Predictors of Acute Kidney Injury and Mortality in Intensive Care Unit at a Teaching Tertiary Hospital

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ABSTRACT

Background and aims: Despite the increased rates of acute kidney injury (AKI) in intensive care units (ICU) and associated mortality, information on the epidemiology of AKI is sparse in sub-Saharan Africa (SSA). We investigated the rates and predictors of AKI and associated mortality in a tertiary ICU.

Materials and methods: This retrospective study analyzed 280 hospital records of patients admitted to the ICU at a tertiary teaching hospital who were aged ≥15 years from January 2017 to May 31, 2018. The outcome parameters of the study were rates of AKI in the ICU, associated risk factors, and mortalities. Acute kidney injury and ICU mortality were established by the multivariate logistic analysis.

Results: The median age was 36 years (IQR 28, 52). The rate of AKI was 52.9%, and the presence of human immunodeficiency virus (HIV) and oliguria was 2.3-fold (0.004) and 4-fold (0.016) positive predictors of ICU-AKI, respectively. Male gender (0.003), diabetes mellitus (DM) (0.010), respiratory disease (0.001), inotropes (0.004), and ventilator support (0.017) were predictors for ICU mortality after controlling for confounders.

Conclusion: The rate of AKI is significantly higher in a referral tertiary hospital in Zambia compared to developed countries and the presence of HIV and noncommunicable diseases such as DM impacts severely on outcomes.

Keywords: Acute kidney injury, Intensive care unit, Mortality, Predictors.

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Study Procedures
Hospital record data were reviewed for age; gender; presence of comorbidities such as diabetes mellitus (DM), HIV, hypertension, cardiovascular, respiratory, and neurological diseases; and also for admission diagnosis and outcome variables (discharge from ICU or mortality). Laboratory records were reviewed to determine the hematomatological and biochemical status of patients for presence of anemia or renal disease, respectively. Patient records were subsequently clustered into AKI and non-AKI groupings.

Study Definitions and Outcomes of the Study
The primary outcomes were presence of AKI, ICU mortality, and associated risk factors. The diagnosis of AKI was based on the AKI-Kidney Disease Improving Global Outcomes (AKI-KDIGO) criteria (rising serum creatinine and reducing urine output <0.5 mL/kg per hour for 6–12 hours). Patients without a record of CKD and/or with estimated glomerular filtration rate above 60 mL/minute/1.73 m² and/or normal imaging findings were considered to have AKI when AKI-KDIGO criteria were met. Sepsis and septic shock were defined according to the survival sepsis guidelines.

Statistical Analysis
Raw data were stored in MS Excel and analyzed using Stata version 13. Nonparametric variables were reported as medians with interquartile ranges while categorical variables were presented as proportions. Comparisons of proportions were established using Mann–Whitney or Pearson’s Chi-squared tests when appropriate at the 5% significance level. Correlates for AKI and ICU mortality were established using the logistic regression analysis.

All factors significant at the 10% level in bivariate analyses were considered in the multivariate logistic regression analysis. The stepwise backward likelihood ratio variable selection method was used with an enter probability of 0.05 and a removal probability of 0.05. Unadjusted odds ratios (OR) and adjusted odds ratios (AOR) together with their 95% confidence intervals were reported.

Results
Characteristics of Participants
Altogether 280 patients’ records were reviewed and their results are reported in Table 1. A total of 143 (51%) ICU patients were from internal medicine, 89 (32%) from surgery, and 48 (17%) from obstetrics and gynecology departments, respectively. The median age was 36 (28, 52) of which 51.1% were male. Overall, 72.3% of the patients were below the age of 50 years, 13.8% were diabetic, 27% hypertensive, and 49.4% had oliguria. Almost 40% of patients were HIV-infected and a higher proportion were males (49.3%) than females (30.3%, p = 0.016). The rate of AKI was 52.9% and ICU mortality was higher in the AKI compared to the non-AKI group (74.1% vs 61.4%, p = 0.022). While no significant difference was observed in rates of AKI between gender (p = 0.173), mortality was significantly higher in males (p = 0.013).

