Outcome of Acute Kidney Injury (AKI) in Coronavirus Disease 2019 (COVID-19) patients

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Abstract

Background: Coronavirus Disease 2019 (COVID-19) is a globally emerging illness, resulting in potential effects on public health and global economies.

Objectives: To assess the incidence of Acute Kidney Injury among patients who are infected with COVID-19, and to evaluate risk factors.

Patients and methods: This study enrolled 100 adult patients infected with COVID-19 and recently diagnosed with polymerase chain reaction (PCR). The patients were submitted to clinical examination and laboratory testing for ESR, CRP, CBC, Serum creatinine, and D-dimer. Patients were also assessed radiologically by CT Chest. High-resolution computed tomography Parenchymal abnormalities on HRCT were assessed. AKI patients were classified based on Acute Kidney Injury Network staging.

Results: The mean age of all studied patients was 48.1 ± 10.8 years and mean BMI of all studied patients was 31.3 ± 4.6 kg/m^2**,** 51 patients were males (51%) and 49 females (49%). There were 35 patients (35%) with a mild infection, 23 patients (23%) with moderate and 42 patients (42%) with severe in the studied patients. The overall AKI prevalence among COVID-19 patients was 18 %. All of them were grade III AKI. Our study revealed that old age, severity of infection, dyspnea, elevated CRP, ALT, AST, PT, INR, Urea and Creatinine were considerable distinct predictors for AKI.

Conclusion: The Prevalence of AKI among COVID-19 patients was 18 %. Old age, the severity of infection, dyspnea, elevated CRP, increased serum urea, Creatinine were significant independent predictors for AKI.

Keywords: AKI; ESRD; COVID-19.

DOI: 10.21608/svuijm.2023.202111.1557

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Received: 10 April, 2023.

Revised: 22 April, 2023.

Accepted: 25 April, 2023.

Published: 17 July, 2023

Cite this article as: Abd Elkader Ahmed Hashim Mohammed, Shimaa Abd Allah Ahmed Mahmoud, Asmaa Abd Elhakim Nafady Hgo, Haggagy Mansour Mohammed, Ghada Mohammed Abd-EL Razek, Dina Badry Mohammed Rabea. (2023). Outcome of Acute Kidney Injury (AKI) in Coronavirus Disease 2019 (COVID-19) patients. *SVU-International Journal of Medical Sciences*. Vol.6, Issue 2, pp: 531-540.

Introduction

In Wuhan, Hubei, China, in December 2019, a cluster of individuals with pneumonia of unknown cause was identified **(Huang et al., 2020).** COVID-19's clinical presentation is varied from asymptomatic and mild upper respiratory tract symptoms to severe diseases with organ failure and death **(Wang et al., 2020).** Additionally, predicting the clinical course or identifying patients who are in danger of deterioration are difficult tasks **(Zhou et al., 2020).**

It's important to highlight that there are considerable regional variations in the clinical and demographic characteristics of COVID-19 individuals **(Lippi et al., 2020).** COVID-19 pneumonia poses a risk to those who have co-morbid conditions. Moreover, COVID-19 individuals with various disease severity levels had considerably diverse blood biomarkers **(Guan et al., 2020).**

Extrapulmonary clinical aspects of COVID-19 influence a variety of other organs, including the renal system (e.g., acute tubular necrosis, acute kidney injury) the cardiovascular system (e.g., pericarditis, acute coronary syndrome, myocarditis, heart failure, and arrhythmias), the gastrointestinal (nausea, diarrhea, abdominal pain, and vomiting), the hepatic system (e.g., elevated bilirubin, aspartate aminotransferase (AST) and alanine aminotransferase (ALT), dermatologic (e.g., urticarial, erythematous rash), ocular (e.g., chemosis and epiphora), neurological system (e.g., dizziness, headache, neuropathy, and encephalopathy) **(Johnson et al., 2020)**.

In terms of pathophysiology, the interaction between the S protein and ACE2 is most likely to be crucial. It has been suggested that the high level of systemic inflammation linked to COVID-19 could hasten the onset of subclinical conditions or result in de novo systemic harm **(Zheng et al., 2020)**.

