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A Study of Acute Kidney Injury in COVID-19

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ABSTRACT

Background: *Severe acute respiratory syndrome coronavirus-2 responsible for the pandemic of COVID-19, has been one of the biggest challenges faced by mankind. The virus predominantly affects the respiratory system. But, the continued study of the disease since the beginning of this pandemic has evolved our understanding of COVID-19 which showed varied presentations with multisystem involvement, leading to acute myocardial infarction, stroke, pulmonary embolism due to its pro-thrombotic nature as well as acute kidney injury.* ***Objectives:*** *To determine the levels of urea and creatinine and to correlate acute kidney injury with the outcome of COVID-19 patients.* ***Materials and Methods:*** *The present study involves 200 patients who were suffering from COVID-19 admitted to a hospital in Bangalore from June 2020 to May 2021, fulfilling the inclusion criteria were analyzed and appropriate data were collected after obtaining informed consent.* ***Results:*** *The majority of the subjects belonged to the >50 y age group. Among the recruited subjects, 117 (58.5%) were male and 83 (41.5%) were female, 170 patients were discharged and 30 patients died. The mean urea levels were 37.82 ± 23.68 mg/dl and mean creatinine values were 0.95 ± 0.85 mg/dl. The Urea levels among the COVID-19 patients who were discharged was 35.98 ± 20.27 mg/dl and among those who died was 52.22 ± 38.01 mg/dl respectively and this was statistically significant (p=0.00). The creatinine levels were 0.88 ± 0.44 mg/dl and 1.32 ± 1.76 mg/dl among the COVID-19 patients who got discharged and expired respectively and this too was statistically significant (p=0.00).* ***Conclusion:*** *The patients suffering from COVID-19 who had developed AKI at the time of presentation had a poor prognosis as well as an increased risk of mortality.*

Keywords: Acute Kidney Injury (AKI), Creatinine, Outcome, Pandemic, Urea

INTRODUCTION

As of 13th November 2021, Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) has affected more than 2,510,000 individuals and caused 5,000,000 deaths worldwide [1]. Other than being a respiratory pathogen, the SARS-CoV-2 has a predilection for the kidneys. Various studies with their data accumulating over time showed that, although SARS-CoV-2 infection primarily causes acute respiratory illness, other organs may also be involved by the virus such as the kidney, and cause complications [2]. 5% to 15% of the COVID-19 cases had renal involvement and showed high mortality of 70%-90%, as recorded in SARS-CoV and MERS-CoV epidemics [3,4].

Kidney Disease Improving Global Outcomes (KDIGO) has defined AKI as an increase in the serum creatinine of 0.3 mg/dl over 48 hours or a 50% increase in baseline creatinine [5]. SARS-CoV-2 acts by binding itself to the ACE2 receptors. These receptors are found to be present greater in the kidney when compared to those in the lungs [6,7]. They are expressed on the brush border apical membrane of the proximal tubule and are also present in the podocytes [7]. However, the impact of AKI may differ from place to place depending on the health care systems, socio-economic status of the patients, education status of the patient, and geography of the locality. Several mechanisms are involved in the pathogenesis of AKI in COVID-19, including direct virus invasion, immune dysfunction, abnormal coagulation, sepsis, drugs, and underlying diseases [8].

Patients with underlying co-morbidities such as diabetes mellitus, hypertension and even Chronic Kidney Disease (CKD) have been found to have a poorer outcome in COVID-19. As such, it was found that CKD patients not

undergoing hemodialysis, exhibited a vulnerability to COVID-19 disease when compared to that of patients on Renal Replacement Therapy (RRT) [9]. The information regarding the development of AKI in patients with COVID-19 is still building up and not completely explored. Thus, in this study, we aim to determine the parameters of renal function i.e., urea and creatinine and to correlate their levels with the outcome of the COVID-19 patients.

Objectives

- To determine the levels of urea and creatinine in COVID-19 patients
- To co-relate acute kidney injury with the outcome of the COVID-19 patients

MATERIAL AND METHODS

This study has been conducted in a hospital in Bangalore, Karnataka, India after obtaining ethical clearance from the Institutional Ethics Committee (No:532/L/11/12/Ethics/ESICMC&PGIMSR/Estt.vol..IV).

The case files of the 200 patients admitted to the Department of General Medicine Triage and COVID Ward/ICU at ESIC MC and PGIMSR from August 2020 to July 2021, fulfilling the inclusion criteria were analyzed and appropriate data were collected after obtaining consent from these patients.

