# COVID-19 Associated Acute Kidney Injury: The Incidence and Associated Factors in Different KDIGO Stages Among the Hospitalized Patients

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**Keywords.** acute kidney injury, COVID-19, hemodialysis, renal replacement therapy

**Introduction.** Acute kidney injury (AKI) is the most common reported renal complication associated with COVID-19. In this study, we evaluated the frequency of AKI, the predisposing factors, and its impact on the patient's outcomes in COVID-19.
**Methods.** By collecting retrospective data, we conducted a cross-sectional study on hospitalized severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infected patients in a COVID-19-designated hospital in Shiraz, Iran, from March 2020 to June 2020. Patients' characteristics and laboratory findings were recorded in data gathering sheets. Data were analyzed using SPSS Software Version 16. A $P$ value < .05 was considered significant.
**Results.** This study was conducted on 980 patients with COVID-19 (mean age: 51.2 ± 16.2 years and men: 54.8%), of which 32.6% developed AKI during their hospitalization period, and 1.3% ended up requiring renal replacement therapy. Patients with higher AKI stages experienced more severe/critical COVID-19 (stage 3: 71.0%, stage 2: 44.8%, stage 1: 6.5%; $P$ < .001). The multivariate analysis showed that the proteinuria had the highest relationship with AKI (OR = 6.77 [95% CI: 4.39 to 10.41], $P$ < .001), followed by in-hospital death (OR = 5.14 [95% CI: 1.86 to 14.47], $P$ = .002). In addition, in-hospital death was more observed in higher stages of AKI (OR = 12.69 [95% CI: 3.85 to 42.09], $P$ < .001).
**Conclusions.** Hospitalized patients with COVID-19 are vulnerable to AKI, especially those who experienced more severe COVID-19 or require mechanical ventilation, which considerably affects the patients' mortality. The high incidence of AKI in our patients demonstrated that it should be considered as one of the common complications of COVID-19, and diagnostic measures, particularly in severe or critical cases, are recommended.

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## INTRODUCTION

The novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), emerged from China in December 2019, and led to the coronavirus disease 2019 (COVID-19), which was officially announced as pandemic by World Health Organization on March 11, 2020.[1] Since that time, more than 190 million people have been infected with the virus around the world and more than 4 million deaths have occurred until August 13, 2021.[2]

Although COVID-19 is mostly asymptomatic or presents mild symptoms, severe diseases can be associated with life threatening complications such as acute respiratory distress syndrome and multiple organ dysfunction, affecting the heart, nervous system, gastrointestinal system, and kidneys.[3]

Acute kidney injury (AKI) is defined as a sudden decrease in renal function that presents with an increase in serum creatinine (sCr), a decrease in urine output, or both.[4] AKI has been reported to be the most common renal manifestation in patients with COVID-19 .[5] Although the exact mechanism of AKI in COVID-19 is unknown, several studies have discussed a number of factors that might play a role in the development of AKI, including direct virus attack and indirect mechanisms including circulatory collapse, hypoxemia, COVID-19-associated coagulopathy, and the host immune response, all of which are correlated with disease severity.[3,6-8] While recent studies demonstrated that AKI could develop as a complication of COVID-19,[5] the related risk factors and their association with different stages of AKI have not been extensively studied. In this study, we evaluated the incidence and mortality of AKI in hospitalized patients with COVID-19, based on the AKI stages, defined by Kidney Disease Improving Global Outcomes (KDIGO) guidelines in order to have a better understanding of the patients' characteristics and laboratory findings that influence their outcomes.

