

CLINICAL AND EPIDEMIOLOGICAL CHARACTERISTICS OF PATIENTS DIAGNOSED WITH COVID-19 IN A TERTIARY CARE CENTER IN MEXICO CITY: A PROSPECTIVE COHORT STUDY

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ABSTRACT

Background: Regional information regarding the characteristics of patients with coronavirus disease (COVID)-19 is needed for a better understanding of the pandemic. **Objective:** The objective of the study to describe the clinical features of COVID-19 patients diagnosed in a tertiary-care center in Mexico City and to assess differences according to the treatment setting (ambulatory vs. hospital) and to the need of intensive care (IC). **Methods:** We conducted a prospective cohort, including consecutive

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patients with COVID-19 from February 26, 2020 to April 11, 2020. Results: We identified 309 patients (140 inpatients and 169 outpatients). The median age was 43 years (interquartile range, 33-54), 59.2% men, and 18.6% healthcare workers (12.3% from our center). The median body mass index (BMI) was 29.00 kg/m² and 39.6% had obesity. Compared to outpatients, inpatients were older, had comorbidities, cough, and dyspnea more frequently. Twenty-nine (20.7%) inpatients required treatment in the IC unit (ICU). History of diabetes (type 1 or 2) and abdominal pain were more common in ICU patients compared to non-ICU patients. ICU patients had higher BMIs, higher respiratory rates, and lower room-air capillary oxygen saturations. ICU patients showed a more severe inflammatory response as assessed by white blood cell count, neutrophil and platelet count, C-reactive protein, ferritin, procalcitonin, and albumin levels. By the end of the study period, 65 inpatients had been discharged because of improvement, 70 continued hospitalized, and five had died. **Conclusions:** Patients with comorbidities, either middle-age obese or elderly complaining of fever, cough, or dyspnea, were more likely to be admitted. At admission, patients with diabetes, high BMI, and clinical or laboratory findings consistent with a severe inflammatory state were more likely to require IC. (REV INVEST CLIN. 2020;72(3):165-77)

Key words: Coronavirus disease-2019. Mexico. Severe acute respiratory syndrome coronavirus 2. Cohort. Coronavirus, 2019-novel coronavirus.

INTRODUCTION

In late 2019, a cluster of patients with pneumonia of unknown etiology was detected in Wuhan, Hubei, China. By January 2020, a new coronavirus (Severe acute respiratory syndrome coronavirus [SARS-CoV-2]) was identified as the causative agent. The World Health Organization (WHO) designated this new entity as coronavirus disease 2019 (COVID-19)^{1,2}. After the first cases were reported, COVID-19 rapidly spread all over the world; on the 11th of March, the WHO declared this novel disease a global pandemic². In Mexico, the first imported cases were described on February 28, 2020, and by the 24th of March, local transmission was detected³. As of April 24, 2020, SARS-CoV-2 infection was confirmed in 2,626,321 subjects and caused over 181,938 deaths globally (12,872 cases and 1221 deaths in our country)^{2,4}.

Several studies have described the clinical and epidemiological characteristics of patients with SARS-CoV-2 infection⁵⁻⁹. The clinical spectrum of COVID-19 ranges from a self-limited upper respiratory tract illness to severe pneumonia with acute respiratory distress syndrome, among other severe manifestations (e.g., acute kidney injury and multi-organ failure)^{1,5,10}. Regional information regarding the clinical and epidemiological characteristics of patients with COVID-19 is needed for a better understanding of the disease. Here, we aimed to describe the clinical and epidemiological features of patients with SARS-CoV-2 infection diagnosed in a tertiary-care center in Mexico City and to assess main differences according to treatment

setting (ambulatory vs. hospital) or by the need of intensive care (IC).

MATERIAL AND METHODS

Study design, setting, and participants

We conducted a prospective cohort study in a tertiary care center located in Mexico City, a 211-bed referral hospital for adults that were converted as a referral center for COVID-19 on March 16, 2020. Preparations for the current pandemic included training of all personnel and changes in hospital infrastructure and organization (i.e., a new triage section and an increase in the IC unit [ICU] capacity from 14 to 40 beds). The general wards distribution and patients flow were redesigned as well. All patients with the requirement of IC were exclusively treated in ICU areas. All consecutive subjects with COVID-19 diagnosed between February 26, 2020s and April 11, 2020, were included using the definitions described by the WHO¹¹. The study was reviewed and approved by the Institutional Review Board (ref. no. 3333). Written informed consent was waived because of the observational nature of the study.

From February 26 to March 23, SARS-CoV-2 infection testing was performed in suspected cases defined as fever or cough plus one extra symptom (i.e., dyspnea, headache, myalgias, arthralgias, and sore throat) in patients with a history of contact with a COVID-19 case or of a recent travel to countries with local

transmission. Since March 24, all suspected cases were tested for COVID-19 regardless of history of previous travels. The need for admission was determined by treating physicians according to our institutional guidelines (Supplementary Fig. 1). Inpatients were followed until discharge or death (last status update was on April 11, 2020); ambulatory patients were evaluated once.

Molecular diagnostic procedures

SARS-CoV-2 testing was carried out on naso/oropharyngeal swabs (two or more samples per patient, with at least one nasopharyngeal swab). Only one patient required a tracheal aspirate for diagnosis. Upper-respiratory samples were transported in a universal transport medium for viruses. Nucleic acid extraction was performed using the NucliSens easy-MAG system® (bioMérieux, Boxtel, The Netherlands). Real-time reverse transcription-polymerase chain reaction was carried out on an Applied Biosystems 7500 thermocycler (Applied Biosystems, Foster City, CA, USA) using primers and conditions described elsewhere¹². The cycle threshold value (Ct-value) for positivity was 38.

