IJKD KIDNEY DISEASES

Association Between Occult Kidney Disease and COVID-19 Mortality: Evidence from a Retrospective Study

Fernando Guerrero-Romero, Gerardo Martínez-Aguilar, Mayela Ríos-Mier, Julia B. Garay-Sierra, Abraham S. Mercado-Sosa, Paulina Flores-Galindo, Luis E. Simental-Mendía*

Unidad de Investigación Biomédica, Delegación Durango, Instituto Mexicano del Seguro Social, Durango, México

Keywords. Occult kidney disease (OKD); Acute kidney injury (AKI); COVID-19; Kidney diseases; Mortality

Introduction. Occult kidney disease (OKD), a term that describes the initial phase of renal failure, is usually overlooked in routine clinical evaluations. Therefore, the goal of this study was to determine whether OKD is associated with the disease severity and mortality in COVID-19 patients.

Methods. A retrospective study was conducted in patients with COVID-19. COVID-19 was considered based on a positive reverse transcriptase-polymerase chain reaction test for SARS-CoV-2. OKD was defined with an estimated glomerular filtration rate < 60 ml/min/1.73 m^2 and creatinine concentrations ≤1.3 mg/dl.

Results. A total of 809 patients with COVID-19 were selected for the study. The frequency of OKD, acute kidney injury, and chronic kidney disease was 7.7%, 15.0%, and 12.4%, respectively. The logistic regression analysis adjusted showed that OKD (OR = 1.86; CI 95%: 1.05-3.32), acute kidney injury (OR = 2.03; CI 95%: 1.42-2.89), and chronic kidney disease (OR = 3.07; CI 95%: 1.90-4.97) were associated with mortality by COVID-19.

Conclusion. Our results indicate that OKD is associated with increased mortality in patients with COVID-19.

IJKD 2026;20:116-21
www.ijkd.org

Brief Communication

INTRODUCTION

The first reports of clinical manifestations associated with COVID-19 mainly focused on the respiratory tract; however, the cumulative evidence showed that infection by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes a systemic disease, including cardiovascular, gastrointestinal, and renal systems.[1]

Angiotensin-converting enzyme 2 (ACE2), a receptor for SARS coronaviruses, counters the effect of the renin-angiotensin system and plays a crucial role in human physiology. In this regard, the SARS-CoV-2 can bind to renal epithelial cells resulting in renal injury and, consequently, disturbances in the fluid, acid-base, and electrolyte homeostasis.[2]

Occult kidney disease (OKD), a term that describes the initial phase of renal failure, is usually overlooked in routine clinical evaluation.[3] A previous study reported a prevalence of OKD of 13.2% in patients with chronic diseases including type 2 diabetes and hypertension.[4] Additionally, female sex, age > 60 years, systemic arterial hypertension, and a body mass index < 25 have been the main factors associated with OKD.[4] To the best of our knowledge, OKD has not been investigated in patients with COVID-19; therefore, the aim of this study was to determine whether OKD is associated with the severity and mortality in COVID-19 patients.

MATERIALS AND METHODS

A cross-sectional retrospective study was conducted in patients with COVID-19 in the General Hospital of Durango, Mexico from March 2020 to March 2021. Eligible participants were men and women over age of 20 years with a positive reverse transcriptase-polymerase chain reaction test (RT-PCR) for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Data regarding body mass index, White Blood Cells (WBC) and Neutrophil counts, Hemoglobin, fasting plasma glucose (FPG), and serum creatinine (SCr) levels, and systolic and diastolic blood pressures were extracted from the hospital records. Patients with incomplete data, and history of pregnancy, heart failure, chronic liver disease, neoplasia, kidney transplantation, dialysis, and use of nephrotoxic drug were exluded from the study. Data were collected at hospital admission.

