

**Review Article****Acute Kidney injury and COVID-19 infection**Katarína Gazdíková<sup>1</sup>, Martina Slováčiková<sup>2</sup><sup>1</sup>Department of General Medicine, Faculty of Medicine, Slovak Medical University in Bratislava, Slovakia<sup>2</sup>Department of Long-term Care of University Hospital in Bratislava, Slovakia and 1st Department of Internal Medicine of Slovak Medical University in Bratislava and University Hospital in Bratislava, Slovakia**Abstract**

COVID-19 infection is currently one of the most discussed medical and socio-economic issues. Generally, it manifests as pneumonia. However, there is a growing body of evidence of multi-organ damage. Manifestations of kidney involvement associated with infection of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus include proteinuria, hematuria, and acute kidney injury (AKI). The presence of AKI negatively affects the prognosis and mortality rate of this infection. The pathogenesis of AKI associated with COVID-19 infection is complex and include the direct and indirect mechanism of renal damage by the virus. Identifying risk factors for AKI development associated with COVID-19 can contribute to improved management as well as patient prognosis.

**Keywords:** COVID-19 infection, risk factors, acute kidney injury, pathogenesis, mortality

**Introduction**

Coronavirus disease (COVID-19) is an infection that has been one of the most frequently discussed medical as a socio-economic issues over the past two years. Common risk factors for COVID-19 infection and its severe course include age, race, male gender, chronic lung disease, cardiovascular disease (CVD), diabetes mellitus (DM), immunodeficiency, kidney and liver disease, obesity/overweight, smoking and polypharmacy [1, 2].

The most common manifestation, that directly threatens the patient's life, is pneumonia. Unfortunately, the lungs are not the only affected organ, but there are currently increasing data on damage to other organs/systems, such as the kidneys, liver, gastrointestinal tract, heart, central nervous system, and bone marrow, which can also adversely affect the course and prognosis of the disease [3].

**Prevalence of AKI in COVID-19 infection**

Manifestations of kidney involvement associated with infection of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus include proteinuria, hematuria, and acute kidney injury (AKI).

Published studies show that AKI that is complicating COVID-19 in-

\*Corresponding Author: Katarína Gazdíková, MD., PhD., Ass. Prof.

Department of General Medicine Faculty of Medicine, Slovak Medical University in Bratislava, Limbova 14, 833 01 Bratislava, Slovakia

Received: June 13, 2022

Published: June 23, 2022

fection varied during the pandemic depending on the type of mutation and vaccination status [4, 5, 6, 7]. Early published reports from China of hospitalized patients with COVID-19 reported rates of AKI at 5 - 29% [8, 9, 10, 11, 12, 13, 14, 15]. In contrast, the rates of AKI among patients hospitalized during the first COVID-19 wave in the United States were substantially higher ranging from 32 to 57% overall, with 9 - 20% developing AKI requiring renal replacement therapy (AKI-RRT) [5, 16, 17]. The patients with COVID-19 infections also had an increased need for RRT, intensive care unit (ICU admission), and mechanical ventilation and they experienced higher rate in-hospital mortality [17]. Published rates of AKI in European cohorts have been similarly high (26%) [18] and smaller European cohorts of ICU patients with COVID-19 have been reported with AKI rates ranging between 50 and 80% [19, 20]. In the recent published COVID-19 cohorts in 15 - 30% of hospitalized patients were developed AKI [5, 6]. This is consistent with the data of the international meta-analyses in which were found a pooled prevalence of AKI in 17% (0.5 - 80.30%) of all patients and 28% of hospitalized patients, a rate that rose to 45% when considering only ICU patients, with AKI-RRT rates of 5 - 9% among all hospitalized patients and 19% among ICU patients [21, 22]. The results of study of Sabaghian et al. [23] demonstrated that 69% of COVID-19 infected patients had AKI during admission and 27.9% exhibited AKI after being admitted.

Notably, AKI appears to disproportionately affect racial and ethnic minorities [5, 17, 24, 25]. A significant risk factor for AKI in COVID-19 infected patients is also male gender [26, 23]. Incidence of AKI in men with COVID-19 is significantly higher than in women with COVID-19. For instance, in one study, the number of male COVID-19 patients with AKI was 34 times higher than that of women (1608 vs 47) [5].

Higher prevalence of AKI were published in the hospitalized kidney transplant recipients and in the patients required hemodialysis (48% and 22%, respectively) [25].

The presence of AKI during COVID-19 infection is clearly an adverse factor associated with poor prognosis and an increased mortality rate [27, 28, 29].

Chan et al. [29] found 50% mortality in the patients with AKI compared to 8% in patients without AKI. In critically ill patients with AKI

**Citation:** Katarína Gazdíková<sup>1</sup>, Martina Slováčiková<sup>2</sup>. Acute Kidney injury and COVID-19 infection. *Int Clin Img and Med Rew.* 2022; 2(3): 1077.

requiring RRT 55% mortality was recorded and, when necessary, mechanical ventilation deemed exceeded 70% [16, 29, 30].

### Pathophysiology of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus infection

The binding of SARS-CoV-2 to the cellular angiotensin converting enzyme 2 (ACE2) receptor [31] is responsible for multi-organ tropism, via the cell's transmembrane spike (S) glycoprotein, which consists of two subunits. The S1 subunit is responsible for binding to the host cell receptor, and S2 enables the fusion of the viral membrane with the infected cell membrane [32]. The co-expression of angiotensin converting enzyme 2 (ACE2) with the transmembrane serine protease 2 (TMPRSS), whose proteolytic activation is required by the spike glycoprotein, is crucial for SARS-CoV-2's entry into the host cells [33]. SARS-CoV-2 in the cytosol of an infected cell begins the translation of its ribonucleic acid (RNA) and virion synthesis. Genome replication occurs in the endoplasmic reticulum (ER) and Golgi complex vesicles. Cells expressing ACE2 messenger RNA (mRNA) in the kidney are epithelial cells in the proximal tubules and podocytes, which can lead to the acute tubular necrosis, endothelial damage, and mitochondrial dysfunction.

