Clinical outcomes of patients hospitalized for COVID-19 and evidence-based on the pharmacological management reduce mortality in a region of the Colombian Caribbean

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**A R T I C L E   I N F O**

**A B S T R A C T**

**Introduction:** Despite the high volume of infections, some clinical aspects of this disease are still unknown. There are currently no studies in Colombia that describe the disease’s clinical and treatment aspects in detail.

**Objective:** Describe the characteristics and clinical management of a group of admitted patients with SARS-CoV-2 infection in a private clinic in Montería, Córdoba-Colombia.

**Patients and methods:** A descriptive observational study was carried out between May and August 2020 in 209 hospitalized patients with a confirmed diagnosis of COVID-19. Upon admittance, clinical, sociodemographic characteristics, comorbidities, and complications were analyzed. Additionally, the effect of the following medications was described: 1—antibiotics (cefepime, piperacillin, tazobactam, meropenem, vancomycin) + low molecular weight heparin (LMWH) + corticosteroids (dexamethasone–methylprednisolone) + colchicine. 2—Antibiotic + LMWH + corticosteroids. 3—LMWH + corticosteroids. 4—LMWH + corticosteroids + colchicine. 5—Other treatments (Tocilizumab).

**Results:** 107 (51%) of the 209 patients with a confirmed diagnosis of COVID-19 passed away. The main comorbidities related to mortality of these hospitalized patients with COVID-19 were obesity and kidney disease (P < 0.05). The main complications associated with fatal outcomes in this group of patients were Acute Respiratory Distress Syndrome (ARDS) and sepsis (P < 0.05). Furthermore, it was evidenced that the colchicine combination showed a significant difference in reducing mortality in hospitalized patients compared to the other therapeutic regimens (P < 0.05).

**Conclusion:** A mortality rate of 51% was found attributable to several factors such as advanced age, obesity, kidney disease, and an average time in days of late consultation. The implementation of the colchicine combination could reduce the mortality rate in this disease.

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**Introduction**

The Annual Report on Global Preparedness from the World Health Organization (WHO) for September 2019 [1] warned of the: “Imminent possibility of a pandemic caused by a lethal respiratory pathogen.” The warning became real in December 2019 with the appearance of a new Coronavirus in Wuhan, China. The new coronavirus quickly crossed geographic boundaries through Asia, Europe, and the Americas. The recent Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) has caused 6,000,000 infections and approximately 1,500,000 deaths [2], with a fatality rate of 3.6%. In Colombia, the number of infections is 1,225,490 cases and 34,761 deaths. The fatality rate is 3.3. In the department of Córdoba, the number of infections is 27,704 and 1,225 deaths with a fatality rate of 7.6% [3].

The disease was unknown before its first outbreak in Wuhan, China. SARS-CoV-2 manifests in flu-like symptoms such as fever,
cough, dyspnea, myalgia, and fatigue. Sudden loss of smell and taste is characteristic of Coronavirus disease 2019 (COVID-19) [4]. In severe cases, it is characterized by pneumonia, acute respiratory distress syndrome, sepsis, and septic shock, leading to death in around 3% of those infected [4]. Although there is currently a high volume of infections, some clinical aspects of the disease remain unknown. There are no studies in Colombia that describe, in detail, the clinical and treatment aspects of the disease.

The main goal of this study is to describe the characteristics and clinical management of a group of hospitalized patients with SARS-CoV-2 infection in a private clinic in Montería, Córdoba-Colombia.

Patients and methods

Type of study and patients

A descriptive observational study was carried out between May and August 2020 in patients with a confirmed diagnosis of COVID-19. Two hundred nine admitted patients with clinical manifestations compatible with SARS-CoV-2 infection were included. The clinical and sociodemographic characteristics, comorbidities, and complications were analyzed (Fig. 1).

