Travel Medicine and Infectious Disease 37 (2020) 101831

Contents lists available at ScienceDirect

Travel Medicine and Infectious Disease

journal homepage: www.elsevier.com/locate/tmaid

Editorial

The kidney and COVID-19 patients – Important considerations

ARTICLE INFO

Keywords
SARS-CoV-2
COVID-19
Renal
Kidney
Outcomes

The ongoing coronavirus disease 2019 (COVID-19) pandemic, has caused substantial damage to the health system globally. The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) primarily affects the lungs, however, this virus can also affect other organs such as intestine, kidney, heart, and brain [1–3]. Kidney dysfunctions are also observed in a large proportion of COVID-19 patients [4]. Initially, the involvement of kidneys was considered negligible, and little attention was paid to the incidence of acute kidney injury (AKI) [5]. Subsequently, AKI incidence in COVID-19 patient was found to be up to 15% in comparison to an earlier suggested range of 3%–9% potentiating the evidence that AKI is common and that the virus can specifically damage the kidneys [6,7]. The incidence of AKI could be up to 25% among critically-ill COVID-19 patients with underlying comorbidities [7]. An autopsy study also showed the virus tropism to the kidney [8]. Other coronaviruses such as the avian infectious bronchitis virus, are also known to cause severe kidney damage in chicken [9,10].

The exact mechanism of SARS-CoV-2 associated renal damage is not fully known. Studies showed that the cellular components required for virus entry such as angiotensin-converting enzyme 2 (ACE2), cellular transmembrane serine protease 2 (TMPRSS2), and cathepsin L (CTSL) are highly expressed in kidneys [8]. Expressions of ACE2 RNA in the small intestine, duodenum and kidneys were found much higher (around 100-fold) than the lung [4]. Furthermore, the co-expression of ACE2 and TMPRSS is reported to be relatively high in the proximal straight tubule cells and podocytes, suggesting favourable condition for localization of the SARS-CoV-2 in kidneys [11]. Studies reporting albuminuria and hematuria in the COVID-19 patients along with the detection of viral RNA from the urine samples further support the potential tropism of the SARS-CoV-2 for the renal tissues [4,12]. The cytokine storm associated along with the direct cytopathic effect of SARS-CoV-2 is suggested as the probable cause of kidney dysfunction [13].

Moreover, the AKI in response to cytokine storm might occur due to renal inflammation, increased vascular permeability, cardiomyopathy and volume depletion leading to cardiorenal syndrome-1 (Fig. 1) [14]. Additionally, injuries of the renal tubules related to the hypoperfusion in response to cytokine storm may also be partly responsible for the kidney injury [13]. The computed tomography of the kidneys revealed a reduction in the density suggesting the renal inflammation and oedema [4].

Kidney dysfunction is characterized by elevated levels of blood urea nitrogen (BUN), creatinine, uric acid and D-dimer, along with proteinuria and hematuria [4]. A study reported that 60% out of 147 COVID-19 patients developed proteinuria, and 48% exhibited hematuria on hospitalization [4]. Elevated levels of BUN was reported in 31% of the total patients and found common in severely ill and deceased cases [4]. A study conducted on 701 consecutive hospitalized COVID-19 patients revealed proteinuria and hematuria in 43.9% and 26.7%, respectively on admission. Moreover, the prevalence of elevated BUN and serum creatinine was reported 13.1% and 14.4% respectively, in the COVID-19 patients [15]. AKI was associated with higher mortality rates, especially when renal replacement therapy is required [7]. In this context, AKI was reported as an independent risk factor for hospitalized COVID-19 patients [4]. Therefore, along with clinical management for pneumonia, potential intervention to protect the kidneys from the virus tropism and cytokine storm must be considered to minimize the mortalities associated with acute renal failure (Fig. 1).

Those COVID-19 patients suffering from the chronic kidney disease and other comorbidities are reported to be at higher risk of a severe form of the disease and they are advised to take extra preventive measures to avoid the exposure of SARS-CoV-2 [16]. A higher number of comorbidities was also found to be associated with this virus tropism for kidney [8]. The COVID-19 posed a new challenge in the form of renal damage directly through virus tropism and indirectly through cytokine storm and increased mortality associated with kidney damage. In this context, clinical care by monitoring and protecting the kidney functions regardless of the patient's comorbidity is utmost necessary to save the patients from unnoticed renal damage during the course of the disease.

https://doi.org/10.1016/j.tmaid.2020.101831
Received 26 June 2020; Received in revised form 14 July 2020; Accepted 23 July 2020
Available online 1 August 2020

