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# Risk Factors for Mortality in Acute Kidney Injury in Intensive Care Units in Togo

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## Abstract

**Context:** Acute kidney injury (AKI) in intensive care unit (ICU) is common and associated with very high mortality. In Togo, a tropical country with limited resources and only one nephrology department in the north, acute kidney injury seems to be a real tragedy with high mortality. Aims: to determine risk factors for mortality in acute kidney injury in the intensive care units. **Methods and Material:** We made a multicentric cross sectional study during 6 months in the four referral centers in northern Togo. Univariate and multivariate logistic regression was used to identify factors associated with mortality. Data were analyzed using RStudio 2023.04.1. **Results:** A total of 12.6% of patients admitted to intensive care had presented with AKI. The mean age was 49.6 ± 17.9. The sex ratio (M/F) was 2.1. Community-acquired AKI was in the majority (67.7%). Oligo anuria was the most frequent functional sign (38.4%). In our series, 81.6% of patients were in KDIGO stages 2 to 3. AKI was organic in 56.2% of cases. Mortality was 44.3%. In multivariate analysis, the main factors predictive of death were: respiratory distress (OR = 2.36; $p < 0.001$), altered consciousness (OR = 2.12; $p = 0.004$), MAP < 60 mmHg (OR = 1.89; $p = 0.004$), hemorrhage as etiology (OR = 2.71; $p = 0.004$) and number of visceral failures (OR = 1.79; $p < 0.001$). **Conclusions:** Acute kidney injury in intensive care is common in northern Togo, and mortality is high. Identification of associated factors should help anticipate prognosis.

## Keywords

AKI, Intensive Care Unit, Dialysis, Epidemiology, Togo

## 1. Introduction

Acute Kidney Injury (AKI) affects more than 13 million people and causes nearly 2 million deaths worldwide every year [1]. In the intensive care setting, its frequency can be as high as 60%, and it is consistently associated with mortality in excess of 40% [1]. Nearly 80% of the socio-economic burden of this disease occurs in developing countries [2]. In Africa, despite the 0by25 initiative of International Society of Nephrology (ISN), which called for a reduction in avoidable deaths due to AKI, research on the subject still shows dramatic results [3]. In Zambia, a study carried out in an intensive care unit revealed a 59% mortality rate in a group of patients with acute kidney injury [4].

The mechanisms of AKI are multiple and often interrelated. AKI occurs most frequently in visceral failure, trauma or sepsis leading to hypovolemia, but also in kidney damage caused by exogenous or endogenous toxic agents [5]. The prognostic factors identified for AKI in the ICU are age, previous health status and severity on admission or inclusion [6]. However, these data are purely for developed countries, whereas African populations are less elderly and less comorbid. Sub-Saharan Africa has few data on the incidence of acute kidney injury in intensive care units, and even less on the factors associated with mortality. In the north of Togo, there are no dialysis centers. As a result, the management of patients with acute renal failure is laborious, especially in intensive care units; mortality appears to be high and the risk factors unknown.

In order to guide public policy in responding to this scourge, this study was carried out with the aim of determining the factors associated with mortality from acute kidney Injury in intensive care units in northern Togo.

## 2. Patients and Methods

### 2.1. Study Setting

The intensive care units of the four largest health facilities in northern Togo served as the study setting. These were: Regional Hospital of Dapaong, of Sokode and of Kara and University Hospital of Kara. These hospitals serve a population estimated at 3,000,000. Togo is a West African country located between the 6th and 11th degrees north latitude, bordered to the north by Burkina-Faso, to the east by Benin, to the west by Ghana and to the south by the Atlantic Ocean. It covers an area of 56,785 $km^2$ and, according to the latest census, had a population of 8,095,498 in 2022. Life expectancy at birth was 63.1 years for men and 68.6 years for women. Togo is subdivided into six (6) major administrative regions from north to south (Savane, Kara, Centrale, Plateau, Grand Lome and Maritime).

