Original Article

Acute Kidney Injury in Patients Hospitalized with COVID-19 in a Tertiary Care Hospital of Islamabad

Acute Kidney Injury with COVID-19

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ABSTRACT

Objective: This study is conducted to find out prevalence, risk factor and outcome of acute kidney injury (AKI) in patients admitted with COVID-19 in Pakistani population.

Study Design: Retrospective, Observational Study

Place and Duration of Study: This study was conducted at the PAF hospital Islamabad from April, 2020 to December, 2020.

Materials and Methods: It involved a review of data from electronic hospital records of patients who were aged18 years or older with laboratory-confirmed COVID-19. We describe the frequency of AKI and, AKI recovery, dialysis requirement and adjusted odds ratios (aORs) with mortality.

Results: Total 191 COVID-19 patients were enrolled, AKI occurred in total 38 (19.8%) patients and out of them 8(4.2%) patients had severe AKI and required dialysis. Regarding AKI staging, stage 1 was present among 18 (9.4%) patients, 06 (3.1%) had stage 2 and 14 (7.3%) had stage 3 AKI. The patients in ICU developed AKI more frequently stage 1 15.4%, stage 2, 7.7%, and stage 3 by 13.5% respectively. Patients with AKI were more likely to have admission in ICU, requirement for mechanical ventilation and requirement for inotropic support. Mortality was very high among patient with AKI 60.5% as compared to patient with no AKI 13.7%.

Conclusion: We found in our study that AKI is a relatively common complication observed among patients hospitalized with COVID-19. It is linked to poor outcome and high mortality.

Key Words: COVID-19, AKI, Dialysis

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INTRODUCTION

Coronavirus Disease 2019 (COVID-19) is caused by the severe acute respiratory coronavirus-2 (SARS CoV-2). It causes acute respiratory illness and first case was reported in Wuhan city of China in December 2019[1]. In January 2020 first case of COVID-19 was reported in Washington USA[2]. COVID-19 was declared as pandemic by World Health Organisation on March 11,2020[3]. After that sharp rise in cases was observed and then it became epicentre of the disease[2,4]. Similar to the observations earlier in China and Italy, a lot of patients with COVID-19 required hospitalization, intensive care admissions and respiratory support worldwide[5,6].

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Along with other clinical presentations, high number of patients presented with acute kidney injury (AKI). Early reports from Italy and China showed that prevalence of AKI had range of 0.5% to 29%[7-13]. US data from Seattle Hospital showed 19% prevalence AKI in ICU admitted patients[14]. Recent study from China utilizing autopsy data showed there was evidence of SARS-CoV-2 causing direct endothelial invasion and tubular damage to the kidneys[15].

Pakistan is one of those countries with high COVID-19 infection rate. But literature on AKI in COVID in Pakistani population is limited. Purpose of this study is to find out prevalence of AKI in patients admitted with COVOD-19, their risk factors and outcome.

MATERIALS AND METHODS

This retrospective cross sectional study was done April 1, 2020 to December 1, 2020 in Pakistan Air Force Hospital Islamabad after approval from institutional ethical review board. Patients were selected according to following criteria;

Inclusion Criteria: Admitted patients of either gender with age≥ 18 years who were confirmed COVID positive by PCR were included in this study.

Exclusion Criteria: We excluded patients with known ESRD prior to admission and patients who were hospitalized for 48 hours.

Data Collection: Data of selected patients was obtained from electronic data system of hospital. Demographics included age, sex, was recorded. Vital signs and laboratory values were obtained.

Definitions of Outcomes: The primary end point was AKI , which is defined as per Kidney Disease Improving Global Outcomes (KDIGO) criteria; a rise in the serum creatinine of 0.3 mg/dl over a 48-hour period or 50% increase in baseline creatinine[16]. AKI stages were defined according to KDIGO; stage 1 as an increase in serum creatinine of ≥0.3 mg/dl or increase to ≥1.5–1.9 times baseline serum creatinine, stage 2 as an increase to >2–2.9 times from baseline serum creatinine, and stage 3 as an increase to more than three times baseline serum creatinine or a peak serum creatinine ≥4.0 mg/dl or if the patient received dialysis during admission.

