

Experience in the management of severe COVID-19 patients in an intensive care unit

Experiencia en el manejo de pacientes graves con COVID-19 en una unidad de terapia intensiva

J. Ojino Sosa-García^{1,5*}, Alan O. Gutiérrez-Villaseñor^{1,5}, Alondra García-Briones^{2,5},
Juan P. Romero-González^{2,5}, Eva Juárez-Hernández^{3,5}, and Octavio González-Chon^{2,4,5}

¹Internal Medicine and Critical Medicine Department, Intensive Care Unit, Hospital Médica Sur; ²Anesthesiology and Critical Medicine Department, Intensive Care Unit, Hospital Médica Sur; ³Clinical Research Department, Translational Research Unit, Hospital Médica Sur; ⁴Management Department, Hospital Médica Sur; ⁵Faculty of Medicine, Universidad Nacional Autónoma de México. Mexico City, Mexico

Abstract

Objective: The objective of this study was to describe the clinical characteristics and management of severe COVID-19 patients. **Methods:** This was observational, descriptive, longitudinal, and retrospective study. **Results:** Fifty-six patients were admitted, of whom 80.3% (n = 45) were male with a mean age of 58 years (46-67). The main comorbidities were obesity, high blood pressure, and diabetes. Symptoms onset time at admittance to the ICU were 9 (7-14) days, of which the most frequent were dyspnea, fever, and dry cough. Laboratory data were lymphopenia; elevation of LDH, fibrinogen, D-dimer, ferritin, and CRP. About 100% of the patients required mechanical ventilation, the median mechanical ventilation time was 12 (6-17) days, and 66% (n = 37) required a prone position. The pharmacological treatment was mainly based on azithromycin, hydroxychloroquine, tocilizumab, and steroids. The most frequent complications were acute kidney injury, venous thromboembolism, and acute myocardial infarction. Mortality rate was 17.8% (n = 10). **Conclusion:** The characteristics of the critically ill patients in our hospital were mostly elderly and obese, with the variables of higher SOFA score and acute kidney injury associated with higher mortality.

Keywords: Coronavirus. COVID-19. Management. Mortality. SARS-CoV-2.

Resumen

Objetivo: Describir las características clínicas y el manejo de pacientes graves con COVID-19. **Método:** Estudio observacional, descriptivo, longitudinal y retrospectivo. **Resultados:** Ingresaron 56 pacientes, el 80.3% (n = 45) de sexo masculino, con un promedio de edad de 58 (46-67) años. Las principales condiciones de comorbilidad fueron obesidad, hipertensión y diabetes. El tiempo de inicio de los síntomas al ingreso fue de 9 (7-14) días, siendo los más frecuentes disnea, fiebre y tos seca. Los datos de laboratorio fueron linfopenia y elevación de deshidrogenasa láctica, fibrinógeno, dímero D, ferritina y proteína C reactiva. El 100% de los pacientes requirieron ventilación mecánica, con una mediana de tiempo de ventilación de 12 (6-17)

Correspondence:

*J. Ojino Sosa-García

Puente de Piedra, 150

Col. Toriello Guerra, Del. Tlalpan

C.P. 14050, Ciudad de México, México

E-mail: drintervista@gmail.com;

jsosag@medicasur.org.mx

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días, y el 66% ($n = 37$) requirieron posición en prono. El tratamiento farmacológico fue a base de azitromicina, hidroxiclороquina, tocilizumab y esteroides, principalmente. Las complicaciones más frecuentes fueron lesión renal aguda, enfermedad tromboembólica venosa e infarto agudo al miocardio. La tasa de mortalidad fue del 17.8% ($n = 10$). **Conclusión:** Los pacientes graves en nuestro hospital fueron en su mayoría personas de la tercera edad y con obesidad, siendo las variables de mayor puntaje SOFA y lesión renal aguda las asociadas con mayor mortalidad.

Palabras clave: Coronavirus. COVID-19. Manejo. Mortalidad. SARS-CoV-2.

