ORIGINAL ARTICLE

ACUTE KIDNEY INJURY IN HOSPITALIZED COVID-19 PATIENTS: A RETROSPECTIVE OBSERVATIONAL STUDY

Mohammad Asim[1], Sartaj Alam[2], Najmush Shakireen[3], Rabia Saeed[1], Arslan Rahat Ullah[1], Zain ul Abideen[4]

[1]Department of Medicine, Northwest General Hospital and Research Center, Peshawar, [2]Department of Nephrology, Peshawar Medical College, Peshawar, [3]Department of Pulmonology, Combined Military Hospital, Peshawar, [4]Department of Physiology, KMU-IMS, Kohat-Pakistan

Background: Published studies have reported that acute kidney injury (AKI) and other kidney related manifestations are associated with COVID-19 and linked with poor outcome. This study aimed to determine the incidence, risk factors and outcomes of AKI in hospitalized COVID-19 patients. **Methods:** This retrospective study of 154 patients involved retrieving data from hospital records confirm COVID-19 infection admitted to the Northwest General Hospital & Research Center, Peshawar from 1st April to 31st July 2020. AKI was defined using kidney disease. Improving Global Outcomes (KDIGO)" guidelines. **Results**: Incidence of AKI was 37.01%. Age, gender, intensive care (ICU) requirement, number of co-morbid, diabetes mellitus, coronary artery disease, chronic kidney disease, chronic obstructive airway disease (COAD), arrhythmias among comorbid and fever and shortness of breath among symptoms were found to be significantly differed between AKI and non-AKI patients. Numerous differences of laboratory results such as serum sodium, potassium, total leukocyte count, absolute lymphocyte count and platelets between both groups were observed (p<0.05). Inflammatory markers including lactate dehydrogenase (LDH), ferritin, d-dimer and C-reactive protein (CRP) were significantly raised in AKI group. Overall mortality was observed to be 38 (24.7%). Moreover, age, ICU requirement; COAD, creatinine, serum sodium, inflammatory markers (LDH, ferritin, d-dimers and CRP), total leukocyte count, absolute lymphocyte count, platelets and support requirement were significantly differed between survivors and non-survivors. Mortality was significantly higher among AKI group, i.e., 52.6% compared to 8.2% in non-AKI group (p<0.001). **Conclusion:** AKI is common among hospitalized COVID-19 patients and is associated with mortality. In all, AKI patients less than half of the patients survived.

Keywords: Acute kidney injury; COVID-19; Inflammatory markers; Inpatient mortality

Citation: Asim M, Alam S, Shakireen N, Saeed R, Rahatullah A, Abideen Z. Acute kidney injury in hospitalized covid-19 patients: A retrospective observational study. J Ayub Med Coll Abbottabad 2022;34(3 Suppl. 1):665–70.

DOI: 10.55519/JAMC-03-S1-9734

INTRODUCTION

Coronavirus disease-2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) primarily affecting the lungs. Recent data have shown that it also affects the nervous system, gastrointestinal system, heart, coagulation system, and kidneys. The incidence of acute kidney injury (AKI) in COVID-19 patients varies from 5–46%. This range is much high in patients requiring intensive care, i.e., 14–76%.[1,2] Contrasting results regarding the incidence of AKI have been published so far. A study from China reported an incidence of AKI in about 5.1% of patients based on data from various hospitals.[3] On the other hand, two independent studies from the United States reported an incidence of 36.6% and 46% of AKI, of whom, 14.3% and 19% required dialysis respectively.[1,4] Exact mechanism of COVID-19 causing AKI is unknown, however, it is believed to be due to the direct effects of the virus on kidney by entering through angiotensin-converting enzyme 2 receptors (ACE2) present in the proximal renal tubules and on podocytes or as a result of the disease severity resulting in cytokines and interleukin storm. A post-mortem study including 26 COVID-19 patients with AKI showed acute tubular injury when observed under light microscope and the presence of viral particles under electron microscopy in the tubular epithelium and podocytes.[5] Acute kidney injury in COVID-19 has higher mortality as compared to other illnesses with AKI. Multiple risk factors of in-patient AKI have been identified which include male gender, older age, diabetes mellitus, hypertension, and history of chronic kidney disease, use of an angiotensin-converting enzyme, non-steroidal anti-inflammatory drugs, mechanical ventilation, and hemodynamic instability.[5,6] There is a scarcity of information describing AKI and its outcomes in COVID-19 patients in Pakistan. Keeping in view, this study was designed to determine the incidence, clinical characteristics, severity, determinants, and outcomes of AKI in hospitalized COVID-19 patients. It will help in early recognition of patients who may need special care during hospitalization.