Severe COVID-19 was defined by an oxygen saturation ≤93%, respiratory rate ≥30 /min, or infiltrates affecting more than 50% of lung parenchyma.[5] Mild COVID-19 was considered by clinically mild symptoms and no sign of pneumonia on imaging; while moderate COVID-19 was characterized by radiological findings of pneumonia, fever, and respiratory symptoms.[6] The eGFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula and CKD was classified as follows: normal (eGFR ≥90 ml/min/1.73 m^2), mild (eGFR 60-90 ml/min/1.73 m^2), moderate (eGFR ≥30-60 ml/min/1.73 m^2), and severe (eGFR < 30 ml/min/1.73 m^2).[7] Chronic kidney disease (CKD) was considered in those patients with a previous history of eGFR < 60 ml/min/1.73 m^2. Mild CKD was considered as eGFR of 60-90 ml/min/1.73 m, while OKD was defined with an eGFR < 60 ml/min/1.73 m^2 and creatinine concentrations ≤1.3 mg/dl with no previous diagnosis of any kidney disease, including acute kidney injury (AKI) or CKD.[8] AKI stage 1 was defined by an increase in serum creatinine levels ≥0.3 mg/dL in 48 hours or an increase in serum creatinine levels ≥1.5 times baseline within the prior 7 days; AKI stage 2 was considered with an increase in serum creatinine levels of 2.0-2.9 times baseline; and AKI stage 3 by an increase in serume creatinine levels of ≥3 times baseline or increase in serum creatinine ≥4.0 or initiation of renal replacement therapy.[9]

Statistical Analysis:

Bivariate analyses were conducted using unpaired Student's t-test (Mann-Whitney U test for skewed data) for numerical variables and χ^2 test for qualitative variables. Differences between more than two groups were estimated using the one-way ANOVA with post hoc Bonferroni. The odds ratio between kidney dysfunction (OKD, AKI, and CKD) and severity and mortality was calculated using multiple logistic regression analysis. Also, an additional logistic regression analysis adjusted by age, sex, diabetes mellitus, and hypertension was performed to control the potential confounders.

RESULTS

Data from 837 clinical records of patients with COVID-19 were reviewed and 28 were excluded because they did not meet the selection criteria. Thus, 809 patients with an average age of 61.5 ± 15.8 years were included in the study.

Patients with severe COVID-19 had a higher neutrophil count (P = .001) and fasting plasma glucose (P = .02) compared to those with non-severe disease. There were no significant differences for other parameters between the study groups. Moreover, the patients who died from COVID-19 were older (P < .001) and had a higher proportion of hypertension (P = .001), OKD (P = .001), and CKD (P < .001). Additionally, individuals who died exhibited higher levels of creatinine (P = .001) and fasting plasma glucose (P < .001), leukocyte (P = .01) and neutrophil (P < .001) counts, as well as a lower hemoglobin concentration (P = .03) compared to the patients who survived (Table 1).

In the overall population, the frequency of OKD, AKI, and CKD was 7.7%, 15.0%, and 12.4%, respectively.

Patients with mild (eGFR 60-90 ml/min/1.73 m^2), moderate (eGFR ≥30-60 ml/min/1.73 m^2), and severe (eGFR < 30 ml/min/1.73 m^2) impairment were different in terms of age (P < .001), diabetes (P < .001), hypertension (P < .001), fasing glucose (P = .01), and hemoglobin concentrations (P < .001), Table 2.

Finally, Table 3 shows the association between renal impairment and outcomes for COVID-19. The logistic regression analysis revealed that OKD (OR = 2.38; 95% CI: 1.40-4.06; P = .001), AKI (OR = 2.57; 95% CI: 1.84-3.58; P < .001), CKD

Table 1. Characteristics of individuals in the study according to severity and survival, n = 724. For severity, 85 patients were not considered due to incomplete data