## MATERIALS AND METHODS

### Study Design and Data Collection

This cross-sectional study was conducted on hospitalized patients infected with SARS-CoV-2 (≥ 18 years) at Shiraz Hazrate Ali-Asghar Hospital (a designated referral hospital for COVID-19 cases in Fars province) affiliated to Shiraz University of Medical Sciences, Iran, from March 20, 2020, to June 20, 2020. A data collection sheet was developed with the information from medical records, including gender, age, signs and symptoms, length of in-hospital stay, routine blood tests, urinalysis, creatine phosphokinase, high-sensitivity C-reactive protein (hs-CRP), comorbid conditions, chest computed tomography (CT) scan results, and history of renal replacement therapy (RRT). All tests were done once within 24 hours after admission, but (sCr) was checked daily for all patients. Patients with missing data, and those with a previous history of CKD or renal transplantation were excluded from the study.

### Definitions

The diagnosis of COVID-19 was confirmed by real-time fluorescence reverse-transcription polymerase chain reaction (RT-PCR) test from a nasal and/or throat swab on admission. In patients with negative initial RT-PCR test results and high clinical suspicion of SARS-CoV-2 infection, the test was repeated 48 hours after the initial test. Fever was defined as a measured axillary temperature of ≥ 37.2 degrees Celsius. According to the KDIGO guideline, AKI was described as increasing sCr by ≥ 0.3 mg/dL within 48 hours from the onset of disease. Furthermore, the KDIGO staging system was used for the classification of the AKI, which defines stage 1 as ≥ 0.3 mg/dL (or 1.5 to 1.9 times) increase in sCr from baseline, stage 2 as a 2 to 2.9 times increase in sCr from baseline, and stage 3 as three times increase in sCr from baseline or ≥ 4 mg/dL increase in sCr or the initiation of RRT.[9] Classifications of COVID-19 severity as mild, moderate, and severe/critical was performed according to the Chinese Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (Trial Version 7).[10] Mild cases were defined as clinical symptoms such as cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhea, loss of taste and smell with no sign of pneumonia on imaging; moderate cases were defined as fever and respiratory symptoms for example trouble breathing or feel short of breath revealed by radiological findings of pneumonia; severe cases were defined as respiratory distress (≥30 breaths/min), oxygen saturation ≤ 93% at rest, and arterial partial pressure of oxygen (PaO2)/fraction of inspired oxygen (FiO2) ≤ 300 mmHg; and critical cases were defined as respiratory failure (requiring mechanical ventilation), shock, along with failure of other organs that require admission in the intensive care unit.[10] Among comorbid conditions, respiratory disease such as chronic obstructive pulmonary disease (COPD) or asthma, cardiac diseases such as ischemic heart disease, heart failure, and arrhythmia, renal disease such as non-dialysis chronic kidney disease, leukopenia on admission, considered as lymphocyte count < $1.1 \times 10^9$/L, elevated serum blood urea nitrogen (BUN), defined as > 20 mmol/L,

and elevated levels of sCr more than 1.1 mmol/L for women and more than 1.3 mmol/L for men., elevated hs-CRP defined as ≥ 10 mg/L, and chest CT scan findings, including ground-glass opacities and parenchymal consolidation, were all supposed to be associated with COVID-19.

### Ethical Issue

The study was conducted in accordance with the Declaration of Helsinki and approved by the local ethics committee of Shiraz University of Medical Sciences (Ethical code: IR.SUMS.REC.1399.071).

### Statistical Analysis

Data were analyzed by using SPSS for Windows, Version 16. Qualitative data were analyzed by using the chi-squared test and expressed as numbers and percentages. Quantitative data were presented as a median, interquartile range, mean, and standard deviation and analyzed by Independent T-test and ANOVA. Multiple binary logistic regression with the conditional forward method and multiple proportional odds ordinal logistic regression was used for analyzing the data. Variables were entered into the model that was significant according to univariate analysis. A $P$ value of < .05 was considered statistically significant.

