Open Access Mini-Review

Journal of Renal Endocrinology

**J Renal Endocrinol** 2020;6:e07.

http://www.jrenendo.com

Nickan Research Institute

# Renal management in COVID-19 pandemic

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**Abstract**

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a single-stranded RNA virus, which belongs to the beta coronavirus family. SARS-CoV-2 infection associates with a broad range of symptoms that starts asymptomatically and then leads to a mild and noninflammatory syndrome. Kidney involvement in COVID-19 disease depends on several factors like direct cytopathic effects of infection through an ACE2 (angiotensin-converting enzyme-2)-dependent pathway, hemodynamic changes, and increased coagulation. Consistent control of serum and urinary creatinine and hemodynamic conditions in patients with kidney disorders results in decreased occurrence of acute kidney injury (AKI) by COVID-19 or reduce its intensity. Improvement of oxygen saturation, using vasoactive peptide to increase kidney perfusion, and active antiviral treatment are some clinical interventions to alleviate disorders in kidney function. Based on the abovementioned considerations, prevention is the most effective way of dealing with COVID-19.

**Keywords:** COVID-19, Acute kidney injury, SARS-CoV-2

**Citation:** Bahrami N. Renal management in COVID-19 pandemic. Renal management in COVID-19 pandemic. J Renal Endocrinol. 2020;6:e07.



## Introduction

Since late 2019, a novel viral disease emerged in Wuhan (China), spread rapidly, and caused an uncontrolled pandemic. This viral disease was called COVID-19, which is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2); a single stranded RNA virus that belongs to the beta coronavirus family (1,2). This infection associates with a broad range of symptoms that starts asymptomatically and then leads to a mild and noninflammatory syndrome. As the symptoms get worse, intensive care unit (ICU) care, mechanical ventilation and renal medications become necessary. Based on scientific researches, SARS and MERS- CoV infections cause renal injuries in 5-15 percent of cases and 60 to 90 percent of patients with this condition die. Based on previous studies, occurrence rate of AKI in patients with COVID-19 is about 3%-9%. However, recent researches in this area report higher rates (2-4). About 40% of hospitalized patients with this disease experience proteinuria or presence of protein in the urine. Additionally, acute kidney injury (AKI) is prevalent among these patients and its intensity (acute or mild) is considered as a negative prognostic factor to determine disease severity. Kidney involvement in COVID-19 disease depends on several factors that we aimed to explain in this mini-review (1-5).

## Direct cytopathic effects of virus

Virus propagation in podocyte and kidney tubule cells may cause proteinuria in patients with COVID-19 and subsequently cause chronic AKI conditions. In addition, it can cause infection in tubular epithelial cells and podocytes through an ACE2-depended pathway and leads to mitochondrial dysfunction, acute necrosis of tubular cells, glomerulonephritis, and leakage of protein into Bowman's capsule (2-5). Expression of angiotensin converting and dipeptidyl peptidase-4 enzymes occur in renal tubular cells and act as main receptors for SARS and MERS-CoV. Huge amounts of ACE2 receptors are found at the surface of kidney and podocyte cells that facilitate viral entry into target cells (2-6).

## Hemodynamic alterations

Different organs of the body act in concert so that disruptions in activity of an organ affect other organs, a phenomenon called organ cross talk.

AKI results from respiratory and kidney failure and causes hypoxia and necrosis. Cardio-renal syndrome is another case that involves heart and kidney. In this disease, disruption in right ventricle by COVID-19 results in fluid accumulation in kidney and subsequently causes AKI. Additionally, left ventricle failure reduces the output of heart and blood supply to kidney (3-7).

## Increased coagulability

Intrinsic immune system activity strengthens coagulation pathways. Cytokine storm and macrophage activation

Received: 22 November 2020, Accepted: 27 December 2020, ePublished: 29 December 2020

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**Implication for health policy/practice/research/ medical education**

Kidney involvement in COVID-19 disease depends on several factors like direct cytopathic effects of infection through an ACE2 (angiotensin-converting enzyme-2)-depended pathway, hemodynamic changes, and increased coagulation.

syndrome caused by viral infection result in excessive activation of coagulation factors, which subsequently causes thrombosis, disseminated intravascular coagulation, and pulmonary cell necrosis (7-10).

