

# Clinical course, biomarkers, management and outcomes of patients hospitalised due to COVID-19 in Colombia

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## Abstract

**Objective:** To analyse the clinic characteristics, risk factors and evolution of the first cohort of hospitalised patients with confirmed infection by COVID-19 in 5 Colombian institutions.

**Materials and methods:** Is a retrospective observational study of consecutive hospitalized patients with a diagnosis of COVID-19 confirmed from March 01 to May 30, 2020 in Colombia.

**Results:** A total of 44 patients were included. The median age was 62 years. 43.2% had a history of smoking, while 69.8% were overweight or obese. 88.6% had at least one comorbidity and 52.3% had three or more comorbidities. Hypertension and dyslipidaemia were the most frequent comorbidities (40.9% and 34.1%, respectively). The 30-day mortality rate was 47.7% with a median of 11 days. The composite outcome occurred in the 36.4%. The biomarkers associated with mortality risk included troponin higher than 14 ng/L (RR: 5.25; 95% CI 1.37-20.1, p = 0.004) and D-dimer higher than 1000 ng/ml (RR: 3.0; 95% CI 1.4-6.3, p = 0.008).

**Conclusions:** The clinical course of SARS-CoV-2 infection in hospitalized Colombian was characterised by a more advanced stage of the infection.

**Keywords:** COVID-19, risk factors, mortality

## Curso clínico, biomarcadores, manejo y desenlaces de pacientes hospitalizados por COVID-19 en Colombia

### Resumen

**Objetivo:** Analizar las características, clínicas, factores de riesgo, y la evolución de pacientes hospitalizados con infección confirmada por COVID-19 en 5 Instituciones de Colombia.

**Material y método:** Es un estudio observacional retrospectivo de pacientes consecutivos hospitalizados con diagnóstico de COVID-19 confirmado entre 01 de Febrero de 2020 y 30 de Mayo de 2020 en Colombia.

**Resultados:** Un total de 44 pacientes fueron incluidos. La mediana de edad fue de 62 años y la mayoría del sexo masculino. El 43.2% tenían historia de tabaquismo, mientras que el 69.8% tenían sobrepeso u obesidad. El 88.6% tenían al menos una comorbilidad y el 52.3% tenían tres o más comorbididades. La hipertensión arterial fue la comorbilidad más frecuente (40.9%), seguido de la dislipidemia (34.1%). La tasa de letalidad a 30 días fue de 47.7% y ocurrió con una mediana de 11 días. El 36.4% presentó el desenlace compuesto. Los biomarcadores asociados con el riesgo de muerte fue troponina > 14 ng/mL (RR:5.25, IC95% 1.37-20.1, p=0.004) y dímero D mayor a 1000 mg/dL (RR: 3.0, IC95% 1.4-6.3, p=0.008).

**Conclusiones:** El curso clínico de la infección por SARS-CoV-2 en colombianos hospitalizados fue un estadio más avanzado de la infección.

**Palabras clave:** COVID-19, Factores de Riesgo, mortalidad

### Introduction

As of December 21, 2019, a group of cases of viral pneumonia had been identified in Wuhan, a metropolitan city in the province of Hubei, China, caused by a new single-stranded RNA virus (SARS-CoV-2) of possible animal origin that has been extensively spreading in humans and causing

respiratory, enteric, hepatic and neurological diseases<sup>1,4</sup>. In February 2020, the World Health Organization designated the disease caused by this virus as COVID-19, which stands for coronavirus disease 2019<sup>1</sup>; COVID-19 has progressively spread and was declared a pandemic on March 11, 2020. COVID-19 has severe impact in terms of morbidity, mortality and costs<sup>2</sup>.

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Worldwide, approximately 15 million confirmed cases of COVID-19 have been reported on all continents, except Antarctica<sup>3</sup>. Latin America and the Caribbean represent the current epicentre of the pandemic due to the vulnerability of some health care systems and considerable heterogeneity in economic, political and social development<sup>4</sup>. Over 6.2 million people have been affected by the disease in this region; Brazil is the most affected country, followed by Peru, Mexico, Chile, Colombia and Argentina<sup>3</sup>. SARS-CoV-2 disease (COVID-19) is predominantly manifested as a lung infection with a range of symptoms characteristic of a mild upper respiratory tract infection; however, 15 to 20% of patients develop severe pneumonia and acute respiratory distress syndrome (ARDS), and 5% of patients develop critical illness associated with shock, cytokine release syndrome, coagulation disorders with consequent multiple organ failure and death<sup>5-7</sup>. The demographic, clinical and laboratory risk factors associated with worse outcomes have been described in the literature; however, the frequency and importance of these factors in the Latin American population have not been described. Our study aims to analyse the clinic characteristics, risk factors and evolution of the first group of hospitalised patients with confirmed COVID-19 infection in 5 institutions in Colombia.

## Materials and method

### Design and population

This is a retrospective longitudinal study of adult patients (> 18 years) diagnosed with SARS-CoV-2/COVID-19 [+] confirmed by real-time reverse transcriptase polymerase chain reaction (RT-PCR) of a nasopharyngeal secretion sample hospitalised in 5 high-complexity hospitals in Colombia and discharged from March 1 to May 30, 2020. The five hospitals were Clínica Universitaria Colombia (Bogotá, Colombia), Clínica Santa María del Lago (Bogotá, Colombia), Clínica Reina Sofía (Bogotá, Colombia), Clínica Iberoamérica (Barranquilla) and Clínica Sebastián de Belalcazar (Cali, Colombia). Patients were recruited consecutively based on compliance with inclusion criteria. Demographic variables, comorbidities, signs and symptoms at admission, chest images, laboratory test, biomarkers, treatment schedules, complications and discharge condition (alive or dead) were extracted from the clinical history.

### Outcomes

The main outcome was the 30-day in-hospital mortality rate; in addition, the composite outcome, defined by a critical care requirement, mechanical ventilation and death, was considered. Other outcomes of interest included frequency of complications, variability in biomarkers and established drug treatment schedules.

**Ethical:** The research was approved by the ethics committee. It is a risk-free study due to its retrospective observational design.