### Kidneys and COVID-19 infection

The kidneys are among the organs that can fail due to COVID-19 infection. Non-acute damages (such as proteinuria or hematuria without renal failure) or acute injuries (such as AKI) are some instances of SARS-CoV-2 infection impacts on kidneys [34, 33].

The pathogenesis of renal damage involves the direct mechanisms of the virus leading to the collapsing glomerulopathy, endothelial damage and activation of coagulation, the renin-angiotensin system and complement, and inflammation, as well as indirect mechanisms due to systemic reactions to viral infection, or the effect of the virus on other distant organs. Significant role in kidney damage play crosstalk (type I cardiorenal syndrome) damage [33, 35, 34, 4]. The severity of the disease is also determined by non-specific factors of critically ill patients, such as artificial ventilation, hypoxia, hypotension, hypovolemia, fever or sepsis, diarrhea, low cardiac output, and nephrotoxic drugs [4]. The most common manifestations of the renal impairment include AKI, hematuria, and proteinuria [36].

The potential mechanisms of renal damage from SARS-CoV-2 infection are shown in Table 1.

### Acute kidney injury risk factors in COVID-19 infected patients

Risk factors for the development of AKI in patients with COVID-19 infection include demographic risk factors, admission factors, and hospitalization-related factors. Demographic factors include older age, male gender, comorbidities as DM, hypertension (HTN), cardiovascular disease (CVD), congestive heart failure (CHF), heart diseases with changes in the electrocardiogram (ECG; ST segment, T wave, QT interval), overweight/obesity, chronic kidney disease (CKD), renal transplantation, liver disease, immunodeficiency (cancer patients, use of immunosuppressants), smoking, and genetic factors - ACE2 polymorphism and the L1 apolipoprotein risk variant (risk of COVID-19 associated nephropathy COVAN) [37].

**Table 1:** Potential mechanisms of renal damage in SARS-CoV2 infection. (adjusted according to [35])

Components of SARS-CoV-2	Mechanism of kidney damage
Cytopathic effect of replication virus	Immune-mediate tissue damage
	Glomerulopathy
	Tubular injury
Renin-angiotensin-aldosteron system abnormalities	Polymorphism in ACE2
	Proinflammatory properties of upregulated AGII
	Upregulation/downregulation of ACE2
Ischemic injury	Septic shock and inflammation
	Hypoxia
	Hypercapnia
	Mechanical ventilation
Rabdomyolysis	Medullary vasoconstriction, intrarenal hypoxia and damage of renal cells by reactive oxygen species
Microthrombi	Inflammatory infiltrations, obstructions and subsequent hypoxia
Hyperinflammation	Cytokine storm
	Complement activation

*ACE2 - angiotensin-converting enzyme 2; AGII – angiotensin II; SARS-CoV-2, severe acute respiratory virus-2*

Notably, AKI appears to disproportionately affect racial and ethnic minorities [5, 17, 24, 25]. The next risk factor for AKI in COVID infected patients is male gender [26, 23]. In the study of Bowe et al. [5] the number of male COVID-19 patients with AKI was 34-times higher than that of women (1608 vs 47).

Risk factors already present at the admission include the severity of the COVID-19 infection, the degree of viremia, respiratory status, the presence of non-respiratory organ manifestations, e.g., diarrhea, leukocytosis, lymphopenia, elevated inflammatory markers, e.g., ferritin, high sensitivity C-reactive protein (hsCRP), D-dimer, hypovolemia/dehydration, rhabdomyolysis, drug use (angiotensin-converting enzyme inhibitors /ACEI/ or angiotensin receptor blockers, statins, non-steroidal anti-inflammatory drugs /NSAID/). Potential risk factors associated with hospitalization include nephrotoxins (drugs, contrast agents), the need for oxygen treatment - non-invasive positive lung ventilation, mechanical ventilation, high positive end-expiratory pressure (fluid overload/hypovolemia) and other characteristics of the critical condition - the need for hospitalization in the ICU, the need for vasopressors, acute distress syndrome [38, 37]. On the other hand the results of Sabaghian et al. [23] study demonstrated that 69% of COVID-19 infected patients had AKI during admission and 27.9% exhibited AKI after being admitted. This consequence shows that drug administration, while patients were admitted, is not an important factor in AKI incidence.

According to Hansrivijit et al. [37] prerenal factors play a key role in the admission of patients with COVID-19 infection, while intrinsic (internal, renal) causes associated with being male, a higher stage AKI (grade 3), a higher basal creatinine value and its high peak, and high serum urea levels play a role in the development of AKI during hospitalization and in patients requiring repletion therapy (RRT). The presence of AKI, whether due to the prerenal or the renal causes, is associated with a high mortality rate.

Sabaghian et al. [23] in the large a complete and comprehensive survey

study focused on reviewing original articles and case reports indexed in various databases such as PubMed/Medline, Embase, and WoS demonstrated that COVID-19 infected patients with AKI in comparison to non-AKI patients had a higher rate of other underlying diseases such as CVD (22.2% vs 16.9%), CHF (9.3% vs 7.7%), history of hyperlipidemia (48.7% vs 38.7%), history of CKD (24.2% vs 11.0%), tumor history (11.1% vs 9.4%), respectively. Arrhythmia with a rate of 91.6% in patients in the AKI group and 11.3% in non-AKI patients had the highest variance between these groups. However, the smoking rate and chronic obstructive pulmonary disease (COPD)/ asthma incidence were not significantly different between the two groups, and even the asthma rate was higher in non-AKI patients than in AKI patients.

The outcomes of Sabaghian et al. [23] review determined two underlying diseases DM and HTN, as a two major risk factors for AKI occurrence in COVID-19 patients; 40% of patients in the AKI group and only 29.5% of patients in the non-AKI group had DM. The HTN rate was 72.8 in AKI patients and 52.1 in non-AKI patients. These results confirm that both HTN and DM factors are very influential in AKI incidence.

In the meta-analysis hospitalized kidney transplant recipients was much higher prevalence of AKI and hemodialysis requirement (48% and 22%, respectively) [25]. These findings are consistent with factors specific for kidney transplant recipients including lower functional reserve of kidney allograft, and the toxic effect of tacrolimus in combination with increased susceptibility to prerenal causes of renal dysfunction (dehydration, hypotension, and metabolic disarray), which are absent in the general population [25].

