Major Article

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Acute kidney injury in a tropical country: a cohort study of 253 patients in an infectious diseases intensive care unit

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ABSTRACT

Introduction: Acute kidney injury (AKI) is a frequent and potentially fatal complication in infectious diseases. The aim of this study was to investigate the clinical aspects of AKI associated with infectious diseases and the factors associated with mortality. **Methods:** This retrospective study was conducted in patients with AKI who were admitted to the intensive care unit (ICU) of a tertiary infectious diseases hospital from January 2003 to January 2012. The major underlying diseases and clinical and laboratory findings were evaluated. **Results:** A total of 253 cases were included. The mean age was 46±16 years, and 72% of the patients were male. The main diseases were human immunodeficiency virus (HIV) infection, HIV/acquired immunodeficiency syndrome (AIDS) (30%), tuberculosis (12%), leptospirosis (11%) and dengue (4%). Dialysis was performed in 70 cases (27.6%). The patients were classified as risk (4.4%), injury (63.6%) or failure (32%). The time between AKI diagnosis and dialysis was 3.6±4.7 days. Oliguria was observed in 112 cases (45.7%). The Acute Physiology and Chronic Health Evaluation (APACHE) II scores were higher in patients with HIV/AIDS (57±20, p-value=0.01) and dengue (68±11, p-value=0.01). Death occurred in 159 cases (62.8%). Mortality was higher in patients with HIV/AIDS (76.6%, p-value=0.02). A multivariate analysis identified the following independent risk factors for death: oliguria, metabolic acidosis, sepsis, hypovolemia, the need for vasoactive drugs, the need for mechanical ventilation and the APACHE II score. **Conclusions:** AKI is a common complication in infectious diseases, with high mortality. Mortality was higher in patients with HIV/AIDS, most likely due to the severity of immunosuppression and opportunistic diseases.

Keywords: Acute kidney injury. Intensive care unit. Infectious diseases. RIFLE criteria.

INTRODUCTION

The incidence of acute kidney injury (AKI) in hospitalized patients is approximately 5%. This incidence is higher in the intensive care unit (ICU) and is accompanied by high mortality, especially when there is a need for dialysis, with indices ranging from 37-88%[1]. AKI is a common complication in critical illness, which is associated with high mortality and has a separate independent effect on the risk of death[1].

As the presence of infection is a risk factor for the development of AKI, this study highlights the roles of infectious diseases in kidney injury. Few studies have investigated the prognostic factors in infectious disease-associated AKI[2,3]. The aim of this study was to investigate the clinical aspects of AKI associated with infectious diseases and the factors associated with mortality using medical record review.

METHODS

The study was conducted at a tertiary infectious diseases hospital. The records of all patients admitted to the ICU from October 2003 to January 2012 were retrospectively evaluated. All patients who developed AKI during their ICU stay were included in the study. The study protocol was approved by the ethical committee of the institution.

The patients were classified according to the RIFLE criteria ("risk", "injury", "failure", "loss" and "end-stage renal disease")[4]. The baseline creatinine level was measured at the moment of hospital admission, or the lowest creatinine level before admission was considered. The RIFLE criteria were considered based on the highest creatinine level achieved by each patient during the hospital stay. The Acute Physiology and Chronic Health Evaluation (APACHE) II was used as the

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gold-standard severity score[5]. Oliguria was defined as urinary volume <400mL/day, despite appropriate fluid replacement.

The patients were divided into two groups, survivors and non-survivors, to investigate whether there were differences in the studied parameters. Non-survivors were included when death occurred after ICU discharge but before hospital discharge.

Statistical analyses were performed using SPSS 17.0 for Windows (SPSS Inc., Chicago, IL, USA) and consisted of univariate and multivariate analyses. Comparisons between the two groups of patients were performed using Student's t test, Fisher's exact test, the Mann-Whitney test and the Chi-square test, when appropriate. A logistic regression model was built for quantitative variables, and association measures were calculated (adjusted relative risk), with a confidence interval of 95%. Multiple logistic regression analysis was used to identify the independent variables used as indicators of the predictors of mortality (dependent variable). In the analyses, p-values below 5% (p-value<0.05) were considered statistically significant.

