

Coronavirus Pandemic

# High mortality at the beginning of the COVID-19 pandemic in a referral center in the metropolitan area of Mexico City

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#### Abstract

Introduction: There is limited information about the coronavirus disease 2019 (COVID-19) disease in Latin-American countries. Our objective was to describe the clinical characteristics and outcomes of COVID-19 patients in Mexico.

Methodology: We conducted a retrospective cohort study with 333 consecutive patients who were admitted to Hospital de Especialidades "Dr. Antonio Fraga Mouret" in Mexico City with COVID-19 between April 1, 2020, and June 30, 2020. Demographic, clinical, laboratory data, treatment details and 30-day outcomes were analyzed.

Results: The patients studied included 52% men (172/233) and the median age was 45 years. Up to 75% (250/333) of patients were classified as overweight or obese. There were 185 (56%) inpatients; 85% (158/185) were hospitalized in the general ward, and 15% (27/185) in the Intensive Care Unit (ICU). Laboratory measurements showed significant differences between inpatients and outpatients such as lymphocyte-count (median 0.8 vs  $1.2 \times 10^9$ /L, p < 0.001), LDH (median 650 vs 294 U/L, p < 0.001), CRP (median 147 vs 5 mg/L, p = 0.007), CK-MB (median, 15 vs 10 U/L, p = 0.008), ferritin (median, 860 vs 392 ng/mL, p = 0.02), and D-dimer (median, 780 vs 600 ng/mL, p = 0.15). These differences were seen between survivor and non-survivor patients as well. The rate of death in mechanically ventilated patients was 94% (67/71). Mortality at 30-day follow-up was 57% (105/185).

Conclusions: We observed that majority of the non-survivors were obese and young. Complications leading to death was observed in majority of the cases.

Key words: COVID-19; epidemiology; Mexico; mortality; pandemic; SARS-CoV-2.

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#### Introduction

The twenty-first century witnessed two global health emergencies involving respiratory pathogens that changed the world. The coronavirus disease 2019 (COVID-19) spread through Asia in late 2019 and spread to Latin America in the begining of 2020. So far there are more than 219 million confirmed cases and over 4.55 million deaths worldwide. The first confirmed case in México was reported on February 28, 2020. Since then there have been more than 275,000 deaths [1]. Mexico currently faces an unprecedented healthcare crisis that has challenged public health policies. During the first quarter of the year, data from cohorts around the globe identified several epidemiological characteristics in patients diagnosed with COVID-19 who required inpatient treatment, especially those who became critically ill [2]. Multiple risk factors such as diabetes, hypertension, cardiovascular disease were identified [3]. In addition, being overweight and obese were associated with a more severe presentation of the disease in Mexico [4]. The prevalence of these chronic diseases may play a decisive role since they are medical issues associated with a more complex sociocultural phenomenon. These sociocultural factors, along with the lack of medical supplies and a collapsed healthcare system coexist in a pandemic and cannot be assessed separately [5]. The clinical presentation of COVID-19 is heterogeneous, and can range from the well-recognized devastating pulmonary damage and multi-organ failure to minor gastrointestinal, neurological, and even dermatological features. These symptoms are still poorly understood. Therefore, the analysis of local epidemiological and clinical data is essential for understanding COVID-19 in our population. We aimed to describe the epidemiological data, clinical characteristics and outcomes of COVID-19 patients treated in a tertiary referral center in the metropolitan area of Mexico City.

# Methodology

This retrospective observational study was performed at the Hospital de Especialidades "Dr. Antonio Fraga Mouret", Instituto Mexicano del Seguro Social in México City. This is a Tertiary Referral Center and is a nine-floor hospital with 550 beds: 524 in the general ward and 26 Intensive care Unit (ICU) beds.

The hospital was converted into a hybrid hospital that received patients who required specialized attention, including COVID-19 suspected and confirmed cases. The beds in the wards were redistributed due to the pandemic to consist of two isolated floors of 70 beds each for suspected or confirmed patients and 12 ICU beds exclusively reserved for COVID-19 patients who required intensive care.

We followed the World-Health Organization (WHO) definitions for inclusion criteria [6]. Patients were divided into four groups: mild, moderate, severe, and critically ill. Mild patients were treated ambulatory, while moderate patients were treated depending on the medical criteria based on assessment.

Confirmation criteria were defined as a positive result of real time Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) assay of nasopharyngeal or lower respiratory tract swabs collected by a healthcare provider following the Center for Disease Control and Prevention (CDC) recommendations [7].

## Data collection

Patients with confirmed COVID-19 admitted to the hospital between April 1, 2020, and May 30, 2020 were included in our study; we included subjects who had available outcomes and their 30-day follow-up assessment. The date of the final follow-up was June 30, 2020. Data was collected from the electronic health records from all patients. The study population was dichotomized into ambulatory and hospitalized groups. The latter group of patients was divided according to hospitalization in the general ward or ICU.