Laboratory risk factors of the AKI [26, 23] are:

- urine - proteinuria, hematuria,
- blood cell count - leukocytosis with neutrophilia and lymphopenia,

- thrombocytosis,
- elevated inflammatory markers - ferritin, interleukin-2R (IL-2R), IL-6, hsCRP, lactate dehydrogenase, procalcitonin,
- vitamin D deficiency,
- elevated coagulation markers - D-dimer,
- renal parameters - elevated creatinine and urea, decreased glomerular filtration.

A summary of the risk factors for AKI associated with COVID-19 infection is shown in Figure 1 [39].

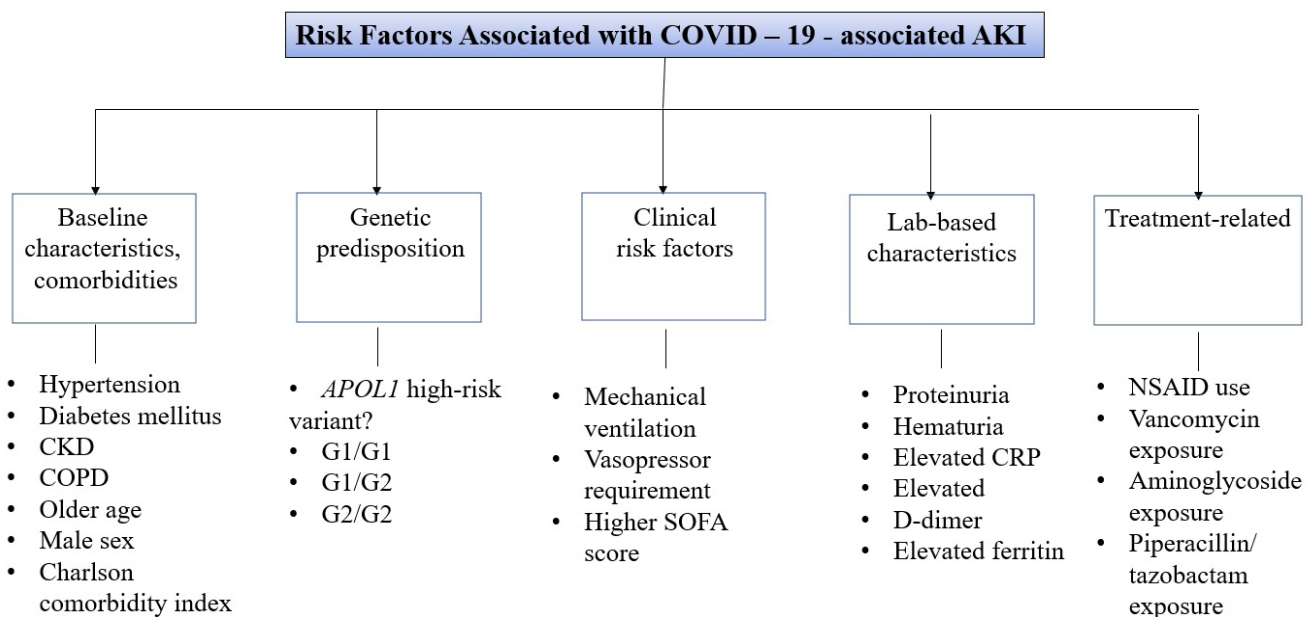
### Pathophysiology of the AKI in patients with COVID-19 infection

The SARS-CoV-2-induced kidney damage is expected to be multifactorial which may be due to its direct and indirect effects.

Directly it can infect the kidney podocytes and proximal tubular cells and based on an ACE2 pathway it can lead to the acute tubular necrosis, protein leakage in Bowman's capsule, collapsing glomerulopathy and mitochondrial impairment. The SARS-CoV-2-driven dysregulation of the immune responses including cytokine storm, macrophage activation syndrome, and lymphopenia can be other causes of the AKI. Organ interactions, endothelial dysfunction, hypercoagulability, rhabdomyolysis, and sepsis are other potential mechanisms of AKI. Moreover, lower oxygen delivery to kidney may cause an ischemic injury [35, 40, 41, 42].

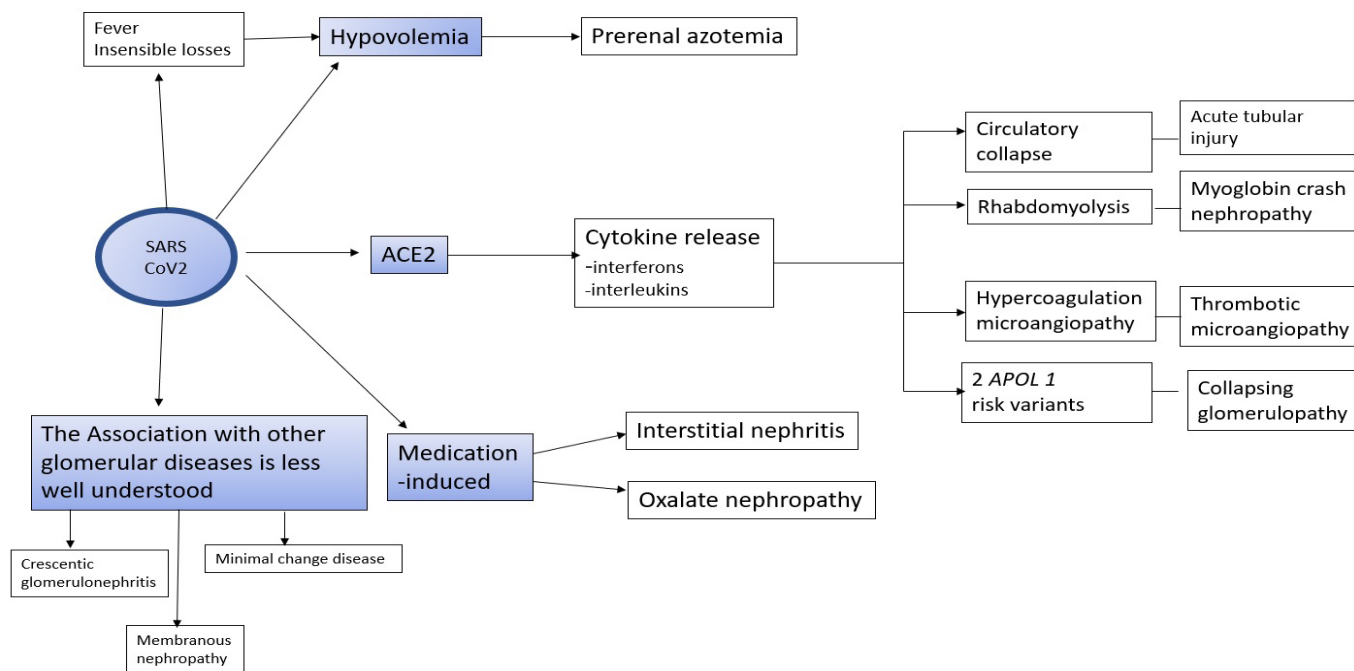
Kidneys can also be affected indirectly by pathophysiological mechanisms such as Acute respiratory distress syndrome (ARDS) caused by COVID-19 infection. SARS-CoV-2 infects alveolar macrophages and lung epithelial cells to amplify viruses and it releases cytokines and chemokines. Infected dendritic cells and the activated macrophages activate immune response extensively and they initiate cytokine storm in the lung. Chemokines release can attract extra inflammatory cells to migrate into the inflammation site that intensify cytokine storm

