

Renal failure in HIV-positive patients—a South African experience

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Abstract

Background. Kidney disease is a major complication of HIV infection, with both acute kidney injury (AKI) and chronic kidney disease (CKD) contributing to morbidity and mortality. Incidence of AKI was reported as 5.9 per 100 patient years in ambulatory patients and ~18% in hospitalized HIV-infected patients, an almost 3-fold higher risk compared with HIV uninfected patients in developed countries. CKD was reported in 6–48.5% of HIV-infected patients in Africa. There is a paucity of data regarding the prevalence and outcomes of AKI in HIV-infected patients in sub-Saharan Africa, the region most affected by HIV.

Methods. A retrospective review of 101 HIV-positive anti-retroviral therapy (ART)-naïve patients presenting with renal failure from 1 October 2005 to 30 September 2006 was undertaken.

Results. A total of 684 patients presented with renal failure, 101 (14.8%) of whom were HIV positive. Ninety-nine (98%) of HIV-positive patients were black and 56 (55%) were male, with mean age 38 ± 9.9 years (range 21–61 years). HIV-positive patients demonstrated severe immunosuppression, with mean CD₄ count of 135 cells/μL (range 1–579 cells/μL). Fifty-seven (56%) HIV-positive patients presented with AKI, 21 (21%) with acute-on-chronic kidney disease and 23 (23%) with CKD; seven patients with AKI were excluded due to lack of records. The causes of AKI in the HIV-positive group included sepsis (60%), volume depletion and haemodynamic instability (19%), toxins (9%), urological obstruction (7%) and miscellaneous (14%). Forty-four per cent of HIV-positive and 47% of HIV-negative patients with AKI demised; *P* = 0.45. Hyponatraemia (*P* = 0.018), acidosis (*P* = 0.018), anaemia (*P* = 0.019) and hyperphosphataemia (*P* = 0.003) were predictors of mortality in HIV-positive patients with AKI. In comparison, predictors of mortality in the HIV-negative group were age (*P* = 0.023) and black ethnicity (*P* = 0.04).

Conclusion. HIV-positive patients, compared with the HIV-negative group, presented with AKI at a younger age and at an advanced stage of immunosuppression. Appropriate support, including dialysis, resulted in similar outcomes in both groups.

Keywords: acute kidney injury; Africa; HIV; renal failure

Introduction

Kidney disease is a major complication of HIV infection, with reports of acute kidney injury (AKI) and chronic kidney disease (CKD), contributing to morbidity and mortality in developed countries. Kidney function is abnormal in as many as 30% of HIV-infected patients and AIDS-related kidney disease has become a relatively common cause of end-stage renal disease requiring dialysis [1–4]. The prevalence of HIV-associated CKD in Africa was reported as 6–48.5% [5]. Acute kidney injury is a common complication among both ambulatory and hospitalized HIV-infected patients, with an estimated incidence of 5.9 per 100 patient-years in ambulatory patients [6] and ~18% in hospitalized HIV-infected patients, [7] an almost 3-fold higher risk compared with HIV-uninfected patients [8]. Risk factors for AKI in HIV infection are lower CD₄ counts, AIDS, hepatitis C and liver disease [7–9].

Immunodeficiency has been considered to play a major role in AKI in HIV-infected populations [10]. Medications used to treat opportunistic infections, as well as anti-retroviral therapy (ART), may be nephrotoxic and result in AKI [5–8]. Hospitalized HIV-infected patients with AKI in New York State acute care hospitals had increased risk of AKI, both in the pre-ART era (OR 4.62) and in the ART era (OR 2.82) [8]. Those with AKI suffered much higher in-hospital mortality (26.6%), compared with a mortality of 4.5% in those without AKI. AKI was associated with an almost 6-fold increase in in-hospital mortality among HIV-infected patients in this study.

The majority of the 34 million people infected with HIV worldwide reside in sub-Saharan Africa, with 5.6 million in South Africa. Sub-Saharan Africa remains most severely affected, with nearly 1 in every 20 adults (4.9%) living with HIV and accounting for 69% of the people living with HIV worldwide [11]. Therefore, the burden of both AKI and

CKD in South Africa would be anticipated to be high, especially as the majority of patients currently present to the public sector hospital facilities in an ART-naïve state. The prevalence of AKI associated with HIV infection in Africa is largely unknown, with few reports of AKI in HIV-positive patients [12, 13]. Ingestion of toxic herbs, infections and diarrhoeal diseases with dehydration resulting in AKI were considered as major factors in this patient population [12].

