https://doi.org/10.37939/jrmc.v27i4.2304

Incidence Of Acute Kidney Injury in Mild, Moderate And Severe Cases Of Coronavirus Disease

Mahvesh Mahmud[1], Ashok Kumar[2], Khurram Baqai[3]

Abstract

Objective: The purpose of this research was to determine the incidence of Acute Kidney Injury (AKI) in COVID-19-affected patients

Methods: This retrospective cohort study was conducted at Ziauddin Hospital Clifton Campus from June to December 2020. Adult patients with AKI or acute-on-chronic kidney disease (ACKD) were included in a retrospective study. Patients infected with SARS-CoV2 and renal involvement were directed towards the ICU/Nephrology departments which have the expertise to perform laboratory analysis, radiography and institution of treatment. Supplemental oxygen use was documented. The research also assessed information about therapy (antivirals, immunomodulators, RRT) and results (renal function recovery or death).

Results: After excluding patients with obstructive AKI, a total of 180 (mean age 50.1 years) of 104 males and 76 females were included in the research. 120 patients were found to have prerenal, and 60 had intrinsic AKI with significant differences between mild, moderate, and severe cases (p=0.004). Acute kidney injury (AKI) survivors had a complete recovery rate of 70%, a partial recovery rate of 22%, and a hemodialysis dependency rate of 8%.

Conclusion: Patients with severe COVID-19 infection often develop more severe AKI, and those in the severe or critical stages often exhibit proteinuria and dipstick hematuria. Long-term follow-up for COVID-19 patients should be done to evaluate its influence on renal outcome, and larger samples are required to elucidate the association between COVID-19 and renal damage.

Keywords: Coronavirus Disease, Renal Replacement Therapy, proteinuria, dipstick hematuria

[1] Associate Professor, Watim Medical College, Rawalpindi; [2] Professor, Ziauddin University, Karachi;[3] Assistant Professor, Ziauddin University, Karachi.
Correspondence: Dr. Mahvesh Mahmud, Associate Professor, Watim Medical College, Rawalpindi. **Email:** mahveshmahmud@yahoo.com.
Cite this Article: Mahmud M, Kumar A, Baqai K. Incidence Of Acute Kidney Injury In Mild, Moderate And Severe Cases Of Coronavirus Disease. JRMC. 2023 Dec. 30];27(4): 601 – 607. https://doi.org/10.37939/jrmc.v27i4.2304.
Received May 23, 2023; accepted October 27, 2023; published online December 30, 2023

1. Introduction

The pandemic of COVID-19 is a major concern on many fronts, with far-reaching negative effects on healthcare, industry, and the economy.[1] The severe acute respiratory syndrome coronavirus 2 (SARS CoV-2) was first identified in December 2019 as a cluster of pneumonia cases of unknown origin in Wuhan, China, and has since rapidly spread worldwide, prompting the World Health Organization to declare the coronavirus disease outbreak a public health emergency of international concern.[2] Asymptomatic infection, moderate upper respiratory sickness, and severe viral pneumonia leading to respiratory failure and death all seem part of the clinical spectrum of SARS-CoV-2 infection.[3] The reported incidence of COVID-19-associated acute kidney injury (AKI) varies, ranging from 2% to 23% across studies.[4,5] However, major meta-analyses reveal an incidence between 10% and 15% of all COVID-19 patients and higher in subgroups of elderly and ICU-admitted patients. Diffuse alveolar destruction is the primary symptom of COVID-19 in the heart, although the virus has also been linked to other organs like the kidney. Recent studies show that up to 37.5% of fatal COVID-19 cases had signs of acute kidney damage.[6] This shows that the kidney is a susceptible organ in COVID-19 patients. The pandemic spread of SARS-CoV2 has altered the daily routines of both patients and healthcare providers. Despite being primarily a respiratory condition, it has been reported that in extreme situations, it may affect other organs and systems.[8] Among them, COVID-19-associated acute kidney damage is particularly interesting because of the high mortality rate related to AKI and the scarcity of data on its intermediate and long-term consequences.[9]