We assessed demographic and epidemiological data, medical history, radiological characteristics, and laboratory values (at admission and 72 hours after) for

all patients. We calculated severity scores and scales commonly used in the COVID-19 pandemic context such as qSOFA, NEWS2, CALL Score, CURB-65 [8-11] for all enrolled subjects. In-hospital evolution, management, complications, and outcomes were captured. Both outpatients and inpatients had a 30-day follow-up. This study was reviewed and approved by the hospital's ethics committee (Registry number R-2020-3501-104).

# Statistical Analysis

The demographic data, clinical characteristics, and laboratory measurements were analyzed with descriptive statistics. Comparisons among survivors and non-survivor patients were performed with the Fisher's exact test or Chi square test for categorical variables when appropriate. The continuous variables were analyzed with Student t test or the Wilcoxon rank sum tests according to the data distribution. A *p* value < 0.05 was considered statistically significant. Analyses were performed using R Project for Statistical Computing; R Foundation, version 3.6.1.

# Results

A total of 955 patients were tested for COVID-19, 415 of them were positive and 540 were negative. We also included 333 patients who tested positive in the final analysis and whose 30-day outcomes were available.

Among the COVID-19 patients included in this study, 52% (172/333) were men, and the median age was 45 years. The most frequent comorbidities were diabetes and hypertension, observed in 42% (139/333) of the patients. In addition, 75% (250/333) of the patients were classified as overweight or obese and the median body mass index (BMI) was 27.6 kg/m<sup>2</sup>. The distribution of the weight classes were as follows: overweight 46% (153/333); obesity class 1: 23% (77/333); obesity class 2: 2.7% (9/333), and obesity class 3: 3.3% (11/333).

# Ambulatory COVID-19 patients

Among the patients included in the study, 148 (45%) were ambulatory patients and were younger than the inpatient group. Median age of the ambulatory patients was 39 yrs whereas median age of the inpatients was 54 yrs (p < 0.001). The ambulatory patients included 57% (85/148) health care workers and their main comorbidities were type 2 diabetes (11%, 16/148) and hypertension (11%, 16/148); 7% (11/148) of them had both type 2 diabetes and hypertension. The CALL Score indicated high risk in only two patients (10

and 13 points, respectively), and the median CALL score of all ambulatory patients indicated low risk (5 points). Almost 99% of the patients (146/148) had a NEWS2 score of low risk with a median score of 2. The most common symptoms were fatigue (92%), myalgias/arthralgias (89%), cough (82%), and headache (79%). Baseline characteristics of the patients and outcomes are shown in Table 1.

#### Hospitalized COVID-19 patients

There were 185 (56%) inpatients, of whom 85% (158/185) were hospitalized in the general ward and 15% (27/185) in the ICU. The inpatients were older (median age: 54 years; IQR: 42-65). History of smoking

was presented in 18% (34/185) patients, and their major comorbidities were diabetes (28.5%, 53/185), hypertension (29%, 54/185), cardiovascular diseases (16%, 30/185) and malignancy (16%, 29/185). There were 135 patients (73%) who were overweight or obese; however, there was no significant difference in BMI between inpatients and outpatients (median 28 kg/m<sup>2</sup> in inpatients vs 27 kg/m<sup>2</sup> in outpatients, p = 0.19). The categories of BMI were as follows: overweight (59%, 80/135); obesity class 1 (32%, 43/135); obesity class 2 (6%, 8/135), and obesity class 3 (8%, 11/135). The most common symptoms were fever (76%), dyspnea (81%), and chest pain (34%). Initial laboratory measurements (Table 2) indicated significantly

Table 1. Demographic data, clinical characteristics treatment and outcomes of all the patients with COVID-19 classified by place of hospitalization.

