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REVIEW

COVID-19 and kidney involvement: pathophysiological approach

COVID-19 y afectación renal: abordaje fisiopatológico

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ABSTRACT

Introduction: due to the great threat posed by COVID-19, the scientific community must have evidence of kidney damage in patients affected by this disease, which would make it possible to carry out actions aimed at its prevention and early detection.
Objectives: deepen knowledge about COVID-19 and its impact on the kidney.
Method: a bibliographic review on COVID-19 and kidney was carried out, in research published in Spanish and English, in the PubMed, Scielo, and Dialnet databases. All documents published in the last five years (2019-2023) were selected, which included the keywords: COVID-19, kidney, kidney disease.
Conclusions: within the systemic involvement caused by COVID-19, the kidney plays a predominant role in its pathophysiology and as a target organ. Kidney disease is in itself a risk factor for morbidity and mortality and acute kidney failure worsens the prognosis; Hence, it is necessary to delve deeper into these topics every day to direct novel diagnostic and therapeutic strategies.

Keywords: COVID-19; Kidney; Renal Disease.

RESUMEN

Introducción: debido a la gran amenaza que representa la COVID-19, la comunidad científica debe tener evidencia del daño renal en pacientes afectados por esta enfermedad, lo cual posibilitaría realizar acciones encaminadas a su prevención y detección precoz.
Objetivos: profundizar en el conocimiento sobre COVID-19 y su afectación al riñón.
Método: se realizó una revisión bibliográfica sobre COVID-19 y riñón, en investigaciones publicadas en idioma español e inglés, en las bases de datos PubMed, Scielo, Dialnet. Se seleccionaron todos aquellos documentos publicados en los últimos cinco años (2019-2023), que incluyeron las palabras clave: COVID-19, riñón, enfermedad renal.
Conclusiones: dentro de la afectación sistémica ocasionada por la COVID-19, el riñón juega un papel preponderante en su fisiopatología y como órgano diana. La enfermedad renal es en sí, un factor de riesgo para la morbimortalidad y el fallo renal agudo empeora el pronóstico; de ahí que se hace necesario profundizar cada día en estos temas para encaminar estrategias diagnósticas y terapéuticas novedosas.

Palabras clave: COVID-19; Riñón; Enfermedad Renal.

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INTRODUCTION

Human coronaviruses are viruses associated with various respiratory diseases, such as severe acute respiratory syndrome and Middle East respiratory syndrome. This has placed this family of viruses in the spotlight of the scientific community due to their high pathogenicity in humans, especially now with the new pandemic caused by the 2019 coronavirus disease (COVID-19).[1]

Due to the serious threat posed by COVID-19, the scientific community must have evidence of kidney damage in patients affected by this disease, which would enable actions to be taken for its prevention and early detection, as it is known that kidney damage in patients with SARS-CoV-2 increases the risk of death.[2]

Much is still unknown about SARS-CoV-2, but early research supports the hypothesis that the severity of COVID-19 is determined by the hyperinflammatory response that occurs in our bodies upon contact with SARS-CoV-2. The severity of the condition is related to the respiratory failure it causes, although some studies do not limit the pulmonary involvement. Research suggests that the mechanism by which SARS-CoV-2 enters the body is closely related to the angiotensin-converting enzyme 2 (ACE2). This enzyme is found in various tissues, including the epithelium of the renal tubular cells. This is why there are reports of COVID-19 patients with severe renal impairment who may develop acute renal failure (a poor prognostic factor).[3]

Objective: To deepen our understanding of COVID-19 and its effects on the kidneys.

METHOD

A review of scientific articles published in peer-reviewed journals and books by specialists in the field was conducted.

A search on vasculitis was conducted in PubMed, Scielo, Swisslinx, and Dialnet. All documents that included the words COVID-19, kidney, and kidney disease published in the last five years were selected.

DEVELOPMENT

The cause of kidney involvement in COVID-19 is likely to be multifactorial, with cardiovascular comorbidity and predisposing factors (e.g., sepsis, hypovolemia, and nephrotoxins) as essential contributors. Cardiorenal syndrome, particularly right ventricular failure secondary to COVID-19 pneumonia, can lead to renal congestion and subsequent acute kidney injury (AKI). Similarly, ventricular dysfunction can lead to low cardiac output, insufficient filling of the arteries, and renal hypoperfusion.[4]

SARS-CoV-2 uses the angiotensin-converting enzyme 2 (ACE-2) receptor for its protein spike, and this binding is primed by the transmembrane serine protease 2 (TMPRSS-2), facilitating entry and spread into receptor cells. The ACE-2 receptor is expressed in type II pulmonary alveolar and capillary endothelial cells.[5]

