Impact of ICU saturation on hospital mortality from COVID-19 in a secondary care center in Iztapalapa, Mexico City

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Research Article

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Abstract

INTRODUCTION: A saturated intensive care unit (ICU) setting and socioeconomic factors such as higher poverty rates have been associated with increased rates of in-hospital mortality in COVID-19 patients. Mexico City has become the national epicenter of the pandemic, with Mexico’s highest death toll. Iztapalapa is the delegation with the highest population density and the most notorious conditions of marginalization in Mexico City. We describe the clinical characteristics and risk factors associated with mortality in 164 patients who received care in a hospital ward setting due to ICU saturation in a hospital in Iztapalapa, Mexico City.

MATERIALS AND METHODS: In this retrospective cohort study, data from confirmed COVID-19 patients hospitalized between April 1, 2020 and May 31, 2020 were collected. Patients were categorized into different subgroups: alive vs. deceased and intubated vs. nonintubated for analysis between groups. A p-value <0.05 was considered statistically significant.

RESULTS: In this setting, 67% of the patients required mechanical ventilation, and 32.3% needed vasopressor support, with an in-hospital mortality of 68.3%. The most common complications during hospitalization were acute kidney injury (36%) and acute respiratory distress syndrome (34.8%). We observed similar factors associated with death as previous studies: male sex, older age, comorbidities, laboratory values indicating increased inflammatory/organ failure markers, and severe disease at admission. Additionally, we found that routine use of intravenous antibiotics was associated with a higher rate of in-hospital mortality (RR 3.45, 95% CI 1.69-7.06, p <0.001).

Background

Novel coronavirus disease 2019 (COVID-19), caused by severe acute respiratory coronavirus-2 (SARS-CoV-2), has become a significant health concern worldwide. As the pandemic has spread, it has persisted in Latin America, creating a substantial demand for hospital admission and critical care. Worldwide reports have shown a mortality rate ranging from 8% to 21% in patients hospitalized for SARS-CoV-2 pneumonia and up to 16-78% in those requiring intensive care unit (ICU) admission. [1]

Mexico has high rates of hypertension, obesity, and diabetes, all of which are risk factors for severe disease after infection with SARS-CoV-2. [2] As of March 15, 2021, Mexico had become the nation with the third-highest number of SARS-CoV-2-related deaths worldwide, and Mexico City was the epicenter of the pandemic, with the country’s highest death toll. [3]

A recent study from a tertiary care center in Mexico City reported in-hospital mortality rates of 30.1% and 49.2% in ICU beds, noting that 45% of the nonsurvivor patients who developed critical illness did not receive invasive mechanical ventilation/ICU care due to the lack of ICU bed availability. [2]

Iztapalapa is the delegation with the highest population density (its population represented 20.5% of the population in Mexico City) and the most notorious conditions of marginalization in Mexico City. [3] By March 15th, 2021, with a total population of 1,815,551 inhabitants in the Iztapalapa delegation,
accumulated COVID-19 confirmed cases of 91,112 had been reported, with 66,373 recovered cases and 5,670 deaths, a fatality rate of 6.2%. At the time of writing, 2,496 active cases had been reported in the second week of March 2021. [4] Prevalent socioeconomic factors such as higher poverty rates, high public transportation use, lack of health insurance, poor formal education level, and overcrowded housing (and other factors that preclude social distancing and preventive measures) are associated with an increased rate of in-hospital mortality in COVID-19 patients. [2]

As the principal tertiary centers for COVID-19 treatment in the metropolitan area of Mexico City reached ICU bed saturation, most Iztapalapa populations with severe or critical COVID-19 receive attention in units with minimal ICU bed availability, such as our center. This study describes the clinical characteristics and risk factors associated with mortality of adults with confirmed SARS-CoV-2 pneumonia who received care in a hospital-ward setting due to ICU saturation in a hospital in Mexico City.

Materials And Methods

2.1.- Study design and setting

This was a retrospective cohort study at a hospital in the Iztapalapa Delegation of Mexico City, Mexico. Our hospital has served as a pandemic hospital since March 2020. During the study period, the ICU bed capacity was only seven beds, but the hospital wards’ capacity was expanded from 36 to 72 beds (all equipped for invasive mechanical ventilation).

We conducted the study in line with the Declaration of Helsinki. The Institutional Ethics Committee approved the study protocol and waived the requirement for written informed consent due to the study’s minimal risk to participants. Privacy and personally identifiable information of the patients were protected, and data collection did not harm the patients.

2.2. Study population

We enrolled patients who had been diagnosed with COVID-19 pneumonia and were hospitalized in the internal medicine department of our hospital between April 1st, 2020, and May 31st, 2020. The inclusion criteria were as follows: (1) patients over 18 years old; (2) patients with COVID-19 confirmed by real-time reverse transcription-polymerase chain reaction (PCR); (3) patients treated only by the internal medicine department medical team; and (4) patients discharged from the hospital due to death or clinical improvement. Exclusion criteria: (1) pregnant patients, (2) patients treated only in the emergency department and intensive care unit, (3) patients referred from other medical units with mechanical ventilation and/or vasopressor support, and (4) those with incomplete data.

Any suspected case with respiratory distress (>30 breaths/minute) or oxygen saturation lower than <90% at room air was hospitalized.

2.3.- Data collection
Patients’ clinical, demographic, radiologic, and laboratory feature data with treatments and hospitalization days were extracted from medical records and collected in a database.

2.4.- Variables

The study’s primary outcome was in-hospital mortality, defined as documented death from any cause during hospitalization. The secondary outcome was the use of mechanical ventilation during hospitalization. Patients were further categorized into different subgroups: alive vs. deceased and intubated vs. nonintubated patients.

2.5.- Statistical analysis

The analyses were computed using IBM SPSS Statistics 22. Regarding data distribution, continuous data are presented as the mean and standard deviation (SD) or median and interquartile range (IQR). Categorical data are reported as frequencies and percentages. Variables were compared between groups using Student’s t-test or a Mann-Whitney U test if numeric or a chi-squared test if categorical. Analysis of risk factors for in-hospital mortality was performed between the groups. A p-value <0.05 was considered statistically significant.

Results

Demographic and clinical characteristics

During the study period, PCR was performed in 265 consecutive patients with suspected SARS-CoV-2 infection; 191 patients (72.1%) were confirmed SARS-CoV-2 cases. Of them, 164 patients (85.8%) met all the study criteria. In this population, 52 patients recovered (31.7%) and 112 (68.3%) died during hospitalization. (Figure 1)

The demographic and clinical characteristics of the patients are shown in Table 1. All patients were residents of Mexico City. The median age was 52.5 years (IQR 44 to 64.5), 68% (n=112) were male, median schooling was 9 years (IQR: 6 to 9), 48.7% (n= 74) were obese, 29% (n =44) were overweight, median BMI was 29.3 kg/m² (IQR 25.5 to 34.7) and 24.3% (n=40) had a history of smoking. A total of 59.7% (n= 98) had comorbidities; diabetes (37.8%) and hypertension (37%) were the most common.

Comparing surviving vs. deceased patients, age (median 47.5 years [IQR: 38-54] vs. 55 years [IQR: 46.5-65.7], p <0.001), diabetes prevalence (21% vs. 45.5%, p 0.003), and smoking index (median of 1 pack/year vs 6 packs/year, p 0.005) were higher in deceased patients. Schooling (median of 9 years [IQR 6 to 12] vs. 7 years [IQR 6 to 9], p 0.01) was lower in deceased patients.

