Predicting mortality in critically ill patients with COVID-19 in the ICU from a secondary-level hospital in Ecuador

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Abstract: Since its molecular isolation on January 7, 2020, the new SARS-CoV-2 coronavirus has spread rapidly, affecting regions such as Latin America. Ecuador received the worst outbreak globally if we count excess mortality per capita. This study describes the clinical, epidemiological and therapeutic characteristics of 89 patients admitted to an intensive care unit (ICU) in a second-level hospital in Quito, Ecuador. Methods: We conducted a retrospective cohort study. We collected data from health records of adult patients with severe COVID-19 admitted to an ICU in Quito, Ecuador, during the first five months of the SARS-CoV-2 outbreak. We used the Wald test to evaluate the categorical predictors of the model at the multivariate level during the regression analysis. Results: 89 patients were recruited. The mean age of the patients was 54.72 years. Men represented 68.54% (n=61) and women 31.46% (n=28). Significant differences in mortality were observed (men 40.98% vs. women 17.76%). LDH and IL-6 at 24 hours after hospital admission were higher among non-survivors than survivors. Persistent hypoxemia (PaO2/ FiO2 <90 mmHg) and IL-6 at 24 hours were also associated with increased mortality. Conclusions: Elevated levels of LDH at 24 hours, IL-6 at 24 hours, lymphocyte and platelet count at 48 hours, neutrophil count at 48 hours and NLR are factors associated with higher motility, risk of failed extubation and reintubation in patients with acute respiratory distress syndrome due to COVID-19.

Key words: COVID-19, ICU, ROC curve, Mortality, Low-Middle Income Country.

Introduction

On 31 December, the Wuhan Municipal Health Committee informed the World Health Organization (WHO) that 27 people had been diagnosed with a type of pneumonia never described before: On 7 January, 2020, Chinese scientists had isolated and sequenced the etiological agent, a novel beta coronavirus later identified as SARS-CoV-2 (severe acute respiratory syndrome coronavirus type -two): The genome of this RNA virus was made available on 12 January, 2020, allowing laboratories in different countries to produce specific primers for the infection diagnosis using real-time reverse transcription-polymerase chain reaction (RT-PCR): On 11 March, 2020, the WHO declared COVID-19 a pandemic after the virus arrived in several countries rapidly: Up to 5 October, 2020, more than 35 million people had been infected, causing more than 1 million deaths worldwide.

In Latin America, a region with high levels of social inequality, mortality rates, and attack rate due to COVID-19, is devastating, especially for those living in poverty: Households in the lowest income group have reduced access to health services, molecular diagnosis, and treatment. Health systems with scarce economic resources and disrupted contact tracing capabilities are often incapable of controlling outbreaks at the community level, affecting mortality and hospital admission trends:

In mid-February 2020, the disease reached Latin America and hit Ecuador abruptly. The first case in Ecuador was officially reported on 27 February, but the only scientific report suggests that the virus has entered the country weeks earlier: In March, the virus had spread massively within Ecuador’s coastal provinces, causing thousands of deaths each day in Ecuador, highlighting Guayaquil, as the first COVID-19 epicenter in Latin America and the worst-hit country in the world:

There is only one report exploring the epidemiological trends of COVID-19 in Ecuador, including a brief description of the clinical presentation among asymptomatic and mildly ill patients; nevertheless, no data is available in terms of the clinical features and outcome among critically ill patients:

This study aims to present the outcome, and clinical characteristics of COVID-19 patients admitted to the intensive care unit in a secondary level hospital in Quito, Ecuador, from 1 April, 2020, to 31 July, 2020.
Materials and methods

Setting
The study was carried out in the Intensive Care Unit in the secondary level hospital Pablo Arturo Suárez Hospital, Quito, Ecuador. Quito is the capital of Ecuador and has a population of 2,781,641. The city is located in the province of Pichincha and has an elevation of 2,850 m above sea level, becoming the second-highest capital city globally.

Study design
A retrospective cohort study of the clinical course and mortality due to COVID-19 among adult patients hospitalized and admitted to the ICU from 1 April to 31 July, 2020.

Population and sample size
Every patient admitted to the ICU with a suspected diagnosis of COVID-19 within the established timeframe was initially included in the study. At the end of the study, we included 89 patients that fulfilled the inclusion criteria, while 12 were excluded from the study.