We therefore reviewed the outcomes of renal failure, with a focus on AKI in HIV-positive ART-naïve patients over a 1-year period.

Subjects and methods

A retrospective review of patients presenting to the adult acute renal service of the Division of Nephrology at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH), a tertiary referral hospital draining the greater Johannesburg area, was conducted during the period 1 October 2005 to 30 September 2006. The study aimed at reviewing data of HIV-positive patients with renal failure and primarily compared HIV-positive and HIV-negative patients with AKI presenting in the same period, matched as closely as possible with regard to age and gender, selected as monthly consecutive referrals after the HIV-positive patients. The identities of all patients were kept confidential.

Demographic data, laboratory results and other information were abstracted from the records of nephrology referrals kept in the 'acute renal' database. Summaries and hospital files were reviewed where available. The University of the Witwatersrand Ethics Committee granted ethics approval unconditionally (Clearance certificate M070427).

Causes of renal failure

Those with haemodynamic instability included pre-renal patients based on the clinician's impression, predominantly those with hypotension and/ or dehydration secondary to gastrointestinal losses but also with conditions such as cardiac failure and haemorrhage. Toxins included contrast agents used for diagnostic investigations, 'Muti' (traditional medicines), drugs such as aminoglycosides and amphotericin B. Urological obstruction included those patients presenting with urinary retention secondary to masses (infectious or neoplastic), prostatic pathology and drugs. Those presentations not included in the above groups were placed into the miscellaneous group.

Study definitions

Hypertension was defined using the South African Hypertension Society guidelines, i.e. SBP > 140 mmHg and/or DBP > 90 mmHg, or known hypertensive patient on medication. Tuberculosis (TB) was diagnosed by the identification of acid-fast bacilli in sputum, bone marrow, TB blood culture or by the attending medical doctor's judgment of the patient's chest X-ray. Serum electrolytes including sodium, potassium, chloride and bicarbonate together with blood urea and serum creatinine were collected on admission. The lowest serum creatinine and the serum creatinine on discharge were collected as well. The days of recovery were calculated by reviewing the serial serum creatinine levels and the lowest levels achieved. Urine dipstick results as well as urine microscopy, culture

and sensitivity were obtained. Proteinuria was obtained from a spot urine protein creatinine ratio (P:C) and/or dipstick proteinuria. The organisms cultured from the blood were documented. Haemodialysis was initiated according to standard indications. The outcome was measured as either recovery or death.

Patients were stratified (opinion-based) into three groups, namely AKI, acute-on-chronic kidney disease (AOCKD) and CKD. The reviewed data that helped stratify the groups included past medical history of CKD, serum creatinine and recovery of serum creatinine within 3 months. Hence, the improvement of renal function was reviewed by the difference in the admission creatinine and the lowest creatinine achieved or independence from dialysis if previously dialysis-requiring.

AKI was defined as an improvement in admission serum creatinine of >50%. This group was further subdivided using the RIFLE criteria into 'Risk', 'Injury' and 'Failure' [11]. Using a serum creatinine of <97 µmol/L as normal (as referenced by the National Health Laboratory Service at the CMJAH), the three groups were categorized as below: Risk: serum creatinine <194 µmol/L, Injury: serum creatinine 195–291 µmol/L and Failure: serum creatinine >291 µmol/L.

Those patients who recovered renal function partially (improvement in serum creatinine <50%) with evidence of underlying CKD were categorized as AOCKD. The definition of CKD applied to those patients whose serum creatinine did not improve after 3 months or with persistent proteinuria. Data collected included in-hospital consultations, thus strict adherence to the definition could not be observed as follow-up data for up to 3 months was not available for most patients, who were lost to follow-up.