Study site

This study was carried out in the State of Córdoba in the Caribbean northwest region. The capital of the State is Montería, with a population of 505,000 inhabitants. The study took place in a private third-level clinic, specialized in the comprehensive management of patients with onco-hematological diseases named Instituto Medico de Alta Tecnología – IMAT. The clinic had 105 beds for the care of patients with COVID-19. The clinic’s building was divided to face the pandemic into two sectors to safely and adequately separate patients with COVID-19 from other patients and healthy people.

Pharmacological treatments

The following drugs were used: 1—broad-spectrum antibiotics (cefepime, piperacillin-tazobactam, meropenem, vancomycin) + low molecular weight heparin (LMWH) + corticosteroids (dexamethasone–methylprednisolone) + colchicine. 2—Antibiotic + LMWH + corticosteroids. 3—LMWH + corticosteroids. 4—LMWH + corticosteroids + colchicine. 5—Other treatments (Tocilizumab). Broad-spectrum antibiotics were prescribed to patients with suspected bacterial coinfection.

Coinfections were diagnosed by radiography or chest tomography, isolation of the germ from respiratory specimens, blood cultures, and molecular detection with PCR. Corticosteroids were administered to patients in need of supplemental O2, with partial oxygen saturation (SpO2) less than 92% [5]. Antithrombotic prophylaxis with low molecular weight heparin (LMWH) was administered to all patients diagnosed with SARS-CoV-2 infection, and therapeutic doses of LMWH were administered to patients with Dimer D > 1000 ng/ml, severe disease, and suspected or confirmed venous thromboembolic events. Colchicine was given for 20 days to all patients with SARS-CoV-2 infection, as long as they did not present gastrointestinal intolerance or a history of hypersensitivity [6]. According to the Colombian consensus’s recommendations for the care, diagnosis, and management of SARS-CoV-2 infection [7], tocilizumab was given.

Inclusion and exclusion criteria

The patients had to be admitted to the hospital ward and meet the criteria for COVID-19 disease classified as moderate, severe, or critical [7,8]. The moderate disease was one with clinical or radiological evidence of pneumonia with clinical of pneumonia (fever, cough, dyspnea, tachypnea) without signs of severe pneumonia, with SpO2 ≥ 90% in room air. Severe disease was one that demonstrated clinical evidence of pneumonia, plus one of the following findings: respiratory rate > 30 breaths/min; severe shortness of breath; or SpO2 < 90% in ambient air. The critical disease was considered if it met Acute Respiratory Distress Syndrome (ARDS) criteria, sepsis, or septic shock [7,8].

The exclusion criteria were the following: patients’ clinical history with the loss of clinical and demographic information more significant than 10%. Patients with a mild diagnosis of Covid-19 disease. Symptomatic patients based on the COVID-19 case definition criteria without evidence of viral pneumonia or hypoxia [7,8]. Patients admitted to hospital for the treatment of diseases other than Covid-19.

Ethical aspects

The consent for the treatment of the patients or relatives was obtained, and they were privately categorized. The work was endorsed by the Ethics Committee of the Instituto de Investigación Biológicas del Trópico (IIBT) and Clinica IMAT. This study was under strict alignment with international ethical standards given by the World Health Organization and the Pan American Health Organization, supported by The Helsinki’s Declaration, and Colombian legislation, resolution number 008430 of 1993 of the Ministry of Health of Colombia.

Statistical analysis

The data were analyzed using the Statistical Package for the Social Sciences version 21 (SPSS). The univariate analysis for the qualitative variables resulted through the calculation of absolute and relative frequencies. In quantitative variables, measures of central tendency were calculated. Moreover, the normality of the quantitative variables was determined by applying the Kolmogorov–Smirnov test. The Bivariate analysis was performed through Pearson’s chi-square test. Multivariate analysis was performed through binomial logistic analysis. The significance of the P-value was set to <0.05 for all analyses performed.