### 2.2. Type and Period of Study

This was a case series study with descriptive and analytical aims; with retrospective data collection over a period of six (06) months, from July 1, 2022 to December 31, 2022.

### 2.3. Study Population

Patients admitted in one of the four ICU of Northern Togo with at least one of the three clinical and biological criteria for AKI as defined by the KDIGO 2012 and followed up during 3 months were included in the study. The criteria for AKI was:

- An increase in serum creatinine of 26.5 µmol/l or 3 mg/l over a 48-hour period; or
- An increase in creatinine of ≥1.5 times the baseline value over a 7-day period; or
- A decrease in diuresis of <0.5 ml/kg/h over 6 hours.

Not included in the study were patients with age < 15 years; known pre-existing chronic renal failure defined by evidence of abnormal creatinine for more than 3 months or small kidneys less than 90 mm on ultrasound; hemodialyzed prior to ICU admission and transferred from another intensive care unit.

### 2.4. Study Procedure

Patients included in the study had at least 3 creatinine measurements: on admission (D0), on day 2 (D2) and on day 7 (D7). Urine collection in the intensive care unit was facilitated by systematic bladder catheterization; diuresis was quantified every hour for the first 48 hours, then every 6 hours.

Data were collected using an electronic xlsform deployed on the Kobo Toolbox platform. The parameters collected were: age (in years), sex, profession, origin defining the notion of community or hospital-acquired AKI, comorbidities, exposure to nephrotoxic agents (modern and/or traditional drugs, iodinated contrast media), general signs, reason for admission, etiology of AKI, stage of AKI, duration of hospitalization in the intensive care unit (in days), data from explorations: physical, biological and radiological; treatment, complications and evolution: death, recovery, CKD. Patients were divided into two groups, "alive" and "deceased", and compared.

### 2.5. Statistical Analysis

Data were analyzed using R 4.3.0 (R Core Team, Vienna) in the RStudio 2023.04.1 environment. Qualitative variables were presented according to their respective numbers and percentages, quantitative variables according to their mean and standard deviation. The Chi2 test and Fisher's exact test were used to compare quantitative variables. The significance level was set at 0.05. The log rank test was used to compare survival curves. A Cox model was used to identify factors predictive of mortality. After univariate analysis, variables that were sufficiently associated ($p < 0.2$) and of significant clinical interest, taking into account the risk of collinearity, were entered into a first model. Using a top-down step-by-step selection procedure, variables with little influence were eliminated, resulting in a reduced model. The validity of the model was then verified by a Schoenfeld test.

### 2.6. Ethical Considerations

From an ethical point of view, informed consent was obtained from patients or their heirs. The data collected were treated anonymously, and confidentiality was respected.

## 3. Results

### 3.1. Descriptive Data

During the study period, 1648 patients were admitted to the various selected intensive care units (Figure 1). Among them, 185 patients were recorded, representing a 12.6% incidence of AKI. The mean age was 49.6 ± 17.9 years, with extremes of 18 and 96 years. Male predominance was 68%, giving a sex ratio of 2.1.

According to patient origin, 67.7% of cases were community-acquired AKI and 32.3% hospital-acquired AKI, of which 68.3% came from medical wards, 21.7% from surgical wards and 10% from gynecology and obstetrics wards. Clinically, the most frequent reasons for hospitalization were respiratory distress in 24.2% of cases, and disorders of consciousness and circulatory distress in 22.7% each.

