

# Retrospective Analysis of Acute Kidney Injury in Hospitalizations with Covid-19

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**Introduction.** Coronavirus Disease 2019 (COVID-19) affected the entire world. While the effects on the lungs are more pronounced, the kidneys are also susceptible, and there is a potential risk of acute kidney injury (AKI) among COVID-19 patients. This study aimed to evaluate the incidence, clinical characteristics, and outcomes of AKI in patients hospitalized with COVID-19.

**Methods.** This study analyzed the incidence, characteristics, and outcomes of AKI in hospitalized patients with COVID-19. Medical records of 755 COVID-19 patients with AKI and 4647 patients without kidney injury admitted between March 2020 and July 2022 were analyzed at Karabuk Training and Research Hospital. We recorded patients' demographic information, length of stay, laboratory results, and the necessity for renal replacement therapy. AKI staging was based on initial and peak values of renal parameters such as serum.

**Results.** The results indicated a high incidence of AKI in COVID-19 patients, particularly in those requiring intensive care units (ICU), where mortality rates were significantly high. The findings revealed that patients with AKI, especially those requiring hemodialysis ( $n = 110$ , 49.32%), had lower rates of recovery and discharge ( $n = 633$ , 83.84%), and significantly higher mortality rates compared to those without AKI ( $P = .032$ ). The mortality rate in patients requiring hemodialysis was 33.64%, underscoring the severity of AKI and the high mortality risk associated with cases necessitating hemodialysis.

**Conclusion.** The development of AKI in COVID-19 patients is associated with a significant increase in mortality risk, indicating the need for further detailed investigations to better understand this condition.

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## INTRODUCTION

Coronavirus Disease 2019 (COVID-19), a pandemic that emerged in 2019 and has affected the entire world, arises from an infection with the SARS-CoV-2 virus. The disease presents with a wide range of symptoms ranging from asymptomatic cases to fever (70-90%), dry cough (60-86%), and shortness of breath (53-80%). Other reported symptoms include fatigue (38%), myalgia

(15-44%), nausea/vomiting or diarrhea (15-39%), headaches, and runny nose (7%).<sup>1-3</sup> The principal complications of COVID-19 include pneumonia (75%), acute respiratory distress syndrome (15%), acute liver damage (19%), cardiac injury (7-17%), coagulopathy (10-25%), acute kidney injury (9%), neurological effects (8%), acute cerebrovascular disease (3%), and shock (6%).<sup>4-8</sup> While the effects on the lungs are more pronounced, the kidneys

are also vulnerable, and there is an increased risk of acute kidney injury (AKI) among COVID-19 patients.<sup>3-9</sup>

AKI is diagnosed and staged according to Kidney Disease Improving Global Outcomes (KDIGO) criteria. Stage 1 AKI is defined as an increase in serum creatinine 1.5-1.9 times baseline or an increase in serum creatinine  $\geq 0.3$  mg/dl or based on urine output  $< 0.5$  ml/kg/h in 6-12 hours or Stage 2 AKI is considered an increase in serum creatinine 2-2.9 times baseline or urine output  $< 0.5$  ml/kg/h in 12 hours and more. Stage 3 AKI is defined as an increase in serum creatinine more than 3 times baseline or urine output  $< 0.3$  ml/kg/h in 24 hours and more or serum creatinine  $\geq 4$  mg/dl and anuria in 12 hours and more or the need for renal replacement therapy is considered.<sup>10-11</sup>

The incidence of COVID-19 associated AKI varies from 0 to 56.9%, depending on whether patients are in the intensive care unit (ICU). It has been reported that AKI may affect more than 20% of hospitalized patients and more than 50% of ICU patients.<sup>12-15</sup> Particularly, AKI associated with COVID-19 can lead to adverse outcomes such as worsening of existing conditions and increased utilization of health resources.<sup>16</sup> In this context, this study aims to retrospectively analyze the incidence, characteristics, and outcomes of acute kidney injury (AKI) in individuals diagnosed with and hospitalized for COVID-19.

## MATERIALS AND METHODS

This retrospective cohort study designed to examine the incidence, characteristics, and outcomes of acute kidney injury (AKI) in hospitalized patients with COVID-19; admitted to Karabuk Training and Research Hospital between March 2020 and July 2022. A total of 755 patients with AKI and 4647 patients without kidney injury were enrolled in the study. The inclusion criteria were COVID-19 patients age above 18 year of age presenting with normal renal function at the time of hospital admission. Patients with a history of nephrotoxic drug use or those who underwent contrast-enhanced imaging procedures during hospitalization were excluded. Favipiravir was administered as an antiviral treatment in patients exhibiting progressive COVID-19 symptoms. However, due to the compromised general health

status of these patients, restrictions imposed by the COVID-19 pandemic that limited renal biopsy procedures unless critically indicated, and the scarcity of existing literature demonstrating renal impairment associated with Favipiravir, AKI potentially related to antiviral therapy was not specifically assessed in our cohort.

