

A short review of male genito-urinary lesions caused by coronavirus disease 2019 (COVID-19)

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Abstract

Coronavirus disease 2019 (COVID-19) is a novel infectious disease that has spread worldwide since it first appeared in December 2019. It can cause pathologies in several organs of the body through direct and indirect mechanisms. After more than two years of study, the effects of COVID-19 on the genitourinary system are now well-evidenced as COVID-19 has considerable effects on the kidneys, testes, vas deferens, epididymis, seminal vesicles, prostate, and penis. Renal invasion is mainly characterized by acute kidney injury. Testicular invasion is characterized by orchitis, testicular epididymitis, etc. Although COVID-19 has been suspected to spread via serum, evidence for the presence of the virus in the semen of patients is currently scarce. COVID-19 also impacts the sexual function of patients to varying degrees, with some patients developing erectile dysfunction. The underlying mechanisms of COVID-19 invasion into the genitourinary system have not been clearly identified, and more clinical studies are required. This review discusses the impact of COVID-19 on the genitourinary system and male health.

Keywords: Acute kidney injury; Coronavirus disease 2019; Erectile dysfunction; Genitourinary system; Semen

The Coronavirus disease 2019 (COVID-19) pandemic is a huge threat to human health and as of May 2022, it has been diagnosed in more than 505 million patients and cumulatively contributed to more than 621,000 deaths in more than 200 countries worldwide. In addition to its major impact on the respiratory system, it has varying degrees of impact on gastrointestinal, cardiovascular, neurological, and genitourinary systems. With an increasing number of infections, there is growing evidence that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) can impair the genitourinary health of patients, particularly men.

As with other coronaviruses, ACE2 and TMPRSS2 play an important role in the infection mechanism of SARS-CoV-2. ACE2 is an important host receptor for SARS-CoV-2 and TMPRSS2 is a host protein that promotes the fusion of the virus with the host cell. Organ tissues with high levels of expression of both proteins are in consequence more susceptible to COVID-19 infection and its consequences. ACE2 and TMPRSS2 were found to be expressed at high levels in a variety of male organs, such as the prostate, testis, vas deferens, etc. Although the expression levels of ACE2 and TMPRSS2 in the testis are controversial, there remains significant evidence that the genitourinary system

is a high-risk site for SARS-CoV-2 invasion. This review summarizes a series of studies over the past 3 years that briefly cover the impact of COVID-19 on urogenital health.

Prostate Dominic Wichmann et al. performed autopsies on 12 deceased patients with COVID-19, of which prostate microthrombi were found in 6 of 9 (2/3) male patients.^[1] However, Alessio Pecoraro et al. suggested that microthrombosis may be a consequence of multi-organ failure in severely diseased patients. They performed a detailed examination of the prostate in 10 patients and the results of their study showed no significant histopathological damage to the prostate during COVID-19 infection.^[2] Despite evidence that COVID-19 does not directly damage prostate tissue, there are still numerous reports of men with clinical manifestations such as prostatitis, benign prostatic hyperplasia and worsening lower urinary tract symptoms, and further research is needed to explain other potential mechanisms by which these symptoms occur.

Testis The association between the testes and COVID-19 is also complex. The testis is considered as a high-risk organ because of its high expression levels of TMPRSS2 and ACE2. Early in the outbreak, SARS-CoV-2 infection caused orchitis^[3] and testicular epididymitis.^[4] Duarte-Neto et al. studied testicular samples from many COVID-19 fatal cases, and all cases showed the SARS-CoV-2 N-capsid protein in mesenchymal cells, supporting cells, spermatogonia, and fibroblasts. Reverse-transcription polymerase chain reaction was conducted to identify COVID-19 viral RNA in 50% (3/6) of the testicular tissue samples. Viral particles were observed in the cytoplasm of mesenchymal cells, supporting cells, spermatocytes, and endothelial cells using electron microscopy. Their study identified testicular damage in patients who suffered fatal COVID-19, attributable to inflammatory damage to the testicular parenchyma caused by SARS-CoV-2 invasion and varied levels of vascular disruption due to secondary ischemia.^[5]

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Semen Based on the evidence of testicular invasion by SARS-CoV-2, the virus may be present in the semen, which could promote COVID-19 transmission. However, Stanley et al. suggested that since ACE2 and TMPRSS2 are not co-expressed in any testicular cell type, sperm cells may not increase the risk of SARS-CoV-2 transmission.^[6] A series of reports supports this view. Song et al. summarized the results of a study of 13 male patients with COVID-19 and observed the absence of SARS-CoV-2 in the semen and testes of male patients infected with COVID-19 during the acute and recovery phases.^[7] Similar results were reported by Pan et al. who examined semen samples in a group of adult Chinese men diagnosed with COVID-19.^[8] Therefore, it is unlikely that COVID-19 is sexually transmitted by men. Temiz et al. also tested 30 patients with COVID-19 and found there was no detection of SARS-CoV-2 in the semen samples. Their findings showed that patients with COVID-19 had significantly decreased sperm morphology and serum sex hormone levels compared to controls.^[9] Enikeev et al. analyzed the semen of patients during hospitalization and 3 months after discharge and found that hormone levels and sperm quality in men were significantly reduced during COVID-19 episodes; however, all variations were temporary, and hormone levels and semen quality returned to normal levels 3 months after discharge.^[10] The evidence for the presence of SARS-CoV-2 in semen is currently minimal. The contrary result was obtained in a study by Li et al. who tested semen from 38 patients and discovered that 6 (15.8%) patients tested positive for SARS-CoV-2, contradicting the results of most studies.^[11] The scientific validity of this remains to be confirmed, considering the small sample size and possibility of contamination when obtaining semen. Thus, we conclude that, despite the generally decreased semen quality in patients with COVID-19, there is almost no SARS-CoV-2 in semen to transmit COVID-19.

Erectile dysfunction (ED) Kresch et al. demonstrated for the first time that SARS-CoV-2 is found in the penis long after the initial infection in humans. They also showed that extensive endothelial cell dysfunction caused by COVID-19 may contribute to ED.^[12] This study provides evidence for the underlying impact of COVID-19 on sexual health. Harirugsakul et al. recruited 153 Thai men with COVID-19 for their study, which showed a high prevalence of ED of 64.7%. They concluded that psychological factors were the cause of ED in most participants and that biological factors did not play a major role.^[13] The current series of studies demonstrated that endothelial dysfunction, testicular damage, and psychological factors contributed to ED due to COVID-19. Although the underlying molecular mechanisms are not completely known, the evidence is sufficient to suggest that COVID-19 results in strong short-term effects on the male reproductive system. A series of large clinical studies are required to illustrate the mechanisms underlying the damage to male sexual function caused by COVID-19.

In conclusion, the available evidence suggests that COVID-19 has had adverse effects on several organs of the genitourinary system, including the kidneys, prostate, testes, and penis. Significant damage to the genitourinary health is possible in patients with COVID-19. Extensive studies are required to understand the long-term effects of SARS-CoV-2 on male urogenital function and mechanisms underlying its effects. As the epidemic continues, a comprehensive assessment of the urogenital health of patients should be conducted to mitigate damage to the urogenital system and reduce the associated sequelae of SARS-CoV-2. In addition, the mental health of patients should be addressed to avoid psychological symptoms,

such as anxiety and depression, which can have a huge impact on male sexual function.

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Statement of ethics

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Conflict of interest statement

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Author contributions

All authors contributed equally in this study.

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