Comparing intubated vs. nonintubated patients, male sex (p 0.036), older age (p 0.024), and a higher smoking index (p 0.002) were observed in patients who needed mechanical ventilation.

Signs and symptoms
Clinical evaluation is summarized in Table 2. The most common symptoms were dyspnea in 82.9% (n=136), cough in 75.6% (n=124), fever in 69% (n=131), myalgias in 44% (n=72) and headache in 40.2% (n=66). On admission, the most common findings at physical examination were pharyngeal hyperemia in 15.2% (n=25) and cyanosis in 8.5% (n=14).

When comparing surviving vs deceased groups, dyspnea (73% in the survivor group vs. 83% in deceased group, p 0.02) and cyanosis (1.9% vs. 11.6%, p 0.03) were more frequently observed in deceased patients. Comparing the intubated vs. nonintubated groups, cyanosis (p 0.03) was associated with the requirement of mechanical ventilation.

At admission, only 17.6% (n=29) of patients presented with fever. During hospitalization, 62.2% (n=109) of patients continued or developed fever. The onset of fever in initially afebrile patients was a median of 2 days after admission (IQR 1-3). Comparing groups, fever at hospitalization (32.7% in the survivor group vs. 76% in the deceased group, p <0.001) and a higher temperature during hospitalization (median 37°C [IQR: 36.8-38.5] vs. 39°C [IQR: 38.2-40], p <0.001) were frequently observed in deceased patients who needed mechanical ventilation.

**Radiographic and laboratory findings**

Radiographic and laboratory features are summarized in Table 3. The most common findings were ground-glass opacities, interstitial abnormalities, and bilateral infiltrates. No difference was found in the radiographic features between groups.

With respect to laboratory findings, low PaO2/FiO2 ratio (mean 213 +/- 107), high WBC count (median 11,050 per mm$^3$, IQR: 7,900-15,100), high neutrophil count (median 9,250 per mm$^3$, IQR:6,475-13,025), high neutrophil-lymphocyte ratio (median 11, IQR: 6.5-19), high lactate dehydrogenase (median 406 U/L, IQR: 322-570), high D-dimer (median 1740 ng/ml, IQR: 728-3380), increased glucose (median 123 mg/dl, IQR: 93-198) and high C-reactive protein (median 21.4 mg/dl, IQR: 12-32) were observed.

After comparing surviving and deceased patients, the deceased group had lower PaO2/FiO2 ratio (mean 274 vs 184, p<0.001), higher WBC count (median 8,700 per mm$^3$ vs 12,000 per mm$^3$, p <0.001), increased neutrophil count (median 6,900 per mm$^3$ vs 10,700 per mm$^3$, p <0.001), higher neutrophil-lymphocyte ratio (median 7.6 vs 13, p <0.001), increased lactate dehydrogenase (median 322 U/L vs 482 U/L, p <0.001), increased D-dimer (median 845 ng/ml vs 2235 ng/ml, p <0.001), elevated glucose (median 101 mg/dl vs 138 mg/dl, p <0.001), and higher C-reactive protein (median 12 mg/dl vs 26.2 mg/dl, p <0.001) levels. The same findings with statistical significance (p <0.05) were observed in patients who needed mechanical ventilation.

**Treatments and complications**

Treatments and complications are described in Table 4. Overall, patients had a median hospital stay of 7 days (IQR: 4-11). Regarding treatment, 98.7% (n=162) had oxygen therapy, 76.2% (n=125) received oral antibiotics, 70.7% (n=116) received intravenous antibiotics, 59.8% (n=98) received hydroxychloroquine, and
25% (n=41) received systemic steroids. The most common complications during hospitalization were acute kidney injury (36%, n=59) and acute respiratory distress syndrome (34.8%, n=57). Sixty-seven percent (n=110) of the patients required invasive mechanical ventilation, and 32.3% (n=53) needed vasopressor support.

Regarding in-hospital mortality, fewer days of hospital stay (median 10 days, IQR: 7-16 vs 5 days, IQR: 3.2-9, p <0.001), higher use of intravenous antibiotics (52% vs 79.5%, p <0.001), higher use of systemic steroids (13.5% vs 30.4%, p 0.02), higher incidence of ARDS (5.8% vs 48.2%, p <0.001) and AKI prevalence (11.5% vs 47.3%, p <0.001), and higher use of vasopressor support (3.8% vs 45.5%, p <0.001) were observed in deceased patients.

Risk factors for death

We summarize the analysis of risk factors for in-hospital mortality in Table 5. Mortality was significantly higher in patients who were male (RR 2.1, 95% CI 1.02-4.51, p 0.04), aged >50 years (RR 2.3, 95% CI 1.49-3.83, p <0.001), had diabetes (RR 3.07, 95% CI 1.28-7.37, p 0.012), had severe pneumonia at admission (RR 14.1, 95% CI 1.66-120.22, p 0.015), PORT/PSI score >91 (RR 6.5, 95% CI 1.33-32.23, p 0.021), SMART-COP score > 5 (RR 6.79, 95% CI 1.65-27.86, p 0.008), SCAP score >10 (RR 4.86, 95% CI 1.18-19.92, p 0.028), had dyspnea at admission (RR 3.55, 95% CI 1.16-10.85, p 0.026), had fever during hospitalization (RR 6.83, 95% CI 2.43-19.13, p <0.001), and were administered intravenous antibiotics (RR 3.45, 95% CI 1.69-7.06, p <0.001).

Discussion

In this study, among patients with confirmed COVID-19 pneumonia who presented during the initial phase of the COVID-19 outbreak in a hospital in the Iztapalapa delegation of Mexico City, in-hospital mortality was 68.3%, which was higher than that found in previous studies. [1, 6-12]

The hospitalization criteria in our hospital may be the cause for this finding. As discussed previously, a considerable number of severely ill or oxygen-dependent patients were hospitalized. Thus, our cohort might represent more severe COVID-19 patients. In this setting of ICU bed unavailability, 67% of the patients hospitalized in a hospital ward required mechanical ventilation, and 32.3% needed vasopressor support.

This study shows the problem of health system saturation and ICU resource rationing during the COVID-19 pandemic. These results were similar to those observed during the pandemic's initial surge in several countries, where over 50% of the critically ill patients who required ICU care died in general hospital wards due to resource constraints. [13]

This investigation showed similar factors associated with death as previous studies. Some comorbidities (such as diabetes mellitus), male sex, older age, increased inflammatory markers, and laboratory values indicating organ failure were associated with a higher rate of in-hospital mortality. [6-8, 10-11]
In this study, we found that routine use of intravenous antibiotics was associated with a higher rate of in-hospital mortality and the need for mechanical ventilation. COVID-19 may mimic bacterial pneumonia, and therefore, antibiotics for possible bacterial coinfections are frequently administered. [14] Langford et al. reported a more frequent unnecessary antibiotic prescription in patients with COVID-19 in the first six months of the global pandemic, mainly due to suspected bacterial coinfections. Despite frequent antibiotic prescriptions, the prevalence of bacterial coinfection and secondary infection in patients hospitalized with COVID-19 was relatively low at 3.5% and 14.3%, respectively. [15]

Studies about the impact of early antibiotic therapy on mortality or critical complications in COVID-19 patients are limited. Buetti et al. reported that early administered antibiotics do not appear to significantly impact mortality or delay hospital-acquired infections in critically ill patients. [14]

