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Assessing the impact of COVID-19 on renal health in recovered patients: a multi-center longitudinal study

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Abstract

The coronavirus pandemic of 2019 has become a global health problem. This article presents an analysis of the scientific literature focusing on the pathogenetic and clinical parallels between the kidneys and SARS-CoV-2, as well as the state of kidney health in patients who have recovered from treatment. The goal is to analyze the effects of COVID-19 on kidney health in recovered patients amid an unprecedented flow of scientific data. This study was conducted in 2020-2023 using modern scientific databases such as Scopus, PubMed, Google and others to examine the impact of COVID-19 on kidney health in recovered patients. The analysis of studies included data from analytical reviews, meta-analyses, and scientific reports of clinical trials, using the following keywords: "kidney disease", "health impact of SARS-CoV-2", "acute kidney injury". The majority of patients infected with coronavirus had kidney damage, comorbidities, and insufficiency of many organs. Deterioration of kidney function after COVID-19 is observed not only in patients with urological diseases, but also in those patients who have not previously had kidney problems. Despite the fact that nephrologists have developed rapid response methods and defined emergency tactics for the management of patients with kidney damage in COVID-19, cases of kidney disease continue to increase, and the percentage of patients in intensive care units is increasing. For better medical outcomes, careful monitoring of renal function and early laboratory diagnostics to determine biochemical markers, both serum, and urine, in patients with COVID-19 and continuous monitoring of these indicators after recovery are recommended.

Keywords: coronavirus, COVID-19, renal function, kidney health, urological diseases.

Introduction

The pandemic has spread to more than 160 countries, with million people have been infected with the coronavirus disease. COVID-19 initially affects the lungs and is accompanied by damage to other organs [1, 2, 3]. Symptoms associated with coronavirus infection can last for more than a month and affect primarily the respiratory system, as well as gastrointestinal, cardiovascular, urinary, bone and muscle, and other multiple organ damage [2, 4, 5].

An increasing number of patients with the virus are reported to have a list of urological symptoms that should not be ignored by nephrologists today. In SARS-CoV-2 disease, the most common symptoms of urological complications are increased urination. The course of coronavirus infection may have its own characteristics in patients with renal failure, including kidney disease, renal transplant recipients and those on haemodialysis.

The onset of viral damage occurs due to the effect on angiotensin-converting enzyme-2 (ACE-2)

receptors, no less important mechanisms of viral damage are reactions of complement system dysfunction, immunological and inflammatory reactions, leading to multiorgan failure. Post-COVID syndrome has been described in patients on the kidneys are manifested by increased creatinine concentration, proteinuria, microhaematuria (Figure 1).

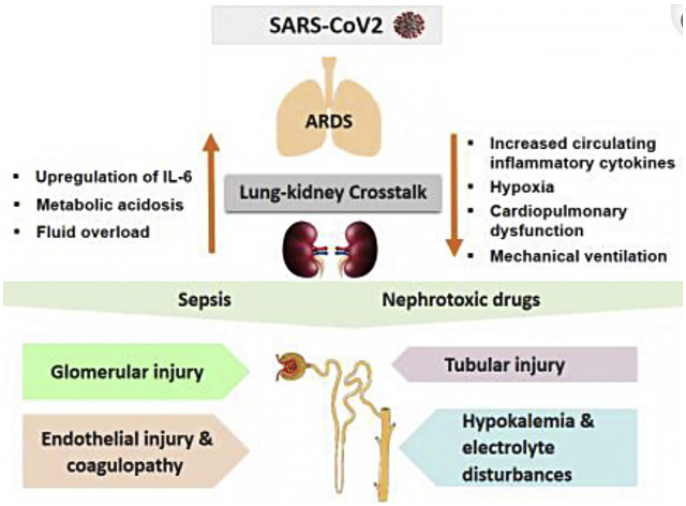


Figure 1 – Crosstalk in the lungs and kidneys, pathomechanism of kidney damage in COVID-19 (2021) [3]

Despite the fact that most patients feel recovered after a coronavirus infection, there is a lot of evidence that raises the problem of post-COVID damage to various organs and tissues, including the kidneys, which leads to impaired physiological functions and problems in the social sphere.

People with COVID-19 have a significantly risk of significant deterioration in kidney function, patients who have not been to hospital with COVID-19 have a nearly 200% risk of end-stage renal disease compared to people who have not had the coronavirus [6].