RESULTS

A total of 253 cases of AKI were recorded, with a mean age of 46±16 years; 72% of the patients were male. The main diseases were human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) (30%), tuberculosis (12%), leptospirosis (11%), meningitis (7.5%), leishmaniasis (4.5%) and dengue (4%), as summarized in **Table 1**. The patients were classified as risk (4.4%), injury (63.6%) or failure (32%). The time between the diagnosis of AKI and dialysis was 3.6±4.7 days. Oliguria was observed in 112 cases (45.7%). Dialysis was performed in 70 (27.6%) cases. The laboratory findings at ICU admission are shown in **Table 2**.

TABLE 1 - General data on critically ill patients with infectious disease-associated acute kidney injury.

Parameter	Patients	
Age (years)*	46±16	
Gender**		
male	181	72.0
female	72	28.0
Primary diagnosis at admission**		
HIV/AIDS	77	30.0
tuberculosis	31	12.0
leptospirosis	28	11.0
sepsis	28	11.0
meningitis	19	7.5
tetanus	14	5.5
pneumonia	12	5.0
visceral leishmaniasis	11	4.5
dengue	10	4.0
viral hepatitis	10	4.0
central nervous system infection	10	4.0
urinary tract infection	3	1.5
Time to develop AKI (days after admission)*	2.8±7.6	
Time to start dialysis (days)*	3.6±4.7	
Dialysis**	70	27.6

HIV/AIDS: human immunodeficiency virus/acquired immunodeficiency syndrome; AKI: acute kidney injury. The values are expressed as the means ± SDs* or as relative frequencies**.

TABLE 2 - Laboratory findings for critically ill patients with infectious disease-associated acute kidney injury.

Parameter	General (n=253)	Survivors (n=94)	Non-survivors (n=159)	p-value
Hemoglobin (mg/dL)	10±2.6	10.55±2.57	10.06±2.67	0.18
Hematocrit (%)	30±7.9	30±8.4	30±8.9	1.0
Platelets (/mm^3)	131,488±111,706	145,838±113,038	125,724±111,601	0.16
Leukocytes (/mm^3)	11,964±10,529	10429±5736	11767±7051	0.12
Serum creatinine (mg/dL)	2.7±1.8	3.2±1.8	3.1±1.7	0.65
Serum urea (mg/dL)	105±68	108±62.15	104±73.5	0.65
Serum sodium (mEq/L)	136±10	135±8.5	136±11	0.44
Serum potassium (mEq/L)	4.4±2.5	4.5±4.07	4.4±1.14	0.76
Blood pH	7.29±0.13	7.36±0.10	7.25±0.13	<0.01
Blood HCO_3 (mEq/L)	16±6.1	18.5±6.2	15.8±5.9	<0.01
AST (IU/L)	346±888	51±49	264±42	<0.01
ALT (IU/L)	172±356	151±22	196±35	<0.01

AST: aspartate aminotransferase; ALT: alanine transaminase; The values are expressed as the means ± SDs. Comparison of survivors vs. non-survivors. Student's t test.

TABLE 3 - Characteristics of critically ill patients with infectious disease-associated acute kidney injury.

Parameter	General (n=253)		Survivors (n=94)		Non-survivors (n=159)		p-value
Anemia	181	73.6	62	34.3	119	65.7	0.14
Need for MV	155	63.5	38	24.5	117	75.5	<0.01
Sepsis	152	62.3	35	23.0	117	77.0	<0.01
Low platelet count	152	62.3	50	32.9	102	67.1	0.11
Oliguria	112	45.7	36	32.1	76	67.9	0.15
Hepatopathy	97	43.1	28	28.9	69	71.1	0.03
Hypotension	67	27.1	16	23.9	51	76.1	0.02
Hyperkalemia	45	18.5	11	24.4	34	75.6	0.06

MV: mechanical ventilation. The values are expressed as the means ± SDs. Comparison of survivors vs. non-survivors. Fisher's exact test.

TABLE 4 - Mortality in critically ill patients with infectious disease-associated acute kidney injury according to the RIFLE criteria.

RIFLE criteria	General (n=253)		Survivors (n=94)		Non-survivors (n=159)	
Risk	11	4.4	5	44.4	6	54.6
Injury	161	63.6	53	32.9	108	67.1
Failure	81	32.0	33	40.7	48	59.2

The values are expressed as relative frequencies. Comparison of survivors vs. non-survivors. Chi-square test. p-value=0.33.