In respiratory viral infection, an altered innate immune function exists in pulmonary tissue due to respiratory viral infection; macrophages are overwhelmed by the increased burden of apoptotic cells and become limited in their capacity to phagocytose bacteria as a result of increasing bacterial growth. Additionally, the initial immune response to a viral lung infection modifies the respiratory tract microbiome, which can, in turn, undermine immune defenses against infectious pathogens. Other inciting mechanisms following viral illnesses include altered epithelial cells that disrupt mucociliary clearance and mucus thickening, impairing immune cell movement. In the specific setting of SARS-CoV-2 infection, fluid- and pus-filled pulmonary alveoli create a nutritive environment for bacteria such as P. aeruginosa and S. aureus. [16]

Nosocomial and ventilator-associated pneumonia associated with multidrug-resistant P. aeruginosa, Acinetobacter baumanii, and K. pneumoniae is common in our center. We did not have microbiology laboratory analyses during the study period in our hospital, so bacterial infections in these patients were unknown. To our knowledge, this is the first research study in which early antibiotic intravenous therapy was associated with higher in-hospital mortality and an increased need for mechanical ventilation in COVID-19 patients. The use of routine intravenous antibiotics, generally broad-spectrum antibiotics, could modify the respiratory tract microbiome. This altered microbiome with impaired immune cells due to SARS-CoV-2 infection could trigger multidrug-resistant pulmonary infections, impacting patient survival.

Respiratory failure is the leading cause of mortality in patients with COVID-19. [17] Myocardial injury, kidney or liver injury, and multiorgan dysfunction are among the other complications leading to death. [18] There are several pathways leading to SARS-CoV-2-related death: those directly attributed to viral infection, those in which the infection partially contributed to the cause of death, and those unrelated to it. In this study, most complications were directly related to SARS-CoV-2. [19]

In a large retrospective cohort study in the United States, risk factors associated with mortality were similar to those identified in our study. Nevertheless, due to the low in-hospital mortality and lower mechanical ventilation use reported, COVID-19 patients present a higher prevalence of acute complications such as ARDS, AKI, and shock. [20] Regarding Mexico, Olivas Martinez et al. reported in a prospective cohort study the same patterns for risk factors for death as our study and showed how lack of ICU bed availability increased patient mortality. The limitation reported in this extensive study was that a considerable
percentage of the patients were transferred to other hospitals due to clinical improvement, clinical deterioration, and saturation of critical care areas, so some clinical outcomes were unknown. [1]

With the findings of previous studies and our results, our group rightfully concluded that in-hospital mortality is associated with a clear pattern. We can expect an increased incidence of acute complications, need for critical care, and higher mortality in a COVID patient with the following risk factors: male sex, older age, presence of comorbidities, laboratory values indicating increased inflammatory/organ failure markers, and severe disease at admission.

In addition to our best efforts, this cohort had the limitation of a small sample size. The population was limited to the Iztapalapa delegation in Mexico City. Extrapolating these findings to other areas in Mexico (with different population densities and ICU bed availability) could be inaccurate.

Conclusions

Patients hospitalized due to COVID-19 pneumonia in a saturated ICU setting had higher mortality than in other studies reported globally. Expanding bed capacity in hospital wards could help mitigate hospital saturation during the COVID-19 pandemic. Nevertheless, a hospital with a low ICU bed capacity could not provide a better outcome for these patients, who had higher mechanical ventilation or vasopressor support requirements. This study reports a critical situation of hospital area overcrowding, elucidating this situation during the COVID-19 pandemic to inform strategies in resource-limited medical units.

Declarations

FUNDING CONSIDERATIONS

This study did not benefit from any funding organization in the public or commercial.

CONFLICT OF INTEREST

None.

AUTHOR’S CONTRIBUTIONS

JM Alanís-Naranjo wrote the initial draft of the manuscript. VM Anguiano-Alvarez, and EF Hammeken-Larrondo contributed to reviewing the manuscript. All authors played a significant role in editing this research article.