Data collection and outcomes

Clinical and epidemiological data were extracted at first evaluation using a standardized case report form¹³; the remainder information was obtained from electronic clinical records. Diabetes was defined as either type 1 or type 2 diabetes mellitus (T2DM). Imaging and laboratory studies were performed accordingly to our local recommendations. In brief, suggested basal laboratory assessment included complete blood cell count, comprehensive metabolic panel, inflammatory markers (i.e., C-reactive protein, ferritin, procalcitonin), creatine kinase, fibrinogen, D-dimer, and lactate dehydrogenase (normal ranges are provided in the Supplementary Table 1). A computerized tomography (CT) scan was performed in all hospitalized patients before admission. The quick Sequential (Sepsis-related) Organ Failure Assessment (qSOFA) score, the National Early Warning Score (NEWS), the MuLBSTA score for viral pneumonia mortality, and the Charlson Comorbidity Index score were calculated for inpatients if data were available¹⁴⁻¹⁷. The primary outcomes were mechanical ventilation, ICU admission, all-cause mortality, and length of stay.

Statistical analysis

Categorical variables were reported as frequencies and proportions. Continuous variables were described using mean, median, standard deviation, and interquartile range (IQR) values as required. Differences between study groups were assessed using the chi-square test, Fisher's exact test, Student's t-test, or Mann-Whitney U test, as appropriate. To identify significant laboratory features that appeared during disease progression, we compared the dynamic profile in eight laboratory tests among inpatients according to their need of IC using generalized linear mixed models adjusted by age and sex. For this analysis, we included only patients with at least two laboratory measures. A two-sided $p < 0.05$ was considered statistically significant. All the analyses were performed using R software, version 3.6.3.

RESULTS

Demographic and presenting characteristics

We included 309 subjects, 140 inpatients, and 169 outpatients (Table 1 and Fig. 1). The median age was 43 years (range, 11-92), 59.2% were men, and 18.6% were healthcare workers (12.3% of them worked at our center). The median body mass index (BMI) was 29.00 kg/m²; 39.6% were overweight, and 39.6% had obesity. The median time from initiation of symptoms to hospital evaluation was 5 days (range, 0-24). The most common symptoms were cough (85.6%), headache (80.7%), fever (79.4%), general malaise (77.1%), and myalgias (72.8%). Anosmia, dysgeusia, and dermatological manifestations were not systematically evaluated; they were observed in 22 of 27 (81.5%), 6 of 9 (66.7%), and 2 of 22 (9.1%) patients, respectively.

Comparison between in- and outpatients

In comparison to outpatients, inpatients were older (median age 49 vs. 39 years) and had more comorbidities (diabetes 22.9% vs. 5.3%; hypertension 32.1% vs. 9.5%; and Charlson Comorbidity Index median 1 vs. 0), Table 1. Furthermore, inpatients presented with fever (93.6% vs. 67.5%), cough (91.4% vs. 80.7%),

Table 1. Comparison of baseline and presenting characteristics between inpatients and outpatients with COVID-19 evaluated at the INCMNSZ (February 26, 2020-April 11, 2020)

Characteristics	No. (%) Total (n = 309)	Inpatients (n = 140)	Outpatients (n = 169)	p-value
Age, median (IQR), years	43.00 (33.00, 54.00)	49.00 (39.00, 61.25)	39.00 (30.00, 49.00)	< 0.001
Sex, male	183 (59.2)	85 (60.7)	98 (58.0)	0.712
Healthcare worker	57 (18.6)	16 (11.4)	41 (24.7)	0.005
Comorbidities				
CCI, median (IQR)	0.00 (0.00, 1.00)	1.00 (0.00, 2.00)	0.00 (0.00, 1.00)	< 0.001
Diabetes	41 (13.3)	32 (22.9)	9 (5.3)	< 0.001
Hypertension	61 (19.7)	45 (32.1)	16 (9.5)	< 0.001
Cardiovascular disease	9 (2.9)	6 (4.3)	3 (1.8)	0.309*
Obesity	67 (39.6)	50 (39.7)	17 (39.5)	0.999
Overweight	67 (39.6)	52 (41.3)	15 (34.9)	0.576
COPD	3 (1.0)	2 (1.4)	1 (0.6)	0.592*
Asthma	9 (2.9)	2 (1.4)	7 (4.1)	0.191*
Immunosuppression	18 (5.8)	8 (5.7)	10 (5.9)	0.999*
Chronic liver disease	3 (1.0)	2 (1.4)	1 (0.6)	0.592*
Smoker (current or former)	47 (15.2)	25 (17.9)	22 (13.0)	0.264
Symptoms				
Days from symptoms onset to hospital admission, median (IQR)	5.00 (2.00, 8.00)	7.00 (4.00, 9.00)	3.00 (2.00, 7.00)	< 0.001
Fever	243 (79.4)	131 (93.6)	112 (67.5)	< 0.001
Cough	262 (85.6)	128 (91.4)	134 (80.7)	0.013
Chest pain	117 (38.2)	53 (37.9)	64 (38.6)	0.994
Dyspnea	124 (40.5)	88 (62.9)	36 (21.7)	< 0.001
Headache	246 (80.7)	107 (77.0)	139 (83.7)	0.18
Irritability	84 (27.9)	34 (25.2)	50 (30.1)	0.412
Diarrhea	94 (30.7)	48 (34.3)	46 (27.7)	0.264
Vomiting	30 (9.8)	18 (12.9)	12 (7.2)	0.145
Shaking chills	182 (59.7)	85 (61.2)	97 (58.4)	0.715
Abdominal pain	39 (12.7)	16 (11.4)	23 (13.9)	0.644
Myalgia	222 (72.8)	106 (76.3)	116 (69.9)	0.264
Arthralgia	199 (65.2)	95 (68.3)	104 (62.7)	0.358
Malaise	236 (77.1)	118 (84.3)	118 (71.1)	0.009
Rhinorrhea	126 (41.2)	44 (31.4)	82 (49.4)	0.002
Sore throat	161 (52.8)	65 (46.8)	96 (57.8)	0.07
Conjunctivitis	73 (23.9)	25 (17.9)	48 (28.9)	0.033
Anosmia	22 (81.5)	9 (64.3)	13 (100.0)	0.041*
Dysgeusia	6 (66.7)	5 (62.5)	1 (100.0)	0.999
Dermatosis	2 (9.1)	2 (9.1)	0 (-)	0.999*

