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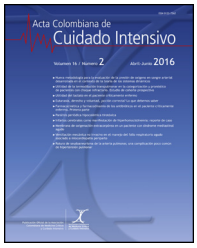

ORIGINAL ARTICLE

Clinical features and prognostic factors of adults with COVID-19 admitted to intensive care units in Colombia: A multicentre retrospective study during the first wave of the pandemic

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KEYWORDS
Coronavirus infections;
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Abstract
Background: A significant number of COVID-19 patients require intensive care unit (ICU) admission. However, ICU mortality in COVID-19 patients varies considerably between studies.
Objectives: To determine the clinical features and outcomes of adults with COVID-19 admitted to ICU in Colombia during the first wave of the pandemic.
Material and methods: A multicentre retrospective study was carried out in 8 ICUs. Adult patients admitted to the ICU with confirmed SARS-CoV-2 infection from March to July of 2020 were included.

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◊ Members of the RAMCOVID study group are present in Appendix A.

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Results: During the study period, 229 adults with COVID-19 were admitted to ICU. Most patients (54.5%) were older than 65 years. Comorbid conditions were documented in 146 (64%) patients, mainly arterial hypertension and diabetes mellitus. The median value of the SOFA score on ICU admission was 5 (interquartile range, 2–12). Regarding complications, 118 (51.5%) underwent mechanical ventilation, 51 (22.4%) required renal replacement therapy, and 85 (35%), vasopressor use. Mortality was 38.4% (88 out of 219 patients). Mortality increased with age (20% in those younger than 40 years and 54.1% in those older than 65 years; $p < .001$). In the multivariate analysis, independent factors associated with mortality were age $\geq$ 65 years (OR, 11.9; 95% CI, 3.20–44.23), SOFA score (OR, 1.21; 95% CI, 1.05–1.39), vasopressor use (OR, 12.8; 95% CI, 3.45–48.17), and renal replacement therapy (OR, 9.0; 95% CI 2.37–34.42).
Conclusions: Critically ill patients with COVID-19 had high mortality mainly related to advanced age, the severity of the disease on admission to the ICU, the use of vasopressors and renal replacement therapy.
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PALABRAS CLAVE
Infecciones por coronavirus;
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Unidad de cuidados intensivos;
Ventilación mecánica;
Mortalidad

Características clínicas y factores pronósticos de adultos con COVID-19 ingresados en unidades de cuidados intensivos en Colombia: un estudio retrospectivo multicéntrico durante la primera ola pandémica

Resumen
Introducción: Un número significativo de pacientes con COVID-19 requieren ingreso en la unidad de cuidados intensivos (UCI). Sin embargo, la mortalidad varía entre los estudios.
Objetivos: Determinar las características clínicas y el pronóstico de los adultos con COVID-19 ingresados en la UCI en Colombia durante la primera ola de la pandemia.
Materiales y métodos: Este estudio retrospectivo multicéntrico se realizó en ocho hospitales. Se incluyeron pacientes con infección confirmada por SARS-CoV-2 de marzo a julio de 2020.
Resultados: Durante el período de estudio, 229 adultos con COVID-19 ingresaron en las UCI. La mayoría de los pacientes (54,5%) tenían más de 65 años. Se documentaron comorbilidades en 146 (64%) pacientes, principalmente hipertensión arterial y diabetes mellitus. La mediana de la puntuación SOFA al ingreso en la UCI fue de 5 (rango intercuartílico, 2-12). En cuanto a las complicaciones, 118 (51,5%) requirieron ventilación mecánica, 51 (22,4%) terapia de reemplazo renal y 85 (35%) uso de vasopresores. La mortalidad fue 38,4% (88 de 219 pacientes). La mortalidad aumentó con la edad (20% en menores de 40 años y 54,1% en mayores de 65 años; $p < 0,001$). En el análisis multivariado, los factores asociados con la mortalidad fueron edad $\geq$ 65 años (OR 11,9; IC 95%, 3,20-44,23), puntuación SOFA (OR 1,21; IC 95%, 1,05-1,39), uso de vasopresores (OR 12,8; IC 95%, 3,45-48,17) y terapia de reemplazo renal (OR 9,0; IC 95%: 2,37-34,42).
Conclusiones: Los pacientes críticos con infección por SARS-CoV-2 tuvieron una mortalidad elevada, principalmente relacionada con la edad avanzada, la gravedad de la enfermedad al ingreso en la UCI y el desarrollo de disfunción orgánica.
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Introduction

In December 2019, a novel coronavirus, now known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), caused an outbreak of respiratory disease in China, and rapidly spread throughout the world.[1] The number of hospitalizations and deaths has increased continuously through 2020, with a significant number of patients with severe illness requiring intensive care unit (ICU) admission and ventilator support. Information about the characteristics and complications of critically ill patients are still emerging. However, ICU mortality varies considerably between studies.[2–4] Better characterization is crucial to direct critical care resource allocation, and to understand the disease in a local context and seeking different factors that can modify the prognosis of patients when outcomes are compared to those of other countries. Remarkably, limited data are available on the clinical features and prognosis of Latin American patients requiring ICU admission.