Statistical analysis

Continuous variables were expressed as mean ± standard deviation or median and interquartile range and compared using the Student *t*-test or the Wilcoxon rank-sum test, as appropriate. Categorical variables were expressed as proportions and compared with the chi-square or Fisher exact test, as appropriate. All statistical tests were two sided, and *P* < 0.05 was considered significant. Univariate multinomial logistic regression was used to determine factors associated with either HIV status or mortality or both among the patients with AKI. The HIV-negative and alive group was used as a reference and was compared with HIV positive and alive, HIV negative and deceased and HIV positive and deceased. The analysis did not control for potential confounders by the use of multivariable multinomial logistic regression, due to missing data in some of the variables and the risk of committing a type III error. Stata 12.0 (Stata Corporation, College Station, TX) was used for data analysis.

Results

In the period reviewed, 684 patients presented with renal failure to the adult acute renal service at the CMJAH. Of these, 101 patients were HIV positive (14.8%), who were predominantly black (98%) and 55% were males. The mean age was 38 ± 9.9 years (range 21–61 years).

HIV-positive patients and renal failure

The majority of the HIV-positive patients presented with AKI (57 patients; 56%), followed by CKD (23 patients; 23%)

and lastly AOCKD (21 patients; 21%). The characteristics of the 101 HIV-positive patients are summarized in Table 1.

Comparison between HIV-positive and HIV-negative patients with AKI

The demographic, clinical and laboratory parameters of the 50 HIV-positive (7 HIV-positive patients were excluded due to lack of records) and 90 HIV-negative patients were reviewed as well as their outcomes (see Table 2). The HIV-positive patients with AKI were divided using the 'RIFLE' classification into three groups; Risk 4 patients (8%), Injury 10 patients (20%) and Failure 36 patients (72%). The HIV-negative group was also divided into three groups; Risk 26 patients (29%), Injury 24 patients (27%) and Failure 40 patients (44%).

HIV-positive patients with AKI presented with more severe renal failure than HIV-negative patients. Using the RIFLE classification, 72% of HIV-positive patients presented in the most severe clinical category (Failure) when compared with 44% of HIV-negative patients ($P=0.014$). Conversely, 29% of HIV-negative patients presented in the least severe clinical category (Risk) when compared with only 8% of HIV-positive patients ($P=0.038$).

Demographics

There were 28 males (56%), with a mean age of 37.4 ± 10.4 years (range 21–67 years) in the HIV-positive group with AKI, compared with 55 males (61%) with a mean age of

45.2 ± 17 years (range 18–84 years) in the HIV-negative group. The majority of the HIV-positive patients were black (49 patients; 98%) and this was statistically significant when compared with the HIV-negative group (67 patients; 74%; $P<0.001$). In the HIV-positive group, the majority of the patients were referred from the internal medicine wards, 37 patients (74%) when compared with the HIV-negative group of 43 patients (48%) ($P=0.019$).

Clinical parameters

Sepsis was the predominant cause of AKI in both groups but was more common in the HIV-positive group (62 versus 43%; $P=0.035$). In the HIV-positive group, 18 (36%) patients were dialysed when compared with 35 (39%) in the HIV-negative group. There were two patients each with diabetes mellitus and hypertension in the HIV-positive group, compared with 13 with diabetes mellitus ($P=0.014$) and 19 with hypertension ($P=0.004$) in the HIV-negative group. TB was diagnosed in 13 patients in the HIV-positive group, when compared with 2 in the HIV-negative group ($P<0.001$). Hepatitis B surface antigenaemia was present in two HIV-positive patients. HIV-positive patients had larger kidney size on ultrasonography than HIV-negative patients (12.16 versus 11.1 cm).

Laboratory parameters

HIV-positive patients on presentation were significantly more hyponatraemic (Na^{2+} 132 versus 139 mmol/L;

