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Article

Risk factors associated with mortality in critically ill patients with SARS-CoV-2 pneumonia in a tertiary hospital in Ecuador

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ABSTRACT

A high mortality rate characterizes SARS-CoV-2 pneumonia in critically ill patients. Numerous risk factors have been identified for this condition. The objective of this study was to determine the risk factors for mortality in critically ill patients with SARS-CoV-2 pneumonia receiving invasive mechanical ventilation. This was an observational, retrospective study of patients in the intensive care unit of a third-level hospital between March 2020 and September 2021. Adults with confirmed SARS-CoV-2 infection and who were in the unit for more than 48 hours were included. Demographic, clinical, laboratory, and mechanical ventilation data were collected. All patients received protocolized treatments. Univariate and multivariate analyses were performed using the R statistical tool, with p-values < 0.05. Of 1024 patients, 203 were analyzed. In the univariate analysis, age, weight, hypertension status, Simplified Acute Physiology Score III, Charlson Comorbidity Index score, neutrophil/lymphocyte ratio, and acute respiratory distress syndrome status significantly differed between the living and deceased patient groups. In the multivariate analysis, the Charlson Comorbidity Index score (OR 1.36, 95% CI 1.12-1.68, p=0.002), acute respiratory distress syndrome (OR 4.16, 95% CI 1.24-16.04, p=0.02), and neutrophil/lymphocyte ratio (OR 1.040, 95% CI 1.00-1.07, p= 0.02) remained statistically significant. The unit's mortality rate was 58.1%. The Charlson Comorbidity Index score, neutrophil/lymphocyte ratio, and acute respiratory distress syndrome status were associated with increased mortality.

Keywords: Pneumonia, Viral Pneumonia, SARS-CoV-2, COVID-19, Sepsis, Adult Respiratory Distress Syndrome, Critical Care, Mechanical Ventilation.

INTRODUCTION

SARS-CoV-2 causes COVID-19, and patients with severe pneumonia requiring admission to the intensive care unit (ICU) have high mortality rates in developing countries [1]. Clinical-epidemiological suspicion and prompt and adequate treatment influence the mortality of these patients. Septic shock and acute respiratory

distress syndrome (ARDS) can complicate the condition of patients with severe pneumonia and increase patient mortality.

During the COVID-19 pandemic, an extensive list of mortality risk factors was identified in patients with severe COVID-19 [2–5]. To date, the number of publications concerning the mortality risk factors in patients with severe SARS-CoV-2 pneumonia admitted to the ICU in our country remains limited [6–8].

The main objective of this study was to determine the risk factors for mortality among critically ill patients with SARS-CoV-2 pneumonia receiving invasive mechanical ventilation (IMV) who were admitted to the ICU of a third-level hospital in Quito, Ecuador, from 2020 to 2021. The secondary objectives were to characterize patients demographically and clinically, determine the frequencies of sepsis and ARDS, and assess patient mortality.

MATERIAL AND METHODS

Study design and context: The study was approved by the Ethics Committee on Human Research of the hospital with the code IESS-HCAM-CEISH-2022-0012. An observational retrospective analytical study was carried out with patients admitted to a 35-bed medical-surgical ICU, a unit that, in 2023, had 1,685 admissions with an average stay of 6 days, 17% mortality, and 91% bed occupancy, and cared for patients with an average age of 55 years, whose most prevalent pathologies were sepsis and acute respiratory failure. This ICU receives patients with clinical and surgical pathologies, such as postoperative care after highly complex surgery, transplants, etc., at the Carlos Andrade Marín Specialty Hospital (HECAM), a 500-bed hospital that belongs to the Ecuadorian Social Security Institute (IESS), in the city of Quito, Ecuador, located 2,800 meters above sea level.

Participants: The study's sample comprised all critically ill patients diagnosed with SARS-CoV-2-caused pneumonia from March 28, 2020, to September 18, 2021. The inclusion criteria were patients over 18 years of age admitted to the ICU with a diagnosis of severe pneumonia confirmed by SARS-CoV-2 real-time polymerase chain reaction (RT-PCR) from a nasal swab or tracheal aspirate, who received IMV during the first 24 hours of admission and who remained in the unit for more than 48 hours. Exclusion criteria were pregnant patients, patients hospitalized for more than 48 hours before ICU admission, patients intubated for more than 48 hours before ICU admission, and patients with insufficient data in their records.