Inclusion criteria
Every patient admitted to the ICU unit with a positive molecular, serological, or clinical diagnosis of COVID-19 (characterized by: fever or chills, cough, dyspnea, anosmia, ageusia, sore throat, or myalgia) was included in the study. The clinical records (HC) of patients admitted with a confirmed result of COVID-19 by RT-PCR or suggestive tomographic pattern (CO-RADS 0 to 3) were included, and cases with a presumptive diagnosis of COVID-19.

Exclusion criteria
Patients with a mild clinical presentation that were not admitted to the ICU or those with respiratory symptomatology that tested negative for SARS-CoV-2 infection through molecular testing (RT-PCR) or tomographic pattern not compatible with COVID-19 (CO-RADS 4 or 5) were included, and cases with a presumptive diagnosis of COVID-19.

Variables and measurements
Our team reviewed the electronic records of every patient that fulfilled the inclusion criteria. (Being admitted to the ICU was one of them). Information concerning epidemiological, clinical, serological, and cytometric variables was collected. Every record was reviewed, and data were retrieved from admission to discharge or death in the ICU during the data collection period.

Statistical analysis
We performed a complete descriptive statistical analysis, calculating every qualitative variable’s absolute and relative values. Mean, and standard deviation measures were used to describe differences and dispersion of the data set.

Assessment of mortality indicators
The APACHE II indicator was found to be higher among non-survivors (28,98) and non-survivors (31.99) 5 being these differences statistically significant (p-value: 0.026).

Ethical considerations
According to human research’s local bioethical principles, anonymized, unidentifiable data from clinical records, excluding case reports, do not require internal review boards’ approval. The physicians involved in collecting clinical data were also the only health providers accessing patients’ clinical records.

Results
General results
During 121 days of follow-up, 89 patients with COVID-19 fulfilled the inclusion criteria. 68.54% (n=61) were men and 31.46% women (n=28). There was no statistically significant difference in mean length of hospital stay (ALOS) between those who survived (9.31 days) versus those who died (10.29 days). The follow-up ended with 66.29% of patients (n=59) discharged from the ICU unit, while 33.71% of them (n=30) died due to COVID-19 (Table 1).

Age and sex differences
The average age of patients admitted to the hospital was 54.7 years, and survivors were 11 years younger (50.9) than non-survivors (62.2), and this difference was statistically significant (p-value: 0.001). Regarding gender, men were three times more likely to die (40.98%, n = 25) from COVID-19 compared to women (17.76%, n = 5) (p-value: 0.032).

Comorbidities and mortality risk
The most frequent comorbidity reported was hypertension (HT) in 20.22% (n=18) followed by obesity 16.85% (n=15) and diabetes mellitus (DM) 9.99% (n=8). The mean body mass index (BMI) was 30.94, with significant differences being observed between survivors (28,98) and non-survivors (31.99)5 being these differences statistically significant (p-value: 0.026).

Ventricular and respiratory parameters
To mitigate end-expiratory alveolar collapse, applied extrinsic PEEP values at 48 hours were significantly lower (7.89 cmH2O) among survivors versus non-survivors (9.26 cmH2O).
and this difference was statistically significant (p-value: 0.015). The maximum PCO₂ at 72 hours was higher among non-survivors (49.34 mmHg), versus survivors (41.37 mmHg), and this difference was statistically significant (p-value: 0.026) (Table 2).

The PaO₂/FiO₂ ratio at 24 and 72 hours was always higher among survivors. For instance, non-survivors reported a PaO₂/FiO₂ of 127.77 mmHg and 136.36 mmHg at 24 and 72 hours, respectively, while survivors had values of 152.97 mmHg and 181.09 mmHg at the same time interval, both differences being statistically significant (p-value: 0.036 and <0.001 respectively).

Survivors remained intubated for seven days while non-survivors for ten days, a difference that is also statistically significant (p-value: 0.002).

Serological biomarkers
Mean lactate dehydrogenase levels (LDH) were higher among non-survivors (1025.47 U/l) versus survivors (891.10 U/l); Likewise, IL-6 presented was 137% higher among non-survivors (140.55 pg/ml) versus survivors (59.3 pg/ml) (p-value: < 0.05). D-dimer and ferritin at 24 and 48 hours did not show significant differences (Table 3).

