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Outcome of Acute Kidney Injury in Critical COVID-19 patients in Karachi, Pakistan: A Single center, Retrospective study

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Abstract

Introduction: The severe acute respiratory syndrome coronavirus2 (SARS-CoV2) is a novel beta-coronaviridae family and its effects on the kidneys have been reported which included the increased requirement of renal replacement therapy during the Covid-19 pandemic. Our study is, thus, designed to determine the outcome among acute kidney injury AKI patients in critically ill patients with covid-19 .

Method and Material: It was a retrospective observational study of COVID-19 patients admitted in SIDH&RC (specialized facility center for COVID-19) from July 2020 to July 2021. The patients were divided into two groups; one with confirmed critical COVID-19 and had AKI during hospital stay and the other group who had confirmed critical COVID-19 and did not develop AKI during hospital stay.

Results: Total 232 patients were included in this study and 92 (39.65%) of these patients had AKI during hospital stay. Most of the patients who had AKI were male 55(59.8%). We found that in this population mortality was not significant in critical COVID-19 patients with AKI. However, patients with AKI had worst survival compared to non-AKI patients ($p<0.05$) and frequently required mechanical ventilation compared to non-AKI patients (70.7% vs 50.7%, $p<0.05$). Such patients had more chance of occurrence of complications: superimposed bacterial infections, NSTEMI, septic shock and progression to severe ARDS, $p<0.05$.

Conclusion: We found that presence of AKI had worst outcomes than non AKI in patients with critical COVID-19.

Keywords: Acute kidney injury (AKI), COVID-19, hemodialysis, survival, mechanical ventilation, myocarditis.

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DOI: 10.53778/pjkd72221

Received Feb 02, 2023 and accepted in revised form June 23, 2023 PJKD 2023;7(2):3-7

Introduction:

The severe acute respiratory syndrome coronavirus2 (SARS-CoV2) is a novel beta-coronaviridae family and its effects on the kidneys have been reported which included the increased requirement of renal replacement therapy during the Covid-19 pandemic.[1] The rapid progression of coronavirus disease 2019 (Covid-19) pandemic showed that lungs are the main organs involved in this disease in the form of viral pneumonia, inflammatory infiltrates and endothelial damage resulting in respiratory failure but other organs like kidneys are also involved resulting in acute kidney injury.[2,3]

Various studies reported that the kidney may serve as a target organ for SARS-CoV-2 because angiotensin-converting enzyme 2 which is the binding for the virus and is highly expressed in proximal tubule cells and podocytes.[4] According to 25th ADQI workgroup consensus report, the pathophysiology of AKI in COVID 19 patients likely relate to direct injury caused by the virus, following patterns of collapsing glomerulopathy, endothelial damage, coagulopathy, complement activation and inflammation or indirectly as part of the systemic involvement of organs in critically ill patients.[5] The data from studies in China showed an AKI incidence ranging from 5% to 29% in hospitalized patients with COVID-19. Although most of these reports identified risk factors for AKI, there have been no direct comparisons to patients negative for COVID-19 that would identify aspects

of AKI risk, course, and outcomes that are unique to COVID-19. It is not yet clear about the extent of AKI caused by Covid-19 and how actually this disease causes AKI.[6-8] Incidence of AKI caused by Covid-19 pandemic has ranges from 5%-29% with inter-center variation which may be due to the difference in demographic features and also underlying co-morbid conditions.[2,3,7,9-11] Jewell et al. showed the frequency of AKI was 39% in a large cohort study.[12] Anees M et al showed that the AKI was present in half (51.1%) of the COVID-19 patients and its significant risk factors were increasing age, prolonged hospital stay, hypoxemia, hypoalbuminemia, DM and raised inflammatory markers.[13]
Our study was, thus, designed to determine the risk factors and outcome of AKI in critically ill patients with covid-19 and their outcomes. This will add local data related to this and will further improve our knowledge about expectations, incidence and outcomes of critically ill COVID 19 patients with AKI Karachi, Pakistan.