### Data analysis

The quantitative variables were analysed using frequency, mean and variance; the categorical data were analysed using

proportional ratios. Bivariate analysis was performed using  $\chi^2$ -squared statistic tests for independence in 2x2 tables and Fisher's exact test for comparison. Hypotheses were confirmed or rejected at  $p < 0.05$ , which was considered statistically significant. Survival functions of time until the event were used to analyse the complications and lethality by Kaplan-Meier curves starting from diagnosis at admission. Exploratory analysis of the associations between mortality and prognostic biomarkers at admission was performed by estimating the relative risk (RR) and odds ratios (OR) with 95% confidence intervals (95% IC).

Based on the collected information, the score on the national early warning score (NEWS) risk scale<sup>8</sup>), Charlson comorbidity index (CCI)<sup>9</sup> corrected for age, APACHE II<sup>10</sup> and the sequential organ failure assessment (SOFA)<sup>11</sup> were estimated for each patient. All analyses are presented according to variable type.

The data analysed during the study are available <http://dx.doi.org/10.17632/cwrd5ysmzp.1>.

## Results

A total of 44 patients were admitted from March to May 2020 to 5 high-complexity hospitals in Colombia. The median age of the patients was 62 years (IQR: 53-72 years), and 79.5% of the patients were older than 50 years. Table 1 summarises the main demographic and admission characteristics of patients with SARS CoV-2/COVID-19 infection.

The median time between the onset of the symptoms and the first consultation at the emergency department was 7 days (IQR: 3-8 days). Systemic symptoms (general malaise, fatigue, myalgia, arthralgia and general deterioration) were reported in 95.5% of the patients, followed by cough (93.2%), high respiratory symptoms (odynophagia and rhinorrhea) (90.9%) and low respiratory symptoms (dyspnoea, retraction and wheezing) (90.9%). Gastrointestinal symptoms, such as diarrhoea, nausea, abdominal pain and emesis, were present in 45.5% of the patients. Anosmia was reported in 9.1% of the patients. Fever was reported by 70.5% of the patients but was documented on admission only in 20.5%.

The results of the majority of admission laboratory tests were normal. However, 36.4% of the patients had lymphopenia at admission and C-reactive protein (CRP) levels higher than 10 mg/L; 25% of the patients had lactate dehydrogenase (LDH) levels higher than 349.9 U/L, and 56.8% of the patients had LDH levels higher than 214 U/L; 16% of the patients had D-dimer levels higher than 1,000 ng/ml; 18.2% of the patients had troponin levels higher than 14 ng/L; and 13.6% of the patients had ferritin levels higher than 1,000 ng/mL. The temporal trend estimates of CRP, D-dimer and troponin are presented in Figure 1. During follow-up, CRP levels increased according to the reports of the first 4 measurements, and the levels decreased after peaking; the D-dimer levels increased regardless of the outcome of the patients, but the highest

**Table 1.** Demographic and clinical characteristics of patients with COVID-19

	Total N (%)	Severe pneumonia N (%)
General	44 (100)	37 (100)
<b>Sex</b>		
Male	29 (65.9)	26 (70.3)
<b>Age (years)</b>		
20-29	2 (4.5)	2 (5.4)
30-39	4 (9.1)	4 (10.8)
40-49	3 (6.8)	3 (8.1)
50-59	11 (25)	9 (24.3)
60-69	8 (18.2)	5 (13.5)
70-79	13 (29.5)	13 (35.1)
80-89	3 (6.8)	1 (2.7)
BMI (n=43)		(n=36)
Normal	13 (30.2)	11 (30.6)
Overweight	15 (34.9)	12 (33.3)
Obesity I	8 (18.6)	7 (19.4)
Obesity II	4 (9.3)	3 (8.3)
Obesity III	3 (7.0)	3 (8.3)
<b>Comorbidities</b>		
High blood pressure (HBP)	18 (40.9)	15 (40.5)
Dyslipidaemia	15 (34.1)	13 (35.1)
Diabetes	8 (18.2)	8 (21.6)
COPD	8 (18.2)	6 (16.2)
CKD	7 (15.9)	5 (13.5)
Coronary artery disease	6 (13.6)	4 (10.8)
Other <sup>a</sup>	13 (29.5)	9 (24.3)
History of smoking	19 (43.2)	16 (43.2)
<b>Number of comorbidities</b>		
No comorbidity	5 (11.4)	4 (10.8)
One comorbidity	6 (13.6)	4 (10.8)
Two comorbidities	10 (22.7)	10 (27)
Three or more comorbidities	23 (52.3)	19 (51.3)
Diabetes + HBP	6 (13.6)	6 (16.2)
<b>Symptoms at admission</b>		
Systemic	42 (95.5)	36 (97.3)
Cough	41 (93.2)	35 (94.6)
Upper respiratory	40 (90.9)	35 (94.6)
Lower respiratory	40 (90.9)	34 (91.9)
Fever	31 (70.5)	26 (70.3)
Gastrointestinal	20 (45.5)	17 (45.9)
Anosmia	4 (9.1)	3 (8.1)
<b>Chest X-ray</b>		
Normal	2 (4.5)	0
Consolidation	8 (18.2)	7 (18.9)
Ground-glass opacity	17 (38.6)	15 (40.5)
Other	17 (38.6)	15 (40.5)

