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Hard outcomes in Critically Ill Patients with ARDS Caused by SARS-CoV-2 Infection: A Retrospective Group Study

Gabriela Maria Mora Martinez[1*], **Theno Alexandro Turrubiates Hernandez**[2], **Porfirio Visoso Palacios**[1], **Josue Gerardo Esparza Correa**[1] and **Alvaro Eduardo Ramírez Gutiérrez**[1]

[1]*Department of Intensive Care, Central South High Specialty Hospital, Mexico City, Mexico*

[2]*Department of Intensive Care, Hospital regional Ciudad Madero, Tamaulipas, Mexico*

***Corresponding Author:** Gabriela Maria Mora Martínez, Department of Intensive Care, Central South High Specialty Hospital, Mexico City, Mexico, E-mail: gabriela.mora.mtz@hotmail.com

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Abstract

Background: The Coronavirus Disease (COVID-19) pandemic has exerted immense pressure on healthcare systems, particularly in the management of patients with Acute Respiratory Distress Syndrome (ARDS). Identifying predictors of survival in critically ill patients is essential for optimizing treatment strategies.

Materials and Methods: A retrospective study was conducted in an Intensive Care Unit (ICU) in Mexico City, spanning from March, 2020 to March, 2023. The study included patients aged 18 years and older with confirmed COVID-19 who required invasive mechanical ventilation. Logistic regression and Kaplan-Meier analyses were performed to evaluate factors associated with mortality.

Results: A total of 157 patients were included, with a mean age of 62.8 years and 74.5% were male. The 90 days survival rate was 41.4%, with a mortality rate of 58.6%. Acute kidney injury (AKI) (OR=3.4), hemodynamic failure (OR=6.5) and elevated lactate levels (OR=0.201) were significantly associated with increased mortality risk. Kaplan-Meier analysis demonstrated significantly reduced survival among patients with AKI, hemodynamic failure and hyperlactatemia.

Discussion: AKI, hemodynamic instability and hyperlactatemia emerged as pivotal predictors of mortality. The high incidence of AKI and associated adverse outcomes highlight the urgent need for management strategies in this vulnerable patient.

Conclusion: The 90 days survival rate was 41.4%. AKI, hemodynamic failure and elevated lactate levels were independently associated with increased mortality, highlighting the necessity for focused and strategic interventions.

Keywords: Pandemic; Hemodynamic failure; Mechanical ventilation; Intensive Care Unit

Abbreviations: ARDS: Acute Respiratory Distress Syndrome; COPD: Chronic Obstructive Pulmonary Disease; AKI: Acute Kidney Injury; SARS-CoV-2: Severe Acute Respiratory Syndrome

Introduction

The COVID-19 pandemic has placed significant pressure on healthcare systems worldwide, particularly in the management of critically ill patients with Acute Respiratory Distress Syndrome (ARDS) caused by SARS-CoV-2 infection. Since the first confirmed case of COVID-19 in Mexico on 27 February, 2020, identifying risk factors has been a priority for health professionals in the country [1-3].

International studies have identified factors such as advanced age, male sex, cardiovascular diseases (especially hypertension), diabetes, Chronic Obstructive Pulmonary Disease (COPD) and malignancies as predictors of severe illness and mortality in COVID-19 patients [4,5]. Approximately, 10% of cases require hospitalization due to pneumonia and 5% develop severe complications such as ARDS, sepsis or multiple organ failure with correspondingly high mortality rates [6-11].

In Mexico, excess mortality has been linked to sociodemographic factors such as an aging population, high levels of socioeconomic marginalization and smaller average household sizes, particularly in central states [12]. Furthermore, chronic diseases have exacerbated clinical outcomes; for instance, diabetes-related mortality was already high before the pandemic, with a 41.6% increase reported in 2020, highlighting the vulnerability of Mexican patients with diabetes [13].

Data suggest that chronic conditions such as diabetes, hypertension and obesity along with advanced age, male sex and indigenous ethnicity, increase the risk of mortality following SARS-CoV-2 infection in the Mexican population [14-18]. However, the factors influencing survival among critically ill patients with ARDS caused by SARS-CoV-2 remain incompletely understood. Although various treatment modalities have been described since the first critical case with ARDS was treated in the Intensive Care Unit (ICU) of the South Central High Specialty Hospital of Petroleos Mexicanos (PEMEX) on 21 March, 2020, management continues to rely primarily on supportive measures, including mechanical ventilation, vasopressor administration and renal replacement therapy [19-24].

