The clinical outcomes of COVID-19 in HIV-positive patients: A systematic review of current evidence

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Abstract

Introduction: Patients with chronic underlying diseases are more susceptible to coronavirus disease 2019 (COVID-19) complications. Recent studies showed people living with HIV (PLWH) are not at greater risk than the general population. Few studies have reviewed the impacts of COVID-19 on PLWH. The purpose of this systematic review was to investigate the impact of COVID-19 on patients infected with HIV.

Methods: We executed a systematic search using four databases of PubMed, Scopus, Science Direct, and Web of Science and screened the records in two steps based on their title/abstract and full text. This study follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist to elevate the validity and reliability of its results.

Results: We reviewed 36 studies. The patients' age was above 20 years in all studies. In almost all studies, the inflammatory parameters were reported high. In most of the studies, all HIV patients completely recovered from the COVID 19 infection. Although CD4 count was not recorded in all studies, the minimum level was reported as 12 cells/µl.

Conclusion: Based on the current review, we concluded that HIV patients at advanced stages (3 or 4) of the disease, whose CD4 counts are low, may show less severe COVID-19 infection symptoms. Similarly, Interference can reduce the severity of immune reactions and subsequent cytokine storms and consequently mitigate the symptoms. Therefore, in most of the studies, the majority of HIV patients showed no severe symptoms and completely recovered from COVID 19 infection.

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INTRODUCTION

At the end of December 2019, cases of a highly contagious infectious disease had been reported in Wuhan, China.\(^1\)\(^–\)\(^7\) Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a new strain of coronavirus and belongs to the Beta coronavirus genus of the Coronaviridae family. Due to the high interpersonal transmission rate, soon SARS-CoV-2 spread globally and turned into a global pandemic.\(^6\)\(^–\)\(^10\) The World Health Organization (WHO) announced its concern about the novel coronavirus on January 30, 2020, and declared the highest level of alarm as a public health emergency.\(^11\) The COVID-19 outbreak was been declared as a global pandemic by WHO on March 11, 2020.\(^12\) As of May 30th, a total of 169 million cases of infected patients were reported around the world and the number of deaths reached 3.52 million.\(^13\) Coronavirus disease 2019 (COVID-19) can affect different organs in the human body. The most common complications of SARS-CoV-2 are respiratory failure and Acute Respiratory Distress Syndrome (ARDS).\(^14\) Risk factors of COVID-19 are related to the type of immune system response and host factors such as age, gender, underlying diseases, and so on.\(^15\)\(^–\)\(^18\)

Patients with chronic underlying diseases can experience COVID-19 complications more than the general population, although recent studies showed people living with HIV (PLWH) are not at greater risk than the general population.\(^19\)\(^,\)\(^20\) HIV attacks a specific type of immune system cells known as a CD4 helper cell and destroys them. When the CD4 count drops below 200 cells/µl, the patient will have progressed to AIDS. According to the Joint United Nations Programme on HIV/AIDS (UNAIDS), the number of PLWH around the world was 37.9 million,\(^21\) and unfortunately, around 12 million of them are not receiving antiretroviral therapy (ART). A recent study revealed 86% of HIV patients receiving ART, have a positive response to it and this leads to undetectable viral load. In conclusion, patients who respond to ART and maintain treatment are not immunocompromised.\(^19\)

Few studies have reviewed the impacts of COVID-19 on PLWH. There is yet no certain answer whether patients infected with HIV are at greater risk of severe illness and worse outcomes. We still need to know whether there are any differences between controlled HIV infection with undetectable viral load and a CD4 count ≥200 cells/µl and uncontrolled HIV infection or AIDS in COVID-19 outcomes. Thus, the aim of this systematic review was to investigate the outcome of COVID-19 among patients infected with HIV.

METHODS

2.1 Study design

We systematically searched four databases, including PubMed, Scopus, Science Direct, and Web of Science to retrieve the related articles based on the keywords used in our search strategy. Two researchers (S. P. M. and S. S.) screened the retrieved articles using the Covidence website (https://www.covidence.org). The screening consisted of two-step title/abstract and full-text screening processes. Utilizing this website eased settling of the discrepancies in the inclusion process. A third researcher (A. K.) addressed the remaining discrepancies. Two researchers (H. M. and A. R.) extracted and summarized the data of the included studies.

2.2 Search strategy

We included the search terms for HIV/AIDS and COVID-19 as presented below:

A. [SARS-CoV-2] (Title/Abstract) OR [COVID-19] (Title/Abstract) OR [2019-nCoV] (Title/Abstract) OR [Novel Coronavirus] (Title/Abstract)
B. [Human Immunodeficiency Virus] (Title/Abstract) OR [HIV] (Title/Abstract) OR [Acquired Immune Deficiency Syndrome] (Title/Abstract) OR [AIDS] (Title/Abstract)
C. [A] AND [B].

2.3 Inclusion criteria

We included all the original articles discussing the COVID-19 status in PLWH. The exclusion criteria are the following:
TABLE 1 Quality assessment of the included studies using NIH tool

| Study                  | Study design       | Score | Quality rating (good, fair, or poor) |
|------------------------|--------------------|-------|--------------------------------------|
| Blanco et al. JL23     | Case series        | 7/9   | Good                                 |
| Brown et al.24         | Prospective cohort | 13/14 | Good                                 |
| Cabello et al.25       | Case series        | 8/9   | Good                                 |
| Calza et al.26         | Case series        | 7/9   | Good                                 |
| Calza et al.27         | Case series        | 6/9   | Fair                                 |
| d’Ettorre et al.28     | Case report        | 8/9   | Good                                 |
| D’Souza et al.29       | Cohort             | 10/14 | Fair                                 |
| Boule et al.30         | Retrospective cohort | 12/14 | Good                                 |
| Del Amo et al.31       | Retrospective cohort | 11/14 | Good                                 |
| Etienne et al.32       | Prospective cohort | 12/14 | Good                                 |
| Geretti et al.33       | Prospective cohort | 13/14 | Good                                 |
| Gudipati et al.34      | Case series        | 7/9   | Good                                 |
| Guo et al.35           | Retrospective cohort | 10/14 | Fair                                 |
| Härter et al.36        | Case series        | 7/9   | Good                                 |
| Ho et al.37            | Case series        | 8/9   | Good                                 |
| Karmen-Tuohy et al.38  | Retrospective cohort | 11/14 | Good                                 |
| Kim et al.39           | Case report        | 7/9   | Good                                 |
| Kowalska et al.40      | Case series        | 8/9   | Good                                 |
| Kumar et al.41         | Case report        | 6/9   | Fair                                 |
| Menghua et al.42       | Case report        | 7/9   | Good                                 |
| Myashita and Kuno43    | Retrospective cohort | 9/14  | Fair                                 |
| Mondi et al.44         | Case series        | 7/9   | Good                                 |
| Nagarakanti et al.45   | Retrospective cohort | 10/14 | Fair                                 |
| Okoh et al.46          | Case series        | 7/9   | Good                                 |
| Patel and Pella47      | Case report        | 6/9   | Fair                                 |
| Ridgway et al.48       | Cohort             | 7/14  | Fair                                 |
| Ruan et al.49          | Case series        | 6/9   | Fair                                 |
| Sachdev et al.50       | Retrospective cohort | 9/14  | Fair                                 |
| Stoeckle et al.51      | Retrospective cohort | 11/14 | Good                                 |

TABLE 1 (Continued)

| Study                  | Study design       | Score | Quality rating (good, fair, or poor) |
|------------------------|--------------------|-------|--------------------------------------|
| Swaminathan et al.52   | Case series        | 7/9   | Good                                 |
| Tesoriero et al.53     | Retrospective cohort | 10/14 | Fair                                 |
| Toombs et al.54        | Case report        | 8/9   | Good                                 |
| Vizcarra et al.55      | Prospective cohort | 11/14 | Good                                 |
| Wang et al.56          | Case report        | 6/9   | Fair                                 |
| Wu et al.57            | Case report        | 7/9   | Good                                 |
| Yang et al.58          | Retrospective cohort | 12/14 | Good                                 |
| Zhang et al.59         | Case report        | 7/9   | Good                                 |

(1) Review articles, letter to the editors, or other studies without original data.
(2) Ongoing studies.
(3) Irrelevant to the aims, settings, and design of this study.
(4) Abstracts, conference abstracts, errata, or other studies lacking full-texts.