MATERIAL AND METHOD

A retrospective study during 1st April – 31st July 2020 was conducted at Northwest General Hospital & Research Center. Data were retrieved from the hospital information and management system. COVID-19 cases admitted in the hospital with at least 24 hours admission time and positive RT-PCR took via nasopharyngeal sampling were included in the final data set. Those patients with age <18 years, dialysis-dependent chronic kidney disease, hospitalization for <24 hours, and ambulatory patients were excluded. Upon satisfying both the inclusion and exclusion criteria, a total of 154 COVID-19 patients were included in the final analysis. Data regarding demographic and clinical information including laboratory parameters were recorded in a structured format. Primary outcomes were the development of AKI as defined by KDIGO criteria and in-hospital mortality.

Frequency and proportions were calculated for categorical variables. For continuous variables, mean and standard deviation (SD) for normally distributed data or median and interquartile range for non-normally distributed data were calculated. Association between categorical variables was computed using Chi-square statistics or Fisher exact test where appropriate. Mean and median differences were calculated using the student independent t-test and Mann Whitney test, respectively. Similarly, ANOVA or Kruskal Wallis test was applied to calculate differences for a variable with more than two categories. P-value less than 0.05 was considered significant in all the statistical analyses. SPSS version 20.0 was used for analyzing the data.

The study was approved by the Independent Ethical Committee of Northwest General hospital & Research Center vide Reference No: NwGH/EC/13.

RE1SULTS

A total of 154 patients who contracted the COVID - 19 and tested positive through RT-PCR were included in the final analysis. The mean age of the patients was 55.13±13.15 (SD) years and males constitute the major portion of the sample population (79.2%). Cough 100 (64.9%), fever 114 (74.0%), shortness of breath (SOB) 102 (66.2%), body aches 49 (31.8%), and chest pain 22 (14.3%), were the major presenting symptoms, while mean duration of these symptoms before admission was 8.00±4.45 (SD) days. The least common symptoms were fatigue, nausea, vomiting, and headache. During the course of treatment 27 (17.5%) patients required intensive care. Diabetes mellitus (DM) and hypertension were the predominant comorbid conditions. The median (IQR) serum creatinine (SCr) was 0.90 (0.40) on admission, while peak SCr was 1.00 (0.67). Median (IQR) SCr was 0.91 (0.54) at the time of discharge. The details are given in Table-1. The incidence of AKI was 37% the study population. Of the total 57 AKI patients, 37 (65.0%) were in stage I, 6 patients (10%) were in stage II and 14 patients (25%) were in stage III (Figure-1).

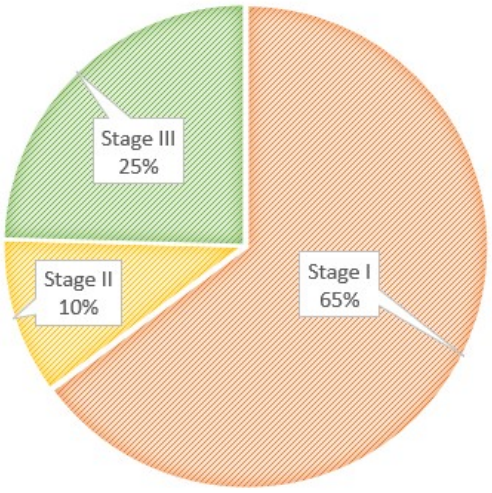

Figure-1: The percentage of AKI stage wise

As shown in table-1, the median (IQR) value of lactate dehydrogenase (LDH) was 490 (385). Median (IQR) ferritin, D-dimers, C-reactive protein (CRP) were 1339 (1523), 929(2027), and 10.0(17.87) respectively. Details regarding other laboratory values of the total patients are given in table-1.
During the hospital stay, non-invasive ventilation was received by 48 (31.2%) patients, while invasive mechanical ventilation (IMV) was received by 22 (14.3%). The overall hospital mortality was 24.7% as shown in table-1.