## RESULTS

During our study period, the total number of hospitalized COVID-19 patients with SARS-CoV-2 positive RT-PCR tests at Aliasghar Hospital, Shiraz, Iran was 980, with a mean age of 51.5 ± 16.3 years; 54.8% (537 cases) of them were men (Table 1). The most commonly reported signs and symptoms were shortness of breath (66.3%), myalgia (42.1%), and dry cough (40.2%). Most patients (76.2%) experienced mild forms of COVID-19. 16.1% and 7.7% of cases experienced moderate and severe or critical disease, respectively. The most common comorbidities reported by patients were hypertension (28.6%) and diabetes mellitus (21.0%). Patients with initial negative RT-PCR tests (2.3%) were admitted due to high clinical suspicion of SARS-CoV-2 infection, in whom the repeated RT-PCR tests turned positive 48 hours after the initial tests. Among all patients, 320 (32.6%) cases developed AKI while 13 (1.3%) required RRT.

Compared with non-AKI patients, AKI patients were significantly older (54.9 ± 16.5 vs. 49.5 ± 15.8 years, $P$ < .001) and predominantly men (62.5% vs. 51.1%, $P$ = .001) (Table 1). The mean leukocyte count was higher ($P$ = .015) in AKI patients, while the mean lymphocyte count was significantly lower than non-AKI patients ($P$ = .002). Among electrolytes, serum sodium and calcium levels were significantly lower in AKI patients ($P$ < .002). Elevated levels of hs-CRP were seen in 47.8% of AKI and 34.0% of non-AKI patients ($P$ < .001). The percentage of AKI patients who required mechanical ventilation were significantly more than non-AKI patients (16.2% vs. 1.8%, $P$ < .001). Hematuria and proteinuria were reported more frequently in AKI patients than in non-AKI patients ($P$ < .001). Patients, who developed AKI during hospitalization, were reported to have more comorbidities including hypertension, diabetes mellitus, cardiac, and renal disease than non-AKI patients ($P$ < .001). The total in-hospital death of all studied COVID-19 patients was 6.3%, which was significantly higher in AKI patients than non-AKI cases ($P$ < .001).

The categorization of AKI into three stages according to KDIGO guidelines demonstrated that 81.2%, 9.0%, and 9.6% of patients were in stages 1, 2, and 3, respectively (Table 2). The stepwise increase in the mean age of AKI patients was associated with increasing severity of AKI ($P$ = .018). Lymphocyte counts demonstrated a stepwise decrease in the more severe stages of AKI ($P$ < .001). In addition, AKI patients with low lymphocyte counts on admission ($P$ < .001) and those who experienced a progressive decrease in their lymphocyte count during hospitalization had significantly higher stages (stage 3) and more severe AKI ($P$ < .001). Elevated BUN and sCr on admission were more frequently detected among patients with severe AKI ($P$ < .001). Patients with stage 3 AKI according to KDIGO classification experienced more severe or critical COVID-9 ($P$ < .001). The results showed a stepwise increase in COVID-19 disease-associated mortality with increasing AKI severity ($P$ < .001).

Among patients with stage 3 AKI, 41.9% required RRT during hospitalization; the mortality of which was 77.0% (Table 3).

The results extracted from logistic regression for AKI are summarized in Table 4 and Figure. The adjusted odds ratio (OR) showed that proteinuria had the greatest association with AKI (OR = 6.77 [95% CI: 4.39 to 10.41], $P$ < .001). BUN, sCr, and creatine phosphokinase were associated with higher