Kidney injuries in patients with COVID-19 can be resulted from severe hypoxia because during this condition adenosine level is increased, which associates with increased vasoconstriction, decreased renal perfusion, and lower GFR (glomerular filtration rate). Procalcitonin > 0.1 ng/mL and eGFR <60 mL/min/1.73 $m^2$ are important risk factors that help diagnose kidney injuries at early stages. In addition, analysis showed that neutrophil and lymphocyte percent, NT-proBNP, hs-cTnI, disruption of the coagulation, and D-dimer are associated with kidney injuries. Therefore, to prevent severe conditions, these factors should be monitored constantly (3-10). Studies have shown that there is a relationship between increase of procalcitonin and cytokine storm caused by SARS-CoV-2, hence; procalcitonin level is associated with disease severity (2-5).

Procalcitonin is a peptide that is released during systemic inflammation specifically bacterial infections. Bacterial endotoxins and systemic cytokines like tumor necrosis factor-α and IL-1β induce procalcitonin synthesis (7-10).

Control of the main factors like serum and urine creatinine and hemodynamic condition in patients with kidney disease reduces the occurrence of AKI or its severity. Lung protective ventilation eliminates the negative effects of cytokine storm on lung and kidney and results in lower damage to respiratory system (8-12).

## COVID-19 occurs in two phases

During the first phase virus propagates and imposes its cytopathic effect. In this stage, antiviral drugs such as chloroquine, hydroxychloroquine, lopinavir, ritonavir, and darunavir are used to control the disease. Second phase of disease initiates 7-10 days after the onset of initial symptoms and associates with risk of death. During this stage pulmonary cell are involved and the need for oxygen increases and ventilation can become necessary. This phase can be triggered by cytokine release syndrome as a form of systemic inflammatory syndrome. Immunosuppressive medicines and immunoregulators can be beneficial in this phase. Relationships of patients with AKI, who do not need dialysis, should be limited (7-15).

Patients that receive dialysis have a higher risk of COVID-19. In addition, patients with acute kidney disorders may have underlying conditions like immune system deficiency and chronic diseases such as diabetes, coronary diseases, obesity, and hypertension; therefore, they have a higher risk of severe symptoms and even death (10-16).

Patients with COVID-19, who receive dialysis, have lower serum cytokines levels and lower numbers of lymphocytes and other immune cells compared to usual patients with COVID-19. However, they have higher risk of death; because of reduced cytokine storm (due to weak immune system), invasive symptoms of disease are lower in these patients (5-15).

Standards determined to dialysis centers during coronavirus outbreak are as follows:

1. Update health advices and information on outbreak and provide guidelines for health care teams even through E-learning.
2. Collect and update personal and professional information of health care team members, patients that receive dialysis and their family members and personnel of same institutes (information about job, daily life, travels and their personal relationships).
3. Continuous monitoring of signs and symptoms of dialysis patients including fever, cough and dyspnea.
4. Reduce group activities such as personnel traffic inside the hospital and group researches.
5. Provide effective communication between health care providers and patients and a way to online control of symptoms in order to decrease the risk of contagion.
6. Self-control of health care providers to prevent the transmission of the disease to dialysis patients because they are more vulnerable to the disease.
7. Reduce dialysis sessions if possible.
8. Provide a suitable condition to disinfect the covers and hands of patients and staff when entering the dialysis room.
9. Avoid eating and drinking at dialysis site.

Patients with COVID-19 and suspected cases should be hospitalized and dialyzed in a separated part of allocated hospitals for this purpose (7-15). There are also some guidelines to more health care;

1. A regular personnel working shift and not shifting this schedule to prevent the transmission and spread of disease
2. Do not change the dialysis center
3. Patients that need vascular access surgery should be assessed in terms of COVID-19 and this surgery should be operated in a specific room with caution.
4. Regular measurement of body temperature and dialysis of patients with COVID-19 at last shift of the day.
5. All equipment that may come into contact with patients or contaminated environment including dialysis apparatus should be disinfected according to standard protocols.