ETHICAL CONSIDERATIONS

The Institutional Ethics Committee approved the study protocol (CEI-1-2021, 501-010-01-21). Privacy and personally identifiable information of the patients were protected, and data collection did not harm the patients.
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Tables
| Variable                        | Overall (N=164) | Death p-value | Mechanical ventilation p-value |
|--------------------------------|-----------------|---------------|-------------------------------|
|                                | NO (N=52)       | YES (N=112)   | NO (N=54)                     | YES (N=110)                     |
| Male gender, n (%)             | 112/164 (68%)   | 31/52 (59.6%) | 31/54 (57.4%)                 | 81/112 (72%)                    |
|                                |                 | 81/112        | 81/110 (73.6%)                |                                |
| Age, median (IQR) -years-      | 52.5 (45-64.5)  | 47.5 (38-54)  | 49.5 (42-56.2)                | 55 (46.5-65)                    |
|                                |                 | 55 (46.5-65.7)|                                |                                |
| Schooling, median (IQR) -years-| 9 (6-9)         | 9 (6-12)      | 9 (6-12)                      | 7 (6-9)                        |
|                                |                 | 7 (6-9)       | 7 (6-9) (64%)                 |                                |
| BMI, median (IQR) -kg/m2-      | 29.3 (25.5-34.7)| 28.6 (25.9-34) | 28.6 (25.7-33.4)              | 30.2 (25.3-36.5)               |
|                                |                 | 30.2 (25.3-36.5) |                                |                                |
| Normal BMI, n (%)              | 34/152 (22.3%)  | 12/51 (23.5%) | 12/53 (22.6%)                 | 22/101 (22%)                    |
|                                |                 | 22/101        | 22/99 (22%)                   |                                |
| Overweight, n (%)              | 44/152 (29%)    | 16/51 (31.3%) | 17/53 (32.1%)                 | 28/101 (28%)                    |
|                                |                 | 28/101        | 27/99 (28%)                   |                                |
| Obesity, n (%)                 | 74/152 (48.7%)  | 23/51 (45.1%) | 24/53 (45.3%)                 | 51/101 (50%)                    |
|                                |                 | 51/101        | 50/99 (50.5%)                 |                                |
| Obese class I, n (%)           | 37/152 (24.3%)  | 12/51 (23.5%) | 14/53 (26.4%)                 | 25/101 (24.7%)                 |
|                                |                 | 25/101        | 23/99 (24.7%)                 |                                |
| Obese class II, n (%)          | 19/152 (12.5%)  | 6/51 (11.7%)  | 3/53 (5.7%)                   | 13/101 (12.8%)                 |
|                                |                 | 13/101        | 16/99 (12.8%)                 |                                |
| Obese class III, n (%)         | 18/152 (11.8%)  | 5/51 (9.8%)   | 7/53 (13.2%)                  | 13/101 (12.8%)                 |
|                                |                 | 13/101        | 11/99 (12.8%)                 |                                |
| Smoking history, n (%)         | 40/164 (24.3%)  | 17/52 (33%)   | 17/54 (31.4%)                 | 23/112 (20.9%)                 |
|                                |                 | 23/112        | 23/110 (20.9%)                |                                |
| Former smoker\(^1\), n (%)    | 20/40 (50%)     | 11/17 (64.7%) | 12/17 (70.6%)                 | 9/23 (39%)                     |
|                                |                 | 9/23          | 8/23 (34.7%)                  |                                |
| Current smoker\(^2\), n (%)   | 20/40 (50%)     | 6/17 (35.3%)  | 5/17 (29.4%)                  | 14/23 (61%)                    |
|                                |                 | 14/23         | 15/23 (65.2%)                 |                                |
| Smoking index\(^3\), median (IQR) - pack/year- | 2.9 (0.7-8.3) | 1 (0.3-2.9) | 6 (1.4-12) | 0.005 | 1 (0.3-2.9) | 6 (1.4-12) | 0.002 |
|-----------------------------------------------|----------------|-------------|-----------|-------|-------------|-----------|-------|
| Alcohol history, n (%)                        | 37/164 (22.5%) | 19/52 (36.5%) | 18/112 (16%) | 0.004 | 19/54 (35.2%) | 18/110 (16.4%) | 0.007 |
| Former drinker\(^4\), n (%)                  | 19/37 (51.4%) | 12/19 (63%) | 7/18 (39%) | 0.1  | 12/19 (63.2%) | 7/18 (39%) | 0.1  |
| Current drinker\(^5\), n (%)                 | 18/37 (48.6%) | 7/19 (37%) | 11/18 (61%) | 0.1  | 7/19 (36.8%) | 11/18 (61%) | 0.1  |
| Drug history\(^6\), n (%)                    | 4/164 (2.4%) | 1/52 (1.9%) | 3/112 (2.67%) | 0.77 | 2/54 (3.7%) | 2/110 (1.8%) | 0.4  |
| Contact with COVID-19 confirmed case within past 14 days, n (%) | 22/164 (13.4%) | 10/52 (19.2%) | 12/112 (10.7%) | 0.13 | 9/54 (16.7%) | 13/110 (11.8%) | 0.39 |
| Comorbidities, n (%)                          | 98/164 (59.7%) | 26/52 (50%) | 72/112 (64%) | 0.08 | 27/54 (50%) | 71/110 (64.6%) | 0.07 |
| COPD, n (%)                                   | 6/164 (3.6%) | 2/52 (3.8%) | 4/112 (3.6%) | 0.9  | 2/54 (3.7%) | 4/110 (3.6%) | 0.9  |
| Diabetes, n (%)                               | 62/164 (37.8%) | 11/52 (21%) | 51/112 (45.5%) | 0.003 | 14/54 (25.9%) | 48/110 (43.6%) | 0.02 |
| Hypoglycemic drugs, n (%)                    | 14/62 (22.5%) | 3/11 (27%) | 11/51 (21.6%) | 0.6  | 3/14 (21.4%) | 11/48 (22.9%) | 0.9  |
| Insulin, n (%)                                | 9/62 (14.5%) | 1/11 (9%) | 8/51 (15.7%) | 0.5  | 2/14 (14.3%) | 7/48 (14.6%) | 0.9  |
| Hypoglycemic drugs with insulin, n (%)        | 8/62 (13%) | 4/11 (36%) | 4/51 (7.8%) | 0.01 | 4/14 (28.6%) | 4/48 (8.3%) | 0.04 |
| No-treatment, n (%)                           | 17/62 (27.4%) | 1/11 (9%) | 16/51 (31.4%) | 0.1  | 1/14 (7.1%) | 16/48 (33.3%) | 0.053 |
| New-onset diabetes, n (%)                     | 14/62 (22.6%) | 2/11 (18.2%) | 12/51 (31.4%) | 0.7  | 4/14 (28.6%) | 10/48 (20.8%) | 0.5  |
| Hypertension, n (%)                           | 61/164 (37%) | 15/52 (28.8%) | 46/112 (41%) | 0.13 | 16/54 (29.6%) | 45/110 (40.9%) | 0.1  |
| Use of ACEI or ARBs, n (%)                    | 34/61 (55.7%) | 5/15 (33%) | 29/46 (63%) | 0.04 | 7/16 (43.8%) | 27/45 (60%) | 0.2  |
| Condition                        | N (% of total) | N (% of cohort) |
|---------------------------------|----------------|-----------------|
| ACEI, n (%)                     | 11/61 (18%)    | 1/15 (6.7%)     |
|                                | 1/16 (6.3%)    | 10/45 (21.7%)   |
| ARBs, n (%)                     | 23/61 (37.7%)  | 4/15 (26.7%)    |
|                                | 19/46 (41.3%)  | 6/16 (37.5%)    |
|                                | 17/45 (37.8%)  | 0.9             |
| CCBs, n (%)                     | 14/61 (23%)    | 3/15 (20%)      |
|                                | 11/46 (24%)    | 4/16 (25%)      |
|                                | 10/45 (22.2%)  | 0.8             |
| Use of >2 drugs, n (%)          | 8/61 (13%)     | 1/15 (6.7%)     |
|                                | 7/46 (15.2%)   | 3/16 (18.7%)    |
|                                | 6/45 (13.3%)   | 0.9             |
| No-treatment, n (%)             | 13/61 (21.3%)  | 3/15 (20%)      |
|                                | 10/46 (21.7%)  | 3/16 (18.7%)    |
|                                | 10/45 (22.2%)  | 0.7             |
| New-onset hypertension, n (%)   | 8/61 (13%)     | 5/15 (33.3%)    |
|                                | 3/46 (6.5%)    | 4/16 (25%)      |
|                                | 4/45 (8.8%)    | 0.1             |
| Hypothyroidism, n (%)           | 7/164 (4.2%)   | 2/52 (3.8%)     |
|                                | 5/112 (4.5%)   | 2/54 (3.7%)     |
|                                | 5/110 (4.5%)   | 0.8             |
| Asthma, n (%)                   | 6/164 (3.6%)   | 5/52 (9.6%)     |
|                                | 1/112 (0.9%)   | 5/54 (9.3%)     |
|                                | 1/110 (0.9%)   | 0.007           |
| Chronic heart failure, n (%)    | 3/164 (1.8%)   | 1/52 (1.9%)     |
|                                | 2/112 (1.7%)   | 1/54 (1.9%)     |
|                                | 2/110 (1.8%)   | 0.9             |
| Peripheral vascular disease, n %| 1/164 (0.6%)   | 0               |
|                                | 1/112 (0.9%)   | 0               |
|                                | 1/110 (0.9%)   | 0.4             |
| Rheumatoid arthritis, n (%)     | 2/164 (1.2%)   | 0               |
|                                | 2/112 (1.8%)   | 0               |
|                                | 2/110 (1.8%)   | 0.3             |
| Coronary heart disease, n (%)   | 2/164 (1.2%)   | 1/52 (1.9%)     |
|                                | 1/112 (0.9%)   | 1/54 (1.9%)     |
|                                | 1/110 (0.9%)   | 0.6             |
| Chronic kidney disease, n (%)   | 7/164 (4.2%)   | 1/52 (1.9%)     |
|                                | 6/112 (5.3%)   | 1/54 (1.9%)     |
|                                | 6/110 (5.5%)   | 0.2             |
| Benign prostatic hyperplasia, n %| 2/164 (1.2%)  | 1/52 (1.9%)    |
|                                | 1/112 (0.9%)   | 1/54 (1.9%)    |
|                                | 1/110 (0.9%)   | 0.6             |
| Atrial fibrillation, n (%)      | 1/164 (0.6%)   | 0               |
|                                | 1/112 (0.9%)   | 0               |
|                                | 1/110 (0.9%)   | 0.4             |
| Epilepsy, n (%)                 | 1/164 (0.6%)   | 0               |
|                                | 1/112 (0.9%)   | 0               |
|                                | 1/110 (0.9%)   | 0.4             |
### Chronic pulmonary thromboembolism, n (%)

|       | 0/164 | 1/52 | 0 | 0.1 | 1/54 | 0 | 0.1 |
|-------|-------|------|---|-----|------|---|-----|
|       | (0.6%) | (1.9%) | | | (1.9%) | | |

