

CKD patients: A high-risk category for severe COVID-19

To the Editor,

We read with interest the research article published by Gerwen et al.¹ in *Journal of Medical Virology*. The study including 3703 patients with confirmed coronavirus disease 2019 (COVID-19) revealed that older age, male gender, or having more than two comorbidities were associated with increased morbidity and mortality. We are in total agreement with these findings and want to represent suggested mechanisms that can clarify the results especially regarding chronic kidney disease (CKD) as a comorbidity.

As COVID-19 caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) spreads throughout the world, almost every individual is at risk for infection. However, some patients are at risk for severe illness and death. Old age and underlying comorbid conditions were associated with increased COVID-19 severity and mortality.² The most important comorbidities were hypertension (HTN) (9.5%–31.2%), diabetes mellitus (8.2%–20%), and other cardiovascular and cerebrovascular diseases (5.6%–40%). Regarding chronic kidney disease (CKD), its prevalence in patients with COVID-19 was 0%–5.6%. Based on this minor percentage, it was uncertain whether CKD should be considered as a true risk factor for COVID-19. Several studies have been conducted to evaluate the correlation between the two pandemics. Although Gerwen et al.¹ study did not document an association between CKD comorbidity and COVID-19 poor outcomes, many studies reported a positive association between CKD and COVID-19 severity and mortality.^{3–5} Mechanisms supporting these findings have not yet been approved.

We hypothesize that complications accompanying CKD are the main reasons for poor outcome in patients with COVID-19. Hypertension, anemia, cardiovascular disease (CVD), and metabolic acidosis are the most important complications of CKD.⁶ Many of these complications have been reported as independent risk factors for COVID-19 poor outcome.

First, hypertension is the most important complication of CKD. The prevalence of HTN in patients with CKD varies from 35.8% in stage 1 to 84.1% in Stages 4 and 5.⁷ Meanwhile, reports from United States, China, and Italy revealed that HTN rates in COVID-19 severely infected patients were 56%, 50%, and 49%, respectively.⁸ As a consequence, HTN was regarded as an independent risk factor for COVID-19 poor outcome including hospitalization, intensive care unit (ICU) admission as well as death.

Second, renin-angiotensin-aldosterone system (RAAS) inhibitors are the first-line antihypertensive agents for patients with CKD. Since these medications result in angiotensin-converting enzyme 2 (ACE2) receptor upregulation, and ACE2 is the main receptor for SARS-CoV-2 entry into human cells, there was a debate

about the fact that these drugs may be associated with increased COVID-19 incidence and severity and some studies called for the discontinuation of these medications.⁹ Due to insufficient evidence, recent guidelines support their continued use and prospective randomized trials are currently ongoing to determine the real correlation between these important HTN medications and COVID-19.¹⁰ However, based on this suggestion, RAAS inhibitors use by patients with CKD may play a role in supporting the positive correlation between CKD and increased COVID-19 severity. Thus, HTN combined with CKD could cause exacerbation of COVID-19, with increased severity and mortality.

Third, a low hemoglobin concentration is associated with a disrupted transport of oxygen to several organs in the body, causing hypoxia, that can in turn contribute to increased COVID-19 severity and mortality. A meta-analysis including 9912 patients with COVID-19 found a significant positive association between the presence of anemia and COVID-19 severity.¹¹ Another study declared anemia as an independent risk factor for severe COVID-19, calling healthcare professionals to be more sensitive to the hemoglobin levels of patients with COVID-19 upon admission.¹² On the other hand, severe COVID-19 is associated with inflammation that can itself affect iron homeostasis, producing anemia. Anemia resulting from COVID-19 is characterized by reduced levels of serum iron and transferrin with normal or increased ferritin levels. This type of anemia is termed “anemia of inflammation.”¹³ Since patients with CKD usually suffer from both chronic inflammation and anemia (prevalence varying between 5.2% and 44.1%),^{14,15} this may partly explain why CKD is a risk factor for poor COVID-19 prognosis.


Finally, the Chinese cohort study of CKD reported that the prevalence of CVD was 9.8% in patients with CKD.¹⁶ Meanwhile, the fatality rate among COVID-19 patients with CVD was 10.5%. In addition, a meta-analysis that studied the burden of CVD in COVID-19 infected patients reported that CVD was significantly associated with both ICU admission and mortality.¹⁷ The high COVID-19 associated mortality in patients with a history of CVD has been explained by multiple mechanisms. Increasing ventricular workload, exacerbating ventricular dysfunction and systemic inflammation that may lead to a hypercoagulable state and thrombotic events are the most important mechanisms.¹⁸ Based on these findings, CVD, an important damaging complication of CKD can play an important role in COVID-19 poor outcome.

In conclusion, CKD-associated complications can explain why CKD results in COVID-19 poor outcomes. While facing a viral second wave, CKD should be considered as a risk factor for COVID-19 severity and mortality. Special care and vaccination should be given

to patients with CKD of varying stages as a way to decrease hospitalization and death from infection.

CONFLICT OF INTERESTS

The authors declare that there is no conflict of interests.

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