Methods

Study Design:

This retrospective, single center study was conducted at Sindh Infectious Disease Hospital and Research Center, which is a specialized facility center only for COVID-19 patients. The patients who were enrolled in the study were all confirmed cases of COVID-19, who were enrolled as critical COVID-19 at the time of admission from July 2020 to July 2021.The patient included in the study had a clear diagnosis by a physician or by medical record and history.

Ethics:

This study was approved by the Dow University of Health Sciences Institutional Review Board (Ref: IRB-2267/DUHS/2021/826)

Data Collection:

We identified 233 patients who fulfilled WHO Criteria for Critical Covid at the time of admission and were above 18 years of age. The data were collected from health management information system (HMIS) and hospital medical record sheets. Demographics, pre-existing condition, disease progression, hospital stay (days), need mechanical ventilation, laboratory parameters and outcomes were gathered and entered in clinical research proforma. The patients included in the study had clear diagnosis by a physician or by medical record.

Inclusion Criteria:

The patients were divided into two groups; one with confirmed critical COVID-19 and had AKI during hospital stay and the other group who have confirmed critical COVID-19 and did not had AKI during hospital stay.

Measurements and Variable Definitions

The identification of AKI was according to the serum creatinine in Kidney Disease: Improving Global Outcome (KDIGO) guidelines.[16] AKI was defined as an absolute increase in serum Cr by ≥0.3 mg/dL within 48 hours or increase in serum Cr ≥1.5 times higher from the baseline value within seven days. AKI is then divided into 3 stage according to the severity to the following KDIGO criteria: Stage 1 AKI is defined as an increase to more than 2 to 2.9 times form the baseline serum Cr within seven days. Stage 2- an increase to more than 3 time from the baseline serum Cr within seven days. Stage 3 AKI defined as more than 3-time increase in serum Cr within 7 days or increase in creatinine to >4 mg/dl or initiation of renal replacement therapy. We considered the baseline serum Cr value as the serum Cr level that was measured on the day of admission. We used the highest serum Cr level after AKI detection to identify the stage of AKI on the basis of KDIGO criteria. Severe AKI was considered as stage 2 or stage 3 AKI. The patients who required renal replacement therapy were automatically met the definition of AKI stage 3. Renal recovery in patients with AKI was defined as a decrease in serum creatinine to a level that was 50% lower than the maximum creatinine reached during hospital stay.

Statistical Analysis:

Tables and graphs were then used to summarize and illustrate the study' s data. The normality of the data was examined using the Kruskal-Wallis test. The median and interquartile ranges are displayed for non-normal distributed continuous data. Numbers and percentages were used for categorical data. Fisher' s and Chi-square

were used for categorical data. Statistical analysis is regarded as significant at p<0.05. Statistical package for social sciences (SPSS) software (version 26.0) and prism GraphPad were used for analysis and graphs (version 8).

Results

A total of 232 patients with critical COVID-19 were hospitalized at SIDH & RC. More than half were male (59.8%) and having median age of 62(52-70) were admitted as critical COIVD-19 patients in hospital. Most of the patients in both groups had pre-existing conditions, in which most of the patients had Hypertension (50%), followed by Diabetes mellitus (32.3%). All demographics and clinical characteristics mentioned in Table.1. Overall, 39% of the patient developed AKI. There was no significant difference regarding clinical features between both groups (Table 1).

Table 1: Demographic and Clinical Characteristics of 232 hospitalized critical COVID-19 patient with/or without acute kidney injury.

