REVIEW ARTICLE
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Potential impact of the COVID-19 in HIV-infected individuals: a systematic review

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SUMMARY

BACKGROUND: Although much has been studied about the SARS-Cov-2 virus, its effects, and the effectiveness of possible treatments, little is known about its interaction with other infectious diseases.

OBJECTIVE: The aim is to study its clinical features and morbidity, and mortality outcomes of COVID-19 patients with HIV/AIDS coinfection.

DATA SOURCES: MEDLINE, Web of Science, Embase, CINAHL, LILACS, Scopus, ClinicalTrials.gov, and Cochrane.

STUDY ELIGIBILITY CRITERIA: Atudies in any language, published after 2019, were describing COVID-19 patients with HIV/AIDS.

STUDY APPRAISAL: JBI Levels of Evidence, Joanna Briggs Institute.

SYNTHESIS METHODS: As shown in the PRISMA flow diagram, two authors separately screened the search results from the obtained titles and abstracts.

RESULTS: Chest CT was observed in patients with pneumonia by SARS-CoV-2 with findings of multiple ground-glass opacities (GGO) in the lungs, there is a need for supplemental oxygenation. One patient developed encephalopathy and complicated tonic-clonic seizures; four patients were transplanted (two, liver; two, kidneys), one patient developed severe SARS-CoV-2 pneumonia and 30 patients died (mortality rate, 11%).

CONCLUSION: HIV did not show any relevance directly with the occurrence of COVID-19. Some studies suggest that HIV-1 infection through induction levels of IFN-I, may to some extent, stop the apparent SARS-CoV-2 infection, thus leading to undetectable RNA. Moreover, some authors suggest retroviral therapy routinely used to control HIV infection could be used to prevent COVID-19 infection.

KEYWORDS: COVID-19. SARS-CoV-2. HIV. Acquired Immunodeficiency Syndrome. Antiretroviral therapy, highly active.

INTRODUCTION

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2; COVID-19) pandemic is unprecedented in scale and speed reaching several countries, affecting countless individuals and causing thousands of deaths around the world. Since HIV infection is a common disease, the concurrence between HIV infection and SARS-CoV-2 can become an important and frequent concern. Therefore, nowadays, it seems essential to clarify whether the HIV infection could alter the clinical course of SARS-CoV-2 infection[1-3].

As the outbreak grew to a pandemic, many centers worldwide raised the concern that immunocompromised patients

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may be at high risk of developing severe respiratory disease (COVID-19)[4-6]. Patients immunosuppressed for various reasons have effects on humoral and cell-mediated immunity and neutrophil function, increasing the risk of severe infections caused by viral agents, such as adenovirus, rhinovirus, norovirus, influenza virus, and respiratory syncytial virus[4,6]. Many of these latter viruses, including coronaviruses, implicate the host response as an important contributor to the disease process; in this respect, dysregulated and excessive innate immune responses appear particularly important drivers of tissue damage during infection[7,8]. These aspects may be relevant when it comes to infection of an immunocompromised host, potentially protected by a weaker immune response against the infection.

However, curiously reviewing the mortality and morbidity reports published on severe acute respiratory syndrome (SARS), middle-east respiratory syndrome (MERS), and more recently on COVID-19, immunosuppression is not mentioned as a risk factor for more severe disease or mortality coronaviruses when compared with the general population, both children and adults[1,3,9]. Mascolo et al.[9] proposed a hypothesis that could explain the interaction between HIV infection and the clinical course of SARS-CoV-2 infection. The latter suggests that patients with conditions that impair the state of the immune system, as immunosuppression for solid organ transplantation or HIV infection, could be protected against severe clinical manifestations, despite the susceptibility to SARS-CoV-2 infection[9,10].

This fact could be explained by the activation of the immune system, especially T cells, which represent a landmark of the histological picture of lung injury related to COVID-19[9]. Additionally, the antiretroviral treatment started (lopinavir/ritonavir, LPV/r) as management of SARS-CoV-2 infections, and it could play a double effect: inhibition of SARS-CoV-2 replication, facilitating the viral clearance and inhibition of HIV replication that could allow a slight activation of the immune response, just enough to contrast the SARS-CoV-2 infections without the beginning of the hyperinflammatory state[9,10]. Furthermore, the antiretroviral (LPV/r) administration could be useful for a potential and not yet confirmed direct anti-SARS-CoV-2 antiviral effect[9-11].

There is much to be clarified about the existing immunological interactions between HIV and SARS-CoV-2, and further studies are urgently required to face this lack of data. For this reason, this study aims to clarify the clinical features and morbidity and mortality outcomes of patients with coinfection COVID-19 and HIV/AIDS.

METHODS

This study adhered to PRISMA guidelines[12]. The review was not registered in PROSPERO, and corresponding authors were not contacted due to time constraints. Ethical approval was not required for this type of study.

Literature Search Strategy

Eligible studies were identified by searching the following databases: MEDLINE, Web of Science, Embase, CINAHL, LILACS, Scopus, ClinicalTrials.gov, Cochrane, and Google Scholar. The studies were identified by a literature search of databases following medical subject heading (MESH) terms: (COVID-19 OR severe acute respiratory syndrome coronavirus 2 OR SARS-CoV-2) AND (Human Immunodeficiency Virus OR HIV OR Acquired Immune Deficiency Syndrome Virus OR Acquired Immunodeficiency Syndrome Virus OR AIDS Viruses OR AIDS Virus).

Reference lists of the identified publications for additional pertinent studies were reviewed. Three researchers (KSM, ACS, and LASS) searched for articles published between December 2019 and July 2020, considering the first case of COVID-19 was registered in the city of Wuhan, China, in December 2019[13].

Inclusion Criteria

Studies meeting the following criteria were included: (a) all the studies that were describing patients affected by the SARS-CoV-2/COVID-19 and with HIV/AIDS, for example, primary case reports, case series, observational studies, randomized controlled trials, and others, (b) there were no language restrictions while selecting the studies, and (c) studies published after 2019.

Selection of Studies

The authors KSM and LASS separately screened the search results using the titles and abstracts. Duplicate studies and reviews were excluded. The author ACS contributed along with the first two went through the full text articles to determine whether the studies meet the inclusion criteria. Discrepancies were resolute for author AKG. The selection of the studies was summarized in a PRISMA flow diagram (Figure 1).

Data Collection and Analysis

Various characteristics of the eligible studies were extracted, including the first authors' last names, year of publication, location of the study (country), study design, primary objective, level of evidence, patients (population), signals and symptoms, mean patients age, patient outcome, laboratory tests, and treatment. Standardized data extraction forms were specifically being created for this review, and