AKI was mentioned often in certain research, but it was only mentioned infrequently among individuals with COVID-19 infection in other studies. Angiotensin-converting enzyme 2 (ACE2) receptor is used by COVID-19 to help the virus enter target organs. The increased expression of the ACE2 receptor in renal cells may lead to an increase in the frequency of AKI events. It's interesting to note that AKI was identified as a significant consequence in hospitalized COVID-19 patients **(Abdalbary and Sheashaa, 2020)**.

The objective of our research was to assess the incidence of Acute Kidney Injury among patients who were infected with COVID-19, and to evaluate risk factors associated with the occurance of acute kidney injury among COVID-19 patients.

Patients and methods

A total of 100 adult patients recently infected with COVID-19 and diagnosed by polymerase chain reaction (PCR) were enrolled. The results of all patients were postives.

Inclusion criteria included: Patients proved as having COVID-19 and aged more than 18 years.

Exclusion criteria included patients younger than 18 years, and End-Stage Renal Disease (ESRD) on regular hemodialysis patients. Patients with major comorbidities or concomitant malignancies were excluded.

The study approval was obtained from Qena Faculty of Medicine institutional ethical committee (IRB NO; SVU-MED-MED018-1-21-3-139). All patients presented informed consent before participation.

All patients underwent the following

A) History and Clinical checking

- Taking full history, including co-morbidities such as Diabetes Mellitus DM, cardiac diseases and Hypertension (HTN) as well as drug intake history.

- Total Clinical checkup: with special emphasis on general and chest examination.
- Anthropometric measurements: weight, height, waist circumference (WC), and the body mass index (BMI) evaluation.

B) Laboratory Investigations: -

The following investigations were performed:

- Complete blood count (CBC) with a differential count.
- Liver function tests (AST, ALT).
- Kidney function tests (urea, creatinine).
- C-reactive protein (CRP).
- Serum Ferritin.
- Serum creatinine (on admission, peak, and discharge), urea,
- **Nasopharyngeal and oropharyngeal swabs** were used for testing COVID-19 (PCR) through Rotor-Gene real-time PCR with a fluorescence system (QIAGEN, GmbH, Germany) before or soon after admission to the assigned hospitals.

C) Imaging:- Patients performed screening with:

- X-ray Chest.
- High-Resolution Computed Tomography HRCT Chest **(Fig. 1)**.