2.4 | Quality assessment

We utilized the National Institutes of Health (NIH) tool to evaluate the quality of the studies. A researcher (A. K.) examined all the studies to ensure the quality of evidence. If an element of the criteria was insufficiently addressed, not applicable, or not reported in a study and it could not be identified indirectly, we did not allocate a score to that element. For cohort and cross-sectional studies, 11–14 was considered good, 6–10 fair, and 0–5 poor. We chose 9–12, 5–8, and 0–4 for good, fair, and poor quality in the case-control studies, respectively. The numbers were 7–9, 4–6, and 0–3 for the case series. Case reports were checked with the same checklist as the case series.

3 | RESULTS

Most of the studies were considered of good quality (25/37). Other studies (12/37) had a fair quality, and we did not classify any studies as poor (Table 1).

Thirty-six studies met the inclusion criteria. The results of these 36 studies are summarized in Tables 2 and 3.
| ID | Study (reference) | Country | Study population | Total cases (HIV + cases) | Age(year) | Sex |
|----|------------------|---------|------------------|--------------------------|-----------|-----|
| 1  | Bhaskaran et al. | UK      | 17,282,905       | 27,480                   | 18–39 years: 6625 (24.1%) 40–49 years: 8093 (29.5%) 60–69 years: 3130 (11.4%) 70–79 years: 937 (3.4%) ≥80 years: 209 (0.8%) Median (IQR): 48 years (40–55) | Male: 17780 (64.7%) Female: 9700 (35.3%) |
| 2  | Blanco et al.    | Spain   | 5                | 5                        | 40, 49, 29, 40, 31 years | Transgender: 2 (40%), Male: 3 (60%) |
| 3  | Cabello et al.   | Spain   | 63               | 63                       | Median (IQR): 46 years (37–52) | Male: 56 (88.9%) |
| 4  | Calza et al.     | Italy   | 9                | 9                        | Median (IQR): 56.2 years (41–73) | Male: 7 (78%) |
| 5  | Calza et al.     | Italy   | 26               | 26                       | Median (IQR): 53.8 years (28–80) | Male: 19 (73%) |
| 6  | Cipolat et al.   | Brazil  | 1                | 1                        | 63 years | Female |
| 7  | D'Ettorre et al. | Italy   | 16               | 11                       | 52 years | Female: 1 (100%) |
| 8  | D'Souza et al.   | USA     | 3411             | 2078                     | Median (IQR): 57 years (26–94) | Male: 956 (46%), female: 1123 (54%) |
| 9  | Davies           | South Africa | 3,460,932     | 3978                     | All patients were above 20 years | Male: 1682 (42.3%), female: 2296 (57.7%) |
| 10 | Del Amo et al.   | Spain   | 77,590           | 77590                    | 20–39 years: 14,506 (19%) 40–49 years: 19,373 (25%) 50–59 years: 32,321 (42%) 60–69 years: 8762 (11%) 70–79 years: 2628 (3%) | Male: 58,120 (75%), female: 19,470 (25%) |
| 11 | Ettiene et al.   | France  | 54               | 54                       | Median (IQR): 54 years (47–60) | Male: 33 (61.1%), female: 21 (38.9%) |
| 12 | Geretti et al.   | England | 47,592           | 122                      | Median (IQR): HIV + group: 56 years (49–62) HIV - group: 74 years (60–84) | Female: HIV + group: 41/121 (33.9%) HIV group: 20/302 (42.9%) |
| 13 | Gudipati et al.  | USA     | 14               | 14                       | Median (IQR): 57.5 years (36–74) | Male: 12 (85.7%), female: 2 (14.3%) |
| 14 | Guo et al.       | China   | 1701             | 1701                     | Mean: 42 ± 14.5 years | Male: 1484 (87.2%), female: 217 (12.8%) |
| 15 | Härter et al.    | Germany | 33               | 33                       | Mean (SD): 48 years (26–82) | Male: 30 (91%), female: 3 (7%) |
| 16 | Ho et al.        | USA     | 93               | 93                       | Median (IQR): 58 years (52–65) | Male: 67 (72%), female: 23 (24.7%) Transgender: 3 (3.2%) |
| 17 | Karmen-Tuohy et al. | USA | 63               | 21                       | Not mentioned | Not mentioned |
| ID | Study (reference) | Country | Study population | Total cases (HIV + cases) | Age(year) | Sex          |
|----|-------------------|---------|------------------|--------------------------|-----------|--------------|
| 18 | Kim et al.39      | Korea   | 1                | 1                        | 29 years  | Male: 1 (100%) |
| 19 | Kowalska et al.40 | Poland  | 34               | 34                       | Median: 40.5 years | Female: 10 (29.4%), Male: 24 (70.6%) |
| 20 | Kumar et al.41    | USA     | 1                | 1                        | 50 years  | Male:1 (100%)  |
| 21 | Menghua et al.42  | China   | 1                | 1                        | 49 years  | Female: 1 (100%) |
| 22 | Miyashita et al.43| USA     | 8912             | 161                      | ≤50 years: 38 51–65 years: 82 ≥66 years: 41 | Male: 125(77%), female: 36 (23%) |
| 23 | Mondi et al.44    | Italy   | 605              | 5                        | 61, 46, 31, 55, 55 years | Male: 4 (80%), Transgender woman: 1 (20%) |
| 24 | Nagarakanti et al.45 | USA  | 277              | 23                       | Median (IQR): 59 years (51–67) | Male: 14 (60.8), female: 9(39.2) |
| 25 | Okoh et al.46     | USA     | 27               | 27                       | Median (IQR): 58 years (50–67) | Male: 15 (55.5%), female: 12 (44.5%) |
| 26 | Patel et al.47    | USA     | 1                | 1                        | 58 years  | Male: 1 (100%)  |
| 27 | Ridgway et al.64  | USA     | 5537             | 8                        | Not mentioned | Not mentioned |
| 28 | Ruan et al.49     | China   | 4                | 4                        | 38, 25, 46, 54 years | Male: 4 (100%)  |
| 29 | Sachdev et al.50  | USA     | 276,807          | 193                      | 48 years (20–76) | Male: 176 (91.2%), female: 12 (6.2%), Transgender female: 5 (2.6%) |
| 30 | Stoeckle et al.51 | USA     | 120              | 30                       | 60.5 years (56.6–70.0) | Male: 24 (80%), female: 6 (20%) |
| 31 | Swaminathan et al.52 | USA  | 6                | 6                        | Mean: 64 years (62, 59, 45, 74, 57, 87 years) | Male: 5 (83%), female: 1 (17%) |
| 32 | Tesoriero et al.53 | USA  | 108,062          | 2988                     | <40 years: 492 pt 40–60 years: 1400 pt >60 years: 1096 | Male: 2109 (70%), female: 879 (30%) |
| 33 | Toombs et al.54   | UK      | 3                | 3                        | 62, 46, 57 years | Male: 2 (66%), female: 1 (34%) |
| 34 | Vizcarr et al.55  | Spain   | 1339             | 51                       | Mean: 53.3 years | Male: 43 (84%), Woman: 8 (16%) |
| 35 | Wang et al.56     | China   | 1                | 1                        | 37 years  | Male: 1 (100%)  |
| 36 | Wu et al.57       | China   | 2                | 2                        | 60 years  | Male: 2 (100%)  |
| 37 | Yang et al.58     | China   | 56               | 3                        | 31, 60, 29 years | Male: 3 (100%)  |
| 38 | Zhang et al.59    | China   | 2                | 2                        | 24, 37 years | Male: 2 (100%)  |
| ID | Signs and symptoms | Duration of disease | Last CD4 count (cells/µl) | Last viral load | Last antiretroviral regimen | Comorbidities | Clinical outcome | Diagnostic parameters during COVID-19 | inflammatory markers | COVID-19Therapy |
|----|-------------------|---------------------|--------------------------|-----------------|-----------------------------|---------------|----------------|-------------------------------|---------------------|----------------|
| 1  | N/A               | N/A                 | N/A                      | N/A             | N/A                         | Hypertension 5290 (19.3%), Chronic respiratory disease 1095 (4.0%), Chronic heart disease 1444 (5.3%), Chronic liver disease 921 (3.4%), Stroke or dementia 559 (2.0%), Other neurological disease 239 (0.9%), Organ transplant 72 (0.3%) | 25 Death in HIV/COVID-19 population | N/A               | N/A               |
| 2  | Fever/cough/ malaise/ headache | 1. 13 years 2. 17 years 3. 7 years 4. 17 years 5. 3 months | 1. 616 2. 445 3. 604 4. 1140 5. 13 | N/A                          | N/A                         | 1. ART at admission remained (Tenofovir+Adefovir, Emtricitabine, Darunavir-boosted Cobicistat) 2. Tenofovir proxifumarate, Emtricitabine plus Lopinavir-boosted Ritonavir (ongoing) 3. Tenofovir proxifumarate, Emtricitabine plus Lopinavir-boosted Ritonavir (for 3 days) | 1. None 2. Hypothyroidism 3. None 4. Asthma 5. None | 1. Cured 2. Still at the hospital 3. Cured 4. Cured 5. Cured | N/A                         | 1. CRP, Ferritin: not done 2. CRP: 30 mg/dl, ferritin:1020 ng/ml 3. CRP:0.72 mg/dl, ferritin:1044 ng/ml 4. CRP: 0.43 mg/dl, ferritin:1044 ng/ml 5. CRP:40 mg/dl, ferritin:1044 ng/ml | Interferon beta-1b hydroxychloroquine Meropenem linezolid Tocilizumab Azithromycin Azithromycin Cefixime Inhaled corticosteroids hydroxychloroquine Azithromycin cefaroline fosamil |