Baseline characteristics	All patients $(n = 333)$	Outpatients $(n = 148)$	General ward $(n = 158)$	ICU (n = 27)
Age median (IOR) years	45 (35-58)	39 (30-46)	54 (42-65)	54 (46-65)
Sex. female	161 (48)	71 (48)	74 (47)	16 (59)
Healthcare worker	93 (28)	85 (57)	7 (4)	10(03)
Comorbidities	<i>y</i> <del>(</del> <u></u> <del>,</del> <del>)</del> <del>,</del>		, (1)	- ( )
Diabetes	69 (21)	16 (11)	46 (29)	7 (26)
Hypertension	70 (21)	16 (11)	50 (32)	4 (15)
Cardiovascular disease	34 (10)	4 (3)	27 (17)	3 (11)
Malignancies	32(10)	3(2)	28 (18)	1 (4)
Physical Examination		- ( )	- ( -)	
Weight, median (IOR) kg	76 (66-84)	78 (65-83.7)	74.5 (65-82)	80 (72.5-91)
Height, median (IQR) m	1.67 (1.60-1.70)	1.69 (1.60-1.70)	1.62 (1.58-1.70)	1.69 (1.60-1.72)
BMI, median (IQR) $kg/m^2$	27.6 (25.2-30.4)	27.6 (25.3-29.7)	27.64 (25.2-30.78)	29.7 (24.9-32.08)
Admission Scores				
qSOFA Score, median (range)	0 (0-3)	0 (0-2)	1 (0-3)	2 (0-3)
NEWS2 Score, median (range)	3 (0-15)	2 (0-6)	7 (1-14)	8 (3-15)
CALL Score, median (range)	9 (4-13)	5 (4-13)	9 (4-13)	9 (6-13)
CURBB-65, median (range)	0 (0-5)	0 (0-2)	1 (0-5)	1 (0-5)
COVID classification				
Mild	116 (35)	116 (78)	0 (0)	0 (0)
Moderate	122 (37)	32 (22)	88 (56)	2 (11)
Severe	62 (19)	0 (0)	49 (31)	13 (48)
Critically ill	33 (10)	0 (0)	21 (13)	11 (41)
Treatment				
Antibiotics <sup>1</sup>	132 (40)	-	109 (69)	23 (85)
Corticosteroids <sup>2</sup>	30 (9)	-	26 (16)	4 (15)
Hydroxychloroquine	71 (21)	-	57 (36)	14 (52)
Macrolide <sup>3</sup>	129 (39)	23 (16)	92 (58)	14 (52)
Antiviral	9 (3)	-	2 (1)	7 (26)
Tocilizumab	8 (2)	-	5 (3)	3 (11)
Convalescent plasma	4 (1)	-	3 (2)	1 (4)
Ruxolitinib	5 (2)	-	4 (3)	1 (4)
Outcomes				
Length of stay, median (IQR) d	7 (3-13)	-	7 (2-12)	17 (11-22)
Discharged alive	234 (70)	148 (100)	82 (52)	4 (15)
Died	99 (30)	0 (0)	76 (48)	23 (85)
30 days follow-up				
Died	14 (4)	8 (5)	6 (4)	0 (0)
Total	113 (34)	8 (5)	82 (52)	23 (85)

ICU: intensive care unit; IQR: interquartile range; INR: international normalized ratio; ARDS: acute respiratory distress syndrome; Fio2: fraction of inspired oxygen; Pao2: arterial partial pressure of oxygen; <sup>1</sup>Antibiotics included penicillin derivatives, fluoroquinolones, and vancomycin; <sup>2</sup>Cortocosteroid included methylprednisolone and prednisone; <sup>3</sup>Macrolides included azithromycin and clarithromycin.

different observations in inpatients in comparison with outpatients, such as, lymphocyte count (median 0.8 vs  $1.2 \times 10^{9}$ / L, p < 0.001), glucose (median 120 vs 93) mg/dL, p < 0.001), LDH (median 650 vs 294 U/L, p <0.001), CRP (median 147 vs 5 mg/L, p = 0.007), CK-MB (median 15 vs 10 U/L, p = 0.008), ferritin (median 860 vs 392 ng/mL, p = 0.02), and D-dimer (median 780 vs 600 ng/mL, p = 0.15). Although there was no statistical significance in D-dimer values between inpatients and outpatients, this inflammatory biomarker level was elevated in critically ill ICU patients and remained high for at least 72 hours longer than the rest of the biomarkers mentioned above. All the prognostic admission scores of inpatients had a higher median than the outpatients with high risk scores in a high proportion of patients, such as NEWS 2.59% (110/185); qSOFA 43% (79/185); CURB-65 17% (31/185) and CALL 44% (82/185). Overall, 38% (71/185) inpatients required invasive mechanical ventilation, of whom 24% (44/185) were treated in the general ward and 15% (27/185) in ICU. The median length of intubation was 2 days (range: 1-48 days) in the general ward and 13 days (range: 2-35) in ICU. The median length of stay of all inpatients was 7 days (range: 1-72 days).

# Treatment and outcomes

Macrolides as COVID-19 therapy were administered to 23 (16%) of the ambulatory patients and 57% (106/185) inpatients. In addition, they received a high percentage of hydroxychloroquine 38% (71/185) and corticosteroids 16% (30/185). There were no significant differences between the survivors and non-survivors with regards to the treatments given with azithromycin, hydroxychloroquine, and corticosteroids (Table 3). Empiric antibiotic therapy was administered to 71% (132/185) of the inpatients, of whom 77% (102/132) received a third-generation cephalosporin. Prophylactic antithrombotic treatment (enoxaparin) was given to 79% (146/185) of the inpatients. Thrombosis as a complication occurred in 3% (11/185)of inpatients. There was no significant difference

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Table 2. Laboratory measurements	at the admission of all the	patients with COVID-19	classified by place of hospitalization.