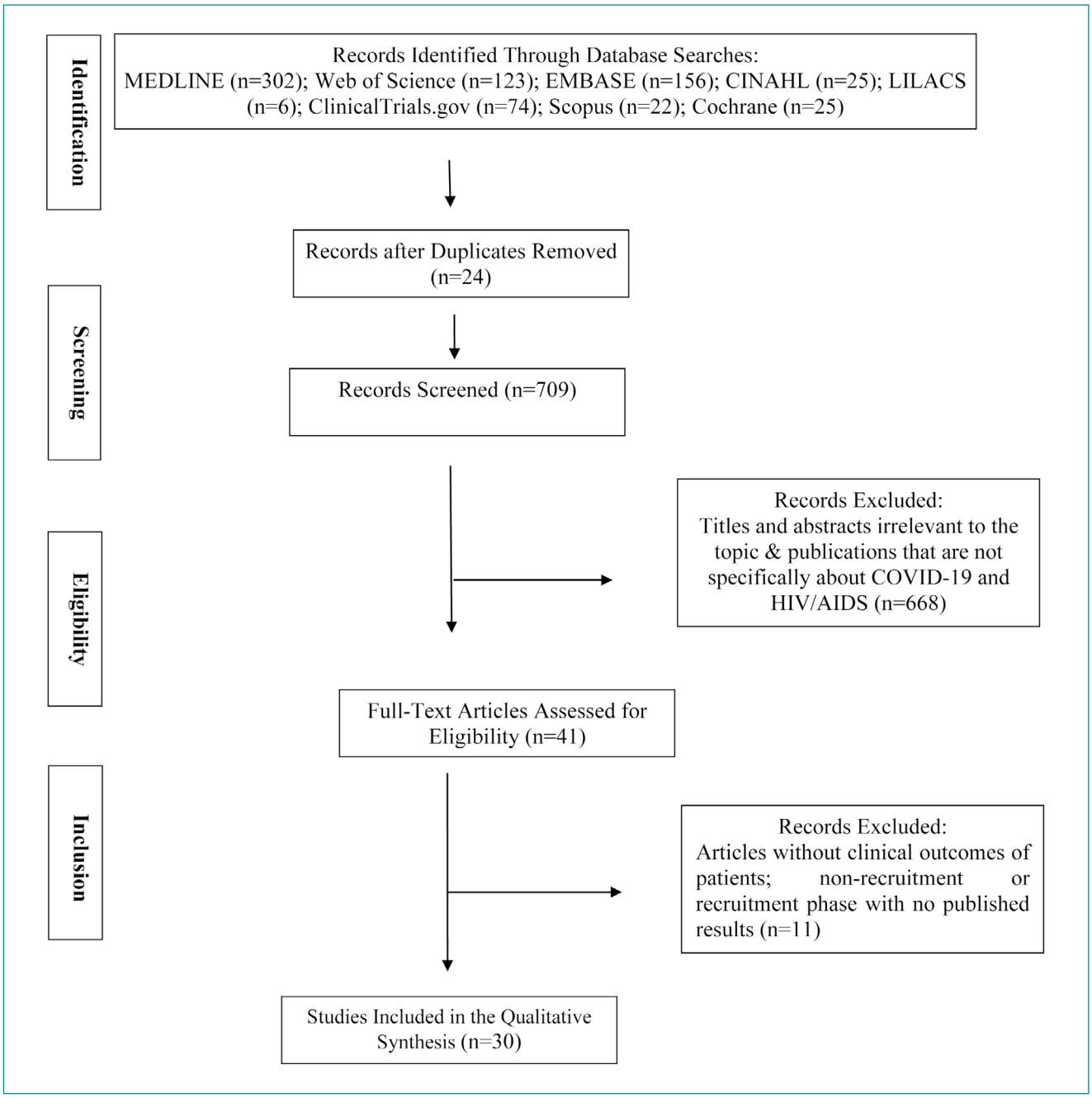

Figure 1. Flow diagram of the search for eligible studies of COVID-19 and HIV/AIDS. CENTRAL=Cochrane Central Register of Controlled Trials.

the results were entered into a database. All data entered were double-checked.

Quality of Evidence

The quality of included studies was assessed using New Joanna Briggs Institute (JBI) Levels of Evidence, developed by the JBI Levels of Evidence and Grades of Recommendation Working Party (October 2013)[14].

RESULTS

Selection of Relevant Studies

The virtual searches retrieved a total of 733 studies (302 from PubMed, 123 from Web of Science, 156 from Embase, 25 from CINAHL, 06 from LILACS, 74 from ClinicalTrials.gov, 22 from Scopus, and 25 from Cochrane). Excluding duplicates (24), 709 articles were selected. After evaluating the title

and abstract, 668 additional articles were excluded. For the 41 studies that had full-text analysis, 30 met the eligibility criteria for this study and were later included in the review. The PRISMA flow diagram for selecting available studies is given in Figure 1.

The characteristics of the included studies are shown in Table 1. The number of participants in each study ranged from 1 to 51. The articles were published in China[15-17,21,31,37,43], Spain[18,23], Uganda[19], Turkey[20], Germany[22], New York[33,34], Austria[25], the United States[24,25,32,40,41], Italy[27,29,44], Japan[28], Cyprus[30], Chicago[35,38], the United Kingdom[36,39], and Singapore[42] in 2020, although COVID-19 was described in 2019[13]. All the articles were in English.

Study Designs

A total of 28 articles were case reports or case series (level of evidence 4.d)[15,16,18-22,24-44] and two were cohort studies (level of evidence 4.b)[17,23]. Thus, the studies included in this review have low levels of evidence according to our classification.

Study Characteristics

In total, 266 patients coinfected with HIV and COVID-19 were included, of whom 209 were men and 57 were women. In the case studies, male patients were 24 and 75 years old[15,16]. Before the observational study, the median age of patients (n=8) was 57.0 years (47.5–61.5)[17].

Clinical Manifestations

The principal clinical manifestations were fever, coughing, shortness of breath, diarrhea or gastrointestinal symptoms, and pneumonia, as shown in Figure 2. The study by Guo et al.[17] showed that till March 3, 2020, 6 of the COVID-19/HIV patients were considered mild cases, 1 was severe, and 1 was a critical case who died. In the study with 33 patients presented by Härter et al.[22], mild clinical cases were 25/33 (76%), severe in 2/33 cases (6%), and critical in 6/33 cases (18%), with 3/33 both patients with known comorbidities. Two other cases of similar deaths were reported by Gervasoni et al.[29] The first was a 47-year-old overweight patient, but without known comorbidities, needed mechanical ventilation, and the second had cardiovascular disease plus a recent diagnosis of lung cancer during hospitalization.

There have also been reports of deaths in other studies. Aydin et al.[20] related the patient, who had potential comorbidities such as obesity, diabetes, hypertension, and chronic obstructive pulmonary disease (COPD), refused to undergo regular treatment for the comorbidities. In the series of cases presented by Suwanwongse and Shabarek[33], all 9 patients mentioned had comorbidities and 7 died – 4 due to hypoxemic respiratory failure and 3 due to septic shock and multiple organ failures. In the study by Shalev et al.[34], of the studied 31 patients, 8 died, of these 4 were above 65 years old, and the other 4 were between 50 and 65 years old. At the time of death, four of them were not ordered to perform cardiopulmonary resuscitation maneuvers. One patient required intubation and mechanical ventilation in the ICU and died of multiple organ failure caused by COVID-19 pneumonitis[36]. Childs et al.[39] mentioned 18 patients in their study, of these 5 died with a mean hospital stay until 8 days, with an interval of 3 and 28 days until death. Okoh et al.[40] reported 27 patients observed in their study and 2 died, who were elderly and had multiple coexisting conditions complicated by septic shock and multi-organ dysfunction syndrome.

Diagnosis

Clinical and epidemiological information are the important factors in the investigative process. Thus, as a travel history for COVID-19 epicenters, direct or indirect contact with persons suspected or confirmed of SARS-CoV-2 infection was decisive on the front line against COVID-19 in the control, treatment, and care as in diagnosis[16,17,19,21,22,24,26,29,35,41-43].

Even though the patients had some main distinctive manifestations of COVID-19, the SARS-CoV-2 tests using reverse transcriptase polymerase chain reaction (RT-PCR) were persistently negative in different samples at various times during the hospitalization period[16,21,24,25,30,37,38,44]. The principles of the diagnostic methods were nasopharyngeal swabs for RT-PCR[15,16,18-35,37,44], nucleic acid test (NAT) of SARS-CoV[17], laboratory test[19,20,22,24,31,37,39,40,42-44], chest radiography[24,27,29-31,34,38,39], computed tomography (CT) of the chest[15-18,20,21,24,28,29,37,41,43,44], brain magnetic resonance imaging (MRI) with and without contrast[41], electrocardiogram (ECG)[41], sputum, aspiration of the lower respiratory tract[23], or bronchoalveolar lavage[22].

Patients' Outcomes

The principal patients' outcomes were as follows:

- Mild lymphopenia with a lymphocyte count of 1.1 × 10^9/L[15,18,20,21,28,31,33,34,36,37,39,41,44];
- Low CD4+ T-lymphocyte percentage[15-17,21-23,28,29,33,34,36,38,39];
- The chest CT indicated the SARS-CoV-2 pneumonia with findings of multiple ground-glass opacities (GGO) in lungs[15,16,20,21,23,25,27-31,33,34,37-39,41,43,44];
- On supplemental oxygen, arterial blood gas analysis revealed: pH 7.41, PCO_2 37.4 mmHg, PO_2 63.9 mmHg, and HCO_3^- 23.4 mmol/L[15,21,25,34,38,44];
- Thirty patients died, so the mortality rate was 11%[17,20,22,29,33,34,36,39,40];

Table 1. Characteristics of the included studies.

Author	Objective	N	Patients' Age	Patient Outcome	Chest Imaging	Treatment	Diagnosis
Zhu et al.[15] (2020)	We reported on an identified unique severe case involving coinfection of SARS-CoV-2 and HIV.	01 man	61	On admission, physical examination revealed a body temperature of 39°C, respiratory rate of 30 breaths per minute and oxygen saturation of 80%, which reached 91% while the patient was given mask flow oxygen at a rate of 5 L/min. On supplemental oxygen, arterial blood gas analysis revealed: pH 7.41, PCO2 37.4 mmHg, PO2 63.9 mmHg, and $HCO_3^{\boxtimes}$ 23.4 mmol/L. Lymphopenia also got worse, with a lymphocyte count of 0.56 × 10^9/L and a low CD4+ T-lymphocyte of 4.75%.	The chest CT indicated the SARS-CoV-2 pneumonia with findings of multiple ground-glass opacities (GGO) in bilateral lungs. The follow-up chest CT displayed progressive GGO and consolidation in lungs.	Isolation at home; anti-HIV drug, lopinavir/ritonavir 400/100 mg per dose, twice daily for 12 days; moxifloxacin 400 mg once daily for 7 days, γ-globulin 400 mg/kg once daily for 3 days; and methylprednisolone 0.8 mg/kg once daily for 3 days.	RT-PCR and chest CT.
Zhao et al.[16] (2020)	We reported a unique case of COVID-19 with preexisting immune dysfunction from previous coinfection of HIV and HCV.	01 man	38	Nasal congestion, runny nose, cough, expectoration, chest tightness, palpitation, and abdominal distension. Low fever of 37.2°C and normal pulse, breath and blood pressure.	A chest CT showed right lower pneumonia.	Oseltamivir and IFN-α inhalation and taking lamivudine, tenofovir, and efavirenz.	RT-PCR and chest CT.
Guo et al.[17] (2020)	We investigated 1178 HIV/AIDS patients in Wuhan and surveyed their health status and whether they were directly contacted with confirmed COVID-19 patients.	07 men and 01 women	The median age of patients was 57.0 years old (47.5–61.5).	Fever, non-productive cough, dyspnea, myalgia, and diarrhea. Till March 3, 2020, 6 of the COVID-19/HIV patients were with mild cases, 1 was with severe case, and 1 was with critical case who died. Six of them had CD4 counts >350/μL, and 2 with CD4 counts between 101 and 350/μL. All patients have a low HIV-VL as less than 20 copies/mL.	NA	All 8 COVID-19 patients' ARV regimens are nucleoside reverse transcriptase inhibitors (NRTIs) and non-nucleoside reverse transcriptase inhibitors (NNRTIs). None of those COVID-19/HIV patients took LPV/r-based ART regimen, which seemed to support the use of LPV/r in PrEP and cope with COVID-19.	CT scan and virus nucleic acid test (NAT).

