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Risk factors for COVID-19 and their association with mortality in Ecuadorian patients admitted to the ICU

A retrospective cohort multicentric study

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Abstract

Several risk factors were associated with mortality in patients with coronavirus disease 2019 (COVID-19) infection in intensive care units (ICU). We assessed the effect of risk factors related to the characteristics and clinical history of the population, laboratory test results, drug management, and type of ventilation on the probability of survival/discharge from the ICU. A retrospective cohort multicentric study of adults with COVID-19 admitted to the ICU between March 2020 and December 2021. Data were collected from 6 hospitals in 5 cities in Ecuador. The primary outcome was ICU survival/discharge. Survival analysis was conducted using semi-parametric Cox proportional hazards models. Of those admitted to the ICU with COVID-19, (n = 991), mean age was 56.76 ± 13.14, and 65.9% were male. Regarding the primary outcome, 51.1% (n = 506) died and 48.9% (n = 485) survived. Of the group that died, their mean age was higher than the survivors (60.7 vs 52.60 years, respectively), and they had a higher prevalence of comorbidities such as arterial hypertension (37.2% vs 20.4%, respectively) and diabetes mellitus (26.9% vs 15.7%, respectively), with $P < .001$. In ventilatory management, 32.7% of patients used noninvasive ventilation and high-flow nasal cannula, and 67.3% required invasive ventilatory support. After adjusting for confounders, Cox regression analysis showed that patients were less likely to be discharged alive from the ICU if they met the following conditions: arterial hypertension (hazard ratio [HR] = 0.83 95% CI 0.723–0.964), diabetes mellitus (HR = 0.80 95% CI 0.696–0.938), older than 62 years (HR = 0.86 95% CI 0.790–0.956), obese (body mass index ≥ 30) (HR = 0.78 95% CI 0.697–0.887), 1 unit increase in SOFA score (HR = 0.94 95% CI 0.937–0.961), PaO_2/FiO_2 ratio <100 mm Hg (HR = 0.84 95% CI 0.786–0.914), and the use of invasive mechanical ventilation (HR = 0.68 95% CI 0.614–0.769). Risk factors associated with increased mortality were older age, obesity, arterial hypertension, and diabetes. Factors such as male gender, chronic obstructive pulmonary disease, acute kidney injury, and cancer reported in other investigations did not have the same effect on mortality in our study.

Abbreviations: BMI = body mass index, COVID-19 = Coronavirus Disease 2019, HR = hazard ratio, ICU = intensive care unit, IMV = invasive mechanical ventilation, m.a.s.l. = meters above sea level, NIV = noninvasive ventilation.

Keywords: COVID-19, intensive care units, mechanical ventilation, risk factors

LF-G and JV-O contributed equally to this work.

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1. Introduction

The first coronavirus disease 2019 (COVID-19) case occurred in China in December 2019. Produced by infection with severe acute respiratory syndrome virus 2,[1] it reached the status of a pandemic in March 2020[2] and has resulted in >770,000,000 cases and over 7 million deaths around the world as of February 2024.[3] According to the Ministry of Health of Ecuador, >1,000,000 confirmed cases were reported, and > 30,000 people died from the disease.[4]

Different authors from different parts of the world have evaluated the severity of COVID-19. One of the most extensive studies revealed that 81% of the cases were mild, 14% severe, and 5% critical, and the case-fatality rate was 2.3%.[5] Even though most COVID-19 cases are classified as mild, the severe and critical cases have become an unprecedented Public Health issue due to the lack of intensive care unit (ICU) beds and the insufficient capacity of most countries to contain the pandemic.[6]

The global burden of COVID-19 cases drives research to understand how risk factors may contribute to COVID-19 disease severity and ICU admission. Thus, a meta-analysis that evaluated 16,561 critically ill COVID-19 patients found that the mean age was 62.6 years, and some of the common comorbidities included hypertension (49.5%), diabetes mellitus (26.6%), and cardiovascular disease (22.2%).[6] Therefore, an adequate provision of services and the capacity of ICUs is a global priority to avoid inequalities in the clinical outcomes obtained from this disease.[6]