**Figure 1** :Risk factors for COVID-19-associated acute kidney injury (adjusted according to [39])



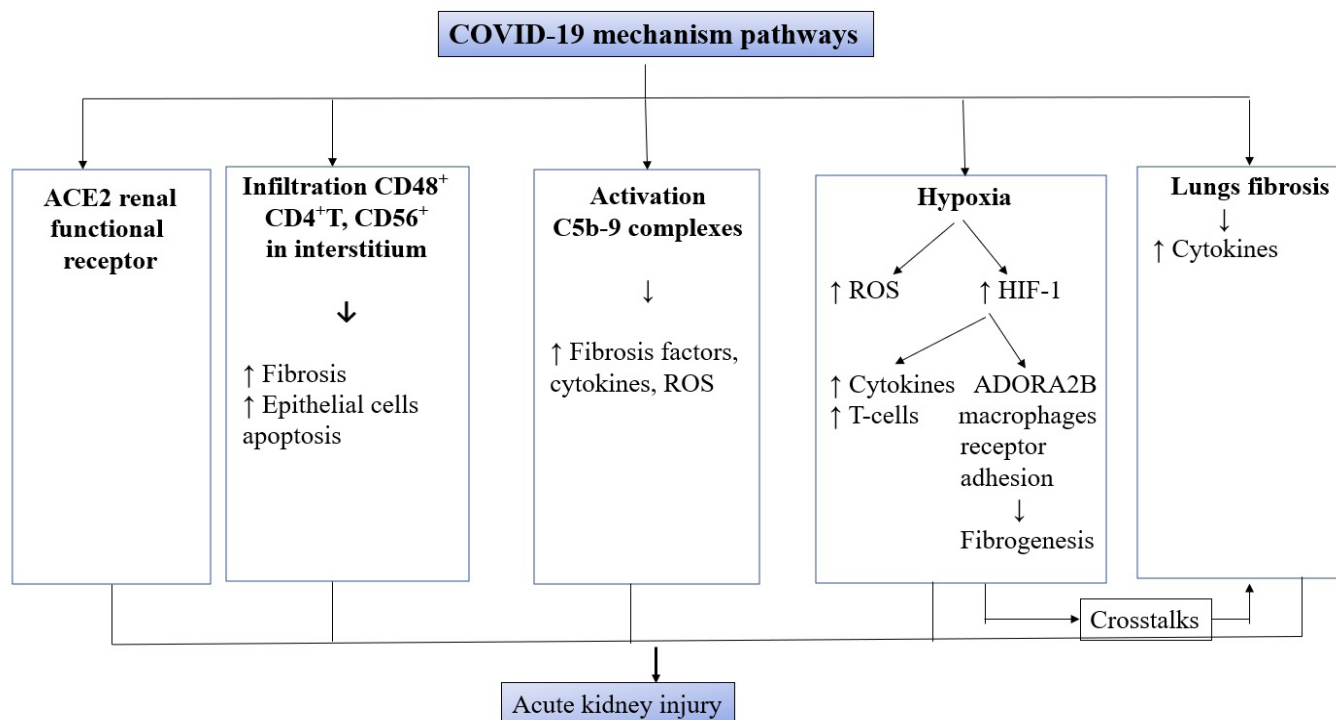
COVID-19 - Coronavirus Infectious Disease 2019, CKD – chronic kidney disease, COPD – chronic obstructive pulmonary, hsCRP –high sensitivity C-reactive protein, NSAID - non-steroidal anti-inflammatory drugs, SOFA, sequential organ failure assessment.

**Figure 2 :**Pathophysiological mechanisms associated with COVID-19–related acute kidney injury (adjusted according to [44])



ACE2 - angiotensin-converting enzyme 2; COVID-19 - Coronavirus Infectious Disease 2019; SARS-CoV-2, severe acute respiratory virus-2

**Figure 3:**Mechanisms of COVID-19 associated acute kidney injury (adjusted according to [45])



ROS – reactive oxygen species, CD – cluster of differentiation, HIF-1 - hypoxia induced factor 1, ACE2 – angiotensin converting enzyme 2

and may have indirect impacts on multiorgan failure, especially kidney, and death. Organ interaction between the damaged lung, the heart and the kidney can deteriorate the viral pathology. Numerous mechanisms including unmasked CVD, cytokine-induced myocardial damage, microangiopathy and viral myocarditis may clarify the main driver of myocardial damage and/or increased levels of troponin in COVID-19 cases. Endothelial dysfunction, microangiopathy, coagulation dysfunction is also involved in the kidney pathology in COVID-19 infection [35, 40].

Hypovolemia, either from diarrheal loss or insensible loss from hyperpyrexia, could lead to tubular injury. Development of secondary infections can cause sepsis-related AKI. Medications are another through the development of interstitial nephritis [43].

