Characteristics and Clinical Course of Adult in-Patients With SARS-CoV-2 Pneumonia in Bogotá, Colombia.

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Abstract

Background: SARS-CoV-2 virus has spread worldwide causing a crisis in healthcare systems. We aimed to describe the clinical characteristics and to explore risk factors of death, critical care admission and use of invasive mechanical ventilation in hospitalized patients with SARS-CoV-2 pneumonia in Bogotá, Colombia.

Methods: We conducted a cross-sectional study of adult patients with laboratory-confirmed SARS-CoV-2 pneumonia. Demographic and clinical data were extracted from electronic records. Univariate and multivariable methods were performed to investigate the relationship between each variable and clinical outcomes at 28 days of follow-up.

Results: Between March 20 and June 30, 2020, 377 adults (56.8% male) were included in the study, of whom 85 (22.6%) died. Non-survivors were older on average than survivors (mean age, 56.7 years [SD 15.8] vs. 70.1 years [SD 13.9]) and more likely male (28 [32.9%] vs. 57 [67.1%]). Most patients had at least one underlying disease (333 [88.3%]), including arterial hypertension (149 [39.5%]), overweight (145 [38.5%]) and obesity (114 [30.2%]). Critical care admission (158 [41.9%]) and invasive mechanical ventilation (123 [32.6%]) was high. Age over 65 years (OR 9.26, 95% CI 3.29-26.01; p=0.00), ICU admission (OR 12.37, 95% CI 6.08-25.18; p=0.00), and arterial pH higher than 7.47 (OR 0.25, 95% CI 0.08-0.74; p=0.01) were associated with in-hospital mortality.

Conclusions: In this study of in-hospital patients with SARS-CoV-2 pneumonia frequency of death was similar to what has been reported. ICU admission and use of invasive mechanical ventilation was high. Risk factors as older age, ICU admission, and arterial pH were associated with mortality.

Background

In December 2019, a cluster of cases of severe pneumonia of unknown cause were identified in Wuhan, China. A novel strain of betacoronavirus called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was identified as the etiologic agent, and coronavirus disease 2019 (COVID-19) the disease it causes [1]. Since then, SARS-CoV-2 has spread worldwide and the number of cases and deaths have followed an exponential trend [2]. As of January 5th, 2021, more than 1.7 million cases and more than 40 thousand deaths of COVID-19 have been reported in Colombia [3].

Conditions such as male sex, increasing age, diabetes, cardiovascular diseases, chronic respiratory diseases, and obesity have been associated with increased risk of death by COVID-19 [4]. Nowadays Latin America is a hotspot for the pandemic, however, there is still a lack of information about the clinical features and prognostic factors of this disease in this region [2].

Latin America and Colombia have singularities that could influence clinical presentation of SARS-CoV-2 pneumonia due to their healthcare systems, their social composition, and the diverse of their geography, that include populations living at high-altitude adapted to hypobaric hypoxia. Determining the regional

clinical features of COVID-19 is essential to expand the knowledge to set health policies. We aimed to describe the demographic and clinical characteristics and to explore risk factors of death, intensive care unit (ICU) admission and use of invasive mechanical ventilation in hospitalized patients diagnosed with SARS-CoV-2 pneumonia in Bogotá, Colombia.

Methods

Study design and participants

This cross-sectional study with an analytical component was conducted in a consecutive sample of hospitalized individuals at a single tertiary care center in Bogotá, Colombia, with community-acquired pneumonia due to SARS-CoV-2 from March 20, 2020 to June 30, 2020, and a follow-up time until 28 days.

Patients 18 years or older admitted to hospitalization with diagnosis compatible with community-acquired pneumonia and a RT-PCR test for SARS-CoV-2 positive in nasopharyngeal swabs were included. Patients with viral coinfection were included, as long as SARS-CoV-2 infection were isolated. We excluded patients that did not have diagnostic imaging to corroborate the diagnosis of pneumonia. Patients transferred to other hospitals were excluded because we were unable to track their outcomes. Patients with hospital-acquired SARS-CoV-2 pneumonia or transferred from other hospitals 48 hours after their initial hospital admission were excluded.

Outcomes

The primary outcome was in-hospital death within 28 days of admission. Patients still in hospital at the latest follow-up point on July 28, 2020 were censored for analyses. Once discharged, patients were considered no longer at risk of death. Secondary outcomes included ICU admission and use of invasive mechanical ventilation.

Data collection

Patients were included through active detection of results of reverse transcription polymerase chain reaction (RT-PCR) for SARS-CoV-2. Demographic data, clinical characteristics, underlying comorbidities, laboratory tests on admission, diagnostic images, treatments for viral pneumonia (antiviral therapy, corticosteroids, antibiotics, ventilatory support, vasopressor support, renal replacement therapy) and outcomes were extracted from electronic medical records. Two researchers independently reviewed the records to double-check the collected data.

Date of illness onset was the first day of symptoms. We used reference values at an altitude of 2,640 meters above sea for assessment of arterial blood gases and hemoglobin levels [5,6]. Chest X-ray features were classified as compatible with viral pneumonia (peripheral ground-glass opacities or consolidations, bilateral or unilateral), compatible with an alternative diagnosis (single lobar consolidation, cavitation, nodules, masses, or reticular pattern) or non-specific (perihilar ground-glass

opacities or consolidations or diffuse ground-glass opacities) [7]. Chest CT features were classified as compatible with viral pneumonia (CO-RADS categories 4 and 5), compatible with an alternative diagnosis (CO-RADS categories 1 and 2) or non-specific (CO-RADS category 3) [8].

Sample size

The sample size was based on the data published of rates of in-hospital mortality (11.7 to 28.3%) and the magnitude of clinical risk factors associated with death (OR 2.46 to 4.08) in patients with SARS-CoV-2 pneumonia [9,10]. Using Fleiss's formula, it was estimated that it would be necessary to include at least 197 participants in order to achieve an 80% power and a 0.05 significance level. The sample size calculation was computed using Epi Info™ version 7.2.3.1 of 2019.