Flow cytometric analysis
Lymphocyte count at 48 hours presented a mean of 753.79 x 10³ / ml in survivors and 537.59 x 10³ / ml in non-survivors (p-value: 0.006). Neutrophilia was found to be significantly higher among non-survivors at 24 hours (11,741.63 x 10³ / ml) in comparison with survivors (9,282.54 x 10³ / ml). For the neutrophil-lymphocyte ratio (NLR) at 24, 48 and 72, non-survivors had significantly higher NLR than survivors (p-value: < 0.001) (Table 4).

Platelet count at 48 hours shows that non-survivors had significantly lower platelet counts (388,172.41 x 10³ / ml) than survivors (330,103.45 x 10³ / ml).

Predictive factors for mortality
PEEP analysis.

The area of the receiver operating characteristic (ROC) curve for PEEP at 48 hours was 0.661 (95% CI 0.535-0.787), maximum PCO₂ at 72 hours 0.650 (95% CI 0.519-0.780), PaFiO₂ at 24 hours 0.636 (95% CI 0.508-0.765), and PaFiO₂ at 72 hours 0.747 (95% CI 0.638-0.857), these areas presented confidence intervals that do not include the value 0.5; therefore, be used to predict mortality for COVID-19.

The cut-off points to predict mortality in the ROC curve using the Youden index of the mechanical ventilation parameters were positive for mortality if 48-hour PEEP ≥8.50 cmH₂O, where the sensitivity was 54%, and specificity was 74% (Figure 1). Positive for mortality if: 72-hour peak PCO₂ ≥46.50 mmHg (sensitivity: 54%, specificity: 77%), 24-hour PaFiO₂ ≤89 mmHg (sensitivity: 30%, specificity: 97%) and PaFiO₂ 72 hours ≤155.50 mmHg (sensitivity: 82%, specificity: 66%).

Biomarker analysis.

The area of the ROC curve for IL-6 was 0.675 (IC95%
Table 2. Correlation between mortality and mechanical ventilation parameters.