The literature is also divided on the effects of the link between AKI and SARS-CoV-2 infection, with some studies documenting no adverse effect on patient evolution and others showing an increase in mortality with rising creatinine, Kidney Disease Improving Global Outcomes (KDIGO) stage, and need for renal replacement therapy (RRT).[5,10-11] Patients with COVID-19-associated AKI have an increased risk of developing chronic kidney disease (CKD).[12] The researchers found that 16% of AKI patients developed CKD within 90 days of study enrollment.[13] The annual

decrease in eGFR relative to controls not infected with COVID-19 was 3.3, 5.2, and 7.7 mL/min/1.73 m^2 in non-hospitalized patients, hospitalized patients, and intensive care patients at least 30 days after COVID-19 infection.[14] Patients with AKI caused by COVID-19 experienced a corresponding decrease in eGFR.[15] Hypoxemic respiratory failure requiring mechanical ventilation or hypotension needing vasopressor usage are major reasons for admitting patients with severe COVID-19 to the intensive care unit.[16] COVID-19-associated AKI may be caused by dehydration, sepsis-induced hypotension, immunologic damage, or microvascular illness. Patients with COVID-19 may suffer acute kidney damage, ranging from prerenal azotemia to acute tubular necrosis due to inadequate oral intake, sepsis, and cytokine storm.[3] In Pakistan there is a lack of data that could help in the diagnosis of those patients who are COVID positive suffering from acute kidney injury. The purpose of this research was to determine the prevalence of AKI in COVID-19-affected patients and demonstrate a correlation between inflammatory markers and COVID-19 severity.

2. Materials & Methods

The Ziauddin Hospital Clifton campus conducted this retrospective research between June – December 2020. Patients hospitalized in the dedicated ICU for COVID-19 patients and the associated nephrology department were included in the study. Those patients were included in the study who met the inclusion and exclusion criteria. One hundred and eighty patients were chosen to participate in the study. All patients were divided into three groups Group I: mild cases, Group II: moderate cases, and Group III: severe cases. Sample size calculation was done to compare proportions where the confidence interval was equal to 95 % with a 5% significance level, taking 80% power of the study. The 180 total sample size was calculated. We divided an equal number of patients into three groups.

Every participant in the research gave informed written permission. The patients included were aged 40-70 years, both male and female. Study participants who were suffering from any severe co-morbid conditions such as liver disease, thyroid disorder, renal disease, and heart failure, were excluded from the study.

Adult patients with COVID-19 infection and AKI or acute-on-chronic kidney disease (ACKD) who were admitted to the Ziauddin Hospital between Jun-Dec 2020 were included in this retrospective study. Patients infected with SARS-CoV2 and renal involvement were directed towards a special unit which was the only COVID-dedicated area of the hospital in the vicinity, with an emergency nephrology department and the ability to perform all laboratory analysis and other requirements for the diagnosis and management required. Laboratory results related to SARS-CoV2 infection included complete blood count, erythrocyte sedimentation rate, C-reactive protein, serum interleukin 6, procalcitonin, and ferritin results were collected, along with demographic information (age, sex, comorbidities). A radiologist performed chest CT scans to see how much of the pulmonary parenchyma was impacted by COVID-19 pneumonia. Supplemental oxygen use was documented. The research also assessed information about therapy (antivirals, immunomodulators, RRT) and results (renal function recovery or death). We examined associations between AKI severity and timing, and several factors linked to COVID-19 severity to assess the effect of the AKI with COVID-19 association on patient outcome according to guidelines.[17] The difference between prerenal and intrinsic AKI was gleaned from the charts according to the nephrologists' assessment based on clinical and laboratory data. Those patients whose renal function recovered to baseline within 48 hours with hydration were classified as having prerenal AKI.

SPSS version 25 was used for the data analysis. (An application for social science statistics) mean and standard deviation were used to represent continuous data, whereas percentages were used to represent dichotomous data. The Chi-square (X^2) test, Fisher's exact test, and the analysis of variance (ANOVA) were employed to compare continuous variables, while the unpaired t-test was used for categorical data. $P = 0.05$ and a 95% confidence interval were used to determine if the findings were statistically significant. Logistic regression analysis, the Spearman rank correlation coefficient test, and the Pearson correlation coefficient test were utilized where suitable.