Demographic, clinical characteristics including presenting symptoms and comorbidities, laboratory parameters, support status, and outcomes were stratified based on AKI and non-AKI group. AKI patients had a mean age (60.33±12.56 years) greater than non-AKI (52.07±12.58 years) and the difference was statistically significant (p<0.001). Those patients who required intensive care had a higher proportion of AKI compared to non-AKI, and a statistically significant association was observed (p<0.001). The mean number of co-morbid conditions was higher in patients with AKI compared to non-AKI (p<0.001). The existing disease conditions that had significant interactions with AKI status were DM, coronary artery disease (CAD), chronic kidney disease (CKD), chronic obstructive airway disease (COAD), and arrhythmias. Among the presenting symptoms, fever and SOB were found to

be significantly associated with AKI status. There were numerous differences in laboratory results between the non-AKI group and AKI group with COVID-19 (Table-1). Serum sodium (Na^+), potassium (K^+) level was significantly higher in the AKI group compared to the non-AKI group, as expected ([140.50(13.75)/ 137 (5.00) Vs 4.54 (1.05)/ 4.00 (0.70]), with higher levels of urea 91 (82.00). Similarly, LDH, ferritin, d-dimer, and C-reactive protein were higher in the AKI group and the differences were significant (p<0.05). These results revealed that AKI represented more severe inflammation. AKI patients had a higher total leukocyte count (TLC) of 12.40 (9.00) vs 10.70 (6.29), lower absolute lymphocyte count (LY) 1.24 (0.86) vs 1.28 (1.04), and platelets 201.19 ± 91.72 vs 274.97±108.67 compared with the non-AKI group. Support in terms of vasopressor use, IMV requirement was higher in AKI group than that among the non-AKI group and the association was statistically significant. Compared with the non-AKI group, the AKI group had significantly higher mortality (p<0.001).

Table-1: Demographic, clinical characteristics, Laboratory parameters, support status and outcome of the study patients (n=154)