N	Severe	Non-severe	*P*	Death	Survival	*P*
	n = 436	n = 288		n = 377	n = 432	
Age, years	61.9 ± 15.4	61.0 ± 15.7	NS	64.9 ± 14.6	58.4 ± 16.0	< .001
Women, n (%)	179 (41.0)	132 (30.2)	NS*	150 (39)	194 (44)	NS*
Oxygen saturation, %	78.8 ± 15.6	96.1 ± 2.0	< .001	82.5 ± 15.8	88.6 ± 13.2	< .001
Diabetes, n (%)	193 (44)	129 (44)	NS*	183 (48)	170 (39)	NS*
Hypertension, n (%)	241 (55)	156 (54)	NS*	229 (60)	211 (48)	.001*
Mechanical ventilation, n (%)	277 (63)	58 (20)	< .001*	230 (61)	31 (7)	< .001*
OKD, n (%)	42 (9.6)	21 (7.2)	NS*	37 (9.8)	26 (6.0)	.001*
CKD, n (%)	59 (13)	32 (11)	NS*	68 (18)	33 (7)	< .001*
Body mass index, kg/m^2	29.5 ± 8.9	29.8 ± 5.7	NS	29.3 ± 9.4	28.3 ± 7.7	NS
Hemoglobin, g/dl	13.9 ± 2.7	13.6 ± 2.5	NS	13.5 ± 2.8	13.9 ± 2.5	.03
Leukocytes ×10^3/µL	13.3 ± 21.4	11.2 ± 9.0	NS**	14.1 ± 22.9	10.9 ± 8.1	.01**
Neutrophils ×10^3/µL	11.0 ± 12.2	8.8 ± 4.8	.001**	11.7 ± 12.8	8.5 ± 4.9	< .001**
Lymphocytes ×10^3/µL	1.0 ± 0.7	1.1 ± 0.6	NS	1.1 ± 2.6	1.2 ± 0.7	NS
Platelets ×10^3/µL	266 ± 113	270 ± 117	NS**	259 ± 117	273 ± 114	NS**
Fasting glucose, mg/dL	193.7 ± 165.2	170.9 ± 114.4	.02**	207.0 ± 182.3	160.1 ± 97.5	< .001**
Creatinine, mg/dL	1.8 ± 2.5	1.8 ± 3.2	NS**	2.1 ± 3.0	1.4 ± 2.6	.001**

OKD: occult kidney disease
CKD: chronic kidney disease
Values are mean ± Standard deviation
NS: not significant
**P*-value was estimated using the χ^2-test
***P*-value was estimated using the Mann-Whitney U test

Table 2. Characteristics of the study population according to the eGFR. n = 702. Patients with CKD were not considered (n = 107)

N	Normal	Mild	Moderate	Severe	*P*
	317	177	135	73	
Age, years	53.0 ± 14.1	67.1 ± 13.5	69.0 ± 12.8	68.8 ± 15.3	< .001
Women, n (%)	127 (40)	75 (42)	63 (46)	34 (46)	NS*
Oxygen saturation, %	87.4 ± 13.5	85.0 ± 15.1	84.2 ± 16.2	85.6 ± 15.1	NS*
Diabetes mellitus, n (%)	103 (32)	67 (37)	63 (46)	45 (61)	< .001*
Hypertension, n (%)	112 (35)	101 (57)	96 (71)	50 (68)	< .001*
Mechanical ventilation, n (%)	83 (26)	63 (35)	49 (36)	22 (30)	NS*
Body mass index, kg/m^2	30.0 ± 7.5	28.6 ± 8.0	29.8 ± 7.7	28.0 ± 9.2	NS
Hemoglobin, g/dl	14.6 ± 2.1	14.1 ± 2.5	13.8 ± 2.4	12.5 ± 2.5	< .001
Leukocytes ×10^3/µL	12.0 ± 24.6	11.6 ± 6.0	13.9 ± 12.3	13.4 ± 8.0	NS
Neutrophils ×10^3/µL	9.7 ± 13.5	9.6 ± 5.8	11.0 ± 5.7	10.8 ± 5.7	NS
Lymphocytes ×10^3/µL	1.1 ± 0.8	1.0 ± 0.6	1.1 ± 0.9	1.7 ± 5.6	NS
Platelets ×10^3/µL	277 ± 115	264 ± 118	267 ± 108	250 ± 112	NS
Fasting plasma glucose, mg/dL	165.5 ± 144.9	180.3 ± 117.5	186.1 ± 129.1	223.8 ± 179.0	.01
Creatinine, mg/dL	0.6 ± 0.1	0.9 ± 0.1	1.4 ± 0.3	3.9 ± 3.6	< .001