<table>
<thead>
<tr>
<th>Mechanical ventilation parameters</th>
<th>Total</th>
<th>Condition at discharge</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Deceased</td>
<td>Survivor</td>
</tr>
<tr>
<td>Ventilatory mode of admission (n (%))</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Volume controlled</td>
<td>14 (15.73)</td>
<td>4 (28.57)</td>
<td>10 (71.43)</td>
</tr>
<tr>
<td>Pressure controlled</td>
<td>75 (84.27)</td>
<td>26 (34.67)</td>
<td>49 (65.33)</td>
</tr>
<tr>
<td>VT 24 hours (mean (SD)) ml/kg</td>
<td>403.15 (61.2)</td>
<td>398.33 (57.41)</td>
<td>405.59 (63.38)</td>
</tr>
<tr>
<td>VT 48 hours (mean (SD)) ml/kg</td>
<td>417.69 (69.08)</td>
<td>411.9 (75.81)</td>
<td>420.63 (65.91)</td>
</tr>
<tr>
<td>VT 72 hours (mean (SD)) ml/kg</td>
<td>424.41 (78.17)</td>
<td>434.21 (88.78)</td>
<td>418.57 (71.49)</td>
</tr>
<tr>
<td>PEEP 24 hours (mean (SD)) cmH2O</td>
<td>9.46 (2.09)</td>
<td>9.83 (2.28)</td>
<td>9.27 (1.99)</td>
</tr>
<tr>
<td>PEEP 48 hours (mean (SD)) cmH2O</td>
<td>8.35 (2.29)</td>
<td>9.29 (2.45)</td>
<td>7.89 (2.08)</td>
</tr>
<tr>
<td>PEEP 72 hours (mean (SD)) cmH2O</td>
<td>7.81 (2.26)</td>
<td>8.46 (2.81)</td>
<td>7.43 (1.79)</td>
</tr>
<tr>
<td>24-hour plateau pressure (mean (SD)) cmH2O</td>
<td>23.19 (4.23)</td>
<td>23.73 (4.65)</td>
<td>22.92 (4.01)</td>
</tr>
<tr>
<td>48-hour plateau pressure (mean (SD)) cmH2O</td>
<td>21.77 (3.83)</td>
<td>22.07 (4.54)</td>
<td>21.61 (3.44)</td>
</tr>
<tr>
<td>72-hour plateau pressure (mean (SD)) cmH2O</td>
<td>21 (3.82)</td>
<td>22.11 (3.92)</td>
<td>20.35 (3.65)</td>
</tr>
<tr>
<td>Driving pressure 24 hours (mean (SD)) cmH2O</td>
<td>13.62 (3.28)</td>
<td>13.53 (3.56)</td>
<td>13.66 (3.17)</td>
</tr>
<tr>
<td>Driving pressure 48 hours (mean (SD)) cmH2O</td>
<td>13.33 (2.94)</td>
<td>13.07 (3.1)</td>
<td>13.47 (2.87)</td>
</tr>
<tr>
<td>Driving pressure 72 hours (mean (SD)) cmH2O</td>
<td>13.42 (3.24)</td>
<td>14 (3.55)</td>
<td>13.07 (3.02)</td>
</tr>
<tr>
<td>PCO2 mean 24 hours (mean (SD)) mmHg</td>
<td>45.77 (13.55)</td>
<td>45.28 (10.92)</td>
<td>46.01 (14.79)</td>
</tr>
<tr>
<td>PCO2 mean 48 hours (mean (SD)) mmHg</td>
<td>45.23 (12.63)</td>
<td>46.53 (12.07)</td>
<td>44.6 (12.95)</td>
</tr>
<tr>
<td>PCO2 mean 72 hours (mean (SD)) mmHg</td>
<td>44.03 (12.86)</td>
<td>49.34 (17.92)</td>
<td>41.37 (8.4)</td>
</tr>
<tr>
<td>PaFiO2 24 hours (mean (SD)) mmHg</td>
<td>144.47 (47.94)</td>
<td>127.77 (44.98)</td>
<td>152.97 (47.52)</td>
</tr>
<tr>
<td>PaFiO2 48 hours (mean (SD)) mmHg</td>
<td>160.78 (47.77)</td>
<td>147.89 (35.14)</td>
<td>167 (51.93)</td>
</tr>
<tr>
<td>PaFiO2 72 hours (mean (SD)) mmHg</td>
<td>166.18 (54.96)</td>
<td>136.36 (41.04)</td>
<td>181.09 (55.25)</td>
</tr>
<tr>
<td>Prone ventilation (n (%))</td>
<td>53 (59.55)</td>
<td>20 (37.74)</td>
<td>33 (62.26)</td>
</tr>
<tr>
<td>Days of prone ventilation (mean (SD))</td>
<td>2.38 (1.42)</td>
<td>2.43 (1.36)</td>
<td>2.35 (1.48)</td>
</tr>
<tr>
<td>Use of relaxant (n (%))</td>
<td>55 (61.8)</td>
<td>17 (30.91)</td>
<td>38 (69.09)</td>
</tr>
<tr>
<td>Days with muscle relaxant (mean (SD))</td>
<td>2.22 (1.46)</td>
<td>2.38 (1.77)</td>
<td>2.14 (1.3)</td>
</tr>
<tr>
<td>Days in MV (mean (SD))</td>
<td>8.49 (5.67)</td>
<td>10.86 (5.26)</td>
<td>7.3 (5.54)</td>
</tr>
<tr>
<td>Mechanical power 24 hours (mean (SD)) j/min</td>
<td>15.77 (4.59)</td>
<td>16.16 (4.26)</td>
<td>15.57 (4.77)</td>
</tr>
<tr>
<td>Mechanical power 48 hours (mean (SD)) j/min</td>
<td>14.92 (4.64)</td>
<td>14.64 (4.31)</td>
<td>15.07 (4.83)</td>
</tr>
<tr>
<td>Compliance 24 hours (mean (SD)) ml/cmH2O</td>
<td>26.49 (12.48)</td>
<td>26.17 (13.89)</td>
<td>26.66 (11.84)</td>
</tr>
<tr>
<td>Compliance 48 hours (mean (SD)) ml/cmH2O</td>
<td>27.42 (13.48)</td>
<td>29.61 (15.64)</td>
<td>26.2 (12.11)</td>
</tr>
<tr>
<td>Compliance 72 hours (mean (SD)) ml/cmH2O</td>
<td>34.32 (10.82)</td>
<td>34.45 (7.71)</td>
<td>34.24 (12.47)</td>
</tr>
<tr>
<td>VT x Kg 24 hours (mean (SD))</td>
<td>6.97 (1.31)</td>
<td>6.91 (1.23)</td>
<td>7 (1.36)</td>
</tr>
<tr>
<td>VT x Kg 48 hours (mean (SD))</td>
<td>7.94 (7.04)</td>
<td>7.1 (1.29)</td>
<td>8.4 (8.68)</td>
</tr>
<tr>
<td>VT x Kg 72 hours (mean (SD))</td>
<td>8.53 (8.55)</td>
<td>7.71 (1.48)</td>
<td>9.05 (10.91)</td>
</tr>
<tr>
<td>Extubation (n (%))</td>
<td>20 (27.40)</td>
<td>14 (70.00)</td>
<td>6 (30.00)</td>
</tr>
<tr>
<td>Successful</td>
<td>53 (72.60)</td>
<td>0 (0.00)</td>
<td>53 (76.81)</td>
</tr>
</tbody>
</table>