Table 1. Spectrum of HIV-positive patients presenting with renal failure

	AKI [n = 57 (56%)]	AOCKD [n = 21 (21%)]	CKD [n = 23 (23%)]	Total (n = 101)
Aetiology (%)				
Sepsis	34 (60%)	15 (48%)	11 (48%)	60
Haemodynamic instability	11 (19%)	2 (10%)	0	13
Toxin	5 (9%)	0	3 (13%)	8
Urological obstruction	4 (7%)	0	0	4
Miscellaneous	8 (14%)	2 (10%)	5 (22%)	15
Dialysed	22 (39%)	8 (38%)	13 (57%)	43
SBP (mmHg)	108 (± 33)	125 (± 37)	157 (± 48)	123 (± 41)
DBP (mmHg)	69 (± 17)	75 (± 22)	93 (± 27)	76 (± 22)
Na (mmol/L)	132 (± 7.05)	134 (± 5)	133 (± 10)	133 (± 7)
K (mmol/L)	4.9 (± 1.32)	4.8 (± 1.0)	5.2 (± 1.6)	5.0 (± 1.3)
Cl (mmol/L)	98 (± 9)	102 (± 9)	99 (± 13)	99 (± 10)
CO ₂ (mmol/L)	14 (± 6)	14 (± 5)	11 (± 6)	14 (± 6)
Urea (mmol/L) (admission)	35 (± 21)	33 (± 22)	52 (± 27)	39 (± 24)
Serum creatinine ($\mu\text{mol/L}$) (admission)	634 (± 416)	678 (± 441)	1445 (± 791)	828 (± 622)
White cell count	10.7 (± 7.9)	10.8 (± 6.3)	12.4 (± 8.3)	11.1 (± 7.7)
Haemoglobin (g/dL)	10.0 (± 2.9)	8.7 (± 3.1)	8.4 (± 2.0)	9.4 (± 2.8)
Platelets ($\times 10^9/\text{L}$)	263 (± 173)	289 (± 175)	268 (± 101)	269 (± 159)
Albumin (g/dL)	26.6 (± 8.0)	27.3 (± 8.1)	26.7 (± 7.8)	26.8 (± 7.9)
Hepatitis B	2 (0.02%)	0	3 (0.03%)	5
Hepatitis C	1 (0.01%)	1 (0.01%)	0	2
Ca (mmol/L)	2.28 (± 0.23)	2.29 (± 0.25)	2.25 (± 0.19)	2.27 (± 0.22)
Mg (mmol/L)	1.11 (± 0.25)	0.94 (± 0.32)	1.00 (± 0.28)	1.04 (± 0.28)
PO ₄ (mmol/L)	2.49 (± 0.95)	1.99 (± 1.2)	2.80 (± 0.99)	2.46 (± 1.04)
Uric acid (mg/dL)	0.70 (± 0.14)	0.57 (± 0.3)	0.49 (± 0.15)	0.60 (± 0.20)
Blood culture: <i>S.pneumonia</i>	3 (3%)	1 (1%)	1 (1%)	5
Staphylococcus	0	0	2 (2%)	2
MRSA	3 (5%)	1 (5%)	0	4
<i>E. coli</i>	2 (4%)	1 (5%)	0	3
Salmonella	2 (4%)	0	0	2
Urine				
Leucocytes+	32 (56%)	13 (62%)	13 (56%)	58 (57%)
Erythrocytes +	20 (35%)	10 (48%)	10 (44%)	40 (40%)
Urine P:C	0.24 (± 0.24)	0.58 (± 0.63)	1.25 (± 1.21)	0.61 (± 0.83)
Urine				
<i>E. coli</i>	4 (7%)	3 (14%)	2 (9%)	9 (9%)
<i>Klebsiella pneumonia</i>	3 (5%)	1 (5%)	0	4 (4%)
CD ₄ count (cells/ μL)	146 (± 156)	75 (± 83)	170 (± 153)	135 (± 146)
CD ₄ <200	36 (63%)	16 (76%)	11 (48%)	63 (62%)
In-hospital mortality	22 (39%)	6 (29%)	5 (22%)	33 (33%)

Table 2. Comparison between HIV-positive and HIV-negative patients presenting with acute kidney injury