Other end point was in hospital mortality.

Statistical Analysis: As the data was not normally distributed (supplement table I) checked using Shapiro-Wilk test so, baseline characteristics were reported as medians and interquartile ranges (IQRs) for continuous variables. Categorical variables were reported as frequencies and percentages. We used M Whitney U /Kruskal-Wallis (non-parametric) tests for continuous variables and chi-squared test for categorical variables. For survival analysis, Kaplan-Meier survival curves was generated, and comparison was done using the log-rank test. Logistic regression models were used to estimate the adjusted odds ratio (aOR) for AKI in patients. SPSS version 23.0 was used for statistical analysis. P-value<0.05 was taken as statistically significant.

RESULTS

Incidence and severity of AKI

Total 191 COVID-19 patients were enrolled, AKI occurred in total 38 (19.8%) patients. Out of them 8(4.2%) patients had severe AKI and required dialysis. Regarding AKI staging, stage 1 was present among 18 (9.4%) patients, 06 (3.1%) had stage 2 and 14 (7.3%) had stage 3 AKI. The patients in ICU developed AKI more frequently stage 1 15.4%, stage 27.7%, and stage 3 by 13.5% respectively (table II).

AKI and Outcome

Patients with AKI were more likely to have admission in ICU, requirement for mechanical ventilation and inotropic support. Mortality was very high among patient with AKI 60.5% as compared to patient with no AKI 13.7% .The results of the Kaplan-Meier survival analysis stratified with AKI are shown in figure II. The curves indicate that the survival among AKI patients is lower than that of the no AKI patients and log-rank test statistics is also statistically significant (p=0.002).

There were 191 COVID-19 patients included in the study with median (IQR) age of 62 (41-83) years, the median (IQR) length of hospital stay was 8 (2-14) days, the median (IQR) creatinine on admission and discharge was 1.07 (0.69-1.45) mg/dL and 1.00 (0.59-1.41) mg/dL respectively, the median (IQR) eGFR on admission and discharge was 66 (31-101) mg/dL and 74 (36-112) mg/dL respectively.

Table No.1: Patient Characteristics of all and those with and without AKI

Patient Characteristics		All (n=191)	AKI (n=38)	No AKI (n=153)	p-value[a,b]
Age (years), median (IQR)		62 (41-83)	67.5 (47.75-87.25)	61.0 (38.5-83.5)	0.009*
Length of Stay (days), median (IQR)		8 (2-14)	8 (1.5-17.5)	7 (1.5-12.5)	0.070
Creatinine admission (mg/dL), median (IQR)		1.07 (0.69-1.45)	1.22 (0.18-2.26)	1.06 (0.71-1.41)	0.04*
Creatinine Discharge (mg/dL), median (IQR)		1.00 (0.59-1.41)	1.98 (0.85-4.81)	0.93 (0.61-1.25)	<0.001*
eGFR admission (mg/dL), median (IQR)		66 (31-101)	52 (2.75-106.75)	68 (37-99)	0.002*
eGFR Discharge (mg/dL), median (IQR)		74 (36-112)	28.5 (20.25-77.25)	80 (49-111)	<0.001*
Specific Gravity		1.02 (1.01-1.03)	1.02 (1.01-1.03)	1.02 (1.01-1.03)	0.024*
White Blood Cells/L, median (IQR)		4.0 (0-8)	6.0 (0-12)	4.0 (1-7)	<0.001*
ALC admission (mg/dL), median (IQR)		1120 (82-2158)	938.5 (307.25-2184.25)	1173 (166-2180)	0.280
ALC Discharge (mg/dL), median (IQR)		1260 (324-2196)	1000 (134-1866)	1320 (367-2273)	0.095
Sex	Male (%)	112 (58.6)	18 (47.4)	94 (61.4)	0.115
	Female (%)	79 (41.4)	20 (52.6)	59 (38.6)	
ICU Admission		52 (27.2)	19 (50.0)	33 (21.6)	<0.001*
Inotropes (%)		20 (10.5)	10 (26.3)	10 (6.5)	0.001*
ACEIsARBs (%)		37 (19.4)	08 (21.1)	29 (19.0)	0.770
Dialysis (%)		08 (4.2)	08 (21.0)	0 (0)	<0.001*
Hematuria (%)		10 (5.2)	09 (23.7)	01 (0.7)	<0.001*
Proteinuria (%)		27 (14.1)	17 (44.7)	10 (6.5)	<0.001*
Leukocyturia (%)		55 (28.8)	22 (57.9)	33 (21.6)	<0.001*
Death (%)		44 (23)	23 (60.5)	21 (13.7)	<0.001*

