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Original Research Paper

General Medicine

STUDY OF RENAL COMPLICATIONS IN COVID 19 PATIENTS IN A TERTIARY SETUP

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ABSTRACT

BACKGROUND: Coronavirus disease 2019 (COVID-19) is a recent viral epidemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). With the increasing stage and severity of AKI, the hazard ratio of death of patients with COVID-19 also increases. Present study was aimed to study various renal complications noted in COVID 19 patients admitted at our dedicated tertiary COVID facility. **MATERIAL AND METHODS:** Present study was hospital based cross sectional observational study, conducted in patients of age ≥18yrs, with COVID RT-PCR positive (oropharyngeal or nasopharyngeal swab)or HRCT-CHEST suggestive of COVID 19 were considered for study. Acute kidney injury was identified according to the Kidney Disease: Improving Global Outcomes definition. **RESULTS:** In present study, out of 770 patients, 86 patients (11.17 %) had AKI diagnosed on admission or during treatment. We noted that significant number of patients developed AKI were > 60 years of age, male, had severe type of COVID 19 infection, with pre-existing morbidities such as diabetes, chronic kidney disease & congestive cardiac failure, difference was statistically significant when compared with non AKI group ($p<0.05$). Among AKI patients, only 20.93 % had AKI on admission, while 79.07 % developed in-hospital AKI. Various parameters were statistically significant for AKI group such as ICU admission (100 % vs 15.94), Hospital Mortality (34.88 % vs 3.8), Mechanical ventilation (82.56 % vs 14.77), Non-invasive ventilation (17.44 % vs 35.67), Vasopressor use (94.19 % vs 25), Vasopressor use >1 type (39.53 % vs 3.8), Diuretics use (77.91 % vs 26.46), Diuretics use >1 type (34.88 % vs 11.55), Corticosteroids (43.02 % vs 30.7), Pulmonary vasodilators (23.26 % vs 3.36).. On admission/first diagnosis of AKI stage 1, 2 & 3 was noted in 48.84 %, 18.6 % & 32.56 % patients respectively. Outcome was favourable in Stage 1 (88.1 %) > Stage 2 (62.5 %) > Stage 3 (32.14 %) while mortality was Stage 3 (67.86 %) > Stage 2 (37.5 %) > Stage 1 (11.9 %)**CONCLUSION:** Patients with age > 60 years, male gender, with preexisting comorbidities (type 2 diabetes mellitus, chronic kidney disease & congestive cardiac failure) are at an increased risk to developing AKI and mortality.

KEYWORDS : COVID 19 infection, preexisting diabetes mellitus, acute kidney injury, chronic kidney disease

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is a recent viral epidemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). COVID-19 has several clinical signs and symptoms such as dry cough, high fever, vomiting, myalgia, sputum production, headache, hemoptysis and diarrhea.[1]

Several clinical outcomes, such as sepsis, acute respiratory distress syndrome (ARDS), respiratory failure, coagulopathy, septic shock, AKI, and acute myocardial injury have been shown to be higher in nonsurvivor patients.[2] Epidemiological data revealed the severe illness rate of COVID-19 infection is as high as 25%, and even though the lungs are the main organs affected, the kidney is also one of the main organs affected in severe illness.[3]

Almost 1 in every 5 cases of COVID-19 admitted to the ICU was noted to require dialysis for severe AKI.[4] Additionally, the relative risk of in-hospital death increases by almost 11 times in COVID patients with AKI.[5] AKI is an independent risk factor for mortality. With the increasing stage and severity of AKI, the hazard ratio of death of patients with COVID-19 also increases.[6] Present study was aimed to study various renal complications noted in COVID 19 patients admitted at our dedicated tertiary COVID facility.

MATERIAL AND METHODS

Present study was hospital based cross sectional observational study, conducted at XXX medical college & hospital, XXX, India working as a dedicated tertiary COVID facility. Study duration was of 1 year (MENTION STUDY PERIOD). Study approval was taken from institutional ethical committee.