6. Medical wastes from patients with confirmed COVID-19 or suspected cases should be considered as infectious medical wastes and disposal according to specific standards.
7. All personnel at different sections should wear waterproof clothes with long sleeves, safety glass, multi-layer glove and surgical masks.

Continuous renal replacement therapy (CRRT) is the most common method used in studies. This method is also preferred in patients with severe AKI. However, some patients can use alternate hemodialysis or alternate renal replacement therapy. Nonetheless, dialysis method should be chosen according to availability of dialysis apparatus. Thrombosis and coagulation are common among patients with COVID-19, thus use of anticoagulants during renal replacement therapy is recommended (6-12).

Peritoneal dialysis can be used instead of CRRT and hemodialysis apparatus. It needs less sources and equipment, but it may increase intra-abdominal pressure and disrupt respiration mechanism specifically in patients with COVID-19. Home hemodialysis is another method that can be used during corona virus pandemic. This method reduces patients contact with health care providers and in this case, dialysis schedule and personal life style of patient are more flexible. But, due to Socioeconomic issues this method has not been developed much (12-19).

Therapeutic plasma exchange is an example of methods used to alleviate the symptoms of COVID-19. In this method, symptoms are reduced through decease in cytokines and antibodies levels, endothelial membrane stabilization and re-regulation of increased blood coagulation. Successful application of this method in some case with severe condition has been reported in previous studies. However, it needs further clinical studies. Out of body, perfusion apparatus like Cytosorb is another option to eliminate the cytokines to reduce symptoms of disease, but it needs more evaluations. Based on reports, mortality and rate of AKI are higher in organ transplant recipients. There is no significant information about regulation of immune system in organ transplant recipients (14-19).

## Conclusion

Patients with underlying disease such as cardiovascular disease, cirrhosis, chronic kidney disease are more vulnerable to COVID-19. They are at high risk of infection and show more severe symptoms. Therefore, patients with chronic kidney disease should be monitored constantly and this condition is considered as an important factor in risk group classification.

Improvement of oxygen saturation, using vasoactive peptide to increase kidney perfusion, and active antiviral treatment are some clinical interventions to alleviate disorders in kidney function.

Based on the abovementioned considerations, prevention is the most effective way of dealing with COVID-19. Diagnostic tests play a critical role in this process. Medicines and equipment shortage during outbreaks are inevitable. Therefore, a comprehensive plan to correct characterizations of symptoms, screening of patients and to record data is necessary.

### Author's contribution

NB is the single author of the manuscript.

### Conflicts of interest

The author declares that she has no competing interests.

### Ethical issues

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the author.

### Funding/Support

None.

