Letter to the Editor

American Journal of Nephrology

Am J Nephrol
DOI: 10.1159/000508089

Received: April 20, 2020
Accepted: April 20, 2020
Published online: June 29, 2020

SARS-CoV-2 Infection Results in Serious Kidney Impairment: More Studies Need to Be Explored

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Dear Editor,

We appreciate the letters by Dr. Bhaskar et al. [1] and by Dr. Silver et al. [2]. In their letters, they put forward some views and comments on our article "Coronavirus Disease 19 Infection Does Not Result in Acute Kidney Injury: An Analysis of 116 Hospitalized Patients from Wuhan, China" [3]. All of the issues raised by them are very important and deserve our attention and considerations. Here, we would like to respond to their comments in the letters and explain their questions about the observations in our paper. We hope that our responses could relieve them of some concerns.

As regards Dr. Bhaskar et al.'s concern about the roles of ACE2 expression in SARS-CoV-2 infection, a recent study shows that the cells with ACE2 expression may act as target cells and be susceptible to SARS-CoV-2 infection, such as type II alveolar cells in the lung [4]. It should be noted that the ACE2 protein has been proved to have an abundant expression in many kinds of cells, including renal tubular epithelial cells. Therefore, it is reasonable to speculate that SARS-CoV-2 may also invade kidney and lead to AKI. However, the information regarding the pathological findings in COVID-19 is limited at present. The reports showed that there were main histological changes in the lung [5,6]. Until now, there are no data and evidence showing that SARS-CoV-2 infection might directly impair the kidney, although SARS-CoV-2 RNA could be detected from urine, including our results [3]. Therefore, in addition to the lung, whether the kidney is the main target organ of SARS-CoV-2 and it causes an obvious AKI need more pathological and virological evidence in the future study. Moreover, data on ACE inhibitor application in COVID-19 are important in this setting and should also be investigated.

As regards Dr. Bhaskar et al.'s concern about mortality in our study, we included 116 patients with COVID-19 hospitalized in the Department of Infectious Diseases. Eleven (11/116, 9.5%) patients were with acute respiratory distress syndrome (ARDS) and were transferred to ICU. Seven out of 11 ARDS patients transferred to ICU died of respiratory failure. As a result, the overall mortality rate of COVID-19 was 6.03% (7/116), while the mortality rate of ARDS patients with COVID-19 in ICU was 63.6% (7/11). There is indeed a high mortality, which is in agreement with the results of the study by Wu et al. [7].

As regards Dr. Silver et al.'s concern about the incidence of AKI in patients with COVID-19, our explanations and answers are as follows. Our department started to treat patients with COVID-19 from the middle of January 2020. Previously, these patients were consultant in "fever clinic," which serves as an outpatient department, and were diagnosed as "unknown origin viral pneumonia" for admission. They were confirmed the diagnosis as COVID-19 by the SARS-CoV-2 RNA test immediately, when PCR detection was available. In that time, our wards were specialized for isolation and treatment of these pa-

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tients. Thirty out of 116 cases with other diseases already hospitalized at the time of their COVID-19 were diagnosed. The others were newly admitted from "fever clinic." All hospitalized patients in our wards were at the acute phase of their illness. The patients clinical categories and comorbidities are presented in table 1 of our paper. The judgment of patients' condition and clinical type is mainly based on the degree of hypoxemia and lung damage [8].

In our paper, AKI was identified according to Kidney Disease: Improving Global Outcomes (KDIGO) [9]. However, few patients without CKD could accurately provide the baseline levels of SCr. When baseline SCr was not available, $SCr_{GFR\text{-}75}$ as surrogate for the baseline SCr was used to diagnose AKI [10]. Renal function and urine were tested weekly in all patients during the treatment of COVID-19. Although the weekly test may not have been sufficiently frequent in certain instances for finding AKI, the high frequency of examination is useful, especially in critical patients.

In this study, 5 patients with ESKD received regular dialysis. The serum creatinine, blood urea, electrolytes, and urine analysis were used to evaluate whether kidney deterioration occurs in them. The symptoms, physical examination results, hemodynamic stability (e.g., blood pressure) were closely monitored as well.

Although AKI is currently reported in critical cases of COVID-19, especially in dead cases as high as 23–32% [11,12], it may be related to severe hypoxemia and/or multiple organ dysfunction syndrome (MODS) induced by inflammatory storm or to high comorbidities. Whether this renal injury is directly caused by SARS-CoV-2 infection is still unclear. In our paper, we did not find a significant AKI in these 11 ARDS cases, including 7 dead patients with ARDS. The critical patients in our study were in small number. Therefore, the differences on kidney impairment from available studies in COVID-19 may associate with the severity of illness.

Many early studies suggested a lower incidence (3–9%) of AKI in those with COVID-19 infection [13–15]. As an early report, our study showed clinical data of 116 hospitalized COVID-19 patients analyzed over 4 weeks for correlation with renal injury. Approximately 10.8% of patients with no prior kidney disease showed elevations in blood urea or creatinine, and 7.2% of patients with no prior kidney disease showed albuminuria. All these patients did not meet the diagnostic criteria of AKI. From these results, we concluded that AKI was uncommon in general population with COVID-19.

Based on the study from SARS-CoV infection in SARS patients in 2003 [16], the data showed that AKI was uncommon, but the mortality was formidably high (91.7%, 33 of 36 cases). Our results were similar and consistent with the presentation of renal injury in SARS. Moreover, in the present study, we also found that unlike a high mortality in SARS complicated with renal injury, none of 5 patients with CKD died from SARS-CoV-2 infection.

Actually, our study showed that a mild renal injury was present rather than AKI in general population with COVID-19. We also suggested that regular monitoring of renal function in COVID-19 patients is necessary, especially in patients with elevated plasma creatinine levels. In the event of signs of AKI, potential interventions, including CRRT, should be used as early as possible.

Finally, our study is a preliminary and retrospective analysis, which had several limitations. Whether SARS-CoV-2 infection results in serious kidney impairment remains to be explored further. It will be crucial to comprehensively characterize larger datasets of COVID-19 patients across hospitals (meta-analyses) to demonstrate if the kidney function is actively impaired due to the viral infection and SARS-CoV-2 could easily lead to kidney damage and if renal diseases are a major high risk factor for aggravating COVID-19 consequences.

Disclosure Statement

We declare no competing interests.

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