A case record form with a follow-up chart was used to record the duration of disease, history of treatment, and complications. COVID-19 infection was be diagnosed by either RT-PCR or Rapid Antigen Test (RAT) technique. Patients underwent biochemical investigations which included complete blood count, liver function test, renal function test, serum electrolytes, serology, CRP, LDH, D-dimer, ABG, and Chest X-ray. Co-morbid conditions like metabolic disorders, endocrine disorders, renal disorders, cardiac disorders, respiratory disorders were confirmed with past medical history.

Inclusion Criteria

Adult patients (aged 18 years and above) with either RT-PCR or Rapid Antigen Test positive for COVID-19 admitted to the Department of General Medicine Triage and COVID Ward/ICU at ESIC MC and PGIMSR from August 2020 to July 2021 and willing to give written informed consent for participation were included in the study.

Exclusion Criteria

The following were excluded from the study:

- Patients who were unwilling to participate in the study
- Patients aged less than 18 years
- Drug-induced AKI
- Known case of Chronic Kidney Disease (CKD)

The patients were monitored and the outcome was measured either as improved (clinical improvement, decreasing trend of inflammatory markers and discharge) or deteriorated (clinically worsening, increasing trend of inflammatory markers, and death of the patient). The patients were discharged as per the discharge policy of the Government of Karnataka after 10 days of symptom onset with no fever or symptoms for 3 consecutive days, maintained oxygen saturation above 95% for 4 consecutive days, showed improvement clinically with no breathlessness, showed a decreasing trend of inflammatory markers and repeat RT-PCR test turned negative.

Method of Statistical Analysis

Data were entered into a Microsoft Excel datasheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. The Chi-square test was used as a test of significance for qualitative data. Continuous data were represented as mean and standard deviation. Pearson correlation was done to find the correlation between two quantitative variables and qualitative variables respectively. A p-value of <0.05 was considered to be significant. Creatinine levels were noted and patients were diagnosed with AKI (the primary endpoint) as per the KDIGO guidelines [5].

RESULTS

As seen in Table 1, most of the cases enrolled for the study are above the age of 50 years i.e. 57%. Of the 200 included in the study, 117 are male and 83 are female.

Table 1 Demographic data

Descriptive Statistics N=200		
Predictors		**Mean ± SD**
Age (in years)	18-30	18 (9.05%)
	30-50	68 (34.0%)
	>50	114 (57.0%)
Gender	Male	Female
	117	83

170 of the 200 patients were discharged in hemodynamically stable condition whereas the remaining 30 succumbed to death as seen in Table 2.

Table 2 Demographic data

Predictors N=200		**Discharge N=170**		**Death N=30**	
Age (in years)	**18-30**	15 (8.82%)		3 (10.0%)	
	30-50	58 (34.12%)		10 (33.33%)	
	more than 50	97 (55.29%)		17 (53.33%)	
Sex		**Male**	**Female**	**Male**	**Female**
		99	71	18	12

Hypertension (HTN) was present in 40% of the patients who were discharged and 36.67% of the patients who died, whereas Diabetes Mellitus (DM) was present in 40.59% and 33.33% of patients who were discharged and died respectively. Thus, we see that HTN and DM are the major comorbidities in the study population as depicted in Table 3.

Table 3 Comorbidities

Comorbidities	**Discharge N=170**	**Death N=30**	**p-value**
Hypertension	68 (40.0%)	11 (36.67%)	0.89
Cardiac Disorder	13 (7.65%)	4 (13.33%)	0.3
Diabetes Mellitus	69 (40.59%)	10 (33.33%)	0.61
Thyroid Disorders	14 (8.24%)	2 (6.67%)	0.92

In the present study, the mean urea levels were 37.82 ± 23.68 mg/dl, and mean creatinine values were 0.95 ± 0.85 mg/dl as depicted in Table 4.

Table 4 Laboratory parameters

Descriptive Statistics N=200	
Predictors	**Mean ± SD**
TLC (× 10^3 cells/cu mm)	9.88 ± 5.25
N%	77.96 ± 15.17
L%	13.38 ± 10.21

NLR	11.71 ± 12.65
UREA (mg/dl)	37.82 ± 23.68
CREATININE (mg/dl)	0.95 ± 0.85
TLC: Total Leucocyte Count, N: Neutrophil, L: Lymphocyte, NLR: Neutrophil-Lymphocyte Ratio	

In Table 5, we see that the Urea levels among those who were discharged and died were 35.98 ± 20.27 mg/dl and 52.22 ± 38.01 mg/dl respectively and this was statistically significant with a p=0.00. The below table has the variables checked for the Significance level (p-value<0.05). Chi-square and fisher-exact were used for categorical variables and t-test was used for continuous variables.

