**Original Article**

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# Incidence and Outcomes of Renal Derangements in Covid-19 Patients of a Tertiary Care Hospital

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*Funding Source: None*
*Conflict of Interest: None*

*Received: Sept 05, 2024*
*Accepted: Jan 10, 2025*

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**ABSTRACT**

Objective: To assess the incidence and outcomes of acute kidney injury in patients diagnosed with Covid-19.

Methodology: This cross-sectional study was carried out in the department of medicine, Shaikh Khalifa Bin Zayed Al Nahyan Hospital/CMH, Rawalakot, AJK, Pakistan from May 2021 to May 2023. Total 676 patients (ages ≥ 18 years) admitted with Covid-19 confirmed through polymerase chain reaction (PCR) having normal renal function tests (RFTs) at admission were included in the study. RFTs were done during admission and patients were followed up for outcome. The kidney disease improving global outcome (KDIGO) staging system was employed to classify the stages of acute kidney injury (AKI). The Clinical Progression Scale (CPS) of WHO, which rates the severity of Covid-19 outcomes from 0 (uninfected) to 10 (death), was utilized.

Results: Patients mean age was 56.1±16.1 years. Among 676 patients, 350 (51.8%) developed AKI. According to clinical progression scale, only 2 (0.3%) patients were uninfected, 540 (79.8%) experienced mild symptoms, 98 (14.5%) were of moderate symptoms, 12 (1.8%) suffered from severe symptoms and 24 (3.6%) were dead. Comprises stage 1 (46%), stage 2 (27.4%) and stage 3 were (26.5%). Among the patients of AKI, 326 (93.1%) were discharged from hospital on home medication and 24 (6.9%) patients died ($p < 0.05$).

Conclusion: Acute kidney injury develops commonly in patients of Covid-19. AKI need to be managed effectively to prevent worst future outcomes.

Keywords: Acute kidney injury, Covid-19, Dialysis, Renal insufficiency.

*Cite this article as: Qayyum W, Naseem A, Nadeem M, Mushtaq S, Tahir R, Ain QT. Incidence and Outcomes of Renal Derangements in Covid-19 Patients of a Tertiary Care Hospital. Ann Pak Inst Med Sci. 2025; 21(1):235-239. doi. 10.48036/apims.v20i1.1322.*

## Introduction

Covid-19 is a respiratory infection triggered by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) which may prove disastrous.[1] SARS-CoV-2 causes mainly respiratory infection result in inflammatory changes i.e., pneumonia and hypoxemia showing the characteristics of acute respiratory distress syndrome (ARDS) in later stages.[2] Although main concern is respiratory system, SARS-CoV-2 may attack kidneys as the virus targets the angiotensin converting enzyme-2 (ACE-2) receptor, which are abundant in kidneys.[3] Acute kidney injury (AKI) following Covid-19 is a major problem deserving plenty of clinical recognition and is a common hazard among the patients of Covid-19.[4] Patients who develop AKI upon admission or after admitting to hospital had a high rate of deaths than those without AKI.[5]

Studies showed varied incidence of AKI in patients of Covid-19. A study done in Italy showed that AKI was in 22.4% patients of Covid-19 with severity stages of 1, 2,

and 3 AKI valued for 58%, 25% and 17%, among 57% patients of Covid-19 compared 25% patients without Covid-19.[7] Kellum et al presented incidence of AKI as high as 43% in hospitalized patients of Covid-19.[8] A recent study in Peshawar found 37% incidence of AKI.[9]

Patients of Covid-19 having comorbidities are associated to severe complications as compared to patients with no comorbidities. A study demonstrated the significant association of comorbidities with the severity of illness.[10] The millions of deaths have been caused due to Covid-19 worldwide which were mainly due to their fatal complications including AKI.[11]

Our study aim was to define the AKI incidence in patients of Covid-19 and to describe different aspects and subsequent consequences of AKI. There is a limited data available in Pakistan regarding AKI incidence in Covid-19 patients, hence we aimed to assess the clinical features and outcomes of AKI in admitted Covid-19 patients.

