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Analysis of 23 Patients with HIV Infection and COVID-19: Descriptive Study

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Abstract

The clinical characteristics, diagnosis methods, medical prognosis, treatment alternatives and prophylaxis of coronavirus SARS-CoV-2 infection in HIV (Human immunodeficiency virus) infected individuals are very similar in patients under HAART with undetectable viral load and CD4+ > 200 cell/µl. The mean incubation time is 5 days (range 2 to 14 days). In HIV-seropositive patients, with high viral load and CD4 < 200 cell/µl, the time between infection for coronavirus and the onset of symptoms is minor. In the general population, 70% to 80% of individuals infected by SARS-CoV-2 develop a mild to moderate disease; 20% to 25% severe forms and 5% develop very severe clinical compromise that requires intensive therapy unit income. In HIV-positive patients these percentages would be 66%, 22% y 12%, respectively. Here we present a series of 23 HIV-seropositive patients coinfected by coronavirus SARS-CoV-2; we analyzed the epidemiology, clinical manifestations and the evolution related with both infections.

Keywords: HIV infection; Covid-19; Suppression of viral replication; Antiretroviral treatment

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Introduction

At the end of December 2019, the appearance of several cases of a rare pneumonia, of unknown etiology, was reported for the first time in Wuhan, Hubei province of China. On January 12, 2020, the causal agent, a new coronavirus, was identified and was initially named nCoV (novel coronavirus) [1]. On January 13, 2020, the first case outside China (Thailand) was diagnosed, in a 61-year-old woman, resident of Wuhan. On January 30, 2020, the WHO (World health organization) determined that it was a Public Health Emergency of International Importance. On February 11, 2020, the WHO designates the nCoV as SARS-CoV-2 due to its similarity to the cause of the SARS outbreak in 2003 and COVID-19 (Coronavirus Infectious Disease 2019) to the new disease. On March 12, 2020, the WHO declared a state of pandemic [2]. SARS-CoV-2 is a virus that infects the epithelial cells of the respiratory system and can cause severe acute respiratory syndrome. It is an RNA virus and belongs to the same family that caused SARS and MERS. It is transmitted by air from an infected person to a susceptible host; it has a short incubation period of 2 to 7 days and can last up to 2 weeks [3]. Superinfection by SARS-CoV-2 in HIV+ patients represent around 1% of total hospitalizations due to COVID-19, while the prevalence of SARS-CoV-2 infection in HIV+ subjects is 0.6% to 1.8%, similar to the general population [4,5].

A series of 23 patients with SARS-CoV-2/HIV coinfection is presented and the epidemiological and clinical characteristics and evolution in relation to both infections are analyzed.

Materials and Method

A retrospective, descriptive and observational study was carried out in which 23 patients with HIV infection and a confirmed diagnosis of SARS-CoV-2 infection by reverse transcriptase polymerase chain reaction were included. Real time (reverse transcription polymerase chain reaction (RT-PCR)) detection of nucleic acids in nasopharyngeal swabs, and its consequence the so-called COVID-19 disease. Patients hospitalized in Unit 17 of Division B of the GCABA Reference Hospital for Infectious Diseases, Francisco J. Muñiz, were included in the period from June to October 2020. This Inpatient Unit received during the period considered to patients with an indication for hospitalization and respiratory symptoms who were swabbed for the detection of SARS-CoV-2 by RT-PCR. The information was obtained from the medical records; Epidemiological characteristics, clinical manifestations, comorbidities, and patterns observed on chest computed tomography (CT) at the time of hospitalization were considered. For imaging studies, chest CT, which was performed in all patients included in this study, a 16-row tomograph was used, with images obtained in axial, sagittal and coronal planes and, in some cases, according to the criteria from the imaging specialist, high-resolution cuts were made. For the analysis of the images obtained, the following patterns of lung

involvement were considered: ground glass (also called ground glass), ground glass with a tendency to consolidation, ground glass with consolidation, cobblestone image, lobar or segmental consolidation, other patterns, and CT normal. The term ground glass opacity (GOVE) describes the opacification of the lung parenchyma that is minor compared to consolidation, such that, despite the increase in density, the pulmonary vessels and the walls of the bronchi continue to differentiate. compromised parenchyma. GOVEs represent a partial occupation of the airspace, they are less opaque than consolidations and, as a consequence, chest CT is more sensitive in their detection than simple chest radiography. Consolidation refers to the occupation of the air space by pathological products (pus, water, blood, etc.).