**Table 1.** Comparison of Laboratory Findings and Clinical Outcomes of Hospital COVID-19 Patients with AKI and Non-AKI

| Variables (number (%) / Mean ± SD) | Total (n = 980) | Acute Kidney Injury | | *P* |
|---|---|---|---|---|
| | | No (n = 660) | Yes (n = 320) | |
| Mean age, year (range) | 51.2 ± 16.2 (18 to 94) | 49.5 ± 15.8 | 54.9 ± 16.5 | < .001 |
| Gender, men | 537 (54.8) | 337 (51.1) | 200 (62.5) | .001 |
| Signs and Symptoms* | | | | |
| Shortness of breath | 650 (66.3) | 433 (65.6) | 217 (67.8) | .517 |
| Myalgia | 413 (42.1) | 262 (39.7) | 151 (47.2) | .027 |
| Dry cough | 394 (40.2) | 218 (33.0) | 176 (55.0) | < .001 |
| Lethargy | 299 (30.5) | 170 (25.8) | 129 (40.3) | < .001 |
| Fever | 289 (29.5) | 182 (27.6) | 107 (33.4) | .062 |
| Sore throat | 61 (6.2) | 27 (4.1) | 34 (10.6) | < .001 |
| Leukocyte count, × $10^9$/L | 6.6 ± 4.2 | 6.3 ± 3.3 | 7.1 ± 5.6 | .015 |
| Lymphocyte count, × $10^9$/L) | 2.4 ± 1.1 | 2.5 ± 1.0 | 2.3 ± 1.1 | .002 |
| Hemoglobin, g/dL | 13.4 ± 1.8 | 13.4 ± 1.7 | 13.2 ± 2.0 | .099 |
| Platelet count, × $10^9$/L) | 205.5 ± 75.9 | 212.1 ± 73.3 | 192.0 ± 79.3 | < .001 |
| Blood urea nitrogen, mmol/L | 16.0 ± 8.8 | 14.1 ± 5.4 | 20.0 ± 12.5 | < .001 |
| Serum creatinine, mmol/L | 1.1 ± 0.6 | 1.0 ± 0.3 | 1.4 ± 0.8 | < .001 |
| Sodium, mmol/L | 139.3 ± 37.3 | 139.6 ± 36.4 | 138.8 ± 38.6 | .002 |
| Potassium, mmol/L | 4.1 ± 0.5 | 4.0 ± 0.5 | 4.1 ± 0.6 | .081 |
| Calcium, mg/dL | 8.4 ± 0.5 | 8.4 ± 0.5 | 8.3 ± 0.6 | .002 |
| Phosphate, mg/dL | 3.0 ± 0.7 | 3.0 ± 0.7 | 3.0 ± 0.7 | .441 |
| Albumin, g/dL | 4.1 ± 0.5 | 4.1 ± 0.5 | 4.1 ± 0.5 | .066 |
| Creatine phosphokinase, U/L | 166.5 ± 24.6 | 135.4 ± 15.5 | 230.7 ± 36.1 | < .001 |
| hs-CRP[+], ≥ 10 mg/L | 377 (38.5) | 224 (34.0) | 153 (47.8) | < .001 |
| Systolic blood pressure, mmHg | 121 ± 15 | 121 ± 15 | 120 ± 15 | .929 |
| Diastolic blood pressure, mmHg | 76 ± 10 | 76 ± 10 | 76 ± 8 | .677 |
| Days of hospital admission | 7.0 ± 5.1 (1 to 42) | 6.6 ± 4.7 (1 to 42) | 8.0 ± 5.6 (1 to 39) | < .001 |
| Administration of mechanical ventilation | 64 (6.5) | 12 (1.8) | 52 (16.2) | < .001 |
| Negative results of initial RT-PCR[++] test | 23 (2.3) | 14 (2.1) | 9 (2.8) | .505 |
| Chest CT consistent with COVID-19 | 329 (33.6) | 192 (29.1) | 137 (42.8) | < .001 |
| Hematuria | | | | |
| Negative | 901 (91.9) | 625 (94.7) | 276 (86.2) | < .001 |
| Positive | 79 (8.1) | 35 (5.3) | 44 (13.8) | |
| Proteinuria | | | | |
| Negative or Trace | 886 (83.9) | 638 (96.7) | 248 (77.5) | < .001 |
| Positive | 94 (16.1) | 22 (3.3) | 72 (22.5) | |
| Comorbid conditions* | | | | |
| Hypertension | 280 (28.6) | 155 (23.4) | 125 (39.1) | <.001 |
| Diabetes Mellitus | 205 (21.0) | 116 (17.6) | 89 (27.8) | <.001 |
| Respiratory disease | 26 (2.7) | 16 (2.4) | 10 (3.1) | .529 |
| Cardiac disease | 83 (8.5) | 33 (5.0) | 50 (15.6) | < .001 |
| Renal disease | 17 (1.7) | 0 (0) | 17 (5.3) | < .001 |
| Severity | | | | |
| Mild | 747 (76.2) | 559 (84.7) | 188 (58.8) | < .001 |
| Moderate | 158 (16.1) | 78 (11.8) | 80 (25.0) | |
| Severe/critical | 75 (7.7) | 23 (3.5) | 52 (16.2) | |
| Outcome | | | | |
| Alive | 918 (93.7) | 649 (98.3) | 269 (84.1) | < .001 |
| Dead | 62 (6.3) | 11 (1.7) | 51 (16.0) | |