The literature has reported multiple factors determining the probability of complication and death of patients with COVID-19, such as advanced age,[7] male gender,[8] chronic non-transmissible diseases such as diabetes mellitus type 2,[9] arterial hypertension,[10] obesity,[11] kidney disease,[12] etc. However, whether these factors have a similar effect in a heterogeneous population such as that of Ecuador is still being determined. Only 1 study using individual data of patients admitted to the ICU reported that being treated at high altitudes is associated with lower COVID-19 mortality.[13] Yet, this study used a small sample size and data from only 2 healthcare centers nationwide. Thus, the present study aims to provide a broader analysis of how several risk factors are associated with the survival/discharge of COVID-19 patients admitted to the ICU.

2. Materials and methods

Using a retrospective cohort multicentric study, we evaluated the association of different risk factors and the survival/discharge rate of patients with COVID-19 treated in ICUs in 5 cities in Ecuador.

2.1. Study setting

Data were collected from 6 tertiary hospital centers (2 hospitals at sea level and 4 high-altitude hospitals) located in the cities of Babahoyo (3 meters above sea level [m.a.s.l.]), Portoviejo (53 m.a.s.l.), Ibarra (2225 m a.s.l.), Cuenca (2560 m.a.s.l.) and Quito (2850 m.a.s.l.). Hospital centers were selected in a way that principal cities from the Coast and Highlands regions were represented. However, not all hospitals could get hospital permissions timely and were excluded from the study (Guayaquil).

2.2. Study sample and data collection

We obtained a consecutive sample from the total number of patients diagnosed with COVID-19 who were treated in the ICU of the participating hospitals between March 2020 and December 2021. The patients met the following inclusion criteria: (i) adult males and females diagnosed with COVID-19 by the real-time polymerase chain reaction method, (ii) admitted to ICU, and (iii) need for invasive (IMV) and noninvasive mechanical ventilation (NIV) as part of the management of COVID-19. Patients who did not meet the inclusion criteria, that is, those who were not diagnosed with COVID-19 by the real-time polymerase chain reaction method, were excluded from the study.

Physicians from the participating ICUs carried out the collection of variables included in this study. Data referring to admission and discharge from the ICU was collected through the REDCap® software from July 2020 to October 2021. Our study obtained the ethical approval of an ad hoc government committee explicitly created to supervise national research activities related to COVID-19 (MSP-CGDES-2021-0065-O). In addition, the committee granted an exemption regarding the use of informed consent due to the COVID-19 pandemic emergency.

2.3. Measures

We collected socio-demographic and health-related variables (comorbidities, laboratories on ICU admission, drug management, and clinical outcomes), including age (binary variable dichotomized by 62), sex, obesity (body mass index [BMI] greater than or equal to 30 vs <30), presence of diabetes type 2, hypertension, cancer, kidney failure acute, capillary refill time, hemoglobin concentration level, creatine concentration levels, SOFA score, PaO_2/FiO_2 ratio, IMV vs NIV, altitude (>1500 m.a.s.l), duration of mechanical ventilation, ICU stays, and hospital length of stay. All the ventilatory parameters were measured at the ICU admission.

2.4. Statistical analysis

Descriptive statistics were used to estimate the incidence of survival among patients diagnosed with COVID-19 and treated in the ICU and to describe the demographic/clinical information retrieved from clinical records. When numerical data did not follow a normal distribution, they were expressed in tables using nonparametric measures, such as median and interquartile range, as seen in Table 1. Categorical variables were reported as counts and percentages. Bivariate analysis was performed with parametric (t test and X^2) and nonparametric (Wilcoxon and Fisher exact test) tests to assess the relationship between the different risk factors and death or survival outcomes and baseline characteristics of the study population. We used semiparametric Cox proportional hazards models to estimate the hazard ratios (HRs) of different risk factors to experience ICU survival/discharge. In the present analysis, HR values <1 should be interpreted as less likely to be discharged alive from the ICU, and HR values >1 as more likely to be discharged alive from the ICU.

Further, in the present study, we did not impute missing data; thus, we conducted a complete case analysis. Results with statistical significance were those with a P-value < .05. Statistical analyses were done using RStudio software, version 1.4.1106.