	Total N (%)	Severe pneumonia N (%)
<b>CAT scan of the chest</b>		
Normal	11 (25)	9 (24.3)
Consolidation	2 (4.5)	2 (5.4)
Ground-glass opacity	25 (56.8)	22 (59.5)
Other	6 (13.6)	4 (10.8)
<b>Vital signs at admission</b>		
Heart rate (bpm)	88 (78 - 100)	88 (78 - 98)
Respiratory rate (bpm)	20 (8 - 22)	20 (18 - 22)
Temperature (°C)	36.8 (36 - 38)	36.8 (36.1 - 37.6)
SBP (mmHg)	124 (108 - 143)	125 (110 - 141)
DBP (mmHg)	78 (69 - 87)	76 (65 - 87)
Saturation (%)	90 (87 - 92)	90 (87 - 92)
Fever (>38) (n, %)	9 (20.5)	6 (16.2)
<b>Laboratory tests at admission</b>		
Leukocytes (10 <sup>6</sup> cells/mL)	8.7 (5.4 - 10.4)	8.82 (6.48 - 10.4)
Lymphocytes (10 <sup>6</sup> cells/mL)	0.9 (0.7 - 1.3)	0.85 (0.65 - 1.08)
Neutrophils (10 <sup>6</sup> cells/mL)	6.79 (4.2 - 8.7)	7.44 (5.24 - 8.72)
Platelets (10 <sup>6</sup> cells/mL)	183.5 (163 - 263)	181 (164 - 246)
Haemoglobin (g/dL)	14.8 (13.6 - 16.2)	14.8 (13.2 - 16.2)
LDH (U/L)	304.5 (249 - 418.5)	311.9 (266.5 - 422)
CRP (mg/L)	134.5 (78.8 - 227.7)	166.11 (109.2 - 256.5)
D-dimer (ng/mL)	498 (368 - 851)	498 (368 - 844)
Troponin (ng/L)	8.5 (6.7 - 18.8)	8.57 (6.9 - 17.4)
AST (U/L)	48.65 (38.4 - 82.7)	48.65 (43 - 82.7)
ALT (U/L)	42.8 (22.3 - 60)	49.15 (31.5 - 60)
Bilirubin (mg/dL)	0.51 (0.4 - 0.7)	0.5 (0.41 - 0.6)
Lactate (mmol/L)	1.33 (1.2 - 1.7)	1.37 (1.2 - 1.6)
Creatinine (mg/dL)	0.97 (0.8 - 1.1)	0.97 (0.74 - 1.1)
Leukocyte/lymphocytes	7.6 (4.9 - 17.1)	8.5 (5.7 - 17.5)
<b>Prognostic biomarkers</b>		
Lymphopenia (<0.8)	16 (36.4)	15 (40.5)
CRP (>10 mg/dL)	16 (36.4)	16 (43.2)
ALT (2 to 5 times)	3 (6.8)	2 (5.4)
AST (2 to 5 times)	5 (11.4)	4 (10.8)
D-dimer (>1000 ng/mL)	7 (15.9)	6 (16.2)
D-dimer (>3000 ng/mL)	2 (4.5)	1 (2.7)
Troponin (>14 ng/L)	8 (18.2)	7 (18.9)
Ferritin (>1000 ng/mL)	6 (13.6)	6 (16.2)
LDH (>350 U/L)	11 (25)	11 (29.7)
LDH (>214 U/L)	25 (56.8)	22 (59.5)

BMI: Body Mass Index; HBP: high blood pressure; COPD: chronic obstructive pulmonary disease; CKD: chronic kidney disease; Dis. disease; LDH: lactate dehydrogenase; CRP: C-reactive protein; ALT: alanine transaminase; AST: aspartate transaminase; CAT: computerised axial tomography. <sup>a</sup>Includes apnoea, heart failure, neoplasms, asthma, arthritis and chronic liver disease.

values were observed in deceased patients. The follow-up of the troponin levels indicated differential results between living and deceased patients, with the troponin levels increasing slightly over time in living discharged patients.

In the follow-up period, 21 deaths occurred, representing a 30-day mortality rate of 47.7%; median time to fatal outcome was 11 days (IQR: 5-21) (Figure 2), and the average time was 15.9 days. A composite outcome (intensive care unit (ICU), mechanical ventilation and death) was present in 36.4% of the patients and was more frequent in men from 70 to 79 years of age with grade I obesity, a history of smoking, high blood pressure and dyslipidaemia. A total of 84.1% of patients required support in the ICU for a median of 2 days (IQR: 1-4) from admission to the emergency room to transfer to the ICU; 70.5% of the patients required invasive ventilator support for a median of 2 days (IQR: 1-4). A total of 27.3% patients required renal support therapy (RST), which corresponds to 12 patients with severe pneumonia. The outcomes are presented in Table 2.

The most common complications included ARDS (65.9%), septic shock (61.4%), cardiovascular complications (54.5%), multiple systemic organ failure (52.3%), acute kidney injury (45.5%) and neurological complications (45.5%). A total of 72.2% patients with severe pneumonia had ARDS, and 51.4% of these patients died. All fatal cases had cardiovascular complications. A total of 55% of the patients with acute kidney injury died.

Exploratory analysis of mortality associated with biomarkers at admission indicated a higher risk associated with troponin levels higher than 14 ng/mL (RR: 5.25; 95% CI 1.37-20.1,  $p = 0.004$ ), D-dimer levels higher than 1000 ng/ml (RR: 3.0; 95% CI 1.4-6.3) and CRP levels higher than 10 mg/L (RR: 5.5; 95% CI 0.42-1.6,  $p = 0.009$ ); the results are presented in Table 3.

Estimation of the risk scales at admission involved the CCI, which could be calculated for all patients; 32 had sufficient information for SOFA and APACHE-II, and 43 had enough information for the NEWS scale. The median NEWS value was 7 points (IQR: 5-8), the median SOFA score was 6 points (IQR: 2.5-10), the median APACHE-II score was 25 points (IQR: 15-40), and the median CCI was 2 points (IQR: 1-4). Nine patients were classified with zero points on the CCI, 15 patients had CCI from 1 to 2, 11 patients had CCI from 3 to 4, and 9 patients had CCI of 5 or higher. According to the American Thoracic Society (ATS) classification, 96.6% of the patients had severe pneumonia, and the median time to death in these patients was 13.5 days (IQR: 8.5-21.5 days).

Treatment of SARS-CoV-2 infection was achieved by implementation of the schemes based on antibiotics (90.9%) and antimalarial agents in combination with antiviral agents (72.7%). Two patients who had positive indications for influenza were treated with oseltamivir, and both patients died. A total of 37 patients had severe pneumonia; 30 of these patients received hydroxychloroquine plus ritonavir/lopinavir, and 36 patients were treated with antibiotics. In addition, 11 of the deceased

**Table 2.** Outcomes and complications

Outcome		Total N (%)	
Mortality		21 (47.7)	
IMV		31 (70.5)	
ICU		37 (84.1)	
Composite		16 (36.4)	
Complications	Total N (%)	Severe pneumonia N (%)	Mortality N (%)
ARDS	29 (65.9)	27 (73)	19 (90.5)
Septic Shock	27 (61.4)	25 (67.6)	18 (85.7)
Cardiovascular	24 (54.5)	20 (54.1)	21 (100)
Multisystemic failure	23 (52.3)	21 (56.8)	17 (81)
Acute kidney injury	20 (45.5)	18 (48.6)	11 (52.4)
Neurological	20 (45.5)	19 (51.4)	9 (42.9)
Gastrointestinal	13 (29.5)	11 (29.7)	9 (42.9)
Thrombotic conditions	4 (9.1)	3 (8.1)	4 (19)

IMV: invasive mechanical ventilation; ICU: intensive care unit; ARDS: Acute respiratory distress syndrome

patients received hydroxychloroquine plus ritonavir/lopinavir, and 19 patients received antibiotics. In patients with a composite outcome, 56.5% received hydroxychloroquine plus an antiviral agent, 62.5% received chloroquine plus an antiviral agent, and 93.8% received an antibiotic.