Pasalina abaractoristics	All patients	Outpatients	General ward	ICU
	(n = 333)	(n = 148)	(n = 158)	(n = 27)
Initial Laboratory measures, median (IQR)				
White blood cell count, $\times 10^{9}/L$	8.7 (6.3-12.1)	7.6 (6.4-10.5)	8.6 (6-11.9)	10.9 (7.6-18.1)
Neutrophil count $\times 10^{9}$ /L	7.1 (4.5-9.8)	5.6 (4.5-7.5)	7.1 (4.1-9.8)	9.1 (5.8-15.9)
Lymphocyte $\times 10^{9}/L$	0.87 (0.55-1.25)	1.2 (1-1.3)	0.79 (0.5-1.2)	0.86 (0.55-1.08)
Hemoglobin, g/dL	14.2 (12.5-15.9)	14.7 (14-15.3)	14 (11.8-15.9)	15.5 (14.2-16.2)
Platelet count $\times$ 10 <sup>9</sup> /L	220 (146-280)	204 (177-278)	202 (132-299)	222 (192-272)
Glucose, mg/dL	112 (93-160)	93 (84-101)	117 (95-162)	149 (114-247)
Creatinine, mg/dL	0.8 (0.6-1.1)	0.7 (0.6-0.9)	0.8 (0.6-1.2)	1.02 (0.7-1.1)
Lactate dehydrogenase, U/L	596 (384-906)	294 (246-366)	636 (437-932)	759 (594-998)
C-reactive protein, mg/L	144 (59-197)	5 (2.9-17.5)	124 (49-194)	166 (141-264)
Procalcitonin, ng/mL	0.29 (0.12-0.77)	0 (0)	0.2 (0.12-0.50)	0.4 (0.3-0.8)
Creatine kinase, U/L	63 (40-144)	52 (40-64)	61 (40-146)	95 (42-250)
Creatine kinase MB U/L	15 (10-24)	10 (10-12)	15 (11-25)	17 (12-28)
Aspartate aminotransferase, U/L	35 (25-51)	22 (20-31)	40 (29-52)	43 (28-68)
Alanine aminotransferase, U/L	32 (23-51)	22 (22-26)	34 (26-52)	39 (22-66)
D-dimer ng/mL	700 (400-2000)	600 (400-600)	690 (390-2000)	1200 (600-2500)
Fibrinogen mg/dL	420 (350-599)	350 (350-375)	385 (313-575)	550 (509-780)
Ferritin ng/mL	856 (620-1189)	392 (373-411)	838 (585-1129)	1132 (784-1392)
INR	1.1 (1-1.2)	1.1 (1 - 1.1)	1.1 (1.05-1.22)	1.1 (1.1-1.2)
Images Studies				
Chest X-Ray				
Normal Chest Ray No. (%)	22 (7)	14 (9)	7 (4)	1 (4)
Unilateral distribution of patchy shadows or	15 (5)	6 (1)	8 (5)	1 (4)
ground-glass opacity, No. (%)	15(5)	0(4)	0(5)	1 (4)
Bilateral distribution of patchy shadows or	179 (54)	30 (20)	125 (79)	24 (89)
ground-glass opacity, No. (%)	177 (54)	50 (20)	125 (77)	24 (07)
CT Scan				
Normal CT scan	2 (1)	2 (1)	0 (0)	0 (0)
Unilateral distribution of patchy shadows or	13 (4)	10(7)	3(2)	0 (0)
ground-glass opacity, No. (%)	15 (4)	10(7)	J(2)	0(0)
Bilateral distribution of patchy shadows or	55 (17)	7 (5)	40 (25)	8 (30)
ground-glass opacity, No. (%)	55(17)	/ (3)	10 (23)	0 (30)

ICU, intensive care unit; IQR, interquartile range; BMI, body mass index; COPD, chronic obstructive pulmonary disease; CT, chest tomography.

between survivors and nonsurvivors who received antithrombotic treatment.