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Table 1. Continuation.

Author	Objective	N	Patients' Age	Patient Outcome	Chest Imaging	Treatment	Diagnosis
Blanco et al.[18] (2020)	We described the first single-center experience of COVID-19 in patients infected with HIV-1, including clinical characteristics, antiviral and antiretroviral treatment, and outcomes.	05 men	The median age of patients was 39.8 years old (29–49).	Two patients had comorbid conditions. Four were virologically suppressed: two with protease-inhibitor (darunavir-boosted cobicistat) and two with integrase inhibitor (dolutegravir)-based ART. CD4 counts were above 400 cells/μL in all patients apart from Patient 5, who was ART naive and a very advanced late presenter. Two patients had upper respiratory tract infections, and three had viral pneumonia, including two requiring admission to the intensive care unit (ICU) with invasive (Patient 2) and non-invasive (Patient 5) mechanical ventilation.	NA	We started all five patients on anti-SARS-CoV-2 treatment on the day of diagnosis. Patient 1 and 5 with darunavir-boosted cobicistat, and patients 2–4 were adapted to lopinavir-boosted ritonavir. We left Patient 1, who had mild infection, on his normal ART. We gave the other patients hydroxychloroquine (patients 2–5) with azithromycin (patients 3–5), and interferon β-1b (patients 2 and 5). We administered concomitant antibacterials in all three patients who had pneumonia (patients 2, 4, and 5), and corticosteroids in two patients (patients 4 and 5) and tocilizumab in one (Patient 2).	RT-PCR and chest CT.
Baluku et al.[19] (2020)	We described a case of HIV/SARS-CoV-2 coinfection.	01 woman	34	On admission (Day 1), she was in a good general condition with no symptoms. There was no wasting, lymphadenopathy, or pallor and her temperature was 36.4°C) (normal). She had a blood pressure of 110/80 mm of mercury (mmHg) and a pulse rate of 84 beats per minute (b/min), both of which were normal. The	NA	Azithromycin (500 mg daily for 5 days), hydroxychloroquine (400 mg twice on day 3 and 200 mg twice daily for the subsequent 5 days), and paracetamol (1 g three times a day for 5 days). Oral	RT-PCR and laboratory test.

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Table 1. Continuation.

Author	Objective	N	Patients' Age	Patient Outcome	Chest Imaging	Treatment	Diagnosis
				respiratory exam was significant for tachypnea (a respiratory rate of 26 breaths/min) with normal oxygen saturation (SpO_2) of 96% on ambient air. There was no respiratory distress, and auscultation of the chest was normal. On Day 3, she reported headache, chest pain, anorexia, and muscle aches but no cough or shortness of breath. Her vitals were normal, except for a respiratory rate of 24 breaths/min and a pulse rate of 97 b/m. On Day 6, she developed watery nonbloody diarrhea without vomiting, abdominal pain or fevers. Clinically, she had dry mucus membranes and the blood pressure was 96/60 mmHg. All symptoms had resolved by Day 12. The respiratory rate was 16 b/min, the pulse rate was 80 b/min, and she had a blood pressure of 126/88 mmHg.		ciprofloxacin (500 mg twice daily for 5 days) and oral rehydration.	
Aydin et al.[20] (2020)	These cases are presented to show the course of coinfection with COVID-19 in HIV-infected cases.	P1 – man	34	With 10 years of known HIV/HBV coinfection but without treatment compliance due to bipolar disorder was admitted with the complaints of dyspnea, dry cough, and fever. On physical examination, there was no pathology other than cachectic appearance, low-grade fever (38°C), and bilateral coarseness in the lungs on auscultation.	Chest CT showed multiple GGO in the bilateral lower lung	Trimethoprim-sulfamethoxazole (TMP-SMX) and oseltamivir	RT-PCR, chest CT, and laboratory test.
		P2 – man	44	Due to HIV infection, it has been using TDF/FTC+dolutegravir for the past 2 years. Although obese patient (body mass index: 35.5 kg/m^2)	X-ray and chest CT showed bilateral patch-like paving stone view, large	Hydroxychloroquine, azithromycin, and oseltamivir.	

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Table 1. Continuation.

Author	Objective	N	Patients' Age	Patient Outcome	Chest Imaging	Treatment	Diagnosis
				had diabetes, chronic obstructive pulmonary disease (COPD), and hypertension, he refused to get regular treatment for these comorbidities. On March 25, 2020, he applied with a complaint of fever, dry cough, and shortness of breath. In the ICU, he suffered a sudden cardiac arrest, despite cardiopulmonary resuscitation, the patient has died.	glass-ground lesions, and was interpreted as mid-advanced viral pneumonia positive		
		P3 – man	35	Has been using TAF/FTC+elvitegravir/cobicistat (EVG/c) for 2 years with the diagnosis of HIV infection and followed up regularly for HIV RNA negative according to the EACS guidelines. On March 29, 2020, he applied with severe weakness, dry cough, and non-bloody diarrhea (5–6 times per day) that had been going on for 11 days. Although there was no pathological finding in the physical examination of the patient and normal oxygen saturation SpO2 95% in room air.	Chest CT showed bilateral peripherally located incomplete ground-glass density infiltrations.	Hydroxychloroquine and oseltamivir.	
		P4 – man	36	Viral suppression continued for 4 years under TAF/FTC/EVG/c treatment, admitted with a dry cough and persistent fever for 6 days.	Chest CT revealed bilateral extended GGO.	Hydroxychloroquine, azithromycin, and oseltamivir	
Wang et al.[21] (2020)	We described a case of HIV/SARS-CoV-2 coinfection.	01 man	37	He denied any other diseases before this onset. The initial physical examination revealed a body temperature of 38.8°C, oxygen saturation (SpO2) 85–90% under ambient air, respiratory rate of 40 breaths/min, blood pressure	The chest CT of this patient showed multiple infiltrations in both lungs, consistent with viral infection. On the second chest	High-flow oxygen and arbidol; methylprednisone, moxifloxacin, and sulbactam/cefoperazone (sulperazone); human	RT-PCR and chest CT.

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Table 1. Continuation.

Author	Objective	N	Patients' Age	Patient Outcome	Chest Imaging	Treatment	Diagnosis
				of 145/93 mmHg, and pulse of 119 bpm. His vital signs remained stable for the first 3 days, apart from dyspnea and chest pain. On 14 February, he developed a high fever of 39.4°C accompanied with dyspnea and palpitations. His body temperature returned to normal, but he still had dyspnea, palpitations, and chest pain and he still needed high-flow oxygen (10 L/min) through a mask.	CT, it showed inflammation absorption compared with the previous one.	serum albumin, thymosin, and ulinastatin; tocilizumab.	
Härter et. al.[22] (2020)	We described our early experiences with COVID-19 and clinical characteristics in patients with documented HIV infection.	30 men and 03 women	The median age of patients (*n* = 33) was 48 years old (26–82).	Two patients with detectable (HIV)-1 viremia needed hospital admission including intensive care treatment and mechanical ventilation, and one of these patients died. Comorbidities other than HIV infection were documented in 20/33 patients, including arterial hypertension (P10), chronic obstructive pulmonary disease (P6), diabetes mellitus (P4), cardiovascular disease (P3), and renal insufficiency (P2). Coinfection with hepatitis B has been documented in five patients: a resolved hepatitis B in four patients, and in one patient a chronic hepatitis B. In one patient, a cured hepatitis C. Common symptoms were cough in 25/32, fever in 22/32, arthralgia/myalgia 7/32, headache 7/32, and sore throat in 7/32. Sinusitis and anosmia occurred in 6/32 for each. At the last available follow-up, 29/32 of patients with documented outcome had recovered from COVID-19. Altogether, 14/33	NA	Antiretroviral regimens included NRTIs in 31, integrase strand transfer inhibitors (INSTI) in 20, protease inhibitors (PI) in 4 and Non-NRTIs in 9 cases. NRTIs were mainly tenofovir alafenamide (16 cases), tenofovir disoproxilfumarate (6 cases) and a cytidine analog, either emtricitabine (P22) or lamivudine (P9).	RT-PCR, laboratory test, bronchoalveolar lavage or sputum.