Consolidation appears as a homogeneous increase in lung parenchymal density that obscures the vessels and walls of the airways. It may present the air bronchogram sign, which refers to the visualization of bronchial lumens with air within a pulmonary parenchymal opacity and therefore implies the patency of the airways. Finally, the crazy-paving pattern is characterized by a thickening of the inter- and intra-lobular septa superimposed on the GOVEs, simulating a cobblestone floor, a finding that is also much more easily identified on chest CT than in the simple radiograph [6].

Comorbidities and risk factors, findings from general laboratory studies, levels of CD4+ T lymphocytes (CD4+ TL), and plasma viral load values for HIV at the time of COVID-19 diagnosis were also taken into account. The results of sputum bacteriology (common germs and AFB), and arterial oximetry.

Results

23 patients were included in the evaluation; 91.3% were men and 8.7% were women, with a median age of 49 years (range: 23 to 68 years). All patients (100%) had symptoms consistent with COVID-19; 13 (56%) presented at least 3 different clinical manifestations included in the diagnostic protocols for suspected this infection in accordance with the regulations of the National Ministry of Health (Table 1). The level of oxygen saturation in peripheral blood could also be evaluated by pulse oximetry in 19 patients with a median saturation of 96% (range: 88% to 99%). In this study, comorbidities were also analyzed since they play a fundamental role in the evolution, prognosis and morbidity and mortality of the COVID-19 disease. Seventeen patients (74%) presented comorbidities; the most common was high blood pressure (HBP), followed by coinfection with Mycobacterium tuberculosis (MTB), community-acquired pneumonia (CAP) and infection with Hepatitis C virus (HCV). The frequency of MTBC/SARS-CoV-2 coinfection in this population is explained by the nature of the Hospital where the study was carried out. The prevalence of comorbidities is expressed in table 2.

Table 1: Clinical Manifestations in 23 patients with SARS-CoV-2 infection/HIV positive symptoms.

Fever	17	73.9%
Cough	13	56.5%
Dyspnea	13	56.5%
Odynophagia	9	39.1%
Headache	9	39.1%
Anosmia	7	30.4%
Myalgias	6	26.1%
Dysgeusia	5	21.7%
Abdominal pain	4	17.4%
Arthralgias	3	13.0%
General discomfort	3	13.0%
pain	2	8.7%
Vomiting	1	4.3%
Diarrhea	1	4.3%
Seizures	1	4.3%
Hyporexia	1	4.3%
Dysarthria	1	4.3%
Weight loss	1	4.3%
Asthenia	1	4.3%
Nausea	1	4.3%
Edema of lower limbs	1	4.3%
Jaundice	1	4.3%
Preauricular phlogosis	1	4.3%

All patients (23/100%) underwent chest CT upon admission, observing the following radiological patterns: the most frequent was the ground glass pattern presented by 16 patients (72.7%), which was distributed bilaterally. Multi-lobar in 15 (68.2%) and unilateral non-multi-lobar in 1 (4.5%). Ground glass (VE) with a tendency to consolidation was found in 4 subjects (18.2%) and ground glass with consolidation in 1 (4.5%). The radiological/tomographic cobblestone pattern was present in 3 patients (13.6%), one patient (4.5%) had consolidation and in another (4.5%) a miliary pattern was observed coinciding with a COVID-19/histoplasmosis coinfection. CT did not show significant alterations in 1 patient (4.5%). The findings on the chest images are summarized in table 1. The distribution of the lesions in VE is summarized in table 2. The rest of the findings obtained on the chest CT are included in table 4.