Determinants of AKI
Table 2 shows factors associated with AKI in bivariate and multivariate analyses. Patients with HIV, cardiac disease, and oliguria were more likely to have AKI compared to those without. HIV-positive patients were about twice [AOR = 2.38, 95% CI (1.33, 4.26)] more likely to have AKI compared to HIV-negative patients. Patients with oliguria were 4.23 [95% CI (2.43, 7.34)] times more likely to have AKI compared to patients without oliguria.

Determinants of ICU mortality
Factors associated with ICU mortality in bivariate and multivariate analyses are shown in Table 3. Male gender, diabetes mellitus, respiratory disease, inotrope, and ventilation support were independently associated with ICU mortality. Compared to female patients, male patients were 75% [AOR = 1.73, 95% CI (1.21, 2.47)] more likely to die in ICU.

Patients with DM were 2.82 [95% CI (1.28, 6.24)] times more likely to die in ICU compared to those without it. Compared to patients without respiratory disease, those with respiratory disease were 2.57 [95% CI (1.43, 4.59)] times more likely to die in ICU. Patients on inotrope support were 77% [AOR = 1.77, 95% CI (1.20, 2.62)] more likely to die compared to those not on the support. Compared to patients not on the ventilation support, those on the ventilation support were 57% [AOR = 1.57, 95% CI (1.08, 2.27)] more likely to die.

Discussion
Our study findings demonstrated the significant high rate of AKI in the ICU in a low-income country and the association between HIV infection and noncommunicable diseases such DM with AKI and mortality among patients admitted to our ICU.

The rate of AKI in our study was 52.9%, which is higher than what is reported in developed countries. However, the reported incidence of AKI in this present study is consistent with findings in LMIC in which the rate may be as high as 60%. The rate of AKI is influenced by several factors that include geographical location, infection rate, and social and economic determinants.

In an observational prospective study of trauma patients in Brazil, Santos et al. found a 33.3% incidence of AKI in ICU while a 40% incidence was found in a multicenter study of ICU in teaching hospitals specializing in surgery and medicine in Egypt. Furthermore, Tejera et al. in Uruguay reported a 50% incidence of AKI among patients hospitalized to ICUs.

Interesting to this study was the twofold positive and highlighted association of HIV with AKI development in the ICU. Acute kidney injury is a common presentation in HIV-infected patients and presence of HIV infection is associated with a fourfold risk of renal disease compared to uninfected HIV patients. Vachiat et al. in a retrospective analysis of 684 patients hospitalized with renal failure in Johannesburg, South Africa, reported a 60% incidence of AKI in the HIV-infected group. In this study, the sepsis rate was significantly high in the HIV-infected vs the uninfected HIV patients. Li et al. reported a 15% incidence of AKI among HIV-infected patients in the United States. In this study, presence of low CD4 count, black ethnicity, and high viral load contributed to AKI development.

Multifactorial HIV- and non-HIV-related factors influence development of AKI in HIV-infected patients. The decreased immunity, nephrotoxic medications for HIV and opportunistic infections, and underlying subclinical renal disease occurring in HIV-infected patients are all significant determinants for AKI development. Furthermore, Wyatt et al. in a U.S. study of pre-highly active antiretroviral therapy (HAART) and post-HAART patients reported
Despite the high death rate in the AKI group, AKI was a negative dependent predictor for ICU mortality. Various studies have reported increased mortality rates in the ICU and worse outcomes of DM patients admitted to the ICU or the influence of male gender in the ICU, a finding in our study.

In our study, the overall ICU mortality rate was 68% and was significantly high in the AKI group vs non-AKI group. The high overall mortality rate is consistent to previous studies. Almost 70 and 40% of our reviewed patients were on ventilation and inotropic supports, respectively. From an analysis that included 200 ventilated patients in the main ICU at a tertiary hospital in India, Sudarsanam et al. found 72% mortality rate. In this study, the type of respiratory failure and the receiving inotrope support predicted ICU mortality.

