The COVID-19 pandemic: consequences for nephrology

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The consequences of the COVID-19 pandemic have been devastating; however, evidence suggests that patients with, or at risk of, kidney disease are disproportionally affected. Patients on dialysis and kidney transplant recipients are at higher risk of adverse outcomes from COVID-19, whereas, conversely, patients with severe COVID-19 are at increased risk of acute kidney injury, with short-term and possibly long-term consequences for nephrological care.

2020 has been a challenge for society and health systems worldwide as a result of COVID-19, which was declared a pandemic by the WHO in March 2020. As of 1 November 2020, the causative virus, SARS-CoV-2, had infected 46 million individuals and caused 1.2 million deaths. Efforts have been invested in the development of mitigation strategies and approaches to manage the acute phase of the illness, as well as in research to provide insights into disease mechanisms. COVID-19 was initially characterized as a febrile respiratory disease but is increasingly recognized as a complex multisystem disease with a wide range of manifestations. Viral injury, uncontrolled inflammation, and the activation of coagulation and complement systems are thought to be important components that underlie disease pathogenesis (Fig. 1).

Early reports, mainly from China, identified underlying chronic kidney disease (CKD) as a risk factor for severe COVID-19 and mortality. A study from New York of over 5,000 individuals with COVID-19 found that age, male sex, heart failure, underlying CKD and a BMI >40 kg/m², were strong predictors of hospital admission and critical illness. The largest study from the UK, which included data from 17 million electronic health records, also identified CKD as a risk factor for mortality in patients with COVID-19, with glomerular filtration rate (GFR) <30 ml/min/1.73 m² and organ transplantation conferring a high risk in multivariate analyses. Patients who receive in-centre dialysis have consistently been shown to be at higher risk of community exposure to SARS-CoV-2 infection. A nationwide study of patients on in-centre dialysis from around 1,300 dialysis facilities in the USA reported the seroprevalence of SARS-CoV-2 antibodies to be 3.5–27.2% — in many places higher than the average of <10% among the general US population.

COVID-19-associated mortality is also high among dialysis and kidney transplant recipients as demonstrated by a population-based registry study of >4,000 patients with a diagnosis of COVID-19 who were receiving kidney replacement therapy (KRT). Among patients on dialysis (n = 3,285), the 28-day mortality risk was 21.1 times higher than the expected 1.2% mortality of propensity-score matched historical controls. In transplant recipients (n = 1,013), the mortality attributable to COVID-19 was 19.9% compared with an expected mortality of 0.2% in the matched control group. The study also identified striking differences between age groups: 28-day mortality among patients on dialysis aged >75 years was as high as 31.4%, with a higher mortality risk for men than women, similar to observations in non-CKD populations. The reason for the sex differences are not fully understood, but hormonal, behavioural and genetic factors have been proposed. Age was likewise an important risk factor for mortality among kidney transplant recipients, evidenced by a mortality of 44.3% among those aged >75 years. Interestingly the mortality risk in this group was higher in women than in men. In both groups, the presence of multimorbidities also affected outcomes. Geographical differences also existed, which are likely associated with the extent of disease spread in different regions.

In addition to the recognition of CKD as a risk factor for poor outcomes among patients with COVID-19, early evidence also identified acute kidney injury (AKI) as an important complication of severe COVID-19. Most often, the AKI is mild to moderate, involving a rise in serum creatinine level and signs of kidney damage such as haematuria and proteinuria. However, a minority experience acute kidney failure requiring kidney replacement therapy (KRT). The consequences of post-AKI kidney damage are severe, with a mortality rate probably as high as 40–60% in ICU patients with AKI. In transplant recipients, the mortality attributable to AKI is 44.3% among those aged >75 years.

In short, SARS-CoV-2 kidney injury is not a mild complication of the virus but an acute multisystem disease with short-term and possibly long-term consequences for nephrology and medicine in general.
Key advances

- Underlying chronic kidney disease (CKD) is a risk factor for severe disease and mortality in patients with COVID-19; COVID-19-related mortality is higher in dialysis and transplant recipients than in the general population.
- Acute kidney injury (AKI) is an important complication of severe COVID-19; critically ill patients in the intensive care unit—particularly those on mechanical ventilation—are more likely than patients with milder disease to require dialysis, which is associated with higher mortality.
- Most patients who survive COVID-19-associated AKI regain kidney function but up to 30% may remain on dialysis at discharge.
- Mitigation strategies to reduce exposure to the SARS-CoV-2 virus are vital to protect high-risk CKD populations; whether COVID-19 will increase the prevalence of CKD in the long term and potentially increase the demand for maintenance dialysis is unclear and requires further investigation.

Whether COVID-19 will escalate the long-term risk of CKD... requires further investigation.