Results

Two hundred and nine patients with a confirmed diagnosis of COVID-19 were analyzed. One hundred out of the 209 were in the
Intensive Care Unit, and the remaining 109 were treated in the general hospitalization ward. In total, 51% perished as a consequence of the infection. The patient’s median age was 60 years old, in which 61% of them were males, and 8.6% were health care workers. The patients’ primary clinical manifestation was respiratory distress, which was observed in 66.5% of patients. In individuals who died with COVID-19, respiratory distress was 83.3% \((P < 0.0001)\). Supplementary critical clinical manifestations were fever (61.7%), cough (58.8%), and adynamic (25.3%). Regarding comorbidities, it was noted that 47% suffered arterial hypertension, 25.3% diabetes mellitus, 18.6% of patients had a history of solid tumors, 17.2% cardiovascular disease, 14.8% kidney disease in various stages, and 14.3% were obese. Moreover, kidney disease and obesity were related to higher mortality in this group of patients \((P < 0.05)\) (Table 1).

Concerning complications, it was evidenced that 48.8% of those admitted presented Acute Respiratory Distress Syndromes (ARDS), and 39.23% sepsis. These complications were present in 90.1% and 70.6% of the deceased patients \((P < 0.0001)\). Other palpable complications were bacterial coinfection (21.1%); the most frequent microorganisms involved in pulmonary bacterial coinfection were: Klebsiella pneumoniae, Pseudomonas aeruginosa, Staphylococcus aureus, and Enterobacter cloacae. The Rhinovirus/Enterovirus viral agents were the most associated with pneumonia (Table 1). A multivariate analysis was carried out to study symptoms, comorbidities, and clinical complications related to the deceased COVID-19 patients. The analysis of the variables projected that symptoms such as respiratory distress are related to a higher rate of mortality by COVID-19 \((P < 0.05)\) \([OR 3.5, 95\% CI 1.7–7.2]\). Furthermore, this analysis showed that comorbidities as obesity and mainly kidney disease could be considered as risk factors related to high fatality rates in these patients \((P < 0.0001)\) \([OR 16 95\% CI 4.4–60]\). On the other hand, the analysis carried out on clinical complications also showed that ARDS and sepsis were two variables with sufficient statistical corroboration linked to fatal outcomes in individuals infected by SARS-CoV-2 \((P < 0.05)\). Likewise,ARDS could be linked to an increase of almost 36 times in the mortality rate \((OR 36, 95\% CI 12–102)\) (Table 2).

As a standard course of treatment given to all admitted patients, the following was the most common combination of antibiotics: antibiotics, low molecular weight heparin, corticosteroids, and colchicine. Fifty-two percent of the patients who received this combination were discharged alive, and this combination was related to reducing the mortality in the total cohort of patients \((P < 0.05)\) \([OR 0.26 95\% CI 0.08–0.71]\) (Table 3).

According to the clinical severity, the impact of treatments was evaluated; however, the present work did not show statistical differences regarding their use \((P > 0.05)\). Critical patients under treatment without colchicine showed higher mortality than those who received colchicine combination \((P < 0.05)\) \([OR 15 (3.04–271.2)]\).

**Discussion**

The present study is the first one of its class in the Republic of Colombia that describes the clinical and treatment aspects of a group of patients with COVID-19. In general, deceased patients tended to be older, with a median age in our population more significant than the ones shown in Asian cohorts \([4,9,10]\), the United States \([11]\), and some Latin American countries \([12,13]\). In the group of patients that did not survive, the predominant symptom was dyspnea; a behavior correlated with a more significant rate of complications and mortality is higher than its presentation in other series of hospitalized patients in cohorts from Asia and Europe \([14,15]\) but is similar to those found in the United States and Latin America \([12,13,16]\).