Introduction

In late December 2019, coronavirus disease 2019 (COVID-19) emerged in Wuhan, Hubei Province, China, when 44 cases of pneumonia of unknown etiology were reported to the World Health Organization, out of which 11 were critically ill patients. Subsequently, the causative virus, called SARS-CoV-2 in connection with severe acute respiratory syndrome, was identified¹.

According to the interactive map to monitor the disease in the world, developed by the Center for Systems Science and Engineering at Johns Hopkins University in Baltimore², by June 5, 2020, 6,724,516 confirmed cases have been reported, with 394,018 deaths from the disease and 2,996,832 recovered patients. The countries that have been most affected by the disease so far are the United States of America with 1,894,753 cases, Brazil with 614,941 cases, Russia with 449,256 cases, and the United Kingdom with 284,734 cases³. In Mexico, 110,026 cases have been reported, out of which 13,170 patients have died⁴.

According to observations published by Wang et al.⁵, the percentage of patients requiring admission to an intensive care unit (ICU) is 26.0%, with the main causes of admission being the presence of organ failure manifested by shock, acute respiratory distress syndrome, arrhythmias, or acute heart failure.

The purpose of this study is to describe the clinical characteristics and management of seriously ill patients admitted to the ICU with a diagnosis of COVID-19, in a tertiary care private hospital in Mexico City, Mexico.

Methods

This study was observational, descriptive, longitudinal, and retrospective study, carried out at *Médica Sur* Hospital ICU from March to June 2020 after approval by the Research Ethics Committee of the Hospital (2020-EXT-461) and informed consent document signature by the patient or his/her legal representative.

Inclusion criteria were: adult patients of either gender, older than 18 years of age, with respiratory function progressive deterioration manifested by dyspnea and hypoxemia, with increased oxygen supply requirements, and suspected or confirmed COVID-19 diagnosis according to clinical and radiological data consistent with COVID-19 and with a reverse-transcription polymerase chain reaction (RT-PCR) SARS-CoV-2-negative test or RT-PCR of a SARS-CoV-2-positive nasopharyngeal sample, respectively. Pregnant patients were excluded from the study.

Evaluated variables included age, gender, body mass index, clinical-demographic characteristics, laboratory tests, chest computed tomography (CT) radiographic findings, prognostic scales (Acute Physiology and Chronic Health Evaluation II [APACHE II], Sequential Organ Failure Assessment [SOFA] and Mexican SOFA [MEXSOFA]) at admission, ventilatory management, pharmacological treatment, complications, and mortality. Data were retrospectively obtained from the medical record at admission, as well as paraclinical tests and targeted treatment data at admission and during patient hospitalization until ICU discharge due to improvement or death or cutoff date on June 5, 2020.

Statistical analysis

Data distribution was determined by the Kolmogorov–Smirnov test. Categorical data are presented as percentages and confidence intervals, and continuous data, with measures of central tendency and dispersion. Statistical analysis was carried out with the SPSS v.20 statistical package.

Results

One hundred and sixty-five patients were admitted to *Médica Sur* Hospital, out of whom 34% ($n = 56$) were admitted to the ICU with a SARS-CoV-2 positive diagnosis confirmed by RT-PCR in 96% of cases ($n = 54$).