The overall rate of death at 30 days of follow-up was 34% (113/333), of whom 2% (8/333) were outpatients, 25% (82/333) in general ward, and 69% (23/333) in ICU. The rate of death in mechanically ventilated patients was 94% (67/71), of whom 66% (44/67) were in general ward and 34% (23/67) were in ICU. The main in-hospital complications included acute respiratory distress syndrome (ARDS) in 45% (84/185), acute kidney injury (AKI) in 30% (56/185), all-cause shock in 29% (54/185) and superinfections in 8% (14/185). AKI, ARDS, and shock were significantly associated with the nonsurvivors group of patients. The nonsurvivor patients were older (median age: 57 years; range: 16-84), had a lower Pao2/Fio2 ratio (median: 168, range: 40-247) at presentation, 90% (94/105) had dyspnea, 86% (86/105) had fever and 41% (43/105) had chest pain The median values of all prognostic admission scores of nonsurvivor patients were in the high-risk categories, and their scores were significantly higher than survivors (Table 3). Some laboratory findings such as neutrophilia, lymphopenia, elevated CRP, CK-MB, LDH, D-dimer, and ferritin had significant differences between nonsurvivors and survivors. These laboratory findings remained present even in the control studies at 72 hrs. (Figure 1).

The procalcitonin levels were significantly higher in nonsurvivor patients during admission; however, we did not document co-infections at the presentation.

## Discussion

This retrospective study described the baseline characteristics and follow-up of the first group of COVID-19 patients from a tertiary referral center in Mexico City, the most densely populated city in Mexico [12]. We found that most patients presented with overweight and obesity as the main associated comorbidity; diabetes and hypertension were also present in a high frequency. Complications and mortality were higher in hospitalized patients than the other cohorts. The death rate was higher in

Table 3. Clinical factors	treatments and laborator	v characteristics of survivor a	and non-survivor COVID-1	9 patient
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Characteristics of patients.	Survivors ( $n = 80$ )	Non-survivors (n = 105)	<i>p</i> -value
Age, median (IQR), years	48 (49-59)	57 (45-68)	0.03
Sex, female	40 (50)	50 (48)	0.86
BMI, median (IQR) kg/m <sup>2</sup>	27.5 (25.5-30.7)	28.1 (24.7-30.8)	0.89
Comorbidities			
Diabetes	18 (23)	35 (33)	0.14
Hypertension	20 (25)	34 (32)	0.35
Symptoms			
Fever	54 (68)	86 (81)	0.03
Cough	66 (82)	89 (84)	0.83
Chest pain	20 (25)	43 (41)	0.03
Dyspnea	55 (69)	94 (90)	< 0.001
Admission Scores, median (range)			
qSOFA Score	1 (0-3)	2 (0-3)	< 0.001
NEWS2 Score	5 (1-12)	9 (2-15)	< 0.001
CURB 65	0 (0-3)	2 (0-5)	< 0.001
Call Score	8 (4-13)	11 (6-13)	< 0.001
Laboratory measures, median (IQR)			
White blood cell count, $x10^{9}/L$	7.9 (5.9-11.1)	9.9 (7-13.4)	0.01
Lymphocyte x10 <sup>9</sup> /L	0.9 (0.6-1.2)	0.6 (0.4-1.1)	0.008
Neutrophil x10 <sup>9</sup> /L	6.1 (4.2-8.8)	7.9 (5.2-11.2)	0.01
Neutrophil-t-lymphocyte ratio	6.7 (3.610.8)	10.6 (5.8-17.9)	< 0.001
C-reactive protein, mg/L	116 (34-154)	169 (122-226)	< 0.001
Creatine Kinase, U/L	57 (40-132)	92 (40-180)	0.06
Creatine kinase MB U/L	12 (10-20)	16 (12-30)	0.006
Procalcitonin, ng/mL	0.1 (0.07-0.25)	0.7 (0.3-1.3)	< 0.001
Lactate dehydrogenase, U/L	523 (382-700)	758 (590-1188)	< 0.001
D-dimer ng/mL	600 (200-1300)	1000 (600-2500)	< 0.001
Ferritin ng/mL, mean (range)	800 (600-987)	980 (690-1392)	0.01
Treatment			
Corticosteroids <sup>1</sup>	13 (16)	17 (16)	1
Hydroxychloroquine	33 (41)	38 (36)	0.58
Azithromycin	14 (18)	12 (11)	0.33
Enoxaparin	68 (85)	77 (73)	0.08

ICU: intensive care unit; IQR: interquartile range; BMI: body mass index; qSOFA: quick Sequential Organ Failure Assessment; NEWS: National Early Warning Score; CALL: Comorbidity, Age, Lymphocyte and LDH; Corticosteroids include methylprednisolone and prednisone.

mechanically ventilated patients, and the deceased patients were younger than reported in previous studies.

