Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Review Article

COVID-19 and the kidney: A matter of concern

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ABSTRACT

Starting from December 2019 in China, SARS-CoV-2, a novel coronavirus strain has rapidly spread to involve more than 150 countries. SARS-CoV-2 is not only responsible for causing pneumonia, but there are also concerns regarding the involvement of other organs such as the heart, liver, and kidneys. Here, we review kidney involvement in COVID 19, the mechanism of kidney injury, and its impact on mortality. Lastly, we focus on the challenges of COVID19 in dialysis and renal transplant patients.

1. Introduction

From the first case, which came into view in Wuhan, China, in December 2019 by a novelstrain of human coronaviruses, the severe acute respiratory syndrome coronavirus 2 (SARSCoV- 2), as of March 24, 2020, there had been around 381,761 cases worldwide. On February 11, 2020, WHO termed it as coronavirus disease 2019 (COVID-19). It has now expanded to more than 150 countries across the world and is responsible for 16,558 deaths.[1] SARSCoV- 2 is a positive-stranded RNA virus that belongs to the Betacoronavirus category. Often pleomorphic, it has a diameter of 60–140 nm. Coronaviruses are members of *Coronavirinae* subfamily, which consists of four genera -Alphacoronavirus, Betacoronavirus, Gammacoronavirus, and Deltacoronavirus — theses are based on their phylogenetic relationships and genomic structures. The alphacoronaviruses and betacoronaviruses can infect only mammals. Some strains of gammacoronaviruses and deltacoronaviruses can also infect mammals· Alphacoronaviruses and betacoronaviruses usually responsible for respiratory diseases in humans. The two viruses, SARS-CoV and MERS-CoV are highly pathogenic forms and can lead to severe respiratory syndrome in humans, but other human coronaviruses strains like (HCoV-NL63, HCoV-229E, HCoV-OC43 and HKU1) can also cause mild upper respiratory diseases.[2] The origin of SARS-Cov-2 is currently unknown, but after its genomic analyses, there is speculation of its evolution from strain found in bats (BatCov RaTG13).[3] Like other respiratory pathogens, human-to-human transmission mainly occurs via aerosol, but transmission by fecal, or direct contact has also been reported. Based on evidence from investigations provided by the China CDC investgations, the incubation time is usually within 3–7 days and can extend up to 2 weeks.[4] Clinical reports suggest that the most frequent symptoms of COVID-19 are fatigue, fever, dry cough, sore throat, dyspnoea, and diarrhea.[5] Leukopenia is the commonly reported laboratory abnormality.[6] Computerized tomography (CT) of the chest is characterized by consolidation or multiple ground-glass opacities involving bilateral sides. Predominantly causing acute respiratory illness, COVID-19 is not confined to only the respiratory system; it may also damage other organs, for instance, the kidneys, heart, gastrointestinal tract, immune, blood, and nervous system.[7] This article attempts to highlight the effect of COVID 19 on the kidneys, with a focus on vulnerable patients undergoing dialysis and renal transplantation.

2. Kidney involvement in COVID-19 infection

A concern of kidney impairment was raised in a report of 710 COVID-19 patients by chen et al. which showed proteinuria and hematuria in 44% of patients and hematuria in 26.9 Manuscript (without Author Details) Click here to view linked References percent at the time of admission. Raised serum creatinine was found in 15.5% of patients. An overall incidence of acute kidney injury (AKI) was reported to occur in 3.2% of patients during the study period.[8] Another study by Zhen Li et al., showed a higher

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prevalence of proteinuria in 63% (32/51) of the patients and raised serum creatinine and blood urea nitrogen in 19% and 27% of the patients respectively. 100% of the patient had abnormalities of the kidneys in CT scans.[9] Till now, there is a scarcity of data on kidney histology of COVID-19 patients.

3. Effect of kidney dysfunction on mortality

In recent studies, after adjustment of multiple cofounders like age, sex, leukocyte count and disease severity, AKI, proteinuria, and hematuria were the independent risk factor for inhospital mortality.[10]

4. Mechanism of kidney injury in COVID-19

Complete pathogenesis of kidney injury in COVID-19 yet to be elucidated, but it appears to be multifactorial and diverse (shown in Fig. 1). Firstly, as some antecodal reports had demonstrated PCR fragments of coronavirus in blood and urine of patients infected with SARS and COVID-19, novel coronavirus may have a direct cytopathic effect of kidney resident cells.[11] The spike (S) protein of SARS-CoV-2 uses angiotensin-converting enzyme II (ACE2) and TRMPSS as a cell entry receptor.[12] ACE2 is highly expressed in kidneys.

Secondly, although no histological evidence is available in the literature, kidney damage may also occur by immune complexes deposition of viral antigen or virus-induced antibody.[13]

Another postulated mechanism is that in critical cases of COVID-19, a very high level of proinflammatory factors such as IL2, IL10, IL7, GSCF, MCP1, and TNFα was found suggesting the occurrence of the cytokine storm that can result in injury to the kidney, heart, lung and other normal cells of the body.[14]

5. Diagnosis

The diagnosis of COVID-19 is mainly established by clinical presentation, history of contact (epidemiological data), and laboratory parameters like leukopenia, CT scan, detection of nucleic acid, serology (IgM/IgG), and enzyme-linked immunosorbent assay (ELISA).[15] According to CDC recommendations, a nasopharyngeal swab specimen is collected to test SARS-CoV-2. Two important technologies for nucleic acid detection are real-time quantitative polymerase chain reaction (RT-PCR) and gene sequencing. Both in-house and commercially assays for the detection of COVID-19 are currently under development.[16]