(Continues)
### TABLE 3 (Continued)

| ID | Signs and symptoms | Duration of disease | Last CD4 count (cells/µl) | Last viral load | Last antiretroviral regimen | Comorbidities | Clinical outcome | Diagnostic parameters during COVID-19 | inflammatory markers | COVID-19 Therapy |
|----|-------------------|---------------------|---------------------------|-----------------|----------------------------|---------------|-----------------|--------------------------------------|----------------------|-----------------|
| 3  | Fever: 66.1%      | HIV infection time | <50 copies/ml             | PI-based therapy: 9.8% | Hypertension: 19%          | Global mortality rate: 3.22% | Ferritin >1000 mcg/L | N/A |
|    | Cough: 66.1%      | (years): 10.8       |                           | INSTI-based therapy: 63.9% | DM: 9.5%                   | CD4 (cell/mm³): 605 | N/A |
|    | Dyspnea: 46.8%    |                     |                           | NNRTI-based therapy: 26.2% | Overweight: 13.1%          | (Median): 391–921 | N/A |
|    | Anosmia: 11.3%    | (days): 6.5–16.5    |                           | TDF-containing regimen: 14.8% | Cardiovascular disease: 12.7% | Nadir CD4 < 200 | N/A |
|    | Ageusia: 9.7%     |                     |                           | TFV (TAF or TDF)-containing regimen: 26.2% | COPD: 4.8% | (cell/mm³): 26.7% | N/A |
|    | Diarrhea: 22.6%   |                     |                           | Smoker: 48.2% | Chronic kidney disease (crl < 30 ml/min): 3.2% | N/A |
|    | Headache: 14.5%   |                     |                           |                  | Tocilizumab: 6.3% | N/A |
|    | Weakness: 25.8%   |                     |                           |                  | N/A |
|    | Myalgia/arthralgia: 24.2% | |                           |                  | N/A |

| 4  | Cough: 7 (77.8%)  | Median (IQR): 21.4 years (13.6–29.4) | Plasm HIV RNA ranged between 66 and 1240 copies/ml, and 7 patients had HIV RNA < 200 copies/ml (77.8%) | Arterial hypertension: 6 (66.7%) | Recovery: 9 (100%) | Six subjects had CD4 + lymphocyte count ranging between 200 and 350 cells/mm³, and 3 subjects had CD4 + lymphocyte count <200 cells/mm³ | N/A |
|    | Myalgia: 7 (77.8%)| Median (IQR): 258 (156–343) (cells/mm³) | | Diabetes mellitus: 2 (22.2%) | | | N/A |
|    | Fatigue: 9 (100%) |                     | 1 boosted protease inhibitor (PI) in 3 cases, 1 integrase strand transfer inhibitor in 4, and 1 nonnucleoside reverse transcriptase inhibitor in 2 | BMI > 30 Kg/m², 1 (11.1%) | | | N/A |
|    | Anosmia and/or ageusia: 3 (33.3%) | | | COPD, 1 (11.1%) | | | N/A |
|    | Dyspnea: 2 (22.2%) |                     | | | | | N/A |

4. Tenofovirdisoproxilumate, Emtricitabine plus Lopinavir-boosted Ritonavir (for 14 days)
5. TenofovirAlafenamide, Emtricitabine, Darunavir-boosted Cobicistat(ongoing)

COVID-19 Therapy: co-trimoxazole corticosteroids
| ID | Signs and symptoms | Duration of disease | Last CD4 count (cells/µl) | Last viral load | Last antiretroviral regimen | Comorbidities | Clinical outcome | Diagnostic parameters during COVID-19 | inflammatory markers | COVID-19 Therapy |
|----|-------------------|---------------------|--------------------------|------------------|-----------------------------|---------------|-----------------|-----------------------------------------|---------------------|-----------------|
| 5  | Fever > 38°C, cough, fatigue, myalgia, and tachypnea | N/A | Above 350 cells/mm³; 22 individuals (85%) | Undetectable HIV viral load in all patients | N/A | N/A | Recovery: 26 (100%) | N/A | CRP (mg/dL), median: 4.2 (0.71–9.2) | Hydroxychloroquine: 50% Exonaparin: 23% |
| 6  | Fever, myalgia, nausea, abdominal pain, diarrhea, hyposmia, hypogeusia, cough, dyspnea | 15 years | CD4: 426 | Undetectable | Tenofovir (TDF), lamivudine (3TC), and dolutegravir (DTG) | Hypertension | Discharged in good conditions | N/A | CRP: 65.5 LDH: 316 | HCQ + Azithromycin |
| 7  | Fever, fatigue | 23 years | 528 cells/µl | N/A | Darunavir/Cobicistat | N/A | Cured | HIV-1 viral load: below level of detection (<37 HIV-1 RNA copies/ml) CD4 count: 242 cells/ml, CD8 count: 336 cells/ml | IL-6: 50.98 pg/ml | N/A |
| 8  | Headache (23%), Myalgias (19%), Shortness of breath (14%), Chills (12%), Fever (6%) and Loss of taste or smell (6%) | N/A | 682 cells/mm³ (median) | Undetectable viral load: 74% | N/A | N/A | Recovered and symptom free: 71.1% Feeling better but not completely recovered: 26.3% Not feeling better: 2.6% | Median CD4 cell count: 682 cells/mm³; 74% had undetectable HIV viral load (<20 copies/mL) | N/A | N/A |