3. Results

Information was collected from 1168 patients admitted to the ICU of the participating units. After applying inclusion and exclusion criteria, the sample was reduced to 991 patients. Of the patients included, 51.1% (n = 506) died and 48.9% (n = 485) survived. Table 1 summarizes the study sample's demographic, clinical, and laboratory characteristics and the results obtained regarding the duration of mechanical ventilation, ICU stays, and hospital stays.

The participants had a mean age of 56.76 ± 13.14 years; 65.9% of the patients were men; and half of the study sample

Table 1

Baseline characteristics of the study sample.

Variable	Overall n = 991	Survival n = 485	Death n = 506	*P*-value	Missing values n (%)
Demographic characteristics					
Age (yr), mean ± SD	56.76 ± 13.14	52.60 ± 12.63	60.75 ± 12.38	<.001	-
< 50	302 (30.5)	195 (40.2)	107 (21.1)	-	-
51–62	331 (33.4)	182 (37.5)	149 (29.4)	-	-
63–70	214 (21.6)	76 (15.7)	138 (27.3)	-	-
> 70	144 (14.5)	32 (6.6)	112 (22.1)	-	-
Male	653 (65.9)	310 (63.9)	343 (67.8)	.199	-
Female	338 (34.1)	175 (36.1)	163 (32.2)	.199	-
Body mass index, median (IQR)	27.77 (25.05–31.11)	27.96 (25.28–31.14)	27.65 (24.80–30.94)	.254	-
Comorbities, n (%)					
Diabetes mellitus	212 (21.4)	76 (15.7)	136 (26.9)	<.001	-
Hypertension	287 (29.0)	99 (20.4)	188 (37.2)	<.001	-
Heart disease (acute myocardial infarction)*	5 (0.5)	0 (0.0)	5 (1.0)	.064	-
Cancer*	4 (0.4)	3 (0.6)	1 (0.2)	.364	-
Morbid obesity*	38 (3.8)	16 (3.3)	22 (4.3)	.413	-
Other disease	341 (34.4)	173 (35.7)	168 (33.2)	.414	-
None	415 (41.9)	235 (48.5)	180 (35.6)	<.001	-
Clinical parameters on admission					
SOFA Score, mean ± SD	6.56 ± 3.99	5.49 ± 3.59	7.59 ± 4.09	<.001	-
APACHE II Score, mean ± SD	15.26 ± 8.18	12.08 ± 6.574	18.29 ± 8.42	<.001	18 (1.8)
Temperature, mean ± SD	36.62 ± 0.71	36.50 ± 0.50	36.55 ± 0.66	.313	401 (39.4)
Systolic blood pressure mm Hg, mean ± SD	123.07 ± 20.20	123.02 ± 17.61	123.11 ± 22.42	.943	-
Cardiac frequency, mean ± SD	91.90 ± 19.51	90.75 ± 0.85	93.00 ± 20.03	.068	-
Respiratory rate, median (IQR)	28 (24–34)	28 (24–34)	28 (24–34)	.780	-
PaO_2/FiO_2 ratio, median (IQR)	96 (70–128)	106 (81–138)	87 (62–115)	<.001	-
Capillary refill time > 3 s, n (%)	111 (11.20)	24 (4.90)	87 (17.20)	<.001	-
Laboratories on ICU admission					
Leucocytes, $x10^3$ cells, median (IQR)	10 320 (6 735–14 520)	9 885 (6 725–13 790)	10 985 (6 790–15 000)	.041	2 (0.2)
Hemoglobin g/dL, median (IQR)	15.20 (14.00–16.50)	15.00 (14.00–16.00)	15.00 (14.00–17.00)	.389	367 (37.0)
Platelets, $10^3/mm^3$, median (IQR)	274 000 (183 000–353 000)	293 000 (218 000–378 000)	248 000 (154 000–335 000)	<.001	3 (0.3)
Glucosa mg/dL, median (IQR)	137 (112–175)	129.5 (109–161.7)	145 (118–187)	<.001	22 (2.2)
pH median (IQR)	7.43 (7.37–7.47)	7.44 (7.40–7.48)	7.41 (7.34–7.46)	<.001	1 (0.1)
PaO_2 (mm Hg) median (IQR)	60.00 (50.00–72.00)	60.00 (51.00–70.00)	59.00 (49.00–74.00)	.935	8 (0.8)
$PaCO_2$ (mm Hg) median (IQR)	33.00 (28.00–40.00)	32.00 (28.00–38.00)	34.300 (29.00–43.00)	<.001	1 (0.1)
Lactate mmol/L, median (IQR)	1.40 (1.10–2.00)	1.40 (1.10–1.80)	1.50 (1.00–2.20)	.129	548 (55.3)
Total Bilirubin mg/dL, median (IQR)	0.73 (0.53–0.97)	0.71 (0.52–0.95)	0.74 (0.54–1.00)	.413	601 (60.6)
Alanine transaminase (ALT) U/L, median (IQR)	52 (32–87)	55 (33–91)	50 (31–80)	.030	144 (14.5)
Aspartate transaminsase (AST) U/L, median (IQR)	53.00 (36.00–79.00)	52.00 (35.00–79.00)	54.00 (37.00–79.00)	.530	143 (14.4)
Ureic nitrogen mg/dL, median (IQR)	21.00 (15.00–30.00)	19.00 (14.00–24.00)	24.00 (17.00–37.00)	<.001	189 (19.1)
Serum creatinine mg/dL, median (IQR)	0.82 (0.67–1.03)	0.80 (0.65–0.97)	0.88 (0.72–1.12)	<.001	528 (53.3)
Prothrombin time (PT) seconds, median (IQR)	11.80 (11.00–13.00)	11.60 (10.95–12.40)	12.00 (11.00–13.20)	.002	428 (43.2)
Partial thromboplastin time (PTT) seconds, median (IQR)	28.90 (24.35–34.00)	28.00 (23.60–33.00)	30.00 (25.00–36.00)	.007	414 (41.8)
C-reactive protein (mg/dL), median (IQR)	114.00 (25.60–240.75)	102.50 (23.78–201.00)	133.00 (27.25–258.00)	.007	713 (71.9)
Procalcitonin (mg/dL), median (IQR)	0.45 (0.19–1.30)	0.31 (0.17–0.88)	0.52 (0.21–1.72)	.001	597 (60.2)
Outcomes					
Duration of mechanical ventilation, days, median (IQR)	10 (6–15)	9 (6–14)	11 (6–16)	.004	20 (2.0)
ICU length of stay, days, median (IQR)	10 (6–16)	10 (6–16)	11 (6–16)	.909	-
Hospital length of stay, days, median (IQR)	15 (9–23)	19 (12–27)	12 (8–19)	<.001	-

