UNIVERSIDAD SIMÓN BOLÍVAR

IMPACTO DE LA FRAGILIDAD Y LA CARGA VIRAL EN LA LESION RENAL AGUDA EN LOS PACIENTES AFECTADOS POR COVID-19

IMPACT OF FRAILTY AND VIRAL LOAD ON ACUTE KIDNEY INJURY EVOLUTION IN PATIENTS AFFECTED BY COVID- 19

Nombre: Lil Geraldine Avendaño Echávez
Cedula: 37440264
Correo: lil.avendano@unisimonbolivar.edu.co

Trabajo de Investigación del Programa
NEFROLOGIA

Tutor:
Dr. Gustavo Aroca Martinez
Dr. Carlos G. Musso

RESUMEN

Introducción: El COVID-19 puede afectar muchos otros órganos además del sistema respiratorio, particularmente en el riñón, el corazón, el tracto digestivo, la sangre y el sistema nervioso. En cuanto a las alteraciones renales, los informes preliminares indicaron una incidencia del 3% al 9% y cada vez hay más pruebas de que la lesión renal aguda (IRA) es frecuente en la infección por SARS-CoV-2, con una incidencia informada de 8-17%, llegando al 35% en pacientes críticos, y que esta condición se considera un factor de mal pronóstico. En este sentido, el desarrollo de IRA en el contexto de la COVID-19 tiene una mortalidad asociada del 91,7%.

Objetivos: Este artículo describe las principales características de los pacientes con COVID-19 que padecen insuficiencia renal aguda (IRA) atendidos en una clínica de alta complejidad en Barranquilla (Colombia), incluyendo sus características particulares, y evalúa el impacto de la carga viral y la fragilidad previa del paciente sobre la evolución clínica de la IRA.

Materiales y Métodos: Los pacientes incluidos en este estudio (n: 48) fueron aquellos con diagnóstico positivo de COVID-19 confirmado por detección PCR de SARS-CoV-2, que habían desarrollado DRA durante su estancia hospitalaria. Se registraron los parámetros séricos y de orina, así como la carga viral del paciente y la escala de fragilidad clínica (CFS). Se exploró un análisis estadístico de los parámetros registrados, como comparaciones y correlaciones entre las variables de interés.

Resultados: De una población de 762 pacientes ingresados en la Clínica de la Costa (Barranquilla, Colombia) con síntomas compatibles con COVID-19, 117 pacientes dieron positivo a SARS-CoV-2 confirmado por PCR, 48 desarrollaron FRA (41% de prevalencia), siendo el la mayoría de ellos clasificados como AKIN 3.

El IRA se documentó 4 ± 3,4 días después del ingreso, y la mayoría de estos pacientes se encontraban en la unidad de cuidados intensivos (75%). Con respecto al subgrupo que desarrolló DRA, la edad media fue de 61 ± 15 años, con un claro predominio del sexo masculino (79%), y valores medios de creatininemia y uremia de 3,35 ± 1,74 mg/dL y 106,91 ± 26,9 mg/dL al diagnóstico, respectivamente con un requerimiento de terapia de reemplazo renal del 29%, y una mortalidad asociada del 73%. La mortalidad de los pacientes con LRA mostró una correlación positiva significativa (33%) con la puntuación de CFS de los pacientes, pero no con su carga viral.

Las anormalidades urinarias documentadas en asociación con AKI fueron, en orden decreciente, proteinuria (35%), hematuria (31%) y leucocituria (4%). En cuanto a los signos y síntomas secundarios a la COVID-19, en el subgrupo de DRA se destacaron: fiebre (100%), disnea (85%), astenia marcada (48%) y mialgia (40%). Entre los marcadores inflamatorios bioquímicos y de compromiso sistémico (directo e indirecto) que más cambiaron (aumentaron) se destacaron: proteína C reactiva, ferritina y dímero D. En relación a los antecedentes de los pacientes que desarrollaron LRA, el 69% eran t robustos (SFC: 1-3), el 21% eran frágiles (SFC: 4-5) y el 10% eran muy frágiles (SFC: 6-7). En cuanto al impacto de la condición de fragilidad previa al desarrollo de LRA secundaria a COVID-19, se observaron recuentos de glóbulos blancos (p= 0,007), niveles de LDH sérica (p = 0,003) y mortalidad (p = 0,006) significativamente más altos documentado entre los pacientes frágiles en comparación con los de los robustos. La mortalidad aumentó un 33% con cada aumento en el grado de fragilidad del paciente (0,33, p = 0,02).