(Continues)
| ID | Signs and symptoms | Duration of disease | Last CD4 count (cells/µl) | Last viral load | Last antiretroviral regimen | Comorbidities | Clinical outcome | Diagnostic parameters during COVID-19 | inflammatory markers | COVID-19 Therapy |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 9 | N/A | N/A | N/A | N/A | Abacavir or Zidovudin | Diabetes | Died: 2.8% | N/A | N/A | N/A |
|   |   |   |   |   | Tenofovir | Hypertension |   |   |   |   |
|   |   |   |   |   | Efavirenz | Chronic kidney disease |   |   |   |   |
|   |   |   |   |   | Lopinavir |   |   |   |   |   |
|   |   |   |   |   | Atazanavir | Chronic pulmonary disease/asthma |   |   |   |   |
|   |   |   |   |   | Dolutegravir | Tuberculosis |   |   |   |   |
| 10 | N/A | N/A | N/A | N/A | Tenofovirdisoproxifumarate/emtricitabine: 12 395 (16%)) |   | Age and gender standardized mortality from COVID-19 in HIV-positive persons (3.7 per 10,000) | N/A | N/A | N/A |
|   |   |   |   |   | TenofovirAlafenamide/emtricitabine: 25 570 (33%) |   |   |   |   |   |
|   |   |   |   |   | Abacavir/lamivudine |   |   |   |   |   |
|   |   |   |   |   | 20 105 (26%) |   |   |   |   |   |
|   |   |   |   |   | Other regimens |   |   |   |   |   |
|   |   |   |   |   | 19,520 (25%) |   |   |   |   |   |
|   |   |   |   |   | Third drug: NNRTI | 15 733 (21%) |   |   |   |   |
|   |   |   |   |   | Protease inhibitor | 14,267 (19%) |   |   |   |   |
|   |   |   |   |   | Integrase inhibitor | 37,622 (50%) |   |   |   |   |
|   |   |   |   |   | Other 9968 (10%) |   |   |   |   |   |
| 11 | N/A | N/A | Median (IQR): 583 (474-773) | HIV viral load < 40 copies: 96.2% | Protease inhibitors based: 9 (16.7%) | Diabetes: 5 (9.3%) | Cured: 43 (86%) | N/A | N/A | N/A |
|   |   |   |   |   | Darunavir: 6 (11.1%) | hypertension: 16 (29.6%) | Still hospitalized: 1 (2%) |   |   |   |
|   |   |   |   |   | Atazanavir: 2 (3.7%) | Other cardiac disease: 4 (7.4%) | Not cured: 5 (10%) |   |   |   |
|   |   |   |   |   | Lopinavir: 1 (1.9%) | Renal insufficiency (crcl<60 ml/min): 3 (5.6%) | death: 1 (2%) |   |   |   |
|   |   |   |   |   | Non-nucleoside inhibitors based: 25 (46.3%) |   |   |   |   |   |
|   |   |   |   |   | Nucleoside inhibitors based: 43 (79.6%) |   |   |   |   |   |
| ID | Signs and symptoms | Duration of disease | Last CD4 count (cells/µl) | Last viral load | Last antiretroviral regimen | Comorbidities | Clinical outcome | Diagnostic parameters during COVID-19 | Inflammatory markers | COVID-19Therapy |
|----|-------------------|---------------------|---------------------------|----------------|-----------------------------|---------------|-----------------|--------------------------------------|----------------------|-----------------|
|    |                   |                     |                           |                | Integrase inhibitors: 33 (61.1%) | Respiratory disease (asthma, chronic bronchitis): 5 (9.3%) |                |                         |                                      |                      |                 |
| 12 | HIV+ group:       | N/A                 | N/A                       | N/A            |                            | Chronic pulmonary disease: (10.8%) |                   |                         |                                      |                      |                 |
|    | Fever: (82.5%)    |                     |                           |                |                            | Asthma: (10.3%) |                   |                         |                                      |                      |                 |
|    | Myalgia: (26.9%)  |                     |                           |                |                            | Chronic kidney disease: (18.1%) |                   |                         |                                      |                      |                 |
|    | Headache: (18.8%) |                     |                           |                |                            | Diabetes, no complications: (13.7%) |                   |                         |                                      |                      |                 |
|    | Cough: (79.3%)    |                     |                           |                |                            | Diabetes, with complications: (7.7%) |                   |                         |                                      |                      |                 |
|    | Dyspnea: (72.7%)  |                     |                           |                |                            | Obesity: (17%) |                   |                         |                                      |                      |                 |
|    | Chest pain: (22.9%) |                   |                           |                |                            | Chronic neurological disorder: (6.9%) |                   |                         |                                      |                      |                 |
|    | Sore throat: (14%) |                     |                           |                |                            | Dementia: (2.5%) |                   |                         |                                      |                      |                 |
|    | Wheeze: (5.9%)    |                     |                           |                |                            | Mild liver disease: (2.5%) |                   |                         |                                      |                      |                 |
|    | Rhinorrhea: (3.1%)|                     |                           |                |                            | Moderate/severe liver disease: (5.1%) |                   |                         |                                      |                      |                 |
|    | Diarrhea: (25.9%) |                     |                           |                |                            | Rheumatological disease: (5.1%) |                   |                         |                                      |                      |                 |
|    | Nausea or vomiting: (21.9%) |   |                           |                |                            | Malnutrition: (4.5%) |                   |                         |                                      |                      |                 |
|    | Abdominal pain: (12.5%) |               |                           |                |                            |                         |                   |                         |                                      |                      |                 |
|    | Fatigue: (43.9%)  |                     |                           |                |                            |                         |                   |                         |                                      |                      |                 |