### Pulmonary hypertension, n (%)

|       | 0/164 | 1/52 | 0 | 0.1 | 1/54 | 0 | 0.1 |
|-------|-------|------|---|-----|------|---|-----|
|       | (0.6%) | (1.9%) | | | (1.9%) | | |

### Pneumonia severity (ATS) *

|       | 66/164 | 5/52 | 61/112 | <0.001 | 9/54 | 57/110 | <0.001 |
|-------|--------|------|--------|---------|------|--------|---------|
|       | (40.2%) | (9.6%) | (54.5%) | | (16.7%) | (51.8%) | |

### NEWS2, median (IQR)

|       | 7 (6-8) | 7 (5.5-7.5) | 8 (6-9) | <0.001 | 7 (6-7.5) | 8 (6-9) | 0.004 |
|-------|---------|-------------|--------|---------|-----------|--------|-------|

### MulBSTA, median (IQR)

|       | 7.5 (5-11) | 7 (4.5-9.5) | 8 (5-11) | 0.2 | 8 (5-11) | 7 (5-11) | 0.9 |
|-------|-------------|-------------|----------|-----|----------|--------|-----|

### PORT/PSI, median (IQR)

|       | 83 (60-107.5) | 56.5 (46-67) | 93 (75-119) | <0.001 | 60 (46.2-70.7) | 91 (71.5-119) | <0.001 |
|-------|---------------|--------------|-------------|--------|----------------|----------------|--------|

### SMART-COP, median (IQR)

|       | 4 (3-5) | 3 (2-4) | 5 (3.7-6) | <0.001 | 4 (2-4) | 5 (3-6) | <0.001 |
|-------|---------|---------|----------|--------|---------|--------|-------|

### SCAP, median (IQR)

|       | 14 (6-20) | 6 (5-11) | 19 (11-25) | <0.001 | 6 (5-11) | 19 (11-25) | <0.001 |
|-------|-----------|---------|-----------|--------|---------|----------|-------|

### SOFA at admission, median (IQR)

|       | 2 (2-3) | 2 (1-2) | 3 (2-3) | <0.001 | 2 (1-2) | 3 (2-3) | <0.001 |
|-------|---------|---------|--------|--------|---------|--------|-------|

### APACHE II, median (IQR)

|       | 9 (7-14) | 7 (5-9.5) | 11 (8-15) | <0.001 | 8 (5-11) | 11 (8-15) | <0.001 |
|-------|----------|---------|----------|--------|---------|----------|-------|

### CHARLSON, median (IQR)

|       | 2 (0-3) | 1 (0-2) | 2 (1-3) | <0.001 | 1 (0-2) | 2 (1-3) | 0.03 |
|-------|---------|---------|--------|--------|---------|--------|-----|

**BMI** = Body Mass Index, **COPD** = Chronic Obstructive Pulmonary Disease, **ACEI** = Angiotensin-Converting Enzyme Inhibitor, **ARB** = Angiotensin II Receptor Blocker, **CCB** = Calcium Channel Blocker, **ATS** = American Thoracic Society.

1.- Patient who has smoked at least 100 cigarettes in his or her lifetime but who had quit smoking at the time of interview.

2.- Patient who has smoked 100 cigarettes in his or her lifetime but who currently smokes cigarettes.

3.- [No. of cigarettes per day * No. of years of smoker] / 20

4.- At least 12 drinks in any one year in lifetime but no drinks in past year.

5.- Patients who have consumed a drink containing alcohol in the last 12 months.

6.- Use of marijuana, cocaine, or inhalants.
We defined the degree of severity of COVID-19 (severe vs. nonsevere) at the time of admission using the 2019 American Thoracic Society guidelines for community-acquired pneumonia.
Table 2.- Signs and symptoms

| Variable                | Overall (N=164) | Death | p-value | Mechanical ventilation | p-value |
|-------------------------|-----------------|-------|---------|------------------------|---------|
|                         |                 | NO (N=52) | YES (N=112) | NO (N=54) | YES (N=110) | NO (N=54) | YES (N=110) |
| Conjunctivitis, n (%)   | 4/164 (2.4%)    | 1 (1.9%) | 3 (2.7%) | 0.7 | 1 (1.9%) | 3 (2.7%) | 0.7 |
| Rhinorrhea, n (%)       | 18/164 (11%)    | 6 (11.5%) | 12 (10.7%) | 0.8 | 8 (14.8%) | 10 (9.1%) | 0.2 |
| Headache, n (%)         | 66/164 (40.2%)  | 26 (50%) | 40 (35.7%) | 0.08 | 28 (51.8%) | 38 (34.5%) | 0.03 |
| Cough, n (%)            | 124/164 (75.6%) | 40 (76.9%) | 84 (75%) | 0.7 | 45 (83.3%) | 79 (71.8%) | 0.1 |
| Odynophagia, n (%)      | 33/164 (20.1%)  | 12 (23%) | 21 (18.7%) | 0.5 | 13 (24%) | 20 (18.2%) | 0.3 |
| Expectoration, n (%)    | 32/164 (19.5%)  | 10 (19.2%) | 22 (19.6%) | 0.9 | 11 (20.4%) | 21 (19.1%) | 0.8 |
| Fatigue, n (%)          | 33/164 (20.1%)  | 15 (28.8%) | 18 (16%) | 0.058 | 12 (22.2%) | 21 (19.1%) | 0.6 |
| Dyspnea, n (%)          | 136/164 (82.9%) | 38 (73%) | 98 (87.5%) | 0.02 | 42 (77.8%) | 94 (85.5%) | 0.2 |
| Nausea or vomiting, n (%)| 17/164 (10.3%) | 7 (13.4%) | 10 (8.9%) | 0.3 | 7 (13%) | 10 (9.1%) | 0.4 |
| Diarrhea, n (%)         | 21/164 (12.8%)  | 6 (11.5%) | 15 (13.4%) | 0.7 | 8 (14.8%) | 13 (11.8%) | 0.5 |
| Hyporexia, n (%)        | 3/164 (1.8%)    | 2 (3.8%) | 1 (0.8%) | 0.1 | 2 (3.7%) | 1 (0.9%) | 0.2 |
| Myalgias, n (%)         | 72/164 (44%)    | 26 (50%) | 46 (41%) | 0.2 | 27 (50%) | 45 (41%) | 0.2 |
| Arthralgias, n (%)      | 61/164 (37.2%)  | 23 (52%) | 38 (34%) | 0.2 | 23 (42.6%) | 38 (34.5%) | 0.3 |
| Chills, n (%)           | 10/164 (5.7%)   | 3 (5.7%) | 7 (6.2%) | 0.9 | 4 (5.4%) | 6 (5.4%) | 0.6 |
|                  | n (%)  | n (%)  | P-value | n (%)  | n (%)  | P-value |
|------------------|--------|--------|---------|--------|--------|---------|
| Thoracic pain, n (%) | 12/164 (7.3%) | 3 (5.7%) | 0.6 | 4 (7.4%) | 8 (7.2%) | 0.9 |
| Diaphoresis, n (%) | 5/164 (3%) | 2 (3.8%) | 0.6 | 3 (5.5%) | 2 (1.8%) | 0.1 |
| Anosmia, n (%)    | 4/164 (2.4%) | 4 (7.6%) | 0.003 | 4 (7.4%) | 0 | 0.004 |
| Seizures, n (%)   | 2/164 (1.2%) | 0 | 0.3 | 0 | 2 (1.8%) | 0.3 |
| Disorientation, n (%) | 3/164 (1.8%) | 0 | 0.2 | 0 | 3 (2.7%) | 0.2 |
| Pharyngeal hyperemia, n (%) | 25/164 (15.2%) | 8 (13.4%) | 17 (15.2%) | 0.9 | 9 (16.7%) | 16 (14.5%) | 0.7 |
| Tonsillitis, n (%) | 8/164 (4.8%) | 2 (3.8%) | 6 (5.3%) | 0.6 | 3 (5.5%) | 5 (4.5%) | 0.7 |
| Rash, n (%)       | 1/164 (0.6%) | 1 (1.9%) | 0 | 0.1 | 1 (1.8%) | 0 | 0.1 |
| Cyanosis, n (%)   | 14/164 (8.5%) | 1 (1.9%) | 13 (11.6%) | 0.03 | 1 | 13 (11.8%) | 0.03 |