Conclusiones: En este estudio, el IRA secundario a COVID-19 (COVAN) mostró una prevalencia del 41% en una población hospitalizada con diagnóstico positivo de SARS-CoV2 por PCR. La mayoría de los casos fueron AKIN 3, con un requerimiento de reemplazo renal del 29% y una mortalidad del 73%. La fragilidad clínica de los pacientes se correlacionó significativamente con la mortalidad por COVAN pero no con la carga viral.

Palabras clave: COVID 19, lesión renal aguda y fragilidad.

UNIVERSIDAD SIMÓN BOLÍVAR

ABSTRACT

Introduction: COVID-19 can affect many other organs in addition to the respiratory system, particularly in the kidney, heart , digestive tract, blood, and nervous system. As for the kidney altera t ions , preliminary reports indicated an incidence of 3%–9% and there is growing evidenc e that acute kidney injury (AKI) is prevalent in SARS-CoV-2 infection, with a repor t ed incidenc e of 8%–17%, reaching 35% in critical patients , and that this condition is considered a poor prognostic factor. In this sense, the development of AKI in the context of COVID-19 has an associated mortality of 91.7%.

Objective: This paper describes the main characteristics of COVID-19 patients suffering from acute kidney injury (AKI) assisted at a high complexity clinic in Barranquilla (Colombia). including their particular features, and evaluates the impact of viral load and prior patient frailty on the clinical evolution of AKI.

Materials and Methods: The patient s included in this study (n: 48) were those with a positive diagnosis of COVID-19 confirmed by PCR detection of SARS-CoV-2, who had developed AKI during their hospital stay. Serum and urine parameters, as well patient ´ s viral load and clinical frailty scale (CFS) were recorded. A statis tical analysis of the recorded parameters, such as comparisons, and correlations between variable s of interest , were explored.

Results: From a population of 762 patients admitted to Clínica de la Costa (Barranquilla, Colombia) with COVID-19- compatible symptoms, 117 patients tested positive for SARS-CoV-2 confirmed by PCR, 48 developed AKI (41% prevalence), being the majority of them classified as AKIN 3.

AKI was documented 4 ± 3.4 days after admission, and most of these patients were in the intensive care unit (75%). With respect to the subgroup that developed AKI, the mean age was 61 ± 15 years, with a clear predominance of males (79%), and average creatininemia and uremia values of 3.35 ± 1.74 mg/dL and 106.91 ± 26.9 mg/dL at diagnosis, respectively with a renal replacement therapy requirement of 29%, and an associated mortality of 73%. AKI patient s ´ mortality showed a significant positive correlation (33%) with patient s ´ CFS score but not with their viral load.

Documented urinary abnormalities in association with AKI were, in decreasing order, proteinuria (35%), hematuria (31%), and leukocyturia (4%). Regarding signs and symptoms secondary to COVID-19, the following stood out in the AKI subgroup: fever (100%), dyspne a (85%), marked asthenia (48%), and myalgia (40%). Among the inflammatory biochemic al and systemic compromise markers (direct and indirect) which changed (increased) the most, the following stood out: C-reactive protein, ferritin, and D-dimer. In relation to the background of the patients who developed AKI, 69% were robus t (CFS: 1–3), 21% were frail (CFS: 4–5), and 10% were very

frail (CFS: 6–7). In terms of the impact of the frailty condition prior to the development of AKI secondary to COVID-19, significantly higher white blood cell counts (p= 0.007), serum LDH levels (p = 0.003), and mortality (p = 0.006) were documented among frail patients when compared with those in robust ones. Mortality increased by 33% with each rise in the patient's degree of frailty (0.33, p = 0.02).

Conclusions: In this study, AKI secondary to COVID-19 (COVAN) showed a prevalence of 41% in a hospit alized populat ion with a positive diagnosis of SARS-CoV2 by PCR. Most cases were AKIN 3, with a renal replacement requirement of 29%, and a mortality of 73%. The clinical frailty of patient s was significantly correlated with COVAN mortality but not with the viral load.