Table 5 Comparing the laboratory parameters between the discharged cases and those who died

Variables	Discharge	Death	p-value
TLC (× 10^3 cells/cu mm)	9.65 ± 5.03	10.32 ± 3.64	0.26
N%	76.83 ± 16.01	84.66 ± 7.65	0.02
L%	14.03 ± 10.75	10.13 ± 5.89	0.04
NLR	11.68 ± 13.44	11.07 ± 6.57	0.41
UREA (mg/dl)	35.98 ± 20.27	52.22 ± 38.01	0.00
CREATININE (mg/dl)	0.88 ± 0.44	1.32 ± 1.76	0.00

The creatinine levels were 0.88 ± 0.44 mg/dl and 1.32 ± 1.76 mg/dl among the COVID-19 patients who got discharged and died respectively with a p-value of 0.00 as well and this too was statistically significant.

Of the 200 study participants, 59 (29.5%) developed AKI. As depicted in Table 6, we see that the percentage of the COVID-19 patients who developed AKI among those who were discharged is 25.88% when compared to those who died which is 50.0% and this difference is statistically significant with a p=0.01.

Table 6 Involvement of the kidney

Variables	Discharge N=170	Death N=30	p-value
Incidence of Acute Kidney Injury	44 (25.88%)	15 (50.0%)	0.01

DISCUSSION

Higher in-hospital mortality is an important complication of AKI in COVID-19 and AKI serves as an important prognostic marker of survival and disease severity [10,11]. The severity of AKI was also related to the mortality rate. Patients requiring higher intensive care support have a higher incidence of AKI with 13.3%-35.2% of patients with a critical disease requiring Kidney Replacement Therapy (KRT) [12-16].

Hypovolaemia, a risk factor for the development of AKI, is a common occurrence in early COVID-19 and hence it is critical to individualize the fluid management [17]. It was demonstrated in a Randomized Clinical Trial (RCT) that fluid and vasopressor resuscitation in patients with septic shock based on dynamic hemodynamic assessment may reduce the risk of AKI and respiratory failure [18].

In the present study, we see that 25.88% of the patients who were discharged developed AKI when compared to 50.0% among those who died and this difference is statistically significant with p=0.01. Lili Chan, et al. (January 2021) concluded that AKI was more common among the hospitalized COVID-19 patients and was associated with higher mortality. And only 30% of the patients with AKI survived with the recovery of renal function by the time of discharge [19].

In the present study Diabetes Mellitus (DM) was a major comorbid condition being present in 40.59% and 33.33% of

patients who were discharged and died respectively. Lim JH, et al. found that comorbid diabetes was more common in AKI patients with COVID-19 than in the non-AKI group. (46.7% *vs.* 27.7%, p=0.04) [20].

The management of AKI in COVID-19 is not significantly different from that of other causes of AKI. AKI can be prevented by strategic early fluid management in hypovolemia or fluid and vasopressor resuscitation in septic shock [21]. The goals of management in COVID-19 patients who already have AKI should be to improve patient outcomes and prevent worsening of kidney function. The management includes avoiding nephrotoxic drugs, optimization of hemodynamics to correct hypovolemia or hypervolemia, management of blood glucose, and standard care in multi-organ failure and shock [21]. The treatment modalities in COVID-19 encompass a variety of nephrotoxic medications and this puts them at a higher risk for AKI, making drug stewardship extremely important. It is important to provide optimal resources for RRT and to begin appropriate RRT modality with the right dose at the right time in those requiring RRT. As there are several mechanisms involved in the pathogenesis of AKI in patients with COVID-19, various treatment modalities targeting these mechanisms such as adoptive T-cell therapy, anticoagulation therapy, and receptor antibodies, need more attention and are an evolving area of research.

The longitudinal effects of COVID-19 associated AKI on kidney function remain largely unknown. James Nugent, et al. noted in their study that the estimated glomerular filtration rate declined by 11.3 mL/min/1.73 m^2 per year faster in patients with COVID-19-associated AKI compared with patients with AKI not associated with COVID-19 [22]. This emphasizes the need to monitor kidney function after hospital discharge among patients with COVID-19-associated AKI.

Limitations

The study is however not without any limitations. This study was conducted in a single center and the sample size was small.

CONCLUSION

The COVID-19 patients who had developed AKI at the time of presentation had a poor prognosis as well as an increased risk of mortality.