	HIV positive (n = 50)	HIV negative (n = 90)	P value
Age (years)	37.4±10.5	45.2 ± 17.0	0.004
Gender (male)	28 (56%)	55 (61%)	0.249
Race (black)	49 (98%)	67 (74%)	<0.001
Co-morbidity			
Hypertension	2 (4%)	19 (21%)	0.004
Diabetes mellitus	2 (4%)	13 (14%)	0.014
Tuberculosis	13 (26%)	2 (2%)	<0.001
HBV co-infection	2 (4%)	-	-
Aetiology			
Sepsis	31 (62%)	39 (43%)	0.035
Haemodynamic	10 (20%)	15 (17%)	0.391
Toxins	5 (10%)	6 (7%)	0.258
Obstruction	4 (8%)	7 (8%)	0.600
Miscellaneous	5 (10%)	21 (23%)	0.040
Referral wards			
Medical	37 (74%)	43 (48%)	0.019
Surgical	4 (8%)	22 (24%)	
ICU	6 (12%)	15 (17%)	
Obstetrics and Gynaecology	3 (6%)	10 (11%)	
Dialysed	18 (36%)	35 (39%)	0.440
Kidney size			
Right	12.1 ± 1.36	11.0 ± 1.64	0.022
Left	12.2 ± 1.48	11.2 ± 1.29	0.040
Electrolytes			
Sodium (mmol/L)	132 ± 7.10	139 ± 9.76	<0.001
Potassium (mmol/L)	4.9 ± 1.28	4.5 ± 1.21	0.042
Chloride (mmol/L)	98 ± 8.74	103 ± 10.67	0.012
CO ₂ (mmol/L)	14.7 ± 5.74	19.4 ± 7.43	<0.001
Urea (mmol/L)	34.5 ± 21.76	23.3 ± 17.67	0.001
Serum creatinine (µmol/L)	619 ± 406.88	455 ± 560.93	0.072
Calcium (mmol/L)	2.3 ± 0.22	2.3 ± 0.18	0.160
Magnesium (mmol/L)	1.1 ± 0.25	0.9 ± 0.30	0.005
Phosphate (mmol/L)	2.5 ± 0.97	1.8 ± 1.04	<0.001
Haemoglobin (g/dL)	10.0 ± 3.01	10.8 ± 3.09	0.137
Albumin (g/dL)	27.2 ± 8.37	28.6 ± 8.56	0.337
Urine P:C	0.26 ± 0.25	0.28 ± 0.36	0.841
In-hospital mortality	22 (44%)	42 (47%)	0.450

$P < 0.001$, t -test), with higher serum potassium (K^+ 4.9 versus 4.5 mmol/L; $P = 0.042$, t -test) and hypochloaemic (Cl^- 98 versus 103 mmol/L; $P = 0.0121$, t -test) compared with the HIV-negative patients. HIV-positive patients were also more acidotic (CO_2 14.7 versus 19.4 mmol/L; $P < 0.001$, t -test). Serum calcium levels were similar; however, HIV-positive patients were more hyperphosphataemic compared with HIV-negative patients (PO_4^{3-} 2.49 versus 1.78 mmol/L; $P < 0.001$, t -test). HIV-positive patients had a higher baseline mean blood urea level (34.5 versus 23.3 mmol/L; $P = 0.001$) and higher serum creatinine (619 ± 407 µmol/L) on admission than the HIV-negative patients (455 ± 561 µmol/L); $P = 0.072$. Haemoglobin levels were similar when comparing HIV-positive (10.0 ± 3.01 g/dL) and HIV-negative patients (10.84 ± 3.09 g/dL). Serum albumin levels were similar in HIV-positive (27.17 ± 8.37 g/dL) and HIV-negative patients (28.58 ± 8.56 g/dL). The urine P:C did not differ between the HIV-positive patients (0.26 g/mmol) and the HIV-negative patients (0.28 g/mmol). Urine P:C on admission in the AKI, AOCKD and CKD group was 0.24, 0.58 and 1.25, respectively, with nephrotic range proteinuria in the AOCKD and CKD groups. However, urine P:C could not be used as a reliable predictor of the outcome as this test was only done in 22 of the 90 HIV-negative patients. Infections due to *Streptococcus pneumoniae*, methicillin-resistant *Staphylococcus aureus*, *Escherichia*

coli (*E. coli*) and *Salmonella* infections were identified more commonly in the AKI group when compared with the CKD group in HIV-infected patients; however, in the CKD group, *S. aureus* was more common. Leucocyturia was present in more than half of all the HIV-positive patients: 32 patients (64%) of the AKI group, 13 (62%) of the AOCKD group and 13 (57%) of the CKD group. *Escherichia coli* was cultured in the urine in all three groups, occurring in 8.9%.

