

Management of COVID-19 at the pandemic's first wave in Ecuador

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Abstract

During March and April 2020, Ecuador was the country with the highest death toll in Latin America due to the coronavirus disease 2019 pandemic. Simultaneously, research was being developed and published globally, and to a certain extent, guided therapeutic approaches in real time, mostly in under-resourced settings. We present the case of a 59-year-old male physician residing in Guayaquil, who presented with severe coronavirus disease 2019, in which mechanical ventilation, prone position, and pulmonary protective ventilatory strategy were used. We discuss the clinical management of the first reported case in the literature of a physician in Ecuador who survived severe acute respiratory syndrome coronavirus 2 infection, as well as the topic of self-medication within health professionals, the management approach that was emerging at the moment in scientific publications and guiding treatment, the role of responsible research and its worldwide impact, and the emotional burdens of the care team who had to make very difficult decisions in extremely adverse circumstances.

Keywords

Coronavirus infections, severe acute respiratory syndrome coronavirus 2, coronavirus disease 2019, pandemic

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Introduction

The first confirmed case of acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in Ecuador was diagnosed on 29 February 2020 and with 17 million citizens, Ecuador was the country with the highest death toll in the region during March and April of that year.¹ A state of emergency was declared on 11 March, and in a very fast pace, new severe cases escalated, leading to the collapse of our health system, specifically at the Guayas Province, where more than 65% of the cases were clustered.^{2,3} Furthermore, in the first 15 days of April 2020, the province of Guayas reported 6703 deaths. When compared to the mortality rate in that same period in 2019, an increase was evidenced in the death toll of the province, rising to 5700 deaths.⁴ Ecuador's health system has a total capacity of 636 hospitals and 29,502 beds—1.4 beds per 1,000 inhabitants—of which 1183 are allocated to intensive care units (ICUs). The province of Guayas has 357 of the total ICU beds of the country, according to data reported by the Institute of Statistics and Censuses (INEC).⁵

As a result of the aforementioned collapse of the healthcare system, the coronavirus disease 2019 (COVID-19) pandemic led to changes in the lifestyle of healthcare workers, causing physical and emotional overload which was associated with psychological stress caused by the potential risk of infection and transmission to family members.⁶ Studies have suggested associations to these comorbidities with the concurrence of

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low availability of protective equipment, fear of infection, being a vehicle of transmission and in some cases, health care workers opting to live alone for fear of transmission to their family members.⁷ Moreover, the lack of screening for early recognition of carriers to prevent the spread of the virus and the lack of adequate training in terms of transmission protection are additional factors that were found to be contributing to fear and anxiety among health professionals.⁸

Huge efforts on research of effective therapeutic approaches were released in scientific articles globally and in a daily basis. Most of them, referring to small clinical trials, in-vitro activity of certain drugs, ventilatory management, and to anecdotic reports.⁹

We describe our experience with the clinical management of one of our colleagues and friend, a critical care physician admitted to the ICU with severe COVID-19 and the first reported case in the literature of a medical doctor to survive in Ecuador. In this case report, we discuss self-medication within health professionals,¹⁰ the management approach that was emerging at the moment in scientific publications,¹¹ the role of responsible research,¹² and the emotional burdens of the care team who had to make very difficult decisions in extremely adverse moments.¹³

Case presentation

We report the case of a 59-year-old male medical doctor living in Guayaquil with a clinical history of chronic hypertension treated with an angiotensin receptor blocker (telmisartam). The patient presented to the emergency department on 23 March with an episode of fever, non-productive cough, malaise, and diarrhea lasting for 10 days. The episode was accompanied with abdominal pain¹⁴ localized in the epigastrium and characterized by an intensity of 8/10. The nasopharyngeal swab real-time polymerase chain reaction (RT-PCR) test for SARS-CoV-2 was positive on the third day. Finally, he reported that he self-medicated 4 days prior with nitazoxanide 500 mg three times a day (TID) and azithromycin 500 mg once a day (QD).

