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Frequency and Outcome of Acute Kidney Injury in SARS–COV2 Patients in Khartoum State

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Abstract:

Background: *Coronavirus disease 2019 (COVID-19) causes multiple organ injuries; acute kidney injury (AKI) is a critical complication due to its high incidence and mortality rate. Many studies have agreed that AKI is an important complication of COVID-19 infection.*

Objective: *To determine the frequency and outcome of AKI among SARS-CoV-2 patients in Khartoum State, as well as identify the associated risk factors that predispose individuals to AKI.*

Study design: *This was a retrospective hospital-based study conducted at Khartoum Teaching Hospital, Royal Care, and Fedail Hospital during the period from September to December 2021 and included all admitted patients with COVID-19. The data were entered in 2021 and analyzed using SPSS version 25.*

Results: *This study covered 170 participants, with a frequency of AKI among the participants of (n=113, 66.5%). The analysis found significant associations between a higher frequency of AKI among patients with sepsis and hemodynamic instability (with a p value < 0.05 in all cases). While the frequency of AKI was higher among patients with comorbidities such as hypertension, diabetes, and CVD, the association was not statistically significant. Management was conservative in (n=35, 31%) of the cases, while RRT was required in (n=78, 69%). The overall mortality was (n=83, 48.8%), which was significantly higher among AKI cases (with p = 0.001).*

Conclusion: *Our study has demonstrated a significant prevalence of AKI among hospitalized COVID patients. Over half of the study population required mechanical ventilation, specifically invasive ventilation. Furthermore, a substantial proportion of patients necessitated RRT, with CRRT being more commonly administered than conventional RRT methods. Notably, hemodynamic instability and sepsis emerged as prominent risk factors for AKI development. Additionally, our study established a significant correlation between the use of vasopressors and the occurrence of AKI. Finally, this study has also shown that AKI increases the mortality rate among COVID patients.*

Keywords: Acute kidney injury, COVID-19, Sepsis, Haemodialysis, Khartoum, Sudan.

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INTRODUCTION

The definition of AKI remained inconsistent until the risk, injury, failure, loss, and end-stage criteria were released (RIFLE). The criteria have defined AKI by changes in serum creatinine from baseline and the reduction in urine output **[1, 2]**. This was followed by the Acute Kidney Injury Network (AKIN) criteria, which proposed another sensitive guideline for diagnosing AKI in 2012. Most recently, Kidney Disease Improving Global Outcome (KDIGO) has released clinical practice guidelines that are built off both RIFLE and AKIN criteria **[2, 3]**.

AKI has been observed in a significant proportion of critically ill patients with SARS-COV-2 infection, particularly those with existing comorbidities. A research article published in the Kidney International journal, investigated the occurrence of AKI in patients hospitalized with Covid-19. The study included 5,449 patients admitted to 13 academic and community hospitals in metropolitan New York, and AKI was defined based on the KDIGO criteria. Among these patients, 1,993 individuals developed AKI, with the highest stages being stage 1 in 46.5%, stage 2 in 22.4%, and stage 3 in 31.1%. Furthermore, 14.3% of these patients required RRT [1]. Another study was a single-center observational study conducted at the Section of Nephrology in the University Hospital of Modena, Italy, and was posted on June 24, 2020. In this specific study, AKI was diagnosed in 69 out of 307 patients, with stage 1 observed in 57.9%, stage 2 in 24.6%, and stage 3 in 17.3% of cases. Hemodialysis was performed in 7.2% of the subjects [4]. A prospective cohort study of 701 patients with COVID-19 done in tertiary teaching hospital in Wuhan in 2020 to determine the prevalence of AKI in COVID-19 patients and to determine the association of abnormal kidney function and death in COVID 19 patients, found that AKI occurred in 5.1% and analysis demonstrated that patients with kidney disease had significantly higher risk for in hospital death [5]. In this context, AKI is linked to elevated mortality rates, particularly when renal replacement therapy is necessary **[6, 7].**

A number of studies have identified alterations in urinary sediment, such as proteinuria and hematuria, as well as signs of urinary SARS-CoV-2 excretion, indicating the possible existence of a renal viral reservoir **[8].** COVID-19 related AKI can have both COVID specific and non-specific causes. COVID-specific factors may include direct cellular harm caused by the virus entering the kidneys via the ACE2 receptor, which is highly expressed in this organ. This can lead to an imbalanced renin-angiotensin-aldosterone system and activate proinflammatory cytokines, which may result in infection and thrombotic events **[9]**. Non-specific causes may involve changes in hemodynamics, right heart failure, high PEEP levels during mechanical ventilation, hypovolemia, administration of nephrotoxic drugs, and nosocomial sepsis **[10].** However, preexisting chronic kidney disease (CKD) that does not require dialysis has not shown an increase in the in-hospital mortality rate among AKI patients. Renal issues persist in a significant number of patients after they are discharged **[3].**

This study aimed to determine the frequency of AKI in COVID patients as well as its associated factors and the mortality rate among patients in local hospitals in Khartoum, Sudan, as a paucity of data, especially from developing countries has been noticed.