The depth of post-COVID renal damage depends on the severity of the disease and the presence of acute renal injury before COVID-19. Researchers have shown that patients with acute renal injury (AKI) associated with COVID-19 had a significant decrease in GFR, increased creatinine concentration, proteinuria, microhaematuria in the long-term period, and required renal replacement therapy. Other risk factors for severe damage were old age, chronic kidney disease (CKD), diabetes, hypertension, history of coronary heart disease, hospitalisation, and long-term hospital stay [7].

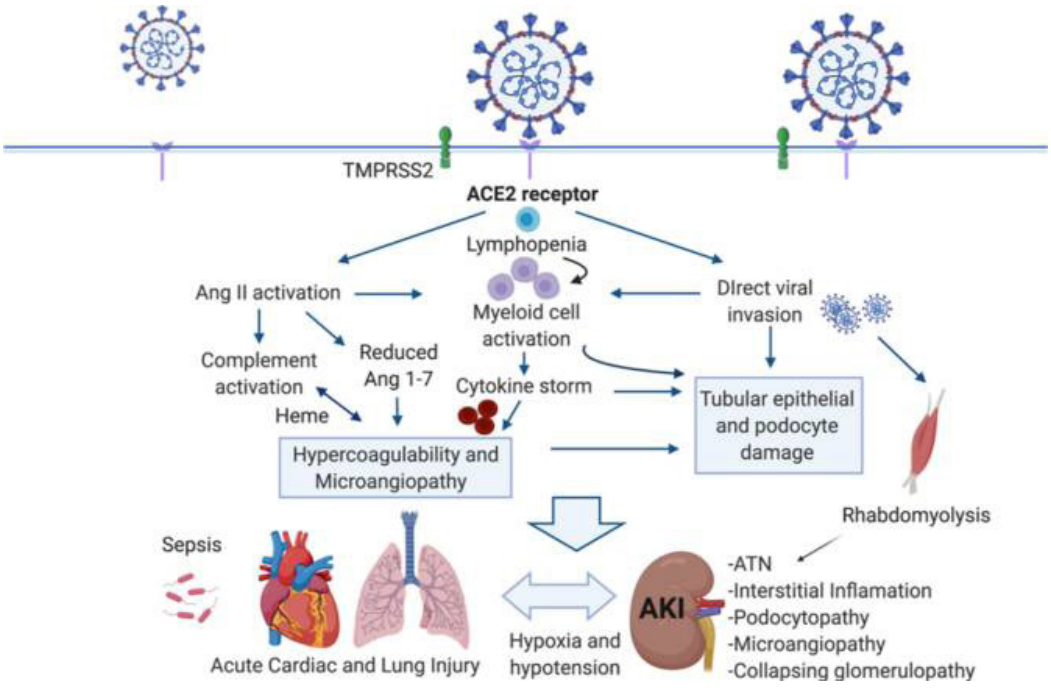
Symptoms of renal dysfunction in patients with infection and SARS range from an increase in the number of red blood cells in the urine (hematuria) to AKI with the development of dialysis [8]. Kidney damage in patients increases dramatically with a decrease in the number of lymphocytes in the peripheral blood and a significant increase in the concentration of procalcitonin, C-protein and interleukins in the blood serum.

Activation of the cytokine pathway in urological diseases leads to the development of multiple organ failure, which often causes death. Researchers have shown that the highest level of T-cell stimulation, which occurs under the influence of the virus, is observed in the exudative stage. At this stage, humoral immunity cells are not detected. At the next stage (proliferation), there is a decrease in the levels of T cells. As a result of autoimmune damage and inadequate immune response, prolonged lymphopenia, and atrophy of lymphoid organs, the number of T-suppressors (CD8+) is increased over T-helper cells (CD4+) [6, 7].

The purpose of this review is to analyse the literature on the impact of COVID-19 on kidney health in recovered patients amidst an unprecedented flow of scientific data.

Material and methods

This study was conducted by analyzing the literature for 2020-2023 using modern well-known scientific databases such as Scopus, PubMed, Google, and others to study the impact of COVID-19 on kidney health in recovered patients. Data from analytical reviews, meta-analyses, and scientific reports of clinical trials were included in our analysis of studies. In this regard, the following keywords were used in the search and analysis: “kidney disease”, “impact of SARS-CoV-2 on health”, “acute kidney injury”. Short and promotional messages were not used in the analysis of the scientific literature. The scientific publications Soliman NA., 2021 (Figure 1); Batlle D, 2020 (Figure 2) were used to create the charts.