[+]high-sensitivity C-reactive protein
[++]reverse transcription polymerase chain reaction
*A patient could have presented with more than 1 characteristic.

odds of developing AKI, among others variable. Patients with cardiac disease were at higher risk of AKI (OR = 2.14 [95% CI: 1.03 to 4.41], *P* = .039).

The variables that were related to the severity

**Table 2.** Comparison of AKI Patient's Laboratory Findings and Clinical Outcomes Based on AKI Stages

| Variables (number (%) / Mean ± SD) | Total (n = 320) | Acute Kidney Injury Stages | | | *P* |
|---|---|---|---|---|---|
| | | 1 (n = 260) | 2 (n = 29) | 3 (n = 31) | |
| Mean age, year (range) | 54.9 ± 16.5 | 53.7 ± 16.0 | 58.6 ± 20.1 | 61.5 ± 15.3 | .018 |
| Gender, men | 200 (62.5) | 160 (61.5) | 22 (75.9) | 18 (58.1) | .276 |
| Leukocyte count, × $10^9$ /L | 7.1 ± 5.6 | 7.0 ± 5.6 | 6.1 ± 2.7 | 10.0 ± 6.3 | < .001 |
| Leukocyte count < 4 × $10^9$ /L | 50 (15.6) | 43 (16.5) | 6 (20.7) | 1 (3.2) | .114 |
| Lymphocytes count, × $10^9$ /L | 2.3 ± 1.1 | 2.4 ± 1.1 | 2.0 ± 1.0 | 1.3 ± 1.1 | < .001 |
| Lymphocyte count < 1.1 × $10^9$ /L | 51 (16.0) | 24 (9.2) | 8 (27.6) | 19 (61.3) | < .001 |
| Progressive decrease in lymphocyte count | 154 (48.1) | 112 (43.1) | 18 (62.1) | 24 (77.4) | < .001 |
| Blood urea nitrogen, mmol/L | 20.0 ± 12.5 | 17.3 ± 7.6 | 22.8 ± 12.2 | 38.8 ± 24.1 | < .001 |
| Blood urea nitrogen > 20 mmol/L | 110 (34.4) | 71 (27.3) | 15 (51.7) | 24 (77.4) | < .001 |
| Serum creatinine, mmol/L | 1.4 ± 0.8 | 1.2 ± 0.4 | 1.4 ± 0.8 | 2.8 ± 1.8 | < .001 |
| Serum creatinine > 1.1 in women / > 1.3 in men | 160 (50.0) | 120 (46.2) | 17 (58.6) | 23 (74.2) | .008 |
| Calcium, mg/dL | 8.3 ± 0.6 | 8.4 ± 0.5 | 8.4 ± 0.4 | 8.0 ± 0.7 | .010 |
| Phosphate, mg/dL | 3.0 ± 0.7 | 3.0 ± 0.7 | 3.0 ± 0.8 | 3.1 ± 0.7 | .222 |
| Albumin, g/dL | 4.1 ± 0.5 | 4.2 ± 0.5 | 4.0 ± 0.5 | 3.6 ± 0.6 | < .001 |
| Uric acid, mg/dL | 5.0 ± 2.1 | 4.5 ± 1.0 | 6.4 ± 2.1 | 7.5 ± 5.0 | < .001 |
| Creatine phosphokinase, U/L | 230.7 ± 36.1 | 192.0 ± 32.0 | 222.4 ± 23.0 | 564.4 ± 57.0 | < .001 |
| Administration of mechanical ventilation | 52 (16.2) | 17 (6.5) | 13 (44.8) | 22 (71.0) | < .001 |
| Hematuria | 44 (13.8) | 23 (8.8) | 8 (27.6) | 13 (42.0) | < .001 |
| Proteinuria | 72 (22.5) | 57 (22.0) | 7 (24.1) | 8 (25.7) | .314 |
| Severity | | | | | |
| Mild | 188 (58.8) | 178 (68.5) | 5 (17.2) | 5 (16.0) | |
| Moderate | 80 (25.0) | 65 (25.0) | 11 (38.0) | 4 (13.0) | < .001 |
| Severe/critical | 52 (16.2) | 17 (6.5) | 13 (44.8) | 22 (71.0) | |
| Outcome | | | | | |
| Alive | 269 (84.0) | 245 (94.2) | 18 (62.0) | 6 (19.4) | < .001 |
| Death | 51 (16.0) | 15 (5.8) | 11 (38.0) | 25 (80.6) | |