Data from the first 24 hours of entry were collected from electronic medical records, using only the worst value when multiple metrics were present. Demographic and clinical variables included age, sex, weight, height, etc.; underlying diseases included obesity, diabetes mellitus, arterial hypertension, congestive heart failure, chronic kidney disease with renal replacement therapy, chronic obstructive pulmonary disease, diffuse interstitial lung disease, and immunocompromised status; severity scores included those from the Charlson Comorbidity Index, Acute Physiology And Chronic Health Evaluation II (APACHE II), Simplified Acute Physiology Score III (SAPS III), and Sequential Organ Failure Assessment (SOFA); complications included the presence of acute respiratory distress syndrome (ARDS), sepsis, septic shock, and acute kidney injury; treatments included steroids (dexamethasone or methylprednisolone), vasoconstrictor support (norepinephrine and/or adrenaline), and intravenous antimicrobials; laboratory variables included lactate dehydrogenase (LDH), creatine phosphokinase (CPK), procalcitonin, leukocytes, neutrophils, lymphocytes, the neutrophil/lymphocyte ratio, D-dimers, interleukin 6, ferritin, C-reactive protein, creatinine, total bilirubin, and mean platelet volume; respiratory variables included the ratio of partial pressure of arterial oxygen divided by fraction of inspired oxygen (PaO_2/FiO_2); ventilatory and pulmonary monitoring parameters included positive end-expiratory pressure (PEEP), compliance, plateau pressure, driving pressure, expiratory resistance, prone position, ratio of tidal volume divided by predicted weight (VT/kg), and recruitment

maneuvers; and outcome variables included the duration of mechanical ventilation, length of stay in ICU, total length of stay, ICU outcome, and outcome at 28 days. In the case of ventilatory variables, respiratory therapy notes were also searched. All patients received management and treatment based on institutional protocols for severe community-acquired pneumonia (CP), COVID-19, sepsis, and ARDS. The data collection instrument was a spreadsheet based on the study variables, with data coding and anonymization.

Definitions: SARS-CoV-2 detection was performed by real-time polymerase chain reaction (RT-PCR). This test detects the nonstructural ORF1a/b region and the nucleocapsid (N) structural protein-encoding gene, both of which are unique to the virus. This process uses internal controls intended to monitor proper processing during sample purification and nucleic acid amplification, as well as to detect the presence of RT-PCR inhibitors. CP was defined based on the criteria of the Infectious Diseases Society of America (IDSA). The severity of CP was defined based on the criteria of the American Thoracic Society (ATS) and the BERLIN consensus for ARDS. The primary outcome was the identification of mortality risk factors, and the secondary outcomes were the frequencies of ARDS and sepsis, and ICU patient mortality.

Statistical analysis: Sample size calculations were not performed because all eligible patients during the study period were included. Categorical variables are reported as counts and percentages, and continuous variables are expressed as medians with interquartile ranges [25–75]. Given the expected skewness of several clinical and inflammatory biomarkers in critically ill patients, non-parametric methods were used for between-group comparisons (Mann–Whitney U test for continuous variables; chi-square or Fisher's exact test for categorical variables, as appropriate), using a two-sided significance level of 0.05.

Some variables had missing data. Analyses were conducted using available data, and denominators are reported where applicable. No imputation was performed. In multivariable logistic regression, cases with complete information on the covariates included in the final model were analyzed (complete-case approach); thus, the effective sample size may be smaller than the total cohort.

To explore variables associated with mortality, two groups were defined (survivors and non-survivors). Candidate predictors for multivariable modeling were selected using a pragmatic approach that considered clinical relevance and univariate associations. A logistic regression model was constructed with mortality as the dependent variable, and model performance was summarized using the area under the ROC curve and the confusion matrix. All analyses were performed in R (version 4.0).