He presented the following initial laboratory findings: white cell count 4300 per mm³ (normal range: 4400–10,300), total neutrophils 3410 per mm³ (normal range: 1780–5380), total lymphocytes 640 per mm³ (normal range: 1180–3740), total monocytes 180 per mm³ (normal range: 250–710), total eosinophil count 60 per mm³ (normal range: 0–6), Ferritin 920 ng/mL (normal range: 30–400), interleukin (IL)-6 13.5 pg/mL (normal range: 0–6.5), D-dimer 2.5 mg/L (normal range: 0–1.9), procalcitonin 0.05 ng/mL (normal range: <0.046), creatinine 0.5 mg/dL (normal range: 0.80–1.20), and Blood Urea Nitrogen (BUN) 19 mg/dL (normal range: 5–20 mg/dL). His individualized prediction of hospitalization risk¹⁵ for a patient with COVID-19 was of 10.5%.

Treatment was started with a continuous infusion of esomeprazole, hydroxychloroquine 200 mg two times a day (BID), azithromycin 500 mg QD, ampicillin/sulbactam (3 g intravenous (IV) every 8 h), and lopinavir/ritonavir 200/50 mg BID.



Figure 1. Chest x-ray demonstrated multiple alveolar consolidations in the right inferior lobe and left superior lobe. Coarse opacities were seen bilaterally in the lung apex. Cardiac silhouette had a normal configuration, and a right venous subclavian catheter pointing toward the innominate vein was observed.

Supplemental oxygen was given via nasal cannula with a rate of 3 L/min, and oxygen saturation was 97%.

On the fourth day after admission, the patient presented with dyspnea, tachycardia, and tachypnea. Presenting oxygen saturation of 90% despite the use of supplemental oxygen via nasal cannula. High flow nasal cannula was initiated. Tocilizumab was initiated with one dose of 400 mg followed by 200 mg due to blood levels of IL6 of 89 (pg/mL) (normal range: 0–6.5). About 12 h later, hydrocortisone 100 mg TID was added to the therapeutic regimen.

On the fifth day of hospitalization, the chest x-ray demonstrated multiple alveolar consolidations in the right inferior lobe and left superior lobe (Figure 1). The patient showed tachypnea and use of accessory muscles of respiration, as well as a deterioration on his level of consciousness. On laboratory findings, he presented with an arterial blood gas analysis showing respiratory acidosis with hypoxemia: pH 7.26; PCO₂ 52.7 mmHg, PO₂ 45.9 mmHg, HCO₃ 20.6 mmHg, and base excess −2.90. Thus, he required endotracheal tube placement and ICU care. The patient was placed in pronation therapy (Figure 2).

The antibiotic coverage was changed to piperacillin/tazobactam 4.5 g IV every 6 h. Sedation and muscular relaxation were accomplished with fentanyl 2 µg/kg/h and rocuronium 0.05 µg/kg/min. Enteral feeding was started via nasogastric tube. Mechanical ventilation parameters at this time were as follows: volume-controlled mode (AC) with tidal volume (TV) of 6 mL/kg of predicted body weight (PBW), a constant

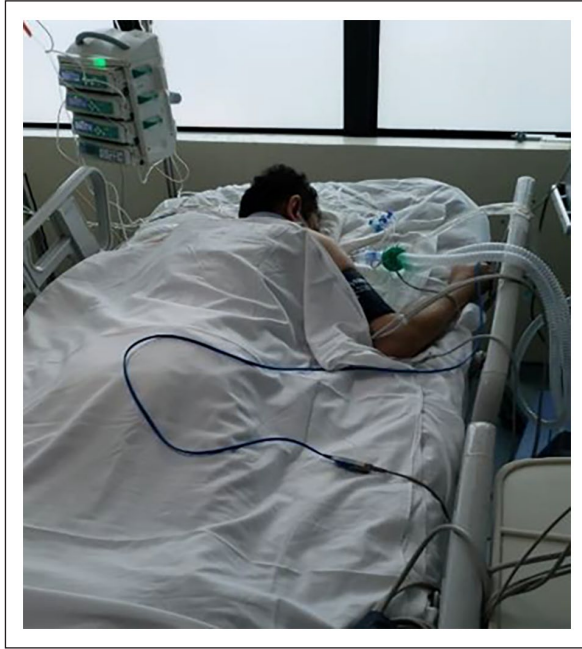


Figure 2. Pronation therapy.

inspiratory flow of 50 L/min, a level of positive-end expiratory pressure (PEEP) of 8 cm H₂O, and respiratory rate of 20 breath/min. The expired TV displayed by the ventilator was reported.