3. Results

After excluding patients with obstructive AKI, a total of 180 (mean age 50.1 years) of 104 males and 76 females were included in the research. 120 patients had prerenal and 60 had intrinsic AKI with significant differences

between mild, moderate, and severe cases (p=0.004). The most common comorbid were diabetes mellitus (12.2%) in severe, hypertension (11.1%), coronary artery disease (9.4%) in mild COVID. 62 patients required renal replacement therapy (RRT). The majority of patients suffered from fever and cough. Five patients died in the severe cases. The other demographic details are listed in Table 1.

Acute kidney injury (AKI) survivors had a complete recovery rate of 70%, a partial recovery rate of 22%, and a hemodialysis dependency rate of 8%. Patients in the severe COVID group required renal replacement therapy (RRT) more frequently than the mild group with the differences being significant. Table 2 shows the variables used for categorizing patients as mild, moderate and severe COVID infections. Figures 1 and 2 show the percentage of dipstick hematuria and proteinuria amongst mild, moderate and severe cases of COVID-19 associated with AKI, with significant 3+ proteinuria seen in patients with severe COVID.

Figure 1 and Figure 2 represent the percentage of proteinuria and dipstick hematuria.

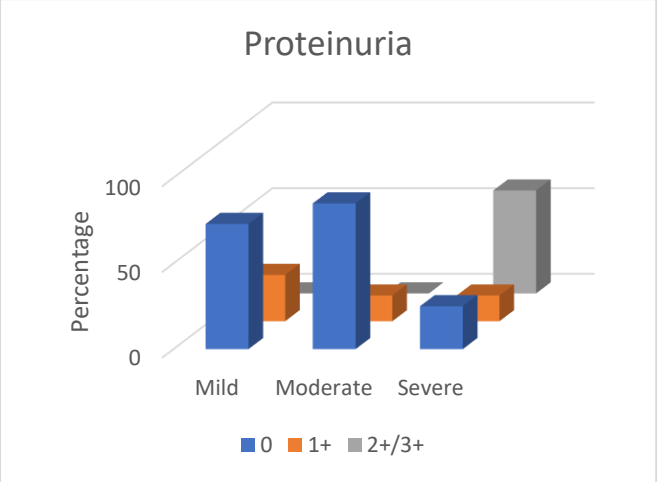

Figure 1: Percentage of Proteinuria

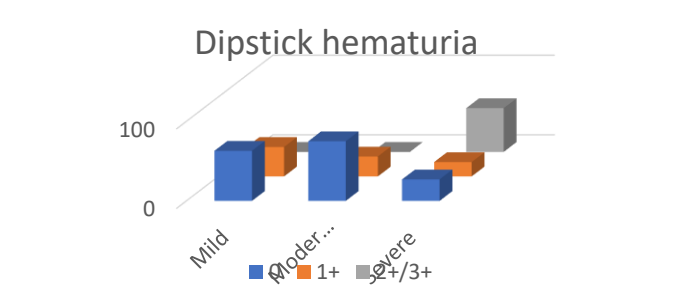

Figure 2: Percentage of Dipstick Hematuria

Table 1: Demographics details of mild, moderate, and severe COVID cases

Variables		Mild n (%)	Moderate n (%)	Severe n (%)	P value
Sex	Male	34 (18.9)	31 (17.2)	39 (21.7)	0.328
	Female	26 (14.4)	29 (16.1)	21 (11.7)	
AKI	Prerenal	54 (30)	36 (20)	30 (16.7)	0.004
	Intrinsic	20 (11.1)	15 (8.3)	25 (13.9)	
Fever	Yes	41 (22.8)	31 (17.2)	47(26.1)	0.008
	No	19 (10.6)	29 (16.1)	13 (7.2)	
Cough	Yes	36 (20)	26 (14.4)	49 (27.2)	<0.001
	No	24 (13.3)	34 (18.9)	11 (6.1)	
Symptoms	Diabetes mellitus, %	3 (1.7)	18 (10)	22 (12.2)	<0.001
	Hypertension %	20 (11.1)	10 (5.6)	8 (4.4)	
	Coronary heart disease, %	17 (9.4)	11 (6.1)	3 (1.7)	
	Chronic kidney disease (eGFR <60 mL/min/1.73m2), %	9 (5)	8 (4.4)	9 (5)	
	Continuous venovenous hemofiltration	6 (3.3)	9 (5)	13 (7.2)	
	History of tuberculosis	5 (2.8)	4 (2.2)	5 (2.8)	
Renal replacement therapy	Required	16 (8.9)	22 (12.2)	39 (21.7)	<0.001
Death	Yes	2 (1.1)	4 (2.2)	5 (2.8)	0.51