RESULTS

Participants

During the study period, 1024 patients were admitted to the unit. Of 1024 patients, 123 did not meet the inclusion criteria; of 901 patients, 577 met the exclusion criteria; and of 324 patients, 121 had incomplete medical records. All 203 patients underwent statistical analysis. Thus, a group of subjects was obtained with median characteristics (interquartile range [Q1-Q3]) of 62 years [52-70] and 72 kilos [65-81], 162 patients were male (79.80%), 56 patients had a body mass index greater than 30 (27.58%), 35 patients had a history of diabetes mellitus (17.24%), 73 patients had a history of arterial hypertension (35.96%), 2 patients had a history of diffuse interstitial disease (0.98%), 5 patients had chronic obstructive pulmonary disease (2.46%), 7 patients had congestive heart failure (3.44%), 11 patients had chronic kidney disease on renal replacement therapy (5.41%), and 10 patients were immunocompromised (4.92%). The median severity scores (interquartile range [Q1-Q3]) were 23 [17-25] for APACHE II, 63.5 [53-73] for SAPS III, 9 [7-12] for SOFA, and 2 [0-3] for the

Charlson Comorbidity Index. The demographic and clinical characteristics between the groups of living and deceased patients are shown in Table 1.

Characteristics	Pneumonia due to SARS-CoV-2, living (n=85)	Pneumonia due to SARS-CoV-2, deceased (n=118)	P<0.05
Age, years, median [Q1-Q3]	57 [49-65]	66 [55-74]	<0.001
Male gender %	77.64 (66/85)	81.35 (96/118)	0.516
Weight, kilos, median [Q1-Q3]	75 [67-85]	70 [65-80]	0.023
Body mass index greater than 30, %	34.11 (29/85)	22.88 (27/118)	0.860
Diabetes mellitus, %	14.11 (12/85)	19.49 (23/118)	0.317
Hypertension, %	27.05 (23/85)	42.37 (50/118)	0.024
Diffuse interstitial lung disease, %	0 (0/85)	1.69 (2/118)	0.227
Chronic obstructive pulmonary disease, %	1.17 (1/85)	3.39 (4/118)	0.315
Congestive heart failure, %	1.17 (1/85)	5.08 (6/118)	0.132
Chronic kidney disease with renal replacement Therapy, %	2.35 (2/85)	7.62 (9/118)	0.101
Immunosuppression, %	3.52 (3/85)	5.93 (7/118)	0.435
APACHE II score, median [Q1-Q3]	22 [16-25]	23 [18-26]	0.219
SAPS III score, median [Q1-Q3]	58.5 [48-70]	66 [56-76]	0.019
SOFA score, median [Q1-Q3]	8 [6-11]	10 [8-12]	0.069
Charlson Comorbidity Index score, median [Q1-Q3]	1 [0-2]	3 [1-4]	<0.001

Q1= quartile 1, Q3= quartile 3, APACHE= Acute Physiology and Chronic Health Evaluation, SAPS = Simplified Acute Physiologic Score, SOFA= Sequential Organ Failure Assessment.

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Table 1. Demographic and clinical variables

The median laboratory variables measured in the first 24 hours in the total group (interquartile range [Q1-Q3]) were lactate dehydrogenase 787.50 [618.25-1116.75], creatine phosphokinase 175 [88-407], procalcitonin 0.77 [0.285-2.070], leukocytes 13 810 [10 900-17 985], neutrophils 11 920 [9340-15825], lymphocytes 850 [545-1270], neutrophil/lymphocyte ratio 13.83 [8.97-22.37], D-dimers 2.22 [0.83-6.90], interleukin 6 103.40 [37.47-220.60], ferritin 1410.15 [909-2333.95], C-reactive protein 24.50 [13.20-39.90], creatinine 1 [0.78-1.60], total bilirubin 0.68 [0.44-0.97], mean platelet volume 10.4 [9.9-11.0], serum lactate 3.30 [2.20-4.40], and arterial PO_2 56.10 [48.75-70]. The laboratory variables for living and deceased patients are shown in Table 2.

Characteristics	Pneumonia due to SARS-CoV-2, living (n=85)	Pneumonia due to SARS-CoV-2, deceased (n=118)	P<0.05
Lactate dehydrogenase, median [Q1-Q3]	787.50 [630-1120]	782.50 [593-1112]	0.602
Creatine phosphokinase, median [Q1-Q3]	162 [65-426]	197 [97-392]	0.125
Procalcitonin, median [Q1-Q3]	0.63 [0.28-1.98]	0.84 [0.29-2.27]	0.965
Leukocytes, median [Q1-Q3]	13340 [10900-17720]	14070 [10905-18150]	0.849
Neutrophils, median [Q1-Q3]	11730 [9020-15150]	12155 [9470-16277]	0.460
Lymphocytes, median [Q1-Q3]	920 [680-1280]	800 [500-1217]	0.660