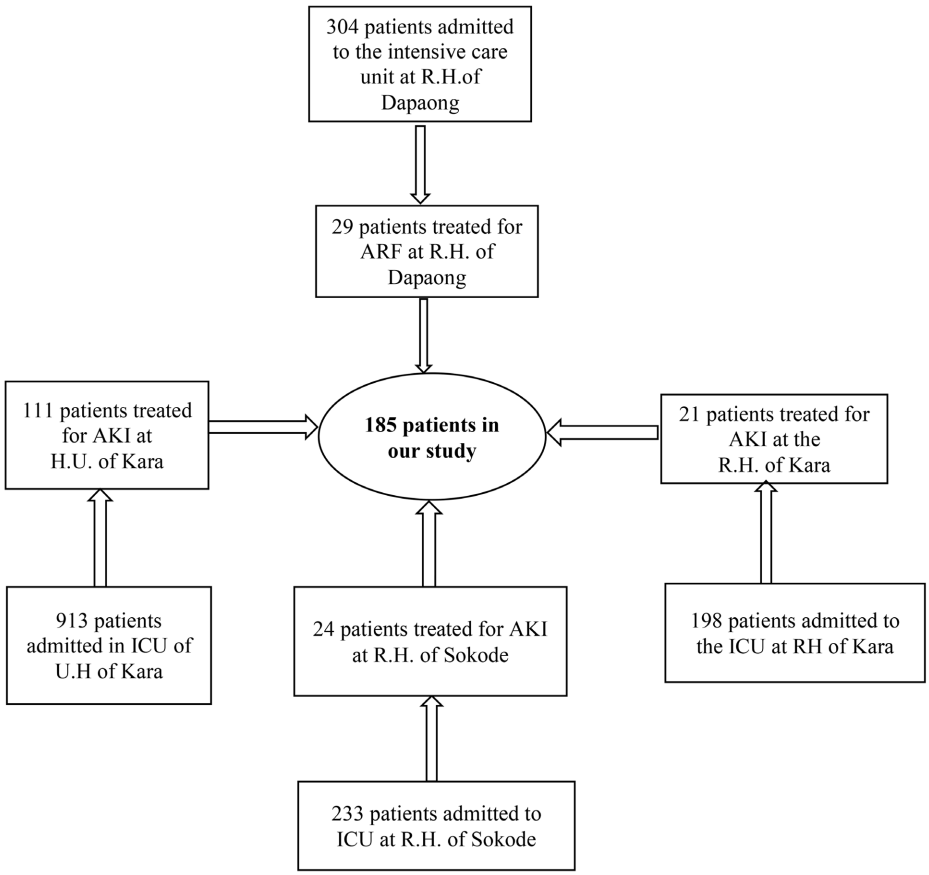


Figure 1. Selection flow chart for the study population. AKI: Acute Kidney Injury; U. H: University Hospital; R. H.: Regional Hospital.

The case fatality rate for AKI was 44.3%, *i.e.*, 82 patients died. In the study, 78 patients (42.2%) had at least one comorbidity, the most frequent being hypertension (23.8%) and diabetes (12%). Prior to hospitalization, patients were exposed to traditional toxicants in 3.8% of cases, and to modern nephrotoxic such as diuretics, non-steroidal anti-inflammatory drugs and aminoglycosides in 11.9% of cases. Clinical symptomatology was represented by hemodynamic disorders with MAP below 60 mmHg in 85.4% of patients, disorders of consciousness in 45.4% of patients, hyperthermia in 37.8% of cases and anuria in 17.3% of cases 3.

The mean creatinine level was 43.1 mg/l ± 25.0 mg/l, with extremes ranging from 15 mg/l to 316 mg/l. Hyperkalemia was present in 16.7% of patients. AKI was KDIGO stage 1 in 18.4% of cases, stage 2 in 48.1% and stage 3 in 33.5%. Organic AKI was predominant in 56.2% of patients, while functional AKI was found in 37.8% and obstructive AKI in 6%. Sepsis was the most common cause in 33.5% of our patients, skin loss and hemorrhage in 21.1% each, and decompensated cirrhosis in 16.5%. Visceral failure was present in 92.4% of patients during their stay in intensive care.

Treatment modalities were mainly vascular filling and antibiotic therapy in 77.8% and 69.2% of cases respectively. Transfusion with a labile blood product was performed in 24.9% of patients. Vasoactive drugs and/or positive inotropes were used in 25.9% of patients, and diuretics in 15.7%. Extra-renal purification was indicated in 59.4% of patients, and 3.8% actually underwent it.

