BRIEF REPORT

DESCRIPTION OF PATIENTS WITH SEVERE COVID-19 TREATED IN A NATIONAL REFERRAL HOSPITAL IN PERU

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ABSTRACT

In order to describe manifestations from patients with coronavirus disease 2019 (COVID-19), sociodemographic variables such as, previous medical history, clinical and radiological manifestations, treatments and evolution of patients were evaluated. This took place from March 6th to 25th, 2020, in the "Edgardo Rebagliati Martins" National Hospital in Lima. Seventeen patients were registered: 76% were male, with an average age of 53.5 years (range 25-94); 23.5% had returned from abroad; 41.2% were referred from other health facilities; 41.2% were admitted to mechanical ventilation; 29.4% (5 patients) died. The risk factors detected were: advanced age, arterial hypertension and obesity. The main symptoms detected were: cough, fever and dyspnea. Frequent laboratory findings were: elevated C-reactive protein and lymphopenia. The predominant radiological presentation was bilateral interstitial lung infiltrate. A first experience in the management of patients diagnosed with severe COVID-19 in Peru is reported.

Keyword: Severe acute respiratory syndrome; Pneumonia, viral; Emergency medical services; Virus diseases; Coronavirus infection; Pandemics (source: MeSH NLM).

INTRODUCTION

The novel coronavirus disease (COVID-19) originated in China in 2019 and is caused by a new virus, called SARS-CoV-2, which stands for severe acute respiratory syndrome coronavirus 2. This disease is characterized by: being directly transmitted, being related to the appearance of severe pneumonia, having an unfavorable evolution in older adults and/or patients with comorbidities, such as hypertension, obesity, diabetes or immunosuppression, and by spreading rapidly throughout the world [1,2]. It was considered a pandemic by the World Health Organization on March 11, 2020 [3,4].

On March 6, 2020, the first person in Peru with COVID-19 was reported. Soon, the number of suspected cases and early hospitalizations increased rapidly. On March 19, the first three deaths occurred [1,3]. As of April 2, 16,518 diagnostic tests were performed and 1,414 cases were positive for SARS-CoV-2; from which 189 were hospitalized, 51 entered the intensive care units and 41 died. Worldwide, at the time, it has been reported that over one million people were infected and more than 50,000 died, the countries most affected were Italy, Spain and, recently, the USA. In South America, Brazil and Ecuador are the countries with the most deaths [5,6].

The Edgardo Rebagliati Martins National Hospital, which provides healthcare to members of the Social Security Health System (EsSalud), is a complexity-level-III facility designated as a reference hospital for COVID-19 patients. This study seeks to describe the clinical

manifestations in patients treated for severe COVID-19 in the emergency service of this national hospital.

THE STUDY

Retrospective observational study conducted in the adult emergency department of the Edgardo Rebagliati Martins National Hospital, located in the district of Jesus María in Lima, Peru. A severe case of COVID-19 is defined as a patient who required hospitalization or died from the disease; and tested positive for SARS-CoV-2 by reverse transcriptase polymerase chain reaction (RT-PCR) analysis of pharyngeal or nasal swabs, processed at the National Institute of Health.

Cases submitted between March 6 and 25, 2020 were included. On March 6, when the first confirmed case was reported in Peru, suspected patients were treated at the hospital, and a few days later they tested positive. Cases with clinical manifestations but negative molecular test for the virus were excluded.

An area in the hospital was set aside to identify, isolate and care for COVID-19 patients. A trained health worker (nurse or nurse technician) was located at the door of the emergency service and asked for the patient's chief complaint and referred the patient to the respiratory triage area if he or she had any acute respiratory symptoms.

The respiratory triage station was located in a separate area of the hospital, where a physician evaluated the suspect patient, according to the institutional flow chart (Figure 1). About 150 patients passed through the triage station daily.

The decision of sending suspected, confirmed or critical patients (dependent on an intensive care unit or mechanical ventilation); to their home for isolation, to the emergency room or into a hospital ward was made by using several methods. These methods were: peripheral capillary oxygen saturation, the rapid sequential organ failure assessment scale (qSOFA) [7] and the risk factors for this disease mentioned in the Peruvian technical standard [1, 8].

We reviewed virtual medical records, laboratory results and the hospital's radiographic system. From these sources, we identified sociodemographic variables, medical history, comorbidities, clinical manifestations and laboratory tests at hospital admission, reviewed the radiological studies performed on each patient, the treatment administered, evolution and hospital stay until the end of the study. The risk factors considered were those established in the technical standards of the Ministry of Health.