* Fisher exact test

was overweight (BMI: 27.77 kg/m² 95% CI 25.05–31.11). Of the group that died, their mean age was higher than the survivors (60.7 vs 52.60 years, respectively), and they had a higher prevalence of comorbidities such as arterial hypertension (37.2% vs 20.4%, respectively) and diabetes mellitus (26.9% vs 15.7%, respectively), with $P < .001$. In addition, they presented higher blood glucose levels at admission (145 vs 129.5 mg/dL), lower PaO_2/FiO_2 ratio levels (87 vs 106 mm Hg), and prolonged capillary refill (17.20% vs 4.9%) compared to patients who survived, with P-value < .001. Since admission, the patients in the group that died presented a tendency to severe disease represented with higher severity scores, APACHE II (18.29 vs 12.08) and SOFA (7.59 vs 5.49), with $P < .001$.

Regarding ventilatory management in the ICU (Table 2), 32.7% (n = 324) of patients used NIV or high-flow nasal cannula, and 67.3% (n = 667) required invasive ventilatory support. Of the 667 patients who received invasive ventilatory support, 179 (26.8%) previously received noninvasive ventilatory support, and 78 (11.7%) received high-flow nasal cannula. Patients who received NIV or high-flow nasal cannula were more likely to die compared to those who received IMV, 27.2% vs 60.7%, P-value < .001, respectively. The patients included in this study received a protective ventilatory strategy, evidenced by tidal volume 7 mL/kg,[6–8] plateau pressure 24.26 ± 5.82 cm H_2O, and driving pressure 14 ± 3.49 cm H_2O. Patients in the group that died had lower lung compliance (27 mL/cm H_2O [20–34]) compared to the group that survived (32 mL/cm H_2O [25–40]).