# Methodology

This prospective cross-sectional study was carried out at Shaikh Khalifa Bin Zayed Al Nahyan Hospital /combined military hospital (CMH), Rawalakot, AJK, Pakistan from May 2021 to May 2023 IRB no 67/SKBZ/CMH/REC The study was carried out following ethical approval from hospital's Ethics Committee, with informed consent acquired from all participants. All patients ≥ 18 years, admitted with relevant sign and symptoms and Covid-19 positive through polymerase chain reaction (PCR) of nasopharyngeal specimens were involved in the study. Patients were enrolled by non-probability consecutive sampling in the study. According to WHO definition, a case of Covid-19 would be rendered as confirmed if PCR assay of specimen is positive collected via nasopharynx or lower respiratory tract.[12] Patients having history of renal stones, renal or prostate surgery, end stage renal disease, who left against medical advice before the completion of their treatment, deranged renal functions at admission and having history of kidney transplant were excluded from the study.

Patients after admission were observed and followed up for the AKI and Covid-19 severity. The patients were categorized according to Clinical Progression Scale (CPS) of WHO. Covid-19 severity outcomes on CPS ranging from uninfected (score 0) to dead (score 10) (Table I).[13] RFTs were repeated at the day 5 of admission and AKI was one of the following: (a) elevated creatinine of ≥ 0.3 mg/dl in 48 hrs or (b) elevated creatinine ≥ 1.5 times the baseline in last 7 days or (c) urine output ≤ 0.5 ml/kg/h for a duration of 6 hrs. As defined by Kidney Disease Improving Global Outcomes (KDIGO) staging, AKI was staged according to severity: (a) Stage 1: creatinine is 1.5-1.9 times the baseline level or shows an elevated of ≥ 0.3 mg/dL, (b) Stage 2: creatinine is elevated to 2.0-2.9 times the baseline level, (c) Stage 3: creatinine is three times the baseline level, increases ≥ 4.0 mg/dL, or requires the renal replacement therapy according to KDIGO staging.[14]

Using a questionnaire we assembled demographic information (age, gender, and qualification), comorbidities, vaccination status against Covid-19, symptoms at presentation, and lab results of renal function tests (RFTs), duration of hospital stay, oxygen demand and ultimate outcome of the patients. KDIGO was used to assess the severity of AKI.

Nominal data was presented in the form of tables and graphs. Categorical variables were computed via frequency and proportions. All numerical variables were introduced as mean with SD. The correlation between comorbidities and AKI severity was assessed by Pearson test. The p value of ≤ 0.05 was rendered significant. All the data was analyzed by using SPSS v 25.

**Table I: Clinical Progression Scale. (Outcomes)**

| Patient state | Description | Score |
|---|---|---|
| Uninfected | Uninfected; no viral RNA detected | 0 |
| Ambulatory mild disease | Asymptomatic; viral RNA detected | 1 |
| | Symptomatic; independent | 2 |
| | Symptomatic; assistance needed | 3 |
| Hospitalized: moderate disease | Hospitalized; no oxygen therapy | 4 |
| | Hospitalized; oxygen by mask or nasal prongs | 5 |
| Hospitalized: severe disease | Hospitalized; oxygen by NIV or high flow | 6 |
| | Intubation and mechanical ventilation, pO2/FiO2 ≥ 150 or SpO2/FiO2 ≥ 200 | 7 |
| | Mechanical ventilation pO2/FIO2 < 150 (SpO2/FiO2 < 200) or vasopressors | 8 |
| | Mechanical ventilation pO2/FiO2 < 150 and vasopressors, dialysis, or ECMO | 9 |
| Dead | Dead | 10 |

# Results

The study included 676 Covid-19 patients. The participants mean age was 56.1±16.1 years. Male population comprised 285 (42.2%) and females were 391 (57.8%). Most of the patients were having fever, myalgia and fatigue 252 (37.3%) or fever, cough and shortness of

breath 214 (31.7%). Small number of patients presented with fever only 19 (2.8%) without any other symptom. Other symptoms included chest pain, headache and diarrhea. Among the total patients, 280 (41.4%) were having no comorbidities. Hypertension was the commonest comorbidity, found in 139 (20.6%) patients followed by hypertension and diabetes combined in 94 (13.9%), diabetes alone in 72 (10.7%), other comorbidities were bronchial asthma, COPD, ischemic heart disease, stroke as shown in Table II.

