AKI in HIV-infected patients before and after the introduction of HAART and also ascertained the impact of AKI on in-hospital mortality in the HAART era. For this purpose, they evaluated all adult patients who were discharged from acute care hospitals in New York State during 1995 (pre-HAART era) and during 2003 (post-HAART era). The presence of AKI was determined by diagnosis code 584 of the International Classification of Diseases, 9th Revision (ICD-9), which identified AKI based on the clinical judgment of the treating physician. There were 52 580 patients with documented HIV infection discharged from hospital in 1995 and 25 114 in 2003. AKI was reported significantly more often during hospitalizations for HIV-infected patients than for uninfected patients in both 2003 (6 versus 2.7%) and 1995 (2.9 versus 1.0%). After adjusting for other covariates, HIV infection remained associated with an increased risk of AKI both in 2003 (OR 2.82, 95% CI 2.66–2.99) and in 1995 (OR 4.62, 95% CI 4.3–4.95). Older age, male gender, black race, diabetes, preexisting CKD and liver disease were independent risk factors of AKI. Hospitalizations of HIV-infected patients that were complicated by AKI were also complicated by much higher in-hospital mortality (27%) than seen in admissions of HIV-infected patients without AKI (4.5%). In multivariate analysis, AKI independently increased in-hospital mortality in HIV-infected patients. In a previous study [16], we also evaluated the incidence, etiology and risk factors of AKI defined by the RIFLE criteria as well as its impact on 60-day mortality in a cohort of critically ill HIV-infected patients. We found that 47% of the patients studied had AKI. The most common etiology of AKI was sepsis (n = 39, 84%). Other less common etiologies of AKI were nephrotoxic drugs administration (n = 4, 8.7%) and volume depletion (n = 3, 6.5%). Older age, hepatitis C virus coinfection, sepsis and severity of illness were predictors of AKI. Patients who experienced AKI had higher mortality than those patients who did not develop AKI, and there was a graded relationship between AKI severity and mortality. After adjusting for other covariates, AKI still remained associated with increased 60-day mortality. Choi et al. [17] conducted an observational cohort study in a national sample of 17 325 HIV-infected persons receiving care in the Veterans Health Administration who survived at least 90 days after discharge from their first hospitalization to examine the association between AKI experienced during their first hospitalization with the development of heart failure, atherosclerotic cardiovascular events, end-stage renal disease (ESRD) and death over a period of two decades. They found a graded and independent association between severity of AKI with heart failure, cardiovascular disease, ESRD and death.

In the present study, the prevalence of AKI (18%) was much higher than that previously reported (6%) in hospitalized HIV-infected patients in the HAART era [15]. It should be remembered that in the study of Wyatt et al. [15], the diagnosis of AKI was determined by diagnosis code 584 of the ICD-9 based on the clinical judgment and documentation of the treating physician, and laboratory values were not reported. Administrative databases may be a powerful tool for the study of AKI, although the low sensitivity of the AKI codes still remains an important caveat [40]. Therefore, in the study of Wyatt et al. [15], the utilization of a diagnostic...
Hypertension is an important risk factor for CKD and cardiovascular disease [26]. In the present study, preexisting hypertension was more common in AKI patients and was associated with increased risk of AKI. This finding suggests that an adequate control of blood pressure in HIV-infected patients beyond the positive impact on CKD and cardiovascular disease could be an important measure to decrease the incidence of AKI in those patients.

The limited number of studied patients does not allow us to definitively conclude about the influence of HAART and more specifically tenofovir-containing regimen in the occurrence of AKI. Therefore, prospective and randomized studies with a large number of patients are still warranted to better determine the precise impact of antiretroviral regimens in renal function among HIV-infected patients who are hospitalized.

We have analyzed the influence of several factors in predicting AKI in hospitalized HIV-infected patients. Some of the tested variables were specific of the HIV-infected population, namely type of HIV, HAART, CD4 lymphocyte count, viral load and AIDS diagnosis. However, from those HIV infection-specific variables, only AIDS was independently associated with increased risk of AKI. We highlight that, although more specific factors related to HIV infection could increase the risk of AKI, common risk factors of AKI (i.e. preexisting hypertension, sepsis and nephrotoxic drugs) could also predict the development of AKI in hospitalized HIV-infected patients. Moreover, in the present study, severe sepsis was a risk factor of in-hospital mortality. Therefore, their prompt recognition and aggressive treatment could be crucial both in diminishing the occurrence of AKI and mortality in this specific population [41, 42].

AKI was simultaneously associated with lengthened time of hospitalization and increased in-hospital mortality. This finding has also previously been demonstrated in HIV-infected patients [15, 16] and in other settings of hospitalized patients [22, 28–36]. The mechanism by which AKI contributes to increased mortality is not completely understood but volume overload, coagulation abnormalities, an increased incidence of sepsis with multiorgan failure, and cytokine or immune-mediated major organ dysfunction are possible explanations for poor outcome among AKI patients [43, 44]. In the present study, sepsis was found much more often among AKI patients and was associated with increased in-hospital mortality; however, after adjusting for sepsis and other covariates with prognostic importance, AKI still remained a predictor of in-hospital mortality. Therefore, the burden of mortality in patients with AKI cannot solely be explained by the high incidence of sepsis in such patients.

Our study has some limitations. First, the single-center nature of the study largely limits its generalizability, and its retrospective design with a relatively small cohort of patients did not allow the evaluation of other confounders with prognostic importance. Second, we did not have daily values of serum creatinine and urine output records; therefore, we were not able to capture all cases of AKI which occurred within the hospitalization.

Despite the aforementioned constraints, however, our study has some virtues. First, AKI was diagnosed and classified by the RIFLE criteria based on serum creatinine determinations. Second, contrary to other studies [15], the etiology of AKI was analyzed, and we also accounted for severity of HIV infection through CDC staging, HIV viral load and CD4 cell count.

Conflict of interest statement. None declared.

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