eGFR: estimated glomerular filtration rate
P-value was estimated using one-way ANOVA with the Bonferroni post hoc test
**P*-value was estimated using the χ^2-test

(OR = 3.59; 95% CI: 2.28-5.66; $P < .001$), mild impairment (OR = 2.19; 95% CI: 1.51-3.18; $P < .001$), moderate impairment (OR = 2.75; 95% CI: 1.81-4.16; $P < .001$), and severe impairment (OR = 5.41; 95% CI: 3.11-9.43; $P < .001$) are significantly associated with increased mortality. An additional analysis, adjusted for age, sex, diabetes, and hypertension, showed that all categories of kidney dysfunction remained associated with increased mortality due to COVID-19. Regarding mechanical ventilation, only mild (OR = 1.64; 95% CI: 1.11-2.40; $P = .03$) and moderate (OR = 1.62; 95% CI: 1.05-2.50; $P = .007$) renal failure were associated in the unadjusted analysis but not after the adjusted analysis. Finally, renal impairment was not associated with severe COVID-19.

Table 3. Logistic regression analysis that evaluates the association between renal impairment (independent variables) with severity and death by SARS-CoV-2 (dependent variables). Patients with estimated glomerulation filtration rate ≥ 90 ml/min/1.73 m^2 were considered as the reference group.

	Mechanical ventilation	Severe COVID-19	Death
	OR (95% CI)	OR (95% CI)	OR (95% CI)
OKD			
Unadjusted	1.44 (0.83-2.48)	1.74 (0.96-3.16)	2.38 (1.40-4.06)
Adjusted*	1.24 (0.69-2.24)	1.68 (0.89-3.17)	1.86 (1.05-3.32)
AKI			
Unadjusted	1.24 (0.88-1.75)	1.15 (0.81-1.64)	2.57 (1.84-3.58)
Adjusted*	1.23 (0.85-1.79)	1.10 (0.75-1.60)	2.03 (1.42-2.89)
CKD			
Unadjusted	1.43 (0.92-2.24)	1.32 (0.82-2.12)	3.59 (2.28-5.66)
Adjusted*	1.35 (0.84-2.17)	1.40 (0.85-2.30)	3.07 (1.90-4.97)
Mild (eGFR 60-90 ml/min/1.73 m^2)			
Unadjusted	1.64 (1.11-2.40)	1.31 (0.88-1.94)	2.19 (1.51-3.18)
Adjusted*	1.42 (0.92-2.18)	1.28 (0.83-1.99)	1.77 (1.17-2.69)
Moderate (eGFR ≥ 30-60 ml/min/1.73 m^2)			
Unadjusted	1.62 (1.05-2.50)	1.24 (0.81-1.90)	2.75 (1.81-4.16)
Adjusted*	1.43 (0.86-2.37)	0.95 (0.58-1.57)	1.70 (1.05-2.76)
Severe (eGFR < 30 ml/min/1.73 m^2)			
Unadjusted	1.21 (0.69-2.12)	1.37 (0.77-2.44)	5.41 (3.11-9.43)
Adjusted*	1.03 (0.55-1.92)	1.01 (0.53-1.93)	3.41 (1.86-6.25)

OR, Odds ratio
CI, confidence interval
OKD, occult kidney disease
AKI, acute kidney injury
CKD, chronic kidney disease
eGFR, estimated glomerulation filtration rate
*Adjusted model by age, sex, diabetes, and hypertension

DISCUSSION

The findings of our study showed that OKD was significantly associated with incresed mortality associated with COVID-19, but not with disease severity. Since OKD is often not diagnosed, our findings highlight the need for early diagnosis to identify individuals at risk of poor prognosis due to COVID-19.