(Continues)
| ID | Signs and symptoms | Duration of disease | Last CD4 count (cells/µl) | Last viral load | Last antiretroviral regimen | Comorbidities | Clinical outcome | Diagnostic parameters during COVID-19 | inflammatory markers | COVID-19Therapy |
|----|-------------------|--------------------|--------------------------|----------------|-----------------------------|---------------|----------------|----------------------------------------|---------------------|---------------|
| 13 | Fever: 7 (50%) Shortness of breath: 7 (50%) Cough: 10 (70%) Diarrhea: 4 (29%) Anosmia, ageusia: 4 (29%) | N/A | Median (IQR): 519.5 (21–1756) N/A | 11 patients <20 1 patient: 25 1 patient: 36 1 patient: 1646 (copies/ml) | N/A | Obesity (N = 8; 57%) Hypertension (N = 8; 57%) Diabetes (N = 6; 43%), chronic kidney disease (N = 5; 36%) and ESRD requiring hemodialysis (N = 2; 14%) | 5 patients died | N/A | N/A | CRP: 6 patients; not available Median: 65 (2.1–21.5 mg/dl) |
| 14 | N/A | Average: 27 ± 11 days CD4 count > 200/µl: 9 (pts with COVID19-HIV coinfection) 9 pts had undetectable viral loads 1406, 82.7%: (NRTIs) and (NNRTIs) 172 (10.1%): LPV/r-based ART, 87 (5.1%): integrase inhibitors (INI)-based ART (62 dolutegravir-based, 19 elvitegravir/cobicistat-based, 4 raltegravir-based, 2 bictegravir-based). 36 individuals (2.1%) were still treatment naïve | N/A | N/A | Nine out of the 11 COVID-19/AIDS patients had relatively high CD4 count (>200/µl) and undetectable HIV viral load (<20 copies/ml). |
| 15 | Cough: 25 (78%) Fever: 22 (69%) Arthralgia/myalgia: 7 (22%) | N/A | Median (IQR): 670/mm³ (69–1715/mm³) N/A | In 30/32 cases: below 50 copies/ml Nucleoside reverse transcriptase inhibitors (NRTIs) in 31 patients, integrase strand transfer inhibitors (INSTI) in 20, protease inhibitors (PI) Documented in 20/33 (60%) patients | N/A | Recovered: 29/32 of patients (91%) Died: 3 | N/A | N/A | N/A |
| ID | Signs and symptoms | Duration of disease | Last CD4 count (cells/µl) | Last viral load | Last antiretroviral regimen | Comorbidities | Clinical outcome | Diagnostic parameters during COVID-19 | inflammatory markers | COVID-19Therapy |
|----|-------------------|-------------------|--------------------------|-----------------|--------------------------|----------------|----------------|---------------------------------|---------------------|----------------|
|    |                   |                   |                          |                 |                          |                |                |                                 |                     |                |
|    |                   |                   |                          |                 |                          |                |                |                                 |                     |                |
| 16 | Fever:            | Median: 20 years  | Median (IQR): 61/89 (69.6%) were on an antiretroviral therapy (ART) regimen: | Recovered:53    | Died:19                 | CRP            | CD4 + : 220 cells/µL | N/A               |                     |                |
|    | 61 (65.6%)        | (15–26, n = 57)   | 554 (339–752) (n = 64)   |                 |                          | (n = 69): Median CRP, 1.37 mg/L | (n = 53) (132–372) |                     |                |
|    | cough:            |                   |                          |                 |                          | (n = 69): Median CRP, 1.37 mg/L | (n = 46) (17–18) |                     |                |
|    | 71 (76.3%)        |                   |                          |                 |                          | (n = 69): Median CRP, 1.37 mg/L | (n = 46) (17–18) |                     |                |
|    | shortness of breath: |                   |                          |                 |                          | (n = 69): Median CRP, 1.37 mg/L | (n = 46) (17–18) |                     |                |
|    | 57 (61.3%)        |                   |                          |                 |                          | (n = 69): Median CRP, 1.37 mg/L | (n = 46) (17–18) |                     |                |
|    | Altered mental status: |                   |                          |                 |                          | (n = 69): Median CRP, 1.37 mg/L | (n = 46) (17–18) |                     |                |
|    | 10/93 (10.8%)     |                   |                          |                 |                          | (n = 69): Median CRP, 1.37 mg/L | (n = 46) (17–18) |                     |                |
|    | Congestion:       | 13 (14%)          |                          |                 |                          | (n = 69): Median CRP, 1.37 mg/L | (n = 46) (17–18) |                     |                |
| ID | Signs and symptoms | Duration of disease | Last CD4 count (cells/µl) | Last viral load | Last antiretroviral regimen | Comorbidities | Clinical outcome | Diagnostic parameters during COVID-19 | inflammatory markers | COVID-19Therapy |
|----|-------------------|---------------------|---------------------------|-----------------|-----------------------------|---------------|-----------------|--------------------------------------|----------------------|-----------------|
|    | Sore throat:      |                     |                           |                 |                             |               |                 |                                      |                      |                 |
|    | 18 (19.4%)        |                     |                           |                 |                             |               |                 |                                      |                      |                 |
|    | Myalgia:          |                     |                           |                 |                             |               |                 |                                      |                      |                 |
|    | 33 (35.5%)        |                     |                           |                 |                             |               |                 |                                      |                      |                 |
|    | Anosmia:          |                     |                           |                 |                             |               |                 |                                      |                      |                 |
|    | 2 (2.2%)          |                     |                           |                 |                             |               |                 |                                      |                      |                 |
|    | Diarrhea:         |                     |                           |                 |                             |               |                 |                                      |                      |                 |
|    | 18/93 (19.4%)     |                     |                           |                 |                             |               |                 |                                      |                      |                 |
|    | Headache:         |                     |                           |                 |                             |               |                 |                                      |                      |                 |
|    | 17 (18.3%)        |                     |                           |                 |                             |               |                 |                                      |                      |                 |

| 17 | N/A               | N/A                 | 298/ml (135–542), N = 19 | N/A             | N/A                         | N/A           | N/A             | Mortality rate: 28.6%               | N/A                  | HIV group:     |
|    |                   |                     | Only 1 patient had a viral load > 50 copies/ml |                 |                             |               |                 | In HIV group                          |                      | Ferritin: 679 ng/mL (338–1446) | 19 |
|    |                   |                     |                           |                 |                             |               |                 |                                      |                      | N = 19          |
|    |                   |                     |                           |                 |                             |               |                 |                                      |                      | CRP: 154.48 ± 94.44 mg/L |   |