On the sixth day since admission and second day of ICU care, due to the presence of arterial hypotension of 80/50 mmHg, volume therapy and vasopressor therapy were started with the administration of 500 mL 0.9% saline solution and norepinephrine 0.02 µg/kg/min, respectively.

On the eighth day of hospital stay, arterial blood gas analysis showed a pH of 7.40, PCO₂ 55.2 mmHg, PO₂ 94.9 mmHg, HCO₃ 33.9 mEq/L, and SaO₂ 93%.

On the ninth day since admission, vasopressor therapy was suspended. Propofol and loop diuretics were added for sedation and improved diuresis, respectively.

On the tenth day of hospitalization and Day 6 of ICU care, sedation was removed, and the patient responded positively with an adequate level of consciousness. Ventilatory parameters were changed to continuous positive airway pressure (CPAP) mode. The following day, the patient was extubated and received 45 L high flow nasal cannula with an FiO₂ of 50%.

On the eleventh day of ICU care, ambient air and high flow oxygen via nasal cannula were alternated with good patient tolerance.

On the twelfth day of ICU care, the patient was saturating 100% with nasal cannula, had adequate diuresis and normal sinus rhythm. An electrocardiograph (ECG) was required prior to the continuation of hydroxychloroquine, and the results were within normal ranges. The patient was transferred to the hospital ward.

On day 16 since hospital admission, antimicrobial therapy was discontinued. In addition, the chest computed

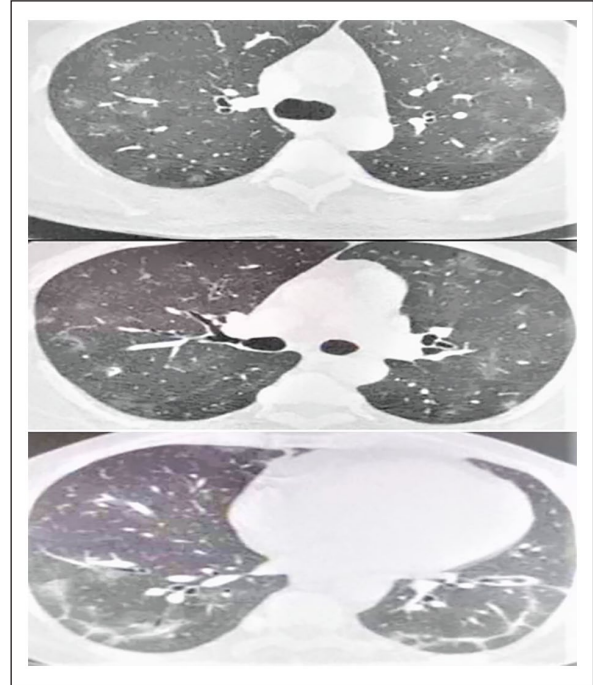


Figure 3. The CT scan of the thorax showed ground—glass opacities and condensation areas of peripheral distribution, both in superior and inferior lobes.

tomography (CT) scan showed improvement in the parenchymal and pleural opacities in lung bases and periphery (Figure 3). Laboratory results reported normal parameters.

On day 19 since hospital admission, the patient reported an overall improvement in his clinical condition. He was ambulating and participating in physical rehabilitation. An antibody test was taken which came back negative for IgM and positive for IgG.

As of today, the patient has returned to clinical practice. See graphical representation of timelines (Figure 4).

Discussion

Since its appearance in December 2019 in Wuhan, China, SARS-CoV-2 has spread to every continent of the world. The high viral load¹⁶ and transmissibility during the initial days of disease presentation may be responsible for its high lethality in vulnerable groups. Therefore, it can easily cause the collapse of many health care systems, especially in developing countries. By 26 February 2020, the first case of COVID-19 in Latin America was reported in Brazil¹⁷ and 3 days later, on February 29, the first case was reported in Ecuador.¹ At that time, during the so-called “first wave,” Brazil and Ecuador constituted the most affected countries in the region and around the world.² The occurrence of public events such as sports games, the return of thousands of migrants on holiday from countries with reports of significant numbers of cases of COVID-19 such as: Italy, Spain,