Statistical analysis

A descriptive analysis of the variables of interest was conducted to report the categorical data by the distribution of frequencies, relative frequencies, and proportions. Continuous variables were expressed as means (standard deviation, SD) and medians (interquartile range, IQR), depending on their distribution.

To evaluate the relationship between variables considered as risk factors and the outcomes logistic regression methods were performed. Quantitative variables distributed not normally were categorized according to data from previous studies for logistic regression. After assessment of collinearity and reduction of input variables by a component matrix, twelve factors with the strongest statistical association with the outcomes on bivariate analysis (p-values <0.05) were included in the multivariate analysis.

All reported p-values were two-tailed and calculated with statistical significance set to $p<0.05$. Statistical analyses were performed using SPSS Statistics version 25.0 (SPSS, Chicago, IL, USA).

Results

Between March 25 and June 30, 2020, 377 adults were admitted with laboratory-confirmed SARS-CoV-2 pneumonia, 214 (56.8%) were male (Table 1). Participants were aged 24-100 years, mean age was 59.7 years (SD 16.4). At the time of end of follow-up, six patients were still in hospital. The first RT-PCR test for SARS-CoV-2 was positive in 368 patients (97.6%), while nine patients (2.4%) had a negative first test and positive second test.

Table 1. Characteristics on admission to hospital and outcomes of the study population.

	Total (n= 377)	Survivor (n= 292)	Non-survivor (n= 85)
Age, years	59.7±16.4	56.7±15.8	70.1±13.9
<50	103 (27.3)	97 (33.2)	6 (7.1)
50–65	130 (34.5)	108 (37.0)	22 (25.9)
>65	144 (38.2)	87 (29.8)	57 (67.1)
Sex			
Female	163 (43.2)	135 (46.2)	28 (32.9)
Male	214 (56.8)	157 (53.8)	57 (67.1)
Symptoms			
Cough	335/360 (93.1)	262/281 (93.2)	73/79 (92.4)
Fever	280/346 (80.9)	219/272 (80.5)	61/74 (82.4)
Dyspnea	258/294 (87.8)	191/222 (86.0)	67/72 (93.1)
Asthenia	136/137 (99.3)	117/118 (99.2)	19/19 (100.0)
Sore throat	106/153 (69.3)	91/128 (71.1)	15/25 (60.0)
Diarrhea	77/154 (50.0)	63/121 (52.1)	14/33 (42.4)
Comorbidities			
Arterial hypertension	149 (39.5)	99 (33.9)	50 (58.8)
Overweight	145 (38.5)	122 (58.2)	23 (27.1)
Obesity	114 (30.2)	90 (30.8)	24 (28.2)
Diabetes mellitus	82 (21.8)	55 (18.8)	27 (31.8)
Chronic obstructive pulmonary disease	34 (9.0)	17 (5.8)	17 (20.0)
Chronic kidney disease	19 (5.0)	10 (3.4)	9 (10.6)
Coronary artery disease	18 (4.8)	13 (4.5)	5 (5.9)
Heart failure	17 (4.5)	10 (3.4)	7 (8.2)
Number of comorbidities			
0	44 (11.7)	32 (11.0)	12 (14.1)
1	169 (44.8)	130 (44.5)	39 (45.9)
2	83 (22.0)	63 (21.6)	20 (23.5)
3	57 (15.1)	48 (16.4)	9 (10.6)
≥4	24 (6.4)	19 (6.5)	5 (5.9)
Smoking status			

Current smoking	7 (1.9)	6 (2.1)	1 (1.2)
Former smoking	38 (10.1)	28 (9.6)	10 (11.8)
Body mass index	27.3 (24.1-30.9)	27.4 (24.8-31.0)	25.8 (22.8-30.9)
Baseline vital signs			
Systolic blood pressure, mmHg	128.0 (116.0-140.0)	127.0 (115.0-138.0)	130.0 (119.3-151.8)
Heart rate, bpm	96.3±17.5	96.0±16.5	97.1±20.7
Respiratory rate, bpm	20 (18-22)	20 (18-21)	20 (19-24)
Pneumonia severity			
CURB-65			
0 or 1	251/342 (73.4)	215/262 (82.1)	36/80 (45.0)
2	79/342 (23.1)	41/262 (15.6)	38/80 (47.5)
≥3	12/342 (3.5)	6/262 (2.3)	6/80 (7.5)
qSOFA			
0 or 1	324/337 (96.3)	267/275 (97.1)	75/80 (93.8)
≥2	13/337 (3.7)	8/275 (2.9)	5/80 (6.2)
Days from illness onset to hospital admission	7 (4-9)	7 (4-10)	6 (4-8)
Days from illness onset to ICU admission	9 (6-11)	9 (7-12)	8 (6-10)
Outcomes			
Invasive mechanical ventilation	123 (32.6)	50 (17.1)	73 (85.9)
ICU admission	158 (41.9)	85 (29.1)	73 (85.9)
ICU length of stay, days	8 (3-15)	7 (3-14)	10 (3-17)
Length of hospital stay, days	9 (6-15)	9 (6-14)	10 (5-18)

Data are presented as mean ± standard deviation, median (interquartile range) or n/N (%), where N is the total number of patients with available data.

There were 85 (22.6%) deaths. Patients who died were older on average than the whole population (Figure 1). Deaths were more likely in male patients, the proportion of women in deaths increased as the population aged.

The median time from first symptom to emergency department admission was 7 days (IQR 4-9). The most common symptoms upon admission included cough, fever, dyspnea, and asthenia (Table 1). Most patients had at least one comorbidity (333 [88.3%]). Arterial hypertension and diabetes mellitus were ones of the most common comorbidities. Two out of three patients suffered from overweight or obesity.