Hypothetical competing mechanisms by which inhibition of the renin-angiotensin system (RAS) with an angiotensin-converting enzyme inhibitor (ACEI) or an angiotensin receptor antagonist (ARA, BRA) may be harmful or protective in COVID-19 infection:

- Hypothesis 1: Coronavirus enters the cell by binding to ACE2; adding an ACEI or ARB could increase the abundance of ACE2 and therefore increase virulence.
- Hypothesis 2: Angiotensin II (Ang II) promotes lung injury by activating the angiotensin type 1 receptor (ATR1), which causes inflammation and fibrosis, and there is also a decrease in Ang II production with an ACEI or an ARB. The actions of Ang II–AT1R with an ARB enhance ACE2-mediated Ang generation and Mas receptor (RMas) activation, which attenuates inflammation and fibrosis and thereby maintains lung injury. Further research is needed to fully understand the role of the RAAS, specifically angiotensin two receptors, and to determine the specific impact of the virus.[6]

Based on this relationship and given the widespread use of angiotensin-converting enzyme (ACE) inhibitors for the control of hypertension or heart and kidney disease, further research is needed to determine whether adding or discontinuing these medications may alter the course of acute COVID-19 infection.[7]

SARS-CoV-2 may also attack renal tubular epithelial cells and lung epithelial cells, and lung damage would be exacerbated by water and salt retention, as evidenced by tubular injury.[8]

Autopsy data indicate that the endothelium is affected in the lung and kidney, likely triggering proteinuria. In addition, viral particles in renal endothelial cells have been reported, suggesting that viremia is a possible cause of endothelial damage in the kidney and a potential contributor to acute kidney injury. Furthermore, SARS-CoV-2 can directly infect the renal tubular epithelium and podocytes via an ACE2-dependent pathway and cause mitochondrial dysfunction, acute tubular necrosis, protein reabsorption vacuole formation, collapsing glomerulopathy, and protein loss in the Bowman's capsule.[9]

AKI can occur at any stage of viral infection, so clinical monitoring and consideration of risk factors, early detection, and diagnosis are essential components of medical care. Kidney involvement in COVID-19 infection is common in hospitalized patients, and increased nitrogenous products such as urea and creatinine, which are frequently elevated in this viral infection, have been considered a cause of mortality. Patients with renal dysfunction are at increased risk of infection, complications, and death. In addition, these patients have pre-existing conditions such as volume overload, left ventricular hypertrophy, and heart failure, which triple mortality.[10]

The deposition of immune complexes composed of viral antigens, specific T lymphocytes, or antibodies can directly damage kidney tissue. However, this has not been proven, and studies on SARS-CoV-2 were negative.

Cytokine storms and inflammatory mediators induced by the SARS-CoV-2 virus can indirectly affect kidney tissue, such as hypoxia, shock, and rhabdomyolysis; these three mechanisms may be related to death in patients with COVID-19.[11]

Related to the immune response, it has been postulated that sepsis causes cytokine storm syndrome and, consequently, acute tubular necrosis and multiple organ dysfunction. In a study of patients who died from SARS-CoV, minimal to severe tubular necrosis

was found in the kidney tissue; however, the cause of death in all seven cases was diffuse alveolar damage.[12]

The involvement of specific inflammatory mediators such as IL-2, IL-7, IL-10, granulocyte colony-stimulating factor, interferon-inducible protein 10, and high concentrations of monocytes in critically ill patients has been postulated.[13]

On the other hand, components of microorganisms known as pathogen-associated molecular patterns are observed, which are released by damaged host cells with elevated cytokines.[14]

In some cases, glomerular ischemia and endothelial cell injury were described with fibrin thrombi within the glomerular capillary loops, reflecting coagulation activation in patients with COVID-19.[15]

Chronic kidney disease (CKD) is associated with poor prognosis and higher mortality in the context of SARS-CoV-2 infection. Patients with CKD have other comorbidities, such as diabetes mellitus (DM) and hypertension (HTN), that also contribute to an increased risk of adverse events. CKD should be a variable to consider in studies to establish the prognosis of patients with COVID-19.[16]

Patients with chronic kidney disease from stage I of the KDIGO (Kidney Disease: Improving Global Outcomes) classification to stage IV or V without renal replacement therapy are immunocompromised, as are patients on peritoneal dialysis, hemodialysis, and even more so patients who have undergone kidney transplantation. Kidney injury is also a manifestation of the problem during this pandemic.[14]

Patients receiving hemodialysis for end-stage renal disease are at greater risk of COVID-19 infection than the rest of the normal population. Most of these patients are elderly and have associated comorbidities, as well as some degree of immunocompetence, which may be associated with poorer survival outcomes.[17]