Characteristics	Total	No AKI N=97	AKI N=57	*p*-value
Age [Mean± SD]	55.13 ±13.15	52.07±12.58	60.33 ±12.56	<0.001
Gender n (%) Male	122 (79.2)	73 (75.3)	49 (86.0)	0.114
Duration of Symptoms [Mean± SD]	8.00 ±4.45	8.37±4.10	7.39 ±4.93	0.195
Length of hospital stay [Median (IQR)]	6.00 (5)	6.00(6)	5.00(6)	0.582
Intensive care requirement n (%)	27(17.53)	5 (5.2)	22 (38.6)	<0.001
Diabetes mellitus n (%)	64(41.56)	34 (35.1)	30 (52.6)	0.033
Hypertension n (%)	66(42.86)	37 (38.1)	29 (50.9)	0.123
Coronary artery disease n (%)	21(13.64)	9 (9.3)	12 (21.1)	0.040
Heart failure rEF n (%)	2(1.3)	1 (1.0)	1 (1.8)	0.702
Chronic kidney disease n (%)	6(3.9)	0 (0.0)	6 (10.5)	0.001
Asthma n (%)	13(8.44)	5 (5.2)	8 (14.0)	0.056
Chronic obstructive airway disease n (%)	4(2.6)	0 (0.0)	4 (7.0)	0.008
Arrhythmias n (%)	3(1.95)	0 (0.0)	3 (5.3)	0.023
Number of Comorbid [Mean± SD]	1.23 ±1.13	0.96±.99	1.68 ±1.23	<0.001
Cough n (%)	100(64.94)	67 (69.1)	33 (57.9)	0.160
Fever n (%)	114(74.03)	79 (81.4)	35 (61.4)	0.006
Sputum n (%)	10(6.49)	7 (7.2)	3 (3)	0.635
Fatigue n (%)	1(0.65)	1 (1.0)	0 (0.0)	0.442
Body aches n (%)	49(31.82)	33 (34.0)	16 (28.1)	0.444
Sore throat n (%)	8(5.19)	6 (6.2)	2 (3.5)	0.470
Shortness of breath n (%)	102(66.23)	58 (59.8)	44 (77.2)	0.027
Chest pain n (%)	22(14.29)	11 (11.3)	11 (19.3)	0.173
Headache n (%)	4(2.6)	3 (3.1)	1 (1.8)	0.614
Diarrhoea n (%)	8(5.19)	5 (5.2)	3 (5.3)	0.977
Vomiting/Nausea n (%)	4(2.6)	2 (2.1)	2 (3.5)	0.586
Creatinine on admission [Median (IQR)]	0.90(0.40)	0.80(0.27)	1.27(0.97)	<0.001
Peak Creatinine [Median (IQR)]	1.00(0.67)	0.80(0.30)	1.86(3.23)	<0.001
Discharge creatinine [Median (IQR)]	0.91 (0.54)	0.80(0.32)	1.79(2.96)	<0.001
Sodium [Median (IQR)]	138.0(6.00)	137(5.00)	140.50(13.75)	0.003
Potassium [Median (IQR)]	4.10(0.86)	4.00(0.70)	4.54(1.05)	0.001
$HCO3^-$ [Mean± SD]	25.57 ±3.41	26.36±2.98	24.18 ±3.69	<0.001
Urea [Median (IQR)]	48.0(51.50)	39(33.00)	91(82.00)	<0.001
INR [Median (IQR)]	1.4(40)	1.40(0.40)	1.30(0.41)	0.247
Lactate dehydrogenase [Median (IQR)]	490(385)	454(317)	654 (453.50)	<0.001
Ferritin [Median (IQR)]	1339 (1523)	1657.05(1338)	2000(1460)	0.018
D-dimers [Median (IQR)]	929(2027)	714(1070)	1383(6466)	0.003
C-reactive protein [Median (IQR)]	10.0(17.87)	8.00(14.00)	19(22.60)	0.002
Alanine transaminase [Median (IQR)]	50.0(66.50)	56(80)	50(66.50)	0.160
Albumin [Mean± SD]	3.43 ±.46	3.46±.43	3.38 ±.50	0.296
Haemoglobin [Mean± SD]	12.92 ±2.12	13.13±1.63	12.56 ±2.75	0.112
Total leukocyte count [Median (IQR)]	11.0(7)	10.70(6.29)	12.40(9.00)	0.001
Absolute lymphocytes [Median (IQR)]	1.27(0.97)	1.28(1.04)	1.24(0.86)	0.282
Platelets count [Mean± SD]	247.66 ±108.47	274.97±108.67	201.19 ±91.72	<0.001
Vasopressor support n (%)	15(9.74)	2 (2.1)	13 (22.8)	<0.001
Non-invasive ventilation (NIV) n (%)	48(31.17)	19 (19.6)	29 (50.9)	<0.001
Mechanical ventilation (IMV) n (%)	22(14.29)	5 (5.2)	17 (29.8)	<0.001
Outcome n (%) Expired	38 (24.7)	8 (8.2)	30 (52.6)	<0.001

Those patients who experienced the AKI were 57 (37%), in these patients the proportions with stages I, II, and III AKI were 65.0%, 10.0%, and 25.0%, respectively. Stages were further stratified by demographic, clinical, and other pertinent information. Peak creatinine and discharge creatinine differed significantly across the three stages. Similarly, serum urea was 80.42±47.16, 142.17±57.84, and 176.14±89.28 in stages I, II, III respectively and the differences were statistically significant. Among the other laboratory parameters, albumin statistically differed among the stages. NIV support was required by 71% in stage III and 83.3% in stage II and 37.8% in stage I and the association were significant across the three stages. The mortality of patients with AKI stages I, II, and III were 43.2%, 66.7%, and 71.4 %, correspondingly.

The differences between survivors and non-survivors were calculated, which showed that non-survivors had a higher mean age (p=0.001). The intensive care requirement was higher in non-survivors compared to survivors and the association was significant. Similarly, those patients who had COAD reported high mortality. Median creatinine at baseline, at peak, and discharge higher in non-survivors compared to survivors and the differences were statistically significant between the groups.

The inflammatory markers such as LDH, ferritin, d-dimers, and CRP levels were higher in non-survivors and the differences were found to be considered significant between the groups. On the other hand, serum albumin was lower in expired patients compared to survivors, i.e., 3.17±0.38 vs 3.51±0.45, (p<0.001). Expired patients had higher TLC (WBC) (14.0(9.50) vs 10.55(6.0), lower lymphocyte count (LY) (0.99(0.66) vs 1.36 (1.02) and platelets 177(132.75) vs 250 (143) compared with survivors and the differences were significant. Vasopressor use, ventilation requirement both invasive and non-invasive was statistically significant between survivors and non-survivors; the details are given in table-2.