Severity of pneumonia evaluated on admission was mild in 251 patients according to CURB-65 score (0 to 1, 73.3%), and 342 had low risk for in-hospital mortality according to a quick SOFA score (0 to 1, 96.3%).

Regarding the most remarkable laboratory findings upon admission to the emergency room, almost half of patients had lymphopenia and it occurred more frequently in non-survivors than in survivors (Table 2). Median concentrations of some systemic inflammation markers were more elevated in non-survivors than in survivors, such as lactate dehydrogenase, C-reactive protein, ferritin and procalcitonin. Likewise, median D-dimer level was higher in non-survivors than in survivors.

Table 2. Laboratory and radiographic findings of the study population on admission to hospital.

	Total (n= 377)	Survivor (n= 292)	Non-survivor (n= 85)
Laboratory findings			
White blood cell count, ×10^9/L	7.545 (5.510-10.035)	7.140 (5.380-9.540)	8.550 (6.235-12.075)
<4	24/376 (6.4)	21/291 (7.2)	3/85 (3.5)
4 to 10	257/376 (68.4)	205/291 (70.4)	52/85 (61.2)
>10	95/376 (25.3)	65/291 (22.3)	30/85 (35.3)
Lymphocyte count, ×10^9/L	1.105 (0.803-1.468)	1.150 (0.890-1.520)	0.810 (0.560-1.250)
<1	156/376 (41.5)	102/291 (35.1)	54/85 (63.5)
≥1	220/376 (58.5)	189/291 (64.9)	31/85 (36.5)
Hemoglobin, mg/dL	14.8±2.0	14.9±1.8	14.5±2.6
<12.5	38/376 (10.1)	20/291 (6.9)	18/85 (21.2)
≥12.5	338/376 (89.9)	271/291 (93.1)	67/85 (78.8)
Platelet count, ×10^9/L	218.000 (177.000-274.750)	225.000 (179.000-281.000)	196.000 (159.000-251.500)
<100	9/376 (2.4)	7/291 (2.4)	2/85 (2.4)
≥100	367/376 (97.6)	284/291 (97.6)	83/85 (97.6)
Lactate dehydrogenase, U/L	344.0 (266.5-462.0)	325.0 (258.0-414.5)	458.0 (310.0-646.0)
≤250	70/365 (19.2)	63/282 (22.3)	7/83 (8.4)
>250	295/365 (80.8)	219/282 (77.7)	76/83 (91.6)
Ferritin, ng/mL	854.0 (472.0-1500.0)	768.5 (470.8-1406.5)	1131.0 (512.5-1942.5)
<600	112/315 (35.6)	90/238 (37.8)	22/77 (28.6)
≥600	203/315 (64.4)	148/238 (62.2)	55/77 (71.4)
C-reactive protein, mg/L	112.3 (63.6-181.7)	101.3 (55.1-167.2)	143.8 (99.1-226.1)
<50	58/309 (18.8)	52/241 (21.6)	6/68 (8.8)
≥50	251/309 (81.2)	189/241 (78.4)	62/68 (91.2)
Procalcitonin, ng/mL	0.27 (0.11-0.93)	0.18 (0.09-0.59)	0.73 (0.25-1.84)
<0.1	15/70 (21.4)	14/48 (29.2)	1/22 (4.5)
0.1 to <0.5	28/70 (40.0)	20/48 (41.6)	8/22 (36.4)
≥0.5	27/70 (38.6)	14/48 (29.2)	13/22 (59.1)

D-dimer, mg/L	0.49 (0.28-0.93)	0.46 (0.27-0.90)	0.65 (0.37-1.14)
<0.5	184/364 (50.6)	156/283 (55.1)	28/81 (34.6)
0.5 to 1.0	101/364 (27.7)	71/283 (25.1)	30/81 (37.0)
>1.0	79/364 (21.7)	56/283 (19.8)	23/81 (28.4)
Creatinine, mg/dL	0.97 (0.79-1.21)	0.90 (0.76-1.12)	1.19 (0.96-1.58)
<1.5	314/363 (86.5)	254/278 (91.4)	60/85 (70.6)
≥1.5	49/363 (13.5)	24/278 (8.6)	25/85 (29.4)
Alanine aminotransferase, U/L	35.0 (22.0-58.5)	38.0 (22.8-61.0)	30.5 (18.3-51.8)
≤40	181/314 (57.6)	128/234 (54.7)	53/80 (66.3)
>40	133/314 (42.4)	106/234 (45.3)	27/80 (33.7)
Arterial pH	7.44 (7.42-7.46)	7.44 (7.42-7.47)	7.43 (7.4-7.46)
<7.40	37/370 (10.0)	19/286 (6.6)	18/84 (21.4)
7.40-7.47	277/370 (74.9)	221/286 (77.3)	56/84 (66.7)
>7.47	56/370 (15.1)	46/286 (16.1)	10/84 (11.9)
SpO2, %	90.5 (86.9-93.9)	91.0 (87.0-94.0)	90.0 (84.2-92.8)
<90	161/370 (38.4)	121/286 (42.3)	40/84 (47.6)
≥90	209/370 (61.6)	165/286 (57.7)	44/84 (52.4)
PaO2/FiO2 ratio	239.0 (198.0-270.0)	246.5 (213.8-274.0)	188.5 (152.5-239.8)
<100	18/370 (4.9)	5/286 (1.7)	13/84 (15.5)
100 to 199	77/370 (20.8)	44/286 (15.4)	33/84 (39.3)
200 to 299	236/370 (63.8)	204/286 (71.3)	32/84 (38.1)
≥300	39/370 (10.5)	33/286 (11.5)	6/84 (7.1)
Viral coinfection	4/63 (6.3)	3/34 (8.8)	1/29 (3.4)
Bacterial coinfection	10/109 (9.2)	5/65 (7.7)	5/44 (11.4)
Chest X-ray features			
Normal	63/354 (17.8)	56/271 (20.7)	7/83 (8.4)
Compatible with pneumonia	257/354 (72.6)	187/271 (69.0)	70/83 (84.3)
Compatible with an alternative diagnosis	10/354 (2.8)	8/271 (2.9)	2/83 (2.4)
Non-specific features	24/354 (6.8)	20/271 (7.4)	4/83 (4.8)
Chest CT features			
Compatible with viral pneumonia	323/344 (93.9)	261/274 (95.3)	62/70 (88.6)