(Continues)

Table 1. Comparison of baseline and presenting characteristics between inpatients and outpatients with COVID-19 evaluated at the INCMNSZ (February 26, 2020–April 11, 2020) (continued)

Characteristics	No. (%) Total (n = 309)	Inpatients (n = 140)	Outpatients (n = 169)	p-value
Physical examination				
Weight, median (IQR), Kg	78.00 (69.00, 88.00)	78.00 (70.00, 88.00)	76.00 (68.50, 89.50)	0.624
Height, mean (SD), meters	1.65 (0.10)	1.65 (0.10)	1.66 (0.09)	0.524†
BMI, median (IQR), kg/m ²	29.00 (25.60, 31.24)	29.10 (25.60, 31.22)	27.60 (25.10, 31.61)	0.309
Temperature, median (IQR), °C	37.00 (36.50, 37.82)	37.20 (36.50, 38.00)	36.70 (36.20, 37.50)	0.002
Heart rate, mean (SD), bpm	97.45 (17.54)	101.39 (18.26)	91.38 (14.48)	< 0.001†
Respiratory rate, median (IQR), rpm	20.00 (18.00, 24.00)	22.00 (20.00, 25.00)	19.00 (17.00, 21.00)	< 0.001
Oxygen saturation**, median (IQR), %	92.00 (88.00, 94.00)	89.00 (86.00, 92.00)	94.00 (93.00, 96.00)	< 0.001
Arterial pressure, median (IQR):				
Systolic, mmHg	122.00 (112.00, 134.00)	120.00 (110.75, 134.25)	125.00 (117.00, 133.00)	0.155
Diastolic, mmHg	78.00 (70.00, 85.50)	75.00 (67.00, 81.00)	80.00 (70.00, 90.00)	0.002
Mean, mmHg	92.33 (83.67, 100.33)	90.50 (83.33, 99.00)	94.67 (86.67, 104.33)	0.006

BMI: body mass index; bpm: beats per minute; CCI: Charlson Comorbidity Index; COPD: Chronic Obstructive Pulmonary Disease; INCMNSZ: Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán; IQR: interquartile range; rpm: breaths per minute.

*Fisher's exact test; †Unpaired student t-test.

**FiO₂ (fraction of inspired oxygen) 21%.

dyspnea (62.9% vs. 21.7%), and malaise (84.3% vs. 71.1%), more often, and less frequently with rhinorrhea (31.4% vs. 49.4%), conjunctivitis (17.9% vs. 28.9%), and anosmia (64.3% vs. 100%). On physical examination, hospitalized patients had a lower capillary oxygen saturation (SpO₂, median 89% vs. 94%), mean arterial pressure (MAP, median 90.5 vs. 94.67 mmHg), a higher heart rate (HR, mean 101.39 vs. 91.38 bpm), and respiratory rate (RR, median 22 vs. 19 rpm).

Comparison of inpatients according to their need for IC

All inpatients had a chest CT-scan compatible with pneumonia. Among these patients, 29 (20.7%) were admitted to intensive-care areas, mostly due to

respiratory failure requiring mechanical ventilation (28 [96.7%]). The median time from symptoms onset to ICU transfer was 11 days (range, 4–36) and the time from hospital admission to ICU transfer 2 days (range, 0–31) (Table 3). We found a higher frequency of diabetes (41.4% vs. 18%) in ICU patients; the remaining basal characteristics were similar between groups (Table 2). Since admission, ICU patients referred abdominal (24.1% vs. 8.1%), and chest pain more frequently (55.2% vs. 33.3%). The latter did not reach statistical significance. On baseline physical examination, ICU patients had a higher BMI (BMI, median 30.5 vs. 28.57), a higher RR (median 26 vs. 22), and a lower SpO₂ (median 83.5 vs. 89). The qSOFA score (median 1.00 [IQR; 1.00, 1.00] vs. 1.00 [IQR; 0.00, 1.00]), MuLBSTA score (median 9 vs. 8), and

Table 2. Comparison of baseline and presenting characteristics of inpatients with COVID-19 according to their requirement of intensive care at the INCMNSZ (February 26, 2020-April 11, 2020)

Characteristics	No. (%) ICU (n = 29)	non-ICU (n = 111)	p-value
Age, median (IQR), years	53.00 (40.00, 64.00)	48.00 (39.00, 60.50)	0.271
Sex, female	9 (31.0)	46 (41.4)	0.419
Healthcare worker	4 (13.8)	12 (10.8)	0.743*
Comorbidities			
CCI, median (IQR)	1.00 (0.00, 3.00)	1.00 (0.00, 2.00)	0.066
Diabetes	12 (41.4)	20 (18.0)	0.016
Hypertension	10 (34.5)	35 (31.5)	0.936
Cardiovascular disease	1 (3.4)	5 (4.5)	0.999*
Obesity	15 (51.7)	35 (36.1)	0.196
Overweight	10 (34.5)	42 (43.3)	0.528
COPD	1 (3.4)	1 (0.9)	0.373*
Asthma	0 (0.0)	2 (1.8)	0.999*
Immunosuppression	3 (10.3)	5 (4.5)	0.362*
Chronic liver disease	1 (3.4)	1 (0.9)	0.373*
Smoker (current or former)	7 (24.1)	18 (16.2)	0.536*
Symptoms			
Days since symptoms onset to hospital admission, median (IQR)	8.00 (6.00, 12.00)	7.00 (4.50, 9.00)	0.21
Fever	28 (96.6)	103 (92.8)	0.685*
Cough	28 (96.6)	100 (90.1)	0.46*
Chest pain	16 (55.2)	37 (33.3)	0.052
Dyspnea	22 (75.9)	66 (59.5)	0.158
Headache	18 (62.1)	89 (80.9)	0.058
Irritability	9 (33.3)	25 (23.1)	0.399
Diarrhea	11 (37.9)	37 (33.3)	0.807
Vomiting	7 (24.1)	11 (9.9)	0.059*
Shaking chills	17 (58.6)	68 (61.8)	0.92
Abdominal pain	7 (24.1)	9 (8.1)	0.024*
Myalgia	23 (79.3)	83 (75.5)	0.85
Arthralgia	21 (72.4)	74 (67.3)	0.76
Malaise	22 (75.9)	96 (86.5)	0.266
Rhinorrhoea	6 (20.7)	38 (34.2)	0.24
Sore throat	17 (58.6)	48 (43.6)	0.219
Conjunctivitis	6 (20.7)	19 (17.1)	0.861
Anosmia	0 (0.0)	9 (75.0)	0.11*
Dysgeusia	0 (0.0)	5 (33.3)	0.206
Dermatosis	0 (0.0)	2 (12.5)	0.94