Mortality associated with renal failure

Overall, 33 of the 101 HIV-positive patients died in hospital, 22 (38.6%) in the AKI group, 6 (2.9%) in the AOCKD group and 5 (2.2%) in the CKD group. Gender did not have an impact on the outcome of AKI. All six HIV-positive patients with AKI admitted to ICU died. An equal percentage (22%) of HIV-positive patients that were dialysed and those that were treated with supportive care only (without dialysis) died. Proteinuria did not predict recovery or death in HIV-positive patients with AKI. Using multinomial logistic regression, the following were significant factors that predicted mortality in HIV-positive patients: hyponatraemia ($P = 0.018$), acidosis ($P = 0.018$), hyperphosphataemia ($P = 0.003$) and anaemia ($P = 0.019$) (see Table 3). In comparison, the predictors of mortality in the HIV-negative group were age ($P = 0.023$) and black ethnicity ($P = 0.04$).

Discussion

HIV-positive patients presented more commonly with AKI (57 of the 101 patients) than with AOCKD and CKD. The younger age of the HIV-positive patients presenting with renal failure (38 ± 9.9 years) was similar to that reported in previous studies (35–46.7 years) [6, 8, 14, 15]. Males represented the majority of patients in previous studies and this study. Patients presenting in our setting with renal failure who were HIV positive were more likely to be black. The only other study showing 99% of the patients presenting with AKI to be black was the study by Rao *et al.* [14]. The studies by Wyatt, Ibrahim and Franceschini each showed the percentage of black patients with AKI to be 54.5, 55 and 61%, respectively [6, 8, 9]. The racial predominance is different to that of other countries, which might be due to epidemiological factors and the spread of HIV. The majority race in South Africa is black and the predominance of black patients that are HIV positive presenting with renal failure is evident.

When the aetiology of renal failure was reviewed, the commonest cause of renal failure was sepsis (60%) followed by volume depletion and haemodynamic instability in HIV-infected patients. Urological obstruction was the least common cause of renal failure (4%). Sepsis was also the predominant aetiology of renal failure in other studies. Rao *et al.* [14] reported that sepsis was the commonest aetiology, occurring in 52% of hospitalized patients. Sepsis was the most frequent cause of AKI in the retrospective review by Peraldi *et al.* [15], accounting for 75% of cases. Other studies showed that sepsis was less common; however, these included ambulatory and not hospitalized patients [9]. Acute kidney injury patients presented in a hypotensive state more frequently (in 19%), compared with AOCKD (10%) and CKD (0%) patients, with a mean BP of $108 (\pm 33)/69 (\pm 17)$ mmHg. The definition of

Table 3. Outcome data (mortality) comparing HIV-positive and -negative patients with acute kidney injury (Reference group HIV-negative and alive patients)

Variables	HIV-positive and alive patients		HIV-negative and deceased patients		HIV-positive and deceased patients	
	OR (95% CI)	P- value	OR (95% CI)	P- value	OR (95% CI)	P- value
Age (years)	0.98 (0.94; 1.01)	0.24	1.03 (>1.00; 1.06)	0.023**	0.98 (0.94; 1.02)	0.27
Gender (female as reference)	0.38 (0.08; 1.95)	0.25	0.25 (0.05; 1.25)	0.092*	0.24 (0.03; 2.03)	0.19
Race (non-Black as reference)						
Black	–	–	2.78 (1.03; 7.45)	0.04**	0.23 (0.03; 2.03)	0.19
Diabetes	0.41 (0.04; 3.84)	0.43	3.00 (0.85; 10.60)	0.09*	–	–
Aetiology (none as reference groups)						
Sepsis	1.71 (0.70; 4.39)	0.26	1.06 (0.46; 2.44)	0.89	2.76 (0.95; 7.98)	0.06*
Haemodynamic instability	1.18 (0.37; 3.76)	0.78	0.72 (0.23; 2.23)	0.57	0.96 (0.26; 3.55)	0.96
Urological obstruction	1.03 (0.23; 4.69)	0.97	0.43 (0.08; 2.34)	0.43	0.41 (0.04; 3.73)	0.45
Miscellaneous	0.45 (0.11; 1.82)	0.27	1.35 (0.51; 3.59)	0.55	0.38 (0.76; 1.9)	0.24
Dialysis	0.47 (0.17; 1.31)	0.15	0.78 (0.33; 1.83)	0.56	1.4 (0.51; 3.86)	0.52
Sodium	0.92 (0.86; 0.99)	0.018**	1.05 (>1.00; 1.10)	0.06*	0.92 (0.85; 0.99)	0.018**
Potassium	1.31 (0.91; 1.90)	0.15	0.86 (0.60; 1.23)	0.41	1.17 (0.78; 1.76)	0.44
Chloride	0.96 (0.91; 1.01)	0.11	1.03 (0.99; 1.08)	0.10*	0.98 (0.93; 1.03)	0.46
CO ₂	0.93 (0.86; 1.01)	0.07*	1.06 (1.00; 1.13)	0.06*	0.90 (0.83; 0.98)	0.018**
Urea (admission)	1.02 (>1.00; 1.05)	0.016**	0.98 (0.96; 1.01)	0.23	1.01 (0.99; 1.04)	0.32
Creatinine (admission)	1.00 (1.00; >1.00)	0.42	1.00 (1.00; >1.00)	0.07*	1.00 (1.00; >1.00)	0.73
Calcium	0.22 (0.02; 2.75)	0.24	2.08 (0.19; 22.60)	0.54	0.72 (0.04; 14.37)	0.83
Phosphate	1.96 (1.16; 3.33)	0.012**	1.18 (0.70; 1.99)	0.53	2.36 (1.33; 4.20)	0.003***
Haemoglobin	0.97 (0.84; 1.14)	0.75	0.97 (0.84; 1.11)	0.62	0.80 (0.67; 0.97)	0.019**
Albumin	0.99 (0.93; 1.05)	0.67	0.99 (0.93; 1.05)	0.64	0.94 (0.88; 1.02)	0.13
Urine P:C	0.58 (0.06; 5.99)	0.65	0.41 (0.02; 7.32)	0.54	0.55 (0.32; 9.49)	0.68