*=p-value <0.05; a=Mann Whitney U test for continuous variables; b=Chi-square test for categorical variables

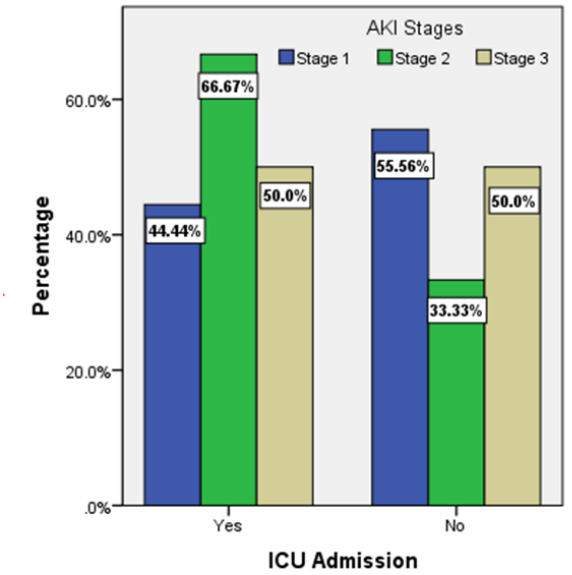

Figure No.1: Graphical Presentation of AKI stages with ICU admissions

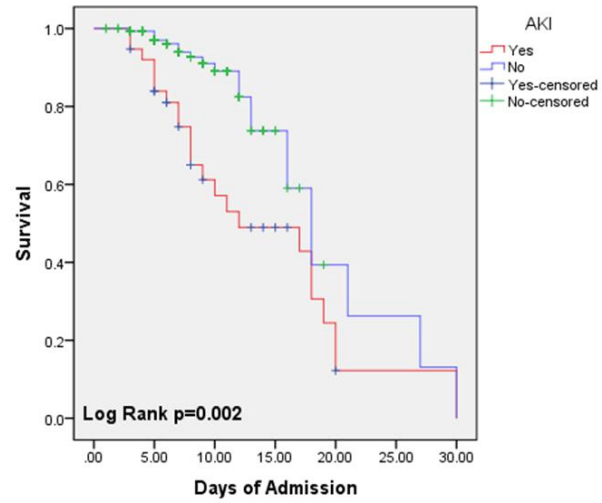

Figure No.2: Survival Probability of AKI cases as compared to no AKI Patients

Regarding protein presence, 1+ protein was found in 21 (11%), 2+ were present in 06 (3.1%). Regarding categorical variables, there were 112 (58.6%) males and remaining 79 (41.4%) were females; 134 (70.2%) were having comorbidities and amongst them major proportion 22 (11.5%) of the patients had hypertension, 17 (8.9%) had hypertension along with diabetes mellitus followed by 14 (7.3%) had hypertension, diabetes mellitus and ischemic heart disease and 11 (5.8%) had obstructive sleep apnea (OSA). There were 52 (27.2%) patients admitted in the ICU, 57 (29.8%) were admitted in HDU and remaining 82 (42.9%) patients were admitted in the ward. O_2 supplementation was invasive in 07 (3.7%), non-invasive among 123 (64.4%) and 61 (31.9%) did not need any supplementation and regarding outcome of patients, 44 (23%) had died.