### 3.2. Analytical Data

In univariate analysis, clinical factors such as confusion, altered consciousness and MAP < 60 mmHg were significantly associated with death, multiplying the risk of mortality in intensive care patients with AKI by 1.77, 3.68 and 2.2 respectively (Table 1).

Etiological and therapeutic factors such as skin loss, hemorrhage, decompensated liver cirrhosis and the use of vasopressor amines multiplied the risk of mortality in the intensive care patient by 3.05, 2.46, 1.94 and 2.2 respectively (Table 1).

For each additional visceral failure, the risk of mortality increased by a factor of 1.87. Patients in stages 2 and 3 of the KDIGO 2012 classification of AKI had a higher risk of mortality compared with those in stage 1 (Table 1).

In multivariate analysis the risk factors for mortality in our population were: respiratory distress (OR = 2.36; 95% CIa [1.42 - 3.91] p value < 0.001), altered consciousness (OR = 2.12; 95% CIa [1.27 - 3.54]; p value = 0.004), MAP < 60 mmHg (OR = 1.89; 95% CIa [1.08 - 3.31]; p value = 0.004), hemorrhage as etiology (ORa = 2.71; 95% CIa [1.19 - 6.19]; p value = 0.004) and number of visceral failures (ORa = 1.79; 95% CIa [1.49 - 2.14]; p value < 0.001) (Table 2).

## 4. Discussion

The incidence of AKI in intensive care units in northern Togo was 12.6%. These

**Table 1.** Univariate analysis using the logistic model of clinical and therapeutic socio-demographic characteristics of cases of death.

| | N | OR* | 95% CI* | *p-Value** |
|---|---|---|---|---|
| Age > median | 185 | 0.97 | 0.57 - 1.65 | 0.9 |
| **Sex** | 185 | | | |
| Female | | - | - | |
| Male | | 0.78 | 0.50 - 1.23 | 0.3 |
| **Comorbidities** | | | | |
| Hypertension | 185 | 1.04 | 0.63 - 1.70 | 0.9 |
| Diabetes | 185 | 0.86 | 0.43 - 1.74 | 0.7 |
| Exposure to a nephrotoxic product | 185 | 0.85 | 0.46 - 1.58 | 0.6 |
| **Functional and general signs** | | | | |
| Glasgow score < 15 | 185 | 3.68 | 2.26 - 5.97 | <0.001 |
| MAP < 60 mmHg | 185 | 2.2 | 1.28 - 3.78 | 0.004 |
| **Source** | 185 | | | |
| Community | | - | - | |
| Hospital | | 1.09 | 0.68 - 1.75 | 0.7 |
| **Department of origin** | 60 | | | |
| Surgery | | - | - | |
| Medicine | | 6.11 | 1.44 - 26.0 | 0.014 |
| **Reasons for admission** | | | | |
| Altered consciousness | 185 | 2.31 | 1.48 - 3.58 | <0.001 |
| Respiratory distress | 185 | 1.86 | 1.20 - 2.89 | 0.006 |
| Anuria | | 0.65 | 0.2 - 2.06 | 0.5 |
| **Etiology** | | | | |
| Hemorrhage | | 2.46 | 1.22 - 4.97 | 0.012 |
| Decompensated hepatic cirrhosis | | 1.94 | 1.13 - 3.32 | 0.015 |
| Severe sepsis | | 2.34 | 1.86 - 4.2 | 0.018 |
| **AKI stage (KDIGO 2012)** | | | | |
| Stage 1 | | - | - | |
| Stage 2 | | 2.22 | 1.03 - 4.78 | 0.043 |
| Stage 3 | | 3.53 | 1.65 - 7.57 | 0.001 |
| **Number of multiple organ failures** | | 1.87 | 1.58 - 2.21 | <0.001 |
| **Treatment methods** | | | | |
| Hemodialysis performed | 33 | 0.29 | 0.04 - 2.18 | 0.2 |
| Vascular filling | | 1.09 | 0.63 - 1.89 | 0.8 |
| Vasopressive amines | | 2.2 | 1.41 - 3.44 | <0.001 |

*OR = Odds Ratio, CI = Confidence Interval, KDIGO = Kidney Disease Improval Global Outcomes.

