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POTENTIAL IMPACT OF THE COVID-19 IN HIV-INFECTED INDIVIDUALS: A SYSTEMATIC REVIEW

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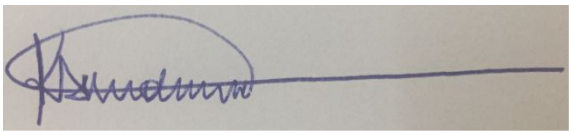

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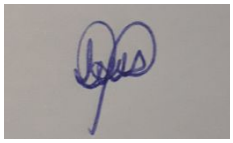

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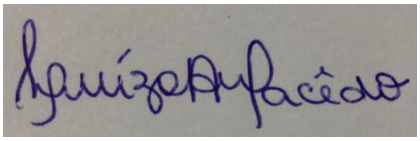

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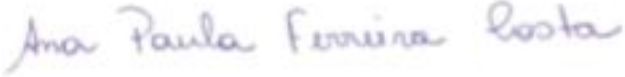

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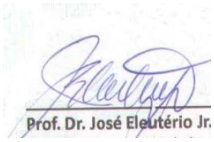

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ABSTRACT

Background: Much has been studied about the virus SARS-Cov-2, its effects, and possibles treatment effective. Nevertheless, little is known about the interactions of this infection with others infectious diseases.

Objective: The aim is to clarify the clinical features and morbidity and mortality outcomes of patients with co-infection COVID-19 and HIV/AIDS.

Data sources: MEDLINE, Web of Science, Embase, CINAHL, LILACS, Scopus, clinicaltrials.gov, Cochrane.

Study eligibility criteria: all the studies that were describing patients affected by the SARS-CoV-2/COVID-19 and with HIV/AIDS; there were no language restrictions while selecting the studies; published after 2019.

Study appraisal: JBI Levels of Evidence - Joanna Briggs Institute.

Synthesis methods: Two authors separately screened the search results using the titles and abstracts. The selection of the studies was summarized in a PRISMA flow diagram.

Results: Chest CT was observed in patients with pneumonia by SARS - CoV - 2 with findings of multiple ground glass (GGO) opacities 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 and two kidneys), one patient developed severe SARS-CoV-2 pneumonia and 30 patients died (mortality rate of 11%).

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

Keywords: Covid-19; SARS-CoV-2; HIV; AIDS; antiretroviral therapy.

1.INTRODUCTION

The SARV-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 SARV-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 may be at high risk of developing severe respiratory disease (COVID-19) (4-6). Patients immunosuppressed for variable reasons have effects on humoral, cell-mediated immunity and neutrophil function, increasing the risk of severe infections caused by viral agents, such as Adenovirus, Rhinovirus, Norovirus, Influenza, 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 SARS, MERS, and more recently on COVID-19, no mention is made on immunosuppression as a risk factor for more severe disease or mortality coronaviruses when compared to the general population, both children and adults (1,3,9). Mascollo et al., (2020) 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 anti-retroviral treatment started (lopinavir/ritonavir) as management of SARS-CoV-2 infections, it could play a double effect: inhibition of SARS-CoV-2 replication, facilitating the viral clearance; 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

(lopinavir/ritonavir) administration could be useful for a potential and not yet confirmed direct anti-SARS-CoV-2 antiviral effect. (9,10,11)

There is much to be clarified about existing immunological interactions between HIV and SARS-CoV-2, 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 co-infection COVID-19 and HIV/AIDS.

2. 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.

2.1. 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. This is justified because the first case of COVID-19 was registered in Wuhan, China, in December 2019 (13).

2.2 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.

2.3 Selection of studies

KSM and LASS separately screened the search results using the titles and abstracts. Duplicate studies and reviews were excluded. A third author contributed (ACAS) along with

the other two went through the full text 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).

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

2.5 Quality of evidence

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

3 RESULTS

3.1 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, 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 (15,16,17,21,31,37,43), Spain (18,23), Uganda (19), Turkey (20), Germany (22), New York (33,34), Austria (25), United States (24,25,32,40,41), Italy (27,29,44), Japan (28), Cyprus (30), Chicago (35,38), United Kingdom (36,39) and Singapore (42) both in 2020, although Covid-19 was described in 2019 (13). All articles were in English.

