Scientific Research Publishing

Open Journal of Internal Medicine, 2023, 13, 8-15
https://www.scirp.org/journal/ojim
ISSN Online: 2162-5980
ISSN Print: 2162-5972

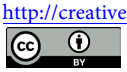
Acute Kidney Injury during Coronavirus Disease in Togo

Yawovi Mawufemo Tsevi*, Lidaw Déassoua Bawe, Kofi Atsu Aziagbe, Badomta Dolaama, Edem Cruz Affanou, Kodjo Agbeko Djagadou, Awalou Mohaman Djibril

Lomé-Commune Regional Hospital, National Center for the Care of COVID-19 in Togo, Sylvanus Olympio University Hospital of Lomé, Lomé, Togo
Email: *tseviclaude@gmail.com

How to cite this paper: Tsevi, Y.M., Bawe, L.D., Aziagbe, K.A., Dolaama, B., Affanou, E.C., Djagadou, K.A. and Djibril, A.M. (2023) Acute Kidney Injury during Coronavirus Disease in Togo. *Open Journal of Internal Medicine*, **13**, 8-15.
https://doi.org/10.4236/ojim.2023.131002

Received: November 23, 2022
Accepted: February 21, 2023
Published: February 24, 2023



Abstract

Background: Acute kidney injury (AKI) is frequently reported in the context of coronavirus infection. The incidence of AKI, particularly in patients hospitalized in intensive care units, is high. The aim was to study the associated factors to mortality in acute kidney injury (AKI) during COVID-19 in Togo. **Method:** This was a cross-sectional analytical study with retrospective data collection. It involved all patients hospitalized at CHR-LC from March 2020 to August 2021 suffering from COVID-19 who presented an AKI. **Results:** We identified 113 cases of acute kidney injury according to the predefined criteria. The prevalence of AKI during COVID-19 was 3.90%. Subjects over 65 years of age were the most represented. The age extremes were 17 and 85 years. The sex ratio (M/F) was 2.89. The main factors significantly associated with the severity of acute kidney injury were diabetes, asthma, HIV infection, and stroke. There was a correlation between the degree of acute kidney failure and severity on admission. Patients with AKI severity 2 and 3 were on hemodialysis. There was a statistically significant correlation between intra-hospital mortality and the severity of acute kidney injury ($p = 0.04$). The intra-hospital mortality rate was 23%. **Conclusion:** Acute kidney injury (AKI) during COVID-19 is a real concern for clinicians. Its medical care involves a multidisciplinary team. Particular emphasis should therefore be placed on the management of co-morbidities and preventive nephroprotection measures.

Keywords

Acute Kidney Injury, COVID-19, Lomé (Togo)

1. Introduction

The coronavirus epidemic called COVID-19, declared as a pandemic and a pub-

lic health emergency of international concern by the WHO, mainly targets the pulmonary alveolus. Although acute respiratory failure is the most severe and common organ dysfunction, acute kidney injury (AKI) is frequently reported in the context of coronavirus infection [1]. The incidence of AKI, particularly in patients hospitalized in intensive care units, is estimated at approximately 6% with, nevertheless, great variability according to the studies, since the figures fluctuate between 0.6% and 29% [2] [3]. Other studies (Chinese, European and American) have shown an association between AKI and excess intra-hospital mortality. Moreover, the risk of death increased with the severity of AKI, after adjustment for age, severity of lung lesions and patient comorbidities [4]. In Africa, a study carried out in Casablanca reported a prevalence of 17% of AKI [5].

In Togo, to our knowledge, this is the first study on acute kidney injury (AKI) in patients with COVID-19. The aim was to study the associated factors to mortality in Acute Kidney Injury (AKI) during COVID-19 at the Lomé Commune Regional Hospital Center (CHR-LC).

2. Method

The study took place at the CHR-LC, national center for the care of COVID-19 in Togo. This was an analytical cross-sectional study with retrospective data collection. This study lasted 18 months from March 2020 to August 2021.

The study population was composed of subjects who had been diagnosed positive for COVID-19 by the PCR test from a nasopharyngeal swab. Included in this study were patients hospitalized at the CHR-LC, aged over 18 and having performed at least two serum creatinine assays. Patients with a history of renal failure at the time of COVID-19 diagnosis and/or treated with hemodialysis were not included in the study.