Parameter	All n=232	AKI n=92 (39.65%)	non-AKI n=140	p-value
Age median (SD)	62 (52-70)	64 (53.5-70)	60 (52-72)	0.701
Male	138 (59.5)	55 (59.8)	83 (59.3)	0.94
Female	94 (40.5)	37 (40.2)	57 (40.7)	
Outcomes				
Discharge	141 (60.8)	54 (58.7)	87 (62.1)	0.599
Mortality	91 (39.2)	38 (41.3)	53 (37.9)	
Comorbities	172 (74.1)	70 (76.1)	102 (72.9)	0.583
DM	75 (32.3)	26 (28.3)	49 (35)	0.283
HTN	116 (50)	47(51.1)	69 (49.3)	0.89
IHD	29 (12.5)	12 (13)	17 (12.1)	0.839
CKD	7 (3)	4(4.3)	3 (2.1)	0.337
AKI Stages				
Stage I	-	43 (46.7)	-	
Stage II	-	25 (27.2)	-	
Stage III	-	24 (26.1)	-	
Laboratory Parameters at Admission				
Creatinine median (IQR)	1.3 (0.89-2)	1.6 (1.08-2.43)	1.1 (0.8-1.6)	0.0001
CRP median (IQR)	100.4(45.5-188)	117 (72-190)	95 (36.5-185)	0.131
TLC median (IQR)	13.5 (9.5-18)	14 (10.05-17.48)	13 (8.9-18.58)	0.537
D-Dimer median (IQR)	1.81 (1.09-4.92)	1.9 (1.1-5.73)	1.6 (0.9-4.2)	0.198
Platelets median (IQR)	226 (167.5-330)	225 (155-306.7)	229 (175-342)	0.172
HB median (IQR)	12.7 (11-14)	12.3 (11-14)	13 (11-14)	0.299
Ferritin median (IQR)	674.6 (353.5-1345.7)	679.3 (347-1359)	654 (351-1334.7)	0.881
LDH median (IQR)	648 (518-1009.5)	747 (539.5-1012)	655 (446-1010)	0.24

Among 92 patients of AKI, 43 (46.7%) had stage I AKI, 25 (27.2%) had stage II AKI and 24 (26.1%) had Stage III AKI. Overall the patients who had AKI had a worse outcome than non-AKI group, as most of the patients required mechanical ventilation (70.7%, p<0.05), prolong hospital stay (median 7, IQR=5-12.7, p<0.05) and more complications occurred in patients who had AKI in which 61(66.3%, p<0.05) had septic shock, 31(33.7%, p<0.05) had myocarditis and patients with AKI had more chances of severe ARDS (78.3%, p<0.05), Table 2. Comparison of mortality among AKI and non-AKI showed no statistical significant difference but when compared the survival distribution among between both group, non-AKI group had a better survival distribution when compared to AKI group, with significant survival distribution (p<0.05) (Figure. 1). In critical COVID-19 patients, it is observed

that within median of 4 days AKI occurred in critical patients. Among 92 patients who developed AKI, 9 of the patient had gone through renal replacement therapy in which only 2 of the patients survived. Out of 92 patients, only 22 patients recovered from AKI.

Table 2: Outcomes of 232 hospitalized critical COVID-19 patients with and without acute kidney injury.

Parameter	All n=232	AKI n=92 (39.65%)	non-AKI n=140	p-value
Mechanical Ventilation	136 (58.6)	65 (70.7)	71 (50.7)	0.003
Outcomes				
Discharge	141 (60.8)	54 (58.7)	87 (62.1)	0.599
Mortality	91 (39.2)	38 (41.3)	53 (37.9)	
Hospital Stay median (SD)	6 (3-10)	7 (5-12.7)	6 (3-9.75)	
Inotropes	139 (59.9)	73 (79.3)	66(47.1)	0.0001
Complication	198 (85.3)	91 (98.9)	107 (76.4)	0.0001
ARDS (Severe)	157 (67.7)	72 (78.3)	85 (60.7)	0.005
Pneumonia	146 (62.9)	72 (78.3)	74 (52.9)	0.0001
NSTEMI	50 (21.6)	31 (33.7)	19 (13.6)	0.0001
Septic Shock	115 (49.6_	61 (66.3)	54 (38.6_	0.0001
Pulmonary Embolism	17 (7.3)	7 (7.6)	10 (7.1)	0.894
Pneumothorax	5 (2.2)	2 (2.2)	3 (2.1)	0.987
Subcutaneous emphysema	6 (2.6)	2 (2.2)	4 (2.9)	0.748
CRS	97 (41.8)	43 (46.7)	54 (38.6)	0.217
NIV	196 (84.48)	73 (79.35)	123 (87.86)	0.095
Mechanical Ventilation at admission	36 (15.51)	19 (20.65)	17 (12.14)	0.095
AKI recovery	x	22 (23.91)	x	x

AKI: Acute Kidney Injury, **NSTEMI**: non ST elevation MI, **CRS**: Cardiorenal syndrome, **NIV**: Non Invasive ventilation.