The aim of the present study was to determine the clinical features and outcomes of adults with coronavirus disease 2019 (COVID-19) admitted to ICU in Colombia during the

first wave of the pandemic. In addition, factors related with mortality were assessed.

Methods

A multicentre retrospective study was carried out in 8 ICUs belonging to the Colombian Association of Critical Medicine and Intensive Care (AMCI). Adult patients admitted to the ICU with confirmed SARS-CoV-2 infection between March and July of 2020 were included. A confirmed case was defined as a person with fever and/or respiratory symptoms, with laboratory-confirmed SARS-CoV-2 infection using real-time polymerase chain reaction in a respiratory sample.

ICU admission criteria and treatment decisions were not standardized and were made by attending physicians at each centre. The investigators at each participating hospital recorded data in a standardized protocol that was sent to the coordinating centre or completed it with a phone mobile application. Data was collected on demographic characteristics, comorbid conditions, clinical signs and symptoms, biochemical analysis, antiviral and antibacterial therapy, and outcomes, including mortality. Biochemical analysis and Sequential Organ Failure Assessment (SOFA) scores were measured at ICU admission. Comorbidities were assessed using modified definitions from the Charlson Comorbidity Index.[5] Tobacco use was recorded when a patient had smoked in the last 6 months. Mortality was defined as death from any cause during hospitalization. All data were carefully reviewed by two clinical investigators before the final validation.

Statistical analysis

The results were analysed using SPSS, version 15.0. All measures of central tendency and proportions were calculated from available data. To detect significant differences between groups, chi-square test or Fisher exact test for categorical variables, and the Mann–Whitney *U*-test for continuous variables, were used. The multivariate logistic regression analysis of factors potentially associated with mortality included the variables that were significant in the univariate analysis and clinically important variables. The result of multivariate analysis was reported as odds ratios (OR) and at 95% confidence intervals (CI). The goodness of fit of the multivariate model was assessed by the Hosmer–Lemeshow test and the accuracy by the area under the receiver operating characteristic (ROC) curve. Statistical significance was established at $\leq$.05. All reported *p* values were two-tailed.

Results

During the study period, 229 adult patients with SARS-CoV-2 infection were admitted to the participant ICU. The demographic, clinical characteristics and outcomes of patients are detailed in Table 1. Most patients (54.5%) were older than 65 years. At least one comorbid condition was documented in 146 (64%) patients, with arterial hypertension, diabetes mellitus, and chronic respiratory diseases being the most common. Multimorbidity (defined as the presence of two or more chronic conditions) was found in 60 (26.4%) patients. The most frequent symptoms on hospital admission were fever, cough, and shortness of breath. Conversely, altered mental status at presentation were infrequent. Antiviral therapy was administered to 119 (52%) patients. Lopinavir/ritonavir was the most frequent antiviral used (93 cases). Antibacterial therapy was administered in 213 (93%) patients. The most commonly used antibiotics were ceftriaxone (108 cases) and clarithromycin (108 cases).

Regarding complications, 118 (51.5%) underwent mechanical ventilation, 51 (22.4%) required renal replacement therapy, and 82 (35.8%) vasopressor support. In-hospital mortality was 38.4% (88 of 229 patients). Mortality increased with age (20% in those younger than 40 years, 28.6% in 40–64 years, and 54.1% older than 65 years; chi-square for trend <.001). Mortality was 63.6% (75 of 118 patients), 84.3% (43 of 51 patients), and 76.8% (63 of 82 patients) among patients requiring mechanical ventilation, renal replacement therapy, and vasopressor support, respectively.