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Table 1. Continuation.

Author	Objective	N	Patients' Age	Patient Outcome	Chest Imaging	Treatment	Diagnosis
				patients were admitted to hospitals. Treatment on intensive care units (ICU) was necessary in 6 of 14 hospitalized patients. Of the 14 patients, requiring treatment in hospitals, 10 have been discharged in the meanwhile. One patient is still in hospital but discharged from ICU. In one patient, a spontaneous pneumothorax could be seen as a complication of persisting cough. Three out of 32 patients with documented outcome had died (P9, P20, and P24).			
Vizcarra et al.[23] (2020)	We compared the characteristics of HIV-infected individuals with COVID-19 with a sample of HIV-infected individuals assessed before the COVID-19 pandemic, and described the outcomes of individuals with COVID-19.	43 men and 08 women.	The median age of patients was 53.3 years old.	Fever was defined as an axillary temperature of 37.3°C or higher. Severe disease was defined as fever or suspected respiratory infection plus respiratory rate greater than 30 breaths per min, oxygen saturation of 93% or less on room air, or acute severe respiratory distress (acute lung infiltrate in chest imaging and ratio of partial pressure of arterial oxygen to fractional concentration of oxygen in inspired air [PaO2/FiO2] of ≤300). Critically ill individuals were those with rapid disease progression and respiratory failure with need for mechanical ventilation or organ failure that needs monitoring in an intensive care unit (ICU). Lymphocytopenia occurred in 15 (43%) of 35 individuals, thrombocytopenia in four (11%), increased alanine aminotransferase in eight (23%), and median PaO2/FiO2 was 462 (IQR 404–474; with	Radiological information was available for 38 (75%) individuals, of whom 17 (45%) had consolidation, 11 (29%) had an interstitial lung pattern, and 21 (55%) had bilateral pulmonary infiltrates.	Regarding ART, a significantly higher proportion of individuals with COVID-19 were receiving tenofovir, either as tenofovir alafenamide (n = 36) or tenofovir disoproxil fumarate (n = 1), before COVID-19 diagnosis (37 [73%]) than those without COVID-19 (487 [38%], p = 0.0036), whereas the use of protease inhibitors or integrase strand transfer inhibitors (INSTIs) was similar in both groups.	RT-PCR, sputum or lower respiratory tract aspirates.

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Table 1. Continuation.

Author	Objective	N	Patients' Age	Patient Outcome	Chest Imaging	Treatment	Diagnosis
				five [10%] patients with a ratio <300) at hospital consultation. Notably, 15 (43%) individuals had increased D-dimer concentrations, and the serum cytokine profile showed high interleukin-6 concentrations in 7 (70%) of 10 analyzed cases.			
Benkovic et al.[24] (2020)	We described patients with covid-19 and HIV.	P1 – man	The median age of patients was 59.7 years old (56–65).	Was diagnosed with HIV in 1995. His only other comorbid condition is hyperlipidemia. He began to feel tired and noticed a decrease in his sense of taste and smell. Although he had no fever or respiratory symptoms, he was concerned when his symptoms did not resolve after 9 days and went to an emergency clinic. Two days after his positive test his symptoms of anosmia and ageusia resolved.	NA	Emtricitabine, tenofovir alafenamide, dolutegravir, and maraviroc.	RT-PCR
		P2 – man		Started to developed subjective fevers and fatigue. A total of 19 days after the initial onset of fatigue he developed a temperature of 102°F (38.9°C) when he went to urgent care. He had no shortness of breath or cough.	Chest X-ray was suggestive of pneumonia.	Emtricitabine, tenofovir alafenamide, etravirine, and abacavir; Lisinopril 10 mg daily.	RT-PCR and chest X-ray.
		P3 – man		Was diagnosed with HIV in 1996. He was discharged home with instructions to self-isolate. After discharged in 1 week, he no longer has any symptoms. Had 2 weeks of non-productive cough and bowel movements. He decided to seek medical attention when he developed a temperature of 100.8°F (38.2°C). In the local emergency	Chest X-ray did not show any consolidation.	Emtricitabine, tenofovir alafenamide, and dolutegravir. rosuvastatin and losartan.	RT-PCR, laboratory test and chest X-ray.

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Table 1. Continuation.

Author	Objective	N	Patients' Age	Patient Outcome	Chest Imaging	Treatment	Diagnosis
				room, the temperature was 100°C, blood pressure was 113/65, heart rate was 75, breathing did not work, and oxygen saturation was 97% in ambient air.			
		P3 – man		Was diagnosed in 2006. He went to the emergency room, temperature was 102.9°F (39.4°C), pulse 83, oxygen saturation 93% on 2 L nasal cannula, blood pressure was 136/71. He was awake, alert, and not showing signs of respiratory distress.	Chest X-ray did not show any consolidation	Oseltamivir 75 mg twice a day for 5 days. Emtricitabine, tenofovir alafenamide, elvitegravir, and cobicistat. Losartan, metformin, atorvastatin, and Coumadin.	RT-PCR, laboratory test and chest X-ray.
Müller et al.[25] (2020)	We described patient with covid-19 and HIV.	01 man	55	In the 1970s, he acquired hepatitis C virus (HCV) infection, probably via factor VIII supplementation, and in 1985, HIV infection. Interferon-based HCV therapy resulted in a sustained virological response. Liver cirrhosis was diagnosed in 2017. In 2018, a solitary hepatocellular carcinoma with a diameter of 55 mm was detected. After successful downstaging by transarterial chemoembolization, the patient underwent uneventful liver transplantation (LT) in January 2019. One year after LT, HIV-PCR was negative. On March 2020, he developed fatigue and fever up to 39.6°C. On March 26, he went to the local hospital in order to be checked for COVID-19. Following worsening symptoms and a positive result for SARS-CoV-2 PCR, he was hospitalized on April 2. The patient presented with fever (39.4°C), fatigue, cough, and tachycardia.	Chest X-ray showed diffuse bilateral infiltrates.	Emtricitabine/tenofovir alafenamide/rilpivirine for HIV is ongoing since 2016. Oxygen and ampicillin/sulbactam.	RT-PCR, laboratory test and chest X-ray.

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Table 1. Continuation.

Author	Objective	N	Patients' Age	Patient Outcome	Chest Imaging	Treatment	Diagnosis
Modi et al.[26] (2020)	We presented a case of an orthotopic liver transplant recipient with well-controlled HIV who successfully recovered from a mild, flu-like illness attributed to SARS-CoV-2.	01 man	32	He developed fatigue, fever, headache, and a dry cough. He presented to the emergency department (ED) and was found to have a temperature of 101°F. The patient was initially instructed to engage in supportive care measures at home; however, the development of chest tightness and shortness of breath prompted presentation to the hospital the following day. He complained of aggravating dry cough, but denied any abdominal symptoms. His vital signs were within normal limits. The patient's respiratory symptoms gradually improved, and he never demonstrated fever or hypoxia. He was discharged home on the sixth day of admission and instructed to maintain isolation for 14 days.	Chest X-ray did not demonstrate any infiltrates. CT imaging was not obtained.	Efavirenz, emtricitabine, and tenofovir disoproxil fumarate. His maintenance immunosuppression consisted of mycophenolate mofetil (MMF), prednisone, and tacrolimus. His ART was changed to raltegravir, emtricitabine, and tenofovir disoproxil fumarate posttransplantation; prednisone was maintained, and tacrolimus was dosed to target a lower trough of 5–9 ng/mL. Hydroxychloroquine was administered outside of a clinical trial for 5 days.	RT-PCR
Riva et al.[27] (2020)	We reported three HIV-positive subjects on antiretroviral (ARV) regimen containing darunavir with good immunovirological status, diagnosed with COVID-19.	P1 – man	62	HIV-positive man was admitted at our ED referring dry cough and fever up to 38.8°C for at least 7 days. In the following days, the patient's respiratory function quickly worsened despite Venturi mask and continuous positive airway pressure therapy, and 1 week after admission, the patient required mechanic ventilation. At the last available follow-up (April 1), the patient is still inpatient with no fever and requiring only low-flow oxygen delivery.	Chest X-ray evidenced a bilateral reticular interstitial thickening.	His ARV regimen consisted of darunavir/cobicistat and lamivudine; doxazosin, metoprolol and amlodipine; lopinavir/ritonavir and hydroxychloroquine. In the ICU, lopinavir/ritonavir and hydroxychloroquine were replaced by tocilizumab and remdesivir.	RT-PCR and chest X-ray.

Continue...

Table 1. Continuation.