OR, odds ratio; CI, confidence interval.

Univariate multinomial logistic regression: *Signifying a trend ($P > 0.05-0.1$), **statistically significance $P > 0.01-0.05$, ***greater statistically significance $P < 0.01$.

AKI could misclassify some patients with non-resolving AKI as AOCKD.

Hyponatraemia was common among all three groups, but most severe in the AKI patients. The study by Agarwal *et al.* [16] reported the incidence of hyponatraemia in HIV-infected patients as 30–60%. The common causes of hyponatraemia were diarrhoea and vomiting. HIV-positive CKD patients presented with more severe hyperkalaemia and acidosis, probably secondary to renal failure or concomitant drugs such as trimethoprim-sulphamethoxazole. Mineralocorticoid deficiency could also account for the hyperkalaemia and hyponatraemia, but was not proven in this study. CKD patients were also appropriately more hypocalcaemic and hyperphosphataemic than other patients, in keeping with chronicity.

The mean CD₄ count of the whole group was 135 cells/ μ L (range 1–579 cells/ μ L), with 63% of patients with AKI with CD₄ counts <200 cells/ μ L. In the study by Franceschini *et al.* [6], only 29% had CD₄ <200 cells/ μ L. The mean CD₄ count in the AOCKD patients was much lower (75 cells/ μ L) than that of AKI patients (146 cells/ μ L) and CKD (170 cells/ μ L) patients. This could possibly be due to the fact that these patients had underlying CKD, and with compromised renal function and lower CD₄ counts, making these patients more susceptible to an acute illness resulting in acute renal dysfunction superimposed on CKD (AOCKD). A recent study from Cape Town reported improved survival of HIV-positive acute dialysis-requiring patients when the CD₄ count was >200 cells/ μ L [13]. The effect of ART on AKI could not be evaluated in this study as all of the patients were ART-naïve; studies have shown that the adjusted odds ratio for AKI in HIV-positive individuals was elevated in both the pre-HAART (4.6) and the post-HAART (2.8) era [17]. Further studies in the post-HAART period are warranted. AKI in HIV-positive patients carries a high mortality; however, there

was no difference in the outcome when compared with HIV-negative patients.

Limitations

This was a retrospective review; thus, there were limitations with missing data; in addition, AKI has many different definitions. The 'RIFLE' classification is universally used; however, different laboratories have different serum creatinine levels and many centres do not accurately measure urine output. We were limited in applying the definition of AKI as the baseline serum creatinine used was the serum creatinine on admission to hospital with advanced AKI in the majority of patients; in addition, most of the patients were managed as in-patients and did not return to out-patient follow-up after discharge from hospital. Thus, the definition of AKI as having normal renal function at 90 days could not be fulfilled. Thus, the term 'probable AKI' would be more appropriate. The patients in the two groups were not ideally matched and our sample size was too small to allow for multivariate analysis.