Table 2: Clinical results of mild, moderate, and severe cases of COVID-19

Variables		Mean	Std. Deviation	P-Value
Age (years)	Mild	51.8	11.7	0.253
	Moderate	48.3	11.4	
	Severe	50.1	11.7	
BMI (kg/m2)	Mild	22.0	3.3	<0.001
	Moderate	21.8	6.2	
	Severe	18.2	4.6	
	Moderate	81.5	0.3	
	Severe	81.5	0.3	
SaO2 (%)	Mild	96.5	0.3	<0.001
	Moderate	95.5	0.3	
	Severe	92.4	0.4	
Ferritin (ng/dl)	Mild	1049.4	498.9	<0.001
	Moderate	2054.7	452.7	
	Severe	2950.0	1053.9	
CRP (mg/l)	Mild	156.8	29.8	<0.001
	Moderate	173.1	30.4	
	Severe	228.1	10.5	
ESR (mm/1hr)	Mild	55.7	2.4	<0.001
	Moderate	73.7	4.2	
	Severe	75.3	2.6	
	Moderate	1.4	0.1	
	Severe	1.2	0.0	
PCT (ng/ml)	Mild	0.2	0.1	<0.001
	Moderate	0.8	0.0	
	Severe	2.4	0.0	
	Moderate	95.2	15.3	
	Severe	96.4	13.8	

4. Discussion

Patients with COVID-19 who develop AKI, hematuria, or proteinuria are at an increased risk of death.[18] We also noted that there were significant differences in the type and severity of AKI with the severity of COVID disease. More patients with severe COVID had intrinsic AKI (signifying more severe damage), and more patients in the severe COVID group required renal replacement therapy. Whether or if the virus also causes direct cytotoxicity is unknown; however, it is thought that hemodynamic alterations and cytokine release play a major role in AKI.[5] The severity of the illness in the individuals evaluated, affects the reported incidence of AKI among patients with COVID-19, particularly those hospitalized.[12] According to Xu Hong et al, there are large observational investigations that showed acute kidney injury in 32%-37% of COVID-19 hospitalized patients. About half of the individuals with AKI had a mild illness (an increase in blood creatinine of 1.5- to 2-fold), whereas the other half had moderate or severe disease (an increase in serum creatinine of more than 2-fold). Twelve per cent to fifteen per cent of individuals were found to have AKI and need Kidney Replacement Therapy (KRT). The need for mechanical breathing and an extended hospital stay was linked to AKI. About half of those with AKI did not fully regain renal function before being released.[19] Age, race/ethnicity, BMI, blood pressure, diabetes, cardiovascular disease, eGFR, interleukin-6, and the need for mechanical ventilation or vasopressors were independent predictors of AKI. Another research with similar results was published.[20, 21]

Within two weeks of ICU admission, 21% of approximately 3000 critically sick patients with COVID-19 had severe AKI needing kidney replacement. About half of these patients did not survive the first 28 days in the hospital.[22] In our study older age, oliguria, and admission to a hospital with few intensive care unit beds increased the chance of death. Three-fourths of patients who made it to release required kidney replacement and over half were still reliant on kidney replacement after two months. The correlation between the need for KRT and the pathophysiology of COVID-19, if any, remains unknown.[23] There has been no research on the long-term effects of KRT for patients with COVID-19. Hospitalized patients with and without COVID-19 were examined for the incidence of AKI in one research.[24] Among the approximately 19,500 patients hospitalized for various causes, the incidence of AKI was 18%; however, it was 31% among the 2600 patients with COVID-19.[14] In this study, the differences in the common risk factors for AKI across the groups did not account for the increased prevalence of AKI observed. Individuals with COVID-19 seemed to have greater levels of C-reactive protein and ferritin, two markers of inflammation, than individuals without COVID-19. Few individuals without COVID-19 had these inflammatory markers examined while hospitalized. Therefore, comparisons of AKI across groups while adjusting for these indicators were not feasible. Another research done by Birkelo, Bethany C showed the comparing outcomes between patients hospitalized for influenza or COVID-19 found that COVID-19 patients had a higher rate of AKI (41 vs 29%) and a higher severity of AKI (stage 3 in 26 vs. 6%). Furthermore, individuals with COVID-19 had greater 90-day mortality than those with influenza (35 vs 9 per cent).[25] The patients included had a mean age of 50