(Continues)

Table 2. Comparison of baseline and presenting characteristics of inpatients with COVID-19 according to their requirement of intensive care at the INCMNSZ (February 26, 2020-April 11, 2020) (continued)

Characteristics	No. (%) ICU (n = 29)	non-ICU (n = 111)	p-value
Physical examination			
Weight, median (IQR), Kg	80.00 (70.00, 90.00)	78.00 (69.00, 87.00)	0.185
Height, mean (SD), meters	1.65 (1.60, 1.70)	1.65 (1.58, 1.72)	0.765
BMI, median (IQR), kg/m ²	30.50 (27.04, 33.87)	28.57 (25.50, 31.20)	0.037
Body temperature, median (IQR), °C	37.30 (36.78, 37.95)	37.20 (36.50, 38.00)	0.382
Heart rate, median (IQR), bpm	109.00 (94.00, 120.00)	101.00 (86.50, 114.00)	0.068
Respiratory rate, median (IQR), rpm	26.00 (22.00, 30.00)	22.00 (19.50, 24.00)	< 0.001
Oxygen saturation (FiO ₂ 21%), median (IQR), %	83.50 (76.00, 88.00)	89.00 (87.00, 92.00)	< 0.001
Arterial pressure, median (IQR)			
Systolic, mmHg	124.00 (110.00, 137.00)	120.00 (112.00, 133.00)	0.857
Diastolic, mmHg	74.00 (62.00, 82.00)	76.00 (68.50, 81.00)	0.877
Mean, mmHg	90.00 (83.33, 97.33)	91.00 (83.33, 100.00)	0.811

BMI: body mass index; bpm: beats per minute; CCI: Charlson Comorbidity Index; COPD: Chronic Obstructive Pulmonary Disease; FiO₂: fraction of inspired oxygen; INCMNSZ: Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán; IQR: interquartile range; rpm: breaths per minute.

*Fisher's exact test.

NEWS score (median 8 vs. 6) were higher at presentation among ICU patients when compared to non-ICU patients (Table 3). As shown in this Table, several differences regarding baseline laboratory exams also were observed.

The dynamic profile of some laboratory tests involved in inflammation was also different. Patients who required ICU had lower lymphocyte counts ($p = 0.03$) and higher WBC and neutrophil counts over time ($p < 0.01$) (Fig. 2). Moreover, the levels of C-reactive protein and lactate dehydrogenase were significantly higher over time in patients who were admitted to the ICU than in those who were not ($p < 0.01$). Platelet counts, levels of D-dimer, and ferritin were also higher in patients who were admitted to the ICU; however, this difference did not reach statistical significance.

Treatment and outcomes

By April 11, the median length of stay of all inpatients was 5 days (IQR, 3–7.75), 6 days (IQR, 3–14) for ICU patients, and 4 days (IQR, 2–7) for non-ICU patients. All inpatients received empiric antibiotic treatment (the length of therapy was not analyzed for the present report). A beta-lactam (i.e., amoxicillin-clavulanate, ceftriaxone, or piperacillin-tazobactam) was administered to 137 (98%) patients and a macrolide (i.e., azithromycin or clarithromycin) to all of them. Moreover, oseltamivir was added in 104 (74.3%) inpatients. At least one antiviral or immunomodulatory therapy currently under evaluation for COVID-19 was administered to 106 patients (76%) (i.e., chloroquine [$n = 44$], hydroxychloroquine [$n = 54$], tocilizumab [$n = 20$], and/or remdesivir vs. placebo [$n = 5$]).

Table 3. Baseline prognostic scores and laboratory findings of inpatients with COVID-19 according to their requirement of intensive care at the INCMNSZ (February 26, 2020-April 11, 2020)