Compatible with an alternative diagnosis	15/344 (4.4)	11/274 (4.0)	4/70 (5.7)
Non-specific features	6/344 (1.7)	2/274 (0.7)	4/70 (5.7)
Pulmonary embolism on CT pulmonary angiography	6/66 (1.6)	6/57 (2.1)	0/9 (0.0)

Data are presented as mean ± standard deviation, median (interquartile range) or n/N (%), where N is the total number of patients with available data.

Chest X-ray was compatible with the suspected diagnosis of pneumonia in 257 (72.6%) patients and it was normal in 63 (17.8%) (Table 2). Chest CT scans were done in 344 patients, CT pulmonary angiographies in 66 patients. Chest CT was compatible with the suspected diagnosis of viral pneumonia in 323 (93.9%) patients. Pulmonary embolism was diagnosed in six cases (1.6%), all of them were survivors.

Pharmacological treatment of patients admitted to hospital with COVID-19 changed over time during enrollment. In this study, 248 (65.8%) patients received systemic corticosteroid therapy, its use was more common in non-survivors than in survivors (73 [85.9%] vs. 175 [59.9%]). Azithromycin (174 [46.2%]), hydroxychloroquine (85 [22.5%]), and lopinavir/ritonavir (79 [21.0%]) were used less frequently.

Regarding the clinical outcomes, a high proportion of patients (158 [41.9%]) were transferred to the ICU; the median ICU length of stay was 8 (IQR 3-15) days (Table 1). Overall, 123 (32.6%) patients received invasive mechanical ventilation and 116 (30.8%) patients received vasopressor therapy. Renal replacement therapy due to sepsis-associated acute renal failure was necessary in 33 (8.8%) patients. The median length of hospital stay was 9 (IQR 6-15) days.

In bivariate analysis age, sex, leukocytosis, history of arterial hypertension, COPD or chronic kidney disease, altered mental status on admission, decreased arterial pH, low levels of peripheral oxygen saturation (SpO2), elevated D-dimer levels, nosocomial bacterial infection and ICU admission were associated with in-hospital death. In the multivariable logistic regression analysis, we found that age over 65 years (reference age <50 years, OR 9.26, 95% CI 3.29-26.01; p=0.00) and ICU admission (OR 12.37, 95% CI 6.08-25.18; p=0.00) were associated with increased risk of death; arterial pH higher than 7.47 (reference pH <7.40, OR 0.25, 95% CI 0.08-0.74; p=0.01) on admission was associated with lower risk of death (Table 3). The logistic model of age, arterial pH and ICU admission had a high discrimination ability for in-hospital mortality (area under the receiver operating characteristic curve of 0.869) (Figure 2). As a proportion of patients did not have measurements on admission of biomarkers such as procalcitonin and ferritin, a sensitivity analysis including these biomarkers for testing the effect of missing data resulted in similar results.

Table 3. Multivariate analysis of risk factors associated with in-hospital death in patients with SARS-CoV-2 pneumonia.

Factors	OR (95% CI)	p-value
Age, years		
<50	1 (ref)	0.00
50–65	2.64 (0.89-7.87)	0.08
>65	9.26 (3.29-26.01)	0.00
Arterial pH		
<7.40	1 (ref)	0.03
7.40-7.47	0.43 (0.19-0.97)	0.04
>7.47	0.25 (0.08-0.74)	0.01
ICU admission	12.37 (6.08-25.18)	0.00

Age over 65 years, male sex, white blood cell count over 10,000 per μL, and SpO2 lower than 90% on admission were associated with use of invasive mechanical ventilation (Table 4). The logistic model of age, male sex, SpO2, and white blood cell count had an acceptable discrimination for invasive mechanical ventilation (area under the receiver operating characteristic curve of 0.761). There were no independent risk factors associated to ICU admission for COVID-19 in the multivariate analysis.

Table 4. Multivariate analysis of risk factors associated with invasive mechanical ventilation in patients with SARS-CoV-2 pneumonia.

Factors	OR (95% CI)	p-value
Age, years		
<50	1 (ref)	0.00
50–65	2.05 (1.03-4.10)	0.04
>65	5.25 (2.66-10.36)	0.00
Male sex	2.36 (1.40-3.97)	0.001
SpO2 <90%	0.38 (0.23-0.63)	0.00
White blood cell count, $\times 10^9$/L		
<4	1 (ref)	0.00
4 to 10	1.77 (0.47-6.64)	0.40
>10	5.73 (1.46-22.46)	0.01

Discussion

To our knowledge, this single-center study is the first report of hospitalized adult patients with SARS-CoV-2 pneumonia in Andean subregion in a high-altitude population (Bogotá is situated at an altitude of 2,640 meters [8,660 feet] above sea level). We observed that COVID-19 hospitalized patients were more likely men over 50 years of age. Demographic characteristics and symptoms of COVID-19 were similar to previous reported data from patients admitted to hospitalization in China, United States, and the UK [11–14]. In our study, in-hospital mortality was 22.6%; age, ICU admission and arterial pH were factors associated with this outcome.

Even though mortality in the present study was consistent with what has been reported, severity of respiratory failure seemed to be worse considering the high proportion of patients admitted to ICU (41.9%) and use of invasive mechanical ventilation (32.6%) in comparison to what was reported in China (26% and 17%, respectively), New York (14.2% and 12.2%, respectively), and the UK (17% and 10%, respectively) [10,13,14]. This could be partially explained because one third (34.2%) of our patients didn't receive corticosteroid therapy for COVID-19, due to part of our population was enrolled before the release of the RECOVERY trial report; although in the dexamethasone group in the RECOVERY trial the use of invasive mechanical ventilation was way lower (5.7%) than in the present study, mortality was similar (22.9%) [15].