Furthermore, patients in the group that died were more likely to require a prone position (63.6% vs 38.6%, respectively), with $P < .001$.

Table 3 shows that patients in the group that died were more likely to require vasoactive drugs (70.9% vs 35.7%) and antibiotic therapy (80% vs 61%, respectively), with $P < .001$. Moreover, fewer deaths were evidenced in patients who received corticosteroids (81.6% vs 73.7%, $P = .003$) and anticoagulants (67.8% vs 60.9%, $P = .022$), with a statistically significant difference.

Cox regression analysis (Fig. 1) showed that adjusting for possible confounding factors, patients with arterial hypertension (HR = 0.83 95% CI 0.72–0.96), diabetes mellitus (HR = 0.80 95% CI 0.69–0.94), who were older than 62 years (HR = 0.86 95% CI 0.79–0.96), and obese (BMI ≥ 30) (HR = 0.78 95% CI 0.69–0.89) were less likely to be discharged from the ICU alive. Patients at high altitudes were more likely to survive or be discharged from the ICU (HR = 1.57 95% CI 1.24–1.99) than those treated at sea level.

Further, 1 unit increase in SOFA score (HR = 0.94 95% CI 0.94–0.96), PaO_2/FiO_2 ratio <100 mm Hg (HR = 0.84 95% CI 0.79–0.91), and the use of IMV (HR = 0.68 95% CI 0.61–0.77) were associated with less probability to be discharged from the ICU alive. We found that creatinine levels greater than or equal to 2 mg/dL, abnormal hemoglobin levels, peripheral perfusion >3 seconds, male sex, and the diagnosis of acute kidney failure or cancer did not obtain a statistically significant difference between groups.

4. Discussion

The findings from this study highlight the critical impact of various risk factors on the mortality of COVID-19 patients admitted to the Intensive Care Units of hospitals in Ecuador. These findings, derived from a cohort of 991 severely ill patients, demonstrate the need for early identification and close monitoring of high-risk individuals to optimize resource allocation and improve clinical outcomes in critical care settings.

Accounting for potential confounding variables, our analysis identified a decreased probability of survival and ICU discharge among patients with comorbidities, specifically arterial hypertension, diabetes mellitus, and obesity. Additionally, we noted a reduced likelihood of survival and ICU discharge for patients aged 62 and older. These crucial findings highlight the pressing need for customized care approaches in critical care medicine, tackling the distinct challenges faced by at-risk patient populations and fostering improved clinical outcomes.

4.1. Comparison with other studies

Our results are aligned with findings obtained in meta-analyses that evaluated risk factors for the severity and death of patients with COVID-19. These studies report a higher risk for older patients with comorbidities such as arterial hypertension, diabetes mellitus, and obesity.[14–16]

Studies that report risk factors exclusively in severe COVID-19 patients who required ICU management report similar results to ours regarding comorbidities and baseline clinical characteristics that increase the risk of death.[17–19] In addition, these patients also presented high results on severity scores such as APACHE II and SOFA at admission.[18]

Patients treated at high altitudes (>1500 m.a.s.l) were more likely to survive or be discharged from the ICU. Our results support the findings from a previous Ecuadorian cohort where high altitude was determined as a protective factor in patients with severe COVID-19 treated at the ICU, arguing that the possible explanation for this phenomenon is the genetic and physiological adaptations to exposure to chronic hypoxia.[20] Major hypobaric hypoxia's molecular and clinical features require analysis of microvasculature, gene expression, proteins, metabolites, and organelles, which is not always feasible or ethical in a hospital setting.[21,22] Despite this, in our study, we assessed hemoglobin levels as possible feature of hypobaric hypoxia. Hemoglobin levels were not statistically different among groups. Other clinical features, such as minute ventilation or pulmonary vasoconstriction, were not possible to assess because of the impairment in ventilatory dynamics due to the infection of COVID-19 and the unnecessary invasive procedure that determining the pulmonary artery pressure could represent over the patients.