Table-2: **Comparison of demographic, clinical characteristics, laboratory parameters, support status, and outcome between survivors and non-survivors**.

Characteristics	Discharged N=116	Expired N=38	p-value
Age [Mean ±SD]	53.16±13.04	61.16±11.72	0.001
Gender n (%) Male	88(75.9)	34(89.5)	0.073
Duration of symptoms Median (IQR)]	7.0(5.0)	7.0(6.0)	0.187
Length of stay Median (IQR)]	5.0(6)	6.0(6.50)	0.199
Intensive care unit n (%)	3.0(2.6)	24.0(63.2)	<0.001
Diabetes mellitus n (%)	46(39.7)	18(47.4)	0.402
Hypertension n (%)	49(42.2)	17(44.7)	0.787
Coronary artery disease n (%)	15(12.9)	6(15.8)	0.656
Heart failure rEF n (%)	2(1.7)	0(0)	0.415
Chronic kidney disease n (%)	5(4.3)	1(2.6)	0.643
Asthma n (%)	8(6.9)	5(13.2)	0.228
Chronic obstructive airway disease n (%)	1(0.9)	3(7.9)	0.018
Arrhythmias n (%)	1(0.9)	2(5.3)	0.088
Number of comorbid [Median (IQR)]	1(2)	1(1)	0.298
Creatinine on admission [Median (IQR)]	0.84(0.40)	1.0(0.53)	0.010
Peak creatinine [Median (IQR)]	0.90(0.50)	1.82(3.24)	<0.001
Discharge creatinine [Median (IQR)]	0.80(0.3)	1.85(3.09)	<0.001
Sodium [Median (IQR)]	137(5)	140(13.75)	<0.001
Potassium [Median (IQR)]	4.0(0.80)	4.33(1.43)	0.108
$HCO3^-$ [Median (IQR)]	26.0(4.0)	25.0(3.95)	0.355
Urea [Median (IQR)]	40(31.50)	92(71.0)	<0.001
INR [Median (IQR)]	1.30(0.33)	1.50(0.40)	0.055
Lactate dehydrogenase [Median (IQR)]	398.50(230.75)	801.50(364)	<0.001
Ferritin [Median (IQR)]	1104.50(1543.75)	2000(792.25)	<0.001
D-dimers [Median (IQR)]	645.0(894)	3576(7921)	<0.001
C-reactive protein [Median (IQR)]	8.00(11.54)	21.50(19.25)	<0.001
Alanine aminotransferase [Median (IQR)]	48.0(65)	50(59.7)	0.819
Albumin	3.51±0.45	3.17±0.38	<0.001
Haemoglobin [Median (IQR)]	13.0(2.23)	12.43(2.29)	0.439
Total leukocyte count [Median (IQR)]	10.55(6.0)	14.0(9.50)	<0.001
Absolute lymphocyte count	1.36(1.02)	0.99(0.66)	0.001
Platelet	250(143)	177(132.75)	<0.001
Vasopressor support n (%)	0(0)	15(39.5)	<0.001
Non-invasive ventilation n (%)	17(14.7)	31(81.6)	<0.001
Mechanical ventilation n (%)	2(1.7)	20(52.6)	<0.001

DISCUSSION

The mean age of our patients included in this study was 55.13, lesser than the studies from United States, United Kingdom, and China (mean age: 66, 68, 73, and 63 years respectively.[3,6–8] Older age was concluded as a risk factor for developing AKI in our study (mean age of AKI patients 60.33±12.56 years). These findings confirm the results reported by Kolhe NV *et al*, and Zahid *et al*.[6,7] No significant relation of AKI with gender was observed among our subjects. Similar results were reported in a study from the UK.[7] However, the male gender has been concluded as a risk factor of AKI among COVID-19 patients in studies done elsewhere.[1,6] Larger trials with multicenter approach may define the exact role of gender among COVID-19 patients.