Regarding gender, females (52.6%) had AKI and among males (47.4%), statistical significance of AKI vs no AKI was found with ICU admissions (p<0.001), inotropes (p=0.001), dialysis (p<0.001), hematuria (p<0.001), proteinuria (p<0.001), Leukocyturia (p<0.001) and death (p<0.001). (Table 1).

The ICU admissions were seen regarding AKI stages as 44.4% having stage 1, 66.67% having stage 2 and 50% having stage 3 were admitted in ICU (Figure I).

Regarding gender, 11.4% females had AKI stage 3, 10.1% had stage 1 AKI and 3.8% had stage 2 AKI and among males, 8.9% had AKI stage 1, 4.5% had stage 3 AKI and 2.7% had stage 2 AKI, statistical significance of various AKI stages was found with ICU admissions (p=0.004), inotropes (p<0.001), dialysis (p<0.001), hematuria (p<0.001), proteinuria (p<0.001), Leukocyturia (p<0.001) and death (p<0.001). (Table 2)

Table No.2: Patient Characteristics of Patients with no AKI and AKI Stages

Patient Characteristics	No AKI (n=153)	Stage 1 (n=18)	Stage 2 (n=6)	Stage 3 (n=14)	p-value[a, b]
Age (years), median (IQR)	61.0 (38.5-83.5)	67 (41.5-92.5)	62.5 (40.25-84.75)	70 (54.25-85.75)	0.048*
Length of Stay (days), median (IQR)	7 (1.5-12.5)	8 (0.75-15.25)	16 (0.75-30.75)	8 (0.75-16.75)	0.174
Creatinine admission (mg/dL), median (IQR)	1.06 (0.71-1.41)	1.04 (0.45-1.63)	0.91 (0.25-1.57)	3.62 (1.32-11.6)	0.002*
Creatinine Discharge (mg/dL), median (IQR)	0.93 (0.61-1.25)	1.45 (0.44-2.46)	1.73 (0.12-3.34)	4.8 (0.04-9.56)	<0.001*
eGFR admission (mg/dL), median (IQR)	68 (37-99)	60 (9.75-110.25)	67.5 (18.5-116.5)	15 (30-62.25)	0.002*
eGFR Discharge (mg/dL), median (IQR)	80 (49-111)	49.5 (1.75-97.25)	34 (17-85)	9.5 (1.75-17.25)	<0.001*
Specific Gravity	1.02 (1.01-1.03)	1.02 (1.01-1.03)	1.01 (1.0-1.03)	1.02 (1.01-1.03)	0.060
White Blood Cells/L, median (IQR)	4.0 (1-7)	5.0 (1-9)	9 (20.5-38.5)	6.0 (2-13)	<0.001*
ALC admission (mg/dL), median (IQR)	1173 (166-2180)	1502.5 (251.5-2753.5)	1166 (857.5-2189.5)	624.5 (67.5-1181.5)	0.029*
ALC Discharge (mg/dL), median (IQR)	1320 (367-2273)	1521.5 (594.25-2448.7	911 (502.5-1319.5	837.5 (283.25-1391.7	0.066

			5)	)	5)	
Sex (%)	Male	94 (83.9)	10 (8.9)	03 (2.7)	05 (4.5)	0.292
	Female	59 (74.7)	08 (10.1)	03 (3.8)	09 (11.4)	
ICU Admission		33 (63.5)	08 (15.4)	04 (7.7)	07 (13.5)	0.004*
Inotropes (%)		10 (50)	03 (15)	03 (15)	04 (20)	<0.001*
ACEIsARBs (%)		29 (78.4)	02 (5.4)	01 (2.7)	05 (13.5)	0.394
Dialysis (%)		01 (12.5)	00 (00)	00 (00)	07 (87.5)	<0.001*
Hematuria (%)		01 (10)	03 (30)	02 (20)	04 (40)	<0.001*
Proteinuria (%)		10 (37)	04 (14.8)	03 (11.1)	10 (37)	<0.001*
Leukocyturia (%)		33 (60)	09 (16.4)	04 (7.3)	09 (16.4)	<0.001*
Death (%)		21 (47.7)	10 (22.7)	05 (11.4)	08 (18.2)	<0.001*