The data was digitized and processed in Microsoft Excel 2013. A descriptive statistical analysis was performed, using central tendency and frequency distribution measurements.

KEY MESSAGES

Motivation for the study: There is limited evidence on the histopathological and inflammatory effects of submicroscopic placental infection by *P. falciparum* and *P. vivax*.

Main findings: Placentas of women who live in the largest endemic area of Colombia, in the northwest of the country, were affected by submicroscopic plasmodial infection (SPPI), not detected with thick drop, but with quantitative polymerase chain reaction (qPCR). The SPPI causes tissue damage in the placenta and affects mediators of processes, such as inflammation, hypoxia, angiogenesis, among others, compared to non-infected placentas. Both *P. vivax* and *P. falciparum* act as pathogens

Implications: Diagnostic and treatment actions for gestational plasmodial infection in prenatal consultation need to be greatly improved and should necessarily include the thick drop test in every control.

The data were taken from secondary sources and were coded to ensure confidentiality and anonymity; only the researchers had access to this data, with prior authorization from the head of the hospital service.

FINDINGS

A total of 17 patients with severe manifestations of COVID-19 were identified. The average age was 53.5 years ranging from 25 to 94; 76% were male; 88.2% lived in the districts of Central and Southern Lima (Miraflores, Jesús María, San Borja, San Isidro, Surquillo, Breña, Rímac, Villa María del Triunfo, Chorrillos and San Juan de Miraflores). Three patients acquired the infection in Europe (from Spain, England and Holland) and one in the USA. From the total of patients, 76% (13 patients) had at least one risk factor for developing severe COVID-19 infection, other risk factors included chronic corticotherapy, pregnancy and human immunodeficiency virus infection. The remaining 23.5% of patients [4] had more than one risk factor at a time (older adult plus high blood pressure or diabetes). Four patients were transferred from private clinics, 2 from another EsSalud facility and 1 from a hospital of the Ministry of Health, all of them were admitted for respiratory symptoms through triage and referred to an assigned ward (Table 1).

Patients were admitted to the hospital with an average time of 7 days with the disease, ranging from 3 to 13 days. The most frequent symptoms were cough, fever and dyspnea; the signs were respiratory rales and polypnea. The
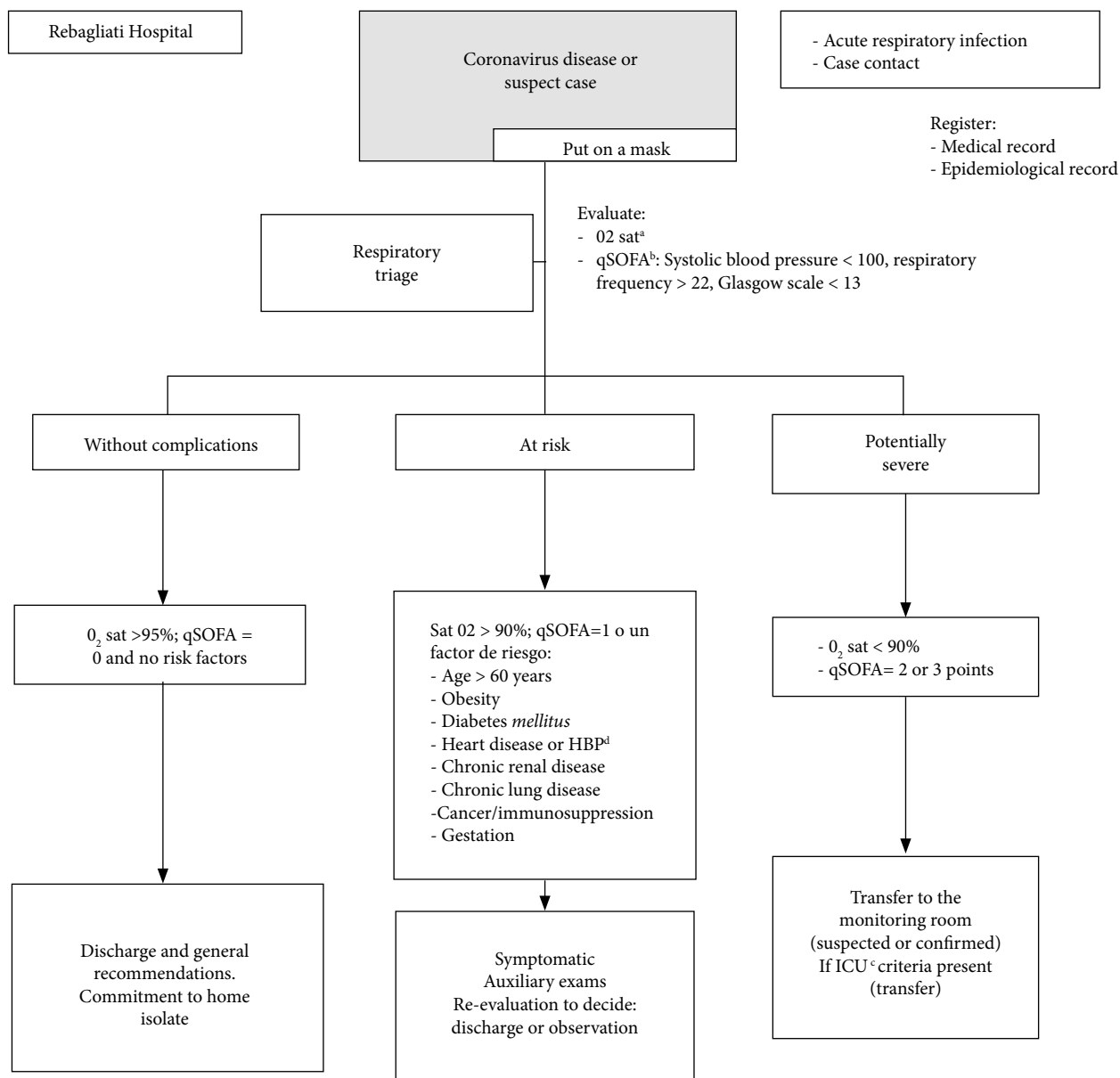
^a O₂ sat: peripheral capillary oxygen saturation; ^b qSOFA: rapid sequential organ failure assessment; ^c ICU: intensive care unit; ^d HBP: high blood pressure