Data were collected from the patients' medical records through the Kobo Toolbox platform, which is the national COVID-19 platform set up to contain all data on COVID-19 positive patients. The parameters studied were:

- Socio-demographic data: age, gender, length of hospitalization;
- Clinical data: history, comorbidities, general signs, renal physical signs and extra renal physical signs;
- Paraclinical data: hemoglobin level, CRP, uremia, creatinine level and GFR (glomerular filtration rate), blood ionogram, HIV serology and hepatitis B and C, and chest CT scan;
- Therapeutic data;
- Evolutionary variables: discharge from hospital, death, complete or partial improvement in renal function.

2.1. Operational Definitions

- Acute kidney injury was defined by a rise in creatinine on admission, confirmed and classified according to the criteria of KDIGO (Kidney Disease

Improving Global Outcomes) for AKI (Acute Kidney Injury) [6].

- The elderly: people whose age ≥ 65 years.
- We defined anemia as a hemoglobin level below 12 g/dl.
- Severity criteria for COVID-19 were: Temperature > 40˚C, Respiratory rate > 30 cycles/min, SpO_2 < 90% on room air or oxygen tolerance > 3 L/min, Systolic BP < 100 mmHg, Diastolic BP < 60 mmHg.

2.2. Data Processing

Data were analyzed using SSPS software. The qualitative variables were presented according to their respective numbers and percentages, the quantitative ones according to their means, standard deviations, medians, interquartile ranges or extremes. A comparative analysis was carried out to look for a difference between the variables collected at inclusion according to KDIGO 2012 stages of acute kidney injury. Chi-square and Fisher tests were used to compare proportions, depending on the situation. The threshold of significance used was $p < 0.05$. Univariate and multivariate logistic regression was performed to investigate factors associated with death.

We obtained verbal authorization from the managers of the said center. The anonymity of the patients was requested in the data sheets to respect medical confidentiality.

3. Results

During our study, 2896 patients with COVID-19 were hospitalized at the CHR-LC, among whom we identified 113 cases of acute kidney injury according to the predefined criteria, *i.e.* a prevalence of 3.90%. The sex ratio (M/F) of our serie was 2.89. Age > 65 ans ($p = 0.02$), known pathological history ($p = 0.000014$), diabetes ($p = 0.05$), asthma ($p = 0.000007$), HIV infection ($p = 0.000002$), fever ($p = 0.000001$) and oligo-anuria ($p = 0.0001$) were associated to the severity of AKI (**Table 1**). C-reactive protein level was high in 62 (54.9%) patients. Hyperkalemia was observed in 7 patients, 5 of whom were in stage 3 of AKI severity. Admission to ICU ($p = 0.04$) and hemodialysis ($p = 0.021$) were associated to the severity of AKI (**Table 2**). The mean uremia was 30.7 mmol/l with a standard deviation of ±1.07. The mean creatinine level was 711 µmol/l with a standard deviation of ±923 µmol/l. In total, 23% of patients died. In univariate analysis, the stage 3 of AKI ($p = 0.04$) and the admission in ICU ($p = 0.05$) were associated with death (**Table 3**). The risk factors statistically associated with death significantly were admitted in ICU (OR = 4.28; 95% CI = 1.22 - 15.02; $p = 0.04$) and stage 3 AKI (OR 3.88; 95% CI = 1.01 - 14.16; $p = 0.04$) (**Table 4**).

4. Discussion

4.1. Factors Associated with the Occurrence of Deaths in Patients with AKI during COVID-19

In our study, on the initial model, mortality was statistically significantly associated

Table 1. Distribution of patients according to clinical data and severity of acute kidney injury.