3.2 Study designs

Twenty-eight articles were the type case report or case series (level of evidence 4.d (15,16,18,19,20,21,22,24,25,26,27,28,29,30,31,32,33,34,35,36,37,38,39,40,41,42,43,44) and two Cohort (level of evidence 4.b) (17,23). Thus, we note that the studies included in this review have low levels of evidence according to classification for levels of evidence from the JBI developed by the Joanna Briggs Institute's Evidence Levels and Recommendation Notes Working Group in October 2013.

3.3 Study characteristics

In total, 266 patients co-infected 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).

3.4 Clinical manifestations

The principal clinical manifestations were fever, coughing, shortness of breath, diarrhea or gastrointestinal symptoms, and Pneumonia, as shown in Table 2. Study of Gun et al. (2020) shows that till March 3, 2020, 6 of the COVID-19/HIV patients were considered mild cases, 1 was severe cases, and 1 was a critical case who died (17). In the study with 33 patients presented by Härter G et al. (2020), 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 (22). Two other cases of similar deaths were related by Gervaoni C et al. (2020), 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 (29).

There have also been reports of deaths in other studies. Aydin Karaosmanoglu and Yasar (2020) (20), related the patient had potential comorbidities such as obesity, diabetes, hypertension and chronic obstructive pulmonary disease (COPD), he refused to do regular treatment for your comorbidities. In the series of cases presented by Suwanwongse and Shabarek (2020) (33), all 9 patients mentioned had comorbidities and 7 died, four due to hypoxemic respiratory failure, and three due to septic shock and failures of various organs. In the study by Shalev et al (2020) (34), of the 31 mentioned patients, 8 died, of these four were over 65 years old, and the other four 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 (2020) (39),

mentions 18 patients in their study of these, five died with a mean hospital stay until 8 days, with an interval of 3 and 28 days until death. Okoh et al (2020) (40), reported 27 patients observed in their study two died, they were elderly and had multiple coexisting conditions complicated by septic shock and multiorgan dysfunction syndrome.

3.5 Diagnosis

Clinic and epidemiology information were 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 were decisive on the front line against COVID-19 both in the control, treatment, and care as in diagnosis (16,17,19,21,22,24,26,29,35,41,42,43).

Even though the patients had some main distinctive manifestations of Covi-19, the SARS-CoV-2 tests using 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 polymerase chain reaction with reverse transcriptase (RT-PCR) (15,16,18-35,37,44), nucleic acid test (NAT) of SARS-CoV (17), laboratory test (19,20,22,24,31,37,39,40,42,43,44), chest radiography (24,27,29,30,31,34,38,39), computed tomography of the chest (CT) (15,16,17,18,20,21,24,28,29,37,41,43,44), brain magnetic resonance with and without contrast (MRI) (41), electrocardiogram (ECG) (41), sputum, aspiration of the lower respiratory tract (23) or bronchoalveolar lavage (22).

3.6 Patients outcome:

The principal patients' outcomes were:

- Mild lymphopenia with a lymphocyte count of 1.1 × 109/L (15,18,20,21,28,31,33,34,36,37,39,41,44);
- Low CD4+ T-lymphocyte percentage (15,16,17,21,22,23,28,29,33,34,36,38,39);
- The chest CT indicated the SARS-CoV-2 pneumonia with findings of multiple ground-glass opacities (GGO) in lungs (15,16,20,21,23,25,27,28,29,30,31,33,34,37,38,39,41,43,44);
- On supplemental oxygen, arterial blood gas analysis revealed: pH 7.41, PCO2 37.4 mm Hg, PO2 63.9 mm Hg, and HCO3− 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);
- One patient developed encephalopathy and complicated tonic-clonic seizures (41);

- Four patients were transplanted, two livers (25,26) and two kidneys (35,36);
- One patient developed severe SARS-CoV-2 pneumonia (30).