Materials and methods

Setting

The study was conducted in an Intensive Care Unit (ICU) adapted for the management of COVID-19 patients at a tertiary care teaching hospital in Mexico City, covering the period from 21 March, 2020 to 20 March, 2023.

Study design

This is an observational, retrospective, longitudinal and comparative study.

Population definition

All patients admitted to the ICU who meet the eligibility criteria are included in this study.

Inclusion criteria: Patients of both sexes aged 18 years and older, with a confirmed diagnosis of COVID-19 through a positive Polymerase Chain Reaction (PCR) test for SARS-CoV-2.

Exclusion criteria: Patients with a negative PCR test were excluded.

Elimination criteria: Patients who died within the first 24 hours of ICU admission and those who did not require invasive mechanical ventilation were eliminated from the analysis.

Primary objective

To determine the 90 days survival rate of critically ill patients with ARDS due to SARS-CoV-2.

Secondary Objective

To identify factors associated with mortality in critically ill patients with ARDS due to SARS-CoV-2.

To determine 90 days survival, according to the factors associated with mortality in critically ill patients with ARDS due to SARS-CoV-2.

Variable operationalization

Demographic variables (age and gender) anthropometric data (weight, height and Body Mass Index (BMI)), comorbidities (diabetes, hypertension, among others) and admission data (PaO_2/FiO_2, SpO_2/FiO_2 and vital signs) were collected to classify the severity of respiratory failure (defined as PaO_2/FiO_2 <300 mmHg or SpO_2/FiO_2 <460 mmHg) and hemodynamic failure (defined as a Mean Arterial Pressure (MAP) <65 mmHg or the need for vasopressor support). The confirmation of the SARS-CoV-2 diagnosis was made by nasopharyngeal PCR test (CFX96 Touch RT-PCR Detection System, United States of America). Indicators of renal function (urine output, serum creatinine and Urinary neutrophil gelatinase-associated lipocalin) were also recorded to classify Acute Kidney Injury (AKI). The number of days on mechanical ventilation, the need and duration of prone positioning, use of neuromuscular blockade, tracheostomy and renal support through hemodialysis were documented. Length of ICU stay and total hospital stay were also recorded. 90 days survival will be assessed, with a patient considered a survivor if they are alive 90 days after hospital admission. Clinical follow-up and medical records will be used for this assessment. Patients discharged before day 90 who have outpatient follow-up, such as follow-up consultations or home visits will also be included. Data were obtained from the critical care unit database.

Statistical analysis

The most prevalent mortality-associated factors were analyzed using descriptive statistics; absolute (n) and relative (%) frequencies were used for categorical variables, while means (X) and Standard Deviations (SD) were calculated for continuous variables. For hypothesis testing, the Student's t-test was used to compare means, the Chi-square test to compare proportions and the Mann-Whitney U test to contrast medians, p-value<0.05 was considered significant. These variables were included in a binary logistic regression model to calculate Odds Ratios (OR) with 95% Confidence Intervals (95% CI). Once the factors associated with mortality with statistical significance were identified, cumulative individual survival probability was estimated using the Kaplan-Meier method and the log-rank test was used to evaluate significant differences in survival between groups defined by the identified risk factors. Additionally, the Pearson correlation coefficient was used to evaluate continuous variables and the Spearman correlation coefficient was applied for the combination of ordinal and continuous variables to assess the relationship between two variables; a p-value of 0.05 was considered significant. Data were processed using SPSS software, version 25.0 (IBM Corporation).

Results

A total of 157 patients were studied, of whom 74.5% (n=117) were male. The mean age was 62.8 ± 11.8 years. Nutritional status, evaluated using Body Mass Index (BMI), had a mean of 30.81 ± 5.90 kg/m²; no patients presented with malnutrition at the time of admission. A total of 12.1% (n=19) were classified as having a normal weight, 38.9% (n=61) were overweight and 49% (n=77) were obese. The most common comorbidity was hypertension, present in 54.8% (n=86) of patients, followed by type 2 diabetes, present in 43.3% (n=68).