A summary of pathophysiological mechanisms for AKI associated with COVID-19 infection are shown in Figure 2 [44] and Figure 3 [45].



## Histopathological changes

The most common injury observed in autopsy and biopsy findings in patients with COVID-19 infection related to AKI is an acute tubular injury [41].

Histopathology showed proximal tubular injury, acute tubular necrosis, intraluminal debris, marked decrease in megalin expression in the brush border and electron microscopy evidence of particles resembling coronaviruses in cisternae of the endoplasmic reticulum in proximal tubule cells and viral particles within the tubular epithelium as well as within podocytes [42, 46].

Glomerular lesions were reported in some of the patients with COVID-19 infection, with collapsing focal segmental glomerulosclerosis (FSGS), also called COVID-associated nephropathy (COVAN), being the most common. Such patients present with nephrotic-range proteinuria and AKI [47, 48, 49, 50, 51, 52, 53]. Similar to HIV-associated nephropathy, COVAN occurred exclusively in Black individuals, and a high proportion tested possessed high-risk apolipoprotein 1 (APO1) genotypes [47, 53]. There are case reports of other glomerular diseases associated with COVID-19 infection, including anti-glomerular basement membrane antibody disease [54], antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis [55], and IgA nephropathy [56].

Factors contributing to AKI associated with COVID-19 infection are listed in Table 2.

Renal transplant recipients are included among the high-risk groups

**Table 2** :Factors contributing to COVID-19 associated renal injury (adjusted according to [4])

Injury	Mechanism of injury
Acute tubular injury	Regional inflammation
	Direct viral infection
	Renal compartment syndrome
	Tissue hypoxia hypoperfusion leading to hypoxaemia, hypotension, hypovolaemia and heart failure
	Nephrotoxic-induced injury (antibiotics or antivirals)
Vascular injury	Endothelitis
	Microthrombi
	Thrombotic microangiopathy
Glomerular injury	Collapsing glomerulopathy (potentially caused by interferon-induced podocyte injury)
	Glomerulonephritis
Interstitial injury	Acute interstitial nephritis; infiltration by immune cells
	Intestinal oedema

because they use immunosuppression, and they are suffering from multiple comorbidities. Moreover, COVID-19 itself poses a significant risk on the kidneys by causing cytokine storm, hypoxia, or rhabdomyolysis, which all may trigger a kidney injury even without transplantation [57]. Immunosuppression seems to be effective for protection the lungs from cytokine storms by reducing the inflammatory response [58]. In kidney transplant patients there is a scarce information on histological findings. In patients with AKI, apart from acute tubular injury, minimal change disease [59], cortical necrosis [60] and collapsing glomerulopathy (COVAN) [61, 62, 63] there have also been described. In addition, very few cases of T-cell or antibody-mediated

rejection have been described, raising the question of whether COVID-19 infection may enhance the alloimmune response [47, 60, 64]. As the mortality rate is higher in patients who are receiving immunosuppressive drugs, therefore calcineurin inhibitor and antimetabolite withdrawal or dose decreasing are recommended for COVID-19 patients [65].

## Prevention and treatment

Treatment of AKI associated with COVID 19 infection is complex. It is aimed primarily at intensive monitoring of vital functions, regular monitoring of urea levels, creatinine, environmental parameters, mineralogram, monitoring of hemodynamic status and monitoring of the development of complications in critically ill patients. In the context of the inflammatory syndrome, fluid resuscitation is important to control fluid balance while avoiding volume target tracking and its consequences, but at the same time, attention should be paid to dehydration, which worsens AKI. Early detection of health damage in COVID-19 infection and implementation of preventive therapeutic and AKI situations are crucial in reducing morbidity and mortality [34].

Early detection and specific therapy of renal changes, including adequate hemodynamic support and avoidance of nephrotoxic drugs, may help to improve critically ill patients with COVID-19 infection [66].

Because COVID-19 infection causes organ-mediated damage by a cytokine storm, the goal of treatment is focused on the reduction or elimination of inflammatory cytokines. In the indicated cases of AKI in critically ill patients with COVID-19 infection is started treatment with renal replacement therapy (RRT). As with AKI from other causes, COVID-19 infection, life-saving RRT, is indicated in oliguria or anuria, severe acidosis, hyperkalaemia, pulmonary edema, uremic pericarditis, hyperosmolemia, metabolic encephalopathy. The need for AKI-RRT is associated with an increased burden of comorbidities and is associated with high mortality. AKI-RRT associated with COVID-19 has high lethality (63% – 79%) and occurs mainly in patients with a high burden of comorbidities and other organ dysfunctions related to the critical state [67, 29, 16, 46, 6, 68]. Patient-level risk factors for AKI-RRT include non-white race; men gender; HTN; DM; anemia; obesity; higher body mass index; CKD; any degree of proteinuria and hematuria; coronary artery disease; CHF; COPD; higher D-dimer; and greater severity of hypoxemia (lower the ratio of the partial pressure of arterial oxygen over the fraction of inspired oxygen /PaO<sub>2</sub>:FiO<sub>2</sub> ratio/) on ICU admission [67, 69, 29, 16, 46, 6, 67, 68, 70, 71]. According Gupta et al. [16] predictors of 28-day mortality in patients with AKI-RRT are older age, severe oliguria, and admission to a hospital with fewer ICU beds or one with greater regional density of COVID-19.

In the published studies, among survivors of AKI-RRT associated with COVID-19 infection, the percentage discharged from the hospital while dependent on RRT varied between 22 - 38% [67, 29, 16, 46, 6, 68, 70, 71]. The main risk factor associated with RRT dependence after an AKI-RRT was the presence of CKD in patients with and without COVID-19 infections [67].

Good management of a patient admitted with COVID-19 can make a significant contribution to preventing the development of AKI as well

as recognizing the early stages of AKI.