4. DISCUSSION

Coronavirus disease 2019 (COVID-19) has spread rapidly around the world since the first reports from Wuhan in China in December 2019, and the outbreak was characterized as a pandemic by WHO on March 12, 2020 (13). Approximately 37,9 million people living with HIV2 are at risk of infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which causes COVID-19 (45).

Several studies have summarized the clinical characteristics of COVID-19 (8), some have reported that the primary chronic diseases, like hypertension, atherosclerosis, and diabetes, the patients have had previously may relevant to the severity of the disease (7-10). However, until now, none 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. (2020) reported the first case of COVID-19 with HIV-1 and HCV co-infection. 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 believe that one potential explanation is that he was taking anti-HIV-1 agents who had been reported to have anti-SARS-CoV-2 effects (47). 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. (2020) also report on an identified unique severe case involving co-infection of SARS-CoV-2 and HIV. CT indicated SARS-CoV-2 pneumonia with findings of multiple ground-glass opacities (GGO) in bilateral lungs, after oral therapy with an anti-HIV drug, lopinavir/ritonavir 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, the patient was in stable condition and discharge (15).

Guo et al. (2020) conducted a more extensive study to find out the risk factors of COVID-19 in HIV/AIDS population, and evaluate the role of antiretroviral therapy 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, Lopinavir/Ritonavir (LPV/r) based antiretroviral therapy (ART) regimen, which seemed to support the use of LPV/r in pre-exposure prophylaxis (PrEP) and cope with COVID-19 [17].

The results finding are conflicting, on the one hand, some authors suggest 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 counts level might waive clinical symptoms. Considering 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 middle east respiratory syndrome (MERS) (17).

The elaboration of this review evidential the small number of studies existing on this topic and that lot of gaps that still need to be filled. Such as the fact 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 that HIV did not show any relevance with the occurrence of COVID-19. On the contrary, some studies have shown that HIV-1 infection through induction levels of IFN-I, may to some extent, stop apparent SARS-CoV-2 infection, thus leading to persistently undetectable RNA. Besides that, some authors suggest retroviral routinely used to control HIV infection could be used to prevent infection by COVID-19. Future studies are needed to prove these possibilities (15,16,17).

Remdesivir, Lopinavir/Ritonavir (LPV/r), Ribavirin, Arbidor, and Chloroquine, etc., have already been tried in COVID-19 treatment, and Remdesivir is now under a registered clinical experiment. The combination 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-6th) also suggested to treat patients with LPV/r. The exact effect of LPV/r in treating the SARS-CoV-2 caused disease still need more observation. Nevertheless, since HIV/AIDS patients might take LPV/r as a routine of the antiretroviral therapy (ART), it

provides a natural study object to observe whether LPV/r can be used as a pre-exposure prophylaxis (PrEP) for SARS-CoV-2, like the PrEP for HIV. These people did not infect HIV, but at high risks can take the antiretroviral drug 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 antiretroviral therapy (ART). Besides that, not everyone can access HIV testing, treatment, and care. Therefore, this is worrying (50).

Potential limitations of the present study include the small number of cases, the time short follow-up, and lack of clinical trials proving that the use of retroviral 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.

5. CONCLUSION

This review points to the existence of conflicts regarding the results obtained in the studies evaluated here. Some authors point 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 suggest HIV-1 infection through 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 routinely used to control HIV infection could be used to prevent infection by COVID-19.