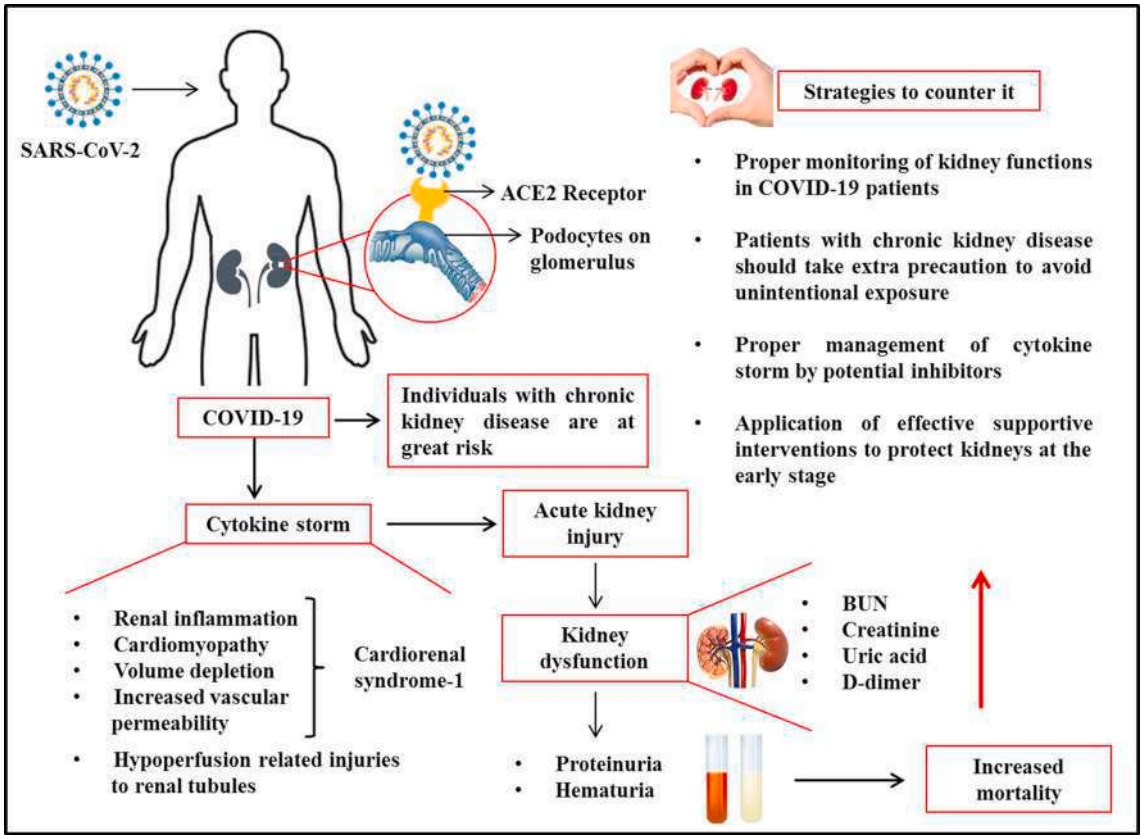

Fig. 1. Probable mechanism of COVID-19 associated kidney damage and strategies to counter it.

Moreover, the application of effective supportive and targeted interventions to protect kidneys at the early stage of SARS-CoV-2 infection is highly recommended [17,18].

CRediT authorship contribution statement

Shailesh Kumar Patel: Conceptualization, Writing - review & editing. **Rohit Singh:** Writing - original draft, Writing - review & editing. **Jigyasa Rana:** Writing - original draft, Writing - review & editing. **Ruchi Tiwari:** Writing - original draft, Writing - review & editing. **Senthilkumar Natesan:** Writing - original draft, Writing - review & editing. **Harapan Harapan:** Writing - original draft, Writing - review & editing. **Kovy Arteaga-Livias:** Writing - original draft, Writing - review & editing. **D. Katterine Bonilla-Aldana:** Writing - original draft, Writing - review & editing. **Alfonso J. Rodríguez-Morales:** Writing - original draft, Writing - review & editing. **Kuldeep Dhama:** Writing - original draft, Writing - review & editing.

Declaration of competing interest

None.

References

[1] Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, Wang B, Xiang H, Cheng Z, Xiong Y, Zhao Y, Li Y, Wang X, Peng Z. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in wuhan, China. J Am Med Assoc 2020;323(11):1061–9. https://doi.org/10.1001/jama.2020.1585.