The median overall hospital stay was 13 days (IQR: 8-22.5 days). The average hospital stay was 6.4 days (SD: 6.8 days), and the average ICU stay was 11.6 days (SD: 11.5 days).

## Discussion and conclusions

In Colombia, the first case of SARS-CoV-2 infection was reported on March 6, and the first death occurred 10 days later; however, the clinical course of patients with SARS-CoV-2 infection has not been documented in Colombia. By mid-July 2020, 218,000 confirmed cases had been registered in Colombia, and 10% of the cases required admission to the hospital<sup>12</sup>.

The baseline characteristics of the study population are similar to those of previously published epidemiological studies with a slightly higher age of hospitalisation than that reported in the initial studies in China (49 years in the initial Huang report<sup>7</sup> and from 55 to 56 years in the subsequent reports by Xu<sup>13</sup> and Wang<sup>14</sup>). In subsequent studies in Italy, Spain and New York, the median age of the population was the same as that reported in our study<sup>6,15,16</sup>.

In patients admitted 7 days after the onset of the symptoms, the most common complaints included general discomfort, cough, fatigue, dyspnoea and, to a lesser extent, odynophagia, vomiting, headache and anosmia, which matches the symptoms reported in the studies in China<sup>7,13,14</sup>. It should be noted that in our group of patients, fever was documented only in

**Table 3.** Relative risk and odds ratio of death according to biomarkers of risk at admission

Biomarker	Mortality		RR (95% CI)	P	OR (95% CI)	P
	Yes	No				
Lymphopenia (<0.8)	7	9	0.83 (0.42 - 1.6)	0.6	0.71 (0.16 - 3.07)	0.6
No	12	11				
CRP (>10 mg/dL)	11	5	5.5 (0.85 - 35.4)	0.009	15.4 (1.32 - 755)	0.009
No	1	7				
ALT (2 to 5 times)	2	1	1.77 (0.64 - 4.93)	0.34	3.33 (0.13 - 215)	0.34
No	6	10				
AST (2 to 5 times)	3	2	1.68 (0.61 - 4.58)	0.34	2.7 (0.2 - 40.8)	0.34
No	5	9				
D-dimer (>1000 ng/mL)	6	1	3 (1.4 - 6.3)	0.008	15 (1.24 - 734.4)	0.008
No	6	15				
D-dimer (>3000 ng/mL)	2	0	2.6 (1.6 - 4.22)	0.09	NC	NC
No	10	16				
Troponin (>14 ng/mL)	6	2	5.25 (1.37 - 2.01)	0.004	18 (1.5 - 268.7)	0.004
No	2	12				
Ferritin (>1000 ng/mL)	3	3	1.5 (0.37 - 5.99)	0.55	2 (0.12 - 37.9)	0.55
No	2	4				
LDH (>350 U/L)	6	5	1.96 (0.78 - 4.9)	0.15	3.12 (0.5 - 19.8)	0.14
No	5	13				
LDH (>214 U/L)	10	15	1.6 (0.27 - 9.33)	0.33	2 (0.13 - 115.3)	0.56
No	1	3				

RR: relative risk; p: p-value; OR: odds ratio; NC: not calculated

20.5% of the patients on admission; however, 70% had fever previously. The frequency of fever varies among the studies; in the largest cohort in Europe, fever was present in 45.4% of the cases<sup>15</sup>, while in China, fever was present in more than 80% of the cases<sup>17-19</sup>. In a study of 1,099 hospitalised patients, Guan et al. reported the presence of fever in 44% of the cases at hospital admission<sup>20</sup>. A total of 93% of the patients had a cough in our study; in other studies, the incidence of cough varied from 48.7% to 65.5%<sup>15,17,19,21</sup>. Dyspnoea was present in 85% of the patients with severe pneumonia, in contrast with the meta-analysis and systematic review of Zhao et al., which reported dyspnoea in 44.2% of patients with severe pneumonia (95% CI: 7.8-80.6) and in 5.7% of patients with non-severe infection (95% CI: 0-10.7%)<sup>22</sup>; moreover, dyspnoea has been reported as a marker of severe and progressive disease<sup>23-25</sup>.

Strikingly, anosmia was only reported by 4 people; however, Menni et al. reported that loss of smell can be a frequent symptom, and anosmia accompanied by fever, fatigue, persistent cough, diarrhoea, abdominal pain and loss of appetite can predict COVID-19 with a specificity of 0.83 (95% CI: 0.81-0.86) and a sensitivity of 0.55 (95% CI: 0.50-0.59)<sup>26</sup>. It is likely that the availability of additional information on the anamnesis of the disease will place a higher emphasis on this symptom and that the incidence of anosmia will be higher than that described in the present study. Similarly, gastrointestinal symptoms occurred in less than 30% of the cases; however, it has been reported that diarrhoea and nausea can precede fever and lower respiratory tract symptoms<sup>27</sup>.