AUTHOR 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 was 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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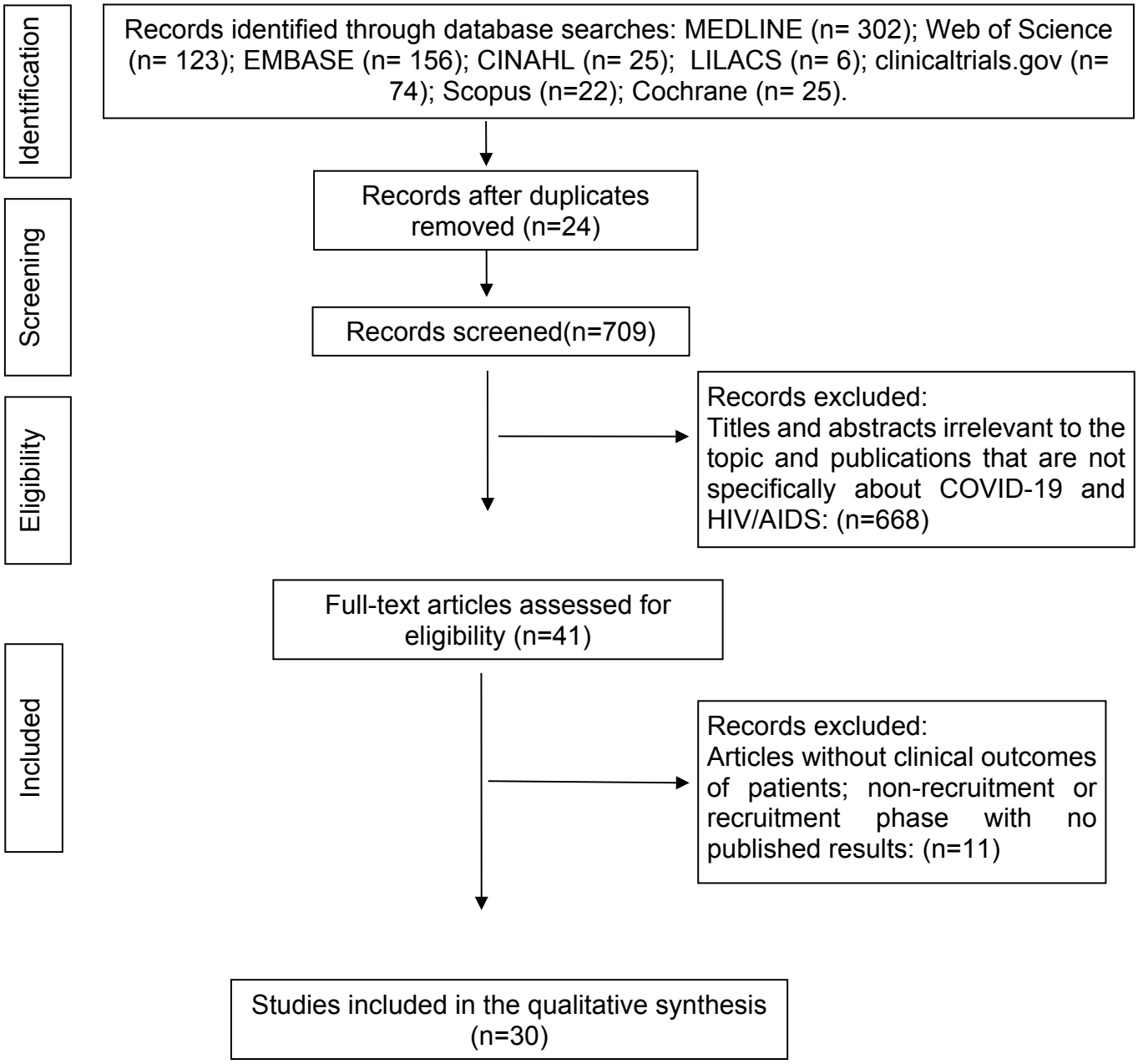

Figure 1 Flow diagram of the search for eligible studies COVID-19 and HIV/AIDS: CENTRAL, Cochrane Central Register of Controlled Trials.

AUTHOR	OBJECTIVE	N	PATIENTS AGE	PATIENT OUTCOME	CHEST IMAGING	TREATMENT	DIAGNOSIS
Guo W, 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 man and 01 woman	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 mild cases, 1 was severe cases, and 1 was critical case who died. Six of them had CD4 counts>350/μl, and 2 with CD4 counts between 101-350/μl. All 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).
Zhu N, et al. (15) (2020)	We report on an identified unique severe case involving co-infection 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 sa- turation of 80%, which reached 91% while the patient was given mask flow oxygen at a rate of 5 liters per minute. On supplemental oxygen, arterial blood gas analysis revealed: pH 7.41, PCO2 37.4 mm Hg, PO2 63.9 mm Hg, and HCO3− 23.4 mmol/L. Lymphopenia also got worse, with a lymphocyte count of 0.56 × 109/L and a low CD4+ T-lymphocyte percentage at 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.