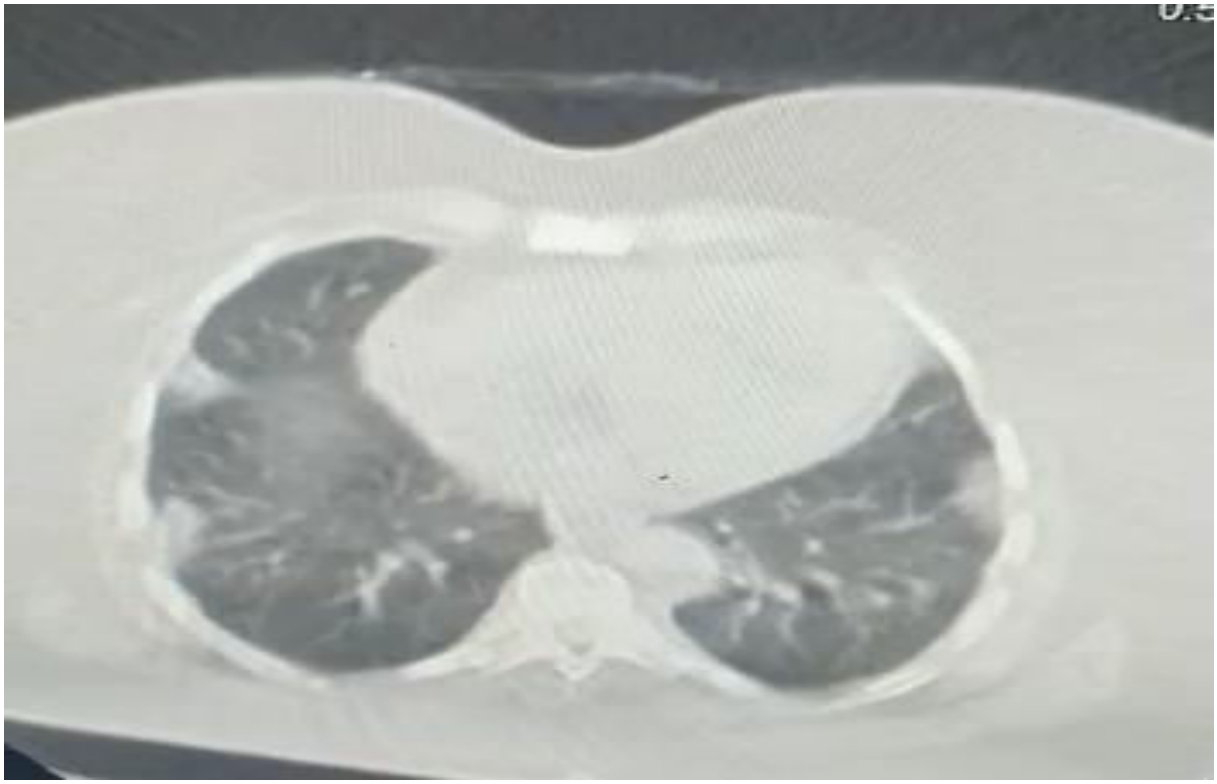

Fig.1. CT Chest of a female shows ground glass opacity

D) Assessment of Acute Kidney Injury

The AKIN classification for AKI is a modified version of the older RIFLE classification, which necessiatates an elevation in serum creatinine by at least 0.3 mg/dl over the course of 48 hours or by a decrease in urine output. In the AKIN classification, AKI is classified into three stages **(Bastin A et al, 2013).** (**Table .1)** shows the stages of AKI.

AKI is only taken into account after adequate hydration and after ruling out urinary obstruction.

Assessment of disease severity

Medical treatment was provided to all patients according to protocols of the ministry of Health and Population, Egypt.The Severity of the disease on admission was classified based on the report of the WHO-China Joint Mission on

COVID-19 **(Gomes, 2020)**. COVID-19 patients were categorized into mild (confirmed tests, with no pneumonia), moderate (confirmed tests with pneumonia), severe (oxygen saturation ≤ 93% at rest; dyspnea with a respiratory rate ≥ 30 breath/min and/or lung infiltrates >50% of the lung field within 24–48 h) and critical (shock, mechanical ventilation due to respiratory failure, or other organ failures that requires intensive care).

Table 1. AKIN classifications for AKI

Stages	Serum creatinine criteria	Urine output criteria
Stage 1	Increase serum creatinine ≥26 μmol/L (N0.3 mg/dL) or increase to more than or equal to 1.5- to 2-fold from baseline	b0.5 mL kg−1 h−1 for N6 h
Stage 2	Increase serum creatinine to more than 2- to 3-fold from baseline	b0.5 mL kg−1 h−1 for N12 h
Stage 3	Increase serum creatinine to more than 3-fold from baseline, or serum creatinine to ≥354 μmol/L with an acute rise of at least 44 μmol/L	b0.3 mL kg−1 h−1 for 24 h

Statistical analysis

The data were analyzed via Statistical Software for Social Sciences (SPSS) version 26.0. Numerical data were shown as mean ± standard deviation (M ±SD) and were compared using Student's t-test. The categorical data were shown as frequency and percentage number (%) and non-parametric data were compared by Chi-square test. P-value < 0.05 was considered significant.

Results

The mean age of all studied subjects was 48.1 ± 10.8 years**,** the mean BMI of all studied patients was 31.3 ± 4.6**,** 51 patients were males (51%), and 49 were females (49%). There were 19 smoker patients (19%), 3 patients (3%) with bronchial asthma, 17 patients (17%) with DM, 12 patients (12%) with CKD, 23 patients (23%) with HTN and 2 patients (2%) with lung fibrosis in the studied patients **(Table 2)**. There were 35 patients (35%) with a mild infection, 23 patients (23%) with moderate, and 42 patients (42%) with severe in the studied patients**.**

Table 2. Demographics data of the studied patients

Variables		Studied patients (N = 100)	
Age (years)	**Mean ±SD**	48.1 ± 10.8	
	Min - Max	30 – 81	
BMI (kg/m²)	**Mean ±SD**	31.3 ± 4.6	
	Min - Max	25.3 – 46.7	
Sex	**Male**	51	51%
	Female	49	49%
Socio Economic Status (SES)	**Low**	67	67%
	Moderate	33	33%
Smoking	**No**	81	81%
	Yes	19	19%