Note: SD = Standard Deviation; * significant differences in means, based on 1 / t test and 3 / Mann Whitney test; ** significant differences in non-survivor condition, based on Chi-square test or Fisher’s exact statistic 2 /
and for LDH at 24 hours 0.691 (IC95% 0.580-0.803), these areas presented confidence intervals that do not include the value 0.5; therefore, they are significant in predicting mortality for COVID-19.

The cut-off points to predict mortality in the ROC curve using the Youden index of the analytical parameters were positive for mortality if IL-6 ≥117 pg / mL, where the sensitivity was 42%, and specificity was 91%. Regarding LDH, it was positive for mortality at 24 hours with a cut-off ≥783 U / L (sensitivity: 90%, specificity: 43%) (Figure 2).

The area of the ROC curve for NLR at 24 hours was 0.704 (95% CI 0.591-0.817), NLR at 48 hours 0.743 (95% CI 0.634-0.851), NLR at 72 hours 0.692 (95% CI 0.578-0.806), and platelets 48 hours 0.633 (95% CI 0.508-0.759), these areas presented confidence intervals that do not include the value 0.5; therefore, they are significant to predict mortality for COVID-19 (Figure 3).

The cut-off points for predicting mortality in the ROC curve using the Youden index of the cytometry parameters were the following: Positive for mortality if NLR 24 hours ≥16.33, where sensitivity was 73% and specificity 64%. Positive for mortality if NLR 48 hours ≥16.33, where the sensitivity was 76% and specificity 67%. Positive for mortality if NLR 72 hours ≥17.12, where the sensitivity was 64% and specificity 74%. Positive for mortality if Platelets ≤364,000 x 10^3 ml, where the sensitivity was 79% and specificity 50%.

SOFA mortality prediction analysis.

For the SOFA mortality predictors, the cut-off point for COVID-19 was determined, the ROC curves showed for SOFA at 48 hours an area of 0.637 (95% CI 0.511-0.763), and for 72 hours of 0.675 (95% CI 0.556-0.794), these areas were significant to predict mortality, the cut-off point established at 48 and 72 hours was positive for mortality if SOFA≥6, at 48 hours, the sensitivity of 79% and specificity 48% were obtained, at 72 hours the sensitivity was 69% and specificity 57% (Figure 4).

The results obtained showed that PaFiO2 72 hours ≤ 155.50 mmHg with p-value 0.009, IL-6 ≥117 pg / mL with p-value 0.011, NLR 24 hours ≥16.33 with p-value 0.013 and NLR 72 hours ≥17.12 with p-value 0.005 are predictors of mortality for COVID-19; where values of PaFiO2 72 hours ≤ 155.50 mmHg, IL-6 ≥117 pg / mL, NLR 24 hours ≥16.33 and NLR 72 hours ≥17.12 presented 9.24, 21.84, 6.13, and 13.33 times more likely not to survive; the mechanical ventilation's cut-off points, analytical and cytometry parameters were determined (Table 5).

The results obtained showed that PaFiO2 72 hours ≤ 155.50 mmHg with p-value 0.009, IL-6 ≥117 pg / mL with...
p-value 0.011, NLR 24 hours ≥16.33 with p-value 0.013 and NLR 72 hours ≥17.12 with p-value 0.005 are predictors of mortality for COVID-19; where values of PaFiO₂ 72 hours ≤155.50 mmHg, IL-6 ≥117 pg/mL, NLR 24 hours ≥16.33 and NLR 72 hours ≥17.12 presented 9.24, 21.84, 6.13 and 13, 33 times more likely to not survive.