Older patients' greater susceptibility may be explained by the poor response of the immune system related to the aging process, known as immunosenescence.[23] In addition, a diminished response of interferon (INF) type 1 has been evidenced, which leads to an inadequate response of TCD8 lymphocytes and allows more significant viral replication.[24]

The higher susceptibility in overweight/obese patients might be explained by the increase of adipose tissue that can act as a reservoir for IL-6 production and secretion, thus amplifying the cytokine storm. Moreover, high levels of cytokines secreted by hypertrophic fat cells in the bloodstream, including IL-6, TNF-α, IL-1, and IL-10, counteract the termination of the antiviral immune response in the lungs, promoting a cytokine storm in patients with COVID-19.[25] Further, the significant predisposition to complications in hypertensive patients may be explained by the deficiency of the vasoprotective, antiproliferative, and anti-inflammatory effects of angiotensin-converting enzyme 2. In

Table 2

Characteristics of Ventilatory Management at Intensive Care Unit Admission.

Characteristics	Overall n = 991	Survival n = 485	Death n = 506	*P*-value	Missing values n (%)
Other types of noninvasive mechanical ventilation (noninvasive mechanical ventilation and high flow nasal canula), n (%)	324 (32.7)	236 (72.8)	88 (27.2)	<.001	-
Invasive mechanical ventilation, n (%)	667 (67.3)	262 (39.3)	405 (60.7)	<.001	-
Tidal volume (mL/kg ideal body weight), median (IQR)	7.0 (6.0–8.0)	7.0 (6.0–9.0)	7.0 (6.0–8.0)	.025	74 (11.1)
Plateau pressure (cm H_2O), mean ± SD	24.26 ± 5.82	23.58 ± 7.38	24.68 ± 4.59	.036	146 (21.9)
Driving pressure (cm H_2O), mean ± SD	14.00 ± 3.49	13.32 ± 3.15	14.40 ± 3.62	<.001	197 (29.5)
PEEP (cm H_2O), mean ± SD	10.10 ± 2.39	9.87 ± 2.05	10.25 ± 2.57	.055	39 (5.8)
< 10	415 (62.2)	168 (40.5)	247 (59.5)	-	
10–12	136 (20.4)	58 (42.6)	78 (57.4)	-	
13–15	70 (10.5)	12 (17.1)	58 (82.9)	-	
>15	7 (1.0)	2 (28.6)	5 (71.4)	-	
Compliance (mL/cm H_2O), median (IQR)	29.0 (22.8–36.0)	32.0 (25.0–40.0)	27.0 (20.0–34.0)	<.001	198 (29.7)
Prone position, n (%)	509 (51.4)	187 (38.6)	322 (63.6)	<.001	-
Tracheotomy n (%)	135 (23.2)	52 (23.3)	83 (23.1)	.012	201 (20.3)

addition, the uncontrolled activity of angiotensin II occurs, which is associated with endothelial dysfunction and inflammation.[26]

Regarding antibiotic use, we found that the group that died had a significantly higher percentage of use of antibiotics, whereas other cohorts found no differences among groups.[27] On the other hand, immunomodulatory treatment with tocilizumab was utilized only in 2.3% of participants in the survival group and 3.8% in non-survivors. This is intriguing because, by May 2021, the RECOVERY trial proved the efficacy of tocilizumab to improve survival and other clinical outcomes in patients with hypoxia and systemic inflammation.[28] The local shortage of access to this treatment was the main reason for the lack of use of this drug.

A meta-analysis that included 69 studies, with a sample of 57,420 adult patients with COVID-19 who received IMV, reported an estimated overall mortality rate of 45% (95% CI 39–52%)[29] and our study reports a mortality rate of 60.7% for patients who received invasive ventilatory support.

