Research Articles

Incidence, treatments, and outcomes of SARS-CoV-2 and HIV co-infections

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Background

We investigated the global threat of co-infection of severe acute respiratory coronavirus 2 (SARS-CoV-2) to patients living with another prevalent viral infection HIV. We have analyzed symptom status, treatment, and outcome of co-infected individuals.

Methods

An extensive literature search of PubMed, preprint databases (bioRxiv, medRxiv, and preprints), and ClinicalTrials.gov was conducted from 1 December 2019 to 28 February 2021. Ninety-two potential studies involving 39,461 HIV and SARS-CoV-2 co-infected patients were analyzed with details of severity, their treatment, and the outcomes.

Results

A total of 39,461 cases of people living with HIV have reported co-infection with SARS-CoV-2 worldwide. Of these coinfected individuals, the symptom status for 3,213 patients (~8%) was available, out of which 44% were severely/critically ill. The collated data show the fatality rate for human immunodeficiency virus (HIV) and SARS-CoV-2 coinfection to be 2.4% and a large proportion was found to have several comorbidities. The most commonly administered antiretroviral therapy to the people living with HIV was tenofovir/emtricitabine; these drugs are already in phase 3 clinical trials for coronavirus disease 2019 (COVID-19). We observed that majority of co-infected patients who survived were those on tenofovir/emtricitabine combination drug therapy for HIV.

Conclusions

The current study demonstrates that patients with HIV may have worse outcomes due to COVID-19 than the general population. However, the HIV/SARS-CoV-2 coinfection needs to be analyzed across multiple countries with a high burden of HIV, and with a much larger cohort to gain a better understanding of the impact of SARS-CoV-2 on people living with HIV.

Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory coronavirus 2 (SARS-CoV-2) remains a serious global public health concern. COVID-19 presentations vary from asymptomatic to severe breathlessness, which can sometimes lead to death. The overall burden of COVID-19 in society seems to have influence from other communicable diseases like human immunodeficiency virus (HIV), malaria, tuberculosis, and certain fungal and bacterial infections.[1–6] To date, USA, India, and Brazil are the countries with the highest cases of COVID-19.[7] Unfortunately, these countries and many others especially in sub-Saharan Africa have a significant burden of HIV [8] that will inevitably result in what Shiau *et al* described as HIV and SARS-CoV-2 syndemic.[9] In the year 2020, ~38 million people were living with HIV and 690,000 people died due to AIDS-related illnesses globally.[8] COVID-19 cases have surpassed HIV in many countries leading to concerns of an emerging syndemic. The burden of HIV is highest in South Africa followed by India and Nigeria. It is also high in the USA (Figure 1).[8] India's COVID-19 burden has been high over two waves and it has the third-highest global HIV burden with over 2 million people infected.[8] To date, the largest population cohort of patients with confirmed concomitant infection of HIV and SARS-CoV-2 are reported from the United Kingdom and South Africa.[10]

Few anti-HIV agents may be promising drug candidates against COVID-19 and several of the multiclass combinations are already in advanced clinical trials against SARS-CoV-2.[11–13] The common classes of antiretroviral therapies (ARTs) are: nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs), integrase strand transfer inhibitors (INSTIs), non-nucleoside reverse transcriptase inhibitors

(NNRTIs), protease inhibitors (PIs), and cytochrome P4503A inhibitors (CYP3A).[14] The drugs belonging to these classes are often used in different combinations depending on multiple factors involved in the HIV infection like the individual's viral load, their T-cell count, HIV strain, the severity of the case, and other chronic illnesses.[14,15] The NRTI drugs tenofovir and emtricitabine are currently in phase 3 clinical trials and may target the RNA-dependent RNA polymerase (RdRp) enzyme of SARS-CoV-2.[11] RdRp may be considered as a significant druggable enzyme to be targeted in coronaviruses. RdRp is error-prone during replication that leads to the utilization of chemically modified nucleoside/nucleotide analogues as substrates instead of natural substrates.[16] The chemically modified substrates cannot be processed further and hence are responsible for stalling the replication process.[16] Another class of ARTs, the protease inhibitors like ritonavir, lopinavir, and darunavir are also in clinical trials for COVID-19.[12,13] The combination of lopinavir and ritonavir was also in clinical trials but seems to be ineffective against SARS-CoV-2 and the use of lopinavir/ritonavir shows hardly any effect on mortality rates for hospitalized COVID-19 patients.[17,18] Darunavir (a protease inhibitor) currently in phase 3 clinical trial in combination with cobicistat (a pharmacokinetic enhancer) increase the activity of darunavir by inhibiting CYP3A4.[13] However, a few studies have reported that darunavir does not show any activity against SARS-CoV-2 *in vitro* but it is too soon to comment on the role of darunavir in patients.[19] The other NRTIs (abacavir, lamivudine) and the PI (atazanavir) may target the RdRp and 3C-like proteinases in SARS-CoV-2 respectively but these drugs currently are not in clinical trials to our knowledge. Other classes of compounds like NNRTIs (efavirenz), INSTIs (bictegravir, elvitegravir, and dolutegravir) are not involved in any clinical phase trials and their effect on SARS-CoV-2 is not yet established to our knowledge.