Table 1. Clinical characteristics of severely ill patients with COVID-19

Baseline characteristics	Patients (%)	95% confidence interval	Reference range
Gender (males)	45 (80.3%)	0.9-0.3	-
Age, years	58 [46-67]	-	-
Comorbidity			
Obesity	28 (50%)	0.37-0.64	-
Hypertension	20 (35.7%)	0.21-0.47	-
Diabetes	14 (25%)	0.12-0.35	-
Clinical manifestations			
Days of onset	9 [7-14]	-	-
Dyspnea	41 (73.2%)	0.62-0.86	-
Fever	39 (69.6%)	0.56-0.81	-
Dry cough	35 (62.5%)	0.50-0.76	-
Myalgia	25 (44.6%)	0.31-0.59	-
Arthralgia	25 (44.6%)	0.31-0.59	-
Chest pain	10 (17.8%)	0.07-0.28	-
Diarrhea	9 (16%)	0.06-0.26	-
Laboratory findings			
Lymphocytes	900 [500-1100]	-	1.2-4 × 10 ³ /μl
Lactate dehydrogenase	343 [285-486]	-	98-192 U/l
D-dimer	1020 [600-3125]	-	0-499 ng/ml
Fibrinogen	699 [493-776]	-	177-410 mg/dl
Ferritin	509 [132.7 – 1058.2]	-	11-306.8 ng/ml
C-reactive protein	211 [125.7 – 306.8]	-	0-7.4 mg/l
Radiological findings			
Ground glass opacity	47 (83.9%)	0.75-0.95	-
Consolidation	39 (69.6%)	0.58-0.83	-
Prognostic scales			
APACHE II	14 [12-19]	-	-
SOFA	7 [6-9]	-	-
MEXSOFA	7 [5-8]	-	-

APACHE II: Acute Physiology and Chronic Health Evaluation II; SOFA: sequential organ failure assessment; MEXSOFA: Mexican sequential organ failure assessment.

Of the 56 patients admitted to the ICU, 80.3% (n = 45) were male, mean age was 58 (46-67) years, and body mass index was 30.1 (27.3-32.4) kg/m². Main comorbid conditions were obesity (50%, n = 28), hypertension (35.7%, n = 20), and diabetes (25%, n = 14) (Table 1).

Median time between the onset of clinical manifestations and ICU admission was 9 (7-14) days, with most common signs and symptoms being dyspnea (73.2%, n = 41), fever (69.6%, n = 39), dry cough (62.5%, n = 35), myalgia and arthralgia (44.6%, n = 25), chest pain (17.8, n = 10), and diarrhea (16%, n = 9) (Table 1).

Most common laboratory findings were lymphopenia (900 [500-1100] × 10³/μL) and elevated lactate dehydrogenase (343 [285-486] U/L), fibrinogen (699 [493-776] mg/dL), D-dimer (1020 [600-3125] ng/mL), ferritin (509 [132.7-1058.2] ng/mL), and C-reactive protein (211 [125.7-306.8] mg/L) (Table 1). The

radiological findings identified by chest CT were ground-glass opacities (83.9%, n = 47) and areas of consolidation (69.6%, n = 39) (Fig. 1).

At ICU admission, the prognosis was determined according to the different scales, with medians being: APACHE II 14 (12-19), SOFA 7 (6-9), and MEXSOFA 7 (5-8), with a mortality likelihood of 15%, 21.5%, and 20%, respectively (Table 1).

Comprehensive approach to patients consisted of advanced airway management and invasive mechanical ventilation with lung protection strategies in 100% of cases. Initial patient measurements were: compliance 37.4 (27-43) mL/cmH₂O, lung compliance pressure 14 (11-16) cmH₂O, plateau pressure 27 (24-29) cmH₂O, and partial pressure of arterial oxygen/fraction of inspired oxygen ratio 70 (50-100). The predominant mechanical ventilation modality was volume-controlled in 82.1% (n = 46), with an initial positive end-expiratory pressure (PEEP) of 12 (12-14) cmH₂O and a fraction of