In Ecuador, almost 85% of the population was fully vaccinated by 2023.[30] This fact contributed to the diminishing of severe COVID-19 cases and mortality rates in the country, as it was observed worldwide where vaccines prevented over 14 million deaths in the first year of the vaccination program.[31] To mitigate the impact of different emerging severe acute respiratory syndrome virus 2 variants, further booster schemes were administered, and nearly 50% of Ecuadorians received the first booster and over 12% the second booster.[30] Nevertheless, Ecuador health policies did not meet the guidelines for vaccination programs. From July to September 2023, the bivalent booster (Original Wuhan variant and Omicron's BA.4 and BA.5 subvariants) was provided to healthcare providers, the elderly, and people with high-risk,[32] but once this program was over, no new programs using bivalent booster were conducted. Afterward, the updated monovalent vaccine (based on XBB.1.5 variant with laboratory-proven efficacy against BA derivatives subvariants[33]) has not been distributed in the Ecuadorian territory, despite that in Latin America, by late 2023 and early 2024, BA.2.86 variant derivatives such as JN.1, are the predominant variants circulating.[34]

Table 3

Drug management of the patients admitted to the ICU.

	Survival n = 485	Death n = 506	*P*-value
Vasoactive, n (%) Yes	173 (35.7)	359 (70.9)	<.001
Antibiotics, n (%) Yes	296 (61.0)	405 (80.0)	<.001
Lopinavir + ritonavir, n (%) Yes	33 (6.8)	76 (15.0)	<.001
Remdesivir, n (%) Yes	3 (0.6)	0 (0.0)	<.001
Hydroxychloroquine, n (%) Yes	9 (1.9)	15 (3.0)	.256
Chloroquine, n (%) Yes	45 (9.3)	101 (20.0)	<.001
Corticosteroids Yes	396 (81.6)	373 (73.7)	.003
Tocilizumab, n (%) Yes	11 (2.3)	19 (3.8)	.172
Anticoagulation, n (%) Yes	329 (67.8)	308 (60.9)	.022
Convalescent plasma, n (%) Yes	4 (0.8)	10 (2.0)	.125