	Severity stage								p
	Total		Stage 1		Stage 2		Stage 3		
	Number	%	Number	%	Number	%	Number	%	
Age ≥ 65 years	33	29.2	5	17.9	1	7.7	27	37.5	0.02
Sex									0.06
Female	39	34.5	11	39.3	8	61.5	20	27.8	
Male	74	65.5	17	60.7	5	38.5	52	72.2	
Known pathological history	92	81.4	16	57.1	8	61.5	68	94.4	0.000014
Hypertension	72	63.7	15	53.6	10	76.9	47	65.3	0.31
Diabetes	43	38.1	14	50.0	9	69.2	20	27.8	0.05
Asthma	3	2.7	0	0.0	3	23.1	0	0.0	0.000007
HIV Infection	10	8.8	2	7.1	6	46.2	2	2.8	0.000002
Obesity	14	12.4	4	14.3	3	23.1	7	9.7	0.38
Cardiopathy	3	2.7	1	3.6	1	7.7	1	1.4	0.40
Symptom at admission									
Fever	35	31.0	10	35.7	13	100	12	16.7	0.000001
Dyspnea	43	38.1	7	25.0	5	38.5	31	43.1	0.24
Cough	13	11.5	6	21.4	0	0.0	7	9.7	0.99
Abdominal pain	6	5.3	2	7.1	0	0.0	4	5.6	0.63
Diarrhea	1	0.9	0	0.0	0	0.0	1	1.4	0.75
Vomiting	2	1.8	0	0.0	0	0.0	2	2.8	0.56
Chest pain	2	1.8	1	3.6	0	0.0	1	1.4	0.66
Oligo-anuria	24	21.2	0	0.0	0	0.0	24	33.3	0.0001
Severity of Covid infection									0.05
Asymptomatic	63	55.8	12	42.9	10	76.9	41	56.9	
Slight	4	3.5	2	7.1	0	0.0	2	2.8	
Moderate	21	18.6	6	21.4	1	7.7	14	19.4	
Severe	16	14.2	6	21.4	0	0.0	10	13.9	
Critical	9	8.0	2	7.1	2	15.4	5	6.9	

HIV: Human Immunodeficiency Virus.

with admission to the intensif care unit and stage 3 severity AKI. These same variables after regression were statistically significantly correlated with mortality. The risk of death was then multiplied by 4 if the patient was admitted to the intensive care unit or had a stage 3 AKI. Indeed, it has been proven in several studies that renal failure is an independent risk factor statistically significantly associated with the occurrence of death [7] [8]. Cheng *et al*. [9] explained this by the

Table 2. Distribution of patients according to paraclinical and therapeutic data and severity of acute kidney injury.

	Severity stage								p
	Total		Stage 1		Stage 2		Stage 3		
	Number	%	Number	%	Number	%	Number	%	
High C-reactive protein	62	54.9	13	46.4	7	53.8	42	58.3	
ESR	24	21.2	5	17.9	6	46.2	13	18.1	
Kalemia									0.25
Hypokalemia	25	22.1	4	14.3	1	7.7	20	27.8	
Hyperkalemia	7	6.2	2	7.1	0	0.0	5	6.9	
Computed tomography arguments									0.11
Pulmonary embolism	2	1.8	1	3.6	0	0.0	1	1.4	
Pneumonia suggestive of COVID-19	20	17.7	8	28.6	3	23.1	9	12.5	
Parenchymal involvement > 20%	22	19.5	6	21.4	5	38.5	11	15.3	
Therapeutic care									
Admission to ICU	25	22.1	8	28.6	2	15.4	15	20.8	0.04
Oxygen therapy	15	13.3	5	17.9	2	15.4	8	11.1	0.65
Corticosteroids	17	15.0	5	17.9	3	23.1	9	12.5	0.55
Chloroquine and Azithromicin	34	30.1	9	32.1	2	15.4	23	31.9	0.47
Anticoagulant	34	30.1	11	39.3	2	15.4	21	29.2	0.28
Ceftriaxone or imipenem	36	31.9	12	42.9	3	23.1	21	29.2	0.32
Hemodialysis	16	14.2	0	0.0	1	7.7	15	20.8	0.021

ESR: Erythrocyte Sedimentation Rate. ICU: Intensive Care Unit.

fact that renal failure aggravates lung injury through several mechanisms, including fluid excretion, direct capillary endothelial injury, and worsening of the inflammatory response. This can significantly increase mortality. The admission of patients to intensive care unit has been correlated as an independent factor of death in certain data from the literature such as that of Sang *et al.* where they found a significant correlation between intensive care unit admission and death [8]. Admission to intensive care unit already implied a multivisceral damage requiring rigorous care, which would favour a higher risk of death.

In the literature, many mortality factors have been repeatedly described during COVID-19 and are simple clinical or therapeutic variables such as age, obesity, comorbidities, severe and critical infection, hypoxemia, dyspnea and intensive care unit admission [8] [9] [10]. Hypoxemia, especially pulsed oxygen saturation below 92%, has been described as an independent factor of death in certain series, particularly in Chinese series such as that of Sang *et al.* where they found a significant correlation between death and signs of respiratory distress [8]. Indeed, hypoxemia could lead to diffuse ischemia, which worsens the already existing renal and extra-renal lesions and would favor a worsening of the prognosis. Positive pressure ventilation could result in microstretching of the

Table 3. Factors associated with death.