To the best of our knowledge, there are no previous reports assessing the presence of OKD in patients with COVID-19, only AKI and CKD have been investigated. Nonetheless, it has been reported that renal function, assessed by eGFR, might decline during the course of COVID-19.[10] Hence, the measurement of eGFR could be an indicator useful for identifying abnormal renal function in COVID-19 patients, including OKD, which often is not detected. Given that the renal function decreases more frequently in patients who were hospitalized due to acute illness such as COVID-19, it should be monitored closely for early diagnosis and optimal management to avoid or reduce future complications arising from decreased kidney function. Although the exact mechanisms linking OKD and COVID-19 are unknown, some mechanisms of renal injury could be involved. In this regard, the main via of renal injury is the overexpression of ACE2 in renal tissue.[11] Furthermore, systemic effects such as host immune clearance, immune tolerance disorders, endothelial dysfunction, thrombus formation, hypoxia, and glucose and lipid metabolism disturbances may also be involved. Finally, the cytokine storm activates macrophages leading to erythro-phagocytosis, anemia, capillary leak syndrome, and thrombosis.[12]

Xi *et al.*[13] found that the eGFR and creatinine clearance decrease by 22% and 24.0% during hospital stay in patients with COVID-19. Furthermore, at hospital admission, they demonstrated that the elevated serum creatinine, blood urea nitrogen, and decreased eGFR are independent risk factors for disease progression.[13] Also, Lv *et al.*,[14] observed that the prevalence of kidney injury is high and usually associated with poor prognosis in patients with SARS-CoV-2 infection.[14] Besides, Peng *et al.*[15] reported that development of AKI, early or late

in the course of the disease, are associated with an increased risk of in-hospital mortality among patients with COVID-19.[15] Zheng *et al*.[16] found that the mortality rate is high in patients with COVID-19 and kidney injury, being 41% in subjects with AKI, 43% in-hospital AKI, and 38% in prehospital AKI.[16]

Thus, our findings are in agreement with the aforementioned reports. Notably, the importance of early detection of OKD in patients with COVID-19 is particularly noteworthy, as it may serve as an early biomarker for high-risk patients and disease progression. Given that the AKI is a negative prognostic factor, its early diagnosis could be helpful for planning prompt and efficacy therapeutic strategies.

It is important to emphasize that the diagnosis of AKI, in addition to a decrease in eGFR and creatinine clearance, may acoompany the presence of proteinuria and hematuria.[16] However, the OKD diagnosis is established by the presence of creatinine levels ≤1.3 mg/dL and decreased GFR. Therefore, OKD is an earlier stage of kidney dysfunction than AKI. Nonetheless, our finding indicates that early kidney dysfunction, such as OKD, at hospital admission is a risk factor for mortality by COVID-19. Therefore, preventive actions are required to reduce the development of impaired renal function and establish an adequate follow-up in patients who have suffered from COVID-19.

Finally, it is worth noting that the results of our study showed no association between kidney dysfunction and severity of COVID-19. This inconsistency might be explained because most patients develop kidney injury during hospitalization,[17] however, we assessed kidney function only on hospital admission. Therefore, further studies are required to clarify our results in this field.

Limitation of the study

The following limitations of this study should be taken into account. First, due to the study design, the causal relationship cannot be assured with certainty. Second, the incidence of kidney injury, diabetes mellitus or hypertension may be underestimated. Finally, we recognize the lack of a healthy control group with negative RT-PCR SARS-CoV-2which may introduce a possible bias.

CONCLUSION

In conclusion, our findings indicate that OKD is associated with increased mortality in patients with COVID-19 independently of well-known risk factors, such as age, sex, diabetes mellitus, and hypertension. Therefore, OKD should be investigated in patients with COVID-19 to implement timely preventive measures to decrease the risk of mortality from this disease. However, since our study was cross-sectional and retrospective, further studies evaluating the causality between OKD and COVID-19, including a control group, are needed to confirm our results.