Neutrophil/lymphocyte ratio, median [Q1-Q3]	12.96 [8.60-18.09]	15.69 [9.69-18.09]	0.031
D-dimers, median [Q1-Q3]	1.40 [0.79-6.21]	2.80 [0.88-6.97]	0.521
Interleukin 6, median [Q1-Q3]	94 [29.47-218.20]	113 [44.20-290]	0.654
Ferritin, median [Q1-Q3]	1408 [836.67-2331.25]	1416.50 [987.25-2333.95]	0.526
C-reactive protein, median [Q1-Q3]	22.90 [12.30-38.45]	25.40 [13.20-40.67]	0.736
Creatinine, median [Q1-Q3]	0.90 [0.70-1.30]	1.10 [0.80-1.90]	0.273
Total bilirubin, median [Q1-Q3]	0.66 [0.44-0.90]	0.69 [0.45-1]	0.861
Mean platelet volume, median [Q1-Q3]	10.30 [9.90-11]	10.50 [9.90-11]	0.762
Lactate, median [Q1-Q3]	3.00 [2.12-4.07]	3.30 [2.30-4.55]	0.823
PO_2 lowest, median [Q1-Q3]	57.80 [51-72]	55.75 [47.02-68.95]	0.490

Q1= quartile 1, Q3= quartile 3, PO_2 = partial pressure of oxygen

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Table 2. Laboratory variables in the first 24 hours

The median variables corresponding to ventilatory support and respiratory monitoring in the first 24 hours (interquartile range [Q1-Q3]) were FiO_2 maximum 1 [0.60-1], highest PEEP 12 [10-14], static compliance 28 [22-35.50], plateau pressure 26 [23-29], expiratory resistance 16 [13-19], highest tidal volume 400 [360-450], highest peak pressure 29 [25-31.75], lowest PaO_2/FiO_2 ratio 72 [55-94.50], VT/kg ratio 6.82 [6.13-7.50], and highest drive pressure 14 [11-16]. The mechanical ventilation variables between the groups of living and deceased patients are shown in Table 3.

Characteristics	**Pneumonia due to SARS-CoV-2, living (n=85)**	**Pneumonia due to SARS-CoV-2, deceased (n=118)**	**P<0.05**
FiO_2 maximum, median [Q1-Q3]	1 [0.60-1]	0.96 [0.60-1]	0.992
Highest PEEP, median [Q1-Q3]	12 [10-14]	12 [10-14]	0.949
Lowest static compliance, median [Q1-Q3]	30 [23.25-36]	28 [21.70-35]	0.441
Plateau pressure, median [Q1-Q3]	26 [22-29]	26 [23-28.50]	0.915
Expiratory resistance, median [Q1-Q3]	16 [13-18]	17 [13-19]	0.850
Highest tidal volume, median [Q1-Q3]	416 [375.25-450]	394 [355.5-441]	0.126
Highest peak pressure, median [Q1-Q3]	30 [25-32]	29 [25-31]	0.559
Lowest PaO_2/FiO_2, median [Q1 - Q3]	72 [56-97.50]	70.23 [55-93.50]	0.803
VT/kg, median [Q1-Q3]	6.88 [6.14-7.54]	6.71 [6.15-7.49]	0.612
Highest drive pressure, median [Q1-Q3]	14 [11-16]	13 [11-15.50]	0.806

Q1= quartile 1, Q3= quartile 3, PO_2 = partial pressure of oxygen, FiO_2 = fraction of inspired oxygen, PEEP= positive end-expiratory pressure, VT= tidal volume, kg = kilograms

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Table 3. Ventilatory variables in the first 24 hours

All patients had median durations of mechanical ventilation (interquartile range [Q1-Q3]) of 13 days [9-20], 15 days in the ICU [10-20], and 19 days in the hospital [12.5-29]. Among complications, 57 patients presented with acute kidney injury (28%). Treatment included steroids in 138 patients (67.98%), vasoactive agents in 188 patients (92.61%), antimicrobials on admission in 186 patients (91.62%), IMV in the prone position in 139 (139/200) patients (69.50%), and recruitment maneuvers in 27 (27/188) patients (14.36%). The data for the living and deceased patient groups are shown in Table 4.