Patients of age ≥18yrs, with COVID RT-PCR positive (oropharyngeal or nasopharyngeal swab)or HRCT-CHEST suggestive of COVID 19 were considered for study. Patients taken discharge against medical advice, lost to follow up were excluded from study

Consent was obtained from all the patients. Patients who did not give the consent were excluded out from the study. The medical records of patients were analysed, history given by patients and epidemiological, clinical, laboratory, and radiological characteristics were noted from medical records. Information recorded included demographic data, medical history, exposure history, underlying co morbidities like diabetes, hypertension cardiovascular disease, and chronic kidney disease.

Acute kidney injury was identified according to the Kidney Disease: Improving Global Outcomes definition.[7] AKI was classified into 3 stages according to the KDIGO guidelines, considering the highest value of serum creatinine recorded during admission.[7] Proteinuria was considered if greater 0,2 g/L in the urine strip and hematuria was the presence of at least 2–5 red cells/field in the urine sediment. Renal

replacement therapy (RRT) techniques were categorized into conventional hemodialysis and continuous veno-venous hemodiafiltration.

Patients diagnosed of AKI in the emergency room were classified as "AKI on admission", and "in-hospital AKI" those developed AKI during the hospital stay.

Data was collected and compiled using Microsoft Excel, analysed using SPSS 23.0 version. Frequency, percentage, means and standard deviations (SD) was calculated for the continuous variables, while ratios and proportions were calculated for the categorical variables. Difference of proportions between qualitative variables were tested using chi- square test or Fisher exact test as applicable. P value less than 0.05 was considered as statistically significant.

RESULTS

In present study, out of 770 patients, 86 patients (11.17 %) had AKI diagnosed on admission or during treatment. We noted that significant number of patients developed AKI were > 60 years of age, male, had severe type of COVID 19 infection, with pre-existing morbidities such as diabetes, chronic kidney disease & congestive cardiac failure, difference was statistically significant when compared with non AKI group ($p<0.05$).

Among AKI patients, only 20.93 % had AKI on admission, while 79.07 % developed in-hospital AKI. Mean days of hospitalization when AKI occurred were 4.3 ± 3.8 days.

Table 1- General Characteristics

Variable	Patients with AKI (N=86)		Patients without AKI (N=684)		P value
	N	%	N	%	
Mean age (in years)	60.11 ± 13.2		56.02 ± 14.3		0.018
Sex					0.034
Male	61	70.93	388	56.73	
Female	25	29.07	296	43.27	
Disease severity					< 0.001
Asymptomatic + mild	2	2.33	459	67.11	
Moderate	4	4.65	184	26.9	
Severe	80	93.02	41	5.99	
AKI					
AKI on admission	18	20.93			
in-hospital AKI	68	79.07			
Day of hospitalization when AKI occurred (days)	4.3 ± 3.8				
Pre-existing morbidity					
Diabetes	41	47.67	133	19.44	< 0.001
Chronic kidney disease	9	10.47	22	3.22	< 0.001
Congestive cardiac failure	7	8.14	26	3.8	< 0.001
Hypertension	39	45.35	251	36.7	0.064
Ischemic heart disease	8	9.3	88	12.87	0.084

We compared various parameters between patients with & without AKI & noted statistically significant parameters for AKI group such as ICU admission (100 % vs 15.94), Hospital Mortality (34.88 % vs 3.8), Mechanical ventilation (82.56 % vs 14.77), Non-invasive ventilation (17.44 % vs 35.67), Vasopressor use (94.19 % vs 25), Vasopressor use >1 type (39.53 % vs 3.8), Diuretics use (77.91 % vs 26.46), Diuretics use >1 type (34.88 % vs 11.55), Corticosteroids (43.02 % vs 30.7), Pulmonary vasodilators (23.26 % vs 3.36). Renal support treatment such as Continuous renal replacement therapy & Extracorporeal membrane oxygenation was used in 15.12 % & 6.98 % patients with AKI.