[2] Rodriguez-Morales AJ, Cardona-Ospina JA, Gutiérrez-Ocampo E, Villamizar-Peña R, Holguin-Rivera Y, Escalera-Antezana JP, Alvarado-Arnez LE, Bonilla-Aldana DK, Franco-Paredes C, Henao-Martinez AF, Paniz-Mondolfi A, Lagos-Grisales GJ, Ramírez-Vallejo E, Suárez JA, Zambrano LI, Villamil-Gómez WE, Balbin-Ramon GJ, Rabaan AA, Harapan H, Dhama K, Nishiura H, Kataoka H, Ahmad T, Sah R. Latin American Network of Coronavirus Disease 2019-COVID-19 Research (LANCOVID-19). Clinical, laboratory and imaging features of COVID-19: a systematic review and meta-analysis. Trav Med Infect Dis 2020 Mar-Apr;34:101623.

[3] Xu Z, Shi L, Wang Y, Zhang J, Huang L, Zhang C, Liu S, Zhao P, Liu H, Zhu L, Tai Y, Bai C, Gao T, Song J, Xia P, Dong J, Zhao J, Wang FS. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. Lancet Respir Med 2020;8(4):420–2. https://doi.org/10.1016/S2213-2600(20)30076-X.

[4] Li Z, Wu M, Yao J, Guo J, Liao X, Song S, Li J, Duan G, Zhou Y, Wu X, Zhou Z, Wang T, Hu M, Chen X, Fu Y, Lei C, Dong H, Xu C, Hu Y, Han M, Zhou Y, Jia H, Chen X, Yan J. Caution on kidney dysfunctions of COVID-19 patients. medRxiv 2020. https://doi.org/10.1101/2020.02.08.20021212.

[5] Wang L, Li X, Chen H, Yan S, Li D, Li Y, Gong Z. Coronavirus disease 19 infection does not result in acute kidney injury: an analysis of 116 hospitalized patients from wuhan, China. Am J Nephrol 2020;51(5):343–8. https://doi.org/10.1159/000507471.

[6] Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, Zhang L, Fan G, Xu J, Gu X, Cheng Z, Yu T, Xia J, Wei Y, Wu W, Xie X, Yin W, Li H, Liu M, Xiao Y, Gao H, Guo L, Xie J, Wang G, Jiang R, Gao Z, Jin Q, Wang J, Cao B. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020;395(10223):497–506. https://doi.org/10.1016/S0140-6736(20)30183-5.

[7] 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 Jun 12. https://doi.org/10.1007/s00134-020-06153-9.

[8] Puelles VG, Lütgehetmann M, Lindenmeyer MT, Sperhake JP, Wong MN, Allweiss L, Chilla S, Heinemann A, Wanner N, Liu S, Braun F, Lu S, Pfefferle S, Schröder AS, Edler C, Gross O, Glatzel M, Wichmann D, Wiech T, Kluge S, Pueschel K, Aepfelbacher M, Huber TB. Multiorgan and renal tropism of SARS-CoV-2. N Engl J Med 2020 May 13:NEJMc2011400. https://doi.org/10.1056/NEJMc2011400.

[9] Coronaviridae Abdel-Moneim AS. Infectious bronchitis virus. In: Bayry J, editor. Emerging and Re-emerging infectious diseases of livestock. Cham: Springer; 2017.

[10] Abdel-Moneim AS, El-Kady MF, Ladman BS, Gelb Jr J. S1 gene sequence analysis of a nephropathogenic strain of avian infectious bronchitis virus in Egypt. Virol J 2006;3:78. https://doi.org/10.1186/1743-422X-3-78.

[11] Pan XW, Xu D, Zhang H, Zhou W, Wang LH, Cui XG. Identification of a potential mechanism of acute kidney injury during the COVID-19 outbreak: a study based on single-cell transcriptome analysis. Intensive Care Med 2020;46(6):1114–6. https://doi.org/10.1007/s00134-020-06026-1.

[12] Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, Liu L, Shan H, Lei CL, Hui DSC, Du B, Li LJ, Zeng G, Yuen KY, Chen RC, Tang CL, Wang T, Chen PY, Xiang J, Li SY, Wang JL, Liang ZJ, Peng YX, Wei L, Liu Y, Hu YH, Peng P, Wang JM, Liu JY, Chen Z, Li G, Zheng ZJ, Qiu SQ, Luo J, Ye CJ, Zhu SY, Zhong NS. China medical treatment expert group for covid-19. Clinical characteristics of coronavirus disease