Characteristics	Pneumonia due to SARS-CoV-2, living (n=85)	Pneumonia due to SARS-CoV-2, deceased (n=118)	P<0.05
Primary ARDS, %	84.70 (72/85)	94.91 (112/118)	0.013
Sepsis, %	95.18% (79/83)	98.30 (116/118)	0.199
Septic shock*, %	83.95% (68/81)	85.21 (98/115)	0.808
Acute renal failure, %	23.52% (20/85)	31.35 (37/118)	0.220
Steroid use, %	67.05% (57/85)	68.64 (81/118)	0.811
Use of vasoactive agents, %	91.76% (78/85)	93.22 (110/118)	0.695
Antimicrobial use, %	95.29% (81/85)	88.98 (105/118)	0.109
Prone ventilation use**, %	63.85% (53/83)	73.50 (86/117)	0.144
Recruitment maneuvers***, %	14.10% (11/78)	14.54 (16/110)	0.932
Days of mechanical ventilation, median [Q1-Q3]	13 [9-21]	14 [10-19]	0.675
Days in ICU, median [Q1-Q3]	16 [11-28]	14 [9-19]	0.067
Days in hospital, median [Q1-Q3]	27 [19-40]	15 [10-20.75]	<0.001

Q1= quartile 1, Q3= quartile 3, ARDS= acute respiratory distress syndrome, ICU= intensive care unit.

* Data available for this variable: n= 196

** Data available for this variable: n= 200

*** Data available for this variable: n= 188

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Table 4. Variables of complications, treatments, and permanence

Primary results

In the univariate analysis, age, weight, arterial hypertension status, SAPS III score, Charlson Comorbidity Index score, the neutrophil/lymphocyte ratio, and ARDS status at admission were significantly different between living and deceased patients. A multivariate analysis was performed on the variables identified in order to identify possible risk factors for mortality: an elevated Charlson Comorbidity Index score, the presence of ARDS, and an increased neutrophil/lymphocyte ratio. The results of this analysis are presented in Table 5 and Figure 1. To validate the obtained model, indicators such as the area under the ROC curve were used, yielding a value of 75.90%, and the confusion matrix was used to assess the model's classification performance in mortality cases, achieving 70% accuracy. 203 patients underwent statistical analysis

	Z statistic	P value	OR	95% CI
Charlson Comorbidity Index score	2.996	0.00273	1.365	1.121-1.688
ARDS	2.220	0.02643	4.165	1.241-16.047
Neutrophil/Lymphocyte ratio	2.195	0.02818	1.040	1.008-1.078

ARDS= acute respiratory distress syndrome, OR= odds ratio, CI= confidence interval

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Table 5: Multivariate analysis for possible mortality risk factors