METHODOLOGY AND MATERIALS

A retrospective hospital-based study was conducted in Khartoum state, which included Khartoum Teaching Hospital, Royal Care Hospital, and Fedail Hospital. The study was conducted over a period of four months from September to December 2021. All patients who had been admitted to the study area mentioned above, during the time of the study, were assessed. A total of 170 patients were studied**.** The inclusion criteria for the study were any patient tested positive for COVID-19 by the PCR test and admitted to the isolation ward of the above mentioned hospitals. COVID severity was assessed in our study population by the Total Severity Score System (TSS). Patients on regular hemodialysis and those under 18 years of age were excluded.

For this study, we have defined AKI as defined by the KIDGO criteria;

AKI is any of the following; Increase in serum Cr by 0.3 mg/dl or more within 48 hours OR increased serum Cr × 1.5 times or more within the last 7 days OR urine output <0.5mL/kg/h for 6 hours. We used the first creatinine level documented since admission as the baseline.

KIDGO staging of AKI was followed;

Stage 1: Increase in serum Cr ≥ 0.3mg/dL or 1.5 –1.9 times from the baseline/ Urine output <0.5 mL/kg/h for 6 hours.

Stage 2: Increase in serum Cr by 2 –2.9 times from baseline/ Urine output <0.5 mL/kg/h for 12 hours.

Stage 3: Increase in serum Cr by 3 times from baseline or serum Cr ≥ 4.0mg/dL or initiation of hemodialysis / Urine output <0.3 mL/kg/h for 24 hours or anuria for12 hours.

According to KIDGO, RRT was commenced due to the development of volume overload, failure to respond to diuretics, and biochemical signs of solute imbalance (azotemia, uremia, hyperkalemia, severe acidosis). RRT used was CRRT and conventional RRT.

Data was collected through a comprehensive questionnaire filled out by us using information obtained from patients' files available during their period of admission. The questionnaire contained the following domains: age, gender, length of hospital stay, oxygen requirement, mechanical ventilator requirement, and complication developed post admission (sepsis, HD instability, liver impairment, CNS depression, other), nephrotoxic medications used, serum creatinine, requirement of RRT, the type of RRT required and the outcome of the patient.

Data was analysied using SPSS 25.0. Cross tabulation was conducted to evaluate potential associations between the frequency of AKI and relevant factors, as well as overall outcomes, using the chi-squared statistical test. The results were presented in tables as numbers and percentages. P-value < 0.05, as well as a 95% confidence interval (CI) not including the null value, was considered statistically significant.

The study obtained ethical clearance from the ethical committee of Sudanese Medical Specialization Board, as well as approval from the hospital administration was taken. The data was kept secure by coding each paper in the file and storing it in locked file cabinets when not in use. Verbal consent was obtained from all participants to enable continuous interactions and ensure feasibility, as determined by the SMSB.

RESULTS

This study included 170 participants. As demonstrated by **Table 1**; nearly two-thirds of them (66.5%) were above sixty years of age, with male gender dominance 62.9%**.** Clinically, the study showed that 39.4% of the participants stayed in the hospital for 1-7 days, while 32.4% stayed in the hospital for more than 14 days.

Table (1) Baseline Characteristics of Studied Population (n=170)

Baseline Characteristics of Studied Population				
Age	**18-39**	**40-59**	**≥ 60**	
	6 (3.5%)	51 (30%)	113 (66.5%)	
Gender	**Male**		**Female**	
	107 (62.9%)		63 (37.1%)	
Serum Creatinine	**Normal Range**		**High**	
	75 44.1%		95 55.9%	
Length of Hospital Stay	**1-7 Days**		**7-14 Days**	**>14 Days**
	67 (39.4%)		48 (28.2%)	55 (32.4)

The frequency of AKI among the participants was (66.5%). AKI was managed conservative in (31%) while (69%) required RRT. All RRT requiring patients received more than three sessions. Patients who underwent haemodialysis required CRRT by (51.3%), while (48.7%) underwent conventional haemodialysis. Participants that received two vasopressor drugs made up (36.3%). As illustrated by **Table 2**.