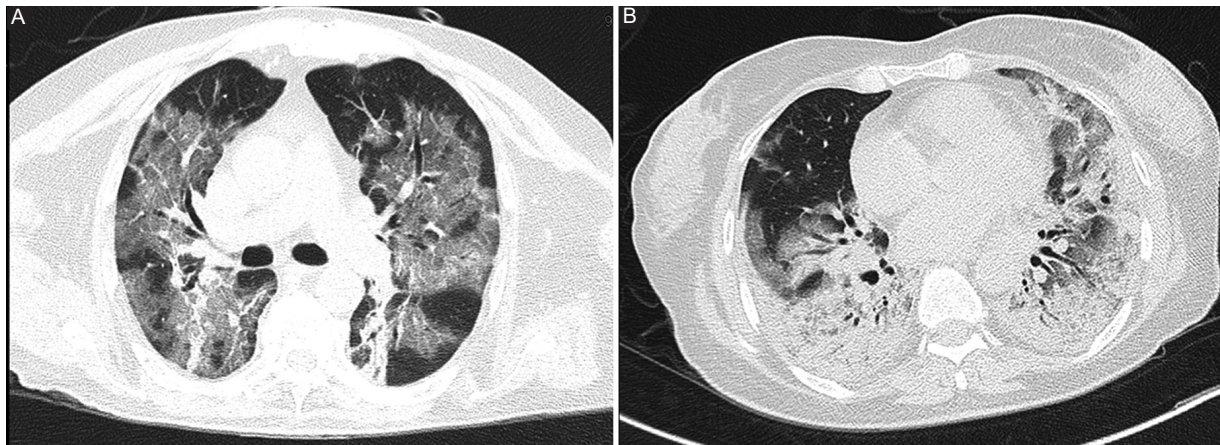


Figure 1. Findings on simple chest computed tomography. **A:** ground glass opacity. **B:** image with areas of bilateral consolidation.

Table 2. Mechanical ventilation parameters in severely ill patients with COVID-19

Parameters	Values	95% confidence interval
Invasive mechanical ventilation	56 (100%)	-
Ventilation modality		
Volume-controlled	450 [350-510] ml	-
PEEP	12 [12-14] cmH ₂ O	-
FiO ₂	70 [50-100]%	-
Prone position	37 (66%)	0.52-0.78
Initial measurements		
Compliance	37 [27-43] ml/cmH ₂ O	-
Lung compliance pressure	14 [11-16] cmH ₂ O	-
Plateau pressure	27 [24-29] cmH ₂ O	-
PaO ₂ /FiO ₂	70 [50-100]	-

FiO₂: fraction of inspired oxygen; PaO₂, partial pressure of arterial oxygen; PEEP: positive end-expiratory pressure.

inspired oxygen (FiO₂) of 73.3%. Mechanical ventilation median time was 12 (6-17) days, and 66% (n = 37) required ventilation in the prone position (Table 2).

Targeted drug treatment consisted of azithromycin (75%, n = 42), hydroxychloroquine (67.8%, n = 38), ritonavir (39.2%, n = 22), lopinavir (30.3%, n = 17), ivermectin (17.8%, n = 10), atazanavir (10.7%, n = 6), remdesivir (3.5%, n = 2), and oseltamivir (10.7%, n = 6). Within adjunctive management, tocilizumab was administered in 53.5% (n = 30) and steroids in 46.4% (n = 26).

Most common complications were acute kidney injury (46.4%, n = 26), venous thromboembolic disease (10.7%, n = 6), and acute myocardial infarction (3.5%, n = 2); there were other less common complications. Of the patients with acute kidney injury, 17.8% (n = 10) required renal replacement management (Table 3).

Of the 56 patients who were admitted to the ICU, four remain hospitalized with ventilatory support, and 42 were withdrawn from mechanical ventilation with

Table 3. Clinical outcomes in seriously ill patients with COVID-19

Outcomes	Patients (%)
Complications	
Acute kidney injury	26 (46.4%)
Venous thromboembolic disease	6 (10.7%)
Acute myocardial infarction	2 (3.5%)
Ischemic cerebrovascular event	1 (1.8%)
Cerebral venous thrombosis	1 (1.8%)
Mesenteric thrombosis	1 (1.8%)
Clinical outcomes	
Days of ICU stay	14 [8-18]
Days of mechanical ventilation	12 [5-14]
Mortality	10 (17.8%)

oxygen supply and were discharged to the specific hospitalization ward for patients with COVID-19 to continue with standard management. Out of them, 39 patients have been discharged from the hospital

Table 4. Comparison of variables according to mortality in surviving and non-surviving patients