Comorbidities	**Non**	64	64%
	Bronchial asthma	3	3%
	DM	17	17%
	CKD	12	12%
	HTN	23	23%
	Lung fibrosis	2	2%

(Table .3) showed highly statistically significant (p< 0.001) decreased ACR after 3 months (49.8 ± 77.9) when compared with basal ACR (56.8 ± 84.9) and ACR at peak (101.5 ± 147.2), and there was highly statistical significant (p< 0.001) decreased Creatinine after 3 months (1.65 ± 1.22) when compared with admission Creatinine (1.9 ± 2.1), Creatinine at peak (3.04 ± 4.5) and Creatinine at discharge (1.98 ± 2.08) **(Table 3).**

Table 3. Albumin Creatinine Ratio (ACR) and Creatinine follow in the studied patients

Variables		**ACR / Creatinine**		**P-value**
		Mean Value	**Standerd Deviation**	
Albumin Creatinine Ratio (ACR) (µg/mg)	**Basal**	56.8	± 84.9	**< 0.001**
	At peak	101.5	± 147.2	
	After 3 months	49.8	± 77.9	
Creatinine (mg/dl)	**At admission**	1.9	± 2.1	**< 0.001**
	At peak	3.04	± 4.5	
	At discharge	1.98	± 2.08	
	After 3 months	1.65	± 1.22	

Our study results revealed that severe COVID-19 was more prominent in older age. There was a considerable (p < 0.001) increased age in severe patients in comparison to mild: moderate patients (**Table .4**). Our study results revealed that dyspnea and increased respiratory rate were associated with the severity of COVID-19 infection. We found statistically significant **(p= 0.002)** elevation in dyspnea in severe patients when compared with mild: moderate patients. Patients with severe infection were found to have a higher percentage of lymphopenia compared with mild and moderate cases. We observed Statistically significant increased liver enzymes in the severe group when compared with the moderate group and mild group. Our study results revealed that increased CRP, high serum levels of ferritin and higher serum values of d-dimer, and lactate dehydrogenase were significantly associated with COVID-19 severity **(Table .4)**.

The overall AKI prevalence among COVID-19 patients was 18 %. All of them were grade III AKI (**Table. 5**). Our study revealed that old age, the severity of infection, dyspnea, elevated CRP, ALT, AST, PT, INR, Urea, and Creatinine were significant independent predictors for AKI, as shown in **(Table. 6).**

Table 4. Relation between clinical and laboratory data

Variables		Mild: Moderate (N = 58)		Severe (N = 42)		P-value
		Mean Value	Standerd Deviation	Mean Value	Standerd Deviation	
Laboratory data	D-dimer (mg/l)	0.66	± 0.47	24.5	± 30.2	**< 0.001**
	LDH (units/l)	220.8	± 137.6	437.2	± 216.2	**< 0.001**
	Ferritin (µg/l)	269.2	± 184.2	483.3	± 199.9	**< 0.001**
	CRP (mg/l)	20.1	± 34.1	63.1	± 44.1	**< 0.001**
	ALT (units/l)	33.6	± 24.3	51.5	± 36.1	**0.004 S**
	AST (units/l)	39.2	± 26.7	57.5	± 35.3	**< 0.001**
	Hb (g/dl)	12.8	± 1.7	12.3	± 2.5	**0.415 NS**
	PLTs (10^3/µl)	238.2	± 77.3	256.7	± 105.3	**0.330 NS**
	WBCs (10^3/µl)	8.4	± 4.0	7.4	± 6.6	**0.023 S**
	A1C (%)	1.7	± 0.7	1.0	± 0.4	**< 0.001**
	PT (sec)	12.9	± 1.0	13.6	± 0.9	**< 0.001**
	INR	1.10	± 0.13	1.24	± 0.17	**< 0.001**
	Urea (mg/dl)	38.8	± 22.8	102.5	± 113.6	**< 0.001**
	Creatinine (mg/dl)	1.08	± 0.96	4.4	± 5.9	**< 0.001**

Using multivariate logistic regression analysis, this table demonstrates that the following factors were predictive for AKI: D-dimer, Lactate Dehydrogenase (LDH), Ferritin, C-reactive Protein (CRP), Alanine Transaminase (ALT), Aspartate Aminotransferase (AST), Hemoglobin (Hb), Platelet (PLTs), White Blood Cells (WBCs), Hemoglobin A1C, Prothrombin Time (PT), International Normalised Ratio (INR), Urea and Creatinine.

