Editorial

Focus on the Crosstalk Between COVID-19 and Urogenital Systems

Not only capable of causing respiratory illness, COVID-19 might also wreak havoc with other organ systems, including the urogenital systems.[1] We discuss the need to consider the crosstalk (referred to mutual effects) between COVID-19 and urogenital systems while preventing the epidemic and treating patients.

The angiotensin-converting enzyme II (ACE2), known to be a cell receptor for human severe acute respiratory syndrome coronavirus (SARS-CoV), also plays a significant role in cellular entry for 2019-nCoV (also known as SARS-CoV-2) via strong interaction with the receptor binding domain of 2019-nCoV with the S-protein.[2] In addition to respiratory organs, up-regulation of ACE2 expression was identified in the urinary system, including the renal proximal tubule cells and bladder urothelial cells,[3,4] as well as the male reproductive system, including Leydig cells and cells in the testicular seminiferous ducts in testis[4].

Indeed, previous studies have reported that affected patients had urinary tract infection; mild proteinuria, hematuria, elevated serum creatinine, elevated urea nitrogen; severe acute kidney injury; and even lethal renal failure representing a strong correlation with intensive care unit admission which could serve as a risk factor for in-hospital death.[5,6] A recent study also suggested that COVID-19 could induce damage to male sex hormones as well.[7] All of these preliminary findings suggest that urogenital systems might be a potentially high risk route of SARS-CoV-2 infection. Due to the possible pathogenicity of the virus to urogenital systems, clinicians must pay close attention to failed organ functionality and focus on the threats posed to the male reproductive system, particularly with regard to the evaluation and proper intervention for infertility in young patients.[4]

Beyond the conventional routes of transmission from respiratory droplets and direct contact, COVID-19 is highly likely to be transmitted by urine, which is in accordance with the Middle East respiratory syndrome coronavirus (MERS-CoV) and SARS-CoV. Several investigators reported isolation of the virus from urine,[1,8] and the National Health Commission of the People's Republic of China warned everyone about contagion of the novel coronavirus via urine of infected patients. Bearing in mind the necessity of close contact with excretions such as urine, the indispensable self-protection for health care workers and others may restrain the risk of COVID-19 transmission.

Nevertheless, the exact mechanism of virus shedding urine is unclear, although 2 mechanisms for SARS-CoV-2 shedding have been proposed. First, sepsis leading to the cytokine storm syndrome could induce renal dysfunction in infected patients with or without underlying chronic renal disease, causing SARS-CoV-2 in the blood to leak from the circulation system into urine. Second, the virus could directly invade the urinary system via binding to ACE2 receptors and lead to shedding in the urine. ‘ Meanwhile, the detection of SARS-CoV-2 or its components (eg RNA, antigens and antibodies) shedding in urine is a reminder that COVID-19 can theoretically be diagnosed based on urinary diagnostics. That is, in addition to the current standard methods of nucleic acid test for nasopharyngeal swab and chest computerized tomography for the diagnosis of COVID-19, urine derived SARS-CoV-2 antigens or antibodies can be used for diagnostic purposes, providing a noninvasive, timesaving and simple test. Thus, we believe validation in an increased number of urine samples is warranted in the future.

More attention should be paid to chronic urological histories of inpatients with COVID-19. It has been suggested that COVID-19 is more likely to infect older adults with serious comorbid conditions, including chronic renal disease and urological malignancies, as a result of the weaker immune systems.[5,9,10]. For example, uremic patients are particularly susceptible to SARS-CoV-2 infection and may exhibit greater variations in infectious and clinical symptoms. In response the Chinese Society of Nephrology and the Taiwan Society of Nephrology issued guidelines for dialysis management.[11] Patients admitted to the

0022-5347/20/2041-0001/0
THE JOURNAL OF UROLOGY®

https://doi.org/10.1097/JU.0000000000001068
Vol. 204, 1-2, July 2020
Printed in U.S.A.

intensive care unit were older and had more comorbid conditions than those not admitted to the unit.[5] Therefore, we suggest that clinicians assess all underlying urological diseases of patients while treating COVID-19, especially older individuals with serious comorbid conditions.

In conclusion, various urogenital illnesses can be induced by virus, and may exacerbate and even cause life-threatening conditions without careful surveillance. Conversely, individuals with chronic urinary diseases may have increased susceptibility to COVID-19 and such underlying comorbidities may result in a poor prognosis without more health care. Identification of the virus and its components (eg RNA, antigens and antibodies) shedding in the urine not only signals the potential route of urine transmission and poses a challenge to the urinary system, but also provides the opportunity to determine if a noninvasive urinary diagnostic test for COVID-19 could assist in diagnosis and spread.

Zhang-song Wu, Zhi-qiang Zhang and Song Wu*
Department of Urological Surgery
The Third Affiliated Hospital of Shenzhen University
Shenzhen University
Shenzhen Following Precision Medical Institute
Shenzhen, China
The First Affiliated Hospital of Guangzhou Medical University
Guangzhou Medical University
Guangzhou, China

*Correspondence: Department of Urological Surgery, The Third Affiliated Hospital of Shenzhen University, Shenzhen University, Shenzhen, 518000 China (telephone: +86-18098928732; email: doctor_wusong@126.com).

REFERENCES

1. Guan W-J, Ni Z-Y, Hu Y et al: Clinical characteristics of coronavirus disease 2019 in China. New Engl J Med 2020; doi:10.1056/NEJMoa2002032.
2. Hoffmann M, Kleine-Weber H, Schroeder S et al: SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. Cell 2020; doi.org/10.1016/j.cell.2020.02.052.
3. Zou X, Chen K, Zou J et al: Single-cell RNA-seq data analysis on the receptor ACE2 expression reveals the potential risk of different human organs vulnerable to 2019-nCoV infection. Front Med 2020; doi:10.1007/s11684-020-0754-0.
4. Fan C, Li K, Ding Y et al: ACE2 expression in kidney and testis may cause kidney and testis damage after 2019-nCoV infection. medRxiv 2020; doi:10.1101/2020.02.12.20022418.
5. Wang D, Hu B, Hu C et al: Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus—infected pneumonia in Wuhan, China. JAMA 2020; doi:10.1001/jama.2020.1585.
6. Yang X, Yu Y, Xu J 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; doi:10.1016/S2213-2600(20)30079-5.
7. Ma L, Xie W, Li D et al: Effect of SARS-CoV-2 infection upon male gonadal function: a single center-based study. medRxiv 2020. doi:10.1101/2020.03.21.20037267.
8. Diao B, Wen K, Chen J et al: Diagnosis of acute respiratory syndrome coronavirus 2 infection by detection of nucleocapsid protein. medRxiv 2020; doi:10.1101/2020.03.07.20032524.
9. Chen N, Zhou M, Dong X et al: Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 2020; **395:** 507.
10. Liang W, Guan W, Chen R et al: Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. Lancet Oncol 2020; **21:** 335.
11. Naicker S, Yang C-W, Hwang S-J et al: The novel coronavirus 2019 epidemic and kidneys. Kidney Int 2020; doi.org/10.1016/j.kint.2020.03.001.