Table (2) AKI in Studied Population

Occurrence of AKI	**YES**		**NO**	**Total**
	113 (66.5%)		57 (33.5%)	N=170
AKI Treatment	**Conservative**		**RRT**	
	35 (31%)		78 (69%)	N=113
Type of RRT	**Conventional**		**CRRT**	
	38 (48.7%)		40 (51.3%)	N=78
Use of Vasopressor	**Vasopressor Used**		**Vasopressor Not Needed**	
	1 Drug	**2 Drugs**		N=113
	39 (34.5%)	41 (36.3%)	33 (29.2%)	

Table (3) the distribution of the participants according to their mechanical ventilator requirement (n = 170)

Mechanical ventilator requirement		Frequency	Percent
Yes		109	64.1 %
No		61	35.9 %
Type (n=109)	**Invasive**	79	72.5 %
	Non invasive	30	27.5 %
Duration (n=109)	**Days 1-7**	24	22 %
	Days 7-14	36	33 %
	Days >14	49	45 %

The analysis revealed significant associations between a higher frequency of AKI among patients with sepsis and hemodynamic instability, with all p-values < 0.05, as detailed in **Table 4**. The study also indicated that the frequency of AKI was higher among patients with comorbidities such as hypertension, diabetes, and CVD, although the association was not statistically significant (p-value > 0.05), as shown in **Table 5**. Lastly, the study demonstrated significantly higher mortality rates among AKI cases (p=0.001), as indicated in **Table 6**.

Table (4) the relationship between some relevant factors and the occurrence of AKI among the participants

Factors		Acute kidney injury						
		Yes (n=113)		No (n =57)		Total (n= 170)		P value
		Freq	%	Freq	%	Freq	%	
Age – Years	18-39	5	4.4	1	1.8	6	3.5	0.296
	59 -40	30	26.5	21	36.8	51	30.0	
	≥ 60	78	69.0	35	61.4	113	66.5	
Gender	Male	74	65.5	33	57.9	107	62.9	0.333
	Female	39	34.5	24	42.1	63	37.1	
Sepsis	Yes	93	82.3	24	42.1	117	68.8	***0.001***
	No	30	17.7	33	57.9	53	31.2	
Hemodynamic instability	Yes	67	59.3	6	10.5	73	42.9	**0.001**
	No	46	40.7	51	89.5	97	57.1	
Nephrotoxic drugs	Yes	13	11.5	4	7.0	17	10.0	0.357
	No	100	88.5	53	93.0	153	90.0	

Table (5) shows the relationship between comorbidities and the occurrence of AKI among the participants

Comorbidities		Acute kidney injury						P value
		Yes (n=113)		No (=57)		Total(n=170)		
		Freq	%	Freq	%	Freq	%	
Isolated Hypertension	Yes	9	8	4	70	13	7.6	0.826
	No	104	92	53	93	157	92.4	
Isolated Diabetes Mellitus	Yes	16	14.2	6	10.5	22	12.9	0.505
	No	97	85.8	51	89.5	148	87.1	
Isolated Cardiovascular Diseases	Yes	1	0.9	1	1.8	2	1.2	0.620
	No	112	99.1	56	98.2	168	98.8	
Hypertension and Diabetes	Yes	26	23	16	28.1	42	24.7	0.470
	No	87	77	41	71.9	128	75.3	
Hypertension and Cardiovascular disease	Yes	1	0.9	1	1.8	2	1.2	0.620
	No	112	99.1	56	98.2	168	98.8	
HTN, DM and CVD	Yes	8	7.1	1	1.8	9	5.3	0.143
	No	105	92.9	56	98.2	161	94.7	

Table (6) shows the relationship between the overall outcome and the occurrence of AKI among the participants

		Acute kidney injury						
		Yes (n=113)		No (n=57)		Total (n=170)		P value
		Freq	%	Freq	%	Freq	%	
Overall outcome	Death	65	57.5	18	31.6	83	48.8	***0.001***
	Discharged	48	42.5	39	68.4	87	51.2	
	Total	**113**	**100.0**	**57**	**100.0**	**170**	**100.0**	

DISCUSSION

Our study aimed to determine the frequency of AKI among SARS-CoV-2 patients in Khartoum state due to the lack of available data on this topic. Although two-thirds of our study participants (66.5%) were above 60 years of age, we did not find a significant association between age and the frequency of AKI. In contrast, a comparable study carried out in the United States, as well as other research conducted in various locations, demonstrated a notable correlation between age and the incidence of AKI **[11-14].**

This study observed a frequency of AKI among participants of 66.5%. Similar rates were observed in a study conducted in Brazil, where the incidence of AKI was 71.2% **[15]**. A study conducted in China showed a contrast, where AKI was found in only 5.1% of patients, and analysis revealed that patients with pre-existing kidney conditions had a significantly higher risk of in-hospital mortality **[16].** The wide-ranging incidence rates of AKI observed across different studies can be attributed to the differing study groups and designs employed, which can yield varying rates of acute kidney failure. However, these findings should not be overlooked, and underscore the need for AKI prevention and treatment to be a priority in managing COVID-19 infections. Furthermore, no significant association between the existence of comorbidities and AKI in participants was found. The majority of our participants did not have any comorbidities. The highest percentage of comorbidities in relation to the presence of AKI was observed in patients with a combination of hypertension and diabetes mellitus at 23%.