In Latin America, several reports have found a case fatality rate and mechanical ventilation use around 24% in hospitalized patients in Brazil [16,17]. However, in the COALITION II trial, that assessed efficacy and safety of adding azithromycin to COVID-19 treatment in Brazilian patients, mortality rate and use of mechanical ventilation was even higher to what we showed (40% and 52% in the control group, respectively) [18].

It has been suggested that some local factors in Latin America could influence clinical presentation of COVID-19 in comparison to Europe, such as the younger age of populations, tropical climate, and the immune regulation induced by helminthic infections or extensive BCG vaccination [19,20]. Colombia has a lower proportion of population over 60 years (13%) in comparison to Italy (29%) or Spain (25%), but at the same time, a lower hospital bed to population ratio and a fragmented healthcare system [21]. These environmental and physiological characteristics may affect the course of COVID-19.

Moreover, PaO2/FiO2 ratio is lower at higher altitudes. Observational studies have been suggested that high-altitude is associated with infectivity and case fatality rate of COVID-19, due to factors such as adaptation to chronic hypobaric hypoxia, angiotensin-converting enzyme 2 expression, ultraviolet radiation and vitamin D production [22]. However, results are conflicting and may be explained by differences in population density, underreporting of cases and barriers of access to healthcare among populations [23–25]. Although altitude does not affect the mortality rate in general patients undergoing invasive mechanical ventilation, specific features of subgroups of patients with acute respiratory distress syndrome in COVID-19 may influence the need of ventilatory support at high-altitude [26]. We theorize that high-altitude hypoxemia could have impacted in severity and course of acute respiratory failure in our COVID-19 population.

On the other hand, this study was conducted in a tertiary care center with one of the largest ICU in Bogotá, so presumably we admitted more severe patients prone to invasive mechanical ventilation from the area. The median duration of symptoms before admission (7 days [IQR 4-9]) was a little bit higher to what was reported in New York and the UK [13,14]; factors not yet assessed and involved in late admission of COVID-19 patients could have affected our results.

In our study, most patients had a mild pneumonia on admission, according to CURB-65 and qSOFA scores. Zhou et al. [10] described in a cohort of 191 patients in Wuhan a CURB-65 score 0 to 1 in most of them (75%) as well. It is possible that clinical prediction rules traditionally used to evaluate severity of community-acquired pneumonia may underestimate risk of mortality or ICU admission in SARS-CoV-2 pneumonia, since they were not developed to predict outcomes in viral pneumonia. Clinical deterioration in COVID-19 occurs later in comparison to bacterial pneumonia (in the present study 9 days from illness onset to ICU admission), so prediction rules at admission might be inaccurate. Data published is conflicting about the performance of these prediction rules in COVID-19 [27−30]. Scores developed for viral pneumonia, such as MuLBSTA, 4C or CALL scores, may better predict the severity in this subset of patients, although they haven't been validated in high-altitude populations [30−33].

Pulmonary embolism in COVID-19 has been described in one out of three patients admitted to ICU, even higher in histopathological studies, suggesting a main role of this complication in adverse patient outcomes [34,35]. In our study, pulmonary embolism occurred in just 1.6% of patients, with no associated deaths. Probably, there was underdiagnosis because CT pulmonary angiography was performed only in 66 patients, due to limitations for its use in ICU patients with acute renal failure, hemodynamic or ventilatory instability.

In the logistic models developed in this study, age and male sex were associated with COVID-19 severity; these results are consistent with the risk factors for poor prognosis previously reported [14,36]. Comorbidities such as arterial hypertension, diabetes mellitus, coronary heart disease, and obesity have been described as factors associated with mortality as well [14,36,37]. In the present study, most patients had at least one underlying disease. The prevalence of obesity (30.2%) was considerably higher than the overall prevalence in Colombian adults (18.7%), suggesting that obesity increases the risk for COVID-19 requiring hospitalization [38].

Inflammatory biomarkers, such as C-reactive protein, ferritin and procalcitonin, have been associated with mortality among COVID-19 patients [36,37]. Likely, since some our patients did not have these markers measured on admission, we could not validate them as independent risk factors. On the other hand, biological variations on biomarkers due to different ethnic backgrounds might modify their prognostic ability in populations like ours. Regarding laboratory findings, in our model for mortality pH in arterial blood gas test on admission was validated as an important biomarker, this factor had not been associated with severe disease before. Most studies in COVID-19 like this have assessed prognostic markers on admission, further studies should address the diagnostic accuracy of markers follow-up.

There are some limitations to our study. First, clinical data collected relied on medical records which might lead to misclassification or recall biases. Nevertheless, we verified thoroughly the collected data; significant underreporting was unlikely because report of clinical characteristics and underlying comorbidities was consistent with existing literature. Second, there were missing data of symptoms and laboratory findings in some cases. This limitation is common in observational studies and might contribute to the underestimation of the true strength of any association. Third, power of statistical analyses may have been affected by the sample size and categorization of variables. Fourth, this study was conducted with hospitalized patients in a single tertiary care center in a high-altitude city, so it is possible that the sickest patients with highest degree hypoxemia were admitted. Patients were included by convenience sampling during the first months of the pandemic to describe the characteristics in our center; thus, our population is not representative of the general population through the whole pandemic. Caution should be exercised about generalizing these data to different settings. Finally, due to the study design we cannot establish a causal connection between risk factors and outcomes; our results and the model developed need a prospective validation.

Conclusions

In summary, in this single-center study of hospitalized patients with SARS-CoV-2 pneumonia clinical characteristics were consistent with existing data. Mortality was similar to what has been reported, however ICU admission and use of invasive mechanical ventilation was higher.