Ang 1-7 – angiotensin 1-7.
ATN – acute tubular necrosis.
ACE2 – angiotensin converting enzyme 2.
SARS-CoV-2 – severe acute respiratory syndrome, coronavirus 2.
TMPRSS2 – transmembrane protease, serine 2.

Figure 2 – Pathogenesis of kidney damage in COVID-19 (2020) [9]

Results and discussion

Impact of COVID-19 on kidney health in patients who have recovered

Urological problems are one of the many complications of coronavirus and a significant risk factor for death. During the pandemic, the number of reports of AKI increased in line with the rise of this severe complication, which followed lower respiratory tract infections and respiratory failure (Figure 2) [9].

Targeting ACE2 with SARS-CoV-2 leads to angiotensin dysregulation, activation of the innate and adaptive immune pathway, and hypercoagulability, resulting in organ damage and ARF associated with COVID-19. Crosstalk between the damaged lungs, heart and kidney can further spread the damage. CD8+ T cells and natural killer cells can inhibit macrophage activation and are potential targets for SARS-CoV-2.

It was found that coronavirus RNA in the kidneys of patients with AKI, compared to the lower incidence of SARS-CoV-2 renal failure in patients without the virus, and RNA was detected in a small number of patients [10]. Researchers have confirmed the link between kidney disease and mortality in hospitalized patients. [11]. It was shown that those patients who had signs of renal dysfunction and who were diagnosed with AKI during treatment in inpatient units had a poor clinical picture against the background of elevated serum creatinine, proteinuria, and hematuria compared to patients with normal levels of these parameters; patients with AKI at stage II had an increased risk of mortality, and at stage III - critical kidney injury with a fatal outcome [11].

In another single-centre study in Wuhan (China), among the total number of patients with confirmed pneumonia, AKI was reported in 4 %, the incidence of AKI continued to increase throughout the study [11].

Kidneys and COVID-19: mechanisms of damage

Scientists suggest the following pathomechanisms of kidney damage in COVID-9:

1) destructive metabolic changes with activation of catabolic processes, cell damage leading to electrolyte disturbances [12]. The accumulation of ACE2 caused by the virus can contribute to an imbalance and activation of the renin-angiotensin system, which leads to inflammation, vasoconstriction, and fibrosis.

Based on reports that virus RNA was identified in kidney tissue in a patient with SARS, data were presented on the isolation of the virus in the patient's urine; the accumulated nucleocapsid antigen of SARS-CoV-2 was found by immunohistochemistry and was identified in renal tubular cells, confirming that the kidneys are a target of the coronavirus [13, 14].

Recently, RNA sequencing of human tissues demonstrated the accumulation of the following genes in the kidneys: CTSL, TMPRSS2, and ACE2, which contribute to SARS-CoV-2 infection [15, 16].

2) Activation of the inflammatory and immune response, enhanced by the release of circulating immune complexes. In this case, the patient has elevated plasma levels of pro-inflammatory cytokines; MIP1A; GCSF and MCP1, indicating the presence of an excessive proinflammatory state in the progression of the disease [17]. High concentrations of circulating pathological mediators interact with renal cells, leading to microcirculatory disorders, tubular damage, and endothelial dysfunction [18].

3) COVID-19 infection leads to coagulopathy, a procoagulant state with vascular damage, patients have microvascular thrombosis, acute renal necrosis, accompanied by glomerular ischaemia and fibrinoid necrosis, i.e., irreversible renal damage [9]. The virus leads to chronic reactive endotheliitis with disseminated vascular damage and is one of the significant causes of clinical symptoms [19]. All this gives grounds for choosing a treatment aimed at stopping viral replication and simultaneously restoring the endothelial state for patients with comorbidities [20].

4) In patients in serious condition with prolonged stay in the hospital, there are a number of factors that further aggravate urological problems, including haemodynamic disorders, nephrotoxic drugs, mechanical ventilation, and sepsis [21].

SARS-CoV-2 and kidney health

Lippi G, 2019, confirmed that the severity of COVID-19 is associated with decreased levels of blood electrolytes in both patients with severe and acute disease [22]. De Carvalho H, in his study, demonstrated the presence of hyponatremia, hypokalemia in patients with infection during treatment in the emergency department [23].