The median age of inpatients was 54 yrs, lower than that in extensive studies reported from New York (NY), USA [13] where the median age was 63 yr (IQR: 52-75y); however some studies from China had a similar median age of 56 yrs (IQR: 42-68) [2,14]. In our study, we found that the median age of non-survivors was 57 yrs, younger than that reported from studies in China ((median: 69 yrs, IQR: 63-76yrs) [14]) and ((median 68 yrs, IQR: 62-77 yrs) [15]) and a cohort of 6493 patients in NY (median 76 yrs, IQR: 65-85 yrs) [16]. Among the hospitalized patients, 135 patients (73%) presented with overweight or obesity and these were the most prevalent comorbidities in our population. Obesity has been described as the main comorbidity associated with COVID-19 in the Mexican population [17]. This is not surprising since in the last evaluation, ENSANUT 2018 [12], 75.2% of Mexican adults aged  $\geq 20$  yrs were overweight or obese. Overweight and obesity are related to a multifactorial chronic inflammatory state and immune dysregulation, a risk factor that would explain the high mortality in

Figure 1. Graphics of the most significant laboratory measurements at presentation and 72 hours after the admission between survivors and nonsurvivors COVID-19 patients.



CK: Creatine kinase; CK-MB: Creatine kinase MB; CRP: C-reactive protein; INR: international normalized ratio.

areas with a high prevalence of overweight and obesity [18].

Other significant comorbidities found were type 2, diabetes and hypertension, present in 28.5% and 29% of the hospitalized patients, which was similar to observations in other parts of the world [13-14]. Despite these being described as risk factors for mortality in other studies [19], we did not find a high proportion among the nonsurvivor patients. However, its prevalence was higher in patients who required hospitalization. Interestingly, Palaiodimos *et al.* [20] reported a multivariate analysis, including these factors, and the results indicated that obesity may be the underlying link between them.

Prognostic admission scores were significantly higher in nonsurvivors compared to survivors. This data suggests that subjects with higher scores could benefit from ICU management; however in Mexico and other Latin American countries this was not possible because of lack of ICU beds (especially at the beginning of the pandemic) [5].

The nonsurvivor patients presented significant laboratory findings such as marked lymphopenia, high LDH, D-dimer, creatine kinase MB, C-reactive protein, ferritin, procalcitonin, and neutrophil/lymphocyte ratio. These findings were similar to previous studies in which these markers have helped determine disease severity and mortality. Some markers such as D-Dimer, ferritin, and procalcitonin were not available in all parts of our country. However, markers such as lymphocytes, DHL or neutrophil/lymphocyte ratio are available in most hospitals and can be used as prognostic markers of the disease [19]. The main complications included ARDS (45%), AKI (30%), and all-cause shock (29%) and were significantly higher in our studies than in the reports from NY [13] and China [14].

Following internal emergency protocols, a high percentage (71%) of patients received empirical antimicrobial therapy, mainly including beta-lactam derivatives, even though we did not find co-infections at admission. Our secondary infection rate was lower (8%) than that reported in a systematic review (15%) [21]. Broad-spectrum antibiotics are commonly administered to COVID-19 patients; it has been reported that up to 75-100% of critically ill patients are administered antibiotics, despite low rate of secondary infections [22]. The disproportionate use of these will result in increase in antimicrobial resistance, mainly in the COVID-19 units, and the risk of novel resistance will play an important role that could be evaluated in the future.

In this study, we did not find significant differences in the treatments between survivor and nonsurvivor patients. Despite the efforts of global researchers, there is no specific treatment to date, although several clinical trials are in progress and the results are promising, and many vaccines are being developed that may help control the global pandemic [3].

The mortality at 30-day follow-up of all patients was 34%, higher than that reported from metropolitan Detroit, USA, that included ambulatory and inpatients and reported a mortality of 16% [23]. The rate of death among hospitalized patients was 54%; this is significantly higher than the cohorts that included hospitalized patients in NY (21%) [13], China (21.9%) [24], and Italy (20.6%) [25].

Patients with mechanical ventilation are challenging for non-intensive care physicians to care for these patients in the general ward. We reported a 94% death rate among patients with mechanical ventilation. This rate is similar to studies in other parts of the world such as New York (88%) [13], China (92%) [26], and US (93.5%) [27]. Studies have reported varied ranges of mortality that can be misinterpreted. Some studies focused on hospitalized patients, while others included all types of patients. Due to the rapid need for information, most cohorts included patients who had not completed outcomes. More specific information can only be objectively assessed over time.

## Limitations

Our study has several limitations. First, this is a retrospective study; most data were acquired via electronic files or phone calls. Furthermore, we did not have a close follow-up in the case of ambulatory patients; not every subject had all laboratory or image studies; some patients were assessed with routine laboratories and a positive SARS-CoV-2 RT-PCR test and were isolated at home and followed remotely during the 30-day period. We did not make adjustments for multiple confounders, so it is impossible to obtain conclusions about factors associated with mortality.