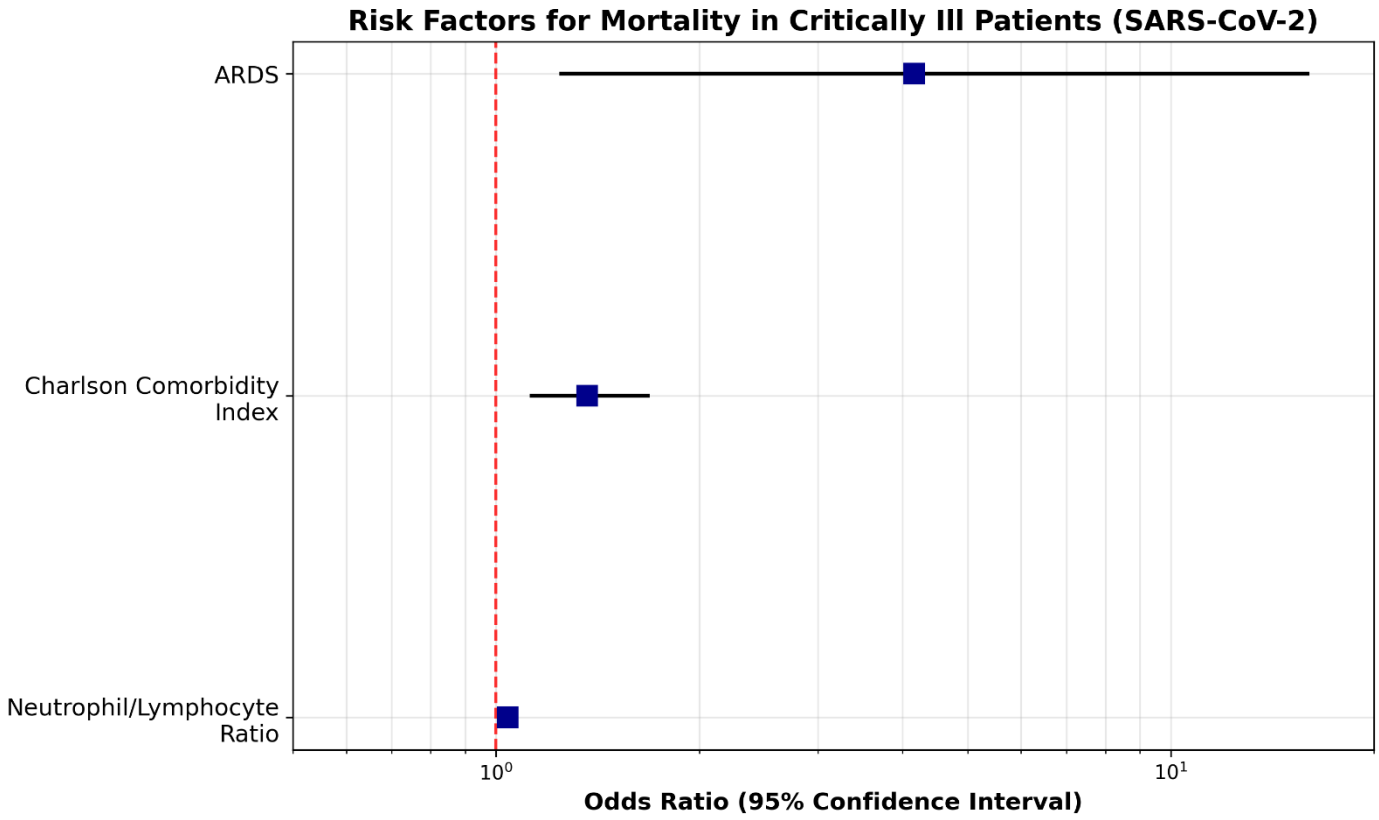

Figure 1. Forest plot of independent risk factors associated with mortality in critically ill patients with SARS-CoV-2 pneumonia. The figure illustrates the Odds Ratios (OR) and 95% Confidence Intervals (CI) for the variables that remained statistically significant in the multivariate model: ARDS (p=0.02), Charlson Comorbidity Index (p=0.002), and Neutrophil/Lymphocyte Ratio (p=0.02). The vertical dashed line at 1.0 represents the null hypothesis. Note: The x-axis uses a logarithmic scale.

Secondary results

A total of 184 patients had ARDS upon admission (90.64%, 95% CI 86.38-94.89); of these, 17 had mild ARDS (9.23%), 86 had moderate ARDS (46.73%), and 100 had severe ARDS (54.34%). A total of 195 (195/201) patients presented with sepsis upon admission to the ICU (97%, 95% CI 94.41-99.61), and 166 (166/196) presented septic shock (84.69%, 95% CI 79.39-89.99). A total of 118 patients died in the ICU (58%, 95% CI 51.09-65.16), and 124 patients died within 28 days of ICU admission (61%, 95% CI 54.13-68.03).

DISCUSSION

SARS-CoV-2, which causes the disease known as "Coronavirus Disease 2019" (henceforth referred to as "COVID-19"), has been shown to cause a spectrum of disease, ranging from asymptomatic to severe cases requiring admission to the intensive care unit (ICU). A study of 72,314 cases classified 81% as mild, with no pneumonia or mild pneumonia; 14% as severe, with the presence of dyspnea, tachypnea, hypoxemia, and pulmonary infiltrates greater than 50%; and 5% as critical, with the presence of ARDS, multiorgan failure, and septic shock [9]. In this study, all patients were critically ill with severe CP, requiring IMV from the time of admission to the ICU; upon admission, more than 90% had a diagnosis of ARDS, and more than 85% had a diagnosis of septic shock.