Upon ICU admission, the mean SpO_2/FiO_2 ratio was 107.31 ± 40 mmHg and the mean PaO_2/FiO_2 ratio was 93.83 ± 41.64 mmHg. The

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prevalence of severe ARDS was 68.2% (n=107), with a mean duration of mechanical ventilation of 16.34 ± 12.43 days. Prone positioning was used in 42% (n=66) of patients, 86.4% (n=57) of whom underwent early pronation, defined as within the first 48 hours of ARDS diagnosis; without statistical significance (OR=1.1, 95% CI: 0,95-1.35, p=0.66). The mean duration of the pronation Maneuver was 49.2 ± 18.77 hours and only 6.1% required a second pronation session. Neuromuscular blockade was used in 49.7% (n=78) of cases and tracheostomy was performed in 29.3% (n=49) of patients. In terms of acid-base balance, the mean pH was 7.32 ± 0.12 (OR=1.24, 95% CI: 1.05-1.45, p=0.44) and the mean partial pressure of carbon dioxide (PCO_2) as 45.19 ± 13.3 (OR=1.15, 95% CI: 0.62 – 2.15, p=0.57). Neither variable showed statistical significance for mortality.

Acute Kidney Injury (AKI) occurred in 70.1% (n=110) of cases, classified based on urinary volumes and the presence of biochemical markers, with a higher prevalence in class 1A (34.5%, n=38). Hemodynamic failure at ICU admission was observed in 74.5% (n=117) of patients, with a mean Sequential Organ Failure Assessment (SOFA) score of 7 points (range: 2-14) and a mean serum lactate level of 1.72 ± 0.74 mM/L.

The mean length of ICU stay was 17.70 ± 13.59 days and the mean total hospital stay was 26.90 ± 19.91 days. Overall mortality was 58.6% (n=92), with a cumulative 90 days survival rate of 41.4%.

For logistic regression analysis, variables that showed statistical significance for mortality were included. Continuous variables such as lactate and SpO_2/FiO_2 were adjusted as dummy variables with cut-off points of 2 mM/L for lactate and 160 mmHg for SpO_2/FiO_2, respectively. The presence of AKI (OR=3.4, 95% CI: 1.702-7.169, p=0.00), hemodynamic failure at ICU admission (OR=6.5, 95% CI: 2.97-14.21, p=0.00) and lactate level (OR=0.201, 95% CI: 0.079-0.515, p=0.00) were independently associated with mortality.

Subsequently, the log-rank test was used to evaluate these variables in relation to 90 days survival, confirming statistical significance for lactate (p=0.00), hemodynamic failure (p=0.00) and AKI (p=0.01), with a p-value<0.05, confirming their association with survival. Moreover, a lower 90 days survival was observed in the group with AKI associated with hemodynamic failure (26.7% *vs* 54.2%, p=0.03, log-rank test) (Figures 1- 4).

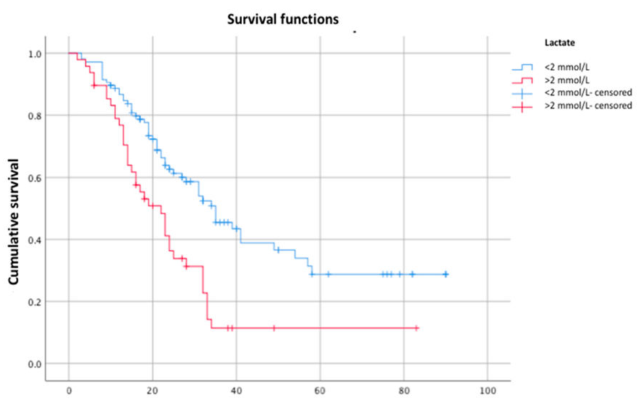

Figure 1: Kaplan-Meier curve showing lower survival in the group of patients with SARS-CoV-2 induced ARDS and elevated serum lactate levels compared to those without elevated levels (p=0.00).

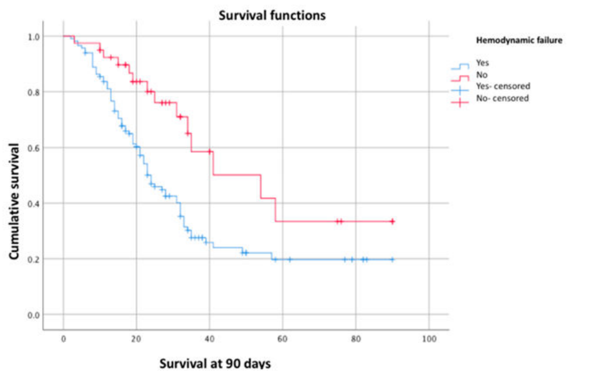

Figure 2: Kaplan-Meier curve showing lower survival in the group of patients with SARS-CoV-2 induced ARDS and hemodynamic failure compared to those without hemodynamic failure (p=0.00).