Blanco L, et al. (18) (2020)	We describe the first single-centre experience of COVID-19 in patients infected with HIV-1, including clinical characteristics, antiviral and antiretroviral treatment, and outcomes.	05 man	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 antiretroviral therapy (ART). CD4 counts were above 400 cells per 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 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, 3, 4, and 5) with azithromycin (patients 3, 4, and 5), and interferon beta-1b (patient 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.
Zhao J, et al. (16) (2020)	We report a unique case of COVID-19 with preexisting immune dysfunction from previous co-infection of HIV and HCV.	01 man	38	Such as 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.

Baluku J, et al. (19) (2020)	We describe a case of HIV / SARS-CoV-2 co-infection.	01 man	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 millimeters of mercury (mm Hg) and a pulse rate of 84 beats per minute (b/min), both of which were normal. The respiratory exam was significant for tachypnea (a respiratory rate of 26 breaths per minute (breaths/min)) with normal oxygen saturation (SPO2) 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 non-bloody diarrhea without vomiting, abdominal pain or fevers. Clinically, she had dry mucus membranes and the blood pressure was 96/60 mm Hg. 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 mm Hg.	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 gram three times a day for 5 days). Oral ciprofloxacin (500 mg twice daily for 5 days) and oral rehydration.	RT-PCR and Laboratory test.
Ozlem AA, 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 computerized tomography (CT) showed multiple ground-glass opacities 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 has been using TDF/FTC+dolutegravir for the past 2 years. Although obese patient (body mass index: 35.5 kg/m2) had diabetes, chronic obstructive pulmonary disease (COPD), and hypertension, he refused to get regular treatment for these comorbidities. On 25 March 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.	X-ray and chest CT showed bilateral patch-like paving stone view, large glass-ground lesions, and was interpreted as mid-advanced viral pneumonia tive.	Hydroxychloroquine, azithromycin, and oseltamivir.	
		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 HIVRNA negative according to the EACS guidelines. On 29 March 2020, he applied with severe weakness, dry cough, and nonbloody 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 ground-glass opacities	Hydroxychloroquine, azithromycin, and oseltamivir	
Wanga M, et al. (21) (2020)	We describe a case of HIV / SARS-CoV-2 co-infection.	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/minute, blood pressure 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/minute) through a mask.	The chest CT of this patient showed multiple infiltrations in both lungs, consistent with viral infection. On the second chest CT showed inflammation absorption compared with the previous one.	High-flow oxygen and Arbidol; Methylprednisone, Moxifloxacin and Sulbactam/cefoperazone (sulperazone); Human serum albumin, thymosin and ulinastatin; Tocilizumab.	RT-PCR and Chest CT.
Härter G, et. al. (22) (2020)	We describe our early experiences with COVID-19 and clinical characteristics in patients with documented HIV infection.	30 man and 03 woman	The median age of patients (n=33) was 48 years old (26-82).	Two patients with detectable HI-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 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).	NA	Antiretroviral regimens included nucleoside reverse transcriptase inhibitors (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.

Vizcarra P, 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 man and 08 woman.	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 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 seven (70%) of ten analysed cases.	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.
Benkovic K, et al. (24) (2020)	Describe 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. Nineteen 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.	His 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. One week after discharge 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 room, the temperature was 100, blood pressure was 113/65, heart rate was 75, breathing did not work and oxygen saturation was 97% in ambient air.	Chest X-ray did not show any consolidation.	Emtricitabine, tenofovir alafenamide and dolutegravir. Rosvustatin and losartan.	RT-PCR, laboratory test and chest X-ray.