^a O_2 sat: peripheral capillary oxygen saturation; ^b qSOFA: rapid sequential organ failure assessment; ^c ICU: intensive care unit; ^d HBP: high blood pressure
Adapted from technical documents of the Ministry of Health of Peru and Spain.

Figure 1. Attention flowchart for patients with confirmed or suspected COVID-19 in the emergency department of a national hospital in Lima, Peru, March 2020.

most frequent laboratory findings were elevated C-reactive protein and lymphopenia. The most frequent radiological finding was bilateral interstitial lung infiltrate (Table 2), no images of pleural effusion were found. Only 1 patient was CT-scanned, because of having abdominal pain, bilateral focal frosted-glass lesions found in the lower pulmonary lobes and had no confirmatory diagnosis at the moment. (Figure 2). Only 2 patients did not have laboratory tests and 4 did not have X-rays due to logistical deficiencies during the first days.

A total of 13 patients received some form of antimicrobial treatment; hydroxychloroquine was available 3 days before the end of data collection for this investigation. All patients received supplemental oxygen and 41.2% ⁽⁷⁾ were admitted to mechanical ventilation.

From the 5 deceased patients, 4 were male (80%), 3 over 70 years old, and 2 had come from Spain, where they acquired the infection. A 38-year-old patient arrived with severe respiratory failure and died 10 hours after being intubated and placed on a mechanical ventilator. One patient was not

Table 1. Epidemiologic characteristics of severe SARS-CoV-2 patients in a national hospital in Lima, Peru, March 2020.

Characteristics	n=17	%
Age group (years)		
Less than 30	1	5.9
from 30 to 39	5	29.4
from 40 to 49	1	5.9
from 50 to 59	4	23.5
60 or more	6	35.3
Gender		
Male	13	76.5
Female	4	23.5
District of origin in Lima		
Center Lima	11	64.7
South Lima	4	23.5
Other	2	11.8
Travel or contact history		
Recent trip to countries with COVID-19	4	23.5
Confirmed contacts	3	17.6
Unknown contacts	10	58.9
Referred from other centers	7	41.2
Risk factors		
Elder age	6	35.3
High blood pressure	4	23.5
Obesity	3	17.6
Diabetes mellitus	2	11.8
Chronic renal disease	2	11.8
Other	3	17.6

