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Letter to the Editor

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Renal Injury in Severe Acute Respiratory Syndrome Coronavirus 2 Infection: An Additional Concern to the Clinicians

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To the Editor

The coronavirus disease 2019 (COVID-19) pandemic is a global concern for public health worldwide. Lung injury is the major outcome of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection; however, damage can occur in multiple organs including the kidney [1, 2]. Previously, it has been shown that SARS virus may be capable of infecting multiple cell types in several organs; pulmonary epithelium and immune cells were identified as the main sites of injury [3]. Organ systems like the lungs, heart, liver, and kidneys rely on and assist one another's functions, so when the virus causes injury in one area, others might be at risk. Moreover, patients with pre-existing illness are at high risk of infection and severe course of COVID-19. Therefore, renal injury is considered as an additional concern in patients with severe COVID-19.

Currently, there are limited data that link underlying kidney dysfunction with severe cases of COVID-19. At this point, it remains unclear to what extent the new coronavirus itself affects kidney function versus contribution from other factors resulting in kidney injury in patients with COVID-19. Some patients with severe COVID-19 showed signs of kidney damage, even those who had no pre-existing kidney disease before they were infected with the SARS-CoV-2 [4]. The prevalence of kidney dysfunction was found up to 16.7% of patients with severe COVID-19 (Table 1) [2, 4-18]. In the relevant COVID-19 studies, serum levels of creatinine and blood urea nitrogen (BUN) were found at increased levels in patients admitted to the intensive care unit (ICU) than other patients [4-8]. In a study, the prevalence of elevated BUN and serum creatinine was 13.1% and 14.4%, respectively in hospitalized COVID-19 patients [4]. The authors observed that patients with increased baseline serum creatinine were more likely to be admitted to the ICU and required mechanical ventilation; indicating that pre-existing kidney dysfunction on admission increases the disease severity [4]. Moreover, the prevalence of kidney injury on admission and the progression of acute kidney disease during hospitalization was high and was correlated with in-hospital death [4].

In a retrospective cohort study consisting of 81 patients critically ill with COVID-19 in an ICU, 50.6% patients experienced acute kidney disease (AKI) [9]. Older age and higher level of serum interleukin 6 (IL-6) were identified as risk factors of AKI in this study. In the USA, a hospital study indicated that 49.3% of the COVID-19 patients had AKI and the patients with AKI had significantly lower baseline estimated glomerular filtration rate (eGFR) [19]. In another study in the USA, AKI was more frequent in COVID-19 patients with respiratory abnormalities, with 89.7% of patients on mechanical ventilation support developed AKI compared to 21.7% of non-ventilated patients [20]. In another study in the same country, AKI was found about 22.2% of hospitalized COVID-19 patients [21]. In New York, of 3,993 hospitalized COVID-19 patients, AKI occurred in 46% patients; among patients with AKI, 19% needed dialysis, and about half of them were died in the hospital [10]. In a retrospective study, it has been observed that patients with acute kidney injury (AKI) and COVID-19 were more likely than patients without COVID-19 to require registered respiratory therapist (RRT), ICU admission, and mechanical ventilation; and were more likely to experience in-hospital death [22].

Although the impact of COVID-19 on the kidney remains unclear, some possible mechanisms could explain the kidney damage in patients with COVID-19. First, immune-mediated inflammation, such as cytokines storm and pneumonia-related hypoxia may cause damage to the kidney cells. Second, acute tubular necrosis (ATN) due to severe infection and hypotension is likely the most common reason for kidney dysfunction in patients with COVID-19. Third, collapsing focal segmental glomerulosclerosis (FSGS) is a rare but well described entity with coronavirus. Fourth, COVID-19-related microangiopathy and hemophagocytic macrophage activation may also cause kidney injury. Fifth, there is a possibility that extremely low levels of oxygen in the blood of severe patients may cause kidney problems. Sixth, the uses of certain medications at high doses may affect kidney functions in COVID-19 patients. In a recent study, it has been observed that patients with acute kidney disease were more likely to have an increased proportion

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Table 1. Renal Function Abnormalities in COVID-19 Patients