FUNDING

No funding was received for conducting this study.

FINANCIAL INTERESTS

The authors declare they have no financial interests.

REFERENCES

1. Xiang HX, Fei J, Xiang Y, et al. Renal dysfunction and prognosis of COVID-19 patients: a hospital-based retrospective cohort study. BMC Infect Dis 2021;21:158
2. Mabillard H, Sayer JA. Electrolyte Disturbances in SARS-CoV-2 Infection. F1000Res. 2020;9:587
3. De Almeida EAF, Lavinas C, Teixeira C, et al. Evaluation of an instrument for screening patients at risk for chronic kidney disease: testing SCORED (Screening for Occult Renal Disease) in a Portuguese population. Kidney Blood Press Res 2012;35:568–572.
4. Balderas-Vargas NA, Legorreta-Soberanis J, Paredes-Solís S, et al. Occult renal failure and associated factors in patients with chronic conditions. Gac Med Mex 2020;156:11-16.
5. Ranieri VM, Rubenfeld GD, Thompson BT, et al. Acute respiratory distress syndrome: the Berlin Definition. JAMA 2012;307:2526–2533.
6. Xia L, Chen J, Friedemann T, et al. The Course of Mild and Moderate COVID-19 Infections-The Unexpected Long-Lasting Challenge. Open Forum Infect Dis 2020;7:ofaa286.
7. Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. Ann Intern Med 2009;150:604–612.
8. Rashid ST, Salman M, Agarwal S, Hamilton G. Occult renal impairment is common in patients with peripheral vascular disease and normal serum creatinine. Eur J Vasc Endovasc Surg 2006;32:294–299.
9. Khwaja A. KDIGO clinical practice guidelines for acute kidney injury. Nephron Clin Pract 2012;120:c179-84.
10. Hong XW, Chi ZP, Liu GY, et al. Characteristics of Renal Function in Patients Diagnosed With COVID-19: An Observational Study. Front Med (Lausanne) 2020;7:409.

11. Pan X wu, Xu D, Zhang H, Zhou W, Wang LH, Cui XG. Identification of a potential mechanism of acute kidney injury during the COVID-19 outbreak: a study based on single-cell transcriptome analysis. Intensive Care Med 2020;46:1114–1116.
12. Faour WH, Choaib A, Issa E, et al. Mechanisms of COVID-19-induced kidney injury and current pharmacotherapies. Inflamm Res 2022;71:39–56.
13. Xia T, Zhang W, Xu Y, et al. Early kidney injury predicts disease progression in patients with COVID-19: a cohort study. BMC Infect Dis 2021;21:1012.
14. Lv W, Wu M, Ren Y, et al. Coronavirus Disease 2019: Coronaviruses and Kidney Injury. J Urol. 2020;204:918–925.
15. Peng S, Wang HY, Sun X, et al. Early versus late acute kidney injury among patients with COVID-19-a multicenter study from Wuhan, China. Nephrol Dial Transplant 2020;35:2095–2102.
16. Zheng X, Yang H, Li X, et al. Prevalence of Kidney Injury and Associations with Critical Illness and Death in Patients with COVID-19. Clin J Am Soc Nephrol. 2020;15:1549–1556.
17. de Almeida DC, Franco MDCP, Dos Santos DRP, et al. Acute kidney injury: Incidence, risk factors, and outcomes in severe COVID-19 patients. PLoS One 2021;16:e0251048.

*Correspondence to:
Luis E. Simental-Mendía, MD, PhD
Predio Canoas 100, Col. Los Angeles, 34077, Durango, Dgo., Mexico
ORCID: 0000-0002-3617-4921
Tell: (+52 618) 8120997
E-mail: luis_simental81@hotmail.com

Received September 2025
Revised December 2025
Accepted February 2026