In relation to the results linked to the HIV/AIDS disease, there was data from 14 patients; 2 (14.2%) patients had a recent diagnosis in the last 6 months. In the rest, the time since the diagnosis of retrovirus infection was greater than 3 years (85.7%). 64.3% (9 patients) were included in the CDC category C3 due to having suffered opportunistic marker infections prior to COVID-19. The CD4+ LT count at the time of SARS-CoV-2 diagnosis was available in all 23 patients in the series; the median was 244 cells/µl; 39% with < 200 cells/µl, 40% between 200 and 500 cells/µl and 21% with > 500 cells/µl. The median VL for HIV, available in 22 patients, was 49 copies/ml. These findings are summarized in table 3. Regarding the evolution, 4 of the 23 patients in this series died (17.39%).

Table 1 presents findings on CT: N: 23 (100%), Patterns: there were patients who presented more than one radiological pattern, Frosted Glass: 16 (72.7%), Bilateral multi-lobar: 15 (68.2%), Unilateral non-multi-lobar: 1 (4.5%), VE with a tendency to consolidate: 4 (18.2%), VE with consolidation: 1 (4.5%), Cobblestone pattern: 3 (13.6%), Lobar consolidation: 1 (4.54%), Miliary pattern: 1 (4.54%) (COVID-19-histoplasmosis coinfection), and Normal CT: 1 (4.54%).

Table 2 presents distribution of EV: N = 16 (100%), VE peripheral distribution: 13 (81.25%), VE central distribution: 1 (6.25%), and VE mixed distribution: 2 (12.5%).

Table 2: Comorbidities detected in patients in this series.

HIV infection	23	100.0%
HTN	5	21.7%
Previous TBC	5	21.7%
Previous NAC	4	17.4%
HCV coinfection	4	17.4%
COPD	2	8.7%
Sick neurological	2	8.7%
Diabetes	1	4.3%
Obesity	1	4.3%
Asthma	1	4.3%

Table 3 presents findings in relation to HIV infection: Date of diagnosis (parameter that was available in 14 patients): N = 14, Recent diagnosis (last 6 months): 2 (14.28%), Diagnosis 3 years ago or more: 12 (85.7%), CDC HI infection stage (available in 14 patients): N = 14, Stage A and/or B: 5 (35.7%), Stage C3: 9 (64.3%), Previous AIDS marker diseases, Pulmonary/disseminated tuberculosis (4 patients), Disseminated cryptococcosis with CNS involvement (1 patient), *Pneumocystis jiroveci* pneumonia (PJP) (2 patients), Diarrhea due to Cryptosporidium (1 patient), Disseminated histoplasmosis (1 patient). Median CD4+ LT available in all patients: (N = 23, 100%): 244 (16.5%), CD4+ LT range (N = 23): 3 to 1078, Less than 200 LT CD4 +: 39%, Between 200 and 500 LT CD4 +: 40%, More than 500 LT CD4 +: 21%, Median Viral Load: available in all patients (N = 23): 49 copies.

Table 4 presents other findings on chest CT: Nodules 2, Cysts 1, Spill 1, Cardiomegaly 1, Cavities 1, Tree in bud 3, Fibrous tracts 3, Bronchiectasis 1, Emphysema 2, Spondylosis 3, DA increase 1, Hepatomegaly 3, Steatosis 1, and Splenomegaly 3.