Only 1 patient had a viral load > 50 copies/ml
| ID | Signs and symptoms | Duration of disease | Last CD4 count (cells/µl) | Last viral load | Last antiretroviral regimen | Comorbidities | Clinical outcome | Diagnostic parameters during COVID-19 | inflammatory markers | COVID-19 Therapy |
|----|-------------------|---------------------|---------------------------|----------------|-----------------------------|---------------|-----------------|-------------------------------------|---------------------|-----------------|
| 18 | Cough, sputum, Chilling, myalgia, Rhinorrhea, sore throat, loss of taste and smell | 5 years | N/A | N/A | GenoSyva<sup>®</sup>: elvitegravir/cobicistat/ emtricitabine/tenofovir | N/A | Improved and discharged (with persistent positive PCR) | CD 4 count: 555/mm³ | Lactate dehydrogenase: 449. 4 ± 239. 8 U/L, N = 5 | N/A |
| 19 | N/A | Median: 5 years (1–14 years) | 557 cells/mm³ | HIV viral load log: median: 4.93 copies/ml (4.2–6) | 82.3% on ART regimen | 52. 9%(18 pts) had comorbidities: Cardiovascular disease:5 Chronic lung disease:2 Diabetes:2 Hypertension:2 Other:7 | Fully recovered:26 Died:2 Still in hospital:6 | Undetectable HIV RNA in 54. 5% | N/A | N/A |
| 20 | Fevers, chills, nasal congestion, and mild cough | 23 years | 435 cells/µl | < 20 copies/ml | Dolutegravir, emtricitabine, and tenofovir alafenamide. | Hypertension, asthma, steatohepatitis, and resolved hepatitis B infection, HIV-associated nephropathy/ focal segmental glomerulosclerosis (FSGS) | Cured | CD4: 395 cells/µl HIV RNA: < 20 copies/mL | No specific treatment | N/A | Interferon atomization |
| 21 | Fatigue, fever, chills, and pharyngeal pain | 8 | Nadir CD4 + count: 224 | Remained undetectable from 2013 | Efavirenz 600 mg, zidovudine 300 mg, | N/A | Cured | N/A | N/A | Interferon atomization | (Continues) |
| ID | Signs and symptoms | Duration of disease | Last CD4 count (cells/µl) | Last viral load | Last antiretroviral regimen | Comorbidities | Clinical outcome | Diagnostic parameters during COVID-19 | inflammatory markers | COVID-19 Therapy |
|----|-------------------|---------------------|---------------------------|-----------------|---------------------------|---------------|-----------------|-------------------------------------|----------------------|-----------------|
| 22 | N/A               | N/A                 | N/A                       | N/A             | N/A                       | Hypertension: 74 | Admission: 36 | Intubated: 19 | Death: 23 | N/A | N/A | N/A |
|     |                   |                     |                           |                 |                           | Diabetes: 46   | N/A             | N/A                   | N/A                  | (5 million bid) |
|     |                   |                     |                           |                 |                           | Dyslipidemia: 55|                 |                      |                      | Ribavirin (150 mg TID) |
|     |                   |                     |                           |                 |                           | Heart Failure: 15|                 |                      |                      | Abidol (200 mg TID) |
| 23 | Asymptomatic: 2   | Pt1: NA             | 1:438                     | <30: 5          | All patient less than 30 | Asthma :1      | 1:438          | Ferritin = 241; | LDH = 207; | HCQ + Tocilizumab |
|     | Fever: 3          | Pt2: 22 years       | 2:112                     | DTG + DRV/r: 1  |                           | Cardiomyopathy:1| 2:1127         | Lym-phocyte = 1252 |               | Pt2,3,4: HCQ |
|     | Dry cough: 3      | Pt3: 3 years        | 3:219                     | DTG + DRV/c: 1  |                           | HBV:1          | 3:219          | Methylprednisolone |                   | Pt5: No specific treatment |
|     | Shortness of breath: 1 | Pt4: 1 years       | 4:127                     | TDF/FTC + EFV: 1|                           | No Comorbidity:2| 4:127          | LDF = 2306 |                   |               |
|     | Myalgia: 1        | Pt5: 20 years       | 5:352                     | TDF/FTC + DTG: 1|                           |                | 5:352          | LDF = 644 |                   |               |
|     |                   | CD4 in hospital     |                           | TAF/FTC/RPV: 1  |                           |                | Cd4 in admission|                      |                      |                |
| 24 | Cough: 20         | N/A                 | N/A                       | Integrate based: 8|                           | Hypertension:15| CD4 > 200: | Lymphocyte = 1056 | Hydroxychloroquine: 11 |
|     | Fever: 18         |                      |                           | NNRTI: 5        |                           | Diabetes mellitus:7| 16/19 pt | (16%) |                   | Azithromycin: 11 |
|     | Dyspnea: 17       |                      |                           | PI + integrase based: 6|                           | Chronic kidney disease:11| 3/19 |            | Procalcitonin (ng/ml): 0.25 (0.07, 0.39) | Ceftriaxone: 8 |
|     | Myalgia: 11       |                      |                           | Not available: 2|                           | Coronary artery disease: 2| CD4 = 101 pt |            | CD4 = 116 1 pt | Remdesivir: 0 |
|     | Diarrhea: 4       |                      |                           | Protease inhibitor based: 1|                           |                | CD4 = 179 1 pt | CD4 = 557 | Steroids: 5 |               |
| ID | Signs and symptoms | Duration of disease | Last CD4 count (cells/µl) | Last viral load | Last antiretroviral regimen | Comorbidities | Clinical outcome | Diagnostic parameters during COVID-19 | Inflammatory markers | COVID-19 Therapy |
|----|-------------------|---------------------|---------------------------|-----------------|-----------------------------|---------------|-----------------|-------------------------------------|---------------------|----------------|
| 25 | Cough: 18<br>Fever: 17,<br>Dyspnea: 17,<br>Fatigue: 13,<br>Myalgias: 9,<br>Diarrea: 4,<br>Nausea/vomiting: 4 | N/A | Median (IQR): 551 (286–710) | <20: 11<br>20–120: 15<br>120: 1 | Integrate based: 9<br>NNRTI: 5<br>PI + integrate: 5<br>Not available: 4<br>NNRTI + integrate: 3<br>PI based: 1 | Hypertension: 16<br> Diabetes mellitus: 9<br>CKD: 10<br>Dialysis: 6<br>CHF: 3<br>CAD: 1<br>COPD: 0 | ICU Care: 3 pt<br>Death: 2 pt | Undetectable<br>Viral Load: 16/18 pt<br>HIV<br>VL = 269001 pt<br>1 pt<br>HIV<br>VL > 2 million<br>1 pt | N/A | Lymph = 17%<br>Procalcitonin, m/L 0.26 (0.08–0.41) | Hydroxychloroquine: 7<br>Azithromycine: 8<br>Remdesivir: 0<br>Steroids: 1<br>Tocilizumab: 0 |
| 26 | Weakness, anorexia, and diarrhea for 2 weeks | N/A | CD4 = 497 (43%) | N/A | Emtricitabine (200 mg) and tenofovir (25 mg) every 24 h, atazanavir (300 mg) every 24 h, and ritonavir (100 mg) every 24 h | Chronic bronchitis, hypertension | Recovered (Discharged) | N/A | Lymph: 23% = 1334 | Hydroxychloroquine + Azithromycin + Zinc Sulfate |
| 27 | N/A | N/A | N/A | N/A | N/A | N/A | N/A | Hospitalized; 6/8 pt<br>ICU admission: 1/8 pt<br>Death: 0/8 pt | N/A | N/A | N/A |
| 28 | Pt1: cough, fever, dyspnea<br>Pt2: fever, cough, and dyspnea<br>Pt3: fever, cough | Pt1: 1 year<br>Pt2: 1 year<br>Pt3: 5 years<br>Pt4: 4 years | Pt1: CD4 = 34<br>Pt2: CD4 = 12<br>Pt3: CD4 = 540 | N/A | 1: No therapy<br>2: No therapy<br>3: EFV/3TC/TDF<br>4: EFV/3TC/TDF | Pt1,2,3 = no comorbidity<br>Pt4: Hypertension, Diabetes, CHD | 1,2 = severe<br>3,4 = moderate<br>All Discharged | Pt1: Procalcitonin = 0.05<br>Pt2: ESR = NA<br>Pt3: ESR = 3 | N/A | N/A | N/A |
| ID  | Signs and symptoms                  | Duration of disease | Last CD4 count (cells/µl) | Last viral load | Last antiretroviral regimen | Comorbidities                                      | Clinical outcome                                      | Diagnostic parameters during COVID-19 | inflammatory markers | COVID-19Therapy |
|-----|-------------------------------------|---------------------|---------------------------|-----------------|-----------------------------|---------------------------------------------------|------------------------------------------------------|----------------------------------|---------------------|---------------|
| Pt4 | Fever, cough, and dyspnea           |                     | Pt4: CD4 = 743            |                 |                             |                                                   |                                                     | N/A                             | N/A                 |               |
| 29  | Cough (38.8%), fever (33.9%), rhinorrhea (25.7%), myalgias (28.4%), headache (26.8%), chills (21.9%), shortness of breath (15.3%), sore throat (15.3%) loss of taste/smell (19.1%) | Year of HIV diagnosis 1985–2010-133 (68.9%) to 2011–2015-26 (13.5%) to 2016–2020-34 (17.6%) | Last CD4 count result: 121 (62.7%) to CD4 count > 500 cells/mm² 60 (31.1%) to CD4 count of 200–500, 12 (6.2%) to CD4 count <200 | N/A                             | Increased incidence of SARS-CoV-2 infection among HIV compared with people without HIV in San Francisco from the date community transmission was reported | Patients interviewed (n = 183) | Any comorbidity: 78 (42.6%) | Lung disease: 8 (4.4%) | ICU admission: 2 (1.1%) | Hospitalized: 14 (7.6%) | Deceased: 0 |
| 30  | Fever 17 (57%), Cough 21 (70%), Sputum production 1 (3%) |                               | CD4 count, median (IQR): 332 (123–526) |                  |                             | Hypertension: 12 (40%) to DM: 8 (27%) | Hypoxemic: 15/30 pt to Intubation: 4/30 pt | Coronary artery disease 2 (7%) to Stroke 0 (0%) | ICU admission: 4/40 pt to Discharged: 24/30 pt | Death: 2/30 pt | Hypertension: absolute lymphocyte count, median 900 (97%) to CRP: 7.6 (2.8–16.5) | Hydroxychloroquine: (67%) systemic corticosteroids: (13%) | Remdesivir (0) |
|     | Dyspnea 7 patients, Sore throat 20 (67%), Rhinorrhea or nasal congestion 1 (3%) |                           | CD4 count < 200 to CD4:CD8 ratio, median (IQR) |                  |                             | Asthma 3 (10%) | Hypoxemic: 15/30 pt to Intubation: 4/30 pt | Coronary artery disease 2 (7%) to Stroke 0 (0%) | ICU admission: 4/40 pt to Discharged: 24/30 pt | Death: 2/30 pt | Hypertension: absolute lymphocyte count, median 900 (97%) to CRP: 7.6 (2.8–16.5) | Hydroxychloroquine: (67%) systemic corticosteroids: (13%) | Remdesivir (0) |
| ID | Signs and symptoms | Duration of disease | Last CD4 count (cells/µl) | Last viral load | Last antiretroviral regimen | Comorbidities | Clinical outcome | Diagnostic parameters during COVID-19 | inflammatory markers | COVID-19Therapy |
|----|-------------------|---------------------|---------------------------|-----------------|-----------------------------|--------------|----------------|---------------------------------------|---------------------|----------------|
| 31 | N/A               | N/A                 | N/A                       | N/A             | N/A                         |              |                |                                       |                     |                |
|    |                   |                     | Last CD4 count (cells/µm³): |                 | ABC/EFV/3TC                  |              |                |                                       |                     |                |
|    |                   |                     | 491,1500, 500,772, 678, 651 |                 | BIC/TAF/FTC                 |              |                |                                       |                     |                |
|    |                   |                     | viral load (copies/ml)     |                 | EVG-c/TAF/FTC               |              |                |                                       |                     |                |
|    |                   |                     | 10,000 (1 pt)              |                 | EFV/TDF/FTC                 |              |                |                                       |                     |                |
|    |                   |                     | Undetectable (4 pt)        |                 |                            |              |                |                                       |                     |                |
|    |                   |                     | CD4: mean 765              |                 |                            |              |                |                                       |                     |                |
|    |                   |                     | Hypertension: 4 pt         |                 | Coronary Disease: 2 pt     |              |                |                                       |                     |                |
|    |                   |                     | 2 Patients: Expired        |                 | Diabetic: 3 Pt              |              |                |                                       |                     |                |
|    |                   |                     | Lymphocyte: 1010, 1770, 1220, 7-80, 560, 620 |                 | LDH: 338, 520, 214 |              |                |                                       |                     |                |
|    |                   |                     | CRP (mg/L): 274, 243.8, NA |                 |                      |              |                |                                       |                     |                |
|    |                   |                     | Procalcitonin: (ng/ml)     |                 |                      |              |                |                                       |                     |                |
|    |                   |                     | 5, 83, 74, NA, NA, 0, 1.0, 42 |                 |                      |              |                |                                       |                     |                |
|    |                   |                     | Pt1: Hydroxychloroquine   |                 |                      |              |                |                                       |                     |                |
|    |                   |                     | Pt2: Hydroxychloroquine + |                 |                      |              |                |                                       |                     |                |
|    |                   |                     | Steroid                   |                 |                      |              |                |                                       |                     |                |
|    |                   |                     | Pt3, 4: No specific treatment |                 |                      |              |                |                                       |                     |                |
|    |                   |                     | Pt5, Hydroxychloroquine    |                 |                      |              |                |                                       |                     |                |
|    |                   |                     | Pt6: Hydroxychloroquine    |                 |                      |              |                |                                       |                     |                |
| 32 | N/A               | N/A                 | N/A                       | N/A             | N/A                         |              |                |                                       |                     |                |
|    |                   |                     | Stage 1                   |                 | N/A                         |              |                |                                       |                     |                |
|    |                   |                     | HIV: 1774                 |                 | N/A                         |              |                |                                       |                     |                |
|    |                   |                     | Total Case: 2988           |                 | N/A                         |              |                |                                       |                     |                |
|    |                   |                     | Hospitalized: 896         |                 | N/A                         |              |                |                                       |                     |                |
| ID | Signs and symptoms | Duration of disease | Last CD4 count (cells/µl) | Last viral load | Last antiretroviral regimen | Comorbidities | Clinical outcome | Diagnostic parameters during COVID-19 | inflammatory markers | COVID-19Therapy |
|----|-------------------|---------------------|---------------------------|-----------------|----------------------------|----------------|-----------------|--------------------------------------|----------------------|----------------|
|    |                    |                     |                           |                 |                            |                |                 |                                      |                      |                |
|    | Stage 2            | HIV: 843            |                           |                 |                            |                |                 |                                      |                      |                |
|    | Stage 3            | HIV: 270            |                           |                 |                            |                |                 |                                      |                      |                |
|    | Others: 101        | viral suppression: Yes: 2628 |                            |                 |                            |                |                 |                                      |                      |                |
|    | Stage 1:           | CD4 ≥ 500 cells/mm³ or ≥26% of total lymphocytes (age ≥ 6 years), CD4 ≥ 1000 cells/mm³ or ≥30% of total lymphocytes (age 1–5 years); Stage 2: CD4 200–499 cells/mm³ or 14%–25% of total |                            |                 |                            |                |                 |                                      |                      |                |