**Table II: Patient demographics, clinical features, laboratory values, and ventilator support level. (n=676)**

| Characteristics | | N | % |
|---|---|---|---|
| Gender | Male | 285 | 42.2 |
| | Female | 391 | 57.8 |
| Comorbidities | None | 280 | 41.4 |
| | Hypertension (HTN) | 139 | 20.6 |
| | Diabetes mellitus (DM) | 72 | 10.7 |
| | HTN, DM | 94 | 13.9 |
| | Asthma | 27 | 4.0 |
| | Asthma, HTN | 34 | 5.0 |
| | Others | 30 | 4.4 |
| Symptoms | Fever, myalgia, fatigue | 252 | 37.3 |
| | Fever, cough, SOB | 214 | 31.7 |
| | Fever, cough | 99 | 14.6 |
| | Nausea, vomiting | 92 | 13.6 |
| | Fever | 19 | 2.8 |
| D Dimers | Positive | 83 | 12.3 |
| | Negative | 593 | 87.7 |
| CRP | Positive | 341 | 50.4 |
| | Negative | 335 | 49.6 |
| Ventilator support | Not required | 660 | 97.6 |
| | Mechanical | 7 | 1.1 |
| | Noninvasive | 9 | 1.3 |
| Vaccination status | Non-vaccinated | 610 | 90.2 |
| | Vaccinated | 66 | 9.8 |

Duration of hospital stay was ≤ 5 days for 374 (55.3%) patients, 6-10 days for 219 (32.3%) and 11–15 days for 83 (12.2%) patients. Most of the patients having < 5 days of stay in hospital were non-AKI. Among the recorded inflammatory markers, D Dimers was found positive for 83 (12.3%) and CRP was positive for 341 (50.4%) patients. Mean ESR was 24.5±18.7. RFT's were repeated at 5th day, and mean serum urea was 8.2±4.7 mmol/L, while mean serum creatinine was 109.3±39.8 mmol/L. During the course of treatment, majority of patients 660 (97.6%) didn't require ventilator support, 9 (1.3%) patients require noninvasive ventilation and only 7 (1.1%) were on mechanical ventilation. Regarding vaccination status, 610 (90.2%) were non vaccinated and remaining 66 (9.8%) patients were vaccinated (Table II). Patients having lower education levels were found to be least vaccinated as compared to those having higher education status.

Considering the Covid-19 severity, according to Clinical Progression Scale (CPS) of WHO, only 2 (0.3%) were uninfected, 540 (79.9%) patients experienced mild symptoms, 98 (14.4%) were of moderate symptoms, 12 (1.8%) suffered from severe symptoms and 24 (3.6%) were dead. Regarding admitted patients of Covid-19, 350 (51.8%) developed AKI, comprises 46% stage 1, stage 2 (27.4%) and 26.6% stage 3 (Table III). While discussing AKI incidence in every category of Covid-19, none of uninfected patients developed symptoms of AKI, 10 (83.3%) patients of severe category developed AKI, 80 (81.6%) of moderate and 11 (2.1%) patients of mild symptoms developed the symptoms of AKI ($p \leq 0.05$). Only 7 patients (2%) who developed AKI were vaccinated while rest of all were non vaccinated (98%). Maximum patients 404 (59.8%) required oxygen supplementation during the hospital stay. Out of these, requirement of 229 (56.6%) patients was < 5L/min $O_2$, 116 (28.8%) were on 5-10 L/min $O_2$ and 59 (14.6%) required > 10 L/min $O_2$. Among 350 patients of AKI, 326 (93.1%) patients were discharged from the hospital on home medication and 24 (6.9%) patients died (Table III).