2019 in China. N Engl J Med 2020;382(18):1708–20. https://doi.org/10.1056/NEJMoa2002032.
[13] Naicker S, Yang CW, Hwang SJ, Liu BC, Chen JH, Jha V. The Novel Coronavirus 2019 epidemic and kidneys. Kidney Int 2020;97(5):824–8. https://doi.org/10.1016/j.kint.2020.03.001.
[14] Ronco C, Reis T. Kidney involvement in COVID-19 and rationale for extracorporeal therapies. Nat Rev Nephrol 2020;16(6):308–10. https://doi.org/10.1038/s41581-020-0284-7.
[15] Cheng Y, Luo R, Wang K, Zhang M, Wang Z, Dong L, Li J, Yao Y, Ge S, Xu G. Kidney disease is associated with in-hospital death of patients with COVID-19. Kidney Int 2020;97(5):829–38. https://doi.org/10.1016/j.kint.2020.03.005.
[16] Henry BM, Lippi G. Chronic kidney disease is associated with severe coronavirus disease 2019 (COVID-19) infection. Int Urol Nephrol 2020;52(6):1193–4. https://doi.org/10.1007/s11255-020-02451-9.
[17] Millan-Oñate J, Rodríguez-Morales AJ, Camacho-Moreno G, Mendoza-Ramírez H, Rodríguez-Sabogal IA, Álvarez-Moreno C. A new emerging zoonotic virus of concern: the 2019 novel coronavirus (COVID-19). Infectio 2020;24:187–92.
[18] Dhama K, Sharun K, Tiwari R, Sircar S, Bhat S, Malik YS, Singh KP, Chaicumpa W, Bonilla-Aldana DK, Rodriguez-Morales AJ. Coronavirus disease 2019 – COVID-19. Clin Microbiol Rev 2020;33(4). e00028-20.

Shailesh Kumar Patel[a], Rohit Singh[a], Jigyasa Rana[b], Ruchi Tiwari[c], Senthilkumar Natesan[d], Harapan Harapan[e,f,g], Kovy Arteaga-Livias[h,i,j], D. Katterine Bonilla-Aldana[j,k,l], Alfonso J. Rodríguez-Morales[i,j,l,m,*], Kuldeep Dhama[a,**]

[a] *Division of Pathology, ICAR-Indian Veterinary Research Institute, Izatnagar, Bareilly, 243 122, Uttar Pradesh, India*
[b] *Department of Veterinary Anatomy, Faculty of Veterinary and Animal Sciences, Rajeev Gandhi South Campus, Banaras Hindu University, Barkachha, Mirzapur, Uttar Pradesh, 231 001, India*
[c] *Department of Veterinary Microbiology and Immunology, College of Veterinary Sciences, UP Pt. Deen Dayal Upadhayay Pashu Chikitsa Vigyan Vishwavidyalay Evum Go-Anusandhan Sansthan (DUVASU), Mathura, India, 281 001, India*
[d] *Indian Institute of Public Health Gandhinagar, Lekawada, Ganghinagar, Gujarat, 382 042, India*
[e] *Department of Microbiology, School of Medicine, Universitas Syiah Kaula, Banda Aceh, Aceh, 2311, Indonesia*
[f] *Medical Research Unit, School of Medicine, Universitas Syiah Kuala, Banda Aceh, Aceh, 23111, Indonesia*
[g] *Tropical Disease Centre, School of Medicine, Universitas Syiah Kuala, Banda Aceh, Aceh, 23111, Indonesia*
[h] *Facultad de Medicina, Universidad Nacional Hermilio Valdizán, Huánuco, Peru*
[i] *Master in Clinical Epidemiology and Biostatistics, Universidad Científica Del Sur, Lima, Peru*
[j] *Latin American Network of Coronavirus Disease 2019-COVID-19 Research (LANCOVID-19), Pereira, Risaralda, Colombia*
[k] *Semillero de Zoonosis, Grupo de Investigación BIOECOS, Fundación Universitaria Autónoma de Las Américas, Sede Pereira, Pereira, Risaralda, Colombia*
[l] *Public Health and Infection Research Group, Faculty of Health Sciences, Universidad Tecnologica de Pereira, Pereira, Colombia*
[m] *Grupo de Investigación Biomedicina, Faculty of Medicine, Fundación Universitaria Autónoma de Las Americas, Pereira, Risaralda, Colombia*

[*] Corresponding author. Master in Clinical Epidemiology and Biostatistics, Universidad Científica del Sur, Lima, Peru.

[**] Corresponding author. Division of Pathology, ICAR –Indian Veterinary Research Institute, Izatnagar, Bareilly, India.
E-mail addresses: arodriguezm@utp.edu.co (A.J. Rodríguez-Morales), kdhama@rediffmail.com (K. Dhama).