**Fever**

|                  | n (%)  | n (%)  | P-value | n (%)  | n (%)  | P-value |
|------------------|--------|--------|---------|--------|--------|---------|
| At home, n (%)   | 131/164 (69%) | 39 (75%) | 92 (82%) | 0.2 | 42 (77.7%) | 89 (80.9%) | 0.6 |
| On admission, n (%) | 29/164 (17.6%) | 6 (11.5%) | 23 (20.5%) | 0.1 | 7 (12.9%) | 22 (20%) | 0.2 |
| Median highest temperature (IQR) - °C | 37 (36.5-37.8) | 37 (36.5-37.6) | 37 (36.5-37.9) | 0.5 | 37 (36.5-37.7) | 37 (36.5-38) | 0.7 |
| During hospitalization, n (%) | 102/164 (62.2%) | 17 (32.7%) | 85 (76%) | <0.001 | 17 (31.5%) | 85 (77.3%) | <0.001 |
| Day of presentation, median (IQR) - days- | 2 (1-3) | 2 (1-3) | 2 (1-3) | 0.7 | 2 (1-3) | 2 (1-3) | 0.4 |
| Median highest | 38.6 | 37 | 39 | <0.001 | 37 | 39 | <0.001 |
| temperature (IQR) - °C | (37.5-39.9) | (36.8-38.5) | (38.2-40) | (36.8-38.5) | (38.2-40) |
|------------------------|-------------|-------------|-----------|-------------|-----------|
| 1.-Axillary temperature ≥38.3°C |             |             |           |             |           |
Table 3.- Radiographic and laboratorial findings

| Abnormalities in Chest X-ray | Overall (N=160) | Death | p-value  | Mechanical ventilation | p-value  |
|------------------------------|----------------|-------|----------|-------------------------|----------|
|                              | NO (N=51)      | YES (N=109) |         | NO (N=53)               | YES (N=107) |         |
| Ground-glass opacity, n (%)  | 115 (71.8%) (68.6%) | 35 (68.6%) | 80 (73.4%) (67.9%) | 36 (73.8%) | 79 | 0.4 |
| Local infiltrates, n (%)     | 12 (7.5%) (6.4%) | 5 (9.4%) | 7 (6.4%) (6.5%) | 5 (9.4%) | 7 (6.5%) | 0.5 |
| Bilateral infiltrates, n (%) | 94 (58.7%) (57.8%) | 31 (60.8%) | 63 (57.8%) (64.2%) | 34 (56.1%) | 60 | 0.3 |
| Interstitial abnormalities, n (%) | 107 (66.8%) (66%) | 35 (68.6%) | 72 (66%) (68.5%) | 37 (65.4%) | 70 | 0.5 |
| Unilateral pleural effusion, n (%) | 13 (8.1%) (7.8%) | 4 (7.8%) | 9 (8.2%) (11.3%) | 6 (7.5%) | 7 (6.5%) | 0.2 |
| Bilateral pleural effusion, n (%) | 4 (2.5%) | 0 | 4 (3.6%) | 1 (1.8%) | 3 (2.8%) | 0.7 |
| Pneumothorax, n (%)          | 1 (0.6%) (1.9%) | 1 (1.9%) | 0 | 1 (1.8%) | 0 | 0.1 |