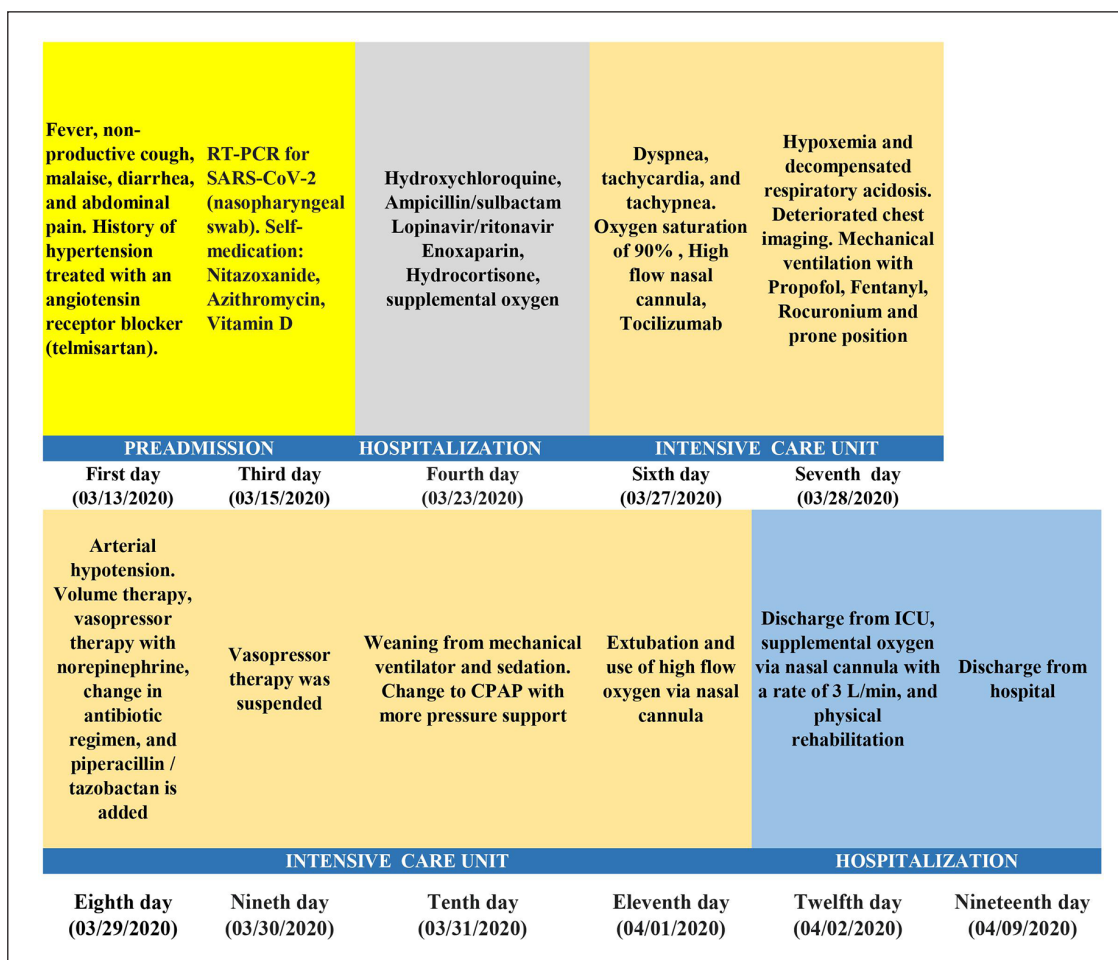


Figure 4. Graphical representation of timelines.

and the United States, and the non-compliance with isolation and social distancing measures all contributed to the peak in cases in the country. Furthermore, the return of migrants implied social gatherings to welcome them as a “local tradition.” These events determined that in 2–3 weeks, the rate of infection and deaths were higher than in cities, such as New York, Madrid, Milan, and Wuhan.^{2,18} Brazil, with 210 million inhabitants, had 5901 deaths by the end of April, with Sao Paulo being the most affected city. New York had a 341% increase in mortality compared to the 485% increase reported in the Ecuadorian province of Guayas, where Guayaquil was the most affected city.