Table 5. description of AKI and prognosis in all studied patients

Variables		Studied patients (N = 100)	
AKI	No	82	82%
	AKI grade III	18	18%
AKI prognosis	CKD	7	38.9%
	ESRD	11	61.1%

Acute kidney injury(AKI), chronic kidney disease (CKD) and end stage renal disease (ESRD)

Table 6. Multivariate logistic regression analysis for factors predictive of AKI

	B	SE	p-value	Odds	95% CL	
Age	0.08	0.024	0.001	1.08	1.03	1.13
Sex	0.32	0.52	0.540	1.37	0.49	3.8
BMI	- 0.06	0.06	0.3	0.93	0.82	1.06
SES	0.018	0.55	0.974	1.01	0.34	3.0
Smoking	- 0.73	0.79	0.355	0.47	0.1	2.2
Fever	1.7	1.06	0.095	5.8	0.73	46.7
malaise	0.94	0.79	0.232	2.5	0.54	12.2
Loss of smell	-19.8	13397	0.999	0.0	0.0	----
Cough	1.73	0.78	0.027	5.7	1.22	26.2
Dyspnea	-1.13	0.54	0.038	0.32	0.1	0.93
Chest pain	-19.8	12710	0.999	0.0	0.0	----
Vomiting	0.11	0.58	0.849	1.11	0.35	3.5
Diarrhea	- 0.66	0.8	0.408	0.51	0.1	2.4
Nausea	- 0.14	0.55	0.795	0.86	0.29	2.5
Pain	- 0.8	0.79	0.308	0.44	0.09	2.11
Melena	- 19.7	28420	0.999	0.0	0.0	----
D-dimer (mg/l)	0.39	0.84	0.642	1.47	0.28	7.6
LDH (units/l)	0.002	0.001	0.147	1.0	0.99	1.0
Ferritin (µg/l)	0.002	0.001	0.119	1.0	1.0	1.0
CRP (mg/l)	0.014	0.005	0.01	1.01	1.0	1.02
ALT (units/l)	0.027	0.008	0.001	1.02	1.01	1.04
AST (units/l)	0.02	0.008	0.003	1.02	1.0	1.03
Hb (g/dl)	- 0.14	0.11	0.215	0.86	0.68	1.08
PLTs (10^3/µl)	0.0	0.003	0.987	1.0	0.99	1.0
WBCs (10^3/µl)	- 0.09	0.07	0.186	0.9	0.78	1.04
A1C (%)	- 2.1	0.69	0.002	0.12	0.03	0.46
PT (sec)	0.66	0.25	0.01	1.9	1.17	3.1
INR	5.3	1.66	0.001	207.3	7.9	5403
Urea (mg/dl)	0.019	0.005	< 0.001	1.01	1.0	1.02
Creatinine (mg/dl)	0.46	0.14	0.001	1.59	1.2	2.1
Bilateral GGO	1.25	0.78	0.111	3.5	0.75	16.4
Crazy-paving app	0.71	0.53	0.178	2.05	0.72	5.8

Using multivariate logistic regression analysis, this table demonstrates that the following factors were predictive for AKI: age, cough, dyspnea, Body Mass Index (BMI), Socioeconomic States (SES), D-dimer, Lactate Dehydrogenase (LDH), Ferritin, C-reactive Protein (CRP), Alanine Transaminase (ALT), Aspartate Aminotransferase (AST), Hemoglobin (Hb), Platelet (PLTs), White Blood Cells (WBCs), Hemoglobin A1C, Prothrombin Time (PT), International Normalised Ratio (INR), Urea, Creatinine and Bilateral Ground Glass Opacity (GGO).

Discussion

Coronavirus Disease 2019 (COVID-19) varies from asymptomatic and gentle upper respiratory infection to extreme kidney affection either by injury to parenchema or thromboemboli to vessels of kidney.

The results of the current study showed that the overall AKI prevalence among COVID-19 patients was 18 %. All of them were grade III AKI.