## Data Collection

Demographic data of the patients (age, sex), place of hospitalization (ICU, General Ward), duration of hospitalization. Moreover, laboratory data including serum creatinine, urea, glucose, potassium, C-reactive protein (CRP), ferritin, D-dimer, procalcitonin, white blood cell (WBC), hemoglobin (HGB), platelet (PLT) were measured, radiological findings and the need for renal replacement therapy were recorded.

## AKI Staging

The staging of AKI was based on the KDIGO criteria. The initial and peak serum creatinine values, changes in glomerular filtration rate, and decreases in urine output were considered to determine the severity of AKI.

## Statistical Analysis

Data analysis was performed using descriptive statistical methods with the SPSS software package, version 24. Continuous data are reported as medians  $\pm$  interquartile ranges (IQR) and for non-normal variables, reported as mean  $\pm$  standard deviation (SD). Categorical variables are presented as percentage frequency distributions. The Kolmogorov–Smirnov test was employed to assess the normality of data distribution. Continuous variables were compared between two groups using the Mann–Whitney U test, while categorical variables were analyzed using the chi-square test. A *P*-value of  $< .05$  was considered statistically significant for all analyses.

## Ethical Approval

The study protocol was approved by the Institutional Review Board under the protocol number 2022/1008 and conducted in accordance with the Declaration of Helsinki. Due to the retrospective nature of the study, patient consent was not required; however, patient privacy and data security were upheld to the highest standards.

## RESULTS

Of a total of 755 COVID-19 patients with AKI included in this study, 433 (57.3%) were male and 322 (42.7%) were female, with a mean age of 54.73 years (range 21- 97). Among the AKI cohort, 337 patients (44.64%) received treatment in general wards, while 418 (55.36%) required ICU admission. The duration of ICU stay ranged from 2 to 70 days (mean  $\pm$  SD: 21.13  $\pm$  6.9 days), whereas the length of hospital stay in general wards ranged from 2 to 33 days (mean  $\pm$  SD: 10.1  $\pm$  5.9 days). Comorbidities were absent in 118 patients (15.63%), while diabetes mellitus (DM) was the most common comorbidity,

**Table 1.** Clinical characteristics of COVID-19 patients with AKI (n = 755)

Variable	n (%) or Mean $\pm$ SD (Range)
Age (years)	54.73 $\pm$ 18.94 (21-97)
Gender	
Male	433 (57.3)
Female	322 (42.7)
Admitting Unit	
Ward	337 (44.64)
ICU	418 (55.36)
Length of Stay (days)	
ICU	21.13 $\pm$ 6.9 (2-70)
Ward	10.1 $\pm$ 5.9 (2-33)
Comorbidities	
No Comorbidity	118 (15.63)
Diabetes Mellitus (DM)	190 (25.17)
Hypertension (HT)	16 (2.12)
Cardiovascular Disease (CVD)	5 (0.66)
Chronic Obstructive Pulmonary Disease (COPD)	7 (0.93)
Cerebrovascular Disease (CD)	1 (0.13)
Cancer (C)	5 (0.66)
DM+HT	62 (8.21)
DM+CVD	70 (9.27)
DM+COPD	14 (1.85)
DM+CD	1 (0.13)
DM+C	5 (0.66)
HT+CVD	41 (5.43)
HT+COPD	0 (0.0)
HT+CD	7 (0.93)
HT+ C	3 (0.40)
CVD+COPD	1 (0.13)
CVD+CD	1 (0.13)
COPD+ C	1 (0.13)
3 vs + Comorbidities	207 (27.42)

\*HT = Hypertension, DM = Diabetes Mellitus, COPD = Chronic Obstructive Pulmonary Disease, C = Cancer, CD: Cerebrovascular Disease, CVD = Cardiovascular Disease

\*\*3 vs+ Comorbidities = Refers to the number of patients with more than three comorbidities.

present in 25.17% of cases. Patients with three or more comorbid conditions accounted for 27.42% of the cohort. The clinical characteristics of COVID-19 patients with AKI are summarized in Table 1.