Older adults and people with pre-existing comorbidities, particularly cardiovascular diseases, high blood pressure and diabetes mellitus, have a significant risk of progression, complications and death<sup>28-30</sup>. In our study, 79.5% of the patients were older

than 50 years, and 75% of the patients were affected with more than 2 comorbidities; the most frequent comorbidities included obesity, high blood pressure, dyslipidaemia, diabetes and a history of smoking. The overall in-hospital mortality of the patients over 60 years of age was 66.7%. These data are similar to the results of Liu et al., who reported a higher risk of disease progression and death in people older than 60 years (OR: 8.5; 95% CI: 1.6-44.8), with a history of smoking (OR: 14.2; 95% CI: 1.5-25) and with respiratory failure (OR: 8.7; 95% CI: 1.9-40)<sup>31</sup>. Similarly, Wu et al. reported a higher case-fatality rate among older adults: ( $\geq 80$  years: 14.8%; 70-79 years: 8.0%; 60-69 years: 3.6%) and among patients with comorbidities, including 10.5% for cardiovascular diseases, 7.3% for diabetes, 6.3% for chronic respiratory diseases, 6.0% for high blood pressure and 5.6% for cancer<sup>29</sup>. In a cohort study in the United States, the United States Centers for Disease Control and Prevention (CDC) COVID-19 response team reported higher mortality in people aged  $\geq 85$  years (range 10%-27%), followed by 3%-11% mortality for ages from 65 to 84 years<sup>30</sup>. As of the current date (July 20, 2020), among all cases of death in Colombia (6,736), the most frequent comorbidities were diabetes mellitus (26.2%), chronic kidney disease (14.8%) and cancer (10.3%). A substantial increase in mortality was observed in older people<sup>12</sup>.

Unlike reported previously in other studies, 37 (84.1%) of 44 patients in the present study developed severe pneumonia and required intensive care management, and 31 patients required mechanical ventilation within 2 days after admission to the hospital. These data differ from data in preliminary reports from China, which indicated a range of 26% to 32% of patients requiring ICU management<sup>13,14,28</sup>. In the United States, the CDC reported an incidence of ICU admission from 7 to 26%<sup>30</sup>, while in Italy, 12% of all detected cases of COVID-19 and 16% of all hospitalised patients were treated in the ICU<sup>32,33</sup>.

The high incidence of ICU admission in our cohort of hospitalised patients may be related to a higher severity of clinical manifestations at admission; the majority of the patients were admitted 1 week after the onset of symptoms, which corresponds to the period of maximum alert for the risk of clinical deterioration<sup>7,14,34,35</sup>. This situation has important implications for health care systems. The overall data for Colombia revealed that approximately 55% of deaths occurred within the first 10 days after hospitalisation<sup>12</sup>, which reaffirms this finding and indicates a need for early detection of the patients at risk of complications. The mortality of the patients admitted to the ICU was 51.3%; however, mortality varied from 39% to 72% depending on the study and is associated with age, comorbidities and complications<sup>27,28,34,35</sup>.

Similar to the cohorts reported in the previous studies, common laboratory test abnormalities of hospitalised patients with COVID-19 included lymphopenia and elevated levels of CRP, LDH and troponin<sup>14,20,36</sup>. Lymphopenia is a marker of impaired cellular immunity and has been reported in 67-90% of the patients with COVID-19<sup>7,37,38</sup>. Elevated levels of D-dimer at admission, as in our patients, have been reported in 46% of hospitalised patients with a longitudinal increase during the hospital stay; in our study, D-dimer levels higher than 1000 ng/mL were significantly associated with an increased risk of mortality<sup>20,28,34,39</sup>.

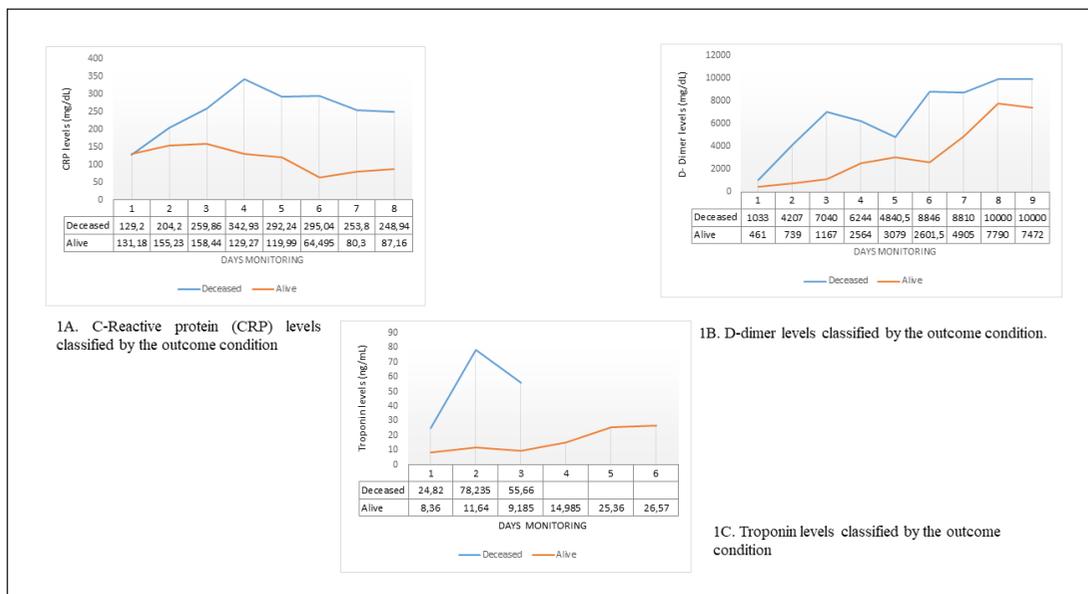
Similar to the previous reports, the radiographic findings mainly included ground-glass opacities and parenchymal consolidations, and only a single patient had normal chest radiography; however, reports of normal chest radiography at the beginning of the disease are frequent<sup>20,40</sup>. On admission, 11 of the 44 patients in our cohort had a normal chest computed tomography (CT) result, and 9 of the patients had severe pneumonia with bilateral ground-glass opacity, thus confirming previously reported observations<sup>41-43</sup>. Considering the variability of the radiographic findings in the CT due to the

evolution time and severity of the disease, the American College of Radiology does not recommend CT as a first-line test for the diagnosis of COVID-19<sup>44</sup>, and the Radiological Society of North America has suggested categorisation of the images to standardise the interpretation and reporting<sup>45</sup>. These guidelines match the observations of the previous studies in critically ill patients<sup>20,46-48</sup>. In patients who developed severe pneumonia, the mean time to dyspnoea ranged from 5 to 8 days, the median time to ARDS ranged from 8 to 12 days, and the mean time to admission to the ICU varied from 10 to 12 days<sup>7,14,34,35</sup>.