Baseline prognostic scores	Median (IQR)		p-value
	ICU (n = 29)	non-ICU (n = 111)	
qSOFA	1.00 (1.00, 1.00)	1.00 (0.00, 1.00)	0.021
NEWS	8.00 (7.00, 10.00)	6.00 (4.00, 8.00)	< 0.001
MuLBSTA	9.00 (8.00, 12.00)	8.00 (5.00, 9.00)	0.006
High risk MuLBSTA	101 (91%)	21 (72%)	0.013
Laboratory findings			
Complete blood count			
White blood cell count, × 10 ⁹ /L	8.1 (5.5, 11.2)	6.0 (4.6, 8.05)	0.002
Neutrophil count, × 10 ⁹ /L	7.2 (4.3, 9.4)	4.4 (3.1, 6.3)	0.001
Lymphocyte count, × 10 ⁹ /L	0.68 (0.5, 1.1)	0.88 (0.62, 1.1)	0.185
Hemoglobin, g/dL	15.50 (14.00, 16.60)	15.60 (14.00, 16.95)	0.422
Platelet count, × 10 ⁹ /L	213.00 (175.00, 283.00)	193.00 (161.00, 231.00)	0.034
Basic metabolic panel			
Creatinine, mg/dL	0.90 (0.74, 1.09)	0.90 (0.70, 1.10)	0.559
Blood Urea Nitrogen, mg/dL	15.40 (10.90, 16.70)	12.30 (10.20, 16.10)	0.067
Sodium, mmol/L	136.00 (133.00, 138.00)	136.00 (133.00, 138.00)	0.741
Potassium, mmol/L	4.00 (3.66, 4.06)	4.02 (3.76, 4.30)	0.107
Liver function tests			
Alanine aminotransferase, U/L	42.00 (26.00, 53.00)	34.00 (22.90, 55.05)	0.349
Aspartate aminotransferase, U/L	56.00 (34.00, 68.00)	34.00 (25.00, 51.50)	0.004
Alkaline phosphatase, U/L	90.00 (63.00, 112.00)	82.00 (64.50, 99.50)	0.299
Total bilirubin, mg/dL	0.59 (0.49, 0.73)	0.50 (0.41, 0.66)	0.118
Albumin, g/dL	3.30 (3.13, 3.80)	4.00 (3.72, 4.20)	< 0.001
Globulin, g/dL	3.34 (2.93, 3.51)	3.10 (2.83, 3.27)	0.047
Acute-phase reactants			
C-reactive protein, mg/dL	13.74 (11.02, 18.98)	6.50 (2.39, 12.91)	< 0.001
Ferritin, ng/mL	646.50 (311.82, 891.25)	335.00 (203.00, 603.00)	0.008
Erythrocyte sedimentation rate, mm/h	34.00 (24.00, 37.50)	19.00 (10.25, 26.00)	0.127
Procalcitonin, ng/mL	0.56 (0.48, 0.80)	0.05 (0.05, 0.11)	< 0.001
Arterial blood gases			
pH	7.46 (7.43, 7.48)	7.45 (7.42, 7.48)	0.616
PaO ₂ , mmHg	63.90 (55.95, 93.50)	59.00 (54.00, 68.00)	0.171
PaCO ₂ , mmHg	31.00 (28.50, 35.35)	32.00 (29.20, 34.00)	0.737
PaO ₂ /FiO ₂ ratio	195.00 (99.83, 252.50)	271.43 (245.71, 302.67)	< 0.001
HCO ₃ , mmol/L	22.00 (19.10, 24.00)	21.80 (20.60, 22.70)	0.47
Lactate, mmol/L	1.15 (1.00, 1.45)	1.00 (0.90, 1.30)	0.18

(Continues)

Table 3. Baseline prognostic scores and laboratory findings of inpatients with COVID-19 according to their requirement of intensive care at the INCMNSZ (February 26, 2020-April 11, 2020) (*continued*)

Baseline prognostic scores	Median (IQR)		p-value
	ICU (n = 29)	non-ICU (n = 111)	
Others			
Fibrinogen, mg/dL	684.00 (485.00, 771.25)	491.00 (415.00, 665.25)	0.008
D-dimer, ng/mL	729.00 (527.00, 1328.72)	454.00 (353.00, 723.50)	< 0.001
Creatinine phosphokinase, U/L	126.00 (68.25, 272.00)	104.50 (57.00, 245.25)	0.593
High-sensitivity troponin I, pg/mL	10.60 (5.62, 16.52)	4.00 (2.80, 5.50)	< 0.001
Lactate dehydrogenase, U/L	488.00 (325.00, 577.00)	266.50 (218.75, 351.75)	< 0.001

FiO₂: fraction of inspired oxygen; ICU: intensive care unit; INCMNSZ: Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán; IQR: interquartile range; NEWS: National Early Warning Score; MulBSTA: Multilobular infiltration, hypo-lymphocytosis, bacterial coinfection, smoking history, hypertension and age score; NIH: National Institute of Health; qSOFA: quick Sequential Organ Failure Assessment.

Anticoagulation (either prophylactic or therapeutic) was given to 127 (90.7%) subjects. By the time of the last status update (April 11, 2020), 65 (46.4%) inpatients were discharged because of improvement, 70 (50%) continued hospitalized, and 5 (3.6%) had died (5/70 [7.1%] among discharged patients). Median age at death was 45 years (range, 33-67); septic shock and severe ARDS were stated as their cause of death.