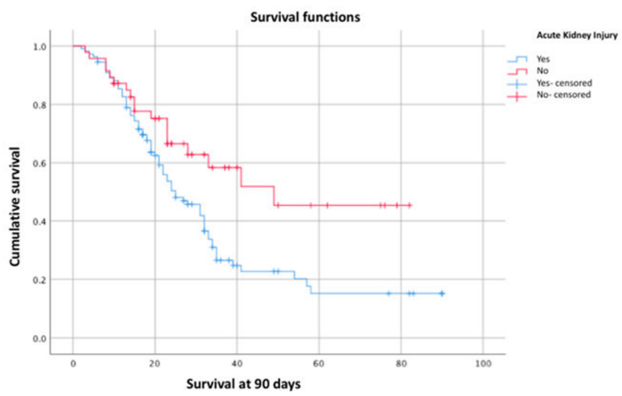

Figure 3: Kaplan-Meier curve showing lower survival in the group of patients with SARS-CoV-2 induced ARDS and Acute Kidney Injury compared to those without acute kidney injury (p=0.01).

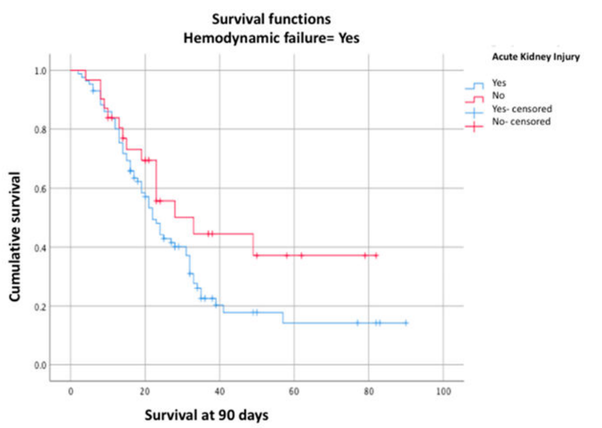

Figure 4: Kaplan-Meier curve showing lower survival in the group of patients with SARS-CoV-2 induced ARDS and hemodynamic failure who presented with acute kidney injury compared to those without (p=0.03).

According to the Pearson and Spearman correlation coefficients, statistically significant correlations were found. The level of PCO_2 and pH showed a moderate negative correlation (r= -0.54, p=0.00). Lactate levels had a weak positive correlation with Acute Kidney Injury (AKI) (r =0.24, p=0.002), while lactate and hemodynamic failure had a weak negative correlation (r= -0.391, p=0.000). A weak positive correlation was observed between mortality and hemodynamic failure (r=0.326, p=0.012). Prone positioning and the use of neuromuscular blockade showed a moderate positive correlation (r=0.702, p=0.000). Additionally, prone positioning had a negative correlation with pH (r= -0.193, p=0.05). Early prone positioning demonstrated a weak positive correlation with pH (r=0.389, p=0.017) and a negative correlation with AKI (r=-0.262, p=0.034).

Discussion

This study highlights the importance of acute kidney injury (AKI), hemodynamic instability and hyperlactatemia as important predictors of survival in patients with ARDS due to COVID-19 [25]. These findings are in line with prior research, which highlights the significant impact of organ dysfunction and metabolic disturbances on patient outcomes [26-29]. Notably, the prevalence of AKI in our study was exceptionally high, recorded at 70%, a stark contrast to the 10.8% reported in the general population of COVID-19 patients [30,31]. Supporting these observations, a meta-analysis of over 22 studies demonstrated a similarly high AKI prevalence of 67% (95% CI: 57-76) and an associated mortality rate of 60.3% among patients with COVID-19 related ARDS [32,33]. Our analysis further confirmed AKI as an independent predictor of 90 days survival, with risk factors such as advanced age, male sex, mechanical ventilation, a BMI exceeding 30 kg/m^2, hypertension and type 2-diabetes being particularly significant contributors.

Hemodynamic failure was another key factor identified in our study, emphasizing the necessity of meticulous monitoring and timely intervention. This finding is consistent with previous studies that have recognized hemodynamic instability as a vital determinant of hospital mortality (OR=1.74, 95% CI: 1.07-2.86) [34]. Furthermore, hypercapnia emerged as a significant contributor to hemodynamic compromise, as elevated PCO_2 levels can lead to systemic vasodilation, reduced myocardial contractility and impaired cardiac performance, thereby worsening hemodynamic failure [35]. In our analysis, a moderate negative Pearson correlation between PCO_2 and blood pH (r=-0.54, p=0.00) reinforced the association of elevated PCO_2 with reduced pH, indicative of respiratory acidosis.