**Table 3.** AKI Stage 3 Patients Who Required Dialysis Treatment

| AKI Stage 3 Patients | Number (%) | Total Sessions med (IQR) | Duration of Sessions (hr), med (IQR) | Death (%) |
|---|---|---|---|---|
| Total RRT[a] Patients | 13 (41.9) | 3 (1 to 3.5) | 4 (2 to 72) | 10 (77.0) |
| HD[b] | 10 (32.2) | 2 (1 to 3) | 2 (2 to 4) | 8 (80.0) |
| CRRT[c] | 3 (9.7) | 3 (1 to 5) | 72 (72 to 72) | 2 (66.6) |

[a]Renal replacement therapy
[b]Hemodialysis
[c]Continuous renal replacement therapy

of the AKI were uric acid and outcome (uric acid: OR = 1.7 [95% CI: 1.32 to 2.22], $P < .001$; outcome: OR = 12.69 [95% CI: 3.85 to 42.09], $P < .001$).

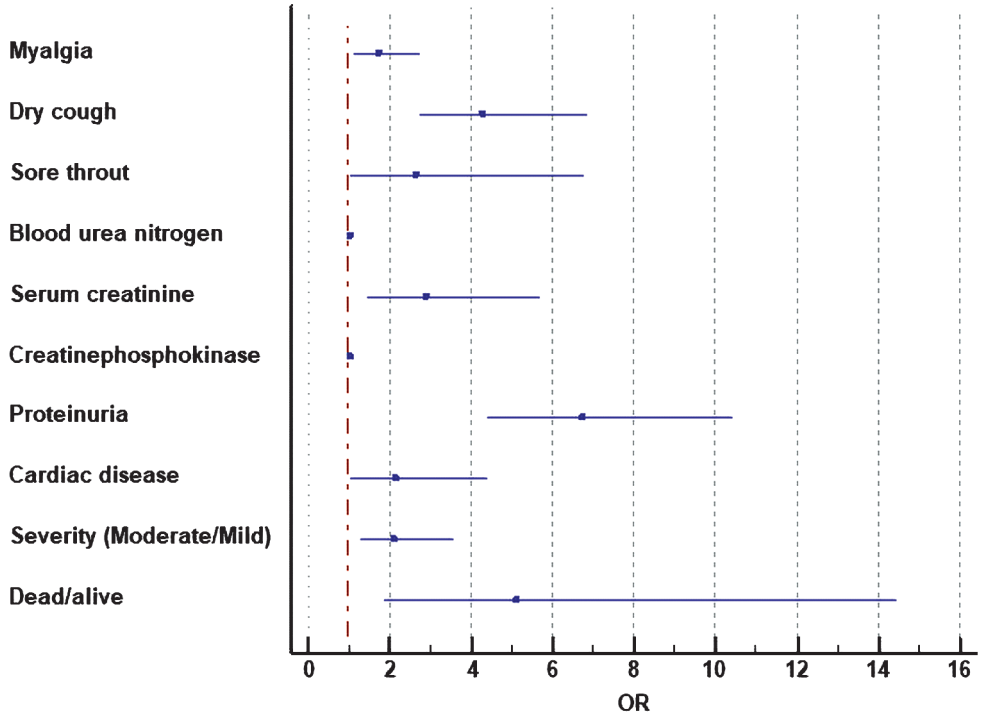
## DISCUSSION

In this cross-sectional study, conducted at Aliasghar Hospital in Shiraz, Iran, the rate of AKI among hospitalized SARS-CoV-2-infected adult patients was about 32.6%. The number of patients with AKI stages 1, 2, and 3 were 26.5%, 2.9%, and 3.1%, respectively. Among all patients with stage 3 AKI, 41.9% required dialysis treatment. The multivariate analysis showed a positive correlation between the severity of COVID-19 and incidence and severity of AKI. Mortality was significantly higher in AKI patients, with an increasing pattern in the more severe stages of AKI. Among the measured risk factors, proteinuria was mainly associated with AKI incidence.