**Table III: Severity of disease, AKI development and outcomes. (n=676)**

| Characteristics | | N | % |
|---|---|---|---|
| Disease severity by clinical progression scale | Uninfected | 2 | 0.3 |
| | Mild | 540 | 76.3 |
| | Moderate | 98 | 14.5 |
| | Severe | 36 | 5.3 |
| | Dead | 24 | 3.6 |
| AKI development | Non-AKI | 326 | 48.2 |
| | AKI | 350 | 51.8 |
| AKI stages | Stage 1 | 161 | 46.0 |
| | Stage 2 | 96 | 27.4 |
| | Stage 3 | 93 | 26.6 |
| Outcomes of AKI | Discharged | 326 | 93.1 |
| | Expired | 24 | 6.9 |

**Table IV: Correlation between comorbidities and severity of illness. (n=676)**

| | Value | Standard error | T value | p value |
|---|---|---|---|---|
| Pearson's (r) | .112 | .039 | 2.919 | .004 |

Using the Pearson correlation (r) test, a positive correlation was found between comorbidities and severity of illness. Patient having more than one comorbidity was found to have more severe illness ($p < 0.05$).

# Discussion

The patient's mean age in this study was 56.1 years, less than the age observed in a study done in China which was 63 years.[15] Studies revealed that advancing age is at stake for establishing AKI in Covid-19 patients.[16] No significant correlation between gender and AKI was found in this study. Comparable findings were found in a study done in UK.[17] Nonetheless, male gender along with diabetes and cardiovascular diseases were established as absolute risk factors of developing AKI.[18] Future trials are required to highlight the role of male gender as a risk of AKI in patients of Covid-19.

In our admitted patients of Covid-19, 51.8% developed AKI. A local study reveals the same results.[19] Ahmed et al reported incidence of AKI to be 41.3% over the span of 4 months highlighting significant association between AKI and mortality.[20] The commonest comorbidities in this study participants were HTN (20.6%) and DM (10.7%). The findings are similar with the results of a study done in New York, which revealed HTN as most common comorbidity (45%) and DM (31%).[21] Local data from Pakistan also revealed HTN as the most common comorbid.[22] In one of the previous studies done in UK 2.6% of patients received kidney replacement therapy, and the major risk factor was chronic kidney disease.[23] Regarding comorbidities, significant association of AKI with COPD, Asthma, ILD and CKD in this study as well as in litreture.[10]

Taking in to account the vaccination status of patients against Covid-19, 90.2% were non vaccinated and only 9.8% patients were vaccinated which indicates that unvaccinated population is more prone to develop Covid-19 infection which then leads to development of systemic complications i.e., AKI. A recent study reveals that Covid-19 vaccination is effective in inhibiting the onset of severe disease and is an important tool to prevent the transmission of virus.[24] A study in Israel shows that there was decreased incidence and signs/symptoms of Covid-19 after having first dose of vaccine.[25]

Regarding the severity of Covid-19 symptoms, only 0.3% were uninfected, 80% patients experienced mild symptoms, 14.4% were of moderate symptoms, 1.8% suffered from severe symptoms and 3.6% were dead. These results are comparable to a study done in Egypt.[26] This study revealed that AKI stage 1 comprised of 46%, stage 2 (27.4%), and stage 3 was 26.5%. In contrast, a study reveals higher percentage of stage 3 as compared to this study, stage 1 comprised 17.1%, stage 2, 25.7%, and stage 3 was 57.2%.[27] AKI staging was seemed to be dependent on severity of respiratory illness, comorbidities, age and vaccination status.

Duration of hospital stay was ≤ 5 days for 55.3% patients, 6-10 days for 32.3% and 11–15 days for 12.2% patients. Patients who developed AKI have more duration of hospital stay as compared to those who didn't develop. According to a study done in Turkey, average hospital stays for patients who developed AKI was 16 days as compared to 9.9 days for non-AKI patients.[28]

There are besides 2.4 million deaths because of Covid-19 globally and majority of them were due to fatal complications including AKI.[11] This study revealed the death rate of 3.6%. The cause of death in majority of patients was respiratory failure and sepsis. A local study revealed mortality rate of 73.2% among severely ill patients requiring hemodialysis.[29]

# Conclusion

In our admitted patients of Covid-19, AKI is a frequent complication related with great number of ICU admissions and duration of hospital stay. This study concludes that renal derangements in Covid-19 patients need to be managed effectively to prevent worst future outcomes. This study highlights the incidence, features, elements of risk and possible complications of AKI in patients of Covid-19 so that urgent and intensive care can be given to effected patients in time.

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