Author	Objective	N	Patients' Age	Patient Outcome	Chest Imaging	Treatment	Diagnosis
		P2 – man	63	On March 18, the patient was admitted to the ED reporting fever up to 38.0°C for at least 11 days with no signs of respiratory distress. On March 28, he was successfully discharged.	The chest X-ray evidenced a bilateral reticular interstitial thickening.	On darunavir-based (given at 800 mg co-formulated with cobicistat, tenofovir alafenamide, and emtricitabine). At hospital admission, darunavir/cobicistat was replaced with lopinavir/ritonavir and hydroxychloroquine, irbesartan.	
		P3 – woman	57	Developing SARS-CoV-2 infection was admitted to our hospital on March 24 reporting fever and cough from at least 10 days. At the last available follow-up (April 1), she was still inpatient waiting for the results of the nasopharyngeal swab to confirm SARS-CoV-2 absence before her discharge.	The chest X-ray evidenced reticular interstitial thickening at the right lung.	On darunavir-based (given at 800 mg combined with cobicistat and raltegravir) and on nebivolol and atorvastatin; hydroxychloroquine.	
Nakamoto et al.[28] (2020)	We described a case was coinfected with SARS-CoV-2 and HIV.	01 man	28	His immune status from HIV infection was not well-controlled due to a lack of ART. Underlying condition: smoker, HBV infection; Day of admission of the disease: 8; Saturation at admission: 97	CT findings at admission: multiple GGO.	ART and hydroxychloroquine.	RT-PCR and chest CT.
Gervasoni et al.[29] (2020)	We described our experience with HIV-positive patients regularly followed by our hospital who were infected with SARS-CoV-2.	36 men and 11 women	The median age of patients was men 51 ± 11 years and women 53 ±	A total of 28 patients tested positive for SARS-CoV-2, including one female asymptomatic patient who was tested because she was a healthcare provider. The COVID-19 diagnosis of the untested patients was based on their clinical symptoms and the presence of risk factors. A total of 13 of the 28 SARS-CoV-2 positive patients were hospitalized; 6	Interstitial pneumonia was diagnosed by means of an X-ray in three cases, and GGO was identified by means of CT in one.	Approximately 80% of the identified patients were receiving integrase inhibitor-based antiretroviral treatment and 11% a protease inhibitor-based regimen (11%); 42% were receiving a tenofovir-based	RT-PCR, chest X-ray, and chest CT.

Continue...

Table 1. Continuation.

Author	Objective	N	Patients' Age	Patient Outcome	Chest Imaging	Treatment	Diagnosis
			12 years old.	had severe lung disease (respiratory rate ≥30 breaths/min, resting percutaneous oxygen saturation ≤93% in room air); 2 of whom required mechanical ventilation: 1 recovered and was discharged and the other died. Another patient with cardiovascular disease and a recent diagnosis of lung cancer died during hospitalization. For comparative purposes, the crude mortality rate of the HIV-negative COVID-19 patients in our hospital (n=502, 67% males, mean age 61±16 years) is currently ~17%. Nearly 64% had at least one comorbidity (82% of the males and 58% of the females), mainly dyslipidemia (32%), arterial hypertension (30%), and hepatitis B or hepatitis C coinfections (11%).		regimen. Fewer than 50% of the patients were given potential anti-SARS-CoV-2 treatments, specifically hydroxychloroquine (17%), azithromycin (15%), lopinavir/ritonavir (11%); one was treated with tocilizumab and remdesivir, and one with tocilizumab alone.	
Iordanou et al.[30] (2020)	We described a case of was coinfected with SARS-CoV-2 and HIV.	01 man	58	The patient had malaise, fever, and dry cough on illness day 1. Breathing difficulty developed on day 4, which led him to seek medical attention. The patient was transferred to hospital. On admission, the patient had a fever (38°C). The oxygen saturation was 92% while the patient was breathing ambient air, the respiratory rate 22 breaths/min, the blood pressure 117/72 mmHg, and the heart rate 105 beats/min. The patient was awake, alert, and fully oriented. He had no comorbidities. The mechanical ventilation aimed at minimizing ventilator-induced lung injury (VILI). Initially, we targeted a tidal volume	Chest radiography was performed, which showed bilateral air space pacifications.	Levofloxacin and oseltamivir. Azithromycin and Chloroquine. Piperacillin-tazobactam and vancomycin. Meropenem and gentamicin, and upon failure to respond, empirical antifungal treatment with caspofungin.	RT-PCR and chest X-ray.

Continue...

Table 1. Continuation.

Author	Objective	N	Patients' Age	Patient Outcome	Chest Imaging	Treatment	Diagnosis
				of 6 ml/kg (Predicted Body Weight), a plateau pressure lower than 30 cm H2O, PaO2 55–80 mmHg, or SpO2 88–95% and pH ≥ 7.25. The oxygenation ratio was the worst on hospital day 9 (PO2/FiO2 185) and gradually improved from that day forward. The patient did not need prone positioning. On hospital day 14, the patient demonstrated a marked elevation of D-dimer to 70,386 ng/mL (from 8,854 ng/mL on day 6), accompanied by a rise in pCO2 and demand for ventilation. Upon initiation to wean the patient from the mechanical ventilation, he developed severe hyperventilation, with high respiratory drive, large tidal volumes, and potentially injurious transpulmonary pressure swing, increasing the risk of Patient Self-Inflicted Lung Injury (P-SILI). Sedation and controlled mechanical ventilation were re-initiated, allowing the lung more time to recover. In that perspective, percutaneous dilatational tracheostomy was performed on hospital day 24 after bronchial secretions resulted in negative for SARS-CoV-2. He was weaned off the ventilator on hospital day 29, and decannulation was performed on hospital day 31. The patient was discharged from the ICU the following day and transferred to a clinic for rehabilitation.			

Continue...

Table 1. Continuation.

Author	Objective	N	Patients' Age	Patient Outcome	Chest Imaging	Treatment	Diagnosis
Wu et al.[31] (2020)	We described the clinical characteristics, clinical manifestations, treatments, and clinical outcomes of both patients.	P1 – man	60	Presented with generalized myalgia for 2 weeks and intermittent fever around 38.3°C for 5 days and was admitted in our hospital. He was diagnosed with stage IV diffuse large B-cell lymphoma and pulmonary tuberculosis in January 2018, for which he received chemotherapy with one cycle of CHOP regimen and seven cycles of EPOCH regimen from April 9 to September 10, 2018. The pulmonary tuberculosis was cured and the lymphoma was significantly regressed. Notably, the patient also had a history of type 2 diabetes for 8 years and received insulin to control blood glucose. During the hospitalization, the patient continued anti-HIV treatment and glucose control with insulin. Fever disappeared 2 days after admission. A total of 5 days later, myalgia, fatigue, and shortness of breath were also significantly mitigated. The patient was considered clinically cured for COVID-19 and was discharged.	A chest CT scan that showed bilateral multiple GGO, prominent on the right lower lobe.	Oxygen, anti-viral (oseltamivir), and antibiotics treatments (moxifloxacin, ceftriaxone, and tazobactam) were given.	RT-PCR, chest CT, and laboratory test.
		P2 – man	47	Attended our hospital after 7 days of fever and non-productive cough. He had a highest body temperature of 39.8°C and generalized myalgia, sore throat, cough, intermittent shortness of breath, and diarrhea. Contrary to case 1 who had known and treated HIV infection, this patient was a newly diagnosed HIV-infected case that was only. He had no fever, cough, and myalgia but still had some dyspnea after labor.	He had performed chest CT scan in local hospital which revealed bilateral multiple GGO.	The patient received oxygen, antibiotic (moxifloxacin), and anti-viral (ribavirin and umifenovir) treatments.	

Continue...

Table 1. Continuation.

Author	Objective	N	Patients' Age	Patient Outcome	Chest Imaging	Treatment	Diagnosis
Patel et al.[32] (2020)	We reported a recovered case of SARS-CoV-2 infection in a HIV-positive.	01 man	58	Medical history of chronic bronchitis, hypertension, and HIV presented to the ED complaining of unresolved symptoms of weakness, anorexia, and diarrhea for 2 weeks. He denied shortness of breath, fever, cough, chest pain, or abdominal pain. His fever spike lasted up to 94 h and maximum body temperature during this time was 39.4°C. After 4 days of hospitalization, he became afebrile and had complete resolution of symptoms. He was discharged on the fifth day of hospitalization after the clinical picture showed marked improvement and was advised to self-isolate at home for a minimum of 14 days. Vital signs taken on admission revealed a blood pressure of 145/68 mmHg, the pulse of 94 beats/min, the body temperature of 37°C, and oxygen saturation of 99% in ambient air. Within 12 h of admission, the patient's temperature went up to 39.3°C.	A chest X-ray done on admission showed clear lungs and no significant abnormalities.	Emtricitabine and tenofovir every 24 h, atazanavir and ritonavir. Oral hydroxychloroquine and oral azithromycin, and zinc sulfate.	RT-PCR
Suwanwongse et al.[33] (2020)	We presented the case series of hospitalized HIV patients with COVID-19 in a single hospital in the South Bronx.	07 men and 02 women	The median age of patients was 58 years old (31–76).	All patients had multiple comorbidities. HIV viral load was very low to undetectable. Active ART (HAART) was discontinued during hospital admission in four patients. Fever, cough, and dyspnea were the most common presenting symptoms among all patients. One patient initially presented with gastrointestinal tract symptoms, including nausea, vomiting, and watery diarrhea. A total of 7 patients eventually died (78%), of which	Chest X-ray abnormalities compatible with COVID-19 pneumonia were found in eight patients and correlated with disease severity.	HAART = DRV, darunavir; DTG, dolutegravir; EVG, elvitegravir; EFV, efavirenz; FER (mg/dL), ferritin; FTC, emtricitabine; HCV, hepatitis C infection; HCQ, hydroxychloroquine. HAART regime: P1 – FTC, TAF, DTG, RTV, DRV; P2 – EVG,	RT-PCR, chest X-ray.