COVID-19: Coronavirus disease 2019

Table 2. Clinical manifestations, auxiliary tests and treatment of patients with severe SARS-CoV-2 virus disease at a national hospital in Lima, Peru, March 2020

Manifestations	n = 17	%
Signs and symptoms		
Cough	14	82.4
Fever	13	76.5
Dyspnea	13	76.5
Polypnea (>20 breaths per minute)	11	64.7
Respiratory Rales	11	64.7
Odynophagia	9	52,9
O$_2$ sat [a] <90%	5	29.4
Hypotension	2	11.8
Diarrhea	2	11.8
Blood analysis		
Increased C reactive protein (between 7 and 34 mg/dL)	12	70.6
Lymphopenia <900 mm^3 (between 150 and 890)	11	64.7
Increased transaminases (>40 U/L)	9	52,9
Hypoxemia (paO2 < 60 mmHg)	6	35.3
Hyperglycemia (>120 mg/dL)	6	35.3
Leukocytosis (>10,000 mm^3)	4	23.5
Chest X-ray patterns on admission (n=13)		
Bilateral diffuse interstitial	6	46.2
Bilateral alveolo-interstitial	4	30.7
Bilateral reticulonodular	3	23.1
Antimicrobial treatment		
Azithromycin	7	41.2
Hydroxychloroquine	5	29.4
Oseltamivir	3	17.6
Other antimicrobial		
Piperacillin-tazobactam	4	23.5
Meropenem and vancomycin	2	11.8
Ceftriaxone	2	11.8
Cefepime, cotrimoxazole or ciprofloxacin	1	5.9
Other medicines used		
Metamizole	9	52.9
Acetylcysteine	8	47.1
Salbutamol	6	35.3
Acetaminophen	3	17.6

O$_2$ sat: peripheral capillary oxygen saturation

hospitalized and died two days after the pharyngeal swab for testing was made, the patient had severe respiratory difficulty before dying at home.

Two patients without risk factors were discharged after 2 and 4 days respectively, due to favorable evolution. At the end of the study, 5 patients remained in intensive care on mechanical ventilation, with an average stay of 7.3 days (ranging from 4 to 14); they presented complications, such as acute renal failure with supportive hemodialysis (2 cases), distributive shock in patients who were receiving inotropic support (2 cases), moderate liver failure (1 case) and low platelet count (one case).

Only 5 patients remained in the general ward for an average of 2 days (ranging from 1 to 5), showing little to no disease progression. One patient was 32 weeks pregnant, received intravenous ceftriaxone, paracetamol and two days later an emergency C-section was performed without complications. The newborn was transferred to the neonatal isolation room and the mother remained in the intensive care unit receiving oxygen by face mask ventilation.