(range: 40-62 years), with the majority male. The most common were diabetes mellitus (12.2%) and CVVH (7.2%) in severe, hypertension (11.1%), and coronary artery disease (9.4%) in mild. Thirty-one out of 33 patients had AKI (mainly stage 3). Acute tubular necrosis (ATN) was seen in the majority of patients (62%), focal segmental glomerulosclerosis (FSGS) was present in one, and many patients experienced complications from other medical conditions (e.g., hypertensive nephrosclerosis) as a result. Another study by Batlle Daniel found that ATN was the most common kidney pathology. Only a subset of individuals with COVID-19 developed glomerular lesions.[26] It is still unclear whether SARS-CoV-2 may directly infect the kidneys. The histopathological investigations showed by Serafinelli Jessica, the presence of COVID-19 patients' kidneys contain virus-like particles.[27] However, these may be subcellular structures inside the endosome (such as clathrin-coated vesicles and multivesicular bodies).[28] It has been shown in several investigations using ultrastructural in-situ hybridization that viral RNA or viral proteins are present in kidney tissue.[29] Other causes of AKI should be investigated similarly to those used for patients in critical condition who also have AKI. Urine samples are not often regarded as extremely contagious.[30] The incidence of AKI was minimal in this group based on a retrospective cohort research that evaluated all 180 confirmed COVID-19 cases. The prevalence of hematuria and proteinuria was not much greater. As compared to the previous research by Li, Qinglin found that the frequency of AKI was 6.7%, with fatality rates reaching up to 91.7%.[31] In recent research of 710 hospitalized patients with COVID-19 illness. However, AKI significantly predicted in-hospital death among COVID-19 patients. Two patients (one with AKI) had elevated serum creatinine levels, but neither had chronic kidney disease. Out of the 710 patients in the Wuhan group, 89 passed away, and 35.5% were classified as very or critically sick.[32] The possible causes of AKI and COVID include sepsis-induced cytokine storm syndrome and coronavirus infection's direct cellular damage to the kidneys.[23,31] Recent studies have shown that the kidneys exhibit significant levels of the receptors for the angiotensin-converting enzyme (ACE2) and the Middle East respiratory syndrome coronavirus (MERS-CoV). Renal impairment resulted from SARS-CoV-2 viremia because the coronavirus travelled from the blood to the kidneys, connected to the ACE2 receptor.[33] The clearance of viral RNA in patients' stools and urine lagged behind that in oropharyngeal swabs, despite the low positive rate of viral RNA in urine (4/58; 6.9%).[34] There was no indication of glomerular disease, whereas acute tubular necrosis was the most prevalent histological sign of AKI in SARS patients. In autopsy specimens from patients with COVID-19, proteinaceous exudates were found in the glomerular Bowman's capsule, along with degeneration of the renal tubular epithelium and exfoliation of tubular luminal hyaline casts, indicating that the kidneys were severely affected. Previous histological research has revealed the presence of intratubular pigmented casts. Congestion with microthrombi and localized fibrosis were also seen in the interstitium.[35,36] After controlling for other potential risk variables, the current research from Wuhan demonstrated that increased serum creatinine, elevated urea nitrogen, AKI, proteinuria, and dipstick hematuria were all independent risk factors for in-hospital mortality.[37] We also found that individuals with COVID-19 who had proteinuria or dipstick hematuria were more likely to be classified as severe or critical and that around half of all severe or critical patients also had albuminuria or hematuria. But there further investigation needs to be done for the correlation between the increased viral load and the increased likelihood of the virus attaching to kidney receptors in these patients. Renal function and cardiac indicators such as lactate dehydrogenase and BNP normalized in our small sample of COVID-19 patients who were followed up, indicating a favourable outlook for these patients. Our research includes a few limitations as we did not have the urine laboratory data from before admission. Therefore, we are not sure whether proteinuria and dipstick hematuria were present before the admission. Second, we could not tell the difference between real hematuria, hemoglobinuria, or myoglobinuria as we just used a dipstick to test for hematuria. However, the frequency of proteinuria and dipstick hematuria in our research was substantially greater than the 4.6% found in the general population in Pakistan.[38]