According to Raina *et al.*'s systematic evaluation of 60 studies involving 43,871 COVID-19 patients, AKI had a pooled incidence rate of about 19.5%.[5] The pooled estimated rate of AKI patients who required RRT and their mortality rate were 39.0% and 52.2%, respectively. While our study findings demonstrated lower rates of RRT requirement and mortality, the authors think that it could be due to our study population which mainly included

**Table 4.** Adjusted Odds Ratio in AKI for Binary Logistic Regression

| Remained Variables | OR | | *P* |
|---|---|---|---|
| | Value | 95% CI | |
| Signs and Symptoms* | | | |
| Myalgia | 1.75 | 1.12 to 2.72 | .012 |
| Dry Cough | 4.31 | 2.72 to 6.82 | < .001 |
| Sore Throat | 2.65 | 1.03 to 6.77 | .042 |
| BUN, mmol/L | 1.05 | 1.01 to 1.09 | .011 |
| Serum Creatinine, mmol/L | 2.89 | 1.47 to 5.68 | .002 |
| Creatine Phosphokinase, U/L | 1.01 | 1.01 to 1.03 | .041 |
| Proteinuria | 6.77 | 4.39 to 10.41 | < .001 |
| Cardiac Disease | 2.14 | 1.03 to 4.41 | .039 |
| Severity | | | |
| Mild | Ref | | |
| Moderate | 2.13 | 1.27 to 3.58 | .004 |
| Severe/Critical | 1.78 | 0.74 to 4.26 | .195 |
| Outcome | | | |
| Dead /Alive | 5.149 | 1.86 to 14.47 | .002 |




Adjusted OR and 95% CI for Significant Variables According to Binary Logistic Regression

patients with mild COVID-19 ending up with less severe AKI and lower rates of RRT requirement and mortality.

According to the findings of our study, older patients are more vulnerable to AKI, and men are at higher risk than women. Several additional studies have also reported the significance of age and gender in AKI incidence.[11-13] However, Mohamed *et al.*[14] showed that males dominated the AKI group and that AKI patients were younger than non-AKI patients.