Sarwal [24] followed 1570 patients with COVID-19 and showed that half of the cases had ESRD, 71.8% had recovery of renal function, while 28.2% of patients were discharged with AKI. These patients had grade III kidney disease, congestive heart failure, and the use of non-invasive mechanical ventilation. Early detection and proper treatment of patients at risk of progression of AKI can improve the results of therapy, reduce the long-term consequences of CKD and have a positive impact on health status [24].

A study of 201 people (average age 45 years) conducted in 2020 [25] found the average time to organ damage in people aged 18 years with severe clinical symptoms after treatment and recovery compared to a control group of the same age and gender. Among those examined, 19% were hospitalised and had a low risk of mortality. It should be noted that 42% of the subjects had 10 or more long-term symptoms of COVID within 4 months after recovery, and 60% of people had serious long-term symptoms, namely shortness of breath, mild heart failure, headache, fatigue and myalgia, lung function, liver and kidney dysfunction [25].

Lumlertgul N and colleagues showed in their study that 7.5% of patients had AKI; stage I was characteristic of 45.7% of these patients of the disease 3 weeks after the onset. Compared to patients with ESRD, there was a higher recovery rate for ESRD. Careful statistical analysis allowed us to identify patients who recovered from AKI, with data showing that half of the early AKI in patients with COVID-19 was mild and patients recovered easily [11].

According to another study of 198 patients followed for 12 days, 118 (59.6%) of patients with COVID-19 had remission of pneumonia [2], and urine tests were negative in the long-term period. It was shown that 4 patients with AKI achieved full recovery of renal function during follow-up, but there was a pattern that patients with severe AKI had more adverse outcomes after severe pneumonia [2, 11]. At the time of hospital discharge, not a significant number of patients were on dialysis, and a greater percentage of patients recovered renal function, with one-third of patients experiencing major adverse renal events at 90 days (MAKE90) [11].

Liberali [7] found a partial deterioration in renal function after coronavirus infection in patients with advanced CKD and transplant recipients, but the short follow-up period did not allow for any firm conclusions in this regard.

Due to the complexity of determining the treatment tactics for patients with chronic nephropathy after COVID-19, they require an individualized approach.

In the therapeutic treatment of patients in this group, more extensive data on the average time to achieve viral clearance and patient's immune response (antibody production) can help adjust

treatment regimens and the logistical components required for this. Patients with urological disease have been shown to have slower viral clearance than the general population, with an average of 32.4 days [7, 26]. It was found that patients' recovery time after infection was longer due to sporadic cases or high viral load.

In summary, infection is a serious medical problem for patients with nephropathy. The results of the Liberali M study [7] show delayed clearance of the virus in this challenging cohort of patients, although there is a satisfactory immune response (presence of specific antibodies). The role of immunological pathomechanisms in urological diseases remains unknown, and elucidation of their peculiarities in the body during the disease will enable the development of relevant vaccines. For those patients who are at risk of morbidity with possible development of pathological conditions of the urological system, it is necessary to take all measures to prevent infection and detect the disease at an early stage [7].

Conclusion

The COVID-19 pandemic has become a public health crisis that has created numerous unprecedented challenges for global health systems. Exposure to COVID-19 continues to lead to kidney disease as more and more reports emerge, so this issue is attracting nephrologists who are actively working on early diagnosis and conceptual treatment. The pandemic is harming patients with urological diseases by disrupting their conservative follow-up care. The ultimate impact of COVID-19 infection on patients with urological diseases remains to be seen. AKI is common among patients hospitalised with COVID-19, the disease occurs in the early stages and is preceded by lung damage.

Recommendations

To optimize treatment, physicians are advised to closely monitor renal function and early urine sediment testing, as well as to determine urinary biochemical markers in patients with COVID-19 and monitor these parameters after recovery. Continuous updating of preventive, diagnostic, and therapeutic strategies is crucial to improve clinical outcomes and reduce morbidity. Researchers need to continuously monitor scientific data in patients with kidney disease after COVID-19 to determine the current state of the problem and to identify unresolved issues. The healthcare system needs to review and improve treatment guidelines for these patients in order to implement a personalized approach.

Prospects for further research

It is important to continue studying the impact of coronavirus on kidney function and the effectiveness of treatment. The next step may be to develop diagnostic guidelines and criteria for identifying those at risk of developing renal dysfunction in COVID-19 and personalised treatment.

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