KeyWords: COVID-19, acute kidney injury, frailty

REFERENCIAS

1. World Heal th Organization. *New Coronavirus* . China; 2020.
2. Gorbalenya AE, Baker SC, Baric RS, et al. The species and its viruses—a stateme n t of the Coronavi rus Study Group. *Biorxiv* . 2020:1-15.
3. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavi rus- infected pneumoni a in Wuhan, China. *JAMA* . 2020;323(11):1061- 1069.
4. Naicke r S, Yang CW, Hwang SJ, Liu BC, Chen JH, Jha V. The Novel coronavirus 2019 epidemic and kidneys. *Kidney Int* . 2020;97(5):824- 828. doi: 10.1016/j.kint.2020.03.001 .
5. Su H, Yang M, Wan C, et al. Renal histopa thological analysis of 26 postmortem findings of patient s with COVID-19 in China. *Kidney Int* . 2020;98(1):219- 227. doi: 10.1016/j.kint.2020.04.003 .
6. Gaba r r e P, Dumas G, Dupont T, Darmon M, Azoulay E, Zafrani L. Acute kidney injury in critically ill patient s with COVID-19. *Intensiv e Care Med* . 2020;46(7):1339-1348. doi: 10.1007/ s0013 4- 020- 06153- 9 .
7. Cheng Y, Luo R, Wang K, et al. Kidney Impai rme nt is associated with in-hospital death of COVID-19 patient s . *medRxiv* . 2020:1- 21. doi: 10.1101/2020.02.18.20023 2 4 2 .
8. Sang L, Chen S, Zheng X, et al. The incidenc e, risk factors and prognosis of acut e kidney injury in sever e and critically ill patients with COVID-19 in Mainland China: a ret rospe c t ive study. Research Square; 2020.
9. Shafi ST. Covid- 19 and acute kidney injury: recent updates . *Pak J Kidney Dis* . 2020;4(2):225- 227.
10. Corman V , Landt O, Kaiser M , Molenkamp R , Meijer A, Chu D , Bleicker T, Brünink S, Schneide r J, Schmidt ML, Mulders D, Haagma ns B, van der Veer B , van den Brink S, Wijsman L, Goder ski G, Romet t e JL , Ellis J , Zambon M , Peiris M, Goossens H, Reusken C , Koopmans M, Drosten C. Detection of 2019 novel coronavi rus (2019- nCoV) by real- time RT-PCR. EURO Surveill. 2020;25(3):23- 30 doi: 10.2807/1560- 7917.ES.2020.25.3.2000 04 5 .

11. KDIGO Clinical practic e guideline for acut e kidney injury. *Kidney Int Suppl* . 2012;2(1):1- 38.
12. Musso CG, Jauregui JR, Macías Núñez JF. Frailty phenotype and chronic kidney disea se: a review of the litera tur e . *Int Urol Nephrol* . 2015;47(11):1801- 1807.
13. King-Vela E, Muñoz J, Rico- Font alvo J, et al. Acute kidney injury in Colombian patient s with COVID-19 who received kidney support therapy with genius® 90 technology. *J Clin Nephrol* . 2020;4(3):056- 060.
14. Gondo- an K, Temel S, Baran Ketencio- lu B, Rabah B, Tutar N, Sungur M. Acute kidney injury in SARS-CoV-2 infected critically ill Patient sTurki sh. *J Nephrol* . 2020;29:185- 189.
15. Chan L, Chaudha ry K, Saha A, et al. on behalf of the Mount Sinai COVID Informa t ics Cente r (MSCIC). AKI in hospitalized patient s with COVID-19. *JASN* Septemb e r 2020. doi: 10.1681/ASN.202005 0 6 1 5 .
16. Cheng Y, Luo R, Wang K, et al. Kidney diseas e is associat ed with in-hospital death of patient s with COVID-19. *Kidney Int* . 2020;97(5):829- 838.
17. Meijer s B, Hilbrands LB. The clinical characteristics of coronavi rus- associat ed nephropa t hy. *Nephrol Dial Transplant* . 2020;35(8):1279- 1281.
18. Shafi ST. Covid- 19 and acute kidney injury: recent updates . *PJKD*. 2020;4(2):225- 227.
19. Molina- Barraga n AM, Pardo E, Galichon P, et al. SARS-COV2 renal impairment in critical care: A ret rospe c t ive study of 42 cases—Kid COVID Stud *y* . Resea r ch Squa r e . doi: 10.21203/ r s .3. r s- 64088/v1 .
20. Golmai P, Larsen, DeVita M, et al. Histopa thologic and ultrastructural findings in postmor t em kidney biopsy material in 12 patient s with AKI and COVID-19. *JASN* . 2020;31:1944- 1947. doi: 10.1681/ASN.202005 0 6 8 3 .
21. Batlle D, Soler MJ, Sparks MA, et al. and on behalf of the COVID. 19 and ACE2 in cardiovascul a r , lung, and Kidney Working Group. Acute kidney injury in COVID-19: emerging evidence of a distinct pathophysiology. *J Am Soc Nephrol* . 2020;31(7):1380- 1383. doi: 10.1681/ASN.202004 0 4 1 9 .
22. Sise ME, Bagge t t MV, Shepa rd JO, Stevens JS, Rhee EP. Case 17- 2020: A 68- year- old man with Covid- 19 and kidney acute injury. *N Engl J Med* . 2020;382(22):2147- 2156.
23. Su H, Yang M, Wan C, et al. Renal histopa thological analysis of 26 postmortem findings of patient s with COVID-19 in China. *Kidney Int* . 2020;98(1):219- 227. doi: 10.1016/j.kint.2020.04.003 .
24. Naicke r S, Yang CW, Hwang SJ, Liu BC, Chen JH, Jha V. The Novel coronavi rus 2019 epidemic and kidneys. *Kidney Int* . 2020;97(5):824- 828.
25. Hernand e z- Arroyo CF, Varghe s e V, Mohamed MMB, Velez JCQ. Urinary sediment microscopy in acute kidney injury associated with COVID-19. *Kidney360* . 2020;1(8):819- 823. doi: 10.34067/KID.000335 20 2 0 .
26. Pujada s E, Chaudhry F, McBride R, et al. SARS-CoV-2 viral load predict s COVID-19 mor tality. *Lancet* . 2020;8(9):e70.
27. Khan S, Chen L , Yang CR, et al. Does SARS-CoV-2 Infect the Kidney? JASN.2020;31: 1-3 doi: https://doi.org/10.1681/ASN.2020081229