Table 2- Treatment Distribution

Variable	Patients with AKI (N=86)		Patients without AKI (N=684)		P value
	N	%	N	%	
ICU admission	86	100	109	15.94	< 0.001
Hospital Mortality	30	34.88	26	3.8	< 0.001
Treatment in hospital		0		0	
Mechanical ventilation,	71	82.56	101	14.77	< 0.001
Non-invasive ventilation	15	17.44	244	35.67	< 0.001
Vasopressor use	81	94.19	171	25	< 0.001
Vasopressor use >1 type	34	39.53	26	3.8	< 0.001
Diuretics use	67	77.91	181	26.46	< 0.001
Diuretics use >1 type	30	34.88	79	11.55	< 0.001
Corticosteroids	37	43.02	210	30.7	< 0.001
Pulmonary vasodilators	20	23.26	23	3.36	< 0.001
Renal support treatment					
Continuous renal replacement therapy	13	15.12			
Extracorporeal membrane oxygenation	6	6.98			

In present study, various complications such as electrolyte disturbances, anemia, acute respiratory distress syndrome, acidosis, coagulation disorders, respiratory failure, secondary infection, hypoproteinemia, sepsis, shock, septic shock, acute heart failure & acute cardiac injury were significantly more in AKI group. ($p<0.001$)

Table 3- Complications

Complications	Patients with AKI (N=86)		Patients without AKI (N=684)		P value
	N	%	N	%	
Electrolyte disturbances	78	90.7	243	35.53	< 0.001
Anemia	71	82.56	101	14.77	< 0.001
Acute respiratory distress syndrome	57	66.28	55	8.04	< 0.001
Acidosis	53	61.63	126	18.42	< 0.001
Coagulation disorders	42	48.84	65	9.5	< 0.001
Respiratory failure	39	45.35	43	6.29	< 0.001
Secondary infection	34	39.53	78	11.4	< 0.001
Hypoproteinemia	34	39.53	104	15.2	< 0.001
Sepsis	29	33.72	59	8.63	< 0.001
Shock	25	29.07	45	6.58	< 0.001
Septic shock	21	24.42	44	6.43	< 0.001
Acute heart failure	8	9.3	11	1.61	< 0.001
Acute cardiac injury	6	6.98	2	0.29	< 0.001

On admission/first diagnosis of AKI stage 1, 2 & 3 was noted in 48.84 %, 18.6 % & 32.56 % patients respectively. Outcome was favourable in Stage 1 (88.1 %) > Stage 2 (62.5 %) > Stage 3 (32.14 %) while mortality was Stage 3 (67.86 %) > Stage 2 (37.5

%) > Stage 1 (11.9 %)

Table 4 Outcome

AKI	Total (%)	AKI recovery	In-hospital mortality
Stage 1	42 (48.84 %)	37 (88.1 %)	5 (11.9 %)
Stage 2	16 (18.6 %)	10 (62.5 %)	6 (37.5 %)
Stage 3	28 (32.56 %)	9 (32.14 %)	19 (67.86 %)
Total	86	56	30

DISCUSSION

The possible mechanisms interacted in renal disturbances by COVID-19, consisted of dehydration (may be due to fever or decreased intake of fluids), cytokine storm syndrome, rhabdomyolysis, hypoxia, etc.[8] Additionally, direct virus invasion to the renal tubular cells and interstitium or glomeruli is possible, since the direct cytopathic effect of virus on various renal cells have been detected previously.[9,10]

Dehydration has various consequences on the kidney, directing to reduction of glomerular filtration rate and acute kidney injury. If volume depletion is not severe, it is reversible with hydration, however if ischemia persists like shock, acute tubular necrosis may happen.

In a review of literature of 16 articles related to AKI and COVID-19, Nerli RB et al.,[11] noted that 49.7% of the admitted patients had comorbidities. 30 patients (2%) out of 1430 patients had chronic kidney disease before admission. A total of 139 patients (9.36%) developed AKI during hospital admission. A total of 51 patients (52%) with AKI died during the course of treatment. Patients with preexisting comorbidities, namely hypertension, type 2 diabetes mellitus, and cardiac and pulmonary disease (chronic obstructive pulmonary disease), are at an increased risk to developing AKI. Patients with deranged serum creatinine and kidney disease are at an increased of needing renal replacement therapy as well as death.[11]