Factors associated with in-hospital death as increasing age, arterial pH, and ICU admission could help to identify patients with poor prognosis. Further studies may help to understand the usefulness of biomarkers follow-up in prognosis and the impact of high-altitude in severity of COVID-19.

List Of Abbreviations

BCG: Bacillus Calmette–Guérin

COVID-19: Coronavirus disease 2019

CO-RADS: COVID-19 Reporting and Data System

COPD: Chronic obstructive pulmonary disease

CT: Computed tomography

ICU: Intensive care unit

RT-PCR: Reverse transcription polymerase chain reaction

SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2

SpO2: Peripheral oxygen saturation

Declarations

Ethics approval and consent to participate

The study was approved by the local Ethics Committee of Universidad del Rosario (Approved number DVO005-1230-CV1269), in accordance with the principles of the Declaration of the Helsinki, and the Proposed International Ethical Guidelines for Biomedical Research Involving Human Subjects of the CIOMS/WHO. Written informed consents were taken from the patients' admissions for data collection. The information provided by the patients was confidential.

Consent for publication

Not applicable.

Availability of data and materials

All data generated or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interest

The authors declare that they have no competing interests.

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Authors' contributions

Study conceptualization and design: All authors. Data collection: JLG, MAI. Statistical analysis: KP. Interpretation of results: All authors. Manuscript preparation: JLG, KP. All authors read and approved the final manuscript. The corresponding author attests that all listed authors meet authorship criteria.

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References

1. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med. 2020;382(8):727–33.

2. World Health Organization. Weekly epidemiological update - 29 December 2020. Published Dec 29, 2020. https://www.who.int/publications/m/item/weekly-epidemiological-update---29-december-2020. Accessed Jan 5, 2021

3. Instituto Nacional de Salud. COVID-19 en Colombia. Published Jan 5, 2021. https://www.ins.gov.co/Noticias/Paginas/Coronavirus.aspx. Accessed Jan 5, 2021

4. Williamson EJ, Walker AJ, Bhaskaran K, Bacon S, Bates C, Morton CE, et al. Factors associated with COVID-19-related death using OpenSAFELY. Nature. 2020;584(7821):430–6.

5. Lasso Apráez JI. Interpretación de los gases arteriales en Bogotá (2.640 msnm) basada en el nomograma de Siggaard-Andersen. Una propuesta para facilitar y unificar la lectura. Rev Colomb Neumol. 2014;26(1):25–36.

6. Coy Velandia LS, Castillo Bohórquez M, Mora AI, Munévar Á, Peña R. YY. Hematological characteristics of blood donors in Bogotá, D.C., Colombia (2.600 m). Rev Med. 2007;15(1):40–7.

7. Smith DL, Grenier J-P, Batte C, Spieler B. A characteristic chest radiographic pattern in the setting of COVID-19 pandemic. Radiol Cardiothorac Imaging. 2020;2(5):e200280.

8. Prokop M, van Everdingen W, van Rees Vellinga T, Quarles van Ufford H, Stöger L, Beenen L, et al. CO-RADS: A categorical CT assessment scheme for patients suspected of having COVID-19 - definition and evaluation. Radiology. 2020;296(2):E97–104.

9. Du R-H, Liang L-R, Yang C-Q, Wang W, Cao T-Z, Li M, et al. Predictors of mortality for patients with COVID-19 pneumonia caused by SARS-CoV-2: a prospective cohort study. Eur Respir J. 2020;55(5):2000524.

10. 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(10229):1054–62.

11. Guan W, Ni Z, Hu Y, Liang W, Ou C, He J, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med. 2020;382(18):1708–20.

12. Cummings MJ, Baldwin MR, Abrams D, Jacobson SD, Meyer BJ, Balough EM, et al. Epidemiology, clinical course, and outcomes of critically ill adults with COVID-19 in New York City: a prospective cohort study. Lancet. 2020;395(10239):1763–70.

13. 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;323(20):2052–9.

14. Docherty AB, Harrison EM, Green CA, Hardwick HE, Pius R, Norman L, et al. Features of 20 133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: prospective observational cohort study. BMJ. 2020;369:m1985.

15. RECOVERY Collaborative Group, Horby P, Lim WS, Emberson JR, Mafham M, Bell JL, et al. Dexamethasone in hospitalized patients with Covid-19 - Preliminary report. N Engl J Med.

2020;NEJMoa2021436.

16. Teich VD, Klajner S, Almeida FAS de, Dantas ACB, Laselva CR, Torritesi MG, et al. Epidemiologic and clinical features of patients with COVID-19 in Brazil. Einstein Sao Paulo. 2020;18:eAO6022.

17. Maciel EL, Jabor P, Goncalves Júnior E, Tristão-Sá R, Lima R de CD, Reis-Santos B, et al. Factors associated with COVID-19 hospital deaths in Espírito Santo, Brazil, 2020. Epidemiol Serv Saude. 2020;29(4):e2020413.

18. Furtado RHM, Berwanger O, Fonseca HA, Corrêa TD, Ferraz LR, Lapa MG, et al. Azithromycin in addition to standard of care versus standard of care alone in the treatment of patients admitted to the hospital with severe COVID-19 in Brazil (COALITION II): a randomised clinical trial. Lancet. 2020;396(10256):959–67.

19. de Freitas E Silva R, Pitzurra R. What are the factors influencing the COVID-19 outbreak in Latin America? Travel Med Infect Dis. 2020;35:101667.

20. Arias-Reyes C, Zubieta-DeUrioste N, Poma-Machicao L, Aliaga-Raduan F, Carvajal-Rodriguez F, Dutschmann M, et al. Does the pathogenesis of SARS-CoV-2 virus decrease at high-altitude? Respir Physiol Neurobiol. 2020;277:103443.