5. Conclusion

Patients with COVID-19 infection, particularly those in the severe or critical stages, often exhibit proteinuria and dipstick hematuria, with more severe AKI and lesser chances of renal recovery. We found that AKI frequently complicates the course of COVID-19 hospitalizations and is associated with increased illness severity,

prolonged hospitalization, and poorer prognosis. Given the extent of the adverse impact of AKI, it is imperative that early detection of comorbidities and renal complications is essential to improve the outcomes of COVID-19 patients. Further research on large scales is warranted to improve our understanding of this disease and design clinical approaches to managing COVID-19-related AKI. Long-term follow-up for COVID-19 patients should also be done to evaluate its influence on renal outcome, and larger samples are required to elucidate the association between COVID-19 and renal damage. These outcomes will be useful to physicians in monitoring and assessing disease progression and patient outcomes.

CONFLICTS OF INTEREST- None

Financial support: None to report.
Potential competing interests: None to report

Contributions:

M.M, A.K, K.B - Conception of study
M.M, A.K, K.B - Experimentation/Study Conduction
M.M, A.K, K.B - Analysis/Interpretation/Discussion
M.M, A.K, K.B - Manuscript Writing
M.M, A.K, K.B - Critical Review
M.M, A.K, K.B - Facilitation and Material analysis

References

1. Onyeaka H, Anumudu CK, Al-Sharify ZT, Egele-Godswill E, Mbaegbu P. COVID-19 pandemic: A review of the global lockdown and its far-reaching effects. Sci Prog. 2021 Apr-Jun;104(2):368504211019854. doi: 10.1177/00368504211019854.
2. Sohrabi C, Alsafi Z, O'neill N, Khan M, Kerwan A, Al-Jabir A, et al. World Health Organization declares global emergency: A review of the 2019 novel coronavirus (COVID-19). International journal of surgery. 2020;76:71-6. doi: 10.1016/j.ijsu.2020.02.034
3. García LF. Immune response, inflammation, and the clinical spectrum of COVID-19. Frontiers in immunology. 2020;11:1441. doi: 10.3389/fimmu.2020.01441.
4. Gabarre P, Dumas G, Dupont T, Darmon M, Azoulay E, Zafrani L. Acute kidney injury in critically ill patients with COVID-19. Intensive care medicine. 2020;46:1339-48. doi: 10.1007/s00134-020-06153-9.
5. Fu EL, Janse RJ, de Jong Y, van der Endt VH, Milders J, van der Willik EM, et al. Acute kidney injury and kidney replacement therapy in COVID-19: a systematic review and meta-analysis. Clinical kidney journal. 2020;13(4):550-63. doi: 10.1093/ckj/sfaa160.
6. Shao M, Li X, Liu F, Tian T, Luo J, Yang Y. Acute kidney injury is associated with severe infection and fatality in patients with COVID-19: A systematic review and meta-analysis of 40 studies and 24,527 patients. Pharmacological research. 2020;161:105107. doi: 10.1016/j.phrs.2020.105107.