In conclusión, this study shows the characteristics and 30-day outcomes of the first consecutive COVID-19 patients who visited a referral center in Mexico City, the epicenter of the pandemic in Mexico. A high proportion of patients had comorbidities such as obesity, diabetes and hypertension. Critically ill patients requiring mechanical ventilation in the general ward had a high death rate.

#### **Authors' Contributions**

Drs. Ordinola and Lopez Luis had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Concept and design: Ordinola, Cervantes, Cobos, Lopez Luis; acquisition, analysis or interpretation of data: Ordinola, Cervantes, Cobos, Perez, González, Lopez Luis; drafting of manuscript: Ordinola, Cervantes, Lopez Luis; critical revision of manuscript for importance intellectual content: Perez, González, Peralta, Carrillo, Olvera, Pineda, Briceño, Vera; statistical analysis: Ordinola, Lopez Luis; administrative, technical, or material support: Perez, González, Peralta, Carrillo, Olvera, Pineda, Briceño, Vera; supervision: Peralta, Vera.

## References

- 1. World Health Organization (2021) WHO coronavirus disease (COVID-19) dashboard. Available: https://covid19.who.int/. Accessed: 3 October 2021.
- Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, Wang B, Xiang H, Cheng Z, Xiong Y, Zhao Y, Li Y, Wang X, Peng Z (2020) Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA 323: 1061–1069.
- Wiersinga WJ, Rhodes A, Cheng AC, Peacock SJ, Prescott HC (2020) Pathophysiology, transmission, diagnosis, and treatment of coronavirus disease 2019 (COVID-19): a review. JAMA 324: 782–793.
- Hernández-Garduño E (2020). Obesity is the comorbidity more strongly associated for COVID-19 in Mexico. A case-control study. Obes Res Clin Prac 14: 375–379.
- 5. Rubin R, Abbasi J, Voelker R (2020) Latin America and its global partners toil to procure medical supplies as COVID-19 pushes the region to its limit. JAMA 324: 217–219.
- World Health Organization (2020) Clinical management of severe acute respiratory infection when novel coronavirus (nCoV) infection is suspected: interim guidance. Available: https://www.who.int/publications-detail/clinicalmanagementof-severe-acute-respiratory-infection-whennovelcoronavirus-(ncov)-infection-is-suspected. Accessed: 19 November 2020.
- Centers for Disease Control and Prevention (2020) Interim guidelines for collecting, handling, and testing clinical specimens from persons under investigation (PUIs) for coronavirus disease 2019 (COVID-19). Available: https://www.cdc.gov/coronavirus/2019-nCoV/lab/guidelinesclinical-specimens.html. Accessed: 24 September 2020.
- Jang JG, Hur J, Hong KS, Lee W, Ahn JH (2020) Prognostic accuracy of the SIRS, qSOFA, and NEWS for early detection of clinical deterioration in SARS-CoV-2 infected patients. J Korean Med Sci 35: e234.
- Ji D, Zhang D, Xu J, Chen Z, Yang T, Zhao P, Chen G, Cheng G, Wang Y, Bi J, Tan L, Lau G, Qin E (2020). Prediction for progression risk in patients with COVID-19 pneumonia: the CALL score. Clin Infect Dis 71: 1393–1399.
- Liu S, Yao N, Qiu Y, He C (2020) Predictive performance of SOFA and qSOFA for in-hospital mortality in severe novel coronavirus disease. Am J Emerg Med 38: 2074–2080.
- Guo J, Zhou B, Zhu M, Yuan Y, Wang Q, Zhou H, Wang X, Lv T, Li S, Liu P, Yang Y, He P, Zhang P (2020) CURB-65

may serve as a useful prognostic marker in COVID-19 patients within Wuhan, China: a retrospective cohort study. Epidemiology and Infection 148: e241.