		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 two liters 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 H, et al. (25) (2020)	Describe 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 human immunodeficiency virus (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,2 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 2nd. The patient presented with fever (39.4°C), fatigue, cough, and tachycardia.	Chest X-ray showed diffuse bilateral infiltrates.	Emtricitabine/tenofovir alafenamide/rilpivirin for HIV is ongoing since 2016. Oxygen and ampicillin/sulbactam.	RT-PCR, laboratory test and chest X-ray.
Modi A, et al. (26) (2020)	We present 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 and was found to have a temperature of 1010F. 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. Computerized tomography (CT) imaging was not obtained.	Efavirenz, emtricitabine and tenofovir disoproxil fumarate. His maintenance immunosuppression consisted of mycophenolate mofetil (MMF), prednisone, and tacrolimus. His antiretroviral therapy (ART) was changed to raltegravir, emtricitabine, and tenofovir disoproxil fumarate post-transplantation; 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 five days.	RT-PCR

Riva A, et al. (27) (2020)	We report three HIV-positive subjects on antiretroviral (ARV) regimen containing darunavir with good immuno virological status, diagnosed with COVID-19.	P1 – man	62	HIV-positive man was admitted at our emergency department 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, one 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, metoprolole and amlodipine; lopinavir/ritonavir plus hydroxychloroquine. In the intensive care unit lopinavir/ritonavir plus hydroxychloroquine were replaced by tocilizumab and remdesivir.	RT-PCR and chest X-ray.
		P2 – man	63	On March 18 the patient was admitted to the emergency department 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 coformulated 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 is 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 nebivolole and atorvastatin; hydroxychloquine.	
Nakamoto T, et al. (28) (2020)	We describe a case of was co-infected with SARS-CoV-2 and HIV.	01 man	28	His immune status from HIV infection was not well-controlled due to a lack of antiretroviral therapy (ART). Underlying condition: Smoker, HBV infection; Day of admission of the disease: 8; Saturation at admission: 97	CT findings at admission: multiple GGO.	Antiretroviral therapy and Hydroxychloroquine.	RT-PCR and Chest CT.

Gervasoni C, et al. (29) (2020)	Describes our experience with HIV-positive patients regularly followed by our hospital who were infected with SARS-CoV-2.	36 man and 11 woman	The median age of patients was man 51 ± 11 years old woman 53 ± 12.	Twenty-eight 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. Thirteen of the 28 SARS-CoV-2 positive patients were hospitalised. Six had severe lung disease (respiratory rate ≥30 breaths/min; resting percutaneous oxygen saturation ≤93% in room air), two of whom required mechanical ventilation: one recovered and was discharged and the othe died. Another patient with cardiovascular disease and a recent diagnosis of lung cancer died during hospitalisation. 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 co-morbidity (82% of the males and 58% of the females), mainly dyslipidemia (32%), arterial hypertension (30%) and hepatitis B or hepatitis C co-infections (11%).	Interstitial pneumonia was diagnosed by means of an X-ray in three cases, and ground-glass opacity 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 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 toxicizumab alone.	RT-PCR, chest X-ray and Chest CT.

Lordanou S, et al. (30) (2020)	We describe a case of was co-infected 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 per minute, the blood pressure 117/72 mmHg, and the heart rate 105 beats per minute. 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 of 6 ml/kg (Predicted Body Weight), a plateau pressure lower than 30 cm H2O, PaO2 55-80 mm Hg, 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 70,386ng/ml (from 8,854ng/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.	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.
Wu Q, 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 two days after admission. Five 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 computed tomography (CT) scan that showed bilateral multiple ground-glass opacities (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 seven 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, myalgia but still had some dyspnea after labor.	He had performed chest CT scan in local hospital which revealed bilateral multiple GGO.	The patient recevied oxygen, antibiotic (Moxifloxacin), and anti-viral (Ribavirin and Umifenovir) treatments.	
Patel RH, et al. (32) (2020)	We report a recovered case of SARS-CoV-2 infection in an HIV-positive.	01 man	58	Medical history of chronic bronchitis, hypertension, and HIV presented to the emergency department 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 hours 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 mm Hg, the pulse of 94 beats per minute, the body temperature of 37°C, and oxygen saturation of 99% in ambient air. Within 12 hours 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 hours, atazanavir and ritonavir. Oral hydroxychloroquine and oral azithromycin, and zinc sulfate.	RT-PCR
Suwanwongse S, 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 man and 02 woman	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 antiretroviral therapy (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. Seven patients eventually died (78%), of which four due to hypoxemic respiratory failure and three from septic shock and multiorgan failures.	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, 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.	RT-PCR, Chest X-ray.