Numerous biomarkers have been studied in patients suffering from COVID19, for example C-reactive protein, interleukin-6, serum amyloid A, lactate dehydrogenase, neutrophil-to-lymphocyte ratio, cardiac troponin, lymphocytes, platelet count, and D-dimer. Out of all these, two, i.e., lower total lymphocytes count and platelet count are seen in severe patients. Neverthless, to discover how different biomarkers behave during the course of illness in COVID19 we need more research and data.[17]

6. COVID-19 in dialysis patients

Confronting SARS-CoV-2 infection is more challenging in dialysis patients. A less efficient immune system makes dialysis patients more prone to severe infectious diseases as compared to the general population. Dialysis patients with COVID-19 may be asymptomatic or may have may subtle manifestation of the infection. To prevent the COVID19 outbreak, dialysis facilities must be prepared.[18] The Chinese Society of Nephrology and the Taiwan Society of Nephrology have provided guidelines for dialysis facilities during the outbreak of the COVID-19. Some essential measures to limit the risk of COVID-19 in dialysis facilities are given in Table 1.[19]

7. COVID-19 in renal transplant patients

Literature regarding impact COVID-19 in renal allograft recipients (RAR) is lacking. Owing to the effect of long-term use of immunosuppressants, they may have an atypical presentation of the infection and are also at high risk of developing severe disease. Recently Guillen et al. reported a case of a COVID-19 infection in a RAR patient, who initially presented with clinical symptoms of

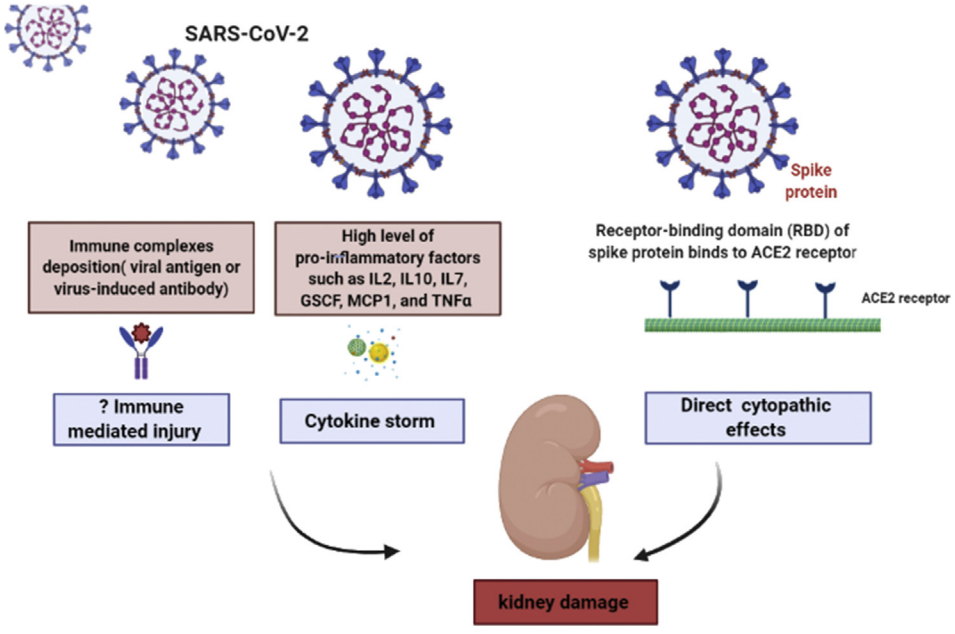

Fig. 1. Pathogenesis of kidney injury by SARS-CoV-2.

Table 1
General measures to mitigate the risk of COVID19 in dialysis facilities.

- Prevention:
  - o Alcoholic solutions dispensers should be provided in waiting rooms of dialysis facilities. Accompanying persons and the patient should use hand sanitizer while entering the dialysis facility.
  - o Patients should be advised to use face masks and instructed to cover nose and mouth when coughing or sneezing. Tissues should be discarded in a plastic-lined waste receptacle.
  - o Patients should be advised to wash hands and fistula arm before initiating dialysis and should properly disinfect the cannulation area.
- Early recognition:
  - o All symptomatic patients should be identified and screened for novel coronavirus infection. Screening should be done at a single entry to the facility
- Immediate referral:
  - o Patients having symptoms like progressive breathlessness or signs of adult respiratory distress syndrome should receive an immediate referral to the hospital.
- Patient placement:
  - o Suspected or confirmed COVID-19 cases should receive hemodialysis in isolation. Separation of at least 6 feet should be maintained between masked symptomatic patients and others.
- Personal protective equipment (PPE):
  - o Dialysis staff should use precautionary measures by using isolation gowns, gloves, masks, and eye protection (shields or goggles).
  - o They should wash their hands with soap and water and use alcoholic based solutions. Surgical masks should be changed every 4–6 h.

gastrointestinal illness with fever, which subsequently developed respiratory symptoms.[20] Although there is no consensus for the treatment of COVID-19 in RAR patients, a reduction of immunosuppressants with low dose methylprednisolone is an acceptable strategy.[21]

8. Conclusion

The occurrence of kidney dysfunction in COVID-19 patients is frequent and is an independent predictor of mortality. The Pathophysiology of kidney involvement in COVID19 is diverse and complex. Early detection is essential to intervene and prevent further kidney impairment. Strict protocols should be followed to mitigate the risk of infection in dialysis patients.

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Not applicable.

Consent for publication

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Availability of data and materials

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Authors' contributions

Priti prepared the manuscript. Vinant, Devinder and Anil analyzed and interpreted patient data. Priti and Vinant were the primary contributors in writing the manuscript.

Declaration of competing interest

The authors declare that they have no competing interests.

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