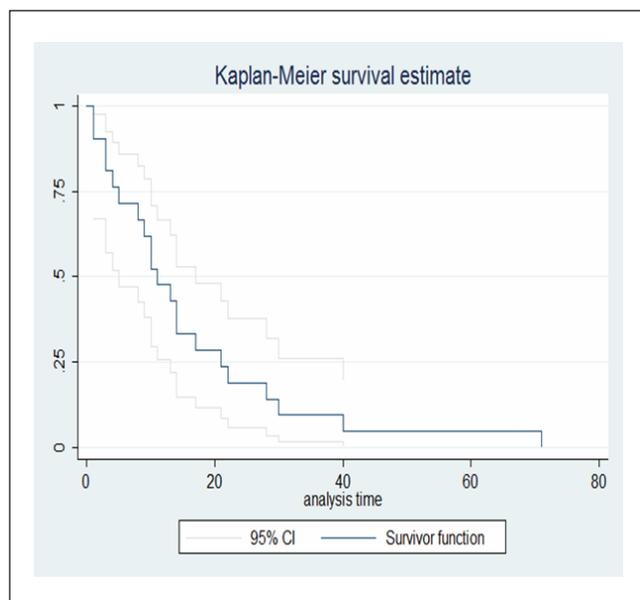
Similar to previous reports, ARDS was the main complication in our patients. ARDS developed in 65.6% of the patients, and 26 patients required mechanical ventilation with 65.5% mortality, which was increased concomitant to the severity of the disease; older patients with comorbidities had a higher probability of mortality<sup>5,39,49</sup>. Acute kidney injury was present in 45.4% of the cases, and renal replacement therapy was indicated in 27.2% of the cases; this is a frequent complication detected in approximately 20-40% of the patients admitted to the ICU<sup>5,50,51</sup>. Therefore, prevention of nephrotoxicity and early detection are very important to establish a timely treatment that impacts morbidity and mortality.

The majority of the patients were treated with antiviral drugs and antibiotic therapy according to the recommendations approved and enforced during the period of the study. In vitro studies with chloroquine or hydroxychloroquine have shown antiviral activity; however, the available evidence has not confirmed the benefits of these antimalarial drugs in patients with SARS-CoV-2/COVID-19 infection<sup>52-54</sup>. Support measures and comprehensive management in hospitalised patients can reduce complications and mortality<sup>55</sup>.

Our study has certain limitations: (i) the study has inherent limitations by design since it is a purely descriptive study



**Figure 1.** Time-dependent changes in C-reactive protein, D-dimer and troponin levels in hospitalised patients with SARS CoV-2/COVID-19



**Figura 2.** Overall survival in patients with SARS-CoV-2/COVID-19

in a small sample without any permissible inference to the general population; however, it provides an overview of the epidemiological situation in hospitalised patients with SARS-CoV-2/COVID-19 infection in Latin America, mainly in Colombia; (ii) at the moment of data collection, Latin America was not at the epicentre of the pandemic; (iii) in the case of some estimates, information was not available for all patients, which may incur a bias because availability of this information can be related to more severe manifestation of the disease and/or transfer to the ICU, where strict monitoring of the patients is performed.

Finally, the clinical course of SARS-CoV-2 infection diagnosis confirmed by RT-PCR in Colombian patients admitted to a high-complexity hospital was similar to that reported in the literature; however, the population was characterised by a more advanced stage of the infection. This report provides a snapshot of the pattern of the pandemic in Colombia and Latin America to guide strategic and clinical decision making and public health policies to ensure reduced potential impact for patients, institutions and the health system.

## Responsabilidades éticas

**Protección de personas y animales:** Los autores declaran que en este artículo no se hicieron experimentos con humanos o animales.

**Confidencialidad de los datos:** Los autores declaran que han seguido los protocolos de su centro de trabajo sobre la publicación de datos de pacientes.

**Derecho a la privacidad y consentimiento informado:** Los autores declaran que en este artículo no aparecen datos de pacientes.

**Conflictos de interés:** Los autores declaran no tener conflictos de interés.

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## Bibliography

1. World Health Organization (WHO). WHO Director-General's remarks at the media briefing on 2019-nCoV on 11 February 2020. 2020.
2. World Health Organization (WHO). WHO Pandemic Phases [Internet]. 2020. Available from: [https://www.who.int/influenza/resources/documents/pandemic\\_phase\\_descriptions\\_and\\_actions.pdf](https://www.who.int/influenza/resources/documents/pandemic_phase_descriptions_and_actions.pdf)
3. Dong E, Du H, Gardner L. An interactive web-based dashboard to track COVID-19 in real time. *Lancet Infect Dis* [Internet]. 2020;20(5):533–4. Available from: [http://dx.doi.org/10.1016/S1473-3099\(20\)30120-1](http://dx.doi.org/10.1016/S1473-3099(20)30120-1)
4. Rodriguez-Morales AJ, Gallego V, Escalera-Antezana JP, Méndez CA, Zambrano LI, Franco-Paredes C, et al. COVID-19 in Latin America: The implications of the first confirmed case in Brazil. Vol. 35, *Travel medicine and infectious disease*. 2020. p. 101613. Doi: 10.1016/j.tmaid.2020.101613
5. 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* [Internet]. 2020 May 26;323(20):2052–9. Doi:10.1001/jama.2020.6775
6. 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* [Internet]. 2020 Apr 28;323(16):1574–81. Doi:10.1001/jama.2020.5394
7. 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(10223):497–506. Doi: 10.1016/S0140-6736(20)30183-5
8. Royal College of Physicians. National Early Warning Score (NEWS): Standardising the assessment of acute illness severity in the NHS. Royal College of Physicians. 2012.
9. 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(5):373–83.
10. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. *Crit Care Med*. 1985 Oct;13(10):818–29.
11. Vincent JL, Moreno R, Takala J, Willatts S, De Mendonça A, Bruining H, et al. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. On behalf of the Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine. Vol. 22, *Intensive care medicine*. United States; 1996. p. 707–10.
12. Instituto Nacional de Salud (INS). Coronavirus (COVID - 2019) en Colombia [Internet]. 2020. Available from: <https://www.ins.gov.co/Noticias/Paginas/Coronavirus.aspx>
13. Xu X, Wu X, Jiang XG. Clinical findings in a group of patients infected with the 2019 novel coronavirus (SARS-Cov-2) outside of Wuhan, China: retrospective case series. *BMJ* [Internet]. 2020 Feb 27;368:m792. Available from: <http://www.bmj.com/content/368/bmj.m792.abstract>
14. 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* [Internet]. 2020 Mar 17;323(11):1061–9. Available from: <https://doi.org/10.1001/jama.2020.1585>
15. Lechien JR, Chiesa-Estomba CM, Place S, Van Laethem Y, Cabaraux P, Mat Q, et al. Clinical and epidemiological characteristics of 1420 European patients with mild-to-moderate coronavirus disease 2019. *J Intern Med* [Internet]. 2020 Apr 30;n/a(n/a). doi:10.1111/joim.13089
16. Aggarwal S, Garcia-Telles N, Aggarwal G, Lavie C, Lippi G, Henry BM. Clinical features, laboratory characteristics, and outcomes of patients hospitalized with coronavirus disease 2019 (COVID-19): Early report from the United States. *Diagnosis (Berlin, Ger)*. 2020;7(2):91–6. Doi: 10.1515/dx-2020-0046
17. Feng Y, Ling Y, Bai T, Xie Y, Huang J, Li J, et al. COVID-19 with Different Severities: A Multicenter Study of Clinical Features. *Am J Respir Crit Care Med*. 2020;201(11):1380–8. doi: 10.1164/rccm.202002-0445OC