Shalev N, et al. (34) (2020)	We describe the characteristics of 31 people living with human immunodeficiency virus hospitalized for severe acute respiratory syndrome coronavirus 2 infection.	24 man and 07 woman	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 antiretroviral therapy (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 R, et al. (35) (2020)	We describes the clinical course of a symptomatic kidney transplant recipient with HIV who tested positive for SARS-CoV-2.	01 man	50	Presented to the Emergency Department (ED) complaining of fevers for two days, with temperatures to 101°F, chills, nasal congestion, and mild cough. The past medical history also 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 antiretroviral therapy (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 tachycardic with heart rate 108/minute, 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.	NA	He received induction immunosuppression with basiliximab and steroid-sparing maintenance 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).	RT-PCR
Toombs J, et al. (36) (2020)	Describe 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; Abacavir + Tazocin. 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; Nevirapina + Doxycyline.	
Li W, 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 per minute, pulse of 119 beats per minute, 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 per minute, pulse of 102 beats per minute, and blood pressure of 125/88 mm Hg. 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.
Ridgway J, et al. (38) (2020)	We report a case series of five PLWH with COVID-19.	P1 – man	38	HIV positive presented to the emergency department (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 tachycardic. 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 perihilar patchy opacities and chest CT showed bilateral ground glass opacities.	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 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.	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, with ceftriaxone transitioned to cefdinir on HD 2. Hydroxycholoroquine.	RT-PCR, Chest X-ray
		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.	Her chest X-ray was unremarkable.	ART regimen of bictegravir, emtricitabine, tenofivir 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 K, et al. (39) (2020)	We report the clinical characteristics of 18 PWH who were hospitalized with confirmed COVID-19.	12 man and 06 woman	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 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.	Most (78%) had bilateral chest radiograph changes consistent with viral pneumonitis and required oxygen therapy.	Two patients were treated with remdesivir [5], and in 2 patients ART was switched to lopinavir/ritonavir. Protease inhibitor; Integrase strand-transfer inhibitor; Non-nucleoside reverse-transcriptase inhibitor; Nucleoside reverse-transcriptase inhibitor; Tenofovir b.	RT-PCR, Chest X-ray and Laboratory test.

Okoh A, et al. (40) (2020)	We report a case series of twenty-seven PLWH with COVID-19.	15 man and 12 woman	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	7 received hydroxychloroquine and 6 were managed with empiric antibiotics for suspected community-acquired pneumonia. Antiretroviral therapy was held during hospitalization.	RT-PCR and Laboratory test.
Haddad S, et al. (41) (2020)	We report 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 two months prior to presentation and recurrent HSV on chronic suppressive therapy presented with abdominal pain, intractable vomiting, and confusion. He became ill six days prior to presentation when the patient started experiencing a dry cough and intermittent fever relieved by antipyretics. On day two 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.	CT chest revealed diffuse patchy nodular ground glass infiltrates. The remainder of imaging studies including CT head were 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.	Hydroxychloroquine, azithromycin, Cefepime, ampicillin, and vancomycin.	RT-PCR, Computerized tomography (CT) and MRI brain with and without contrast and EEG.
Sun W, et al. (42) (2020)	We report here a case of HIV and SARS-CoV-2 coinfection in a PLHIV on long-term antiretroviral therapy 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 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.	His chest radiograph was clear with no infiltrates or consolidation.	Tenofovir, lamivudine, and efavirenz.	RT-PCR and Laboratory test.

Chen J, et al. (43) (2020)	This report provides 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 subpleural regions of the middle and lower lobes of the right lung, with involvement of adjacent interlobar pleura.	Antiretroviral therapy (ART) (tenofovir; lamivudine; favirenz) 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.
Giambene S, et al. (44)	We report 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 'ground-glass' opacities, in the absence of signs of bleeding or signs of pulmonary embolism	Antiretroviral therapy STR with arunavir/ cobicistat/ emtricitabine/ tenofovir alafenamide. Hydroxycloroquine, azithromycin, sarilumab.	RT-PCR, Chest CT and Laboratory test.