Death: 207
| ID | Signs and symptoms | Duration of disease | Last CD4 count (cells/µl) | Last viral load | Last antiretroviral regimen | Comorbidities | Clinical outcome | Diagnostic parameters during COVID-19 | inflammatory markers | COVID-19 Therapy |
|----|-------------------|---------------------|---------------------------|-----------------|-----------------------------|---------------|-----------------|---------------------------------------|-----------------------|----------------|
| 33 | N/A               | Pt1: 18 years       | CD4: Pt1: 180 Pt2: 50 Pt3: 3,890 | N/A             | Pt1: Raltegravir 400 mg BD Lamivudine 50 mg OD Abacavir 600 mg OD | Pt1: Hypertension, ESRD, Renal transplant, Diabetes Pt2: G6PD Pt3: Hypertension, Diabetes, Obesity | Pt1: Death Pt2,3: CPAP (Discharged later) | N/A | Lymphocyte: Pt1: 230 Pt2: 1130 Pt3: 1100 CRP, mg/dL Pt1: 260 Pt2: 51 Pt3: 78 | Prednisolone Specific Treatment |
|    |                   | Pt2: 7 years        |                            |                 |                             |               |                 | N/A |                          |                         |                  |
|    |                   | Pt3: 8 years        |                            |                 |                             |               |                 |                          | N/A                  |                  |
| 34 | Fever: 36 (71%)   | 19.5 years (9.3–28.6) | Recent CD4: 565 (296–782) | N/A             | Protease inhibitors 11 (22%) NNRTI 8 (16%) INSTI 41 (80%) Tenofovir (TAF or TDF) 37 (73%) | Any 32 (63%) Hypertension 18 (35%) Cardiovascular disease 14 (27%) Diabetes 7 (14%) Chronic kidney disease 6 (12%) Chronic liver disease 24 (47%) | Total Case: 51 Admit: 28 (55%) => 22 noncritical disease 6 critical disease 2 deaths 21 recovered 5 still admitted | N/A | Lymphocyte: 1,200 (800–1,800) Serum ferritin, ng/mL (n = 7) 972 (366–2791) Procalcitonin, ng/mL: 0.08 (0.04–0.13) | No specific antiviral therapy hydroxychloroquine azithromycin ritonavir boosted |
| ID | Signs and symptoms | Duration of disease | Last CD4 count (cells/μl) | Last viral load | Last antiretroviral regimen | Comorbidities | Clinical outcome | Diagnostic parameters during COVID-19 | inflammatory markers | COVID-19 Therapy |
|----|-------------------|---------------------|-------------------------|-----------------|-----------------------------|---------------|-----------------|--------------------------------------|---------------------|-----------------|
| 35 | Fever, dry cough, chest pain | N/A | CD4 cell count = 34/ul, CD8 cell count = 737/ul | N/A | N/A | N/A | 1 Pt: Mechanical Ventilation + ICU admission (Still admitted) | | | Lymphocyte: 1550 |
|    |                   |                     |                         |                 |                             |               |                 | CRP: 96.5 LDH: 423                     |                     | Methyprednisolone then Tocilizumab |
| 36 | Pt1: Myalgia, fever, dyspnea, productive cough | Pt1: 6 years diagnosed | N/A | N/A | N/A | Pt1: Tenofovir disoproxil fumarate, lamivudine and efavirenz | Pt1: stage IV diffuse large B-cell lymphoma, pulmonary tuberculosis, Diabetes | Pt1: Moderately ill and discharged | Pt1: Lymph = 900 Procalcitonin (PCT) = 0.19 ng/ml; C-reactive protein (CRP) = 191.21 mg/L | | Oseltamivir + Umifenovir |
|    | Pt2: New diagnosed |                     |                         |                 |                             |               |                 |                                      |                     | Pt2: Ribavirin + Umifenovir |
|    | Fever, nonproductive cough, |                     |                         |                 |                             |               |                 |                                      |                     |                     |
| ID | Signs and symptoms | Duration of disease | Last CD4 count (cells/µl) | Last viral load | Last antiretroviral regimen | Comorbidities | Clinical outcome | Diagnostic parameters during COVID-19 | inflammatory markers | COVID-19 Therapy |
|----|-------------------|-------------------|------------------------|----------------|----------------------------|----------------|----------------|-------------------------------|-------------------|----------------|
| 37 | N/A               | N/A               | CD4:                   | N/A            | Pt1: AZT/3TC/NVP           | N/A            | N/A            | N/A                           | Lymphocyte count:  | N/A            |
|    |                   |                   | Pt1 = 420             |                | Pt2: TDF/3TC/EFV           |                |                | Pt1: Lymph= 670               | Procalcitonin=     | Pt2: Arbidol then Tocilizumab |
|    |                   |                   | Pt2 = 550             |                | Pt3: STRIBILD              |                |                | Pt2: Procalcitonin= 0.05       |                  | Pt2: Arbidol the Methylprednisolone then Tocilizumab |
|    |                   |                   | Pt3 = 21              |                |                           |                |                | Pt3: Lymphocyte= 1550          |                   | Pt3: Arbidol then Tocilizumab |
| 38 | Pt1: Fever, fatigue, poor appetite, shortness of breath, sore throat | Pt1,2= New HIV | Pt1: CD4 = 13 | N/A | Pt1 –                   | N/A            | N/A            | Pt1: Lymphocyte= 1080          |                  | Pt1: Arbidol then Tocilizumab |
|    |                   |                   | Pt2: CD4 = 23         |                | Pt2 –                     |                |                | Pt2: Procalcitonin: 0.03       |                  | Pt2: Arbidol the Methylprednisolone then Tocilizumab |
|    |                   |                   |                       |                |                           |                |                | Pt2: CRP = 96.51               |                  | Pt3: Arbidol then Tocilizumab |
Forty percent of the studies were from the USA, 20% from China, 11.4% from Italy, 11.4% from Spain and the remainder were from Germany, France, UK, South Korea, Poland, and South Africa. All the articles were published between January and December 2020. The study population in the explored articles ranged from one patient (in case reports) to 3,460,932 patients in a large cohort study from South Africa (Table 2).