In a study from the United States of America of a cohort of over 5000 patients 36.6% of patients developed acute kidney injury (AKI) according to KDIGO criteria. Furthermore, AKI may be associated with an ongoing requirement for renal support and prolonged hospitalization thereby imposing a significant health and resource burden.[12]

Lowe, R et al.,[13] studied 81 patients admitted adult intensive care unit suffering from SARS-CoV-2 infection, all patients had acute hypoxic respiratory failure and needed either noninvasive or invasive mechanical ventilatory support. 44% had evidence of AKI (Stage I-33%, Stage II-22%, Renal Replacement Therapy (RRT)-44%). All patients with AKI stage III had RRT. Age, diabetes mellitus, immunosuppression, lymphopenia, high D-Dimer levels, increased APACHE II and SOFA scores, mechanical ventilation and use of inotropic or vasopressor support were significantly associated with AKI. The peak AKI was at day 4 and mean duration of RRT was 9 days. The mortality was 25% for the AKI group compared to 7% in those without AKI. Among those received RRT and survived their illness, the renal function recovery is complete and back to baseline in 92% of patients.

Sharma PK et al.,[14] studied renal profile of COVID-19 infected patients. 64 (21.3%) patients had deranged renal function tests with abnormal blood urea nitrogen and serum creatinine. Overall, 56 patients (18.6%) without chronic kidney disease showed mild increase of BUN or serum creatinine. 35 patients (11.6%) had high blood urea nitrogen and 18 patients (6%) had raised creatinine.

Sampathkumar et al.,[15] identified risk factors for COVID-19 Associated AKI, unique to Indian population such as hypotension, hypoxemia, extensive pulmonary involvement, ventilatory support, male sex, hyponatremia, high neutrophil to lymphocyte ratio, and lower absolute monocyte count, higher indices of inflammatory markers (interleukin-6, C-reactive protein) and coagulopathy (d-Dimer), and low serum albumin, some of which have also been reported in other studies.

In study by Paek JH et al.,[16] out of 704 patients, 28 (4.0%) developed AKI. Of the 28 patients with AKI, 15 (53.6%) were found to have AKI stage 1, 3 (10.7%) had AKI stage 2, and 10 (35.7%) had AKI stage 3. Among these patients, 12 (42.9%) recovered from AKI. In the patients with AKI, the rates of admission to intensive care unit (ICU), administration of mechanical ventilator (MV), and in-hospital mortality were significantly higher than in patients without AKI. Multivariable analysis revealed that old age, high neutrophil-to-lymphocyte ratio, elevated creatinine kinase, and severe AKI were independent risk factors for in-hospital mortality. Severe AKI was associated with in-hospital death.

Blanca Tarragóna et al.,[17] analyzed 41 patients with a mean age of 66.8 ± 2.1 years, 90.2% males, and with a history of chronic kidney disease (CKD) in 36.6%. 56.1% of patients presented with severe pneumonia or acute respiratory distress syndrome (ARDS), and 31.7% required intensive care. AKI etiology was prerenal in 61%, acute tubular necrosis in the context of sepsis in 24.4%, glomerular in 7.3% and tubular toxicity in 7.3% of the cases. Proteinuria in 88.9% and hematuria in 79.4% of patients. 48.8% of patients required renal replacement therapy (RRT). Median length of stay was 12 days and 22% of the population died. Patients who developed AKI during hospital stay presented with higher C-reactive protein, Lactate dehydrogenase-LDH and d-dimer values, more severe pulmonary damage, more frequent intensive care unit-ICU admission, treatment with lopinavir/ritonavir and biological drugs and RRT requirement.

The increased incidence of AKI in COVID-19 patients could be due to the synergistic effect of all of these factors and also by state of dehydration, toxic tubular damage, and drug-induced nephrotoxicity.[18] Healthcare providers should be aware of that antiviral drugs like remdesivir and lopinavir/ritonavir could cause drug-drug interactions with calcineurin inhibitors. It is therefore recommended to use these drugs with extreme caution.[19] The current management of COVID-19 associated AKI includes supportive treatment, avoiding nephrotoxic drugs, and early start, when possible, of renal replacement therapy.[20]

CONCLUSION

Patients with age > 60 years, male gender, with preexisting comorbidities (type 2 diabetes mellitus, Chronic kidney disease & Congestive cardiac failure) are at an increased risk to developing AKI and mortality. COVID 19 infection with above high risks are prone for AKI & require expert treatment at a tertiary center.