**Table 2.** Multivariate analysis of sociodemographic, clinical and therapeutic characteristics of fatal cases.

| | Initial model | | | Final model | | |
|---|---|---|---|---|---|---|
| | OR[1] | 95% CI* | *p-Value* | ORa* | 95% CIa* | *p-Value* |
| Respiratory distress | 2.64 | 1.47 - 4.75 | 0.001 | 2.36 | 1.42 - 3.91 | <0.001 |
| Altered consciousness | 2.41 | 1.40 - 4.17 | 0.002 | 2.12 | 1.27 - 3.54 | 0.004 |
| MAP < 60 mmHg | 1.96 | 1.05 - 3.64 | 0.003 | 1.89 | 1.08 - 3.31 | 0.004 |
| Bleeding | 5.11 | 1.52 - 17.2 | 0.008 | 2.71 | 1.19 - 6.19 | 0.001 |
| Number of multiple organ failures | 1.83 | 1.48 - 2.25 | <0.001 | 1.79 | 1.49 - 2.14 | <0.001 |

*OR = Odds Ratio, CI = Confidence Interval, [1]ORa = Adjusted Odds ratio, ICa = adjusted Confidence Interval.

data seem similar to those of Touré in Mali and Bennis in Morocco, who found a frequency of 12.3% and 14% of AKI respectively [7] [8]. However, they are quite different from the results of Banda, who found a frequency of 59% in Zambian intensive care units [4]. It has been established that the incidence of AKI in the ICU varies according to the type of patient recruitment (general ICU, medical ICU, surgical ICU) and the diagnostic criteria used [7]. In our study, the majority (67%) of patients came directly from their homes. In addition, the diagnostic criteria for acute renal failure were not the same. In sub-Saharan Africa, the diagnostic criteria for AKI are largely based on creatinine levels. Yet creatinine is a biomarker of renal function, and lags behind renal injury by several hours [9]. What's more, its determination, which is not always available, is still carried out by the Jaffe method, which remains inaccurate, as chromogens other than creatinine interfere with the result, leading to errors [10]. In our study, not only was the diagnosis of AKI based on elevated creatinine in 82.7% of cases, but also the method used to measure creatinine was the Jaffe method. This may constitute a bias in patient recruitment.

Several studies have demonstrated that the development of AKI in the intensive care unit (ICU) or intensive care unit (ICU) is associated with increased morbidity and mortality. In a study of 279 ICU patients, mortality was 71.7% versus 14.4% ($p < 0.001$) in the AKI group compared with the non-AKI group [11]. In this study, the development of AKI was an independent predictor of mortality, increasing the risk of death by a factor of 10 [11]. In our series, the mortality rate was 44.3%. According to the multivariate model, mortality was associated with several factors: the number of visceral failures, respiratory distress, MAP < 60 mmHg, altered consciousness, and hemorrhage as etiology.

The number of visceral failures or dysfunctions associated with AKI is a major prognostic factor [6]. The more organ dysfunctions there are, the higher the risk of AKI.

The excess mortality associated with respiratory failure, hypotension and shock has been mentioned since the earliest studies of AKI [12]. This is illu-

strated by the correlation between mortality and the use of mechanical ventilation in most series [13] [14]. Indeed, mechanical ventilation may suggest the presence of respiratory or circulatory distress, and hence low mean arterial pressure. In his series, Consentino reported a mortality rate of 80% in the group requiring mechanical ventilation versus 57% in the non-ventilated group ($p = 0.006$) [14]. The most serious complications of AKI are PAO and metabolic acidosis, which result in respiratory distress. These complications are responsible for the majority of deaths.