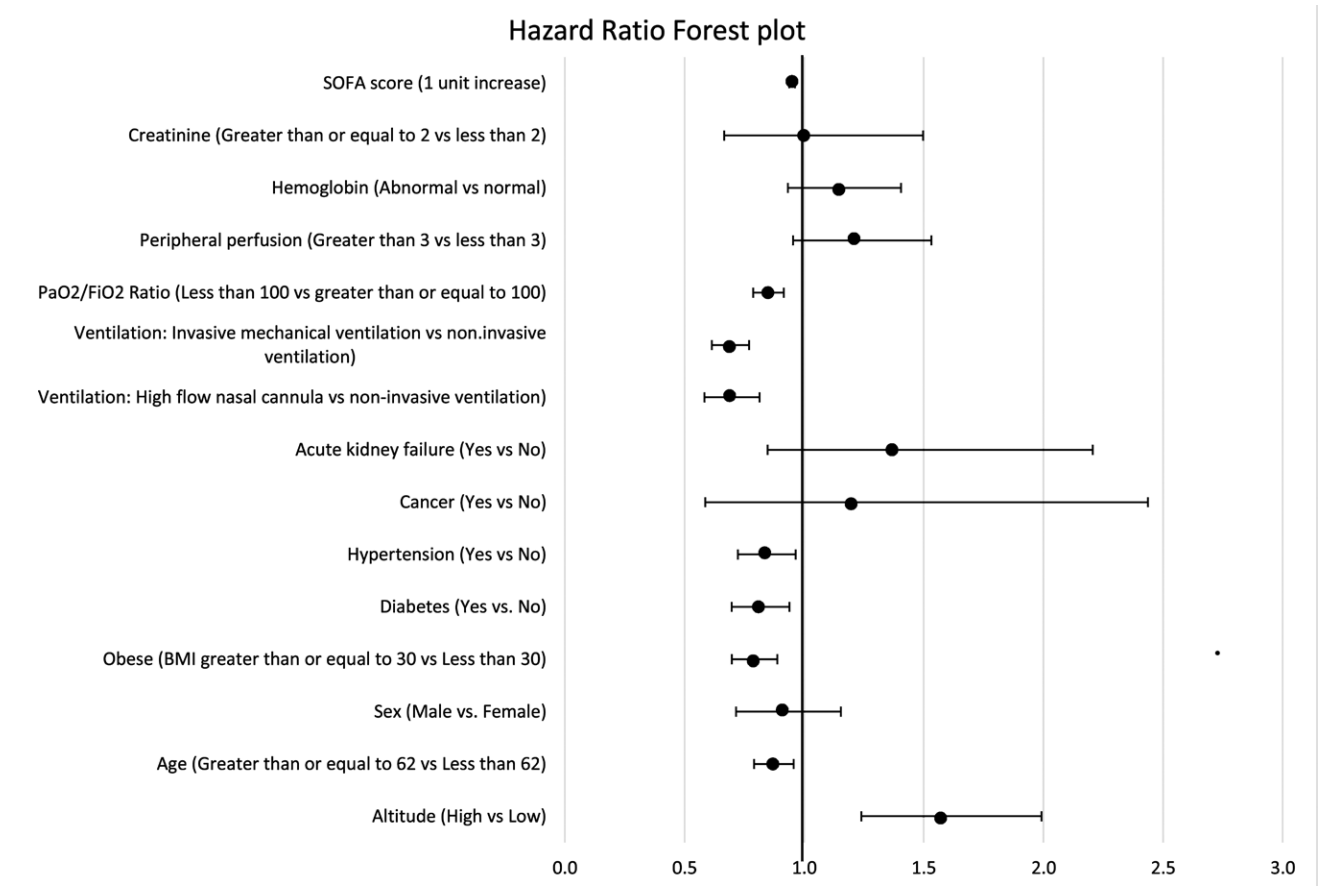

Figure 1. Multivariable Cox proportional hazards regression analysis of factors associated with mortality.

4.2. Strengths and limitations

Our study has different strengths and limitations. Compared to a prospective cohort study conducted with a similar and larger population in Latin America, our study obtained equivalent results concerning COVID-19 severity risk factors such as age and obesity. Still, it differed on other risk factors, such as anemia (assessed through abnormal hemoglobin levels instead of hematocrit).[35] Besides, our population was the largest cohort analyzing risk factors in COVID-19 patients in Ecuador and included numerous sites along the country, compared with other similar local studies.[13,20] Also, our study evaluated different comorbidities as a single risk factor rather than a unique variable for all comorbidities. It explored the clinical outcomes of using several drug treatments for severe COVID-19. Between its limitations, we did not assess important variables such as self-care at discharge mainly because our retrospective design did not allow us to obtain information different than that collected at the medical registries. The high missing values in specific laboratory parameters due to the shortage of laboratory supplies during the pandemic limited us from incorporating them in our regression model or obtaining statistical significance (e.g., hemoglobin and creatinine) so we cannot rule out the possibility of residual confounding. Further, due to regulatory/administrative permissions and logistic issues some hospitals were excluded from the study population that might cause a selection bias. However, we anticipated that its effect would be minimal due to the important final sample size analyzed.

4.3. Implications of the findings

The present study has important clinical implications for medical practitioners in managing patients infected with the virus. The study's findings, which highlight the critical role of various factors, could provide healthcare professionals with crucial insights into improving patient outcomes. For instance, clinicians can use these findings to develop targeted interventions and treatment plans for patients with COVID-19 based on their risk factors. Ultimately, the study's findings may also inform public health policy and decision-making, particularly in countries with similar geographic and demographic profiles to Ecuador. Further, the COVID-19 pandemic highlighted the fragility of the Ecuadorian healthcare system. Thus, human and supply resources significantly impacted the decision-making process, particularly during periods of high incidence when patient demand far exceeded resource supply. Consequently, prioritization of patient care was required based on factors such as the probability of survival and recoverable years of life. Similar deficiencies and practices were observed in other low- and middle-income countries globally.[36–38]

5. Conclusions

In summary, in this multicentric cohort study of patients diagnosed with COVID-19 admitted to the ICUs in Ecuador and who required ventilatory support as part of their management, the risk factors associated with increased mortality were older age, obesity, arterial hypertension, and diabetes. Factors such as male gender, chronic obstructive pulmonary disease, acute kidney injury, and cancer reported in other investigations were not found to have the same effect on mortality in our study.

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