DISCUSSION

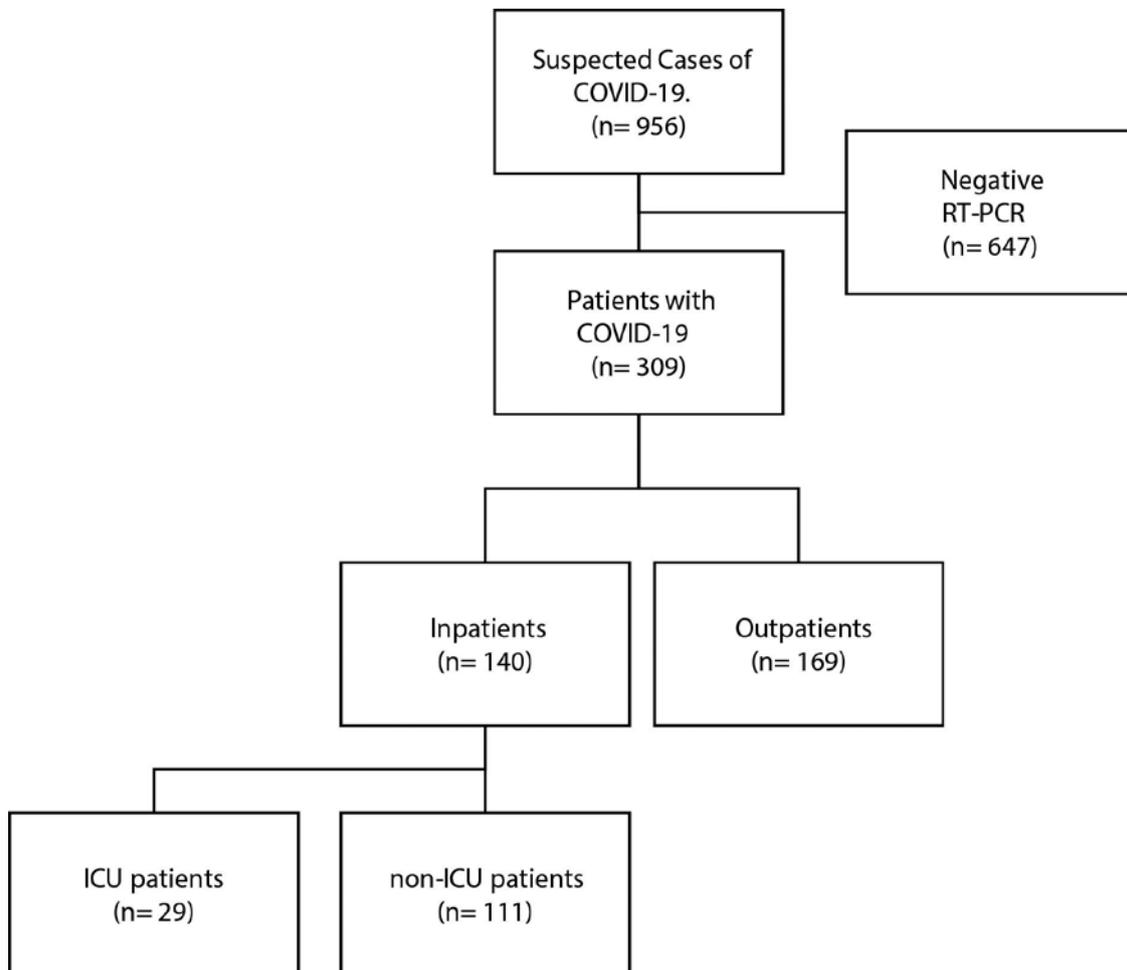
In this study, we described the experience of a tertiary care center in Mexico City recently converted to a referral center for COVID-19. Our results provide a comprehensive description of the clinical and epidemiological features of the first wave of patients diagnosed with COVID-19. We were able to identify several clinical, epidemiological, and laboratory differences between patients according to their treatment setting (ambulatory vs. hospital) or by their need of IC. These findings could be useful for clinicians during hospitalization decision-making and in predicting the need of IC.

Overall, patients were mostly middle-aged obese or overweight men who came into the emergency room within 1 week of symptoms onset. Most COVID-19

cohort studies have focused on hospitalized subjects with several features that are shared by ours, such as presenting symptoms (mainly fever and/or acute respiratory symptoms) and a predominance of male sex^{1,8,18,19}.

Interestingly, while the median age of our patients was similar to the reported in some series from China (median, 47-56 years), our population was younger than those from other cohorts (e.g., the United States of America, median 63 years)^{1,8,19}, even after analyzing out- and inpatients, and the need for IC. Age is a well-known factor that impacts negatively on the outcome in COVID-19 infection and other infections, presumably due to immunosenescence²⁰. The predominance of middle-aged subjects in our population (even those that require IC), contrasts with the findings from other reports^{1,19,21}. These findings could be explained in part by the high prevalence of overweight and obesity in our cohort. Kass et al. found a significant inverse correlation between age and BMI among COVID-19 patients (i.e., younger inpatients were more likely to be obese). Likewise, Lighter et al. reported an odds ratio for requiring IC of 1.8 (95% confidence interval [CI], 1.2-2.7) and 3.6 (CI, 2.5-5.3) in patients < 60 years with a BMI between 30 and 34 or equal or > 35, respectively^{22,23}. This assumption is also supported by our finding that a higher BMI was more frequently found among our inpatient population, as well as in patients who required IC.