Continue...

Table 1. Continuation.

Author	Objective	N	Patients' Age	Patient Outcome	Chest Imaging	Treatment	Diagnosis
				4 due to hypoxemic respiratory failure and 3 from septic shock and multiorgan failures.		FTC, TAF, cobicistat; P3 – FTC, TDF, RAL; P4 – FTC, TAF, ATV, cobicistat; P5 – FTC, TAF, DTG; P6 – EVG, FTC, TAF, cobicistat; P7 – Do not take; P8 – FTC, TDF, DTG; P9 – EFV, FTC, TAF.	
Shalev et al.[34] (2020)	We described the characteristics of 31 people living with HIV hospitalized for severe acute respiratory syndrome coronavirus 2 infection.	24 men and 07 women	The median age of patients was 60.7 years old (23–89).	At least 1 comorbidity was identified in 22 patients. The most common were hypertension in 21, diabetes mellitus 13, and obesity 9. Thirteen patients were current or former smokers and 8 were diagnosed with asthma or chronic obstructive pulmonary disease. Twenty-three patients presented with fever (defined as a temperature of >38.0°C) or developed fever during admission. Twenty-eight patients received supplemental oxygen and 8 required invasive mechanical ventilation. Disease severity was distributed as follows: mild, 1; moderate, 2; severe, 2; and critical in 7 patients. At the time of analysis, 8 patients had died, 21 were alive and discharged, and 2 were alive and hospitalized. Thirteen patients were discharged home and 8 to a care facility.	Chest radiography was performed in 30 patients, 20 of whom displayed abnormalities consistent with viral pneumonia.	All subjects were taking ART at the time of admission. Hydroxychloroquine used in 24 patients, followed by azithromycin in 16. Corticosteroids were used in 8 and the interleukin 6 receptor (IL-6R) antagonist tocilizumab in 2 patients. 1 used drug remdesivir and another patient sarilumab. ART regimens containing tenofovir prodrugs or protease inhibitors were prescribed in 17 and 7 patients, respectively.	RT-PCR, chest radiography.
Kumar et al.[35] (2020)	We described the clinical course of a symptomatic kidney transplant recipient with	01 man	50	Presented to the ED complaining of fevers for two days, with temperatures to 101°F, chills, nasal congestion, and mild cough. The past medical history also	NA	He received induction immunosuppression with basiliximab and steroid-sparing maintenance	RT-PCR

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Table 1. Continuation.

Author	Objective	N	Patients' Age	Patient Outcome	Chest Imaging	Treatment	Diagnosis
	HIV who tested positive for SARS-CoV-2.			includes hypertension, asthma, steatohepatitis, and resolved hepatitis B infection. The patient denied shortness of breath, chest or abdominal pain, diarrhea, or vomiting. The patient was diagnosed with HIV infection in 1997, initiated ART at that time, and has had long-term viral suppression. In the ED, the patient was hypertensive with blood pressure 172/95 mmHg and tachycardia with heart rate 108 beats/min, but he appeared well and had temperature 98.9°F and oxygen saturation 100% on room air. The patient had ongoing symptoms reported through the monitoring program including anosmia and ageusia one day after discharge, fatigue, and fevers.		immunosuppression with tacrolimus and mycophenolate mofetil. At and since time of transplant, the ART regimen consisted of dolutegravir, emtricitabine, and tenofovir alafenamide. He was also receiving maraviroc v. placebo as part of a randomized clinical trial (NCT02741323).	
Toombs et al.[36] (2020)	We described patient with covid-19 and HIV.	P1 – man	62	He had received a renal transplant and also had type 2 diabetes (T2DM) and hypertension. He was intubated and ventilated on ITU and died from multi-organ failure precipitated by COVID-19 pneumonitis.	NA	Raltegravir; lamivudine; sbacavir + tazocin. It was immunocompromised from tacrolimus and mycophenolate treatment.	NA
		P2 – man	46	With glucose-6-phosphate dehydrogenase (G6PD) deficiency, had been ART naïve until 5 days prior to admission after he had been lost to follow up since diagnosis in 2013.		Atovaquone in view of G6PD deficiency. truvada; dolutegravir + levofloxacin.	NA
		P3 – woman	57	With a history of stroke, T2DM, hypertension and obesity, was a nurse in an older persons care home with confirmed COVID-19 infections at the time of admission. She also was covered for added bacterial infection and was discharged in a good condition.		Descovy; nevirapine + doxycycline.	

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Table 1. Continuation.

Author	Objective	N	Patients' Age	Patient Outcome	Chest Imaging	Treatment	Diagnosis
Li et al.[37] (2020)	We reported COVID-19 patients coinfected with HIV and analyzed the clinical and laboratory features of them.	P1 – man	37	Physical examination of the patient revealed a body temperature of 38.8°C, respiratory rate of 40 breaths/min, pulse of 119 beats/min, and blood pressure of 145/93 mmHg. The patient had an intermittent fever and chest pain, and the highest body temperature was 39.4°C. Most importantly, the patient presented fluctuating dyspnea symptoms for a long time. The clinicians evaluated the symptoms and examinations comprehensively and speculated that the patients might suffer from immunodeficiency diseases. Then HIV detection results showed that the patient was HIV-positive. At last, the patient was transferred to a special hospital for infectious diseases and received further therapy.	CT scan images of the lung showed that the high-density area was gradually increased.	Was given symptomatic supportive treatment such as intermittent low flow oxygen, lianhua qingwen capsule, and antiviral therapy with abidor.	RT-PCR, chest CT, and laboratory test.
		P2 – man	24	The patient stated that he had got an intermittent fever accompanied by cough, fatigue, poor appetite, dizziness, chest tightness, and shortness of breath after activity since 8 February. Physical examination of the patient revealed a body temperature of 36.5°C, respiratory rate of 22 breaths/min, pulse of 102 beats/min, and blood pressure of 125/88 mmHg. The patient had an intermittent fever and cough, and the highest body temperature was 40.2°C. Most importantly, the symptom of dyspnea had gradually worsened. At last, the patient was transferred to a special hospital for infectious diseases and received further therapy.	CT scan of the lung showed that the high-density area was gradually increased.	Was given symptomatic supportive treatment such as intermittent low flow oxygen, antiviral therapy with abidor, and antibodies therapy toward to interleukin 6 (IL-6) receptor with tocilizumab.	RT-PCR, chest CT, and laboratory test.

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Table 1. Continuation.

Author	Objective	N	Patients' Age	Patient Outcome	Chest Imaging	Treatment	Diagnosis
Ridgway et al.[38] (2020)	We reported a case series of five PLWH with COVID-19.	P1 – man	38	HIV positive presented to the ED with 7 days of fever, dry cough, shortness of breath (SOB), headache, and myalgias. He also had 3 days of diarrhea. Medical history included diabetes mellitus type 2 with a hemoglobin A1C of 9.9%, obstructive sleep apnea, hyperlipidemia, hypertension, and obesity. On presentation, he was febrile to 39.3°C and tachycardia. His oxygen saturation was 94% on room air (RA). He was admitted due to evidence of viral pneumonia, elevated LFTs, and uncontrolled diabetes mellitus.	Chest X-ray showed peripheral patchy opacities and chest CT showed bilateral GGO.	Empiric ceftriaxone and azithromycin; hydroxychloroquine.	RT-PCR, chest X-ray, and chest CT.
		P2 – woman	50	HIV positive presented to the ED with 1 week of cough productive of white sputum, daily fevers, and progressive SOB as well as 1 day of headache. Her only significant comorbidity was obesity. On presentation, she was afebrile with a temperature of 36.6°C, and had an oxygenation saturation of 88% on RA, which improved to 93% with 2 L nasal cannula (NC). On HD 2, her oxygenation status slightly worsened and she required 3–4 L oxygen by NC. Her oxygenation improved and she was discharged on HD 4.	Chest X-ray showed mild multi-focal patchy airspace consolidation in the left lower lobe.	Azithromycin and ceftriaxone, cefdinir.	RT-PCR, chest X-ray.
		P3 – woman	51	HIV positive presented to the ED with 1 week of cough productive of yellow sputum, myalgias, SOB, 4 days of fever, and 1 day of watery diarrhea. Her only medical history was a remote history of latent tuberculosis treated with isoniazid	Chest X-ray showed bilateral perihilar and basilar patchy airspace and interstitial opacities.	ART regimen of elvitegravir, cobicistat, emtricitabine, and tenofovir alafenamide. Ceftriaxone and azithromycin for empiric CAP treatment,	RT-PCR, chest X-ray.