Discussion

The first studies carried out in Europe and the US showed little impact of COVID-19 infection on patients with HIV. In a follow-up cohort of 5,683 patients with HIV, from the Hospital Clinic of Barcelona, COVID-19 was diagnosed in 53 of them (0.9%) [7]. Similarly, patients with retrovirus infection represented 0.8% of the 5,700 patients hospitalized for COVID-19 in 12 hospitals in New York [8]. In a systematic review of 25 studies (mostly from the US and China) that included 252 patients, it was found that the risk of HIV-infected patients, both of SARS-CoV-2 infection and of disease progression baseline, was similar to that of the uninfected. As in the general population, comorbidities and advanced age were the risk factors for severity and mortality in HIV/COVID-19 co-infection [5]. Something similar was observed in a larger study carried out in Spain. In a cohort of 77,590 people with HIV (in 60 hospitals) receiving antiretrovirals, risk factors for hospitalization, admission to the intensive care unit, and mortality similar to those of the general population were identified [9].

A recent systematic review on COVID-19 demonstrated that in countries with a high prevalence of HIV/MTB co-infection, TB was a risk factor for COVID, increasing severity and mortality, regardless of the stage of retrovirus infection [10].

However, with the development of the different variants of SARS-CoV-2 and the inclusion of a greater number of HIV-positive people in the studies, the first conclusions began to change. Thus, a WHO study that included 15,500 HIV-positive patients from 24 countries showed that retrovirus infection was an independent risk factor for severe COVID-19 disease, the need for hospitalization, and mortality [11].

In this large population of HIV-positive subjects, as in the general population, age over 65 years, male gender, diabetes and high blood pressure were risk factors that were associated with greater in-hospital mortality and serious illness at the time of delivery. the internment. In this series, the mortality of those patients infected by the retrovirus with mild to moderate disease ($SO_2 \geq 90\%$ without the need for O_2 supplements; respiratory rate ≤ 30 per minute without the need for oxygen therapy or mechanical ventilation) at the time of hospitalization was 16.8%, while for those with severe COVID-19 disease ($SO_2 < 90\%$; respiratory rate > 30 per minute; ICU admission; requirement for inotropes or vasopressors and need for O_2 or assisted respiration) it was 34.9% [11]. In a systematic review that included 252 HIV-positive patients with SARS-CoV-2 superinfection, 90.5% of the deceased patients were over 50 years old, 85.7% were men, and 64.3% had multiple comorbidities [5]. Defects in the immune response, both B and T, can potentially be associated with a more severe and prolonged clinical course of COVID-19 disease. This occurs especially in patients infected by the retrovirus, with low CD4 and persistent viral replication, in the absence of ART or with a lack of response to ART [12]. The antibody response may not be adequate in the HIV+ population, both to infection and vaccination. However, in HIV+ subjects on ART with a good virological and immunological response, two studies verified levels and duration of neutralizing IgM and IgG antibodies similar to the general HIV population [13,14]. A third study demonstrated a lower neutralizing antibody response [15].

As we could see in the series presented, the clinical presentation of SARS-CoV-2 infection and its variants does not differ in HIV-positive patients on HAART with good clinical, virological, and immunological response, compared to the general population. Fever, cough, fatigue, dyspnea, headache, myalgia, odynophagia, loss of taste and smell are the most common clinical manifestations in the general population

Table 3: Laboratory findings on admission.

Parameter	N	Normal value	Obtained values (Median)
White blood cells	23	3600 to 11000	5200/mm³
Lymphocytes	23	20.5% to 46.5%	1350/mm³
Urea	23	10 to 50 mg/dl	31 mg/dl
LDH	23	230 to 460 U/L	404 U/L
Quick time	23	70 to 120%	82%
Platelet count	23	150,000 to 400,000/mm3	196,000/mm³
Blood glucose	23	70 to 110 mg/dl	98 mg/dl
Ferritin	Value available in 15 patients	30 to 400 ng/ml	895 ng/ml
D-dimer	Value available in 13 subjects	0 to 500 ng/ml	678 ng/ml
Sodium	Available level in 13 patients	135 to 140 mmol/L	138 mmol/L

Table 4: COVID-19 differential diagnosis with OI.