Discussion

In our study the frequency of AKI was 39.65% among COVID-19 patients who were critical at the time of admission. There was a significant difference between the survival distribution. Overall hospital mortality for critical ill patients with COVID-19 was 39.2%, compared to 41.3% in patients with AKI. Patients with AKI stage I 21(38.9%), stage II 16(29.6%) and stage III 17(31.5%) survived. 22 of the AKI patients recovered to their baseline renal function during hospitalization and 32 recovered after discharged. Patient who gone through renal replacement therapy, only 2 out of 9 patients survived. Most of the patient who had AKI had a long period of hospital stay and required mechanical ventilation as compared to non-AKI patients.

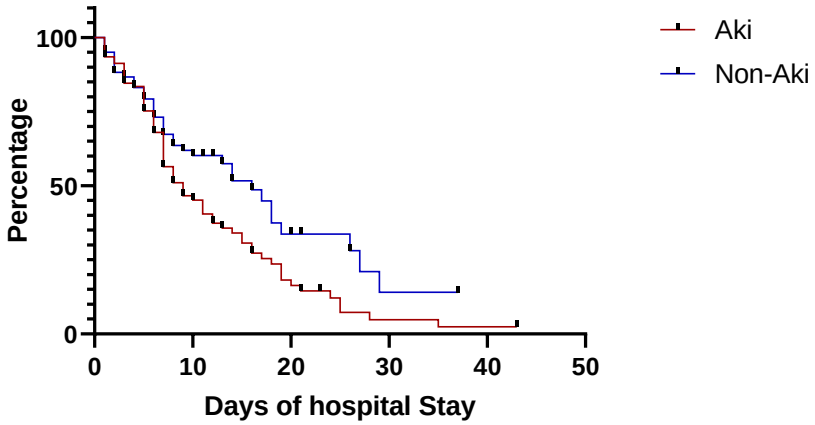

Fig 1: Kaplan–Meier survival estimates mortality of 232 critical COVID-19 patients between with AKI (red curve) and without AKI (blue curve).

AKI is an independent risk factor for increased mortality in critical patients but in our study mortality not found significant.[15,16] The reported incidence of AKI among critically ill COVID-19 patients in earlier cohorts from China was approximately 20%-30% and it is regarded as a marker of disease severity.[17-18] Although the incidence

of AKI in our study is higher than these reports, it is comparable to the other international studies.[19-20] We found that hypertension as a pre-existing condition significantly impacted mortality. A meta-analysis of 71 studies including 216,843 patients found a substantial link between hypertension and death.[21] In our study, there was no significant difference between DM, IHD and mortality between both groups. In most of the studies critical COVID-19 patients requiring mechanical ventilation reported incidence of AKI was as high as 75%, similarly in our study 70% of the patient required mechanical ventilation compared to non-AKI critically ill patients (70.7% vs 50.7%, $p<0.05$).[22-24] Patients in our population who had acute renal injury complication demonstrated severe outcomes and acute kidney injury was recognized as a predictor.[25,26]

The limitation of our study was that it was a retrospective study and and low sample size. The effects of COVID-19 are felt strongly throughout the world, but surprisingly, rich countries were more severely impacted than developing ones. The various epidemiological factors that were seen throughout the epidemic may be the cause. As we've already indicated, a wealthy economy, a high GDP, high levels of education, and a sense of hygiene did not offer any protection against the pandemic.[27,28] In our community, the epidemiology and demographics of COVID-19 are different. Therefore, mortality was not as high as other studies reported despite the presence of typical risk factors predicting a worse outcome.

Conclusion:

We concluded that AKI is more frequent in patients with critical Covid-19 and it occurs early in the disease course. It was not associated with higher mortality compared to the non AKI group.

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