The majority of cases of pneumonia caused by the novel coronavirus (SARS-CoV-2) have been observed in individuals aged 20-59 years, with notable exceptions in Italy, Germany, and Korea, where the majority of cases have been observed in individuals aged 65+[10]. Among all patients, approximately 51% were men. Our group of patients was mostly over 60 years old, possibly because the hospital in this study serves a higher percentage of older patients. There was a clear predominance of males.

Notably, there was a low overall Charlson Comorbidity Index score upon admission, 2 points, which would estimate a 10-year survival rate of 90% and could be explained by the fact that many patients with chronic diseases did not reach the hospital at the peak of the pandemic and possibly died at home. However, it is striking that, with this score, there was a significant difference between living and deceased patients; the Charlson Comorbidity Index could be considered a risk factor for death in this study.

Risk factors

Previous studies have identified several risk factors associated with mortality, such as cardiovascular diseases, diabetes mellitus, hypertension, neoplasia, chronic lung disease, and advanced age [10]. Other publications have mentioned advanced age [2], especially those over 65 years of age [3,4], male sex [3], and the presence of diabetes mellitus [11] as risk factors for mortality in patients with severe COVID-19. This finding was evaluated through a meta-analysis of mortality in patients with COVID-19, which revealed that mortality in COVID-19 patients is twice as high as that in nondiabetic patients. Variables that include severity upon ICU admission, measured by scales such as the APACHE II (an increase of 5 points) [2] and SOFA [12], are also associated with increased mortality.

Laboratory findings, such as oxygen saturation values and a PaO_2 /FiO_2 ratio less than 100 [2], in addition to several inflammatory markers upon admission and during the ICU stay, such as elevated procalcitonin, D-dimers greater than 1 µg/L [12], elevated lactate, a peripheral lymphocyte count (PLC) less than 0.95×10^9/L [13] and increased platelet count [2,4] are also associated with a greater risk of death.

Medical complications during the evolution of the disease, described as risk factors for death, include acute renal failure, cardiac arrest, and septic shock [2,4], the latter of which was observed in the context of frequent nosocomial infections in this group of patients.

This study revealed that the presence of chronic diseases, as indicated by a high Charlson Comorbidity Index score, a diagnosis of ARDS upon admission to the unit, and a high neutrophil/lymphocyte ratio (NLR) could be considered risk factors for mortality (Figure 1).

Charlson Comorbidity Index

Evidence suggests that the Charlson Comorbidity Index should be used to risk-stratify patients hospitalized with COVID-19, with a score ≥ 3 associated with a poor prognosis and higher mortality, and that for each point increase in the score, there is a 16% increase in the risk of death [14]. Other reviews mention a cutoff value of >4 adjusted for age, with an AUC of 0.709 ($p = 0.001$), a sensitivity of 68%, and a specificity of 62% [15]. These results are consistent with our findings in the deceased patient group.

ARDS

The mortality of ARDS as a complication of CP depends on the severity of its presentation: mild-moderate-severe, with values of 30-34-50%, respectively [16]. In the case of patients with COVID-19 admitted to the ICU with ARDS, there is variability in mortality, with values of 27-89%, depending on the country [17]; however, this risk factor would be the only one in which we could intervene and improve the prognosis, for example,

by protocolizing the diagnosis and treatment of this complication. In our study, the presence of ARDS quadrupled the risk of death.

Neutrophil/lymphocyte ratio

An elevated NLR has been proposed as a risk factor for death in critically ill patients with COVID-19. There is evidence of the usefulness of the NLR for predicting disease severity and mortality in patients with COVID-19, with area under the ROC curve values of 0.85 (95% CI 0.81-0.88) for severity and 0.90 (95% CI 0.87-0.92) for mortality [18]. Cutoff values have been established. In a study of 2071 patients with COVID-19 admitted to the ICU, King et al. reported that an NLR greater than 7.45 increased the probability of death by 1.32 times (95% CI 1.14-1.54)[19]. Our study has a median that doubles the aforementioned cutoff value, but the probability of death is slightly lower.

Sepsis and ARDS

The frequency with which sepsis occurs as a secondary complication of viral infections remains uncertain. A prospective study from Southeast Asia published in 2018 found that viruses accounted for up to 33% of sepsis cases in adults. Furthermore, approximately one-third of adults requiring admission to the intensive care unit for CP have a viral infection [20].

