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Editorial

Is Podocyte Injury During COVID-19 Infection Contributes To Proteinuria and A Threat To Renal Failure?

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The recent global outbreak of coronavirus is originated in the city of Wuhan (China) as unusual bilateral pneumonia in December 2019 [1,2]. The infectious agent causing pneumonia was identified as a novel coronavirus using high-throughput sequencing [3], and the WHO named this new virus as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV2) and associated disease as COVID-19 [4]. SARS-CoV2 is an RNA virus and is 96% identical to bat coronavirus [2]. Nevertheless, the intermediate host responsible for the present outbreak of COVID-19 remains unknown. This virus belongs to the betacoronavirus family and characterized by SS RNA. This virus is zoonotic and can infect a variety of animals and livestock and members of betacoronavirus family were associated with two earlier outbreaks SARS-CoV and MERS-CoV (Middle East Respiratory Syndrome) in 2003 and 2012, respectively. COVID-19 becomes the worldwide health emergency as more than 210 Countries and Territories are affected with a death toll of about 450,000 and increasing.

SARS-CoV2 can be transmitted by direct contact or via droplets and the most common symptoms are dry cough, fever, and fatigue whereas diarrhea is occasional. However, the clinical features of SARS-CoV2 infection can be asymptomatic or presented with a range of mild to moderate respiratory illness, acute pneumonia, and severe respiratory failure with high mortality. Besides respiratory illness, kidney dysfunction and proteinuria are the predominant complications occurring in critically ill COVID-19 patients from China, Italy, and the USA [5-9]. Initial studies reported very less burden of kidney injury, however, a recent prospective study observed ~ 44% and 27% of COVID-19 patients had proteinuria and hematuria [6]. COVID-19 Patients with renal abnormality had a significantly higher risk of in-hospital death, suggesting that renal dysfunction is associated with the severity of the disease and poor survival rate [6]. Proteinuria indicates damage to the Glomerular Filtration Unit (GFU) of the kidney wherein podocytes are the principal component of GFU. Podocytes provide epithelial coverage to the glomerulus capillaries and play a pivotal role in the ultrafiltration of blood and curb protein loss into the urine. Podocytes have limited potential for replication and podocyte injury is centric to glomerular dysfunction [10].

SARS-CoV2 infects by binding to angiotensin-converting enzyme 2 (ACE2) of host cells [2]. ACE2 expressed by an array of cells localized to lungs, intestine, blood vessels, liver, pancreas, adipose tissue, testes, and kidney. Single-cell transcriptomic analysis revealed a significant co-expression of ACE2 and TMPRSS2 (Transmembrane Serine Protease) in podocytes suggesting these cells are the potential host for SARS-CoV2 and exhibit preferential tropism for this virus [11]. ACE2 expression by glomerular podocytes is comparable to that of lungs and intestine [11]. Encapsulated SARS-CoV2 viral particles were observed in podocytes from the postmortem examination of COVID-19 patients [12] suggesting podocytes are bonafide targets for viral infection. Furthermore, elevated ACE2 expression was observed in the settings of diabetic nephropathy [13]. One could speculate that increased ACE2 may attract greater infectivity by a virus that possibly explains the high mortality in diabetic subjects with COVID-19 infection.

Although initial reports suggested COVID-19 infection is a respiratory illness subsequent studies suggest that renal abnormalities are more common and are associated with higher mortality. In addition to the global burden of diabetes and diabetic nephropathy, the acute incidence of COVID-19 pandemic could be an additional threat for renal health and it is of great concern in the patients with pre-existing kidney ailments. The most frequent comorbidities of COVID-19 are hypertension and diabetes that are often treated with ACE inhibitors, which tend to increase ACE2 expression [14] that may impose a greater risk of infection by the virus. We are in a need to understand the cellular and molecular events that occur in SARS-CoV2 associated podocytopathy. Injured podocytes often shed in urine and podocytes harboring viral particles if shed in urine may contribute to the disease transmission. In addition to the direct cytopathic effect of the virus, immune-mediated mechanism, cytokine damage, and septic shock are considered a possible mechanism that elicits kidney damage in COVID-19 patients [15]. As podocytes express a significant amount of ACE2 and are a bonafide target for SARS-CoV2 infection and are play a central role in renal filtration, podocyte injury during COVID-19 infection is a great challenge for the patients to deal with and to the nephrologist to strategize treatment options.

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