| Abnormalities in Chest CT | Overall (N=24) | Death | p-value  | Mechanical ventilation | p-value  |
|---------------------------|----------------|-------|----------|-------------------------|----------|
|                           | NO (N=9)      | YES (N=15) |         | NO (N=9)               | YES (N=15) |         |
| Ground-glass opacity, n (%) | 21 (87.5%) (77.8%) | 7 (77.8%) | 14 (93%) (100%) | 6 (66.7%) | 15 | 0.01 |
| Local infiltrates, n (%)   | 1 (4.2%) | 0 | 1 (6.7%) | 0 | 1 (6.7%) | 0.4 |
| Bilateral infiltrates, n (%) | 22 (91.7%) (100%) | 9 (100%) | 13 (86.7%) (100%) | 9 (100%) | 13 | 0.2 |
| Interstitial abnormalities, n (%) | 5 (20.8%) | 2 (22%) | 3 (20%) (22%) | 2 (22%) | 3 (20%) | 0.8 |
| Unilateral pleural effusion, n (%) | 2 (8.3%) | 1 (11%) | 1 (6%) (22%) | 2 (22%) | 0 | 0.057 |
| Bilateral pleural effusion, n (%) | 1 (4.2%) | 0 | 1 (6%) | 0 | 1 (6.7%) | 0.4 |
| Characteristic                          | Overall       | Death          | p-value | Mechanical ventilation | p-value |
|----------------------------------------|---------------|----------------|---------|------------------------|---------|
|                                        | NO            | YES            |         | NO                     |         |
|                                        | 213 (107.1)   | 274 (104.5)    | <0.001  | 280 (97.5)             | <0.001  |
| PaO2/FiO2 ratio, mean (+/-SD)          |               |                |         |                        |         |
| White cell count, median (IQR) – per mm³| 11,050 (7,900- | 8,700 (6,550- | <0.001  | 8,850 (6,925-          | <0.001  |
|                                        | 15,100)       | 11,575)        |         | 11,400)                |         |
| Neutrophil count, median (IQR)- per mm³-| 9,250 (6,475- | 6,900 (4,800- | <0.001  | 6,900 (5,000-          | <0.001  |
|                                        | 13,025)       | 10,100)        |         | 9,950)                 |         |
| Lymphocyte count, median (IQR) -per mm³-| 800 (600 -   | 1,000 (700-   | 0.005   | 900 (700-              | 0.03    |
|                                        | 1,200)        | 1,450)         |         | 1,400)                 |         |
| Neutrophil-lymphocyte ratio, median (IQR) | 11 (6.5-19) | 7.6 (3.8-12.2) | <0.001  | 7.8 (3.8-13.2)         | <0.001  |
| Monocyte count, median (IQR) -per mm³-| 500 (300-700) | 600 (300-700) | 0.3     | 600 (300-700)          | 0.2     |
| Platelet count, median (IQR) -per mm³-| 244,500 (187,000- | 280,500 (178,250- | 0.1     | 259,500 (172,750-      | 0.4     |
|                                        | 328,500)      | 405,750)       |         | 405,250)               |         |
| Hemoglobin, median (IQR) -g/dl-        | 14.4 (13-15.4) | 14.2 (13.3-15.4) | 0.8   | 14.2 (13.2-15.4)       | 0.7     |
| Lactate dehydrogenase, median (IQR) -U/L| 406 (322-570) | 322 (235-392) | <0.001  | 340 (236-402)          | <0.001  |
| Aspartate aminotransferase, median (IQR) -U/L- | 49 (34.7-68.2) | 44.5 (28.5-62) | 0.09   | 45.5 (29.2-65.7)       | 0.2     |
| Parameter                          | Median (IQR)         | Median (IQR)         | Median (IQR)         | Median (IQR)         | Median (IQR)         |
|-----------------------------------|----------------------|----------------------|----------------------|----------------------|----------------------|
| Alanine aminotransferase, median  | 33.5 (24-52)         | 33 (24-62)           | 34.5 (23-51)         | 0.7                  | 33 (24.2-62.5)       |
| (IQR) -U/L-                       |                      |                      |                      |                      | (23.7-52)            |
| Total bilirubin, median           | 0.7 (0.5-0.9)        | 0.7 (0.5-0.9)        | 0.7 (0.5-0.9)        | 0.9                  | 0.7 (0.5-0.9)        |
| (IQR) -mg/dl-                     |                      |                      |                      |                      | (0.5-0.9)            |
| Creatine kinase, median           | 119.5 (52-270)       | 71 (31-169)          | 130 (70-275)         | 0.006                | 62.5 (31.5-166)      |
| (IQR) -U/L-                       |                      |                      |                      |                      | (73.5-277.7)         |
| Creatinine, median (IQR) -mg/dl-  | 0.8 (0.7-1.4)        | 0.7 (0.5-0.8)        | 0.9 (0.7-1.6)        | <0.001               | 0.8 (0.5-0.9)        |
| D-dimer, median (IQR) -ng/ml-     | 1740 (728-3380)      | 845 (387-2190)       | 2235 (821-3527)      | <0.001               | 970 (488-2230)       |
| C-reactive protein, median (IQR)  | 21.4 (12-32)         | 12 (5.8-23)          | 26.2 (16-34.7)       | <0.001               | 13.3 (7.6-26.6)      |
| -mg/ml-                           |                      |                      |                      |                      | (14.8-34)            |
| Procalcitonin, median (IQR) -ng/ml-| 0.5 (0-2)           | 0 (0-0.5)            | 0.5 (0-2)            | <0.001               | 0 (0-0.5)            |
| Glucose, median (IQR) -mg/dl-     | 123 (93-198)         | 101 (87-131)         | 138 (101-215)        | <0.001               | 102 (90-136.5)       |
| Sodium, median (IQR) -mEq/L       | 137 (133-141)        | 137 (133-140)        | 137 (132-142)        | 0.2                  | 137 (133-140)        |
| Chloride, median (IQR) -mEq/L     | 102 (99-107)         | 102 (99-106)         | 102 (98-109)         | 0.5                  | 102 (99-107)         |
| Potassium, median (IQR) -mEq/L    | 4.1 (3.7-4.5)        | 3.8 (3.6-4.1)        | 4.2 (3.8-4.8)        | <0.001               | 3.9 (3.6-4.1)        |
| Calcium, median (IQR) -mg/dl-     | 7.7 (7.4-8.1)        | 7.9 (7.5-8.3)        | 7.7 (7.3-8)          | 0.03                 | 7.9 (7.4-8.1)        |
| Phosphor, median (IQR) -mg/dl-    | 3.4 (2.8-4.2)        | 3.3 (2.8-3.8)        | 3.5 (2.8-4.5)        | 0.1                  | 3.4 (3-3.9)          |
| Magnesium, median (IQR) -mg/dl-   | 2.1 (1.9-2.4)        | 2 (1.8-2.2)          | 2.2 (1.9-2.6)        | <0.001               | 2 (1.8-2.2)          |
|                                 |                      |                      |                      |                      | 2.2 (1.9-2.6)        | <0.001               |
|                          |       |       |       |       |       |       |
|--------------------------|-------|-------|-------|-------|-------|-------|
| **Erythrocyte sedimentation rate, median (IQR) -mm/hr** | 18 (10-30) | 17 (13-26.5) | 18 (10-30) | 0.8 | 17.5 (13-29.2) | 18 (9.7-30) |
| **Brain natriuretic peptide, median (IQR) – pg/ml** | 49 (11.6-136) | 14.2 (2-67.5) | 68.6 (23.9-163) | **0.008** | 24.1 (9.8-82.7) | 64.4 (21.6-145) |

*Reference ranges:* PaO2/FiO2 ratio, >300; white cell count, 4,600 to 10,200/mm3; neutrophil count, 2,000 to 6,900/mm3; lymphocyte count, 600 to 3,400/mm3; neutrophil-lymphocyte ratio, 1-3; monocyte count, 0 to 900/mm3; platelet count, 142,000 to 424,000/mm3; hemoglobin, 12.2 to 18.1 g/dL; lactate dehydrogenase, 100 to 170 U/L; aspartate aminotransferase, 0 to 38 U/L; alanine aminotransferase, 0 to 41 U/L; total bilirubin, 0.1 to 1 mg/dL; creatine kinase, 26 to 140 U/L; creatinine, 0.8 to 1.4 mg/dL; D-dimer, 0 to 400 ng/mL; c-reactive protein, 0 to 0.7 mg/dL; procalcitonin, 0 to 0.5 ng/mL; glucose, 70 to 110 mg/dL; sodium, 136 to 145 mEq/L; chloride, 95 to 110 mEq/L; potassium, 3.5 to 5.3 mEq/L; calcium, 8.5 to 10.3 mg/dl; phosphor, 2.5 to 4.5 mg/dL; magnesium, 1.7 to 2.8 mg/dL; erythrocyte sedimentation rate, 0 to 10 mm/hr; brain natriuretic peptide, 0 to 100 pg/ml.
| Characteristic                  | Overall (N=164) | Death | p-value | Mechanical ventilation | p-value |
|--------------------------------|-----------------|-------|---------|------------------------|---------|
|                                | NO (N=52)       | YES (N=112) |         | NO (N=54) | YES (N=110) |   |
| Oral antibiotics<sup>1</sup>, n (%) | 125/164 (76.2%) | 42/52 (80.8%) | 3 | 43/54 (79.6%) | 82/110 (74.5%) | 0.4 |
| Intravenous antibiotics, n (%)  | 116/164 (70.7%) | 27/52 (52%) | <0.001 | 24/54 (44.4%) | 92/110 (83.6%) | <0.001 |
| Oseltamivir, n (%)              | 5/164 (3%)      | 3/52 (5.8%) | 0.1    | 3/54 (5.6%) | 2/110 (1.8%) | 0.1 |
| Hydroxychloroquine<sup>2</sup>, n (%) | 98/164 (59.8%) | 31/52 (59.6%) | 0.9    | 30/54 (55.6%) | 68/110 (61.8%) | 0.4 |
| Ivermectin<sup>3</sup>, n (%)  | 8/164 (4.8%)   | 1/52 (1.9%) | 0.2    | 1/54 (1.85%) | 7/110 (6.3%) | 0.2 |
| Tocilizumab, n (%)              | 3/164 (1.8%)   | 1/52 (1.9%) | 0.9    | 1/54 (1.85%) | 2/110 (1.8%) | 0.9 |
| Systemic steroid, n (%)         | 41/164 (25%)   | 7/52 (13.5%) | 0.02   | 9/54 (16.7%) | 32/110 (29.1%) | 0.08 |
| Hydrocortisone, n (%)           | 13/164 (7.9%)  | 2/52 (3.8%) | 0.1    | 3/54 (5.6%) | 10/110 (9.1%) | 0.9 |
| Methylprednisolone, n (%)       | 13/164 (7.9%)  | 1/52 (1.9%) | 0.05   | 1/54 (1.9%) | 12/110 (10.9%) | 0.1 |
| Prednisone, n (%)               | 2/164 (1.2%)   | 2/52 (3.8%) | 0.03   | 2/54 (3.7%) | 0 | 0.006 |
| Dexamethasone, n (%)            | 13/164 (7.9%)  | 2/52 (3.8%) | 0.1    | 3/54 (5.6%) | 10/110 (9.1%) | 0.9 |
| Oxygen therapy<sup>4</sup>, n (%) | 162/164 (98.7%) | 51/52 (98%) | 0.5    | 52/54 (96.3%) | 110/110 (100%) | 0.04 |
| Acute respiratory distress syndrome<sup>5</sup>, n (%) | 57/164 (34.8%) | 3/52 (5.8%) | <0.001 | 0 | 57/110 | <0.001 |
| Acute kidney injury<sup>6</sup>, n (%) | 59/164 | 6/52 (48.2%) | <0.001 | 6/54 | 53/110 | <0.001 |
|                               | (36%) | (11.5%) | (47.3%) | (11%) | (48.2%) |
|-------------------------------|-------|---------|---------|-------|---------|
| **Rhabdomyolysis**<sup>7</sup>, n (%) | 2/164 (1.2%) | 0 | 2/112 (1.8%) | 0.3 | 0 | 2/110 (1.8%) | 0.3 |
| **Use of renal replacement therapy, n (%)** | 1/164 (0.6%) | 1/52 (1.9%) | 0 | 0.1 | 0 | 1/110 (0.9%) | 0.4 |
| **Vasopressor support, n (%)** | 53/164 (32.3%) | 2/52 (3.8%) | 51/112 (45.5%) | <0.001 | 1/54 (1.8%) | 52/110 | <0.001 |
| **Days of hospital stay, median (IQR) -days-** | 7 (4-11) | 10 (7-16) | 5 (3.2-9) | <0.001 | 9 (6-14.2) | 6 (4-9) | <0.001 |