Continue...

Table 1. Continuation.

Author	Objective	N	Patients' Age	Patient Outcome	Chest Imaging	Treatment	Diagnosis
				for 9 months. On presentation, her oxygen saturation was 93% on RA, and she was given 2 L oxygen by NC. She was admitted to rule out acute coronary syndrome. Her temperature was 36.4°C on admission, but increased to 39.3°C the second day of admission.		with ceftriaxone transitioned to cefdinir on HD 2. Hydroxychloroquine.	
		P4 – woman	53	HIV positive and a history of esophageal strictures status post stenting complicated by bronchoesophageal and tracheoesophageal fistulas presented with 1 week of nausea, vomiting, intermittent diarrhea, dehydration, and cough of productive sputum. She endorsed chills, but denied any fever. She denied any sick contacts. On presentation, she was febrile to 39°C and had oxygen saturation of 97% on RA.	Chest X-ray was unremarkable.	ART regimen of bictegravir, emtricitabine, tenofovir alafenamide, ritonavir, and darunavir; cefdinir and azithromycin for empiric.	RT-PCR
		P5 – woman	47	HIV positive presented to the abdominal pain with nausea and vomiting, intermittent chest pain, dyspnea on exertion, and chills. Heart failure with ejection fraction of 15% with implantation of implantable cardioverter defibrillator (ICD), chronic obstructive pulmonary disease, hypertension, and morbid obesity.	Chest X-ray showed cardiomegaly but no infiltrate. Abdominal CT showed wedge-shaped splenic infarction.	ART regimen of tenofovir disoproxil fumarate, emtricitabine, darunavir, ritonavir, and raltegravir.	RT-PCR, chest X-ray, and chest CT.
Childs et al.[39] (2020)	We reported the clinical characteristics of 18 PWH who were hospitalized with confirmed COVID-19.	12 men and 06 women	52 (49–58).	The commonest presenting symptoms were fever, shortness of breath, and cough. Seven patients reached the composite endpoint; these patients had similar HIV and demographic characteristics	Most (78%) had bilateral chest radiograph changes consistent with viral pneumonitis and required oxygen therapy.	Two patients were treated with remdesivir, and in 2 patients, ART was switched to lopinavir/ritonavir. Protease inhibitor;	RT-PCR, chest X-ray, and laboratory test.

Continue...

Table 1. Continuation.

Author	Objective	N	Patients' Age	Patient Outcome	Chest Imaging	Treatment	Diagnosis
				compared to those who did not reach this endpoint. At the time of writing, 5 patients had died, 12 patients were successfully discharged from hospital, and 1 patient remains an inpatient. There was a trend toward more common use of protease inhibitor-containing antiretroviral regimens among those with COVID-19.		integrase strand-transfer inhibitor; Non-nucleoside reverse-transcriptase inhibitor; nucleoside reverse-transcriptase inhibitor; tenofovir b.	
Okoh et al.[40] (2020)	We reported a case series of 27 PLWH with COVID-19.	15 men and 12 women	58	The top 4 common symptoms at presentation were fever, cough, dyspnea, and fatigue, which had started over a median duration of 3 days before presentation. More than half of the patients had a history of systemic hypertension and about one-third reported diabetes mellitus or chronic kidney disease. After a median hospital course of 10 days, 3 patients required intensive unit level of care and 2 of them had died. The deceased subjects were elderly patients, with multiple coexisting conditions whose course was complicated by septic shock and multiorgan dysfunction syndrome.	NA	A total of 7 received hydroxychloroquine and 6 were managed with empiric antibiotics for suspected community-acquired pneumonia. ART was held during hospitalization.	RT-PCR and laboratory test.
Haddad et al.[41] (2020)	We reported a case of a middle-aged man with COVID-19 who developed acute encephalopathy and tonic-clonic seizure activity.	01 man	47	Well-controlled HIV. Maintained on dolutegravir-lamivudine with last CD4 count of 604 cells/cu mm and an undetectable viral load 2 months prior to presentation and recurrent HSV on chronic suppressive therapy presented with abdominal pain,	CT chest revealed diffuse patchy nodular ground-glass infiltrates. The remainder of imaging studies including CT head	Hydroxychloroquine, azithromycin, cefepime, ampicillin, and vancomycin.	RT-PCR, CT, and MRI brain with and without contrast and EEG.

Continue...

Table 1. Continuation.

Author	Objective	N	Patients' Age	Patient Outcome	Chest Imaging	Treatment	Diagnosis
				intractable vomiting, and confusion. He became ill 6 days prior to presentation when the patient started experiencing a dry cough and intermittent fever relieved by antipyretics. On day 2 of hospitalization, the patient was found to have worsening encephalopathy, agitation, and new-onset left-sided ptosis. He subsequently developed witnessed tonic-clonic seizure complicated by a tongue laceration leading to respiratory arrest requiring intubation and sedation. Hospital course was further complicated by acute kidney injury which resolved after discontinuation of acyclovir on day 6 of presentation when HSV PCR was negative. On day 6 of hospitalization, the patient's level of consciousness improved off sedation, and he was successfully extubated.	was unremarkable. CT scan of the chest with coronal (left) and cross-sectional (right) views showing diffuse patchy peripheral ground-glass infiltrates most consolidative within the right lower lobe.		
Sun et al.[42] (2020)	We reported here a case of HIV and SARS-CoV-2 coinfection in a PLHIV on long-term ART in Singapore.	01 man	37	Fever (38.6°C at maximum), sore throat, dry cough, and headache for the duration of 6 days. The CD4+ T-cell count was 201 cells/μL (12%) on diagnosis (2010). His viral load has been undetectable since February 2011, and the CD4+ T-cell count increased to 900 cells/μL (36%) by 2015. On presentation, the patient looked clinically well	His chest radiograph was clear with no infiltrates or consolidation.	Tenofovir, lamivudine, and efavirenz.	RT-PCR and laboratory test.

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Table 1. Continuation.

Author	Objective	N	Patients' Age	Patient Outcome	Chest Imaging	Treatment	Diagnosis
				and was afebrile (37.2°C) with normal blood pressure and heart rate. His oxygen saturation was 100% on room air, and his respiratory rate after admission was 20 breaths per min.			
Chen et al.[43] (2020)	This report provided reference for the diagnosis and treatment of HIV-infected patients with COVID-19.	01 man	24	Was admitted to our hospital with a 1-day history of fever (37.8°C) and dry cough.	CT showed multiple high-density patchy shadows with unclear boundaries in the sub-pleural regions of the middle and lower lobes of the right lung, with involvement of adjacent interlobar pleura.	ART (tenofovir; lamivudine; efavirenz) for 2 years. After COVID-19 diagnosis, he was given lopinavir/ritonavir combined with interferon inhalation for treatment.	RT-PCR, chest CT, and laboratory test.
Di Giambenedetto et al.[44] (2020)	We reported the case of a 75-year-old male patient, with a history of 23 years since HIV diagnosis.	01 man	75	A 7 days history of high fever, diarrhea, and cough. In the days immediately following, clinical conditions worsened, with persistent fever and worsening dyspnea, requiring a progressive increase in oxygen supplementation up to a FiO2 of 0.6, two distinct episodes of hemoptysis. After some days, we observed a progressive improvement in clinical conditions, with the resolution of fever and improvement of respiratory parameters and gas exchange.	CT scan of the lungs was showing bilateral consolidations and GGO, in the absence of signs of bleeding or signs of pulmonary embolism	ART STR with darunavir/cobicistat/emtricitabine/tenofovir alafenamide. Hydroxychloroquine, azithromycin, sarilumab.	RT-PCR, chest CT, and laboratory test.

NA: not applicable.