Discussion

This original research is the first report of the clinical characteristics of severely ill patients with COVID-19 who have been clinically managed in a secondary-level hospital ICU in Quito, Ecuador. The results showed that older age and sex are positively associated with mortality. These results are similar to several reports available⁹,¹⁰. The average age of our admitted patients was 54 years, considerably younger populations than other countries. In China, two reports found that the mean age of patients admitted to the ICU was between 64 and 66 years, on average ten years older than our population¹¹,¹². In other continents, the age of the admitted patients is also higher. For instance, in Italy and Spain, the average age is 79 years¹³-¹⁶. Mejia et al. 2020 published the only available study with results similar to ours in a cohort of Peruvian patients. They
found that the median age of the admitted patients was 59 years\textsuperscript{17}. Although there is no clear information on why older men are at higher risk of dying due to COVID-19, a higher proportion of comorbidities among men may play a significant role, and the presence of unhealthier lifestyles\textsuperscript{18}, along with immunosenescence phenomena. It has also been hypothesized that men have a higher angiotensin-converting enzyme-2 (ACE-2) receptor, which might play an important role. Previously published studies suggest that the ACE-2 receptor plays a role in other coronaviruses-related diseases such as Severe Acute Respiratory Syndrome (SARS) or Middle East Respiratory Syndrome (MERS), finding higher concentrations of ACE-2 receptors among men\textsuperscript{18,19}.

In terms of respiratory parameters, persisting hypercapnia for more than 72 hours, the PaFiO\textsubscript{2} ratio at 24 and 72 hours < 140 mmHg and PEEP greater than 9 cmH\textsubscript{2}O were also associated with increased risk of mortality. External positive pressure ventilation increases intrathoracic pressure and does so more potently when the lungs are highly compliant\textsuperscript{20}. Moderate PEEP levels are required to ventilate adequately and achieve normoxia. In our results, maintaining PEEP levels greater than 8 mmHg after 48 hours was associated with a poorer prognosis. Although the impact of COVID-19 within the lungs is not quite the same as other diseases causing ARDS, the role of adequate ventilatory management is fundamental.

Gatinonni et al., defined two phenotypic patterns in the clinical presentation of COVID-19, a Low (L) phenotype in which there is low elastance, low shunt and poor recruit ability with little response to PEEP and a High (H) phenotype, with high elastance, high shunt and favorable response to alveolar recruitment with PEEP\textsuperscript{21,22}.

Regarding the presentation of the L and H phenotypes in ARDS due to COVID 19, we consider that their presentation was variable, if we take into account the relationship between compliance and PaO\textsubscript{2} / FiO\textsubscript{2}, as reported by Panwar\textsuperscript{23}, patients with lower PaO\textsubscript{2} / FiO\textsubscript{2}, like those with low compliance died. However, these variables can be very heterogeneous because there could be H patterns with PaO\textsubscript{2} / FiO\textsubscript{2} greater than 150 and in other L phenotypes with PaO\textsubscript{2} / FiO\textsubscript{2} <150mmHg. Both PaO\textsubscript{2} / FiO\textsubscript{2} and compliance have always been considered a marker of severity; in our work, the patients who had lower values were the most serious and of them, those who died had low compliance from admission, as mentioned. In other studies, patients that improved PaO\textsubscript{2} / FiO\textsubscript{2} and compliance pattern L had better survival\textsuperscript{22,23}.

Our study also found that elevated levels of IL-6\textsuperscript{24}, LDH at 24 hours, lymphopenia at 48 hours, neutrophilia at 24 hours, and high NLR from admission to 72 hours were also associated with more significant mortality. Previous works have evaluated this, which may indirectly indicate a reaction due to the massive inflammatory response or the cytokine storm constantly related with more severe clinical presentations\textsuperscript{24,25}. These results are similar to those previously reported worldwide; however, it is interesting to note that ferritin and the D-dimer biomarker have not achieved enough statistical power to predict mortality\textsuperscript{12,26}. Furthermore, our findings support the use of cytometric analysis that is often affordable and available in low-resource settings.