Table No.3: Adjusted and Unadjusted OR for AKI presence in patients

Variables	Unadjusted OR	Adjusted OR	p-value
ICU Admission	3.64 (1.729-7.648)	0.46 (0.114-1.88)	0.282
Proteinuria	11.58 (4.68-28.63)	3.10 (0.832-11.54)	0.092
Leukocyturia	5.0 (2.36-10.59)	1.59 (0.562-4.50)	0.382
Hematuria	47.17 (5.75-386.69)	10.74 (1.03-111.91)	0.047*
Dialysis	34.32 (4.08-288.99)	18.17 (1.57-210.40)	0.020*
Inotropes	5.11 (1.94-13.41)	2.39 (0.62-9.24)	0.206
Outcome	9.64 (4.34-21.38)	6.98 (1.76-27.71)	0.006*

*p<0.05; OR=Odds Ratio

DISCUSSION

AKI is frequently observed in covid-19 and carries poor outcome. In our study AKI occurred in total 38 (19.8%) patients and out of them 8(4.2%) patients had severe AKI and required dialysis. Regarding AKI staging, stage 1 was present among 18 (9.4%) patients, 06 (3.1%) had stage 2 and 14 (7.3%) had stage 3 AKI. The patients in ICU developed AKI more frequently stage 1 15.4%, stage 2, 7.7%, and stage 3 by 13.5% respectively. It was higher from what was reported from Singapore which showed incidence of AKI was 8.1%, out of them , (68%) were at AKI stage 1 ,(16%), were at in stage 2 and (16%) stage 3. It further showed that AKI was associated with high mortality[17]. Data from Mexico showed prevalence more than our data and there prevalence of AKI was 58.6%. In-hospital mortality was significantly higher in patients those patients who had stage AKI stage 3 and AKI stage 2 (68.7%) or those who required dialysis compared with those with AKI stage 1[18]. These findings were similar to our study.

One large study from US done on 22,122 patients from different hospitals showed incidence of AKI among Covid-19 patients to 30.6%. and dialysis requiring AKI 8.5%[19]. These findings were very much comparable to our findings. Another study of 3993 patients from USA showed very high prevalence of AKI (46%) of which 19% required dialysis. The proportion of stages were as follows stage 1,2 and 3 AKI were were 39%, 19%, and 42%, respectively. 24% of COVID-19 patients were admitted to ICUand (76%) of them experienced AKI. In hospital mortality was 50% in patients with AKI as compared to 8% without AKI[20]. This study showed high prevalence of AKI among US population. One multicenter study of US population published of almost 6,000 patients showed almost similar results. AKI was found in (36.6%) of patients. The peak stages of AKI were stage 1 in 46.5%, stage 2 in 22.4% and stage 3 in 31.1%. Out of these patients, 14.3% required renal replacement therapy. AKI was primarily seen in patients on mechanical ventilation[21].

The variations in the prevalence of AKI in COVID-19 if different countries and regions may be partly explained by the fact that they these studies use different inclusion criteria. Second different ethnic, demographic groups and presence of comorbid also play a major role in the outcome of the disease. That may be the reason few studies have very high prevalence and few have very low prevalence of AKI.

CONCLUSION

We found in our study that AKI is a relatively common complication observed among patients hospitalized with COVID-19. It is linked to poor outcome and high mortality.

Author's Contribution:

Concept & Design of Study:	Muhammad Sajid Rafiq Abbasi
Drafting:	Maryam Masud, Khawar Sultan
Data Analysis:	Uzma Rehman, Sajid Nasim, Rukhsana Manzoor
Revisiting Critically:	Muhammad Sajid Rafiq Abbasi, Maryam Masud
Final Approval of version:	Muhammad Sajid Rafiq Abbasi

Conflict of Interest: The study has no conflict of interest to declare by any author.

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