21. Amariles P, Granados J, Ceballos M, Montoya CJ. COVID-19 in Colombia endpoints. Are we different, like Europe? Res Soc Adm Pharm. 2021;17(1):2036–9.

22. Pun M, Turner R, Strapazzon G, Brugger H, Swenson ER. Lower incidence of COVID-19 at high altitude: facts and confounders. High Alt Med Biol. 2020;21(3):217–22.

23. Cano-Pérez E, Torres-Pacheco J, Fragozo-Ramos MC, García-Díaz G, Montalvo-Varela E, Pozo-Palacios JC. Negative correlation between altitude and COVID-19 pandemic in Colombia: a preliminary report. Am J Trop Med Hyg. 2020;103(6):2347–9.

24. Intimayta-Escalante C, Rojas-Bolivar D, Hancco I. Letter to the Editor: Influence of altitude on the prevalence and case fatality rate of COVID-19 in Peru. High Alt Med Biol. 2020;21(4):426-427.

25. Woolcott OO, Bergman RN. Mortality attributed to COVID-19 in high-altitude populations. High Alt Med Biol. 2020;21(4):409-416.

26. Jibaja M, Ortiz-Ruiz G, García F, Garay-Fernández M, de Jesús Montelongo F, Martinez J, et al. Hospital mortality and effect of adjusting PaO2/FiO2 according to altitude above the sea level in acclimatized patients undergoing invasive mechanical ventilation. A multicenter study. Arch Bronconeumol. 2020;56(4):218–24.

27. Satici C, Demirkol MA, Sargin Altunok E, Gursoy B, Alkan M, Kamat S, et al. Performance of pneumonia severity index and CURB-65 in predicting 30-day mortality in patients with COVID-19. Int J Infect Dis. 2020;98:84–9.

28. Nguyen Y, Corre F, Honsel V, Curac S, Zarrouk V, Fantin B, et al. Applicability of the CURB-65 pneumonia severity score for outpatient treatment of COVID-19. J Infect. 2020;81(3):e96–8.

29. Carriel J, Muñoz-Jaramillo R, Bolaños-Ladinez O, Heredia-Villacreses F, Menéndez-Sanchón J, Martin-Delgado J, et al. CURB-65 as a predictor of 30-day mortality in patients hospitalized with COVID-19 in Ecuador: COVID-EC study. Rev Clin Esp. 2020;

30. Knight SR, Ho A, Pius R, Buchan I, Carson G, Drake TM, et al. Risk stratification of patients admitted to hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: development and validation of the 4C Mortality Score. BMJ. 2020;370:m3339.

31. Xu R, Hou K, Zhang K, Xu H, Zhang N, Fu H, et al. Performance of two risk-stratification models in hospitalized patients with coronavirus disease. Front Med. 2020;7:518.

32. Ji D, Zhang D, Xu J, Chen Z, Yang T, Zhao P, et al. Prediction for progression risk in patients with COVID-19 pneumonia: The CALL score. Clin Infect Dis. 2020;71(6):1393–9.

33. Liang W, Liang H, Ou L, Chen B, Chen A, Li C, et al. Development and validation of a clinical risk score to predict the occurrence of critical illness in hospitalized patients with COVID-19. JAMA Intern Med. 2020;180(8):1081–9.

34. Klok FA, Kruip MJHA, van der Meer NJM, Arbous MS, Gommers D a. MPJ, Kant KM, et al. Incidence of thrombotic complications in critically ill ICU patients with COVID-19. Thromb Res. 2020;191:145–7.

35. Nadkarni GN, Lala A, Bagiella E, Chang HL, Moreno PR, Pujadas E, et al. Anticoagulation, bleeding, mortality, and pathology in hospitalized patients with COVID-19. J Am Coll Cardiol. 2020;76(16):1815–26.

36. Chen R, Liang W, Jiang M, Guan W, Zhan C, Wang T, et al. Risk factors of fatal outcome in hospitalized subjects with coronavirus disease 2019 from a nationwide analysis in China. Chest. 2020;158(1):97–105.

37. Wang K, Zuo P, Liu Y, Zhang M, Zhao X, Xie S, et al. Clinical and laboratory predictors of in-hospital mortality in patients with coronavirus disease-2019: a cohort study in Wuhan, China. Clin Infect Dis. 2020;71(16):2079–88.

38. Ministerio de Salud y Protección Social. Encuesta Nacional de la Situación Nutricional ENSIN 2015. Colombia. Published Mar, 2020. https://www.minsalud.gov.co/sites/rid/Lists/BibliotecaDigital/RIDE/VS/ED/GCFI/libro-ensin-2015.pdf. Accessed Dec 29, 2020