Patients who died were older, more frequently Afrodescendant and smokers, and more often had arterial hypertension and diabetes mellitus. They were also more likely to have higher values in their SOFA score, D-dimer, and lactate dehydrogenase. Similarly, renal replacement therapy and vasopressor use were documented more frequently in patients who died (Table 1). In the multivariate analysis, independent factors associated with mortality were age $\geq$ 65 years (OR, 11.9; 95% CI, 3.20–44.23), SOFA score (+1-point increase) (OR, 1.21; 95% CI, 1.05–1.39), vasopressor use (OR, 12.8; 95% CI, 3.45–48.17), and renal replacement therapy (OR, 9.0; 95% CI, 2.37–34.42). The goodness of fit of the multivariate model was 0.74 and the discriminatory power was 0.90 (95% CI, 0.86–0.94). Similar results were found if multivariate analysis was restricted to patients that required mechanical ventilation.

Discussion

This multicentre study of critically ill patients with SARS-CoV-2 infection reveals that this disease affected mainly older patients with comorbidities. In addition, critically ill patients frequently developed severe organ failure requiring respiratory, renal, and vasopressor support. During hospital admission, 38% of critically ill patients died, being this frequency higher among patients that required mechanical ventilation (64%). Independent factors associated with mortality were old age ($\geq$65 years), the severity of the disease at ICU admission (evaluated by the SOFA score), and the need for renal and vasopressor support.

The present results are consistent with data from studies that evaluated outcomes in critically ill patients with COVID-19.[2–4] In a systematic review and meta-analysis, Armstrong et al.[2] documented that in patients with complete ICU admissions with COVID-19 infection, mortality rate was 41.6% (95% CI, 34.0–49.7%). Moreover, we also performed a subgroup analysis in mechanically ventilated patients, because ICU criteria decisions were not standardized in the present study, and it was likely that non-severe cases had been admitted due to the uncertainty around progression of the disease during the early period of the

Table 1 Demographic and clinical features, and laboratory findings of adults with COVID-19 admitted to ICU.

Variables	All patients (*N* = 229)	Patients who survived (*N* = 141)	Patients who died (*N* = 88)	*p*-value
Age, median (IQR), years	62 (52–71)	58 (48–67.5)	67.5 (56.5–74.5)	<.001
Male sex	138 (60.3)	85 (60.3)	53 (60.2)	.99
Afro-descendant	16 (7)	6 (4.3)	10 (11.4)	.04
Body mass index, median (IQR)	26.7 (24.4–30.4)	27.2 (25.3–30.8)	26.1 (23.6–30)	.10
Comorbidities	146 (64)	78 (55.7)	68 (77.3)	.001
Arterial hypertension	104 (45.4)	52 (36.9)	52 (59.1)	.001
Chronic cardiac disease	18 (7.9)	8 (5.7)	10 (11.4)	.12
Chronic pulmonary disease	26 (11.4)	15 (10.6)	11 (12.5)	.66
Diabetes mellitus	48 (21)	20 (14.2)	28 (31.8)	.001
Chronic kidney disease	13 (5.7)	5 (3.5)	8 (9.1)	.07
Smoker	11 (4.8)	3 (2.1)	8 (9.1)	.02
Clinical features				
Fever	162 (70.7)	106 (75.2)	56 (63.6)	.06
Cough	157 (68.6)	96 (68.1)	61 (69.3)	.84
Dyspnoea	171 (74.7)	105 (74.5)	66 (75)	.92
Headache	22 (9.6)	18 (12.8)	4 (4.5)	.04
Gastrointestinal symptoms	38 (16.6)	24 (17)	14 (15.9)	.82
Altered consciousness	21 (9.2)	9 (6.4)	12 (13.6)	.06
Laboratory findings				
PaO2/FiO2, median (IQR)	107.5 (73–200)	145 (79–200)	100 (70–163)	.06
Leucocytosis (≥12000 cell/mm3)	88 (38.4)	41 (29.1)	47 (53.4)	<.001
Lymphopenia (≤1200 cell/mm3)	82 (36)	48 (34.3)	34 (38.6)	.50
D-dimer, ng/ml, median (IQR)	965 (400–2765)	746 (383.5–1373.5)	1326 (424–5052)	.003
Ferritin, ng/ml, median (IQR)	1188 (683.5–1650)	1184 (792.9–1650)	1226 (529.2–1650)	.59
LDH, U/litre, median (IQR)	455 (372.5–604)	398 (342–455)	549 (452–709)	<.001
SOFA score	5 (2–12)	3 (1–10)	10 (5–12)	<.001
Treatment				
Antiviral therapy	119 (52)	75 (53.2)	44 (50)	.63
Antibiotic therapy	213 (93)	127 (90.1)	86 (97.7)	.02
Corticosteroids	130 (56.8)	83 (58.9)	47 (53.4)	.41
Complications				
Mechanical ventilation	118 (51.5)	43 (30.5)	75 (85.2)	<.001
Renal replacement therapy	51 (22.4)	8 (5.7)	43 (49.4)	<.001
Prone position	101 (44.1)	40 (28.4)	61 (69.3)	<.001
Vasopressor use	82 (35.8)	19 (13.5)	63 (71.6)	<.001
Tracheostomy	19 (9.1)	9 (7.1)	10 (12.3)	.19