Lactate levels were also identified as an independent factor impacting 90 days survival (OR=0.201, 95% CI: 0.079-0.515, p=0.00). While traditionally associated with anaerobic metabolism, hyperlactatemia in critically ill COVID-19 patients may also reflect more complex metabolic disturbances, including systemic inflammation and mitochondrial dysfunction [36,37]. This multifactorial elevation highlights the need for a detailed interpretation of lactate levels. Our findings revealed a weak positive correlation between elevated lactate and AKI risk (r=0.24, p=0.002) as well as a weak negative correlation between lactate levels and hemodynamic failure (r= -0.391, p=0.000), potentially indicating variations in tissue perfusion [32-36]. These correlations have significant implications for clinical management, highlighting the importance of early identification and personalized interventions.

For instance, targeted strategies for the timely management of AKI and hemodynamic instability could markedly improve patient outcomes. Despite the widespread use of prone positioning and other ventilatory interventions in severe ARDS, our study did not observe a survival benefit, pointing to the need for further research to refine these approaches. Prone positioning was strongly correlated with neuromuscular blockade use (r=0.702, p=0.000), indicating frequent concurrent implementation in severe cases. However, our findings revealed no survival benefit from early prone positioning (OR=1.1, 95% CI: 0.95-1.35, p=0.66) [38-40]. Moreover, prone positioning was negatively correlated with pH (r=-0.193, p=0.05), suggesting an association with metabolic or respiratory acidosis [35].

The mean duration of prone positioning in our study was 49.2 ± 18.77 hours, classified as prolonged. Despite initial assumptions that extended sessions might improve outcomes, recent data from a group of 753 patients showed no benefit in 60 days mortality, even for sessions exceeding 36 hours [33]. Interestingly, early pronation demonstrated a weak positive correlation with pH (r=0.389, p=0.017), possibly indicating an acid-base homeostatic advantage when performed promptly. Furthermore, early pronation was weakly negatively correlated with AKI occurrence (r=-0.262, p=0.034), suggesting a potential renal protective effect [31,35].

Several significant correlations between physiological variables and ventilatory interventions further highlight the necessity of optimizing ventilation strategies. Early initiation and personalized adjustment of prone positioning duration, guided by oxygenation indices and vigilant monitoring of acid-base disturbances especially hypercapnia and acidosis are essential for achieving optimal patient outcomes. This approach exemplifies the importance of personalized management in treating ARDS patients. Future research should continue to examine these complex relationships and their implications for improving ARDS management.

Conclusion

In our group study of critically ill patients with ARDS due to SARS-CoV-2 infection who required mechanical ventilation, the cumulative 90 days survival rate was 41.4%. Survival was independently associated with the presence of AKI (p 0.01, log-rank test), hemodynamic failure (p=0.00, log-rank test) and elevated lactate levels (p=0.01, log-rank test). Notably, a substantial decline in 90-days survival was observed when AKI was accompanied by hemodynamic failure, with survival dropping to 26.7%.

Our patient population exhibited several well-documented risk factors for severe disease and ARDS. However, our findings underscore that, in critically ill patients requiring mechanical ventilation for COVID-19-related ARDS, AKI and hemodynamic failure are strongly associated with decreased survival. These results emphasize the need for targeted strategies to manage these complications and potentially improve outcomes in this vulnerable patient group.

Limitations

This study has some important limitations. The retrospective design may have introduced biases, particularly due to inconsistently recorded or missing data, affecting the accuracy of certain variables.

Additionally, the variability in treatment protocols during the early stages of the pandemic could have influenced the outcomes and comparability of the findings. The absence of detailed ventilatory data limited our ability to fully evaluate the impact of ventilation strategies on patient outcomes. Moreover, the inclusion of patients in extremely critical conditions may restrict the generalizability of our results to less severe cases. Future research should consider prospective designs, more comprehensive data collection and a broader range of patient severities to enhance the robustness and applicability of findings.

Ethical considerations

This study was approved by the Research Committee and the Ethics and Research Committee under the numbers 17-21, 20-21 and 26-21, ensuring the confidentiality and protection of patient data. Since this was an observational study without intervention, informed consent was not required.

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