As shown in Table 2, statistically significant changes were observed in laboratory parameters between admission and discharge in AKI cohort. Hemoglobin (HGB) and platelet (PLT) counts increased significantly ( $P < .05$ ). Conversely, admission levels of D-dimer, ferritin, procalcitonin, C-reactive protein (CRP), and white blood cells (WBC) counts were significantly elevated and decreased significantly by discharge ( $P < .05$ ). Furthermore, a significant upward trend was observed in peak urea and creatinine levels during hospitalization. The mean urea levels increased from 60 mg/dL upon admission to 118 mg/dL at peak hospitalization, and the mean serum creatinine levels elevated from 0.89 mg/dL to a peak of 1.84 mg/dL ( $P < .05$ ). These elevations in the urea and serum creatinine levels reflect the occurrence of AKI and a marked deterioration in renal function, underscoring the necessity for meticulous renal monitoring in patients hospitalized with COVID-19.

According to Table 3, among 755 patients diagnosed with AKI, 332 (43.97%) were classified as stage 1, 200 (26.49%) as stage 2, and 223 (29.54%) as stage 3. Mortality rates across AKI stages were analyzed using the chi-square test. In stage 3 AKI, 110 of the 223 patients (49.32%) required hemodialysis, and mortality occurred in 37 (33.64%) of those patients who received dialysis. When including stage 3 patients who did not require dialysis, the total mortality rate was 28.25% ( $n = 62$ ). Additionally, among stage 3 AKI patients, 195 (26.23%) were managed in the ICU, while 28 (3.71%) received care in general wards. In stage 2, the mortality rate for ICU-managed patients was 30.36% ( $n = 34$ ), while it was only 2.27% ( $n = 2$ ) in ward-managed patients. Similarly, among stage 1 AKI patients, ICU management was associated with a mortality rate of 19.81% ( $n = 22$ ), whereas general ward management had a significantly lower mortality rate of 0.90% ( $n = 2$ ).

Overall, the mortality rate in the AKI cohort was 16.16% (122/755), significantly higher than the 4% (186/4647) mortality rate observed in the non-AKI cohort ( $P = .032$ ). Clinical improvement was achieved in 633 (83.84%) AKI patients compared to 4461 (96%) non-AKI patients (Table 4).

**Table 2.** Laboratory results in COVID-19 Patients with AKI (n = 755)

Laboratory Parameter	Admission (Mean ± SD, Range)	Discharge (Mean ± SD, Range)	P
HGB (g/dL)	10.4 ± 5.34 (3.8-18.7)	12.4 ± 1.97 (7.9-17.6)	< .05
Platelet (10 <sup>3</sup> /μl)	180.5 ± 106.62 (5-1426)	301 ± 129.44 (13-1177)	< .05
WBC (10 <sup>3</sup> /μl)	13.35 ± 9.56 (1.57-95.01)	6.73 ± 3.54 (0.37-40.64)	< .05
Urea (mg/dL)	60 ± 27.31 (14-212)	118 ± 68.89 (24-399)	< .05
Creatinine (mg/dL)	0.89 ± 0.24 (0.16-1.3)	1.84 ± 1.30 (1-9.82)	< .05
Potassium (mEq/L)	5.1 ± 0.84 (3.1-9.5)	4.08 ± 0.48 (3.5-5.4)	< .05
D-Dimer (ng/mL)	2.54 ± 7.53 (0.19-35)	0.87 ± 2.35 (0.19-21)	< .05
Ferritin (ng/mL)	604.75 ± 595.60 (7.2-1650)	277.65 ± 447.89 (6.6-1650)	< .05
Procalcitonin (ng/mL)	0.32 ± 14.39 (0.01-75)	0.06 ± 2.13 (0.01-43.57)	< .05
CRP (mg/L)	138.51 ± 101.69 (0.5-612)	23.15 ± 41.55 (0.0-274)	< .05
Glucose (mmol/L)	233.0 ± 144.75 (54-1246)	109.0 ± 57.60 (60-390)	< .05

\*\*P-value; Mann-Whitney U test was used for continuous variables.