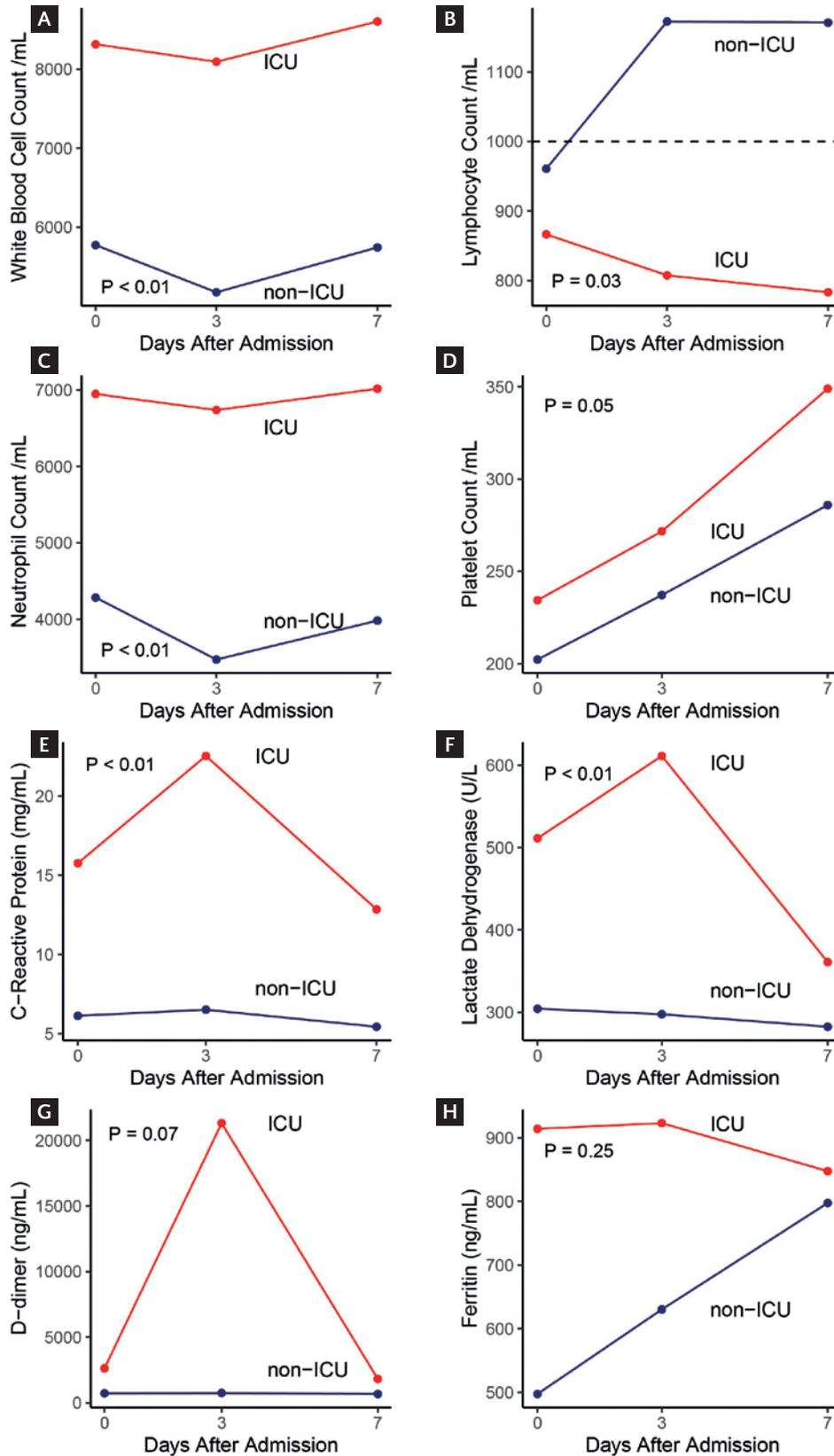
Figure 1. Flow chart of the patient selection process. COVID-19: coronavirus disease 2019; ICU: intensive care unit.



Several underlying mechanisms possibly explain the relationship between obesity and COVID-19 severity. These could be mechanical in nature (e.g., restrictive lung ventilatory defect), pro-inflammatory or immune dysregulatory, or even related to a higher prevalence of other comorbidities such as diabetes and hypertension among obese patients²². The association between BMI with the severity of COVID-19 might be of paramount importance in Mexico, where the prevalence of overweight and obesity among adults is 39.1% and 36.1%, respectively²⁴. Consequently, this emerging risk factor could trigger a wave of young patients presenting with severe COVID-19 with requirements of IC and, therefore, with the possibility of jeopardizing the public and private health-care service capacity in our country. Further studies are warranted to corroborate our findings.

Comprehensive knowledge of the factors related to COVID-19 complications as well as their early identification is essential components for identifying subjects that could safely receive ambulatory care. Compared to outpatients, inpatients were older and reported T2DM and hypertension more often. We also found a higher proportion of people living with diabetes among ICU patients than in non-ICU patients. As in the case of aging, the presence of comorbidities (e.g., diabetes and hypertension) is well-known risk factors for COVID-19 complications²⁵⁻²⁸. Both, inpatients and patients with ICU requirements presented with symptoms and signs suggestive of pneumonia more frequently⁸. In contrast, outpatients complained more about upper respiratory tract symptoms, maybe indicative of an earlier stage of the disease.

Figure 2. Dynamic profile of laboratory findings in inpatients with coronavirus disease-19 according to their need for intensive care. ICU: intensive care unit. Mean laboratorial measures over time among ICU and non-ICU patients were compared using mixed effects linear models.



When compared to non-ICU inpatients, patients with requirement of IC presented several laboratory parameters (at baseline and over time), that were suggestive of a more intense inflammatory response, a more severe pro-thrombotic state, and a higher frequency of cardiac and liver involvement. All of these features have been previously related to worse outcomes, including the need of IC and death^{1,8,9,18,29,30}.

These features (i.e., clinical, epidemiological, and laboratorial) could be useful in hospitalization-decision making, simplifying early identification of complications, and improving their prediction. In fact, our institutional guidelines are based on a simple evaluation at triage aimed at the early identification of complications and their related factors. Our guidelines contemplate two predictive bedside scores to identify patients with complications and patients at risk of worse outcomes (i.e., qSOFA and NEWS). Both are recommended for sepsis screening and have been shown to predict mortality and IC requirements³¹. According to our findings, these scores were higher in ICU patients when compared to non-ICU subjects. We also found a higher MuLBSTA score, a tool that was explicitly developed to assess 90-day mortality in patients with viral pneumonia¹⁷. Although we found all of them useful, further studies are required to assess their diagnostic and predictive capability for complications and worse outcomes in patients with COVID-19.

This study has several limitations: (a) the patients included are part of a still ongoing cohort study, and thus the results represent preliminary data on the initial evaluation of COVID-19 patients during the 1st weeks of the pandemic; (b) since many patients are currently hospitalized, their follow-up still is limited, and therefore, several endpoints are unknown; (c) outpatients were not systematically followed-up during this stage, and thus in some patients their outcomes are unknown; (d) this preliminary data does not allow to analyze the impact of treatment modalities; moreover, the mortality analysis is limited in that patients evaluated for this outcome represented only half of the included population; and (e) these data come from a single tertiary care center, and therefore, the availability of laboratory tests, facilities, and/or treatment modalities may not be generalized to every center in Mexico and Latin America.

In conclusion, patients with COVID-19 diagnosis were middle-aged obese or overweight men. Older individuals with comorbidities presenting with fever, cough, or dyspnea were most likely to be admitted. Inpatients with history of diabetes, high BMI, and clinical or laboratory features compatible with a severe inflammatory state were more likely to require IC.