Variable	Survivors (n = 46)	Non-survivors (n = 10)	p
Demographic data			
Age	56 [46-66]	67 [46-74]	0.588
Gender (males)	77.8% (35)	90% (9)	0.667
Body mass index	30.1 [26.8-32.8]	30 [26.9-32.7]	0.874
Comorbidity			
Obesity	51.1% (23)	50% (5)	1.000
Hypertension	31.1% (14)	50% (5)	0.288
Diabetes	24.4% (11)	20% (2)	1.000
Clinical manifestations			
Symptom onset	9 [7-13]	9 [6-26]	0.775
Dyspnea	71% (32)	90% (9)	0.0423
Fever	71% (32)	60% (6)	0.479
Dry cough	66.7% (30)	50% (5)	0.469
Inflammation markers			
Lymphopenia	800 [500-1075]	1000 [700-1650]	0.295
Lactic dehydrogenase	343 [227-439]	598.5 [336.5-962.5]	0.650
Fibrinogen	699 [459-811]	493 [493-699]	0.250
D-dimer	935 [582-1490]	3200 [1970-35200]	0.083
Ferritin	524.3 [149.5-1026.4]	452.7 [0-1116]	1.000
Prognostic scales			
APACHE II	14 [11.5-19]	14.5 [11.7-22.5]	0.874
SOFA	7 [6-8]	8 [7-10.2]	0.027
MEXSOFA	7 [5-8]	7 [4.7-8.0]	0.866
Mechanical ventilation			
Compliance	37 [27.2-47.4]	35.5 [26.5-40.7]	0.755
PaO ₂ /FiO ₂	65 [50-100]	100 [85-100]	0.052
Prone position	66.6% (30)	70% (7)	1.000
Ventilation days	12 [6-16]	14 [5-18]	0.665
Targeted treatment			
Azithromycin	73.3% (33)	80% (8)	1.000
Hydroxychloroquine	68.9% (31)	70% (7)	1.000
Ritonavir	40% (18)	40% (4)	1.000
Lopinavir	28.9% (13)	40% (4)	0.479
Tocilizumab	55.6% (25)	40% (4)	0.490
Steroids	57.8% (26)	80% (8)	0.287
Complications			
Acute kidney injury	40% (18)	80% (8)	0.035
Venous thromboembolic disease	6.7% (3)	30% (3)	0.066
Acute myocardial infarction	2.2% (1)	10% (1)	0.333

FiO₂: fraction of inspired oxygen; PaO₂: partial pressure of arterial oxygen.

due to improvement of their condition. Median ICU length of stay was 14 (8-18) days (Table 3).

ICU mortality rate was 17.8% (n = 10), with main causes of death being pulmonary thromboembolism, acute myocardial infarction, stroke, and disseminated intravascular coagulation (Table 3).

In the comparison of clinical variables according to mortality, non-surviving patients showed a higher SOFA score (7 [6-8] vs. 8 [7-10.2]; p = 0.027) and a higher percentage of acute kidney injury (40% [n = 18] vs. 80% [n = 8]; p = 0.035) (Table 4).

Discussion

The population of Latin America has epigenetic characteristics that are different from those of other continents and even from those of the United States of America and Canada; however, COVID-19 behavior is not different from that described in the literature. In Mexico, among the epidemiological characteristics of the disease, it predominates in the male gender, with an average age of 45 years, and mainly affects those older than 60 years, with main comorbid conditions

being hypertension, diabetes, obesity, smoking, chronic kidney failure, and chronic obstructive pulmonary disease, among others. On the other hand, the percentages of hospital and ICU occupancy are 44% and 38%, respectively, with an overall mortality rate of 11.9%⁶.

Among the epidemiological characteristics of the critically ill patients who were admitted to the ICU, there is a predominance of the male gender, with a 4:1 ratio, which is similar to that observed in the rest of the nation and in countries such as China, Italy, and the United States of America⁵⁻¹³. As for age, severely ill patients were older than 60 years^{6,9-13} and had comorbidities, such as obesity, hypertension, and diabetes, which have been reported in different case series worldwide⁵⁻¹³. It is important mentioning that, in this population, obesity predominates as a risk factor, which is correlated with the elevated prevalence of this condition in the country, which is 32% in people older than 20 years¹⁴. On the other hand, the first ICU-admitted cases were imported from Italy ($n = 3$), the United States ($n = 3$), Spain ($n = 1$), and Turkey ($n = 1$), and the rest were due to community transmission.