DECLARATIONS

Conflict of Interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

REFERENCES

[1] World Health Organization. "Coronavirus disease 2019 (COVID-19)." 2021.

[2] Pan, Xiu-Wu, et al. "Acute kidney injury during the COVID-19 outbreak." *Nephrology Dialysis Transplantation,* Vol. 35, No. 9, 2020, pp. 1635-41.

[3] Chu, Kwok Hong, et al. "Acute renal impairment in coronavirus-associated severe acute respiratory syndrome." *Kidney International,* Vol. 67, No. 2, 2005, pp. 698-705.

[4] Yeung, Man-Lung, et al. "MERS coronavirus induces apoptosis in kidney and lung by upregulating Smad7 and FGF2." *Nature Microbiology,* Vol. 1, No. 3, 2016, pp. 1-8.

[5] KDIGO. "Kidney disease: Improving global outcomes (KDIGO) acute kidney injury." https://kdigo.org/guidelines/acute-kidney-injury/

[6] Serfozo, Peter, et al. "Ang II (angiotensin II) conversion to angiotensin-(1-7) in the circulation is POP (prolyloligopeptidase)-dependent and ACE2 (Angiotensin-Converting Enzyme 2)-independent." *Hypertension,* Vol. 75, No. 1, 2020, pp. 173-82.

[7] Ye, Minghao, et al. "Glomerular localization and expression of angiotensin-converting enzyme 2 and angiotensin-converting enzyme: Implications for albuminuria in diabetes." *Journal of the American Society of Nephrology,* Vol.

17, No. 11, 2006, pp. 3067-75.

[8] Qian, Jingyi, et al. "Pathogenesis of acute kidney injury in coronavirus disease 2019." *Frontiers in Physiology,* Vol. 12, 2021, p. 84.

[9] Gibertoni, Dino, et al. "COVID-19 incidence and mortality in non-dialysis chronic kidney disease patients." *PLoS One,* Vol. 16, No. 7, 2021, p. e0254525.

[10] Cheng, Yichun, et al. "Kidney disease is associated with in-hospital death of patients with COVID-19." *Kidney International,* Vol. 97, No. 5, 2020, pp. 829-38.

[11] Zhou, Fei, et al. "Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: A retrospective cohort study." *The Lancet,* Vol. 395, No. 10229, 2020, pp. 1054-62.

[12] Argenziano, Michael G., et al. "Characterization and clinical course of 1000 patients with coronavirus disease 2019 in New York: Retrospective case series." *BMJ,* Vol. 369, 2020.

[13] Huang, Chaolin, et al. "Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China." *The Lancet,* Vol. 395, No. 10223, 2020, pp. 497-506.

[14] Pei, Guangchang, et al. "Renal involvement and early prognosis in patients with COVID-19 pneumonia." *Journal of the American Society of Nephrology,* Vol. 31, No. 6, 2020, pp. 1157-65.

[15] House, Napier. "ICNARC report on COVID-19 in critical care 01 May 2020." 2020.

[16] Goyal, Parag, et al. "Clinical characteristics of Covid-19 in New York city." *New England Journal of Medicine,* Vol. 382, No. 24, 2020, pp. 2372-74.

[17] Ostermann, Marlies, Kathleen Liu, and Kianoush Kashani. "Fluid management in acute kidney injury." *Chest,* Vol. 156, No. 3, 2019, pp. 594-603.

[18] Douglas, Ivor S., et al. "Fluid response evaluation in sepsis hypotension and shock: A randomized clinical trial." *Chest,* Vol. 158, No. 4, 2020, pp. 1431-45.

[19] Chan, Lili, et al. "AKI in hospitalized patients with COVID-19." *Journal of the American Society of Nephrology,* Vol. 32, No. 1, 2021, pp. 151-60.

[20] Lim, Jeong-Hoon, et al. "Fatal outcomes of COVID-19 in patients with severe acute kidney injury." *Journal of Clinical Medicine,* Vol. 9, No. 6, 2020, p. 1718.

[21] Nadim, Mitra K., et al. "COVID-19-associated acute kidney injury: Consensus report of the 25th Acute Disease Quality Initiative (ADQI) Workgroup." *Nature Reviews Nephrology,* Vol. 16, 2020, pp. 747-64.

[22] Nugent, James, et al. "Assessment of acute kidney injury and longitudinal kidney function after hospital discharge among patients with and without COVID-19." *JAMA Network Open,* Vol. 4, No. 3, 2021, p. e211095.