- National Institute of Statistics and Geography (2018) National Survey of Health and Nutrition (ENSANUT). Available: https://ensanut.insp.mx/encuestas/ensanut2018/doctos/metodo logia/ensanut\_2018\_diseno\_conceptual.pdf. Accessed September 23, 2020. [Article in Spanish].
- Richardson S, Hirsch J S, Narasimhan M, Crawford JM, McGinn T, Davidson KW, The Northwell COVID-19 Research Consortium, Barnaby DP, Becker LB, Chelico JD, Cohen SL, Cookingham J, Coppa K, Diefenbach MA, Dominello AJ, Duer-Hefele J, Falzon L, Gitlin J, Hajizadeh N, Harvin TG, Zanos TP (2020) Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City Area. JAMA 323: 2052–2059.
- 14. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, Xiang J, Wang Y, Song B, Gu X, Guan L, Wei Y, Li H, Wu X, Xu J, Tu S, Zhang Y, Chen H, Cao B (2020) Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 395: 1054–1062.
- 15. Chen T, Wu D, Chen H, Yan W, Yang D, Chen G, Ma K, Xu D, Yu H, Wang H, Wang T, Guo W, Chen J, Ding C, Zhang X, Huang J, Han M, Li S, Luo X, Zhao J, Ning Q (2020) Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. BMJ 368: m1091.
- Mikami T, Miyashita H, Yamada T, Harrington M, Steinberg D, Dunn A, Siau E (2021) Risk factors for mortality in patients with COVID-19 in New York City. J Gen Intern Med 36: 17– 26.
- 17. Ortiz-Brizuela E, Villanueva-Reza M, González-Lara MF, Tamez-Torres KM, Román-Montes CM, Díaz-Mejía BA, Pérez-García E, Olivas-Martínez A, Rajme-López S, Martinez-Guerra BA, de-León-Cividanes NA, Fernández-García OA, Guerrero-Torres L, Torres-González L, Carrera-Patiño FA, Corral-Herrera EA, Hernández-Alemón AN, Tovar-Vargas M, Serrano-Pinto YG, Espejo-Ortiz CE, Ponce-de-León A (2020) Clinical and epidemiological characteristics of patients diagnosed with COVID-19 in a tertiary care center in Mexico City: a prospective cohort study. Rev Invest Clin 72: 165–177.
- Dietz W, Santos-Burgoa C (2020) Obesity and its implications for COVID-19 mortality. Obesity 28: 1005.
- Du RH, Liang LR, Yang CQ, Wang W, Cao TZ, Li M, Guo GY, Du J, Zheng CL, Zhu Q, Hu M, Li XY, Peng P, Shi HZ (2020) Predictors of mortality for patients with COVID-19 pneumonia caused by SARS-CoV-2: a prospective cohort study. Eur Respir J 55: 2000524.
- 20. Palaiodimos L, Kokkinidis DG, Li W, Karamanis D, Ognibene J, Arora S, Southern WN, Mantzoros CS (2020) Severe obesity, increasing age and male sex are independently associated with worse in-hospital outcomes, and higher in-hospital mortality in a cohort of patients with COVID-19 in the Bronx, New York. Metabol Clin Exp 108: 154262.
- Lansbury L, Lim B, Baskaran V, Lim WS (2020) Co-infections in people with COVID-19: a systematic review and metaanalysis. J Infect 81: 266–275.
- Clancy CJ, Buehrle DJ, Nguyen MH (2020) PRO: the COVID-19 pandemic will result in increased antimicrobial resistance rates. JAC - Antimicrobial Resistance 2: dlaa049.
- Suleyman G, Fadel RA, Malette KM, Hammond C, Abdulla H, Entz A, Demertzis Z, Hanna Z, Failla A, Dagher C, Chaudhry Z, Vahia A, Abreu Lanfranco O, Ramesh M, Zervos MJ,

Alangaden G, Miller J, Brar I (2020) Clinical characteristics and morbidity associated with coronavirus disease 2019 in a series of patients in metropolitan Detroit. JAMA 3: e2012270.

- 24. Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, Huang H, Zhang L, Zhou X, Du C, Zhang Y, Song J, Wang S, Chao Y, Yang Z, Xu J, Zhou X, Chen D, Xiong W, Xu L, Song Y (2020) Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. JAMA Internal Medicine 180: 934–943.
- 25. Giacomelli A, Ridolfo AL, Milazzo L, Oreni L, Bernacchia D, Siano M, Bonazzetti C, Covizzi A, Schiuma M, Passerini M, Piscaglia M, Coen M, Gubertini G, Rizzardini G, Cogliati C, Brambilla AM, Colombo R, Castelli A, Rech R, Riva A, Galli M (2020) 30-day mortality in patients hospitalized with COVID-19 during the first wave of the Italian epidemic: a prospective cohort study. Pharmacol Res 158: 104931.
- 26. Hua J, Qian C, Luo Z, Li Q, Wang F (2020) Invasive mechanical ventilation in COVID-19 patient management: the experience with 469 patients in Wuhan. Critical Care 24: 348.

27. Gupta S, Hayek SS, Wang W, Chan L, Mathews KS, Melamed ML, Brenner SK, Leonberg-Yoo A, Schenck EJ, Radbel J, Reiser J, Bansal A, Srivastava A, Zhou Y, Sutherland A, Green A, Shehata AM, Goyal N, Vijayan A, Velez J, STOP-COVID Investigators (2020) Factors associated with death in critically ill patients with coronavirus disease 2019 in the US. JAMA Internal Medicine 180: 1436–1447.

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