28. Braun F, Hube r T, Puelles V. Proximal tubula r dysfunction in patient s with COVID-19: what have we learnt so far? Kidney Int . 2020 Nov; 98(5): 1092–1094. doi: 10.1016/j.kint.2020.09.002
29 . González C, Yama E, Yomayus a N, et al. [Colombian Consens us of Exper t s on Evidenc e- Informed Recomme n d a t ions for the Prevent ion, Diagnosis and Manageme n t of SARS-CoV-2 / COVID-19 Acute Kidney Injury]. Rev. Colomb. Nefrol. [Interne t] . 2 de junio de 2020 [citado 1 de noviembr e de 2020];7(Supl.2). https:// revis t an ef rologia.org/index.php/ r cn/ a r t icle/view/473
30. Lee J, Silberzweig J, Akchurin O, et al. Characteristics of Acute Kidney Injury in Hospitalized COVID-19 Patients in an Urban Academic Medical Center. CJASN. 2021;16:1-3 doi: https://doi.org/10.2215/CJN.07440520
31 . Jingyuan Liu, Yao Liu, Pan Xiang et al. Neut rophil- to-Lymphocyte Ratio Predicts Sever e Illness Patient s with 2019 Novel Coronavirus in the Early Stage. https://doi.org/10.1101/2020.02.10.2002 1 5 8 4
32. Fei Zhou, Ting Yu, Ronghui Du et al. Clinical cour se and risk factors for mort ality of adult inpatients with COVID-19 in Wuhan, China: a ret rospective cohort Study. Lancet 2020; 395: 1054- 62
33. Qiurong Ruan , Kun Yang, Wenxia Wang et al. Clinical predictor s of mortality due to COVID-19 based on an analysis of data of 150 patient s from Wuhan, China. Intensive Care Med 2020. Intensive Care Med (2020) 46:846–848 https://doi.org/10.1007/ s001 34- 020- 05991- x
34. Páramo Fernánd e z J. Coagula ción, Dímero D y COVID-19. Sociedad Español a de Trombosis y Hemos t a si a (SETH) https://www. s e t h. e s /index.php/noticia s/not icias /not icias- de- la- seth/1588- coagula cion- dimero- d-y-covid- 19.html
35. Pérez G. Coronavi rus . Impacto cardiovascular . Sociedad Interamericana de Cardiología. http://www. sia c a rdio.com/noved ad e s / covid- 19/coronavi rus- y-suimpacto- cardiovascul a r /
36. Driggin E, Madhavan MV, Bikdeli B, Chuich T, Laracy J, Bondi- Zoccai G,Brown TS, Nigoghos si an CD, Zidar DA, Haythe J, Brodie D, Beckman JA, Kirtane AJ, Stone GW, Krumholz HM, Parikh SA, Cardiovascul a r Conside r a t ions for Patient s , Health Care Worker s , and Heal th Systems During the Coronavi rus Disease 2019 (COVID-19) Pandemi c, Journal of the American College of Cardiology (2020), doi:https://doi.org/10.1016/j.jacc.2020.03.031.
37. Qin C, Zhou L, Hu Z et al. Dysregulation of immune response in patients with COVID-19 in Wuhan, China. Clint Infect Dis 2020. https://doi.org/10.1093/ cid/ciaa
38. Meht a P, McAuley DF, Brown M, Sanchez E, Tatte r s all RS, Manson JJ. COVID-19: conside r cytokine storm syndrome s and immunosupp r e s s ion. Lancet 2020. https://doi.org/10.1016/S0140- 6736(20)30628- 0