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NEPHROLOGY - LETTER TO THE EDITOR

Acute kidney injury associated with COVID-19: another extrapulmonary manifestation

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Dear Editor,

Since December 2019, the world has been learning about a new coronavirus, SARS-CoV2, a virus associated with COVID-19 disease. A characteristic of this coronavirus is damage to the pulmonary interstitium and its consequent viral pneumonia; however, it is known that it is capable of damaging other systems and organs [1].

Several studies have shown evidence of the presence of kidney damage and its relationship with mortality. One of these is the multicenter and retrospective study by Li et al., which involved 193 patients hospitalized for COVID-19, finding frequent alterations in the tests on admission: 59% presented with proteinuria, hematuria in 44%, BUN elevated in 14% of patients, hypoalbuminemia in 58% and 10% had elevated serum creatinine. Findings highlight the importance of tracking in examinations from admission to the emergency department or hospitalization. In addition, in this study, significant differences in serum creatinine (SCr), BUN, proteinuria and hematuria were observed among severe and non-serious patients infected with SARS Cov-2 and higher levels were observed in the deceased, associated with a risk factor 5.3 times higher for mortality than in patients without acute kidney injury (AKI) [2]. Similar findings were found in the prospective cohort study involving 701 patients, published by Cheng et al., who analyzed the proportional risks of renal symptomatology finding: elevated BUN (HR 7.15, 95% CI 4.92–10.39), elevated SCr (HR 2.99, 95% CI 2.00–447), hematuria 1+ (HR 4.64, 95% CI 2.24–9.62) and proteinuria 1+ (HR 4.12, 95% CI 1.97–8.62) all with statistically significant results [3].

Conversely, Wang et al. did not find progression to AKI in patients with COVID-19, reporting that 5 of 116 patients studied had pre-existing chronic kidney disease (CKD), without progression to AKI. Of the patients without CKD, 7% reported albuminuria and 10.8% mild increases in BUN and serum creatinine. However, the alterations were corrected in both cases and there was no progress to acute kidney injury. Of this cohort studied, 6.3% (seven patients) died, none had AKI or CKD [4].

It is known that the virus uses the angiotensin II-converting enzyme (ACE2) as a receptor for its entry into the cell; however, the transmembrane serine 2 protease is fundamental for this process since it breaks the bond between the virus protein S and ECA2 allowing the release of peptides by the virus that facilitate membrane fusion and thus infection of the host cell [5]. Studies have demonstrated the expression of ECA2 and TMPRSS2, a gene encoding serine 2 transmembrane protease, in podocytes and cells of the proximal rectus tubule, important structures in protein filtration and urine in general, which may be affected by the harmful effects of the virus on them, leading to alterations in renal function tests and acute renal failure [5]. The expression of these enzymes assumes that the cells of the kidney epithelium and its functional unit are targets of infection and replication of SARS CoV-2, theory that is supported by the detection of virus antigens in postmortem samples of renal tissue of COVID-19 patients who presented with AKI and by the presence of the virus in the urine of infected individuals [6, 7].

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In addition to the cytopathic effect, a severe immunological reaction would be triggered, leading to infiltration of macrophages and lymphocytes into the renal tubular interstitium as well as fibrosis and alterations in the microvasculature with their consequent tubular damage; therefore, acute tubular necrosis and AKI are produced not only due to the direct effect of the virus, but also due to the immune reaction produced [6].

Likewise, the renin–angiotensin–aldosterone system is also altered by SARS-CoV-2 by massively occupying ACE2, raising blood levels of angiotensin II, which has been associated with viral load [8], this increase could mean in a vasoconstriction of the afferent artery of the nephron, causing a decrease in blood flow in the nephron and therefore alterations in the glomerular filtration rate; however, this theory needs studies for its validation. Furthermore, blood volume and sodium levels would be increased, not only by the increased activity of aldosterone due to the increase of angiotensin II, but also by the decrease of angiotensin 1–7, a product of angiotensin II degradation by ECA2, which has a natriuretic and vasodilator effect [8].

It is presumed that the virus reaches the renal parenchyma through the bloodstream, since it has been shown that approximately 15% of patients with renal injury present the RNA of the virus in the blood [9].

On the other hand, AKI induced by SARS-CoV-2 also affects patients with previous renal disorders; studies claim that CKD is associated with severe disease in those infected with COVID-19 with an OR of 3 (95% CI 1.09–8.47) [10], as well as 25% of elderly patients with pre-existing basic diseases, higher risk population, died by COVID-19, were complicated by presenting AKI in a study published by Chen et al. [11]. In addition to this, a series of cases of seven patients with a history of renal transplantation and COVID-19 respiratory infection in South London showed that these people usually present atypical symptoms and more complications than in immunocompetent individuals; since four of these patients required ICU and one died [12, 13], it is therefore recommended in some documents that immunosuppressive management should be minimized or discontinued for a certain time [14].

In conclusion, the kidney and its functional unit are targets of SARS-CoV-2, producing extrapulmonary symptoms and even being a risk factor for developing severe disease and mortality. Therefore, it is suggested that special attention be paid to the evolution of renal function tests and an action aimed at the protection of renal function since the admission of patients with COVID-19.

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