Cui et al (2020) found the incidence of AKI equal to 18.1% among COVID-19 patients in Hubei Province, China. This results are similar as our results.

El-Sayed et al. (2021) analyzed the data from 734 COVID-19 cases to estimate AKI incidence in where in Egypt COVID-19 patients. The overall rate of AKI was remarkably higher in cases with COVID-19 (14%).

Our result was in line with **Hamilton et al. (2020).** who reported that 20.3% of 1032 patients included in the analysis had a diagnosis of AKI.

Gulzar et al. (2021) reviewed 586 COVID‑positive admitted patient's data. The majority of patients were males (>88%) and the median age of the sample was 48.30 (21–92) years. There were **23.03%** of cases developed AKI during hospitalization.

There were lower AKI occurrences in the early research on patients suffering from COVID-19. A systematic review involving 24 reports including 4963 individuals with COVID-19 revealed that the frequency rate of AKI was 4.5% **(Williamson et al., 2020)**.

Also, lower incidences were reported ~~in a~~ local study in El-Minia University Hospital by **Refat et al**, who reported that the incidence of AKI in hospitalized COVID cases was 5.3% **(Refat et al., 2020).** Similarly, among 536 SARS-1 patients, there were 36 (6.7%) infected people evolved acute kidney injury **(Zou et al., 2020).**

However, our results are lower compared to those of an US study, which demonstrated that 36.6% of 5,449 patients progressed to AKI **(Hirsch et al., 2020).**

In a meta-analysis of 11 cohort studies involving 5336 patients with COVID-19 infection, AKI incidence in hospitalized patients was 4%. However, the in-hospital mortality with AKI was up to **32%**, and the rate of mortality with AKI was 16 times more than without AKI **(Mou et al., 2020)**.

This diversity in the studies could be attributed to the variations in age and the ethnicity of patients, sample size, inclusion criteria, sampling procedures, and methods of detecting AKI. It also may be due to the difference in the definition of AKI as well as the use of anticoagulation, presence of comorbidities or period of hospitalization.

Our study revealed that old age, the severity of infection, dyspnea, hematemesis, elevated CRP, ALT, AST, PT, INR, Urea, and Creatinine were significant independent predictors for AKI.

Data were gathered from the medical records of 100 individuals who were diagnosed with COVID-19 infection in a recent retrospective cohort study. The incidence of AKI in our study was 18%. While oxygen saturation was significantly lower than in the non-AKI group, age and BMI were significantly greater in the AKI group (P 0.0001). The administration of immune-suppressive medications (P = 0.042), a high score on the sequential organ failure evaluation, critical severity, and invasive respiratory assistance were all substantially linked with AKI (P 0001). AKI cases had considerably greater levels of D-dimer, creatinine kinase, and creatinine, although the glomerular filtration rate was significantly reduced (P 0.001). AKI and increased mortality were substantially linked (P 0.001). Creatinine, glomerular filtration rate, disease severity and D‑dimer were potentially independent predictors for AKI **(Mohamed et al., 2022).**

Zahid et al.(2020) identified many risk factors for AKI in their study as patients with AKI were more probably to have a hypertension history, be male, and suffer severe respiratory failure needing mechanical ventilation. Furthermore, increased BMI elevated the probability of progressing severe AKI**.**

Furthermore, at the early stage of COVID-19, **Xu et al.(2020)** examined the impact of age and sex on AKI. They discovered that individuals over the age of 70 and those who were male, displayed

higher serum levels of uric acid, urea nitrogen, and creatinine**.**

Moreover, **Azeem et al.(2021)** revealed that patients who developed incident AKI were older and were more likely to have other comorbidities.

Cui et al.(2020) also reported that most of cases in the AKI group were critical (52.4%) **Hamilton et al.(2020)** reported that at baseline, patients expressed a higher serum creatinine were more predisposed to have AKI compared with those in the non-AKI category.

In research by **El-Sayed et al.(2020)** those with AKI showed greater levels of inflammatory parameters and kidney function tests than those without AKI, including CRP, D-dimer, serum creatinine, and blood urea)**.**

Conclusion

The Prevalence of AKI among COVID-19 cases was 18 %. Our study revealed that old age, the severity of infection, dyspnea, hematemesis, elevated CRP, increased serum urea and Creatinine were significant independent predictors for AKI.

Conflict of intrest: None.

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