Figures
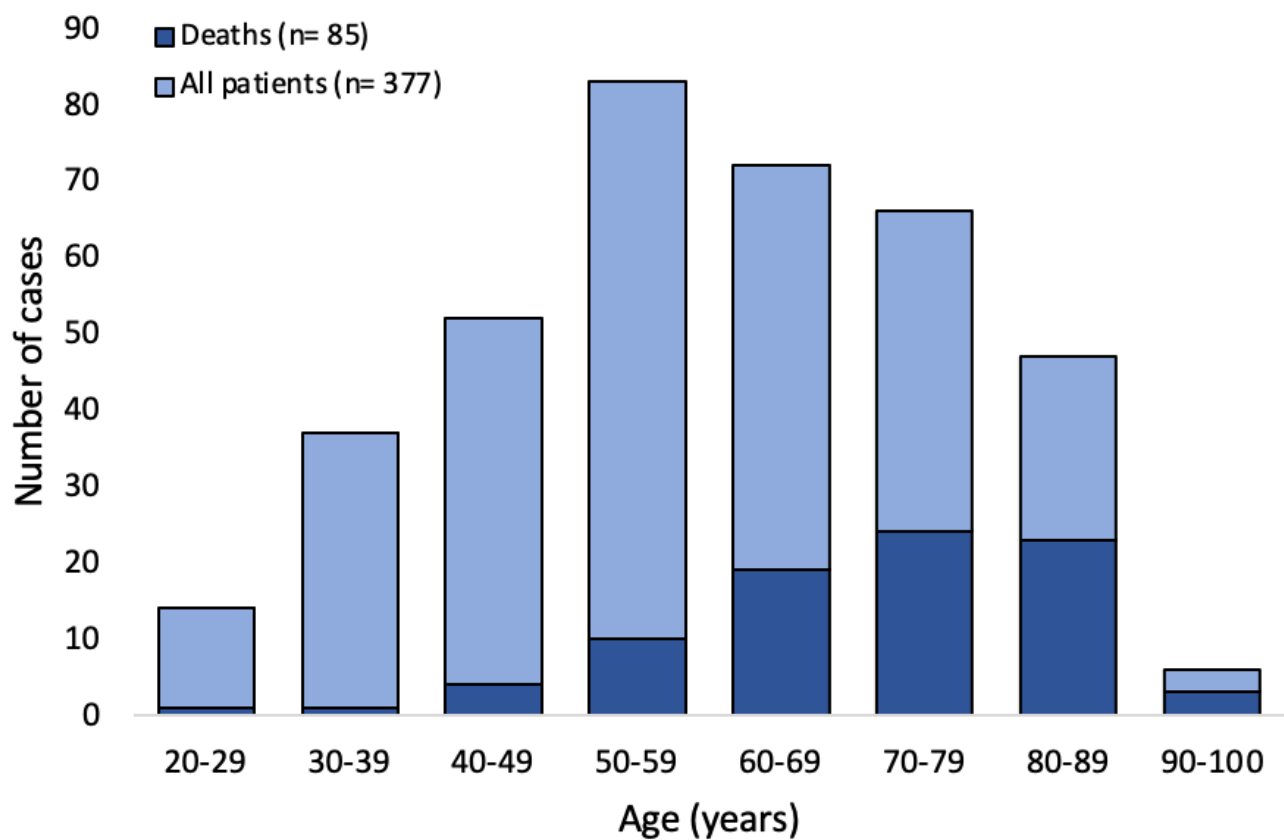
Figure 1

Cases and deaths distribution by age of patients with SARS-CoV-2 pneumonia.
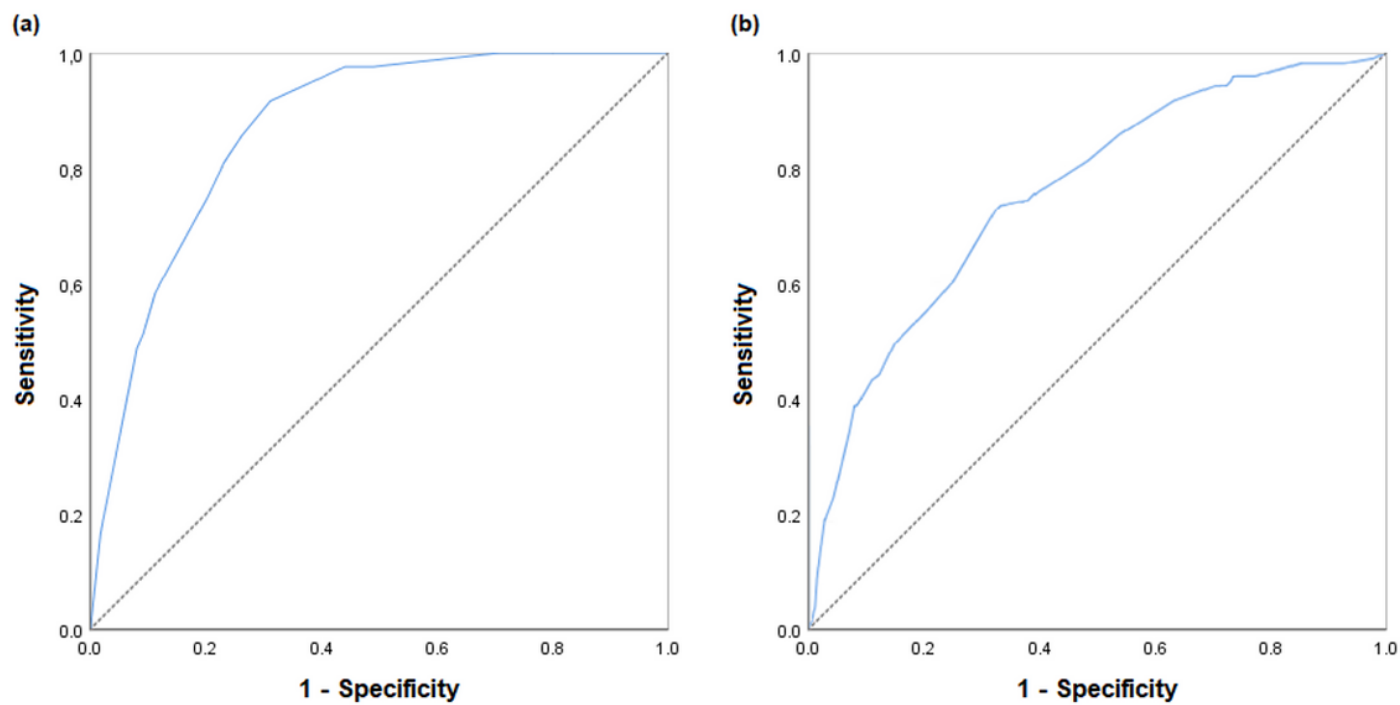
Figure 2

Receiver operating characteristics (ROC) curves for (a) the model of age, ICU admission and arterial pH for in-hospital mortality (area under the curve 0.869), and (b) the model of age, male sex, peripheral oxygen saturation and white blood cell count for invasive mechanical ventilation due to SARS-CoV-2 pneumonia (area under the curve 0.761).