LETTER TO THE EDITOR

Potential risk of the kidney vulnerable to novel coronavirus 2019 infection

Fan Zhang and Yumei Liang
Department of Nephrology and Laboratory of Kidney Disease, Hunan Provincial People’s Hospital, Hunan Normal University, Changsha, China

Submitted 2 March 2020; accepted in final form 30 March 2020

TO THE EDITOR: In December 2019, an outbreak of acute respiratory illness, since named coronavirus disease 2019 (COVID-19) by the World Health Organization, emerged in Wuhan, Hubei, China. As of March 28, 2020, there had been 512,701 confirmed cases and 23,495 deaths documented globally (12a). COVID-19 has become a global health threat. Through the efforts of experts and scientists all over the world, our understanding of COVID-19 has grown considerably. Researchers performed deep sequencing analysis from lower respiratory tract samples and identified a novel coronavirus that has since been named novel coronavirus 2019 (2019-nCoV), now severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It has been confirmed as the cause of COVID-19 (14). This is the third epidemic caused by a coronavirus in the 21st century, after SARS (caused by SARS-CoV) and Middle East respiratory syndrome (MERS).

Studies have shown that both 2019-nCoV and SARS-CoV shared the same cell entry receptor, angiotensin-converting enzyme 2 (ACE2) (5, 13). In this way, ACE2 expression patterns in different organs, tissues, and cell types could uncover the potential risk to 2019-nCoV infection. ACE2 is expressed in humans in the epithelia of the lung, small intestine, heart, liver, and kidney (8). In autopsy samples obtained from patients with SARS, immunohistochemical examination revealed SARS-CoV virions, RNA, and antigen in the lung and other organs, including the kidney (4). One in vitro study (11) established that SARS-CoV with proximal tubular epithelial cells showed persistent and productive infection, which was partly correlated with ACE2 expression. Using state-of-art single cell techniques, Zou et al. (15) stratified organs into high and low risk according to the expression level of ACE2. In their analysis, the kidney should be listed as high risk. These findings indicate that 2019-nCoV infection of kidney cells.

Clinical manifestations of COVID-19 in parts of China have been recently reported (1, 6, 12). In accordance with ACE2 expression in organs, besides respiratory symptoms, nonrespiratory symptoms such as fatigue, myalgia, and diarrhea have also been reported. Acute kidney injury (AKI) has been reported as one of the complications that occur during the progression of COVID-19 in both patients comorbid with kidney disease and those who are not (6, 12). One study (12) of 138 patients with COVID-19 reported that 4% of patients with COVID-19 had AKI (12). Huang et al. (6) reported on 41 patients with COVID-19, among whom 10% had elevated creatinine (>133 μmol/L) on admission and 7% had AKI. Laboratory tests showed that the level of blood urea and creatine increased progressively in the progression of COVID-19. The incidence of AKI in patients with COVID-19 is similar to that found in patients with SARS; one retrospective analysis showed 6% of patients SARS to have AKI (2). In an analysis of 536 patients with SARS, 6.7% developed acute renal impairment, and the involvement of the kidney in SARS cases has been associated with a high (91.7%) mortality rate (3). Similarly, patients with COVID-19 who received care in intensive care units were more likely to have AKI than patients that did not receive care in intensive care units (12). All these findings indicate that AKI could be one of the risk factors for mortality in patients with COVID-19.

The pathophysiological mechanisms of AKI could be multifactorial, including direct infection with 2019-nCoV, immune and inflammatory responses induced by viral infection, and systemic toxic reaction resulting from respiratory failure. These mechanisms may be closely associated with death in severe cases of COVID-19.

Since the routes of transmission have contributed greatly to the rapid spread of 2019-nCoV, this reminds us that urine samples should be tested to exclude a potential alternative route of transmission except respiratory droplets and direct contact (7, 10). Special care of renal function should be taken into account when treating patients with COVID-19. Such information calls for patient care regarding renal function of patients currently under emergency and potential postcure care units were more likely to have AKI than patients that did not receive care in intensive care units (12). All these findings indicate that AKI could be one of the risk factors for mortality in patients with COVID-19.

The pathophysiological mechanisms of AKI could be multifactorial, including direct infection with 2019-nCoV, immune and inflammatory responses induced by viral infection, and systemic toxic reaction resulting from respiratory failure. These mechanisms may be closely associated with death in severe cases of COVID-19.

The pathophysiological mechanisms of AKI could be multifactorial, including direct infection with 2019-nCoV, immune and inflammatory responses induced by viral infection, and systemic toxic reaction resulting from respiratory failure. These mechanisms may be closely associated with death in severe cases of COVID-19.