Reference	Group	Patients number	Chronic kidney disease number (%)	Creatinine (µmol/L)[a]	BUN (mmol/L)[a]	% of patients with abnormal kidney function
Arentz et al, 2020 [11]	Hospitalized	21	10 (47.6)	128.2 (8.8 - 397.8)	NA	NA
Chan et al, 2020 [10]	Non-AKI	2,158	81 (4)	70.7 (61 - 80)	13 (10 - 19)	NA
	Presence of AKI	1,835	339 (18)	129.9 (93 - 212)	31 (18 - 51)	NA
Chen et al, 2020 [2]	Hospitalized	99	NA	75.6 (25)	5.9 (2.6)	Creatinine: 3; BUN: 6
Cheng et al, 2020 [4]	Hospitalized	701	36 (5.1)	77 (31)	5.7 (3.9)	Creatinine: 14.4; BUN: 13.1
Guan et al, 2020 [5]	Severe[b]	173	3 (1.7)	NA	NA	4.3
	Non-severe	926	5 (0.5)	NA	NA	1.0
Huang et al, 2020 [12]	Severe[b]	13	0	79 (53.1 - 92.7)	NA	15
	Non-severe	28	1 (4)	73.3 (57.5 - 84.7)	NA	7
Liu et al, 2020 [6]	Severe[b]	13	NA	74.2 (28.3)	3.3 (2.7 - 3.7)	NA
	Mild	27	NA	64 (13.3)	3.2 (2.5 - 4.4)	NA
Mo et al, 2020 [13]	Severe[b]	85	4 (4.47)	79 (65 - 96)	NA	NA
	Mild	70	2 (2.9)	65 (58 - 78)	NA	NA
Regina et al, 2020 [14]	No-ventilation	163	26 (16)	88.5 (70 - 112.7)	NA	NA
	Ventilation	37	2 (5.4)	97 (82 - 127)	NA	NA
Rubin et al, 2020 [15]	Severe[b]	71	4 (6)	115.6	10.1	NA
Shi et al, 2020 [16]	Hospitalized	81		75.4 (29.8)	NA	NA
Wang et al, 2020 [7]	Severe[b]	36	2 (5.6)	80 (66 - 106)	5.9 (4.3 - 9.6)	NA
	Non-severe	102	2 (2.0)	71 (58 - 84)	4 (3.1 - 5.1)	NA
Xia et al, 2020 [9]	Presence of AKI	41	41 (100)	104 (74 - 188.5)	12.5 (8.6 - 27.8)	NA
	Non-AKI	40		65.5 (48 - 80)	7.1 (5.5 - 10.6)	NA
Xu et al, 2020 [8]	Hospitalized	62	NA	72 (61 - 84)	NA	5
Yang et al, 2020 [17]	Survivors	20	12 (60)	80.7 (32.3)	NA	NA
	Non-survivors	32	3 (9.4)	76.3 (24.4)	NA	NA
Zhao et al, 2020 [18]	Severe[b]	30	1 (3.3)	NA	NA	16.7
	Mild	61	0	NA	NA	0

[a]Data were presented as mean (SD) or median (IQR); [b]Severe: patients admitted to the intensive care unit (ICU). COVID-19: coronavirus disease 2019; SD: standard deviation; IQR: interquartile range; BUN: blood urea nitrogen; AKI: acute kidney injury; NA: data were not available.

of glucocorticoid and diuretics treatment on admission [4]. Lastly, the virus itself infects the kidney cells. In a recent study, it has been shown that SARS-CoV-2 uses angiotensin-converting enzyme 2 (ACE2) as a receptor to entry into target cells [23]. Recent data on human tissue RNA-sequencing suggested that ACE2 is more highly expressed in the kidney than in the lungs and heart [24]. Therefore, kidney damage might be caused by the virus through the ACE2-dependent pathway. Although, kidney dysfunction directly by the virus is still debatable and there are some studies that did not find the presence of SARS-CoV-2 in the biopsied kidney tissue [25-27].

Despite the limited data on kidney involvement in COVID-19, acute kidney injury appears to multifactorial and involve a complex process driven by the virus itself, cytokine storm, microangiopathy, hypercoagulation, and drugs effects. It is known that hypertension and diabetes can damage blood vessels of the kidneys; therefore, coexisting of these disease conditions can increase hospital mortality from COVID-19. Therefore, severe COVD-19 patients with renal injury require more attention during hospitalization. While kidney injury in COVID-19 is still not well understood, further research is needed to explore the exact causes of kidney damage in patients with SARS-CoV-2 infection.

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Conflict of Interest

The author declares no conflict of interest.

Informed Consent

Not applicable.

Author Contributions

FI conceived the idea and drafted the letter.

Data Availability

The author declares that data supporting the findings of this study are available within the article.

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