7. Nadim MK, Forni LG, Mehta RL, Connor Jr MJ, Liu KD, Ostermann M, et al. COVID-19-associated acute kidney injury: consensus report of the 25th Acute Disease Quality Initiative (ADQI) Workgroup. Nature reviews Nephrology. 2020;16(12):747-64. doi: 10.1038/s41581-020-00356-5.u6u
8. Post-COVID-19 global health strategies: the need for an interdisciplinary approach. Ageing clinical and experimental research. 2020;32(8):1613-20. doi: 10.1007/s40520-020-01616-x
9. Tan BW, Tan BW, Tan AL, Schriver ER, Gutiérrez-Sacristán A, Das P, et al. Long-term kidney function recovery and mortality after COVID-19-associated acute kidney injury: An international multi-centre observational cohort study. Eclinicalmedicine. 2023;55:101724. doi: 10.1016/j.eclinm.2022.101724.
10. Wainstein M, MacDonald S, Fryer D, Young K, Balan V, Begum H, et al. Use of an extended KDIGO definition to diagnose acute kidney injury in patients with COVID-19: A multinational study using the ISARIC–WHO clinical characterisation protocol. PLoS medicine. 2022;19(4):e1003969. https://doi.org/10.1371/journal.pmed.1003969
11. Silver SA, Beaubien-Souligny W, Shah PS, Harel S, Blum D, Kishibe T, et al. The prevalence of acute kidney injury in patients hospitalized with COVID-19 infection: a systematic review and meta-analysis. Kidney medicine. 2021;3(1):83-98. e1. doi: 10.1016/j.xkme.2020.11.008.
12. Long JD, Strohbehn I, Sawtell R, Bhattacharyya R, Sise ME. COVID-19 Survival and its impact on chronic kidney disease. Translational Research. 2022;241:70-82. doi: 10.1016/j.trsl.2021.11.003.
13. Lumlertgul N, Pirondini L, Cooney E, Kok W, Gregson J, Camporota L, et al. Acute kidney injury prevalence, progression and long-term outcomes in critically ill patients with COVID-19: a cohort study. Annals of intensive care. 2021;11(1):1-11. doi: 10.1186/s13613-021-00914-5.
14. Palvesky P, Radhakrishnan J, Townsend RR. COVID-19: Issues related to acute kidney injury, glomerular disease, and hypertension. UpToDate; 2020.
15. Zhang W, Liu L, Xiao X, Zhou H, Peng Z, Wang W, et al. Identification of common molecular signatures of SARS-CoV-2 infection and its influence on acute kidney injury and chronic kidney disease. Frontiers in Immunology. 2023;14. https://doi.org/10.3389/fimmu.2023.961642
16. Bhatraju PK, Ghassemieh BJ, Nichols M, Kim R, Jerome KR, Nalla AK, et al. Covid-19 in critically ill patients in the Seattle region—case series. New England Journal of Medicine. 2020;382(21):2012-22. doi: 10.1056/NEJMoa2004500
17. Robbins-Juarez SY, Qian L, King KL, Stevens JS, Husain SA, Radhakrishnan J, Mohan S. Outcomes for Patients With COVID-19 and Acute Kidney Injury: A Systematic Review and Meta-Analysis. Kidney Int Rep. 2020 Jun 25;5(8):1149-1160. doi: 10.1016/j.ekir.2020.06.013.
18. Chaudhri I, Moffitt R, Taub E, Annadi RR, Hoai M, Bolotova O, et al. Association of proteinuria and hematuria with acute kidney injury and mortality in hospitalized patients with COVID-19. Kidney and Blood Pressure Research. 2020;45(6):1018-32. doi: 10.1159/000511946.