Among the total studied population of 3,993,400 COVID-19 patients, 89,343 patients had COVID19-HIV coinfection, among which 72% (ranged from 42.3% to 100%) were male, 0.01% (11 patients) were transgender. Patients' gender was not available in two studies. Patients' age was above 20 years in all studies. As the review revealed, nine studies did not mention the ART regimen for HIV + patients. At the time of the COVID-19 diagnosis, the most common symptoms were fever, cough, myalgia, and headache. Additionally, most of the patients had various comorbidities such as hypertension, diabetes mellitus, asthma, renal insufficiency, cardiovascular disease, etc.

Laboratory values including CRP, ferritin, and Interleukins levels were available in about two-third of the studies. But in almost all the studies with inflammatory tests results, the values were elevated. In most of the studies, all HIV patients completely recovered from the COVID-19 infection. In 8 studies, mortality was reported ranging from 1% to 36%. Although CD4 count was not recorded in all the studies, the minimum level was reported as 12 cells/µl.

4 | DISCUSSION

We found that HIV patients at advanced stages (3 or 4) of the disease with low CD4 count and weak immune systems show less severe COVID-19 symptoms. However, some studies showed controversial results which contradict our primary hypothesis. The main reason for these contradictory results was the scarcity of existent literature and inconsistency of evidence that limited our ability to address and reasonably argue our main hypothesis. This may also be due to simultaneous symptoms and underlying comorbidities that come along at advanced stages of HIV infections and could perplex and obscure the typical presentation of COVID-19 in such patients. Despite these contradictory results, the majority of studies included in this review indicate mild or no typical symptoms of COVID-19 in HIV patients, particularly in those at the advanced stages of HIV disease. This review also found an unexpected high recovery rate in these patients after COVID-19 infection, which contradicts the common knowledge of higher morbidity and mortality rate in immunocompromised patients.

SARS-CoV-2 is a new strain of coronavirus, which is the causal agent of COVID-19. The usual symptoms of COVID-19 are fever, cough, headache, shortness of breath, tiredness, loss of taste or smell, and gastrointestinal symptoms such as diarrhea, anorexia, nausea, and abdominal pain,1 of which, many are due to the cytokine storm caused by the host's immune system. To control these symptoms, corticosteroids have been used now and then by clinicians around the world which indicates the substantial role of immune system function interfered with SARS-CoV-2. Application of Canakinumab, a humanized monoclonal antibody against IL-1β in a sub-group of hospitalized patients with COVID-19 and subsequent swift reduction in the systemic inflammatory response and oxygenation improvement by Claudio Ucciferri et al. also manifests the fundamental role of the immune system and inflammatory cytokines in the SARS-CoV-2 pathophysiology.55,66 The human immunodeficiency virus targets the body's natural immune system and causes immune deficiency. This immune deficiency can lower the severity of the immune system reactions such as cytokine storms and subsequently the accompanying symptoms. This could explain the milder symptoms, lower morbidity, and less mortality among HIV-positive patients infected by COVID-19 as the primary fatal condition in COVID patients is caused by the cytokine storm which subsequently leads to multiorgan dysfunction and death. The hypothesis was supported by some of the included studies in the present review, while, some contradictory results were also observed.

In the present review, a CD4 count less than 500 was assumed as a cutoff point. Thus, the patients with a mean CD4 count less than 500 were considered immunodeficient and assumed to be at advanced stage patients. In the study conducted by Calza et al. all the nine HIV-positive patients with CD4 count less than 258 fully recovered, which supports the hypothesis of our study.26 Additionally, in Kumar et al.’s and Patel RH.'s study, the patients had a CD4 count less than 500 and again completely recovered.41,47 Similar findings were reported by Mondi A et al.44 In contrast, in Karmen-Tuohy et al.’ study contradictory results were reported. Although the median CD4 count of patients was lower than 500 and the patients were immunodeficient, the mortality rate was higher (28%).39 Likewise, in the study by Blanco et al., all the patients with CD4 count > 500 were cured, but one of the two patients with CD4 count < 500 remained in the hospital due to the severity of illness that may have been due to comorbidities as is reported by authors.23 However, the findings of the Ruan L et al’ study were completely against our hypothesis. In this
study, all the patients with CD4 count > 500 experienced moderate-severity clinical outcomes; while, all the patients with CD4 count < 500 had severe clinical outcomes. 

4.1 Limitation

Despite the limited available evidence, the findings of the present review authenticate the primary hypothesis arguing less severe clinical outcomes in HIV patients at the advanced stages. Although this could be mainly due to the inability of the immune system in HIV patients to provoke the cytokine storm, which is believed to be the main responsible event for severe clinical outcomes in COVID patients, the contradictory results inform future studies to explore further the possible underlying causes of such an observation.

5 CONCLUSION

In conclusion, the results of the present study suggest that HIV patients at advanced stages (3 or 4) of the disease, when CD4 counts are low and their immune system is compromised, manifest less severe symptoms and less mortality following COVID-19. This has been attributed to the inability of HIV-positive individuals’ immune systems in provoking the cytokine storm that caused the severe clinical outcome in COVID patients. By a similar mechanism, it seems that corticosteroids mitigate the severity of symptoms in COVID patients with a healthy immune system.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTIONS

Conception and design of the study: Esmaeil Mehraeen, SeyedAhmad SeyedAlinaghi; acquisition of data: Amirali Karimi, Seyed Peyman Mirghaderi, Amirata Fakhfouri; analysis and interpretation of data: Hengameh Mojdeganlou, Alireza Barzegary; drafting the article: Esmaeil Mehraeen, Mehrzad MohsseniPour, Solmaz Saeidi; revising it critically for important intellectual content: SeyedAhmad SeyedAlinaghi, Armin Razi; final approval of the version to be submitted: Esmaeil Mehraeen, Amir Masoud Afsahi, Omid Dadras, Marcarious M. Tantuoyir.

DATA AVAILABILITY STATEMENT

The authors stated that all information provided in this article could be shared.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

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