TABLE 5 - Risk factors for death in critically ill patients with infectious disease-associated acute kidney.

Parameter	RR	95% CI
Metabolic acidosis	4.9	2.7-8.7
Sepsis	4.3	2.4-7.6
Need for MV	3.7	2.1-6.5
Hyperkalemia	3.0	1.5-6.0
Hypotension	2.1	1.1-4.0
Use of vasoactive drugs	6.7	3.7-11.9

MV: mechanical ventilation; RR: relative risk. CI: confidence interval. The values are expressed as the means ± SDs.

The comparison of survivors and non-survivors revealed higher frequencies of mechanical ventilation, sepsis and hypotension among the non-survivors, as shown in **Table 3**.

The mean APACHE II score was 50±22. The scores were higher in patients with HIV/AIDS (57±20, p-value=0.01) and dengue (68±11, p-value=0.01) and were lower in patients with tuberculosis (33±19, p-value=0.0001) and leptospirosis (34±18, p-value=0.0002) compared with the total sample score.

The distribution of survivors and non-survivors according to the RIFLE criteria was as follows: Risk (44.4% vs. 54.6%, p-value=0.31), Injury (32.9% vs. 67.1%, p-value=1.66) and Failure (40.7% vs. 59.2%, p-value=1.20) **(Table 4)**.

Death occurred in 159 cases (62.8%). Mortality was higher in patients with HIV/AIDS (76.6%, p-value=0.02) and was lowest in those with leptospirosis (28.5%, p-value=0.0009). The risk factors for death are described in **Table 5**.

DISCUSSION

AKI is a common complication in critically ill patients and is associated with substantial increases in morbidity and mortality. The course of many infectious diseases can be complicated by AKI, as demonstrated in this study.

In this study, the mean age was 46 years, and 72% of the patients were male. Males have consistently predominated in reports on the incidence of AKI as a complication in infections, such as HIV[6,7], leptospirosis[8] and other community-acquired AKI. The reasons for such gender differences are unclear but are likely associated with work activities.

The cause of AKI in the ICU is commonly multifactorial; it frequently develops from a combination of hypovolemia, sepsis, medications and hemodynamic perturbations[9]. Sepsis is the most common cause of AKI in the general ICU, accounting for up to 50% of cases[10]. Silva Jr et al.[7] detected AKI in 37% of 532 HIV/AIDS patients. In the present study, the main causes of ICU admission were HIV/AIDS (30%), tuberculosis (12%) and leptospirosis (11%).

There are few prospective data regarding the appropriate timing of the initiation of dialysis; thus, the question of appropriate timing remains unanswered and controversial[11-13]. In the literature, the need for dialysis in patients with leptospirosis varies from 16-40%[14,15]. In the present study, dialysis was performed in 27% of cases, and the length of time between AKI diagnosis and the start of dialysis was 3 days.

The RIFLE criteria were independently associated with hospital mortality in a multivariable analysis[7,16,17]. However, in our study, the RIFLE criteria were not an independent predictor of mortality. This fact may have been due to the specific systemic conditions in infectious diseases that override renal lesions in determining mortality.

Multiple studies of patients with AKI and sepsis[18,19] and mechanical ventilation[20,21] have consistently demonstrated the increased risk of death. Mortality among HIV patients varies from approximately 25-70% and is significantly higher among patients with AKI[7,22]. Choi et al.[23] reported 48% mortality in HIV-infected patients with an estimated glomerular filtration rate (eGFR) of less than 60 and albuminuria. In the present study, 63% of the patients died. Mortality was higher in patients with HIV/AIDS. The risk factors for death in the present study were metabolic acidosis, sepsis, the need for mechanical ventilation, hypotension, hyperkalemia and the use of vasoactive drugs, similar to the findings of previous studies[2,7,24].

In summary, AKI is a common complication in infectious diseases, with high mortality. Dialysis was instituted in few cases (27%) and was started late when it was employed. Mortality was higher in patients with HIV/AIDS, most likely due to the severity of immunosuppression and opportunistic diseases. Better knowledge of the factors associated with bad prognoses in ARF cases is important for improving prevention and treatment, especially among critically ill patients.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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