Therapeutic measures in managing this condition can impact normal kidney function in the context of a patient with acute and/or chronic kidney injury, so certain aspects should be considered when formulating any of the possible treatments. Indicators such as glomerular filtration rate (GFR), stage of chronic kidney disease, and the need for dialysis therapy are necessary for drug prescription in patients with kidney disease and COVID-19 infection.[18,19]

In patients with chronic kidney disease on hemodialysis with COVID-19, no differences in symptoms were observed between sexes, and lymphopenia and elevated inflammatory markers were present at the time of diagnosis, mainly in symptomatic patients.[20]

These findings show that SARS-CoV-2 can cause severe damage to healthy and previously affected kidneys, which may be at greater risk of infection due to the neoexpression of viral receptors.[21]

COVID-19 disease continues to represent an immense clinical challenge, no longer considered a respiratory disease but rather a multisystemic condition with widespread involvement of different organs and systems, including the renal tissue. Current evidence indicates that SARS-CoV-2 can invade mainly proximal tubule cells and podocytes through the ACE-2 receptor. Viral infection could cause kidney injury through a direct cytopathic effect and immune response-mediated damage, which warrants further research and study to understand better this area's impact and, consequently, the most appropriate measures to consider in its identification and management.[22]

Nephrologists worldwide face the challenge of addressing the complications of COVID-19 in an already fragile population. The combination of targeted viral, extracorporeal, and immunosuppressive treatments is essential in managing kidney disease and COVID-19 patients. Still, due to the complexity of their condition, diverse expertise is required.[23]

CONCLUSIONS

Within the systemic involvement caused by COVID-19, the kidney plays a significant role in its pathophysiology and as a target organ. Kidney disease is itself a risk factor for morbidity and mortality, and acute kidney failure worsens the prognosis; hence, it is necessary to delve deeper into these issues every day to develop innovative diagnostic and therapeutic strategies.

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

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AUTHOR CONTRIBUTION

Conceptualization: Yangel Fuentes Milián, Patricia Prieto Milián.
Research: Yangel Fuentes Milián, Patricia Prieto Milián.
Methodology: Yangel Fuentes Milián, Patricia Prieto Milián.
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REFERENCES

1. Vargas JG, Ávila N, Hurtado D, Cárdenas-Roldán J, Peña D, Ortiz G. Lesión Renal Aguda en COVID-19: puesta al día y revisión de la literatura, Acta Colombiana Cuidados Intensivos, Elsevier,2020, 30;(20) 1-11. Disponible en: https://doi.org/10.1016/j.acci.2020.10.004

2. González Milán ZC, Alarcón González R, Escalona González SO. Daño renal en pacientes con COVID-19. Rev. Cub. Inv. Biomédicas. 2021 [acceso: 02/05/2021];40(2):e808. Disponible en: http://www.revibiomedica.sld.cu/index.php/ibi/article/view/808

3. Hidalgo-Blanco MÁ, Andreu-Periz D, Moreno-Arroyo MC. COVID-19 en el enfermo renal. Revisión breve. Enferm Nefrol [Internet]. 2020 Jun [citado 2023 Ago 26] ; 23(2): 122-131. Disponible en: http://scielo.isciii.es/scielo.php?script=sci_arttext&pid=S2254-28842020000200002&lng=es

4. Zarzosa SG, Lucas JH, Llorente B, Trascasa M, Molina R, Serrano C, et al. Acute renal failure in COVID-19 patients on mechanical ventilation. Rev Chil Anest. 2021; 49(6):867–73.

5. Shetty AK. Mesenchymal Stem Cell Infusion Shows Promise for Combating Coronavirus (COVID-19) Induced Pneumonia. Aging and Disease. 2020;11(2):462-4. DOI: 10.14336/AD.2020.0301

6. Singhal T. A Review of Coronavirus Disease-2019 (COVID-19). The Indian Journal of Pediatrics (April 2020) 87(4):281–286 https://doi.org/10.1007/s12098-020-03263-6

7. Vaduganathan M, Vardeny O, Michel T, McMurray JJV, Pfeffer MA, Solomon SD. Renin-Angiotensin-Aldosterone System Inhibitors in Patients with Covid-19 N Engl J Med. 2020;382:1653-9.

8. Diao B, Feng Z, Wang C. Human kidney is a target for novel severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2). Infection. 2020;12(1):2506. DOI: 10.1101/2020.03.04.20031120v2

9. Soler MJ, Macia Heras M, Ortiz A, del Pino y Pino MD, Salgueira Lazo M. Impacto de la pandemia COVID-19 en los servicios de Nefrología españoles. Nefrología [Internet]. 2020; 40(6):579–84. Disponible en: https://doi.org/10.1016/j.nefro.2020.08.002

10. Pincay Luna MY, & Alcocer Diaz S. (2023). Perfil renal asociado a mortalidad por Covid 19 en pacientes de la unidad de cuidados intensivos a nivel de Latinoamérica . Revista Científica Arbitrada Multidisciplinaria PENTACIENCIAS, 5(3), 112–123. https://doi.org/10.59169/pentaciencias.v5i3.524