Our study found that 64.1% of our study population required mechanical ventilation of those, 72.5% were on invasive ventilation. Thus, 72.5% experienced severe manifestations of the COVID. Furthermore, 45% of patients who required mechanical ventilation relied on this intervention for more than 14 days, suggesting the prolonged and challenging nature of their respiratory distress. In addition, it was noted that 70% of the participants that developed AKI received vasopressors. Of which 36.3% received two vasopressor drugs. Prior research supports the notion that the use of vasopressors can further impede the flow of blood to tissues in instances where there is insufficient circulating blood volume **[17]**. Administering fluids and vasoactive medications to patients with AKI can cause fluid overload and exacerbate the condition by increasing intravascular volume. Therefore, it is essential to manage fluids and vasoactive medications carefully while closely monitoring hemodynamics. Furthermore, Moledina et al. **[18]** and Rodrigo et al. **[19]** reported that death associated with vasopressors was also an independent risk factor for KDIGO stage 3. There is no yet information regarding what drugs can be used safely in patients with AKI as well septic shock.

In this study, significant associations were found between a higher frequency of AKI among patients with sepsis and hemodynamic instability (p values < 0.05 in all) **[20].** Preventing S-AKI is challenging because most patients have already developed AKI by the time they seek medical attention. Moreover, David D Leedahl et al found that the co-occurrence of septic shock and AKI increases the risk of death by double compared to either condition in isolation **[21].** Furthermore, hemodynamic instability is commonly seen in critical illness and significantly affects patient outcomes in the ICU by hindering tissue perfusion and oxygen delivery, which can result in multi-organ dysfunction, including AKI **[22, 23].** Thus, it is essential to have early detection tools for AKI in individuals with sepsis to minimize delays in diagnosis and treatment.

The findings of this study indicate that the majority of patients suffering from AKI required RRT. Specifically, 69% of patients required RRT, while only 31% were managed conservatively. These results highlight the importance of appropriate management for patients with AKI, as prompt initiation of RRT can potentially improve outcomes and reduce mortality rates. More than half of the patients requiring haemodialysis underwent continuous renal replacement therapy 51.3%, as opposed to conventional haemodialysis (48.7%). This suggests that CRRT was the preferred option for managing AKI patients in this study population. The use of CRRT more commonly than conventional therapy can be correlated to the high rate AKI associated with sepsis and haemodynamic instability, as well as the high need for invasive ventilation among our study population.

Regarding outcomes, mortality rates were significantly higher among AKI patients. In Wuhan, China, COVID-19 patients with kidney disease had a significantly higher risk for in-hospital death **[16].** A systematic review reported that 52% of COVID-19 patients with AKI died, highlighting the strong association between AKI and increased odds of death **[24].** Similarly, in Turkey, Arikan et al reported an overall in-hospital mortality rate of 38.9% among patients with AKI **[25].** These findings demonstrate that the high death rate is one of the most significant indicators of the risk of AKI among COVID-19 patients, despite varying rates reported in different studies.

LIMITATIONS

This studies limitation are; a small sample size of 170 patients that are all of the same ethnic group, black Africans. Thus our study lacks diverse ethnicity. Most of our study population did not have comorbidities which made it difficult to obtain a reliable data regarding the relation between comorbidities and the development of AKI in the study population.

CONCLUSION

This paper has found that COVID-19 patients have an increased risk of AKI. More than half of our study population required mechanical ventilation, particularly invasive ventilation. We found that a higher number of patients required renal replacement therapy (RRT). All patients requiring RRT received more than three sessions. Continuous renal replacement therapy was more frequently used than conventional RRT. Haemodynamic instability and sepsis were significant predisposing factors for developing AKI. Our study has found a significant association between the occurrences of AKI in patients that received vasopressors. Most of our study population received two vasopressor drugs. This study has also shown that AKI increases the mortality rate among COVID patients.

Authors Contributions

[1] Supervisor**,** researched and analysed existing literature, revised final paper critically and finally approved the manuscript.

[2] Proposed research idea, researched and analysed existing literature, collected the data, and drafted the article.

[3] Supervisor, analysed data, revised final paper critically and finally approved the manuscript

[4] Designed initial draft, interpreted data, revised final draft and approved the manuscript.

[5] Drafted the article, revised it critically and finally approved the manuscript.

[6] Drafted the article, revised it critically and finally approved the manuscript.

[7] Drafted the article, revised it critically and finally approved the manuscript.

Data availability statement

The data that support the findings of this study are openly available in PubMed at pubmed.ncbi.nlm.nih.gov

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