Despite the high death rate in the AKI group, AKI was a negative dependent predictor for ICU mortality. Various studies have reported increased mortality rates in the ICU and worse among patients with AKI compared to those without AKI. Through a retrospective analysis of 152 admissions to the ICU, Peres et al. reported 36% overall mortality rate with 52% vs 5.8% in the AKI and non-AKI groups, respectively, of which mechanical ventilation predicted a 10-fold mortality rate. Our study findings are similar to Peres et al. who reported AKI as a negative predictor for ICU mortality.

In our study, the presence of DM and respiratory disease strongly predicted ICU mortality by almost threefold each. Sudarsanam et al. in an observational study of 200 mechanically ventilated patients at a tertiary hospital in India also found respiratory disease as a 2.7-fold predictor of ICU mortality. Previous studies have shown conflicting outcomes of DM patients admitted to the ICU or the influence of male gender in the ICU, a finding in our study. The increased levels of inflammatory cytokines associated with hyperglycemia may explain the poorer outcomes in DM patients. Esposito et al. reported increased levels of inflammatory cytokines, interleukin (IL) 6, 18, and TNFα, that were associated with acute levels of hyperglycemia. However, Siegelaar et al. in a meta-analysis that indexed 141 articles showed no overall ICU survival benefit in nondiabetics. However, 1.4-fold mortality rate was observed in DM patients admitted to surgical ICU in this study.
High levels of inflammatory cytokines have been found in hospitalized septic males vs females. Nasir et al. in Karachi found 60.7 ± 13.4 pg/mL vs 28.1 ± 7.2 pm/mL IL6 in males vs females, respectively. The major limitation to the study was that many records were unavailable due to the nonelectronic health recordkeeping. Additionally, the study was retrospective with a small sample size for major conclusions.

**Table 2: Predictors of acute kidney injury in intensive care unit**

| Characteristic          | Crude OR | 95% CI  | p value | Adjusted OR | 95% CI  | p value |
|-------------------------|----------|---------|---------|-------------|---------|---------|
| Age (years)             |          |         |         |             |         |         |
| <50                     | 0.93     | 0.72–1.21 | 0.605   |             |         |         |
| >50+                    | 1        |         |         |             |         |         |
| Gender                  |          |         |         |             |         |         |
| Male                    | 1.18     | 0.93–1.49 | 0.173   |             |         |         |
| Female                  | 1        |         |         |             |         |         |
| Diabetes mellitus       |          |         |         |             |         |         |
| Yes                     | 1.11     | 0.78–1.59 | 0.553   |             |         |         |
| No                      | 1        |         |         |             |         |         |
| Hypertension            |          |         |         |             |         |         |
| Yes                     | 1.27     | 0.96–1.68 | 0.096   |             |         |         |
| No                      | 1        |         |         |             |         |         |
| HIV positive            |          |         |         |             |         |         |
| Yes                     | 1.78     | 1.23–2.59 | 0.003   | 2.38        | 1.33–4.26 | 0.004  |
| No                      | 1        |         |         | 1           |         |         |
| Sepsis                  |          |         |         |             |         |         |
| Yes                     | 1.90     | 1.48–2.44 | <0.001  |             |         |         |
| No                      | 1        |         |         |             |         |         |
| Cardiac disease         |          |         |         |             |         |         |
| Yes                     | 1.34     | 0.96–1.87 | 0.084   |             |         |         |
| No                      | 1        |         |         |             |         |         |
| Respiratory disease     |          |         |         |             |         |         |
| Yes                     | 0.75     | 0.51–1.11 | 0.153   |             |         |         |
| No                      | 1        |         |         |             |         |         |
| Oliguria                |          |         |         |             |         |         |
| Yes                     | 3.25     | 2.42–4.35 | <0.001  | 4.23        | 2.43–7.34 | 0.016  |
| No                      | 1        |         |         | 1           |         |         |
| NSAIDs                  |          |         |         |             |         |         |
| Yes                     | 0.90     | 0.71–1.15 | 0.903   |             |         |         |
| No                      | 1        |         |         |             |         |         |
| Anemia                  |          |         |         |             |         |         |
| Yes                     | 1.04     | 0.78–1.37 | 0.811   |             |         |         |
| No                      | 1        |         |         |             |         |         |
| Inotropes support       |          |         |         |             |         |         |
| Yes                     | 1.41     | 1.09–1.82 | 0.008   |             |         |         |
| No                      | 1        |         |         |             |         |         |
| Ventilator support      |          |         |         |             |         |         |
| Yes                     | 1.22     | 0.94–1.59 | 0.136   |             |         |         |
| No                      | 1        |         |         |             |         |         |