During this global pandemic, a large number of health professionals were infected by SARS-CoV-2.¹⁸ This could have been associated with the lack of adequate protective equipment, with some studies in the region reporting that “7 out of 10 healthcare workers did not have the necessary resources (PPE) to care for patients with COVID-19.”¹⁹ In addition, there was a disproportionate exposure to SARS-CoV-2 due to excessive workload with agglomeration of hospital areas and late recognition of symptoms of COVID-19 among health workers.¹⁸

Moreover, in the Americas, the highest proportion of cases was reported in the United States of America (45%) and Brazil (29%), while the highest lethality rates in Latin America were reported in Ecuador (5.8%). According to data from the Coronavirus Resource Center at Johns Hopkins University, as of 2 April 2020, Panama had 0.76 COVID-19-related deaths per 100,000 inhabitants (32 deaths total), and Ecuador 0.57 (98 deaths total). Ecuador recorded 21,500 excess deaths until 17 June 2020, translating into a higher rate with 1000 deaths in excess per million inhabitants.²⁰

The COVID-19 syndrome presents with early exponential viral replication, proliferation, organic damage by cytokine release, and endothelial damage with platelet aggregation and thrombus formation. Therefore, when there is clinical and epidemiological suspicion based on radiological, biochemical, and microbiological tests, treatment must be initiated early, independently of the swab test result.²¹ Furthermore, an early sequential therapy with multiple drugs before the establishment of critical illness,²² could have positively influenced the progression of the disease in our patient. However, there are no conclusive studies in favor of early multiple therapeutics monitored by telemedicine at the moment this study was

written.²³ In this context, the use of medication such as remdesivir, convalescent plasma, antiviral antibodies, corticosteroids, and anticoagulants is associated with an effective multimodal treatment rather than monotherapy.²⁴ At the time of this patient's medical care, there was not enough information available from clinical trials focusing on how to control early viral replication, cytokine storm and thrombosis in outpatients with COVID-19. At that stage, there was an urgent need for early innovations.

At the beginning of the pandemic in our region, which was one of the first affected around the world, we used therapies that are currently part of the recommendations of the majority of clinical guidelines^{25,26} and have proven therapeutic efficacy. Supported by the results of the RECOVERY²⁷ and REMAP-CAP²⁸ studies, these therapies were undoubtedly decisive in the recovery and survival of our patient. Medications used included azithromycin, nitazoxanide, hydroxychloroquine, lopinavir/ritonavir, tocilizumab, corticosteroids, and enoxaparin due to high levels of D-dimer. Prone positioning as a protective mechanical ventilation strategy was also implemented.²⁹

In daily medical practice, therapeutic decisions in the ICU require a medical indication and incorporate the will of the patient, which applies to the different stages of care. Such decisions are made with the medical team and with the participation of the patient and family. Intensive care teams around the world have adopted and implemented these standards in recent decades.³⁰

Many ethical concerns were raised by us during this case, as evidence-based treatments were still lacking. However, our patient wanted any possible treatment to be tried even if it failed to work, and we chose to respect his autonomy and decision-making capacity. At the same time, we had to take beneficence and nonmaleficence into consideration, and we realized that by no means, we were pursuing inadequate or futile treatment in view of the circumstances. Looking back, we think that we made the best possible decisions with the resources and information available to us.

During this pandemic, numerous scientific papers have endorsed and rejected^{31,32} certain aspects that support the evidence for hydroxychloroquine treatment in COVID-19. Despite this, we believe that in our situation, hydroxychloroquine could have had a positive effect used early in our patient, especially when combined with other drugs that can reduce viral replication.

Conclusion

We present the clinical management of the first reported case in the literature of a physician in Ecuador who survived severe SARS-CoV-2 infection. We discuss the challenges met by the critical care team, the decision-making process during the adverse circumstances imposed by the COVID-19 pandemic and the role that ongoing research played in the therapeutic approach. We conclude that scientific research

anchored in transparency and robust methodology is urgently needed to guide therapeutic efforts worldwide and specially in low-resource settings like ours.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Disclosure statements

Appropriate written informed consent was obtained for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Ethical approval

The institution where the case report was made does not require ethical approval to report individual case

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Informed consent

Written informed consent was obtained from the patient for publication.

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