Several laboratory data are identified as predictors of severity and mortality in COVID-19, such as elevated D-dimer, lymphopenia, increased LDH, thrombocytopenia, increased C-reactive protein, elevated ferritin and IL-6, among others\textsuperscript{27-34}. In our study, the factors associated with mortality were LDH values at 24 hours, IL-6, the lymphocyte and platelet count at 48 hours, the neutrophil count at 48 hours, and the NLR in all its measurements; the latter, together with IL-6, reached a predictive level. These results are consistent with the existing evidence in the world. Interestingly, D-dimer and ferritin at 24 and
48 hours did not present a significant association with mortality, a finding that contradicts the existing evidence at that time.

The most frequent comorbidities in our patients were: hypertension, obesity and diabetes mellitus (DM). For diabetes and hypertension, there was no statically significant difference in terms of risk of mortality; nevertheless, when evaluating body mass index, higher BMI was associated with a greater risk of dying (Table 1), as described in other studies. A clinical report from Wang et al. showed statistically significant differences in terms of mortality among patients with chronic hypertension. On the other hand, other studies found that hypertension was not an independent factor in increasing mortality, opposing hypercholesterolemia and DM.

In general terms, the overall mortality in our center seems to be adequate compared to other countries. In Ecuador, we found that 33.7% of patients succumbed in the ICU unit due to COVID-19. A recently published report from China, including 517 patients, reported an overall mortality rate of 37.7%. These numbers seem to be lower than other reports coming from Europe. For instance, in Italy, Grasselli et al. 2020 included 1,715 patients, and they found that the overall mortality was superior to 48%. In Spain, a national cohort of 736 patients reported mortality rates greater than 42%. On the other hand, information emerging from the USA shows that mortality was significantly lower in a cohort of 1,392 patients. They reported an overall mortality of 23.6%.

In Latin America, reports are scarce. We found that in Peru, the overall mortality rate among severely ill COVID-19 patients was 32.4%. However, in this study, cut-off points for serological biomarkers and mechanical ventilation variables analysis were not determined, which might give a more in-depth insight into our results. At the beginning of the pandemic, corticosteroids’ use was controversial, and their use focused on quenching the so-called “cytokine storm”. During the first few months of the outbreak, few scientific societies recommended using systemic corticosteroids to treat ARDS. Nevertheless, in our hospital, we adopted the SARS and MERS guidelines, which could be associated with our relatively low mortality rates compared to other centers.

Limitations

Our results came from an intensive care unit of 7 beds. Therefore, collecting a representative sample was more prolonged than in other centers. It is essential to point out that a molecular analysis for COVID-19 using RT-PCR was not always available in situ; therefore, the diagnosis was based on radiological and clinical suspicion, and the confirmatory molecular or serological confirmation sometimes arrived days later.

Conclusions

The values of LDH at 24 hours, IL-6 and lymphocyte and platelet count at 48 hours, the neutrophil count at 48 hours, and the NLR are factors associated with mortality and were even determining factors for failure in the extubation and reintubation. The clinical and physiopathological presentation of COVID-19 suggested a strong activation of the pro-inflammatory response; this meant that in our hospital, even without solid evidence, we indicated corticoids, a measure that was later validated by RCTs and meta-analyses. This would essentially justify the non-elevated mortality in our series of patients.

Although analytical markers such as IL 6 and LDH are acceptable and well-known parameters for managing critical patients, their availability is not universal, and IL 6 is expensive. Finding a surrogate such as the NLR, which has a predictive value in its measurements at 24 and 72 hours that is not depreciable: makes the findings of this study relevant by providing a cost-effective instrument derived from the standard blood count to establish the risk of death and severity in COVID-19.

Ethics approval and consent to participate

According to human research’s local bioethical principles, anonymized, unidentifiable data from clinical records, excluding case reports, do not require internal review boards’ approval. The physicians involved in collecting clinical data were also the only health providers accessing patients’ clinical records.

Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare no conflicts of interest.

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Authors’ contributions

JLV was entirely responsible for conceptualizing the study and directing the team when collecting information. He drafted the first version of the manuscript and reviewed the final version. MPM, FEJ, SAM, WTM, LS, GJ, EI, EC, and CM were responsible for collecting information from the ICU unit and contributing equally to the data analysis. EVG was responsible for completing the dataset and completing the first draft of the manuscript. EOP was responsible for critically reviewing the first draft, completing the manuscript’s final version, and critically reviewing the entire analytical process around data collection.

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Bibliographic references