18. Lechien JR, Chiesa-Estomba CM, De Siaty DR, Horoi M, Le Bon SD, Rodriguez A, et al. Olfactory and gustatory dysfunctions as a clinical presentation of mild-to-moderate forms of the coronavirus disease (COVID-19): a multicenter European study. *Eur Arch Oto-Rhino-Laryngology* [Internet]. 2020;277(8):2251–61. Doi:10.1007/s00405-020-05965-1
19. Chen L, Deng C, Chen X, Zhang X, Chen B, Yu H, et al. Ocular manifestations and clinical characteristics of 534 cases of COVID-19 in China: A cross-sectional study. *medRxiv* [Internet]. 2020 Jan 1;2020.03.12.20034678. doi: 10.1111/aos.14472
20. 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* [Internet]. 2020 Feb 28;382(18):1708–20. Doi:10.1056/NEJMoa2002032
21. Sun L, Shen L, Fan J, Gu F, Hu M, An Y, et al. Clinical features of patients with coronavirus disease 2019 from a designated hospital in Beijing, China. *J Med Virol* [Internet]. 2020 May 5;n/a(n/a). doi:10.1002/jmv.25966
22. Zhao X, Zhang B, Li P, Ma C, Gu J, Hou P, et al. Incidence, clinical characteristics and prognostic factor of patients with COVID-19: a systematic review and meta-analysis [Internet]. *medRxiv*; 2020. Doi: 10.1101/2020.03.17.20037572
23. Tian S, Hu N, Lou J, Chen K, Kang X, Xiang Z, et al. Characteristics of COVID-19 infection in Beijing. *J Infect* [Internet]. 2020;80(4):401–6. Doi: /10.1016/j.jinf.2020.02.018
24. Yang W, Cao Q, Qin L, Wang X, Cheng Z, Pan A, et al. Clinical characteristics and imaging manifestations of the 2019 novel coronavirus disease (COVID-19): A multi-center study in Wenzhou city, Zhejiang, China. *J Infect*. 2020 Apr;80(4):388–93. Doi: 10.1016/j.jinf.2020.02.016
25. Chen J, Qi T, Liu L, Ling Y, Qian Z, Li T, et al. Clinical progression of patients with COVID-19 in Shanghai, China. *J Infect* [Internet]. 2020;80(5):e1–6. Available from: <https://doi.org/10.1016/j.jinf.2020.03.004>
26. Menni C, Valdes A, Freydin MB, Ganesh S, El-Sayed Moustafa J, Visconti A, et al. Loss of smell and taste in combination with other symptoms is a strong predictor of COVID-19 infection. *medRxiv* [Internet]. 2020 Jan 1;2020.04.05.20048421. doi: 10.1038/s41591-020-0916-2
27. Pan L, Mu M, Yang P, Sun Y, Wang R, Yan J, et al. Clinical Characteristics of COVID-19 Patients With Digestive Symptoms in Hubei, China: A Descriptive, Cross-Sectional, Multicenter Study. *Off J Am Coll Gastroenterol | ACG* [Internet]. 2020;115(5). Doi: 10.14309/ajg.0000000000000620
28. Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, et al. Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China. *JAMA Intern Med* [Internet]. 2020 Jul 1;180(7):934–43. Available from: <https://doi.org/10.1001/jamainternmed.2020.0994>
29. Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention. *JAMA* [Internet]. 2020 Apr 7;323(13):1239–42. Available from: <https://doi.org/10.1001/jama.2020.2648>
30. CDC COVID-19 Response Team. Severe Outcomes Among Patients with Coronavirus Disease 2019 (COVID-19) — United States, February 12–March 16, 2020. *MMWR Morb Mortal Wkly Rep* 2020. 2020;69(12):343–6.
31. Liu W, Tao Z-W, Wang L, Yuan M-L, Liu K, Zhou L, et al. Analysis of factors associated with disease outcomes in hospitalized patients with 2019 novel coronavirus disease. *Chin Med J (Engl)* [Internet]. 2020 May 5;133(9):1032–8. doi: 10.1097/CM9.0000000000000775
32. Onder G, Rezza G, Brusaferro S. Case-Fatality Rate and Characteristics of Patients Dying in Relation to COVID-19 in Italy. *JAMA*. 2020 Mar. doi:10.1001/jama.2020.4683
33. Grasselli G, Pesenti A, Cecconi M. Critical Care Utilization for the COVID-19 Outbreak in Lombardy, Italy: Early Experience and Forecast During an Emergency Response. *JAMA* [Internet]. 2020 Apr 28;323(16):1545–6. Available from: <https://doi.org/10.1001/jama.2020.4031>
34. 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* [Internet]. 2020;395(10229):1054–62. Available from: [http://dx.doi.org/10.1016/S0140-6736\(20\)30566-3](http://dx.doi.org/10.1016/S0140-6736(20)30566-3)
35. Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *Lancet Respir Med* [Internet]. 2020;8(5):475–81. Available from: [http://dx.doi.org/10.1016/S2213-2600\(20\)30079-5](http://dx.doi.org/10.1016/S2213-2600(20)30079-5)
36. Goyal P, Choi J, Pinheiro L. Clinical Characteristics of Covid-19 in China. *Nejm*. 2020;100(1):1–3. DOI: 10.1056/NEJMc2005203
37. Goyal P, Choi JJ, Pinheiro LC, Schenck EJ, Chen R, Jabri A, et al. Clinical Characteristics of Covid-19 in New York City. *N Engl J Med* [Internet]. 2020 Apr 17;382(24):2372–4. Available from: <https://doi.org/10.1056/NEJMc2010419>