	Similarities	Differences
TBC	Cough, dyspnea, fever	Subacute/chronic evolution - Productive cough. Radiological pattern (cavitation, tree in bud). The greater the immunosuppression, the greater the similarity with COVID-19
PJP	Cough, dyspnea, radiological pattern	Subacute/acute evolution
Cryptococcosis	Headache, fever, sometimes lung involvement	Cough, dyspnea, radiological pattern, diarrhea
Disseminated histoplasmosis	Subacute/chronic evolution, meningeal signs	Subacute/chronic evolution, reticulo-nodular/miliary pattern, skin lesions

and also in HIV positive people with a good response and adherence to HAART. This clinical presentation could also be observed in the series analyzed and in others consulted [16].

Regarding the evolution, in 2 series analyzed, 66.5% of patients presented mild to moderate symptoms, 21.7% had severe manifestations and 11.8% required ICU admission [5,17].

The diagnosis of HIV/SARS-CoV-2 co-infection is based on the same methods used for the general population. RT-PCR detection of the viral genome is the gold standard laboratory test. It is performed on nasopharyngeal or oropharyngeal swabs with a sensitivity in this population of 65% to 75%; and a specificity of 99%. The rapid test for viral antigens in nasal and pharyngeal swabs has a sensitivity that varies from 30% to 80% and depends on the moment in which the sample is collected in relation to the onset of symptoms [18].

Pulmonary involvement was the most frequent form of presentation of the disease in these subjects, as in the general population. The changes observed in lung parenchyma can be seen through chest X-ray with a sensitivity of 69% in symptomatic patients or, even better, with chest tomography that shows a sensitivity of 97% at the time of presentation of symptoms [5,19]. In the series presented, chest CT was performed on all patients, with radiological patterns similar to those of the general population (Table 1). In this sense, in a series analyzed, those patients with high clinical suspicion and an initial negative RT-PCR for SARS-CoV-2 who presented a chest CT in which changes compatible with COVID-19 were detected, in a second or third RT-PCR, these same patients had (+)20 results.

In HIV-positive subjects, it is important to include differential diagnoses of lung pathologies linked to immunodeficiency and that may present similar or overlapping radiological findings, especially PJP. PJP is the opportunistic infection (OI) most frequently referred to in the literature as a misdiagnosis of COVID-19 [20]. The clinical presentation and radiological findings may be similar to COVID-19. It is one of the most common OIs in patients who are unaware of their HIV infection status with CD4 counts <200 cells/µl. Without adequate treatment, mortality is 20 - 40% [21,22].

In these patients, clinical suspicion, history/physical examination, and rapid test/serology for HIV are of fundamental importance for diagnosis [21,22].

In relation to the prognosis of HIV/SARS-CoV-2 coinfection, the progressive increase in the median age of the HIV+ population in recent years, the immunosenescence that is added to the immunodeficiency associated with the retrovirus, the LT CD4+ count < 200 cells/µl worsens the prognosis, makes differential diagnoses difficult and increases, and also increases the risk of long COVID-19. Other elements of unfavorable prognosis include a detectable viral load, having suffered opportunistic infections in the previous 6 months and increased rates of neoplasms, cardiovascular disease and neurological disease, renal involvement and other comorbidities associated with HIV [23]. Finally, regarding treatment, those patients on ART with a good clinical, virological, and immunological response should be treated identically to the general population. ART should not be interrupted if it is effective and drug interactions should be monitored [24].

Conclusion

The clinical characteristics, diagnosis, prognosis, prophylaxis, and treatment of SARS-CoV-2 coronavirus infection in HIV-infected patients are very similar to those of the general population when they are virologically suppressed with treatment. antiretroviral and have a CD4+ lymphocyte count greater than 200 cells/µl. In immunosuppressed patients or without antiretroviral treatment, the prognosis is worse and opportunistic AIDS infections should be included in the differential diagnosis, especially those that compromise the respiratory system. Fortunately, the extensive vaccine coverage that exists in 2023 makes severe symptomatic disease much less frequent.

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Conflict of Interest

The authors declare that they have no conflicts of interest.

Ethics Statement

The work has been approved by the ethics committee responsible in the workplace.

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