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SUPPLEMENTARY DATA

Supplementary data are available at Revista de Investigación Clínica online (www.clinicalandtranslational-investigation.com). These data are provided by the corresponding author and published online for the benefit of the reader. The contents of supplementary data are the sole responsibility of the authors.

REFERENCES

1. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA*. 2020; 323:1061-9.
2. World Health Organization. Situation Reports. Available from: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports>. [Last accessed on 2020 Apr 24].
3. Dirección General de Epidemiología. Aviso Epidemiológico Enfermedad COVID-19 Por SARS-CoV-2 (Actualización). Available from: <https://www.gob.mx/salud/documentos/aviso-epidemiologico-enfermedad-covid-19-por-sars-cov-2-actualizacion>. [Last accessed on 2020 Apr 26].
4. Unidad de Inteligencia Epidemiológica y Sanitaria. Comunicado Técnico Diario COVID-19. Available from: https://www.gob.mx/cms/uploads/attachment/file/548251/Comunicado_Tecnico_Diario_COVID-19_2020.04.24.pdf. [Last accessed on 2020 Apr 26].
5. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet*. 2020;395:507-13.
6. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72314 cases from the Chinese center for disease control and prevention. *JAMA*. 2020;323:1239-42.

7. Chen T, Wu D, Chen H, Yan W, Yang D, Chen G, et al. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. *BMJ*. 2020;368:m1091.
8. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med*. 2020;382:1708-20.
9. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet*. 2020;395:1054-62.
10. Durvasula R, Wellington T, McNamara E, Watnick S. COVID-19 and kidney failure in the acute care setting: our experience from Seattle. *Am J Kidney Dis*. 2020; Epub ahead of print.
11. World Health Organization. Clinical Management of Severe Acute Respiratory Infection When Novel Coronavirus (2019-nCoV) Infection is Suspected: interim Guidance. Available from: <https://www.who.int/docs/default-source/coronaviruse/clinical-management-of-novel-cov.pdf>. [Last accessed on 2020 Mar 13].
12. Corman VM, Landt O, Kaiser M, Molenkamp R, Meijer A, Chu DK, et al. Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. *Eur Surveill*. 2020;25:2000045.
13. Dirección General de Epidemiología. Lineamiento Estandarizado para la Vigilancia Epidemiológica y por Laboratorio de Enfermedad por 2019-nCoV. Available from: <https://www.gob.mx/salud/documentos/79208>. [Last accessed on 2020 Apr 26].
14. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40:373-83.
15. Seymour CW, Liu VX, Iwashyna TJ, Brunkhorst FM, Rea TD, Scherag A, et al. Assessment of clinical criteria for sepsis: for the third international consensus definitions for sepsis and septic shock (sepsis-3). *JAMA*. 2016;315:762-74.
16. Smith GB, Prytherch DR, Meredith P, Schmidt PE, Featherstone PI. The ability of the national early warning score (NEWS) to discriminate patients at risk of early cardiac arrest, unanticipated intensive care unit admission, and death. *Resuscitation*. 2013;84:465-70.
17. Guo L, Wei D, Zhang X, Wu Y, Li Q, Zhou M, et al. Clinical features predicting mortality risk in patients with viral pneumonia: the MuLBSTA score. *Front Microbiol*. 2019;10:2752.
18. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. 2020;395:497-506.
19. Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW, et al. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York city area. *JAMA*. 2020;2020:e206775.
20. Nikolich-Zugich J, Knox KS, Rios CT, Natt B, Bhattacharya D, Fain MJ. SARS-CoV-2 and COVID-19 in older adults: what we may expect regarding pathogenesis, immune responses, and outcomes. *Geroscience*. 2020;42:505-14.
21. Grasselli G, Zangrillo A, Zanella A, Antonelli M, Cabrini L, Castelli A, et al. Baseline characteristics and outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the Lombardy region, Italy. *JAMA*. 2020;323:1574-81.
22. Kass DA, Duggal P, Cingolani O. Obesity could shift severe COVID-19 disease to younger ages. *Lancet*. 2020; Epub 2020 May 4.
23. Lighter J, Phillips M, Hochman S, Sterling S, Johnson D, Francois F, et al. Obesity in patients younger than 60 years is a risk factor for Covid-19 hospital admission. *Clin Infect Dis*. 2020;2020:ciaa415.
24. Instituto Nacional de Estadística y Geografía. Encuesta Nacional de Salud y Nutrición (ENSANUT) 2018. Available from: <https://www.inegi.org.mx/programas/ensanut/2018>. [Last accessed on 2020 May 8].
25. Guan WJ, Liang WH, Zhao Y, Liang HR, Chen ZS, Li YM, et al. Comorbidity and its impact on 1590 patients with Covid-19 in China: a nationwide analysis. *Eur Respir J*. 2020;2020:2000547.
26. CDC COVID-19 Response Team. Preliminary estimates of the prevalence of selected underlying health conditions among patients with coronavirus disease 2019-United States, February 12-March 28, 2020. *MMWR Morb Mortal Wkly Rep*. 2020;69:382-6.
27. Zheng YY, Ma YT, Zhang JY, Xie X. COVID-19 and the cardiovascular system. *Nat Rev Cardiol*. 2020;17:259-60.
28. Hussain A, Bhowmik B, do Vale Moreira NC. COVID-19 and diabetes: knowledge in progress. *Diabetes Res Clin Pract*. 2020;162:108142.
29. Shi S, Qin M, Shen B, Cai Y, Liu T, Yang F, et al. Association of cardiac injury with mortality in hospitalized patients with COVID-19 in Wuhan, China. *JAMA Cardiol*. 2020;2020:e200950.
30. Ruan Q, Yang K, Wang W, Jiang L, Song J. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. *Intensive Care Med*. 2020;46:846-8.
31. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The third international consensus definitions for sepsis and septic shock (sepsis-3). *JAMA*. 2016;315:801-10.