In terms of treatment, dialysis was indicated in 59.4% of cases, but was carried out in only 3%. In a meta-analysis of 41 studies involving 1,401 adults and 1937 children, of the 70% of adults who required dialysis, only 33% had access to it [15]. According to the authors, the inaccessibility of dialysis facilities contributes to increased mortality in sub-Saharan Africa [15]. Although we did not find this associated factor in statistical analysis, it is easy to understand that the absence of this treatment is a major handicap. The treatment of serious complications such as hyperkalemia (16.4%), acute pulmonary edema (APO) and acidosis remains ineffective in our series. This raises the problem of under-equipped intensive care units in Africa [16]. Hypovolemia remains the primary mechanism of AKI in intensive care units [17].

A closer look at the factors associated with mortality reveals a number of features specific to our population. The study population is young, rural, with a predominance of community-acquired renal failure.

Contrary to Western data [6], age is not a factor associated with ICU mortality in our setting. In sub-Saharan Africa, AKI mainly affects young, economically active adults aged around 40 [18] [19]. The average age of $49.7 \pm 17.9$ years in our population was similar to that of Bennis [7], who also reported a male predominance. This data is common to several works except those that include several patients from obstetric gynecology departments [20].

Since KDIGO 2012, the notion of community versus hospital-acquired AKI has emerged [21]. Hospital-acquired AKI is multifactorial and occurs in subjects associating several comorbidities with a poor prognosis. In our study, in which patients were recruited from the intensive care unit, the predominance of community-acquired AKI (67.6%) reflects the delay in transfer. According to Lengani in Burkina Faso, it is the severity of symptoms or the extent of disability that motivates referral to healthcare facilities in Africa [22]. In our series, the top three reasons for hospitalization were respiratory distress (24.2%), consciousness disorders (22.7%) and circulatory distress (22.7%). Altered consciousness was also found to be predictive of death in AKI ($p = 0.004$). A prospective multicenter study by Liano *et al.* in Spain showed that the prognosis of AKI in the ICU was particularly poor for comatose patients [23]. The clinical expression of AKI in the ICU is multifaceted. Anuria was the first functional sign in our series. It reflects the late referral of patients, as it has been established that it occurs several hours after renal aggression and leads to the classification of AKI as KDIGO stage 3. The majority of patients were in stages 2 and 3.

Several pathophysiological factors were found concomitantly in the same patients. Although statistically insignificant, drugs with nephrotoxic potential, including aminoglycosides and diuretics, were found in high proportions. Indeed, studies have shown that these drugs are misused in AKI, with the risk of aggravating the initial mechanism, either through direct toxicity of the drug, favored by the drop in blood volume and the concentration of free metabolites, or through disruption of intra-glomerular hemodynamics [24]. Several traditional toxicants were also found in our series, although the causal link has not been formally established. In Togo in particular, and in Africa in general, the course of treatment is marked by traditherapy (treatment with plants and unapproved root decoctions). There are two main reasons for this: the importance of cultural beliefs and the high cost of treatment in a poor population.

In sub-Saharan Africa, the etiology of AKI is predominantly infectious [9] [25]. Rural populations, like our own, are often confronted with precarious sanitary conditions and limited access to medical infrastructures [15]. As infectious pathologies are not controlled, most patients develop AKI associated with them [9] [26]. The majority of etiologies found in our work were septic, and this was reflected by the presence of an inflammatory syndrome with a mean leukocyte count of 16.1 ± 2.9 G/l.

The main limitation of this study is that the factors associated with mortality were not studied concomitantly in the group without renal failure. The diagnosis of AKI itself, based solely on creatinine measurement, remains controversial, as does the fact that diuresis is not used as a criterion, given the organization of intensive care units.

## 5. Conclusion

Acute Kidney Injury (A is common in intensive care units, with a poor prognosis. In our context, it occurs in young male subjects, with hypovolemia as the main mechanism. Its high mortality is associated with factors such as respiratory distress, altered consciousness, MAP < 60 mmHg, hemorrhage as etiology and the number of visceral failures. Identifying these factors associated with death in Acute Kidney Injury should enable us to anticipate prognosis and adapt specific management. Simple strategies for systematic screening of target groups in emergency departments, with early intervention, could be implemented and evaluated in a future study.

## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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