38. Terpos E, Ntanasis-Stathopoulos I, Elalamy I, Kastritis E, Sergentanis TN, Politou M, et al. Hematological findings and complications of COVID-19. *Am J Hematol* [Internet]. 2020 Jul 1;95(7):834–47. Available from: <https://doi.org/10.1002/ajh.25829>
39. Petrilli CM, Jones SA, Yang J, Rajagopalan H, O'Donnell L, Chernyak Y, et al. Factors associated with hospital admission and critical illness among 5279 people with coronavirus disease 2019 in New York City: prospective cohort study. *BMJ* [Internet]. 2020 May 22;369:m1966. DOI: 10.1136/bmj.m1966
40. Shi H, Han X, Jiang N, Cao Y, Alwalid O, Gu J, et al. Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: a descriptive study. *Lancet Infect Dis* [Internet]. 2020;20(4):425–34. Available from: [http://dx.doi.org/10.1016/S1473-3099\(20\)30086-4](http://dx.doi.org/10.1016/S1473-3099(20)30086-4)
41. Zhao W, Zhong Z, Xie X, Yu Q, Liu J. Relation Between Chest CT Findings and Clinical Conditions of Coronavirus Disease (COVID-19) Pneumonia: A Multicenter Study. *Am J Roentgenol* [Internet]. 2020 Mar 3;214(5):1072–7. Available from: <https://doi.org/10.2214/AJR.20.22976>
42. Bernheim A, Mei X, Huang M, Yang Y, Fayad ZA, Zhang N, et al. Chest CT Findings in Coronavirus Disease-19 (COVID-19): Relationship to Duration of Infection. *Radiology* [Internet]. 2020 Feb 20;295(3):200463. Available from: <https://doi.org/10.1148/radiol.2020200463>
43. Cao Y, Liu X, Xiong L, Cai K. Imaging and clinical features of patients with 2019 novel coronavirus SARS-CoV-2: A systematic review and meta-analysis. *J Med Virol* [Internet]. 2020 Apr 3;n/a(n/a). Available from: <https://doi.org/10.1002/jmv.25822>
44. American College of Radiology A. ACR Recommendations for the use of Chest Radiography and Computed Tomography (CT) for Suspected COVID-19 Infection. 2020.
45. Simpson S, Kay FU, Abbara S, Bhalla S, Chung JH, Chung M, et al. Radiological Society of North America Expert Consensus Statement on Reporting Chest CT Findings Related to COVID-19. Endorsed by the Society of Thoracic Radiology, the American College of Radiology, and RSNA. *Radiol Cardiothorac Imaging* [Internet]. 2020 Mar 25;2(2):e200152. Available from: <https://doi.org/10.1148/ryct.2020200152>
46. Lauer SA, Grantz KH, Bi Q, Jones FK, Zheng Q, Meredith HR, et al. The Incubation Period of Coronavirus Disease 2019 (COVID-19) From Publicly Reported Confirmed Cases: Estimation and Application. *Ann Intern Med* [Internet]. 2020 Mar 10;172(9):577–82. Available from: <https://doi.org/10.7326/M20-0504>
47. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia. *N Engl J Med* [Internet]. 2020 Jan 29;382(13):1199–207. Available from: <https://doi.org/10.1056/NEJMoa2001316>
48. 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* [Internet]. 2020;395(10223):507–13. Available from: [http://dx.doi.org/10.1016/S0140-6736\(20\)30211-7](http://dx.doi.org/10.1016/S0140-6736(20)30211-7)
49. Liu Y, Sun W, Li J, Chen L, Wang Y, Zhang L, et al. Clinical features and progression of acute respiratory distress syndrome in coronavirus disease 2019. *medRxiv* [Internet]. 2020 Jan 1;2020.02.17.20024166. doi: 10.1101/2020.02.17.20024166
50. Cheng Y, Luo R, Wang K, Zhang M, Wang Z, Dong L, et al. Kidney disease is associated with in-hospital death of patients with COVID-19. *Kidney Int* [Internet]. 2020 May;97(5):829–38. Doi: 10.1016/j.kint.2020.03.005
51. 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* [Internet]. 2020;395(10239):1763–70. Available from: [http://dx.doi.org/10.1016/S0140-6736\(20\)31189-2](http://dx.doi.org/10.1016/S0140-6736(20)31189-2)
52. Chacón, K, Pinzón C, Barrera A, Low E, Yomayusa N. Eficacia y seguridad de cloroquina, hidroxicloroquina y azitromicina en pacientes con COVID-19: Resumen de evidencia. *Rev Colomb Nefrol*. 2020;7(1). Doi: 10.22265/acnef.7.Supl.2.469
53. World Health Organization (WHO). WHO discontinues hydroxychloroquine and lopinavir/ritonavir treatment arms for COVID-19 [Internet]. 2020. Available from: <https://www.who.int/news-room/detail/04-07-2020-who-discontinues-hydroxychloroquine-and-lopinavir-ritonavir-treatment-arms-for-covid-19#:~:text=WHO today accepted the recommendation,19 treatment for hospitalized patients.>
54. RECOVERY Collaborative Group. Effect of Hydroxychloroquine in Hospitalized Patients 4 with COVID-19: Preliminary results from a 5 multi-center, randomized, controlled trial. 2020.
55. Liu K, Fang Y-Y, Deng Y, Liu W, Wang M-F, Ma J-P, et al. Clinical characteristics of novel coronavirus cases in tertiary hospitals in Hubei Province. *Chin Med J (Engl)* [Internet]. 2020;133(9). Doi: 10.1097/CM9.0000000000000744