This high mortality rate is perhaps due to the delayed reporting of symptoms by the affected patients. (Average 9.1 days), which has been evidenced as an adverse prognostic factor \([17]\). We believe
that delay in attention is correlated to misinformation given at the beginning of this pandemic in our region. People's perception of the disease was misled when national authorities placed several restrictions to contain the virus, flatten the curve, and relieve the health care system. People believed they would get sicker at hospitals than at home. The misinformation and fear negatively impacted timely clinical care [16]. As described in some international media [18], this infodemic could impact morbidity and mortality. This topic should be evaluated with other studies that consider social factors, race, religion, educational level, and gender [19–21].

On the other hand, comorbidities such as kidney disease and obesity seem to be, according to studies in The United States, China, and Spain [14,22,23]. However, because the clinic is a regional referral center for cancer patients, the proportion of patients with solid tumors and hematological tumors was higher (25.8%). Cancer comorbidity could have influenced the results, being associated with a higher fatality rate in cancer patients [24].

In the multivariate analysis, the variable of obesity behaved as a factor that increases mortality risk and enters agreements with other findings in additional cohorts. It is an independent risk and prognostic factor for the greater severity of the disease [25,26]. In obese patients, it has been proposed that the low metabolic and cardiorespiratory reserve may lead to immune hyperreactivity and greater severity of the disease [27]. Chronic kidney disease (CKD) was associated with a progressive increase in the rate of hospital-diagnosed COVID-19 [28] and has significantly higher mortality.
than patients without kidney disease [29], behaving as a significant independent predictor of COVID-19 mortality [30]. We found a greater risk of mortality in the group of patients with chronic kidney disease, similar results found in New York, the United States, and Mexico City [31].

The most frequently encountered complications were sepsis and ARDS; the multivariate analysis showed an increased risk of mortality in patients who presented these complications [32]. Ninety percent of the deceased patients presented ARDS, which leads to a more significant number of days of ventilation and short-term mortality [33] similar to that published by Tzotzos et al. [34], who describe results of a global survey of studies that report ARDS associated with COVID-19.

The combination of broad-spectrum antibiotics, low molecular weight heparin, corticosteroids, and colchicine were included. Considering that approximately half of the patients were admitted to the ICU, antibiotics were consistent with those described in other series [10,35,36]. However, the present study had bacterial infection at a higher rate (58%) than those reported by Lansburri et al. [37], who reported 7% of patients hospitalized in the general ward and 14% of those hospitalized in the ICU had bacterial infection. In previous studies, 90% of the patients received empirical antibiotic treatment [38].

LMWH was administered in prophylactic doses according to weight in all patients with confirmed SARS-CoV-2 infection based on data suggesting a procoagulant pattern [39]. Likewise, in patients with hypercoagulability associated with severe inflammation states [40] with an increase in the incidence of venous thromboembolism [41–43]. According to other our finding related to LMWH is that its administration reduces mortality in patients with complicated forms of this disease [44,45].

Based on the evidence at the date of the RECOVERY study [5], glucocorticoids in all patients who needed supplemental oxygen were started. Based on clinical benefit data found in the GRECO study [6], colchicine was used in 54.2% of the hospitalized patients with good gastrointestinal tolerance. In the multivariate analysis, colchicine showed a reduction in the risk of mortality. In other words, patients treated with the colchicine combination had less chance of dying than those who received the combination without colchicine (Table 3).

Our work has some weaknesses. The study was conducted in a single medical center, which probably introduced a selection bias and limited the findings' extrapolation. Furthermore, a proportion of patients were admitted with severe disease, limiting the ability to evaluate the relationship between independent variables and mortality.

In conclusion, the present work reveals that during the pandemic's maximum peak, mortality from COVID-19 was 51%. These data related to higher mortality would be attributed to several related factors such as the advanced age of the hospitalized population, comorbidities such as kidney disease and obesity, and an average time in late consultation days. Furthermore, the present study showed that the colchicine combination was reducing mortality in COVID-19 disease. However, our findings need to be confirmed with a bigger casuistic and in other populations.

**Ethical approval**

This research was approved by the ethics and research committee of Oncomedica S.A.

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