NSAIDs, nonsteroidal anti-inflammatory drugs; HIV, human immunodeficiency virus; OR, odds ratio; CI, confidence interval

**Conclusion**

The outcome of AKI among patients admitted to the ICU was highly impacted by HIV and DM comorbidities. Extra care and attentiveness should be employed toward such patients in a setting of limited resources. To our knowledge, this is the first study examining the impact of HIV and DM in the ICU setting in Zambia.
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Table 3: Predictors for ICU mortality

| Characteristic              | Crude OR | 95% CI     | p value | Adjusted OR | 95% CI     | p value |
|-----------------------------|----------|------------|---------|-------------|------------|---------|
| Age (years)                 |          |            |         |             |            |         |
| <50                         | 0.69     | 0.51–0.93  | 0.016   |             |            |         |
| >50+                        | 1        |            |         |             |            |         |
| Gender                      |          |            |         |             |            |         |
| Male                        | 1.38     | 1.07–1.78  | 0.014   | 1.73        | 1.21–2.47  | 0.003   |
| Female                      | 1        |            |         | 1           |            |         |
| Diabetes mellitus           |          |            |         |             |            |         |
| Yes                         | 2.51     | 1.37–4.61  | 0.003   | 2.82        | 1.28–6.24  | 0.010   |
| No                          | 1        |            |         | 1           |            |         |
| Hypertension                |          |            |         |             |            |         |
| Yes                         | 1.43     | 1.04–1.97  | 0.029   |             |            |         |
| No                          | 1        |            |         | 1           |            |         |
| HIV positive                |          |            |         |             |            |         |
| Yes                         | 1.08     | 0.76–1.52  | 0.675   |             |            |         |
| No                          | 1        |            |         | 1           |            |         |
| Sepsis                      |          |            |         |             |            |         |
| Yes                         | 1.25     | 0.96–1.61  | 0.092   |             |            |         |
| No                          | 1        |            |         | 1           |            |         |
| Cardiac disease             |          |            |         |             |            |         |
| Yes                         | 1.46     | 0.99–2.16  | 0.056   |             |            |         |
| No                          | 1        |            |         | 1           |            |         |
| Respiratory disease         |          |            |         |             |            |         |
| Yes                         | 1.94     | 1.30–2.89  | 0.001   | 2.57        | 1.43–4.59  | 0.001   |
| No                          | 1        |            |         | 1           |            |         |
| Oliguria                    |          |            |         |             |            |         |
| Yes                         | 1.25     | 0.96–1.63  | 0.093   |             |            |         |
| No                          | 1        |            |         | 1           |            |         |
| NSAIDs                      |          |            |         |             |            |         |
| Yes                         | 1.03     | 0.79–1.32  | 0.848   |             |            |         |
| No                          | 1        |            |         | 1           |            |         |
| Anemia                      |          |            |         |             |            |         |
| Yes                         | 0.88     | 0.65–1.19  | 0.882   |             |            |         |
| No                          | 1        |            |         | 1           |            |         |
| Inotropes support           |          |            |         |             |            |         |
| Yes                         | 1.92     | 1.41–2.60  | <0.001  | 1.77        | 1.20–2.62  | 0.004   |
| No                          | 1        |            |         | 1           |            |         |
| Ventilator support          |          |            |         |             |            |         |
| Yes                         | 1.73     | 1.31–2.28  | <0.001  | 1.57        | 1.08–2.27  | 0.017   |
| No                          | 1        |            |         | 1           |            |         |

NSAIDs, nonsteroidal anti-inflammatory drugs; HIV, human immunodeficiency virus; ICU, intensive care unit; OR, odds ratio; CI, confidence interval

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