			95% confidence interval		p
	Number	OR	Inferior	Superior	
Sex	113				
Female					
Male		0.64	0.26	1.59	0.34
Known pathological history	92	0.52	0.18	1.47	0.21
Hypertension	72	1.09	0.43	2.75	0.84
Diabetes	43	1.02	0.41	2.51	0.96
Asthma	3	0.76	0.68	0.84	0.33
HIV Infection	10	0.34	0.04	2.87	0.30
Stroke	14	0.90	0.23	3.50	0.88
Obesity	14	1.40	0.40	4.89	0.59
Cardiopathy	3	1.70	0.14	19.53	0.67
Symptom on admission					
Fever	35	1.24	0.49	3.15	0.64
Dyspnea	43	0.83	0.33	2.06	0.68
Cough	13	1.58	0.44	5.61	0.48
Abdominal pain	6	1.73	0.30	10.02	0.53
Diarrhea	1	0.22	0.16	0.32	0.06
Vomiting	2	0.77	0.69	0.85	0.43
Chest pain	2	0.77	0.69	0.85	0.43
Oligo-anuria	24	1.15	0.40	3.28	0.79
AKI severity according to KDIGO					
Stage 1	8				
Stage 2	6	1.84	0.55	6.09	0.32
Stage 3	12	4.52	1.11	18.38	0.04
Admission to ICU	25	2.21	0.51	3.88	0.05
Oxygen therapy	15	1.83	0.57	5.95	0.30
Corticosteroids	17	2.07	0.68	6.29	0.19
Chloroquine and Azithromicin	34	1.64	0.65	4.11	0.28
Anticoagulant	34	1.64	0.65	4.11	0.56
Ceftriaxone or imipenem	36	0.94	0.36	2.41	0.89
Hemodialysis	16	0.74	0.19	2.83	0.66

OR: Odds Ratio; HIV: Human Immunodeficiency Virus; Stroke; ICU: Intensive Care Unit.

Table 4. Multivariate analysis of risk factors associated with death.

	Initial model				Final model			
	95% confidence interval				95% confidence interval			
	OR	Inf.	Sup.	p^1	aOR	Inf.	Sup.	p^2
Age ≥ 65 years	1.19	0.30	4.70	0.81				
AKI severity according to KDIGO								
Stage 1								
Stage 2	1.84	0.55	6.09	0.32				
Stage 3	4.52	1.11	18.38	0.04	4.28	1.22	15.02	0.02
Admission in ICU	0.81	0.26	2.57	0.03	3.88	1.01	14.16	0.04
Oxygen-therapy	0.58	0.16	2.16	0.42				
Corticosteroids	0.48	0.12	1.91	0.30				
Chloroquine and Azithromicin	0.45	0.14	1.42	0.18				
Anticoagulant	0.84	0.30	2.36	0.74				
Ceftriaxone or imipenem	1.50	0.51	4.37	0.46				
Hemodialysis	1.07	0.24	4.83	0.93				

OR: Odds Ratio; AOR: Adjusted Odds Ratio; AKI: Acute Kidney Injury; Inf: Inferior; Sup: Superior; ICU: Intensive Care Unit.

alveoli, resulting in the release of cytokine pro-inflammatory factors and stimulation of the renin-angiotensin system, which would subsequently modify renal perfusion.

4.2. Methodological Limitation

Our study has suffered from some shortcomings, namely, the absence of biology data such as 24-hour proteinuria, urinary strip, cytology and renal pathological anatomy. We relied on the presence of two creatinine values to evaluate the severity of AKI according to the KDIGO for AKI stages [6]. The absence of blood creatinine at discharge for some patients did not allow the evaluation of renal function when patients were discharged from the hospital. However, this is one of the first studies in Togo on renal damage during COVID-19.

5. Conclusion

Acute kidney injury during COVID-19 is a real concern for clinicians. Its medical care implies a better knowledge of the profile of patients suffering from it. Stage 3 AKI is a poor prognostic factor. It is essential to emphasize the avoidance of nephrotoxic drugs and the early realization of a minimum assessment of creatinine in patients suffering from COVID-19 for early and appropriate care.

Declaration

All the authors participated in the development of the survey sheet, the data collection, the data analysis and the drafting of the manuscript.

Conflicts of Interest

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

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