### References

1. Cozzolino M, Piccoli GB, Ikizler TA, Ronco C. The COVID-19 infection in dialysis: are home-based renal replacement therapies a way to improve patient management? J Nephrol. 2020;33:629-31. doi: 10.1007/s40620-020-00784-3.
2. Barros Camargo L, Quintero Marzola ID, Cárdenas Gómez JC, Mendoza Daza LT, Quintana Pájaro L. Acute kidney injury associated with COVID-19: another extrapulmonary manifestation. Int Urol Nephrol. 2020;52:1403-4. doi: 10.1007/s11255-020-02507-w.
3. Kellum JA, van Till JWO, Mulligan G. Targeting acute kidney injury in COVID-19. Nephrol Dial Transplant. 2020;35:1652-1662. doi: 10.1093/ndt/gfaa231.
4. Wang J, Wang Z, Zhu Y, Li H, Yuan X, Wang X, et al. Identify the Risk Factors of COVID-19-Related Acute Kidney Injury: A Single-Center, Retrospective Cohort Study. Front Med (Lausanne). 2020;7:436. doi: 10.3389/fmed.2020.00436.
5. Cravedi P, Mothi SS, Azzi Y, Haverly M, Farouk SS, Pérez-Sáez MJ, et al. COVID-19 and kidney transplantation: Results from the TANGO International Transplant Consortium. Am J Transplant. 2020;20:3140-8. doi: 10.1111/ajt.16185.
6. Gabarre P, Dumas G, Dupont T, Darmon M, Azoulay E, Zafrani L. Acute kidney injury in critically ill patients with COVID-19. Intensive Care Med. 2020;46:1339-48. doi: 10.1007/s00134-020-06153-9.
7. Lynch MR, Tang J. COVID-19 and Kidney Injury. R I Med J (2013). 2020;103:24-28.
8. Rombolà G, Brunini F. COVID-19 and dialysis: why we should be worried. J Nephrol. 2020;33:401-3. doi: 10.1007/s40620-020-00737-w.
9. Ronco C, Reis T, Husain-Syed F. Management of acute kidney injury in patients with COVID-19. Lancet Respir Med. 2020;8:738-742. doi: 10.1016/S2213-2600(20)30229-0.
10. Naicker S, Yang CW, Hwang SJ, Liu BC, Chen JH, Jha V. The Novel Coronavirus 2019 epidemic and kidneys. Kidney Int. 2020;97:824-828. doi: 10.1016/j.kint.2020.03.001.
11. White CA, Kappel JE, Levin A, Moran SM, Pandeya S, Thanabalasingam SJ; CSN COVID-19 Rapid Response Team. Management of Advanced Chronic Kidney Disease During the COVID-19 Pandemic: Suggestions From the Canadian Society of Nephrology COVID-19 Rapid Response Team. Can J Kidney Health Dis. 2020;7:2054358120939354. doi: 10.1177/2054358120939354.
12. Li J, Li SX, Zhao LF, Kong DL, Guo ZY. Management recommendations for patients with chronic kidney disease during the novel coronavirus disease 2019 (COVID-19) epidemic. Chronic Dis Transl Med. 2020;6:119-123. doi:

10.1016/j.cdtm.2020.05.001.
13. Kliger AS, Cozzolino M, Jha V, Harbert G, Ikizler TA. Managing the COVID-19 pandemic: international comparisons in dialysis patients. Kidney Int. 2020;98:12-16. doi: 10.1016/j.kint.2020.04.007.
14. Alberici F, Delbarba E, Manenti C, Econimo L, Valerio F, Pola A, et al. Brescia Renal COVID Task Force. Management of Patients on Dialysis and With Kidney Transplantation During the SARS-CoV-2 (COVID-19) Pandemic in Brescia, Italy. Kidney Int Rep. 2020;5:580-585. doi: 10.1016/j.ekir.2020.04.001.
15. Kliger AS, Cozzolino M, Jha V, Harbert G, Ikizler TA. Managing the COVID-19 pandemic: international comparisons in dialysis patients. Kidney Int. 2020;98:12-16. doi: 10.1016/j.kint.2020.04.007.
16. Goicoechea M, Sánchez Cámara LA, Macías N, Muñoz de Morales A, et al. COVID-19: clinical course and outcomes of 36 hemodialysis patients in Spain. Kidney Int. 2020;98:27-34. doi: 10.1016/j.kint.2020.04.031.
17. Vasudevan A, Mantan M, Krishnamurthy S, Pais P, Mathew G, Hari P, et al. Managing Children with Renal Diseases During the COVID-19 Pandemic. Indian Pediatr. 2020;57:641-51. doi: 10.1007/s13312-020-1893-8.
18. Shen Q, Wang M, Che R, Li Q, Zhou J, Wang F,et al. Consensus recommendations for the care of children receiving chronic dialysis in association with the COVID-19 epidemic. Pediatr Nephrol. 2020;35:1351-7. doi: 10.1007/s00467-020-04555-x.
19. 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. J Am Soc Nephrol. 2020;31:1157-65. doi: 10.1681/ASN.2020030276.