NA: Not Applicable

Table 2. Clinical manifestations

Author	Fever	Coughing	Chest tightness/ palpitation	Shortness of breath/ Dyspnea	Diarrhea or abdominal distension	Desaturation	Myalgia	Nasal runny or nasal congestion	Pneumonia
Guo W, et. al. (17) (2020)	Yes	Yes	No	Yes	Yes	No	Yes	No	Yes
Zhu N, et al. (15) (2020)	Yes	No	No	Yes	No	Yes	No	No	Yes
Blanco L, et al. (18) 2020)	Yes	Yes	No	Yes	No	Yes	No	No	Yes
Zhao J, et al. (16) (2020)	Yes	Yes	Yes	No	Yes	No	No	Yes	Yes
Baluku J, et al. (19) (2020)	Yes	No	Yes	Yes	Yes	No	Yes	No	No
Ozlem AA, et al. (20) (2020)	Yes	Yes	Yes	Yes	Yes	No	No	No	No
Wang M, et al. (21) (2020)	Yes	No	Yes	Yes	No	Yes	No	No	No
Härter G, et al. (22) (2020)	Yes	Yes	No	No	No	Yes	Yes	No	No
Vizcarra P, et al. (23) (2020)	Yes	Yes	No	Yes	Yes	No	Yes	No	No
Benkovic S, et al. (24) (2020)	Yes	Yes	No	No	Yes	No	No	No	No
Müller H, et al. (25) (2020)	Yes	Yes	No	No	No	No	No	No	No
Modi A, et al. (26) (2020)	Yes	Yes	Yes	Yes	No	No	No	No	No
Riva A, et al. (27) (2020)	Yes	Yes	No	No	No	No	No	No	No

Nakamoto T, et al. (28) (2020)	No	No	No	No	No	Yes	No	No	No
Gervasoni, et al. (29) 2020)	Yes	Yes	No	Yes	Yes	No	Yes	No	Yes
Lordanou S, et al. (30) (2020)	Yes	Yes	No	Yes	No	No	No	No	No
Wu Q, et al. (31) (2020)	Yes	No	No	Yes	No	No	Yes	No	No
Patel RH, et al. (32) (2020)	Yes	Yes	No	Yes	Yes	No	Yes	No	Yes
Suwanwongse K, et al. (33) (2020)	Yes	Yes	No	Yes	Yes	Yes	Yes	No	No
Shalev N, et al. (34) (2020)	Yes	No	No	No	No	No	Yes	No	Yes
Kumar R, et al. (35) (2020)	Yes	Yes	No	No	No	No	No	Yes	No
Toombs J, et al. (36) (2020)	Yes	Yes	No	Yes	No	Yes	No	No	No
Li W, et al. (37) (2020)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
Ridgway J, et al. (38) (2020)	Yes	Yes	Yes	No	No	Yes	Yes	No	Yes
Childs K, et al. (39) (2020)	Yes	Yes	No	Yes	No	Yes	No	No	No
Okoh A, et al. (40 (2020)	Yes	Yes	No	Yes	No	No	No	No	No
Haddad S, et al. (41) 2020)	Yes	Yes	No	Yes	Yes	No	Yes	No	No
Sun LJ, et ali. (42) (2020)	Yes	Yes	No	No	No	No	No	No	No

Chen J, et al. (43) (2020)	Yes	Yes	No	No	No	No	No	No	No
Giambene S, et al. (44) (2020)	Yes	Yes	No	Yes	Yes	Yes	No	No	No

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	X
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	X
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	X
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	X
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	X
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	X
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	X
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	X
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	X

PRISMA 2009 Checklist

Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	X
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	X

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	X
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	X
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	X
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	X
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	X
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	

PRISMA 2009 Checklist

Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	X
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	X
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	X
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	X

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POTENTIAL IMPACT OF THE COVID-19 IN HIV-INFECTED INDIVIDUALS: A SYSTEMATIC REVIEW

RUNNING HEADLINE: IMPACT OF THE COVID-19 IN HIV-INFECTED INDIVIDUALS

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