The pathophysiological mechanisms of AKI could be multifactorial, including direct infection with 2019-nCoV, immune and inflammatory responses induced by viral infection, and systemic toxic reaction resulting from respiratory failure. These mechanisms may be closely associated with death in severe cases of COVID-19.

GRANTS
This work was supported by Hunan Provincial People’s Hospital RENSHU Funding Project RS201801.

DISCLOSURES
No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS
F.Z. drafted manuscript; Y. L. edited and revised manuscript. F.Z. and Y. L. approved final version of manuscript.

REFERENCES
1. Chang D, Lin M, Wei L, Xie L, Zhu G, Dela Cruz CS, Sharma L. Epidemiologic and clinical characteristics of novel coronavirus infections
involving 13 patients outside Wuhan, China. *JAMA* 323: 1092–1093, 2020. doi:10.1001/jama.2020.1623.

2. Choi KW, Chau TN, Tsang O, Tso E, Chiu MC, Tong WL, Lee PO, Ng TK, Ng WF, Lee KC, Lam W, Yu WC, Lai JY, Lai ST; Princess Margaret Hospital SARS Study Group. Outcomes and prognostic factors in 267 patients with severe acute respiratory syndrome in Hong Kong. *Ann Intern Med* 139: 715–723, 2003. doi:10.7326/0003-4819-139-9-200311040-00005.

3. CHU KH, Tsang WK, Tang CS, Lam MF, Lai FM, To KF, Fung KS, Tang HL, Yan WW, Chan HW, Lai TS, Tong KL, Lai KN. Acute renal impairment in coronavirus-associated severe acute respiratory syndrome. *Kidney Int* 67: 698–705, 2005. doi:10.1111/j.1523-1755.2005.67130.x.

4. Gu J, Gong E, Zhang B, Zheng J, Gao Z, Zhong Y, Zou W, Zhan J, Wang S, Xie Z, Zhuang H, Wu B, Zhong H, Shao H, Fang W, Gao D, Pei F, Li X, He Z, Xu D, Shi X, Anderson VM, Leong AS. Acute renal impairment in coronavirus-associated severe acute respiratory syndrome. *Nature* 579: 270–273, 2020. doi:10.1038/s41586-020-2012-7.

5. Hoffmann M, Kleine-Weber H, Krüger N, Mueller MA, Drosten C, Pöhlmann S. The novel coronavirus 2019 (2019-nCoV) uses the SARS-coronavirus receptor ACE2 and the cellular protease TMPRSS2 for entry into target cells. *bioRxiv*. In press. doi:10.1101/2020.01.31.929042.

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, Liang R, Gao Z, Jin Q, Wang J, Cao B. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China [Erratum in *Lancet* 395: 496, 2020]. *Lancet* 395: 497–506, 2020. doi:10.1016/S0140-6736(20)30183-5.

7. Lei H, Li Y, Xiao S, Lin CH, Norris SL, Wei D, Hu Z, Ji S. Routes of transmission of influenza A H1N1, SARS CoV, and norovirus in air cabin: comparative analyses. *Indoor Air* 28: 394–403, 2018. doi:10.1111/ina.12445.

8. Li W, Wong SK, Li F, Kuhn JH, Huang IC, Choe H, Farzan M. Animal origins of the severe acute respiratory syndrome coronavirus: insight from ACE2-S-protein interactions. *J Virol* 80: 4211–4219, 2006. doi:10.1128/JVI.80.9.4211-4219.2006.

9. Otter JA, Dunskey C, Yezli S, Douthwaite S, Goldenberg SD, Weber DJ. Transmission of SARS and MERS coronaviruses and influenza virus in healthcare settings: the possible role of dry surface contamination. *J Hosp Infect* 92: 235–250, 2016. doi:10.1016/j.jhin.2015.08.027.

10. Pacciarini F, Ghezzi S, Canducci F, Sims A, Sampaolo M, Ferioli E, Clementi M, Poli G, Conaldi PG, Baric R, Vicenzi E. Persistent replication of severe acute respiratory syndrome coronavirus in human tubular kidney cells selects for adaptive mutations in the membrane protein. *J Virol* 82: 5137–5144, 2008. doi:10.1128/JVI.00096-08.

11. 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. *JAMA* 323: 1061–1069, 2020. doi:10.1001/jama.2020.1585.

12.World Health Organization. Coronavirus disease (COVID-19) Pandemic. Coronavirus Disease (COVID-19) Outbreak Situation [Online]. https://www.who.int/emergencies/diseases/novel-coronavirus-2019 [28 March 2020].