Conclusion

Outcomes of AKI were similar in HIV-positive and HIV-negative patients in this study; however, the HIV-negative patients were older and presented with more chronic comorbidities such as hypertension and diabetes.

Dialysis should be offered when indicated and aggressive fluid resuscitation, antibiotics as well as other supportive care should be emphasized, as it is likely that a higher percentage of patients will recover.

Acknowledgements. We thank the Charlotte Maxeke Johannesburg Academic Hospital and Department of Nephrology staff for

their assistance. The data form part of a thesis for a Masters in Internal Medicine at the University of the Witwatersrand, Johannesburg, South Africa.

Conflict of interest statement. None declared.

References

1. Gupta SK, Eustace JA, Winston JA *et al.* Guidelines for the management of chronic kidney disease in HIV-infected patients: recommendations of the HIV Medicine Association of the Infectious Diseases Society of America. *Clin Infect Dis* 2005; 40: 1559–1585
2. Gupta SK, Mamlin BW, Johnson CS *et al.* Prevalence of proteinuria and the development of chronic kidney disease in HIV-infected patients. *Clin Nephrol* 2004; 61: 1–6
3. Szczech LA, Gange SJ, van der Horst C *et al.* Predictors of proteinuria and renal failure among women with HIV infection. *Kidney Int* 2002; 61: 195–202
4. Szczech LA, Hoover DR, Feldman JG *et al.* Association between renal disease and outcomes among HIV-infected women receiving or not receiving antiretroviral therapy. *Clin Infect Dis* 2004; 39: 1199–1206
5. Fabian J, Naicker S. HIV and kidney disease in sub-Saharan Africa. *Nat Rev Nephrol* 2009; 5: 591–598
6. Franceschini N, Napravnik S, Eron JJ Jr *et al.* Incidence and etiology of acute renal failure among ambulatory HIV-infected patients. *Kidney Int* 2005; 67: 1526–1531
7. Choi AI, Li Y, Parikh C *et al.* Long term consequences of acute kidney injury in the HIV-infected. *Kidney Int* 2010; 78: 478–486
8. Wyatt CM, Arons RR, Klotman PE *et al.* Acute renal failure in hospitalized patients with HIV: risk factors and impact on in-hospital mortality. *AIDS* 2006; 20: 561–565
9. Ibrahim F, Naftalin C, Cheserem E *et al.* Immunodeficiency and renal impairment are risk factors for HIV-associated acute renal failure. *AIDS* 2010; 24: 2239–2244
10. Lopes JA, Melo MJ, Viegas A *et al.* Acute kidney injury in hospitalized HIV-infected patients: a cohort analysis. *Nephrol Dial Transplant* 2011; 26: 3888–3894
11. UNAIDS Report on the global AIDS epidemic 2012 (November 2012) <http://www.unaids.org/en/> (7 December 2012, date last accessed)
12. Naicker S, Abboud O, Gharbi MB. Epidemiology of acute kidney injury in Africa. *Semin Nephrol* 2008; 28: 348–353
13. Arendse C, Okpechi I, Swanepoel C. Acute dialysis in HIV-positive patients in Cape Town, South Africa. *Nephrology* 2011; 16: 39–44
14. Rao TK, Friedman EA. Outcome of severe acute renal failure in patients with acquired immunodeficiency syndrome. *Am J Kidney Dis* 1995; 25: 390–398
15. Peraldi MN, Maslo C, Akposso K *et al.* Acute renal failure in the course of HIV infection: a single-institution retrospective study of ninety-two patients and sixty renal biopsies. *Nephrol Dial Transplant* 1999; 14: 1578–1585
16. Agarwal A, Soni A, Ciechanowsky M *et al.* Hyponatremia in patients with the acquired immunodeficiency syndrome. *Nephron* 1989; 53: 317–321
17. de Silva TI, Post FA, Griffin MD *et al.* HIV-1 infection and the kidney: an evolving challenge in HIV medicine. *Mayo Clinic Proc* 2007; 82: 1103–1116

Received for publication: 5.7.12; Accepted in revised form: 9.9.13