**Table 3.** Relationship between AKI stage and mortality (n = 755)

Acute Kidney Injury Diagnosis (N=755)						
AKI Stage	n (%)	AKI Stage	n (%)	AKI Stage	n (%)	P
AKI 1	332 (43.97)	AKI 2	200 (26.49)	AKI 3	223 (29.54)	.03
Death (n = 122)	24 (7.23)	Death	36 (18.00)	Death	62 (28.25)	
Treated in ICU	111 (14.70)	Treated in ICU	112 (14.83)	Treated in ICU	195 (26.23)	.07
Treated in Hospital Ward	221 (29.27)	Treated in Hospital Ward	88 (11.66)	Treated in Hospital Ward	28 (3.71)	
Need for Hemodialysis	AKI 1: 0	Need for Hemodialysis	AKI 2: 0	Need for Hemodialysis	AKI 3: 110 (100)	< .005
				Death in Patients Needing Hemodialysis	37 (33.64)	

**Table 4.** Comparison of mortality rates of AKI and non-AKI cohorts.

AKI Diagnosed (n=755)	n (%)	Non-AKI (n=4647)	n (%)	P
Recovery and Discharge	633 (83.84)	Recovery and Discharge	4461 (96.00)	.08
Total Death	122 (16.16)	Total Death	186 (4.00)	.032
Death in Patients Requiring Hemodialysis	37 (33.64)	Death in Patients Requiring Hemodialysis	0 (0%)	< .005

\*P ≤ .05 was considered significant.

These findings highlight the substantial negative impact of AKI, particularly dialysis-requiring AKI, on survival outcomes in COVID-19 patients (Table 4).

## DISCUSSION

The high incidence of AKI in COVID-19 patients necessitates an understanding of its impact on survival and renal outcomes.<sup>1-7</sup> Previous studies were limited by small sample sizes or incomplete follow-up, or did not primarily focus on survival or renal outcomes.<sup>16-20</sup> The current study, which included 4647 hospitalized COVID-19 patients with 99% endpoint completion and a comparison of outcomes and mortality with the evolving component of AKI, provides a clear assessment of survival and renal outcomes in this patient population. We found that in-hospital mortality

was highest in patients diagnosed with AKI stage 3, followed by AKI stage 2, stage 1 and those without AKI (AKI 3, 29.54%; AKI 2, 18.0%; AKI 1, 7.23%; and non-AKI, 4% deaths/mean 25 patient days, respectively). The high rate of in-hospital deaths, especially in COVID-19 patients who experienced AKI requiring dialysis, reveals the need for shared decision-making in critical illnesses (33.64%).

We used mortality rates to address confounding variables in the association between increased risk of death in COVID-19 and AKI. The findings continued to show that AKI stages 1–3 remain significant risk factors for in-hospital mortality. This suggests an independent correlation between AKI and mortality, potentially serving as a marker for greater disease severity. Consistent with our findings, recent publications have reported an association between AKI and in-hospital death

among those hospitalized with COVID-19.<sup>11</sup> Early reports from Wuhan, China found that the risk of death associated with AKI was increased even after adjusting for age, sex, disease severity, and comorbidities, ranging from 1.9 to 4.7 times.<sup>21</sup> A recently published study from New York comparing COVID-19 admissions to a historical cohort found that patients diagnosed with AKI had a significantly higher risk of death compared to those without AKI.<sup>22</sup>

A multicenter study of ICU patients at 64 centers in the United States found that decreased renal function during ICU admission was associated with an odds ratio of 2.4 for 28-day mortality.<sup>23–25</sup> Despite the heterogeneity of published studies in terms of geographic location, patient population, and disease severity, it is clear that AKI is associated with an increased risk of death in COVID-19 patients.

Renal outcomes in AKI patients vary, with increased mortality rates that are particularly noticeable in those requiring dialysis (Table 4). Patients diagnosed with AKI stage 3 experience a difficult clinical course. Among the 755 patients diagnosed with AKI, 110 (14.57%) underwent hemodialysis treatment and 73 (66.36%) of these patients survived and did not require hemodialysis at the time of discharge. The stage of acute kidney injury is of great importance in determining the initiation of hemodialysis. The mortality rate increases with the advancement of AKI stages. (Table 3 and Table 4). COVID-19 patients who experience any stage of AKI during hospitalization should be closely followed up to evaluate their ongoing renal function after discharge, regardless of whether they require dialysis or whether their renal function improves.

## CONCLUSION

In conclusion, we found that the development of AKI during COVID-19 hospitalization is associated with a significant increase in mortality risk, which appears to be even higher in patients with AKI who subsequently require dialysis. Further well-designed studies are warranted to better elucidate the impact of AKI severity and staging on clinical outcomes in patients with COVID-19.

## LIMITATIONS OF THE STUDY

The retrospective nature and single-center design of the study introduces potential limitations.

## CONFLICT OF INTEREST

No conflict of interest was declared by the authors.

## FUNDING DISCLOSURE

The authors declared that this study received no financial support.

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