DISCUSSION

Severe cases of COVID-19 described in this study correspond to the first cases treated in a hospital in the early stage of the pandemic in Peru. They were similar to cases reported in China and the USA, which describe a disease affecting mainly male population, starting with cough and other respiratory symptoms, with an average disease duration of seven days [10-13]. Fever and dyspnea are less frequent symptoms and it would not be appropriate to take them as diagnostic or severity criteria [12]. Instead, we propose to consider objective data, such as capillary oxygen saturation or easy-to-apply clinical scores to improve treatment
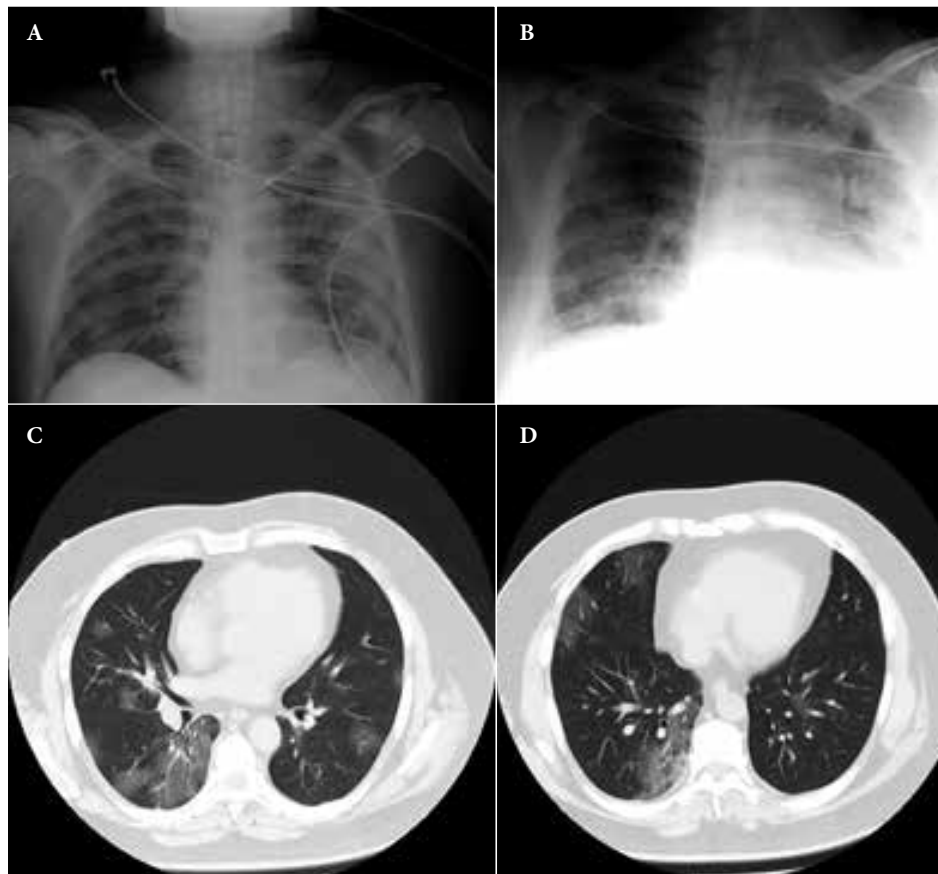
Figura 2. Patients with severe SARS-CoV-2 pneumonia. (A) Chest X-ray of a 25-year-old male with bilateral reticulonodular pattern. (B) Chest X-ray of a 47-year-old male with alveolar pattern and bilateral air bronchogram. (C & D) Chest CT scan images of a 53-year-old male with bilateral multilobular ground-glass focal lesions

decision making, mainly, in primary care conditions [7]. Gastrointestinal symptoms are atypical and rare [9].

Only 35% of the studied population was over 60 years, less than China and USA reports for severe cases. This could be due to the lower number of older adults in the Peruvian population, or because our data only represents the first stage of the epidemic. Also, a contributing factor could be that this disease entered the country through international travel, mainly by air, and transmitted by young people. There are also comorbidities, such as arterial hypertension and obesity, which are mentioned as risk factors for the development of the severe form of the disease [9-12].

Reports regarding auxiliary tests used in COVID-19 are scarce. In our study the increase of acute-phase reactants, such as C-reactive protein and lymphopenia predominated, similar to China and USA reports. The considered cut-off point for lymphopenia in this study was of less than 900 lymphocytes per mm³ compared to 1,500 per mm³ which was the value considered in the USA. The higher frequency of increased values for liver enzymes, such as transaminases,

compared to that observed in other countries, is notable [9-12].

In this series of cases, radiological images correspond mainly to simple chest X-ray images, but multifocal and bilateral lung lesions are still evident, similar to those reported in China and Korea [14-18]. However, the best evaluation method for this disease is the computerized tomography, since it allows to determine the prognosis and the therapeutic measures to be applied, being advisable to extend its use in this group of patients.

There is no approved treatment for COVID-19. In this study, broad-spectrum antibiotics are associated, similar to those used in other countries [10]. Azithromycin was used from the beginning, mainly as part of the treatment for atypical pneumonia, whereas hydroxychloroquine could be used weeks later, when it was authorized for hospital use. The need for invasive ventilatory support was relatively low, but it could be due to the fact that this is a small series of cases and that at the beginning of the pandemic its use was delayed.

Mortality in this case series was less than the 50% found in intensive care patients in USA [12], this is due to the fact that this study includes emergency room patients in which the observation period was shorter. In addition, organizational problems during the first days in the hospital may have influenced the patient's evolution, due to the lack of hematological, biochemical and radiological examinations as a result of personal and environmental biosecurity issues. There were several limitations, including the small number of cases, incomplete clinical data and auxiliary examination results, and non-uniform diagnostic criteria. Concomitant infection with other viruses and bacterial complications were not investigated. However, this is an exploratory study that provides evidence of the first cases treated in a Peruvian hospital during the COVID-19 pandemic.

In conclusion, this study presents one of the first experiences in a Peruvian hospital regarding the diagnosis and treatment of adult patients with severe COVID-19, characterized by bilateral pneumonia, high prevalence in men, the presence of comorbidities, the need for supplementary oxygen and significant mortality.

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