11. Caicedo Mesa A, et al. Pandemia de COVID-19 y enfermedad renal: ¿Qué sabemos actualmente?. Rev. colom. nefrol. [online]. 2020, vol.7, suppl.2, pp.221-248. Epub May 10, 2021. ISSN 2500-5006. https://doi.org/10.22265/acnef.7.supl.2.438

12. Chu KH, Tsang WK, Tang CS, Lam MF, Lai FM, To KF, et al. Acute renal impairment in coronavirus-associated severe acute respiratory syndrome. Kidney Int 2005;67(2):698-705. Available from: https://doi.org/10.1111/j.1523-1755.2005.67130.x

13. Xianghong Y, Renhua S, Dechang C. Diagnóstico y tratamiento de la nueva neumonía por coronavirus: no se puede ignorar la lesión renal aguda. Chin Med J (Engl) 2020. Available from: https://doi.org/10.3760/cma.j.cn112137-20200229-00520

14. Hernández-Rivera JCH, Silva-Rueda RI, Salazar-Mendoza M, Pazos-Pérez F, Pérez-López MJ, Bermúdez-Aceves L, et al. COVID-19 generalidades y enfermedad renal. Artículo de revisión. Gac Med Bilbao. 2021;118:143–159

15. Fragale G, Baña Matías T, Magenta M, Beitia V, Karl A, Cortés L, et al . Valor pronóstico del compromiso renal en COVID-19. Rev. nefrol. dial. traspl. [Internet]. 2022 Mar [citado 2023 Ago 25] ; 42(1): 4-10. Disponible en: http://www.scielo.org.ar/scielo.php?script=sci_arttext&pid=S2346-85482022000100004&lng=es

16. Escalona-González S, González-Milán Z, Ricardo-Paez B. Enfermedad renal crónica como causa importante de mortalidad en pacientes con COVID-19 en Cuba. Revista Cubana de Medicina [Internet]. 2022 [citado 25 Ago 2023]; 61 Disponible en: https://revmedicina.sld.cu/index.php/med/article/view/2704

17. Ikizler T. COVID-19 y Unidades de Diálisis: ¿Qué sabemos ahora y qué debemos hacer? AJKD. 2020;76(1):1-3 DOI: 10.1053/j.ajkd.2020.03.008

18. Zhang F, Liang Y. The potential risk of kidney vulnerable to novel coronavirus 2019 infection. Am J Physiol Physiol 2020:ajprenal.00085.2020. Available from: https://doi.org/10.1152/ajprenal.00085.2020

19. Izzedine H, Jhaveri KD, Perazella MA. COVID-19 therapeutic options for patients with Kidney Disease. Kidney Int 2020;0. Available from: https://doi.org/10.1016/j.kint.2020.03.015

20. de Armas Gil Tomás, Herrera Oropesa Yeneisis, Barroso Cruz Jorge, Joseph Planas Harold Ricardo, Rey Torres Ailyn Bárbara, Fuentes Abreu Jorge et al . La COVID-19 en pacientes con enfermedad renal crónica en hemodiálisis. Rev Cub Med Mil [Internet].

2021 Mar [citado 2023 Nov 02] ; 50(1): e859. Disponible en: http://scielo.sld.cu/scielo.php?script=sci_arttext&pid=S0138-65572021000100010&lng=es

21. Coello Roberto D., Salgado Walter, Pazmiño Gomez Betty J., Vazquez Vanina, Veron Delma. La pandemia de COVID-19 y el riñón, Guayas, Ecuador. Rev. nefrol. dial. traspl. [Internet]. 2020 Dic [citado 2023 Nov 02] ; 40(4): 279-294. Disponible en: http://www.scielo.org.ar/scielo.php?script=sci_arttext&pid=S2346-85482020000400279&lng=es

22. Flores Gavino Aldo, Espinoza Anchaygua Ricardo, Herrera-Añazco Percy, Rodriguez-Morales Alfonso J.. SARS-COV-2 y su efecto a nivel de tejido renal: Una revisión narrativa. Acta méd. Peru [Internet]. 2021 Ene [citado 2023 Nov 02] ; 38(1): 53-57. http://dx.doi.org/10.35663/amp.2021.381.1885

23. Treviño-Becerra Alejandro, Grajales-García Dulce P., Feria Ramírez José A.. COVID 19 y enfermedad renal crónica. Gac. Méd. Méx [revista en la Internet]. 2022 Ago [citado 2023 Nov 03] ; 158(4): 187-189. Disponible en: http://www.scielo.org.mx/scielo.php?script=sci_arttext&pid=S0016-38132022000400187&lng=es