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REFERENCES

1. Rothan HA, Byrareddy SN. The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak. J Autoimmun. 2020;109:102433.
2. E. Murillo-Zamora, X. Trujillo, M. Huerta, M. Ríos-Silva, O. Mendoza-Cano, Male gender and kidney illness are associated with an increased risk of severe laboratory-confirmed coronavirus disease, BMC Infect. Dis. 20 (1) (2020) 674.
3. Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, Wu Y, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. Lancet Respir Med. 2020;8(5):475-481.
4. Silver SA, Beaubien-Souligny W, Shah PS et al. The Prevalence of Acute Kidney Injury in Patients Hospitalized with COVID-19 Infection: A Systematic Review and Meta-analysis. Kidney Med 2021; 3:83-98.e1.
5. Lin L, Wang X, Ren J, et al. Risk factors and prognosis for COVID-19-induced acute kidney injury: a meta-analysis. BMJ Open 2020; 10:e042573.

6. Prasad N, Agrawal SK, On behalf of COVID-19 Working Group of Indian Society of Nephrology. COVID 19 and acute kidney injury. Indian J Nephrol 2020; 30:161-5.
7. Khwaja A. KDIGO clinical practice guidelines for acute kidney injury. Nephron - Clin Pract. 2012;120:c179–84.
8. Valizadeh R, Baradaran A, Mirzazadeh A, Bhaskar LVKS. Coronavirus-nephropathy; renal involvement in COVID-19. J Renal Inj Prev. 2020; 9(2): e18.
9. Li W, Moore MJ, Vasilieva N, Sui J, Wong SK, Berne MA, et al. Angiotensin-converting enzyme 2 is a functional receptor for the SARS coronavirus. Nature. 2003;426:450-4.
10. Hamming I, Timens W, Bulthuis ML, Lely AT, Navis G, van Goor H. Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus. A first step in understanding SARS pathogenesis. J Pathol. 2004;203:631-7.
11. Nerli RB, Sharma M, Ghagane SC, Gupta P, Patil SD, Shubhashree M, et al. Acute kidney injury in patients with COVID-19. Indian J Health Sci Biomed Res 2020;13:64-7.
12. 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
13. Lowe, R., Ferrari, M., Nasim-Mohi, M. et al. Clinical characteristics and outcome of critically ill COVID-19 patients with acute kidney injury: a single centre cohort study. BMC Nephrol 22, 92 (2021).
14. Sharma PK, Aggarwal V, Sapariya N, Baweja S, Nagori R, Chabbra MK. Renal profile of COVID-19 infected patients admitted in a tertiary care hospital in Western Rajasthan. Int Surg J 2020;7:2332-6.
15. Sampathkumar, Hanumaiah H, Rajiv A, et al. Incidence, Risk Factors and Outcome of COVID-19 Associated AKI- A Study from South India. J Assoc Physicians India 2021; 69:28-31.
16. Paek JH, Kim Y, Park WY, Jin K, Hyun M, Lee JY, et al. (2020) Severe acute kidney injury in COVID-19 patients is associated with in-hospital mortality. PLoS ONE 15(12): e0243528
17. Tarragón B, Valdenebro M, Serrano ML, Maroto A, Llópez-Carratalá MR, Ramos A, Rubio E, Huerta A, Marques M, Portolés J. Acute kidney failure in patients admitted due to COVID-19. Nefrologia (Engl Ed). 2021 Jan-Feb; 41(1): 34- 40.
18. Fortarezza F, Pezzuto F. COVID-19 nephropathy: what could pathologist say? J Nephropathol. 2020;9(4):e32.
19. Michaels MG, La Hoz RM, Danziger-Isakov L, Blumberg EA, Kumar D, Green M, Pruett TL, et al. Coronavirus disease 2019: Implications of emerging infections for transplantation. Am J Transplant. 2020.
20. 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) 97:829–38.