The period of clinical manifestations onset at ICU admission in the study population was 9 days, which is similar to that reported in other case series (7-10 days)^{8,11,13}. The most common signs and symptoms were dyspnea, fever, and dry cough, which are similar to those described in seriously ill patients who required admission to an ICU^{12,13}.

The most common laboratory findings were lymphopenia and lactate dehydrogenase and D-dimer elevation, which are similar to observations described in the general population^{5,7-9,11-13}, and ferritin^{9,11} and C-reactive protein elevation^{7,9}. Another characteristic finding in the study population was fibrinogen elevation, which is associated with a higher risk of thrombotic events in patients with COVID-19. Among the tomographic data, the main ones were ground-glass opacities and areas of consolidation, as reported in the general population and in severely ill patients^{5,7,8,11-13}.

Regarding the scores on the prognostic scales at critically ill patients ICU admission, they were 14 for APACHE II and 7 for SOFA, unlike the scores reported by Wang et al.⁵, which in their study were 17 and 5 points, respectively; this difference could be due to the degree of respiratory dysfunction in our population.

The criterion for critically ill patients ICU admission was respiratory function progressive deterioration manifested by dyspnea and hypoxemia, with the need

for advanced airway management and invasive mechanical ventilation, and for this reason, this procedure was resorted to in 100% of cases, unlike other studies, in which a variability of 47% to 88% of cases is reported, due to the use of other oxygen delivery strategies, such as high-flow nasal cannula or non-invasive mechanical ventilation^{5,10-12}. Mean compliance was 37 mL/cm H₂O and lung compliance pressure was 14 cm H₂O, which were higher and lower, respectively, than those reported by Bhatraju et al.¹³. Within initial mechanical ventilation parameters, PEEP was 12 cm H₂O and FiO₂ was 73.3%, which are similar values to those described by Grasselli et al.¹⁰. The ventilation strategy in prone position was provided in 66% of cases, which is higher than reported in other studies (27-50%)¹⁰⁻¹².

The recommendations for targeted pharmacological treatment in severely ill patients admitted to the ICU were based on the institutional clinical guidelines, which were developed by hospital clinical experts in accordance with scientific evidence and experience from studies reported in other countries. Initial treatment consisted of coadministration of azithromycin/hydroxychloroquine¹⁵, lopinavir/ritonavir¹⁶, and tocilizumab¹⁷. Steroids were administered to 46.4% of patients, similarly as reported in other series^{7,11}. Therapeutic options for management included remdesivir compassionate use¹⁸. It is important mentioning that targeted treatment was continuously adjusted according to the generation of scientific evidence on the effectiveness and safety of all different interventions; however, it cannot be assured that clinical outcomes are due to their application in our population.

Among the complications of the study population, 46.4% of the patients had acute kidney injury, as in other studies, as one of the main complications^{5,7,8,11,12}. On the other hand, our patients developed venous thromboembolic disease and acute myocardial infarction as the second and third complications, similar to that reported by Zhou et al.¹¹.

The mortality rate of seriously ill patients with COVID-19 in the ICU was 17.8%, which is lower than that published in other series of patients with the same characteristics (26-97%)⁹⁻¹³, with the presence of a higher SOFA score and acute kidney injury being the variables with statistical significance in non-surviving patients.

The main limitations of the study are its retrospective, single-center nature, and its small sample size, which is why the results of the correlation

measurements between the different interventions should be taken with caution until a larger number of patients is studied.

Conclusion

The main characteristics of the patients who required admission to the ICU in our hospital center are that they were mostly older adults, with obesity and high values of inflammation and thrombosis markers. The presence of a higher SOFA score and acute kidney injury as the variables that were most commonly associated with mortality stands out. Although it is true that there is currently no single intervention that has demonstrated effectiveness and safety in COVID-19, multisystemic support and multidisciplinary teamwork strategies have a positive impact on critically ill patients' clinical outcomes.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this research.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

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