In the prevention of development of AKI in COVID-19 infected patients we can recommend:

- increase attention to fragile, polymorbid patients and patients with risk factors for severe COVID-19 infection,
- ensure adequate hydration (per os, i.v, via hospitalisation),
- prevent of hypovolemia and hypoperfusion,
- adjust of chronic medication (antihypertensives - ACEI, angiotensin II receptor antagonists/, diuretics, minerals, peroral antidiabetics), hypnotics, sedatives, beta-blockers for the risk of accumulation,
- avoid polypharmacy and polypragmasy, the prescription cascade,
- prevent of drug damage: caution when administering NSAIDs, antibiotics (aminoglycosides), dose adjustment for existing renal disease according to renal function,
- control urine pH with correction,
- important precautionary measures include an early vaccination at all population with fousation at-risk groups.

### Conclusion

Management of patients with COVID-19 infection needs to be approached comprehensively, accepting its potential for multi-organ damage, including AKI. Potential risk factors that significantly increase the risk of developing AKI, which is associated with poorer prognosis and an increased mortality rate, need to be identified in a timely manner. Therefore, it is necessary to focus on general risk factors, risk factors present at the admission of the patient, as well as those occurring during hospitalization. COVID-19 infection needs to be viewed comprehensively.

AKI frequently complicates the course of infection COVID-19 hospitalizations and is associated with increased severity of illness, prolonged duration of hospitalization, and poor prognosis. Given the extent of the adverse impact of AKI, early detection of comorbidities and renal complications is essential to improve the outcomes of COVID-19 patients. Increased attention needs to be paid to risk groups of patients with COVID-19 infection already in the general practitioner's office. In patients with risk factors for the development of AKI, there is a need to follow strategic measures, possibly consider hospitalization despite the easier course of COVID-19 infection.

### Reference

1. Gandhi RT, Lynch JB, Rio CD. Mild or Moderate Covid-19. *N Engl J Med* 2020; 383:18. doi: 10.1056/NEJMcp2009249.
2. ERA-EDTA Council, the ERACODA Working Group. Chronic kidney disease is a key risk factor for severe COVID-19: a call to action by the ERA-EDTA. *Nephrol Dial Transplant* 2021; 36:1. <https://doi.org/10.1093/ndt/gfaa314>.
3. Gavriatopoulou M, Korompoki E, Fotiou D, Ntanasios-Stathopoulos I, Psaltopoulou T, et al. Organ-specific manifestations of COVID-19 infection. *Clin Exp Med* 2020; 20(4):493–506.
4. Legrand M, Bell S, Forni L, Joannidis M, Koyner JL, et al. Pathophysiology of COVID-19-associated acute kidney injury. *Nat Rev Nephrol* 2021; 17:751–764.
5. Bowe B, Cai M, Xie Y, Gibson AK, Maddukuri G, et al. Acute Kidney Injury in a National Cohort of Hospitalized US Veterans with COVID-19. *Clin. J. Am. Soc. Nephrol* 2020; 16:14–25.

6. Charytan DM, Parnia S, Khatri M, Petrilli CM, Jones S, et al. Decreasing Incidence of Acute Kidney Injury in Patients with COVID-19 Critical Illness in New York City. *Kidney Int Rep* 2021; 6:916–927.
7. Husain-Syed F, Birk HW, Ronco C. Coronavirus Disease 2019 and Acute Kidney Injury: What Have We Learned? *Kidney Int Rep* 2021; 6:872–874.
8. Chen N, Zhou M, Dong X, Qu J, Gong F, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: A descriptive study. *Lancet* 2020; 395:507–513.
9. Cheng Y, Luo R, Wang K, Zhang M, Dong L, et al. Kidney Disease is Associated with In-hospital Death of Patients with COVID-19. *Kidney Int* 2020; 97(5):829–838.
10. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med* 2020; 382:1708–1720.
11. Wang J, Wang Z, Zhu Y, Li H, Yuan X, et al. Identify the Risk Factors of COVID-19-related acute kidney injury: A single-Centre, retrospective cohort study. *Front Med* 2020; 7:436. doi: 10.3389/fmed.2020.00436.
12. Wang L, Li X, Chen H, Yan S, Li D, et al. Coronavirus Disease 19 Infection Does Not Result in Acute Kidney Injury: An Analysis of 116 Hospitalized Patients from Wuhan, China. *Am J Nephrol* 2020; 51:343–348
13. Huang C, Wang Y, Li X, Ren L, Zhao J, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020; 395:497–506.
14. Yang X, Yu Y, Xu J, Shu H, Xia J, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: A single-centered, retrospective, observational study. *Lancet Respir Med* 2020; 8:475–481.
15. Lin L, Wang X, Ren J, Sun Y, Yu R, et al. Risk factors and prognosis for COVID-19-induced acute kidney injury: A meta-analysis. *BMJ Open* 2020; 10:e042573.
16. Gupta S, Coca SG, Chan L, Melamed ML, Brenner SK, et al. AKI Treated with Renal Replacement Therapy in Critically Ill Patients with COVID-19. *J Am Soc Nephrol* 2021; 32(1):161–176.
17. Fisher M, Neugarten J, Bellin E, Yunes M, Johns TS, et al. AKI in Hospitalized Patients with and without COVID-19: A Comparison Study. *J Am Soc Nephrol* 2020; 31:2145–2157.
18. Kolhe NV, Fluck RJ, Selby NM, Taal MW. Acute kidney injury associated with COVID-19: A retrospective cohort study. *PLoS Med* 2020; 17: e1003406.
19. Fominskiy EV, Scandroglio AM, Monti G, Calabro MG, Landoni G, et al. Prevalence, Characteristics, Risk Factors, and Outcomes of Invasively Ventilated COVID-19 Patients with Acute Kidney Injury and Renal Replacement Therapy. *Blood Purif* 2021; 50:102–109.
20. Chaibi K, Dao M, Pham T, Gumucio-Sanguino VD, Di Paolo FA, et al. Severe Acute Kidney Injury in Patients with COVID-19 and Acute Respiratory Distress Syndrome. *Am J Respir Crit Care Med* 2020; 202:1299–1301.
21. Silver SA, Beaubien-Souligny W, Shah PS, Harel S, Blum D, et al.