In our patients who experienced AKI, the mean leukocyte count was significantly higher, and the mean lymphocyte and platelet counts were significantly lower. Our findings confirmed the results of other studies. [15-16]

Furthermore, in our study, AKI patients had higher levels of BUN and sCr in comparison with non-AKI ones at the time of admission. The

same findings were reported by Zhang *et al*.[15] and Hirsch *et al*.[11] Our results also demonstrated that creatine phosphokinase was significantly higher in AKI patients; this is similar to the reports of Cui *et al*.[17] Proteinuria and hematuria were much more prevalent in our AKI patients, consistent with the study of Fisher *et al*.[12] which reported a significantly greater rate of proteinuria among their AKI patients. In this study, patients with AKI were more likely to have comorbidities than patients without AKI, except for those with respiratory diseases; Hirsch *et al*.[11] also found that their AKI patients had a much higher rate of comorbidities.

Patients with AKI had a higher prevalence of moderate, severe or critical COVID-19 cases, and a lower prevalence of mild COVID-19 instances, as compared to patients without AKI. A study conducted by Cui *et al*.[17] showed a higher rate of critical COVID-19 in AKI patients. The mortality rate of our AKI patients was significantly higher than non-AKI ones, which was also observed in similar studies conducted in this area.[11, 13, 16-18]

The mean leukocyte count, blood urea nitrogen and serum creatinine, creatine phosphokinase, proteinuria, and hematuria showed an increasing stepwise pattern in more severe stages of AKI when we evaluated laboratory findings and outcomes of patients in different AKI stages. Also, patients with severe stages of AKI experienced severe COVID-19 and required ventilator support, and eventually showed worse outcomes. Hirsch *et al*.[11] reported similar results to our study that showed an increased stepwise pattern in severe stages of AKI, in which worse outcomes were noted among patients who suffered severe stages of AKI.

The pathophysiology of AKI in COVID-19 has been discussed in several studies. There is evidence that the SARS-CoV-2 virus attacks the surface of renal podocytes and proximal straight tubule cells, where virus cell entrance mediators such as angiotensin-converting enzyme 2 receptors are more abundant.[3, 19-23] Overactivation of immune responses, hypercoagulability, viral sepsis, and drug nephrotoxicity are other contributing mechanisms involved in the pathophysiology of AKI in these patients.[3, 19, 21, 24]

## LIMITATIONS

This study had several limitations. Considering the high prevalence of COVID-19 in our country with several peaks due to different SARS-CoV-2 mutations, although our hospital was one of the main COVID-19 referral centers in southern Iran, the measured AKI incidence cannot be generalized to the general population. Also, we did not have kidney biopsy information, 24-hour urine tests, and patients' medications. In addition, we only measured the in-hospital mortality rate.

## CONCLUSION

AKI is a common complication in hospitalized COVID-19 patients. There are positive correlations between severity of COVID-19 and incidence and severity of AKI. Therefore, AKI diagnostic measures should be addressed, especially in severe or critical COVID-19 cases. Future research should consider the long-term outcomes in COVID-19 patients with AKI and the rate of chronic RRT requirement in this population.

## CONFLICT OF INTEREST

The authors declared that they had no conflict of interest.

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## AUTHORS' CONTRIBUTIONS

All authors have contributed to the research's concept and design and the manuscript's writing and revision and have approved the manuscript for submission.

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The study was conducted in accordance with the Declaration of Helsinki, and all experiments were performed in accordance with relevant guidelines and regulations. The local ethics committee of Shiraz University of Medical Sciences approved it (Ethical code: IR.SUMS.REC.1399.071). The current retrospective study was conducted on the basis of informed consent obtained at the admission time, including research aspects. The informed consent was obtained again when additional information was needed. The authors thank Shiraz University of Medical Sciences, Shiraz, Iran, the Center for Development of Clinical Research of Nemazee Hospital, and Dr. Nasrin Shokrpour for editorial assistance.

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