During the pandemic caused by a SARS-CoV-2-type virus, a percentage of the population presented severe respiratory illness associated with sepsis and septic shock plus organ dysfunction [21]. In this study, more than 90% of the patients had sepsis upon admission to the unit, and more than 80% met the septic shock criteria based on the SEPSIS-3 consensus. The low procalcitonin values (<1) are striking, suggesting a viral etiology. Importantly, the high NLR values reveal a moderate degree of physiological stress in these patients, possibly explained by viral sepsis; however, this contrasts with the high use of antimicrobials upon admission of these patients, mainly due to the lack of knowledge of this epidemic, the use of empirical treatments without further evidence, and the lack of resources to establish rapid bacteriological diagnoses.

The most common clinical presentation of severe COVID-19 is acute respiratory failure compatible with ARDS, defined using the Berlin diagnostic criteria [22]. In patients with severe SARS-CoV-2 pneumonia, unique characteristics of ARDS have been described, especially a dissociation between the severity of hypoxemia and lung mechanics, with relatively high compliance and features rarely observed in most cases of ARDS [23]. In this group of patients, more than 90% met the criteria for moderate or severe ARDS at admission to the unit, with a median PaO2/FiO2 of less than 100; that is, most patients had moderate-to-severe ARDS. All patients were managed with a protective strategy, including low VT, plateau pressures <30, and moderate PEEP. Steroids were used to treat only 68% of patients, even though, at the beginning of the pandemic, their use was not protocolized, and IMV in the prone position was used in 70% of patients. In addition, unlike the group described by Gattinoni, these patients' compliance was low from the beginning.

Before the COVID-19 pandemic, prone ventilation was a strategy used for hypoxemia refractory to other treatments in the management of patients with moderate-severe ARDS, as demonstrated by the Spanish study from Álvarez-Lerma et al., with a value of 18.2% [24], and the APRONET study, where the frequency of use of the prone position in patients with severe ARDS was 32.9% [25]. There was insufficient scientific evidence for the use of corticosteroids in the management of CP before the pandemic, and there are even reports of increased mortality in patients whose pneumonia was caused by influenza. In the study by Álvarez-Lerma et al., only 40.3% of participants used corticosteroids [24]. Since the emergence of SARS-CoV-2, the use of dexamethasone has been protocolized, as evidenced by the findings of the RECOVERY group trial [26].

Mortality

The mortality in patients with CP admitted to the ICU can reach 34-36% [27]. These percentages can increase when pneumonia is complicated by septic shock or with ARDS, with values of 30- to 50% [16].

The overall mortality of patients with COVID-19 admitted to the ICU was determined to be 30-40%; however, when mortality was analyzed by country income level, mortality among patients in ICUs in high-income countries was as low as 10.6%, and that among patients in low-income countries was as high as 79.8% [28]. In Latin America, the reported mortality of critically ill patients with COVID-19 receiving IMV was 57%, reaching up to 63.3% in some countries [29,30]. The ICU mortality in this study was similar to that reported in low-income countries for patients with severe ARDS and septic shock.

Limitations

This was a single-center, retrospective study, which may limit generalizability and is subject to residual confounding. Eligibility criteria related to timing and record completeness may introduce selection bias (including the requirement for ICU stay >48 hours and the exclusion of patients with prolonged pre-ICU management), potentially underrepresenting very early deaths and affecting mortality estimates. Missing data were present for some variables; analyses were performed using available data without imputation, and complete-case multivariable modeling may have reduced the effective sample size. The study period (March 2020–September 2021) spanned different phases of the pandemic with evolving clinical protocols, and no temporal stratification was performed. Information on microbiologically confirmed co-infections/superinfections was not systematically available and therefore was not included. Findings should be interpreted as exploratory associations rather than causal risk factors.

CONCLUSIONS

This study identifies the Charlson Comorbidity Index score, ARDS, and the neutrophil/lymphocyte ratio as key determinants of mortality in critically ill patients with SARS-CoV-2 pneumonia receiving invasive mechanical ventilation. These findings provide valuable evidence for the Ecuadorian and Latin American contexts—regions with limited prior data—confirming that, despite differences in healthcare resources and altitude, these biomarkers remain robust predictors of poor outcomes. The observed mortality aligns with the high rates reported in low-to middle-income countries, highlighting the need for targeted interventions in these settings.

Patents: Not applicable.

Supplementary Materials: Not applicable.

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