- The Prevalence of Acute Kidney Injury in Patients Hospitalized with COVID-19 Infection: A Systematic Review and Meta-analysis. *Kidney Med* 2021; 3:83–98.
22. Robbins-Juarez SY, Qian L, King K, Stevens JS, Husain SA, et al. Outcomes for Patients with COVID-19 and Acute Kidney Injury: A Systematic Review and Meta-Analysis. *Kidney Int Rep* 2020; 5:1149–1160.
  23. Sabaghian T, Rommasi F, Omid F, Hajikhani B, Nasiri MJ, et al. COVID-19 in patients with and without acute kidney injury. *Bratisl Med J* 2022; 123(5):372–380.
  24. Teixeira JP, Barone S, Zahedi K, Soleimani M. Kidney Injury in COVID-19: Epidemiology, Molecular Mechanisms and Potential Therapeutic Targets. *Int J Mol Sci* 2022; 23:2242. <https://doi.org/10.3390/ijms23042242>.
  25. Jayant K, Reccia I, Bachul PJ, Al-Salmay Y, Pyda JS, et al. The Impact of COVID-19 on Kidney Transplant Recipients in Pre-Vaccination and Delta Strain Era: A Systematic Review and Meta-Analysis. *J Clin Med* 2021; 10:4533. <https://doi.org/10.3390/jcm10194533>.
  26. Liu J, Wang T, Cai Q, Huang D, Sun L, et al. Acute Kidney Injury and Early Predictive Factors in COVID-19 Patients. *Front Med* 2021; 8:604242. doi: 10.3389/fmed.2021.604242.
  27. Rudnick MR, Hilburg R. Acute Kidney Injury in COVID-19: Another Challenge for Nephrology. *Am J Nephrol* 2020; 51(10):761–763.
  28. Wang W, Xu Y, Gao R, Lu R, Han K, et al. Detection of SARS-CoV-2 in Different Types of Clinical Specimens. *JAMA* 2020; 323:1843–1844.
  29. Chan L, Chaudhary K, Saha A, Chauhan K, Vaid A, et al. AKI in Hospitalized Patients with COVID-19. *J Am Soc Nephrol* 2021; 32(1):151–160.
  30. Karagiannidis C, Mostert C, Hentschker C, Voshaar T, Malzahn J, et al. Case characteristics, resource use, and outcomes of 10 021 patients with COVID-19 admitted to 920 German hospitals: an observational study. *Lancet Respir Med* 2020; 8(9):853–862.
  31. Behzad S, Aghaghazvini L, Radmard AR, Gholamrezanezhad A. Extrapulmonary manifestations of COVID-19: Radiologic and clinical overview. *Clin Imaging* 2020; 66:35–41.
  32. Hoffmann M, Kleine-Weber H, Schroeder S, Krüger N, Herrler T, et al. SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor. *Cell* 2020; 181(2):271–280.
  33. Khan S, Chen L, Yang C-R, Raghuram V, Khundmiri SJ, et al. Does SARS-CoV-2 Infect the Kidney? *J Am Soc Nephrol* 2020; 31(12):2746–2748.
  34. Ronco C, Reis T, Husain-Syed F. Management of acute in patient with COVID. *Lancet Respir Med* 2020; 8(7):738–742.
  35. Smarz-Widelska I, Grywalska E, Morawska I, Forma A, Michalski A, et al. Pathophysiology and Clinical Manifestations of COVID-19-Related Acute Kidney Injury-The Current State of Knowledge and Future Perspectives. *Int J Mol Sci* 2021; 22(13):7082.
  36. Higgins V, Sohaei D, Diamandis E, Prassas I. COVID-19: from an acute to chronic disease? Potential long-term health consequences. *Crit Rev Clin Lab Sciences* 2021; 58(5):297–310.
  37. Hansrivijit P, Gadhiya KP, Gangireddy M, Goldman JD. Risk Factors, Clinical Characteristics, and Prognosis of Acute Kidney Injury in Hospitalized COVID-19 Patients: A Retrospective Cohort Study. *Medicines* 2021; 8(1):4. <https://doi.org/10.3390/medicines8010004>.
  38. Nadim MK, Forni LG, Mehta RL, Connor Jr MJ, Liu KD, et al. COVID-19 associated acute kidney injury: consensus report of the 25th Acute Disease Quality Initiative (ADQI) Workgroup. *Nat Rev Nephrol* 2020; 16:747–764.
  39. Menez S, Parikh ChR. Overview of acute kidney manifestations and management of patients with COVID-19. *Am J Physiol Renal Physiol* 2021; 321:F403–F410. doi:10.1152/ajprenal.00173.2021.
  40. Ahmadian E, Khatib SMH, Soofiyan SR, Abediazar S, Shoja MM, et al. Covid-19 and kidney injury: Pathophysiology and molecular mechanisms. *Rev Med Virol* 2021; 31:e2176.
  41. Izzedine H, Jhaveri KD. Acute kidney injury in patients with COVID-19: an update on the pathophysiology. *Nephrol Dial Transplant* 2021; 36(2):224–226.
  42. Su H, Yang M, Wan C, Yi L-X, Tang F, et al. Renal histopathological analysis of 26 postmortem findings of patients with COVID-19 in China. *Kidney Int* 2020; 98(1):219–227.
  43. Varga Z, Flammer AJ, Steiger P, Haberecker M, Adermatt R, et al. Endothelial cell infection and endotheliitis in COVID-19. *Lancet* 2020; 395(10234):1417–18.
  44. Ng JH, Hirsch JS, Hazzan A, Wanchoo R, Shah HH, et al. Outcomes Among Patients Hospitalized With COVID-19 and Acute Kidney Injury. *Am J Kidney Dis* 2021; 77(2):204–215. <https://doi.org/10.1053/j.ajkd.2020.09.002> PMID:32961245.
  45. Khouchlaa A, Bouyahya A. COVID-19 nephropathy; probable mechanisms of kidney failure. *J Nephropathol* 2020; 9:e35. 10.34172/jnp.2020.35.
  46. Werion A, Belkhir L, Perrot M, Schmit G, Aydin S, et al. SARS-CoV-2 causes a specific dysfunction of the kidney proximal tubule. *Kidney Int* 2020; 98(5):1296–1307.
  47. Akilesh S, Nast CC, Yamashita M, Henriksen K, Charu V, et al. Multicenter Clinicopathologic Correlation of Kidney Biopsies Performed in COVID-19 Patients Presenting with Acute Kidney Injury or Proteinuria. *Am J Kidney Dis* 2021; 77(1):82–93.
  48. Larsen CP, Bourne TD, Wilson JD, Saqqa O, Sharshir M. Collapsing Glomerulopathy in a Patient With COVID-19. *Kidney Int Rep* 2020; 5(6):935–039.
  49. Peleg Y, Kudose S, D'Agati V, Siddall E, Ahmad S, et al. Acute Kidney Injury Due to Collapsing Glomerulopathy Following COVID-19 Infection. *Kidney Int Rep* 2020; 5(6):940–945.
  50. Velez JCQ, Caza T, Larsen CP. COVAN is the new HIVAN: the re-emergence of collapsing glomerulopathy with COVID-19. *Nat Rev Nephrol* 2020; 16(10):565–567.
  51. Sharma Y, Nasr SH, Larsen CP, Kemper A, Ormsby AH, et al. COVID-19-Associated Collapsing Focal Segmental Glomerulosclerosis: A Report of 2 Cases. *Kidney Med* 2020; 2(4):493–497.
  52. Nasr SH, Kopp JB. COVID-19-Associated Collapsing Glomerulopathy: An Emerging Entity. *Kidney Int Rep* 2020; 5(6):759–761.
  53. Shetty AA, Tawhari I, Safar-Boueri L, Seif N, Alahmadi A, et al. COVID-19-Associated Glomerular Disease. *J Am Soc Nephrol*