The most common comorbidities in our study population were hypertension (42.9%) followed by DM (41.6%). A multicenter analysis from Pakistan also reported hypertension being the most common comorbid.[9] Among comorbidities, a significant association of AKI was observed with DM, CAD, COAD, CKD, arrhythmias, and a number of comorbid conditions. Some of these risk factors including older age, DM, and cardiovascular disease were also reported in multiple centers studies.[4,8,9] Increase in the number of comorbid was also reported as a risk factor of AKI in a study from the UK.[7] Implication of number comorbid diseases

Incidence of AKI was high in our subjects affecting more than one-third of the patients. AKI was reported in 37.01% of our patients which is on the higher side compared to that reported in other studies, i.e., 5.1–36%.[3,4,7, 10–13] This is also higher than the AKI in non-COVID19 disease patients as reported by Kolhe NV *et al*,.[7] This slightly higher incidence of AKI in our study can be explained due to strict inclusion criteria, a greater number of comorbid conditions, Asian population and lower number of subjects. Of the total AKI patients, 37 (65%) had stage I AKI followed by stage III (14, 25%) and stage II (6, 10%). On comparing stages of AKI, serum urea, serum albumin, and use of non-invasive ventilation were significantly associated among all parameters.

The relationship of AKI with respiratory failure is linear as higher stage AKI was found in severe COVID-19 patients with a more invasive need for ventilation. This was also observed in our results, where the need for intensive care was more in patients with AKI when compared to non-AKI (38.6% Vs 5.2%). Results published by Hirsch *et al*.,[4] also showed significant percentages among both groups (53.2% vs 9.7%) $p<0.001$. Similarly, NIV in 50.9% and IMV in 29.8% were observed in AKI as compared to 19.6% and 5.2% in non-AKI individuals, respectively. These results were parallel to a multicenter analysis where 53.6% of patients with AKI needed mechanical ventilation compared to 3.5% in the non-AKI group ($p<0.001$).[4] Regarding the use of vasopressor, 22.8% of our subjects with AKI needed vasopressor support as compared to 2.1% in the non-AKI group ($p<0.001$). Also, all of our patients who received vasopressor support during admission could not survive ($p<0.001$). These values also correlate with the findings of Hirsch JS *et al.* in this context.[4] The severity of AKI with respiratory failure, a higher number of mechanical ventilation, and increased mortality among ventilated patients in our study strongly support the link between respiratory failure and AKI among hospitalized COVID-19 patients**.**

COVID-19 triggers cytokine storm and sets the stage for multi-organ failure along with AKI through several mechanisms such as immune dysregulations which further cause intrarenal inflammation and cause increase vascular permeability. Multifactorial causative pathways play an important role in the development of AKI in COVID-19 patients that lead to acute tubular necrosis.[14] As COVID-19 is a prothrombotic state itself, prothrombotic coagulopathy contributing AKI cannot be ruled out. In our study, serum ferritin, lactate dehydrogenase and C-reactive protein was done at the time of admission showed significant relation with AKI. Also, these markers along with d-dimers were highly statistically significant in patients who could not survive. These statistics validate the findings reported by Arshad et al where CRP levels more than 7 times predicted in-hospital mortality in COVID-19 illness.[15] In addition to these values, serum urea level, bicarbonate, and total leukocyte were found significantly raised in our patients of the AKI group compared to non-AKI.

Cheng *et al* reported a 16.1% incidence of inpatient deaths with a sharp increment to 33.7% in patients with high baseline creatinine.[3] More data have shown similar higher values of in-hospital mortality such as Kolhe *et al*. 71.1% and Rudnick *et al*. 60.5%.[2,7] Our study confirmed AKI as a risk factor of in-hospital mortality (52.6%) in COVID19 patients with AKI compared to 8.2% in non-AKI group. Stage 3 AKI showed the highest percentage of mortality followed by stage 2 and stage 1 AKI. Similar results were reported by others as for stage 3 AKI.[2] Among the reported studies, in-hospital deaths were 34.8–72% in the US and 16.1–86% in China.[3,4,8,11,16] Furthermore, age and the presence of COAD were strongly linked with in-patient deaths. In our study, there was no significant relation between AKI and d-dimers however mortality was

significantly higher in our subjects with high d-dimers values.

This study has some limitations. Worth mentioning is a retrospective design and single-center study with a low sample size. We were not able to have long-term follow-up of these patients. Urine output was not included in the AKI determination due to missing data.