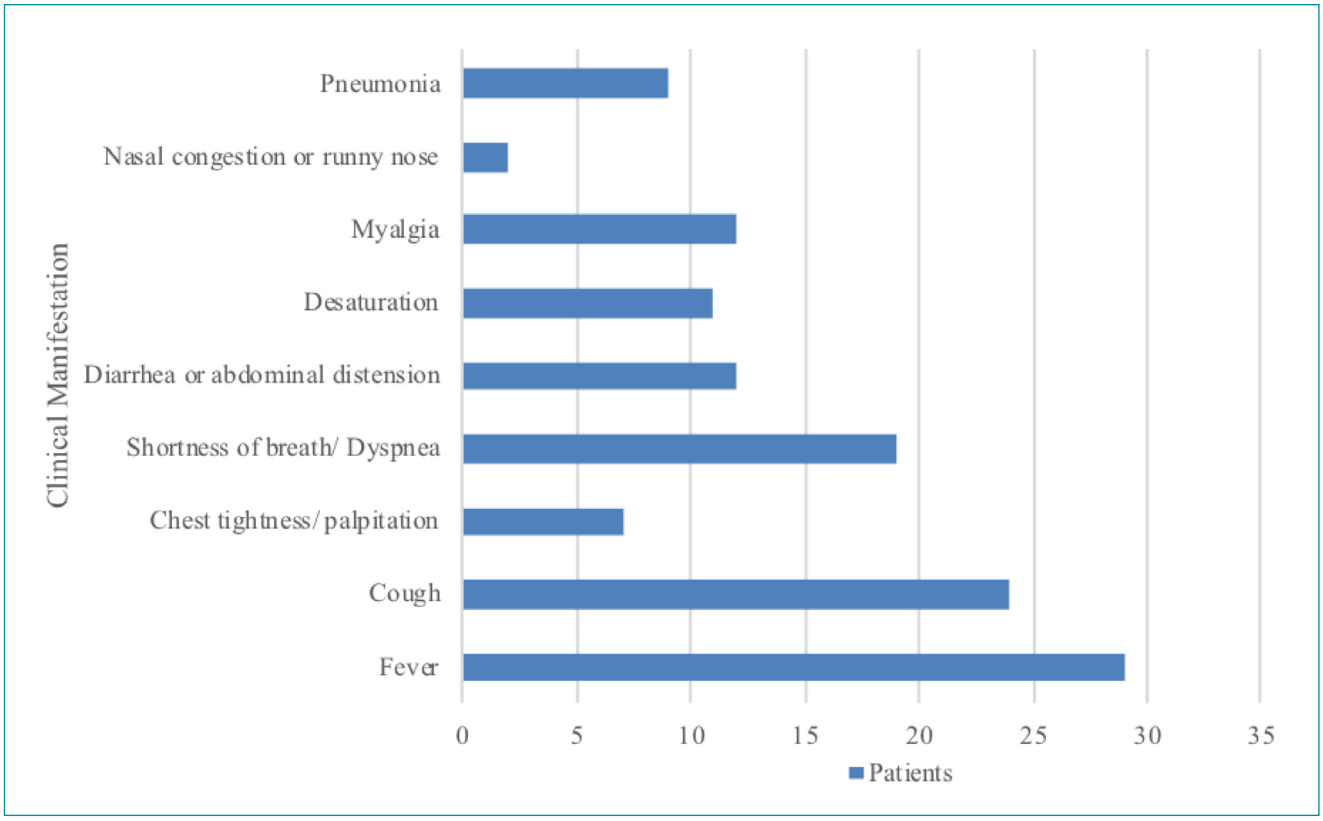

Figure 2. Clinical manifestation of patients with COVID-19 and HIV/AIDS.

- One patient developed encephalopathy and complicated tonic-clonic seizures[41];
- Four patients were transplanted, two of them for liver[25,26] and other two for kidney[35,36];
- One patient developed severe SARS-CoV-2 pneumonia[30].

DISCUSSION

Coronavirus disease 2019 (COVID-19) has spread rapidly around the world since the first reports from Wuhan, China, in December 2019, and the outbreak was characterized as a pandemic by the WHO on March 12, 2020[13]. Approximately 37.9 million people living with HIV-2 are at risk of infection with SARS-CoV-2, which causes COVID-19 infection[45].

Several studies have summarized the clinical characteristics of COVID-19, and some studies have reported that the primary chronic diseases, such as hypertension, atherosclerosis, and diabetes, the patients have had previously, may relevant to the severity of the disease[7-10]. However, until now, none of the study has been conducted to evaluate the morbidity and severity of COVID-19 in HIV/AIDS. Assuming that patients are with compromised immunity and also in a chronic disease state, HIV/AIDS patients were presumed to be at a higher risk of getting infected by the novel virus for their susceptibility to even opportunistic pathogens[17].

Recently, Zhao et al.[16] reported the first case of COVID-19 with HIV-1 and HCV coinfection. Although the test of SARS-CoV-2 RNA was persistently negative on the different specimens at various times, the plasma anti-SARS-CoV-2 antibody was positive. The authors believed that one potential explanation is that the patient who was taking anti-HIV-1 agents had been reported to have anti-SARS-CoV-2 effects[46]. These data are consistent with the notion that some anti-HIV-1 agents may have preventive and/or therapeutic effects against SARS-CoV-2. Another possibility is that the activated type I interferon (IFN-I) may help suppress SARS-CoV-2[16].

Zhu et al.[15] also reported on an identified unique severe case involving coinfection of SARS-CoV-2 and HIV. CT indicated SARS-CoV-2 pneumonia with findings of multiple GGO in bilateral lungs, after oral therapy with an anti-HIV drug, LPV/r 400/100 mg per dose twice daily for 12 days, as was advised by the Chinese health authority for the treatment of SARS-CoV-2 infection, and moxifloxacin 400 mg once daily for 7 days, γ-globulin 400 mg/kg once daily for 3 days, and

methylprednisolone 0.8 mg/kg once daily for 3 days through the intravenous route. The patient showed a marked clinical and radiological improvement, and the patient was in stable condition and discharged.

Guo et al.[17] conducted a more extensive study to find out the risk factors of COVID-19 in HIV/AIDS patients and evaluated the role of antiretroviral therapy (ART) in preventing or treating COVID-19. This study found that in the HIV/AIDS population, all of those combined COVID-19 patients had relatively normal CD4 counts, which indicated a relatively normal immune function, factors such as the gender, of the CD4 counts, or the HIV-VL, or the ART regimen did not show any relevance with the occurrence of COVID-19. None of those COVID-19/HIV patients took remdesivir, LPV/r-based ART regimen, which seemed to support the use of LPV/r in pre-exposure prophylaxis (PrEP) and cope with COVID-19[17].

The results of these findings are conflicting, on the one hand, some authors suggested that an immune system debilitated probably facilitates the dominant infection, or more accurately, causes the pathological changes to give rise to the symptoms. On the other hand, other authors also indicated that a compromised immune system with a lower CD4 count levels might waive the clinical symptoms. Considering that there were a lot of asymptomatic SARS-COV-2-infected individuals being reported, although we do not have effective strategies to screening all of the HIV/AIDS patients, we may speculate that some of them may be infected but present with no symptoms. This finding probably supports the hypothesis that a lower active immune status might protect the human body from a severe viral attack other than the immune storm, such as SARS and MERS[17].

The elaboration of this review evidenced that few studies exist on this topic and that lot of gaps still need to be filled. The fact is that the studies point out one possible influence of HIV-1-induced immune dysfunction on the immune responses to and clearance of SARS-CoV-2; at the same time, HIV did not show any relevance with the occurrence of COVID-19. On the contrary, some studies have shown that HIV-1 infection through the induction levels of IFN-I may, to some extent, stop the apparent SARS-CoV-2 infection, thus leading to persistently undetectable RNA. Besides that, some authors suggested that retroviral drugs routinely used to control HIV infection could be used to prevent the infection by COVID-19. Future studies are needed to prove these possibilities[15-17].

Remdesivir, LPV/r, ribavirin, arbidol, and chloroquine, and others have already been tried in COVID-19 treatment, and remdesivir is now under a registered clinical experiment. The combination of protease inhibitor, LPV/r, was proved to target both HIV and coronaviruses, and the national guidelines for diagnosis and treatment of COVID-19 (from the 1st to 6th) also suggested to treat patients with LPV/r. The exact effect of LPV/r in treating the SARS-CoV-2-caused disease still needs more observation. Nevertheless, since HIV/AIDS patients might take LPV/r as a routine of the ART, it provides a natural study object to observe whether LPV/r can be used as PrEP for SARS-CoV-2, like the PrEP for HIV. These people were not infected by HIV, but were at high risks and suggested to take the antiretroviral drugs every day to prevent the infection[11,12].

However, in 2018, only 62% of adults and 54% of children living with HIV in low- and middle-income countries were receiving lifelong ART. Besides that, not everyone can access HIV testing, treatment, and care. Therefore, this is worrying[47].

The potential limitations of the present study include few number of cases, the shorter follow-up time, and lack of clinical trials proving that the use of retroviral drugs as prophylaxis for COVID-19 is safe. The latter limitations serve as an incentive for the production of clinical trials with a larger number of patients and with a longer follow-up time, as well as the production of randomized clinical trials that assess the safety and the effectiveness of antiretroviral drugs.

CONCLUSION

This review points to the existence of conflicts regarding the results obtained in the studies evaluated in this study. Some authors pointed out one possible influence of HIV-1-induced immune dysfunction on the immune responses to and clearance of SARS-CoV-2, although the HIV did not show any relevance directly with the occurrence of COVID-19. Some studies suggested that HIV-1 infection through the induction levels of IFN-I may, to some extent, stop apparent SARS-CoV-2 infection, thus leading to persistently undetectable RNA. Besides that, there is an assumption that retroviral drugs routinely used to control HIV infection could be used to prevent the infection by COVID-19.

AUTHORS' CONTRIBUTIONS

Medeiros KS, Sarmento AC, Silva LASS and Macêdo LTA were responsible for the study conception and design, acquisition of data, analysis and interpretation of data, drafting of manuscript, and critical revision. Eleutério Jr. J and Costa APF were responsible for the manuscript critical revision. Gonçalves AK was responsible for the study conception and design, acquisition of data, analysis and interpretation of data, drafting of manuscript and critical revision.

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