- 2021; 32(1):33-40.
54. Predecki M, Clarke C, Cairns T, Cook T, Roufousse C, et al. Anti-glomerular basement membrane disease during the COVID-19 pandemic. *Kidney Int* 2020; 98(3):780-781.
  55. Uppal NN, Kello N, Shah HH, Khanin Y, De Oleo IR, et al. De Novo ANCA-Associated Vasculitis with Glomerulonephritis in COVID-19. *Kidney Int Rep* 2020; 5(11):2079-2083.
  56. Huang Y, Li XJ, Li YQ, Dai W, Shao T, et al. Clinical and pathological findings of SARS-CoV-2 infection and concurrent IgA nephropathy: a case report. *BMC Nephrol* 2020; 21:504.
  57. Alebrahim-Dehkordi E, Reyhanian A, Saberianpour S, Hasanpour-Dehkordi A. Acute kidney injury in COVID-19; a review on current knowledge. *J Nephropathol* 2020; 9(4):e31.
  58. Fishman JA, Grossi PA. Novel coronavirus-19 (COVID-19) in the immunocompromised transplant recipient: #Flatteningthe-curve. *Am J Transplant* 2020; 20:1765-1767.
  59. Yamada M, Rastogi P, Ince D, Thayyil A, Mansilla A, et al. Minimal change disease with nephrotic syndrome associated with coronavirus disease 2019 after apolipoprotein L1 risk variant kidney transplant: a case report. *Transplant Proc* 2020; 52:2693-2697.
  60. Kudose S, Batal I, Santoriello D, Xu K, Barasch J, et al. Kidney biopsy findings in patients with COVID-19. *J Am Soc Nephrol* 2020; 31:1959-1968.
  61. Doevelaar AN, Hölzer B, Seibert FS, Bauer F, Stervbo U, et al. Lessons for the clinical nephrologist: recurrence of nephrotic syndrome induced by SARS-CoV-2. *J Nephrol* 2020; 33:1369-1372.
  62. Noble R, Tan MY, McCulloch T, Shantier M, Byrne C, et al. Collapsing glomerulopathy affecting native and transplant kidneys in individuals with COVID-19. *Nephron* 2020; 144:589-594.
  63. Lazareth H, Péré H, Binois Y, Chabannes M, Schurder J, et al. COVID-19-related collapsing glomerulopathy in a kidney transplant recipient. *Am J Kidney Dis* 2020; 76:590-594.
  64. Toapanta N, Torres IB, Sellarés J, Chamoun B, Serón D, et al. Kidney transplantation and COVID-19 renal and patient prognosis. *Clin Kidney J* 2021; 14(Suppl 1):i21-i29.
  65. Yilmaz G, Ebru O, Ibrahim B, Ulkem C. Assessment of clinical outcomes in renal transplant recipients with COVID-19. *J Med Virol* 2021; 93:6760-6764.
  66. Sabaghian T, Kharazmi AB, Ansari A, Omid F, Kazemi SN, et al. COVID-19 and Acute Kidney Injury: A Systematic Review. *Front Med* 2022; 9:705908. doi:10.3389/fmed.2022.705908.
  67. Samaan F, Carneiro de Paula E, de Lima Souza FBG, Mendes LFC, Rossi PRG, et al. COVID-19-associated acute kidney injury patients treated with renal replacement therapy in the intensive care unit: A multicenter study in São Paulo, Brazil. *PLoS ONE* 2022; 17(1):e0261958. <https://doi.org/10.1371/journal.pone.0261958>.
  68. Hirsch JS, Ng JH, Ross DW, Sharma P, Shah HH, et al. Acute kidney injury in patients hospitalized with COVID-19. *Kidney Int* 2020; 98(1):209-218. <https://doi.org/10.1016/j.kint.2020.05.006> PMID: 32416116.
  69. McAdams MC, Li M, Xu P, Gregg LP, Patel J, et al. Using dipstick urinalysis to predict development of acute kidney injury in patients with COVID-19. *BMC Nephrology* 2022; 23:50. <https://doi.org/10.1186/s12882-022-02677-y>.
  70. Iftimie S, Lopez-Azcona AF, Vallverdu I, Hernandez-Flix S, de Febrer G, et al. First and second waves of coronavirus disease-19: A comparative study in hospitalized patients in Reus, Spain. *PLoS One* 2021; 16(3):e0248029. <https://doi.org/10.1371/journal.pone.0248029>. PMID:33788866.
  71. Sharif N, Opu RR, Ahmed SN, Sarkar MK, Jaheen R, et al. Prevalence and impact of comorbidities on disease prognosis among patients with COVID-19 in Bangladesh: A nationwide study amid the second wave [published online ahead of print, 2021 Jun 26]. *Diabetes Metab Syndr* 2021; 15(4):102148.