1.- Azithromycin 500 mg PO qDay for five days.

2.- Hydroxychloroquine 400 mg PO twice daily for two doses, then 200 mg twice daily for five days

3.- Ivermectin 0.2 mg/kg/day PO for 4 days.

4.- Use of supplemental oxygen by nasal cannulas, simple face mask, or non-rebreather mask during hospitalization.

5.- In non-intubated patients, sudden respiratory failure with a PAO2 / FiO2 ratio <200 or new bilateral opacities in hospitalization; on intubated patients, a PAO2 / FiO2 ratio <200 or new bilateral opacities in hospitalization.

6.- Decreased urine output under 0.5 ml/kg/hr for more than 6 hours, either an elevation in serum creatinine equal to or greater than 0.3 mg/dl or an increase equal to or greater than 50% within 48 hours in hospitalization.

7.- Dark urine color with myoglobinuria plus creatine kinase > 1000 U / L or an increase of 5 times its normal value in hospitalization.
Table 5.- Risk factors associated with mortality

| Risk Factor                              | Unadjusted RR | Adjusted RR |
|------------------------------------------|---------------|-------------|
|                                          | RR | 95% CI | p-value | RR | 95% CI | p-value |
| Age >50 years                            | 2.3 | 1.49-3.83 | <0.001 |     |        |         |
| Male gender                              | 1.45 | 0.93-2.27 | 0.1     |     |        |         |
| Smoking history                          | 0.66 | 0.42-1.04 | 0.09    |     |        |         |
| Smoking index ≥10                        | 1.74 | 0.66-4.6  | 0.19    |     |        |         |
| Schooling ≤6 years                       | 1.6 | 0.98-2.63 | 0.049   |     |        |         |
| Obesity (BMI >30 k/m²)                   | 1.15 | 0.73-1.81 | 0.5     |     |        |         |
| BMI Classification                       |     |         |         |     |        |         |
| Overweight                               | 0.8 | 0.55-1.43 | 0.63    | 0.8 | 0.36-1.78 | 0.58 |
| Obese class I                           | 1.04 | 0.61-1.77 | 0.8     | 1.08 | 0.44-2.62 | 0.8 |
| Obese class II                          | 1.07 | 0.53-2.16 | 0.8     | 1.19 | 0.39-3.57 | 0.7 |
| Obese class III                         | 1.23 | 0.56-2.69 | 0.58    | 1.45 | 0.46-4.53 | 0.52 |
| Smoking history adjusted by age          |     |         |         | 0.42 | 0.18-0.94 | 0.035 |
| Smoking index ≥10 adjusted by age        |     |         |         | 2.08 | 0.45-9.49 | 0.3  |
| Condition                                      | OR  | 95% CI        | p-value | Adjusted by                                                                 |
|------------------------------------------------|-----|---------------|---------|----------------------------------------------------------------------------|
| Diabetes                                       | 2.26| 1.26-4.07     | 0.003   | age, gender and BMI                                                         |
| Hypertension                                   | 1.5 | 0.91-2.59     | 0.08    | age, gender and BMI                                                         |
| Severe pneumonia (ATS 2019)                    | 6   | 2.5-14.23     | <0.001  | age, gender, BMI, diabetes, hypertension, smoking history.                 |
| NEWS2 score ≥7                                 | 1.58| 1.01-2.47     | 0.047   | age, gender, BMI, diabetes, hypertension, smoking history.                 |
| PORT/PSI ≥91                                   | 6.08| 2.56-14.41    | <0.001  | age, gender, BMI, diabetes, hypertension, smoking history.                 |
| SMART-COP ≥5                                   | 6.07| 2.56-14.39    | <0.001  | age, gender, BMI, diabetes, hypertension, smoking history.                 |
| SCAP ≥10                                       | 3.92| 2.45-6.29     | <0.001  | age, gender, BMI, diabetes, hypertension, smoking history.                 |
| SOFA ≥3                                        | 3.64| 1.84-7.2      | <0.001  | age, gender, BMI, diabetes, hypertension, smoking history.                 |
| APACHE II ≥10                                  | 2.79| 1.59-4.89     | <0.001  | age, gender, BMI, diabetes, hypertension, smoking history.                 |
|                |   |   | <0.001 | Adjusted by age, gender, BMI, diabetes, hypertension, smoking history. |
|----------------|---|---|--------|---------------------------------------------------------------------|
| CHARLSON ≥2    | 2.4 | 1.43-4 | <0.001 |                                                                     |
| Dyspnea        | 1.72 | 1.11-2.75 | 0.026 |                                                                     |
| Cyanosis       | 5.07 | 0.75-33.96 | 0.028 |                                                                     |
| Fever on hospitalization | 3.33 | 2.06-5.39 | <0.001 |                                                                     |
| Use of intravenous antibiotics | 2.2 | 1.45-3.43 | <0.001 |                                                                     |

Figures
Figure 1

Flowchart of the study design. SARS-CoV-2, severe acute respiratory syndrome coronavirus 2. PCR, polymerase chain reaction. IMV, invasive mechanical ventilation.