Data are reported as *n* (%), unless otherwise state. ICU, intensive care unit; IQR, interquartile range; LDH, lactate dehydrogenase; SOFA, Sequential Organ Failure Assessment.

pandemic. Mortality in COVID-19 patients that required ventilator support has been varied, ranging from 20% to 88%.[6,7] Our mortality in mechanically ventilated patients was similar to that reported in other countries.[7]

In the univariate analysis of this study, Afro-descendants had a higher risk of mortality. Similarly, Golestaneh et al.[8] found that blacks have a higher mortality with COVID-19 incompletely explained by age, comorbidities, and available metrics of sociodemographic disparity. Moreover, as described in other studies,[9,10] we also found that comorbidities such as arterial hypertension and diabetes mellitus were more frequent in patients who died. A meta-analysis documented that diabetes mellitus in patients with COVID-19 is related to a two-fold increase in mortality as well as severe disease, as compared to nondiabetic patients.[9] Other factors related to mortality in the present study were high levels of d-dimer and lactate dehydrogenase. These biomarkers have been associated with poor prognosis and have been included in severity scores developed to evaluate the risk of complications in COVID-19 patients.[11,12]

In our cohort, mortality was significantly associated with older age, with 60% mortality in those age 65 and above as compared with 20% in those under age 40. Mortality was also associated with severity of illness on arrival to the ICU, and the need for ICU interventions for severe organ dysfunction including renal replacement therapy and vasopressor support. In this regard, in a metanalysis, the mortality rate of patients with acute kidney injury was 52% (range, 7%–100%).[13] Similarly, Pei et al.[14] documented, according to 2012 Kidney Disease Improving Global Outcomes (KDIGO)

definitions, a mortality of 75% in stage 2, and 90.9% in stage 3. Moreover, we also documented a high mortality among patients requiring vasopressor support. The frequency of vasopressor support reported in COVID-19 patients that required ICU admission ranges from 35 to 94%. The reasons for vasopressor support remain poorly documented, and includes hypovolemia, sepsis, deep sedation during mechanical ventilation, pulmonary embolism, or myocarditis.[15] Nevertheless, the complete profile of these complications in COVID-19 patients required further research.

The present study was conducted in geographically diverse settings all over Colombia, during the first months of the COVID-19 pandemic. The strengths of the study are its multicentre design, the large number of patients included, and the comprehensive clinical data collection. However, our study has some limitations that should be acknowledged. First, physicians did not use a uniform strategy for determining ICU admission, and so factors other than disease severity may have contributed to site-of-care decisions. In this regard, we performed a subgroup analysis in patients with mechanical ventilation, a definitive criterion for ICU admission, and found similar results in prognosis factors. Second, due to the retrospective design, some clinical and laboratory findings were not available for all patients. Third, any link between ICU capacity and healthcare system measures and the reported outcomes were not evaluated. Finally, we did not assess the viral load or shedding, and its relationship with the outcomes.

In conclusion, critically ill patients with COVID-19 had a high mortality mainly related to advanced age, the severity of the disease on admission to the ICU, the use of vasopressors and renal replacement therapy. Future research should evaluate and identify treatments that prevent the development of organ failure and improve COVID-19 patient outcomes.

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Conflict of interest

All authors had no potential conflicts of interest.

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Appendix A. Other members of the Network for Research in COVID-19 of the Colombian Association of Critical Medicine and Intensive Care (RAMCOVID study group)

Emiro Buendia, Samir Viloria and Didier Sanjuan (Universidad del Norte and Hospital Universidad del Norte); Yudy Aguilar and Luz E. Botero (Universidad Pontificia Bolivariana and Clínica Universitaria Bolivariana); Carlos Renowitzky (Clínica Centro); Daniela Arango-Isaza (Hospital Manuel Uribe Ángel); Patricia Medina-González and Hernán F. Guillen-Burgos (La Misericordia Clínica Internacional); Ana M. Pinza-Ortega (Fundación Hospital San Pedro); David Yepes (Universidad CES and Clínica CES).

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