19. Xu H, Garcia-Ptacek S, Annetorp M, Bruchfeld A, Cederholm T, Johnson P, et al. Acute kidney injury and mortality risk in older adults with COVID-19. Journal of nephrology. 2021;34:295-304. doi: 10.1007/s40620-021-01022-0.
20. Huang C, Soleimani J, Herasevich S, Pinevich Y, Pennington KM, Dong Y, et al., editors. Clinical characteristics, treatment, and outcomes of critically ill patients with COVID-19: a scoping review. Mayo Clin Proc. 2021 Jan;96(1):183-202. doi: 10.1016/j.mayocp.2020.10.022.
21. Graidis S, Papavramidis TS, Papaioannou M. Vitamin D and Acute Kidney Injury: A Two-Way Causality Relation and a Predictive, Prognostic, and Therapeutic Role of Vitamin D. Front Nutr. 2021 Mar 4;7:630951. doi: 10.3389/fnut.2020.630951.
22. Legrand M, Bell S, Forni L, Joannidis M, Koyner JL, Liu K, et al. Pathophysiology of COVID-19-associated acute kidney injury. Nature Reviews Nephrology. 2021;17(11):751-64. https://doi.org/10.1038/s41581-021-00452-0
23. Farouk SS, Fiaccadori E, Cravedi P, Campbell KN. COVID-19 and the kidney: what we think we know so far and what we don't. Journal of nephrology. 2020;33:1213-8. doi: 10.1007/s40620-020-00789-y.
24. Bruchfeld A. The COVID-19 pandemic: consequences for nephrology. Nature Reviews Nephrology. 2021;17(2):81-2. doi: 10.1038/s41581-020-00381-4.
25. Birkelo BC, Parr SK, Perkins AM, Greevy Jr RA, Hung AM, Shah SC, et al. Comparison of COVID-19 versus influenza on the incidence, features, and recovery from acute kidney injury in hospitalized United States Veterans. Kidney International. 2021;100(4):894-905. doi: 10.1016/j.kint.2021.05.029
26. Batlle D, Soler MJ, Sparks MA, Hiremath S, South AM, Welling PA, et al. Acute kidney injury in COVID-19: emerging evidence of a distinct pathophysiology. Journal of the American Society of Nephrology. 2020;31(7):1380-3. doi: 10.1681/ASN.2020040419.
27. Serafinelli J, Mastrangelo A, Morello W, Cerioni VF, Salim A, Nebuloni M, et al. Kidney involvement and histological findings in two pediatric COVID-19 patients. Pediatric Nephrology. 2021;36(11):3789-93. DOI: 10.1007/s00467-021-05212-7.
28. Bullock, HA, Goldsmith CS, Zaki SR, Martines RB, Miller SE. Difficulties in differentiating coronaviruses from Subcellular Structures in Human Tissues by Electron Microscopy. Emerging Infectious Diseases . 2021 Ap ;27(4), 1023-1031. DOI:10.3201/eid2704.204337.
29. Hopfer H, Herzig MC, Gosert R, Menter T, Hench J, Tzankov A, Hirsch HH, Miller SE. Hunting coronavirus by transmission electron microscopy–a guide to SARS-CoV-2-associated ultrastructural pathology in COVID-19 tissues. Histopathology. 2021 Feb;78(3):358-70.
30. Zaki N, Alashwal H, Ibrahim S. Association of hypertension, diabetes, stroke, cancer, kidney disease, and high-cholesterol with COVID-19 disease severity and fatality: A systematic review. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2020;14(5):1133-42. DOI: 10.1016/j.dsx.2020.07.005.
31. Li Q, Zhang T, Li F, Mao Z, Kang H, Tao L, et al. Acute kidney injury can predict in-hospital mortality in elderly patients with COVID-19 in the ICU: a single-center study. Clinical interventions in aging. 2020:2095-107. DOI: 10.2147/CIA.S273720
32. Liang W, Liang H, Ou L, Chen B, Chen A, Li C, Li Y, Guan W, Sang L, Lu J, Xu Y. Development and validation of a clinical risk score to predict the occurrence of critical illness in hospitalized patients with COVID-19. JAMA internal medicine. 2020 Aug 1;180(8):1081-9. DOI:10.1001/jamainternmed.2020.2033
33. Zhuang MW, Cheng Y, Zhang J, Jiang XM, Wang L, Deng J, et al. Increasing host cellular receptor—angiotensin-converting enzyme 2 expression by coronavirus may facilitate 2019-nCoV (or SARS-CoV-2) infection. Journal of medical virology. 2020;92(11):2693-701. DOI: 10.1002/jmv.26139
34. Douangboupha V. Applied Epidemiology of Infectious Diseases in Lao People's Democratic Republic (Lao PDR): The Australian National University (Australia); 2022.
35. Khismatullin RR, Ponomareva AA, Nagaswami C, Ivaeva RA, Montone KT, Weisel JW, Litvinov RI. Pathology of lung-specific thrombosis and inflammation in COVID-19. Journal of Thrombosis and Haemostasis. 2021 Dec 1;19(12):3062-72.DOI: 10.1111/jth.15532.
36. National Health Commission & National Administration of Traditional Chinese Medicine. Diagnosis and treatment protocol for novel coronavirus pneumonia (Trial Version 7). Chinese Medical Journal. 2020 May 1;133(09):1087-95. DOI: 10.1097/CM9.0000000000000819.
37. Pei G, Zhang Z, Peng J, Liu L, Zhang C, Yu C, et al. Renal involvement and early prognosis in patients with COVID-19 pneumonia. Journal of the American Society of Nephrology. 2020;31(6):1157-65.
38. Jafar TH, Chaturvedi N, Gul A, Khan AQ, Schmid CH, Levey AS. Ethnic differences and determinants of proteinuria among South Asian subgroups in Pakistan. Kidney international. 2003 Oct 1;64(4):1437-44. DOI: 10.1046/j.1523-1755.2003.00212.