CONCLUSION

The incidence of AKI is high in COVID-19 hospitalized patients and the magnitude of the inflammatory response, age, gender; fever, and shortness of breath are among the risk factors for the development of AKI. Moreover, AKI is associated with a high risk for mortality.

Grant support and financial disclosure: None.
Conflict of interest: None.

AUTHORS' CONTRIBUTION

NS: Analysis and interpretation of data, drafting the manuscript. MA and SA: Concept and design, critical review, final approval. RS: Acquisition of data, interpretation of data. ARU and ZUA: Final approval, drafting the manuscript

REFERENCES

1. Chan L, Chaudhary K, Saha A, Chauhan K, Vaid A, Zhao S, *et al*. AKI in hospitalized patients with COVID-19. J Am Soc Nephrol 2021;32(1):151–60.
2. Rudnick MR, Hilburg R. Acute Kidney Injury in COVID-19: Another Challenge for Nephrology. Am J Nephrol 2020;51(10):761–3.
3. Cheng Y, Luo R, Wang K, Zhang M, Wang Z, Dong L, *et al*. Kidney disease is associated with in-hospital death of patients with COVID-19. Kidney Int 2020;97(5):829–38.
4. Hirsch JS, Ng JH, Ross DW, Sharma P, Shah HH, Barnett RL, *et al*. Acute kidney injury in patients hospitalized with COVID-19. Kidney Int 2020;98(1):209–18.
5. Nadim MK, Forni LG, Mehta RL, Connor MJ, Liu KD, Ostermann M, *et al*. COVID-19-associated acute kidney injury: consensus report of the 25th Acute Disease Quality Initiative (ADQI) Workgroup. Nat Rev Nephrol 2020;16(12):747–64.
6. Zahid U, Ramachandran P, Spitalewitz S, Alasadi L, Chakraborti A, Azhar M, *et al*. Acute kidney injury in COVID-19 patients: An inner city hospital experience and policy implications. Am J Nephrol 2020;51(10):786–96.
7. Kolhe NV, Fluck RJ, Selby NM, Taal MW. Acute kidney injury associated with COVID-19: A retrospective cohort study. PLoS Med 2020;17(10):e1003406.
8. Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW, *et al*. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area. JAMA 2020;323(20):2052–9.
9. Ul-Haq Z, Shahzad M, Khattak MI, Fazid S, Ullah N, Shireen A, *et al*. Clinical Characteristics, Mortality and Associated risk factors in COVID-19 patients reported in ten major hospitals of Khyber Pakhtunkhwa, Pakistan. J Ayub Med Coll Abbottabad 2020;32(4 Suppl 1):633–9.
10. Chen T, Wu D, Chen H, Yan W, Yang D, Chen G, *et al*. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. BMJ 2020;368:m1091.
11. Mohamed MM, Lukitsch I, Torres-Ortiz AE, Walker JB, Varghese V, Hernandez-Arroyo CF, *et al*. Acute kidney injury associated with coronavirus disease 2019 in urban New Orleans. Kidney360 2020;1(7):614–22.
12. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, *et al*. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China. JAMA 2020;323(11):1061–9.
13. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, *et al*. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020;395(10229):1054–62.
14. Su H, Yang M, Wan C, Yi LX, Tang F, Zhu HY, *et al*. Renal histopathological analysis of 26 postmortem findings of patients with COVID-19 in China. Kidney Int 2020;98(1):219–27.
15. Arshad AR, Khan I, Shahzad K, Arshad M, Haider SJ, Aslam MJ. Association of Inflammatory Markers with Mortality in COVID-19 Infection. J Coll Physicians Surg Pak 2020;30(10):158–63.
16. Gong Y, Hou J. Claudin-14 Underlies Ca++-Sensing Receptor–Mediated Ca++ Metabolism via NFAT-microRNA–Based Mechanisms. J Am Soc Nephrol 2014;25(4):745–60.

Submitted: June 15, 2021	*Revised: November 16, 2021*	*Accepted: MArch 22, 2022*

Address for Correspondence:

Najmush Shakireen, Ihtesham House, Opposite PTCL Colony, Warsak Road, Peshawar-Pakistan
Cell: +92 313 951 1139
Email: dr.nwgh@gmail.com