Kidney Issues Associated with COVID-19 Disease

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Infection with SARS-CoV-2 and the resulting COVID-19 can cause both lung and kidney damage. SARS-CoV-2 can directly infect renal cells expressing ACE2 receptors, resulting in kidney damage, and acute kidney injury (AKI) has been reported in COVID-19 hospitalized patients. The pathophysiology of COVID-19-associated AKI is multifactorial. Local and systemic inflammation, immune system dysregulation, blood coagulation disorders, and activation of the renin-angiotensin-aldosterone system (RAAS) are factors that contribute to the development of AKI in COVID 19 disease. COVID-19 patients with kidney involvement have a poor prognosis, and patients with chronic kidney disease (CKD) infected with SARS-CoV-2 have an increased mortality risk. CKD patients with COVID-19 may develop end-stage renal disease (ESRD) requiring dialysis. In particular, patients infected with SARS-CoV-2 and requiring dialysis, as well as patients who have undergone kidney transplantation, have an increased risk of mortality and require special consideration. Nephrologists and infectious disease specialists face several clinical dilemmas in the prophylaxis and treatment of CKD patients with COVID-19. This entry presents recent data showing the effects of COVID-19 on the kidneys and CKD patients and the challenges in the management of CKD patients with COVID-19, and discusses treatment strategies for these patients.

Keywords: chronic kidney disease ; COVID-19 ; hemodialysis ; kidney transplantation ; peritoneal dialysis ; SARS-CoV-2

COVID-19 has a broad clinical spectrum. In the context of COVID-19 disease, the organ most commonly affected is the lung. The kidney is another organ that can be affected by SARS-CoV-2 [1].

SARS-CoV-2 invades cells by binding its spike protein to the angiotensin-converting enzyme2 (ACE2) receptor on the cell surface [1]. Therefore, SARS-CoV-2 can affect any system in which ACE-2 receptors are present, including cardiovascular, nervous, immune, gastrointestinal, and renal systems [1].

In addition to the spike protein, SARS-CoV-2 encodes several accessory proteins, including ORF3a, ORF3b, ORF6, ORF7a, ORF7b, ORF8, ORF9b, and ORF9c. These accessory proteins play various roles in viral replication, immune evasion, and pathogenesis. Studies have shown that SARS-CoV-2 can directly infect renal cells expressing ACE2 receptors, resulting in kidney damage [2]. The virus can disrupt normal kidney function and cause inflammation and injury. The presence of SARS-CoV-2 RNA was detected in kidney tissue samples from COVID-19 patients, indicating active virus replication in the kidneys. In addition, some accessory proteins of SARS-CoV-2 were found to contribute to kidney injury. The ORF3a protein, for example, has been associated with the promotion of apoptosis and inflammation in kidney cells. It can disrupt ion transport mechanisms and impair renal filtration function [2][3]. Other studies suggest that dysregulation of the Renin-Angiotensin-Aldosterone System (RAAS), which plays a critical role in regulating blood pressure and fluid balance, may also be involved in kidney complications associated with COVID-19 [4]. The interaction between the spike protein and the ACE2 receptor may disrupt the RAAS and lead to kidney dysfunction.

It should be noted that research into the specific mechanisms underlying renal problems associated with COVID-19 is ongoing and our understanding is constantly evolving. Nevertheless, the available evidence suggests that accessory proteins of SARS-CoV-2, together with the interaction between the spike protein and the ACE2 receptor, contribute to kidney complications in COVID-19 patients.

SARS-CoV-2 activates the immune system, resulting in the production of cytokines known as cytokine release syndrome [5]. This dysregulated immune response can cause systemic inflammatory syndrome, acute distress syndrome, and multi-organ damage. This inflammatory response persists even when the viral load decreases [5].

Infection of endothelial cells causes endotheliitis, which leads to vasoconstriction. Furthermore, the synergistic effect of inflammation and hypercoagulability leads to hypoperfusion, organ ischemia, and tissue damage [6].

SARS-CoV-2 is detected in the renal parenchyma [7]. Proteinuria, hematuria, and elevated BUN and creatinine levels have been noted in SARS-CoV-2 patients. Tubular damage and collapsing glomerulopathy were observed in affected patients [8][9]. Acute tubular damage characterized by mild focal acute tubular necrosis is the predominant finding in renal biopsies from COVID-19 patients with AKI [9]. In addition, peritubular erythrocyte aggregation and glomerular fibrin thrombi with ischemic collapse have been reported [9]. Moreover, collapsing glomerulopathy associated with COVID-19 is characterized by podocyte damage [10]. The collapsing glomerulopathy associated with COVID-19 has been associated with high-risk APOL1 genotypes [11]. The relationship between COVID-19 and CKD appears to be bidirectional and complicated.

The risk of dying in hospital is higher in hospitalized COVID-19 patients with acute kidney injury (AKI) or CKD (46.4%) than in hospitalized patients without AKI or CKD (7.3%) [12]. Interestingly, hospitalized patients affected with AKI or CKD require renal replacement therapy after discharge [12].

According to secondary meta-analyses [13] and nationwide analyses [14], hospitalized COVID-19 patients with CKD, including CKD stages 3–5, maintenance dialysis, and kidney transplantation, had a higher mortality rate than COVID patients without CKD [14]. An increased mortality rate of over 25–30% has been reported in hemodialyzed patients with COVID-19 [15][16]. Hemodialysis (HD) patients have several comorbidities such as diabetes and cardiovascular disease, which makes them more susceptible to SARS-CoV-2 infection [17]. In addition, HD patients have a weaker immune system, and CKD is considered a secondary immunodeficiency that increases the risk of infection and leads to increased mortality [17]. Therefore, special considerations should be made in medical management and prophylaxis.

Management of COVID-19 kidney transplant patients is another challenge. The balance between medical treatment of COVID-19 and immunosuppressive drugs to prevent graft rejection is an important clinical problem [18]. In addition, renal transplant patients usually present with atypical symptoms that complicate the diagnosis of COVID-19 [18].

CKD patients or ESRD patients on dialysis and kidney transplant patients are at increased risk of infection. Vaccination against SARS-CoV-2 has been reported to reduce severe infections and deaths in both CKD patients and renal transplant patients [18][19]. However, isolated cases of glomerulopathy have been reported after vaccination against COVID-19 [20].

The medical management of COVID-19 CKD patients is more complicated. Drug treatment includes anti-inflammatory (nonsteroidal) agents, anticoagulants, monoclonal antibodies, and multiple antiviral therapies alone or in various combinations [21].

Even after the approval of various antiviral therapies and vaccines, the mortality rate is not under control because new variants of the virus with altered genome sequences continue to emerge [21].

Long-term effects of COVID-19 on renal function have been reported [22]. Further studies are needed to explore and understand the long-term effects of the COVID-19 pandemic. Although the World Health Organization declared the end of the COVID-19 global emergency on 5 May 2023, COVID-19 remains a public health threat.

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