Given the significance of the high number of people living with HIV globally, here we discuss available data on co-infection of HIV and SARS-CoV-2, their incidence, fatality rates, and the possible effectiveness of antiretroviral therapy (ART) against COVID-19.

METHODS

INFORMATION SOURCES AND LITERATURE SEARCH

A detailed literature search was performed, and the reports were taken into consideration from 1st December 2019 to 28th February 2021. A comprehensive literature search from PubMed, preprint databases (bioRxiv, medRxiv, and Preprints), reference lists, and ClinicalTrials.gov was done to identify articles for inclusion. The keywords/subject headings used for the relevant literature were "HIV (Human immunodeficiency virus) AND COVID-19 (Coronavirus)", OR HIV and SARS-CoV-2. Descriptive analysis was conducted as per the 'rapid review' methodology.[20] The rapid review simplify the components of the systematic review process to produce information in a short period of time.[20]

INCLUSION AND EXCLUSION CRITERIA

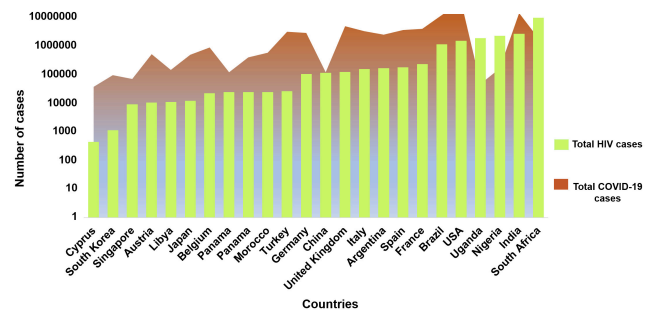Case studies, case series, cross-sectional studies, cohorts,

Figure 1. The burden of HIV and COVID-19 cases in various countries.

The data for HIV has been taken for the most recent available year from UNAIDS (2018-2020). For COVID-19, WHO data have been considered as of 03rd February 2021. Y-axis denotes log10 of the number of cases for HIV and cumulative COVID-19 cases while X-axis denotes the corresponding countries.

editorials, and short letters that reported single or aggregate clinical data on the coinfection of HIV and SARS-CoV-2 were considered. Articles (reviews, newspaper articles) not reporting original clinical data on the HIV and SARS-CoV-2 coinfections were not included in the current study. Articles in the English language were considered while those in other languages were excluded.

DATA EXTRACTION

The data was extracted, reviewed, and validated by RC. Data were extracted based on publication date, study type, country, gender, and sample size. The severity index for COVID-19 for patients was classified as asymptomatic (if specified in the articles), mild/moderate (either specified in the articles or if the patient did not require admission to ICU/supplemental oxygen therapy), and severe/critical (either specified in the articles or if the patients were admitted to ICU/required supplemental oxygen/ventilation/died). The case fatality rate percentage was calculated by using the formula = total number of deaths among HIV and SARS-CoV-2 cases/ total number of HIV and SARS-CoV-2 cases from respective country *100.

PATIENT AND PUBLIC INVOLVEMENT

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

RESULTS

The selection of studies is shown as a flowchart in Figure 2. Our search strategy identified 1341 potential publications on HIV/SARS-CoV-2 co-infections. After screening the abstracts and removing irrelevant articles, we assessed 92 publications that met our inclusion criteria. The details of case studies, case series, cross-sectional studies, cohorts, editorials, and short letters that reported single or aggregated clinical data are shown in Table 1. From our review, the first case report of HIV and SARS-CoV-2 co-infection emerged from Wuhan (China) in January 2020 of a male in his 60s suffering from COVID-19 - related pneumonia who

was eventually discharged in a stable condition.[21] Another case from Wuhan with a preexisting dysfunctional immune system due to the co-infection of HIV-1 and HCV (Hepatitis C Virus) was reported to have COVID-19.[22] Interestingly, unlike the previous case, this patient repeatedly tested negative for SARS-CoV-2 RNA, and later tested positive for IgM antibody against SARS-CoV-2.[22] Two possible explanations for the undetectable SARS-CoV-2 RNA leading to negative RT-PCR test results were postulated by the authors; first - the patient was already on antiretroviral treatment (ART) (lamivudine, tenofovir, and efavirenz) which was considered to be effective against SARS-CoV-2; and second – the high levels of type I interferon (IFN-I) in HIV-1 may have cleared the SARS-CoV-2 infection.[22] Few studies have also pointed out that SARS-COV-2 in its early infection phase seems to be more sensitive towards IFNs.[23] After China, Singapore was the second country to report HIV and SARS-CoV-2 case in which the patient had mild symptoms of COVID-19 and was already on ART for HIV.[24]

GLOBAL DISTRIBUTION OF HIV/ SARS-COV-2 CO-INFECTIONS AND CASE FATALITY RATES

Currently, numerous countries are reporting HIV/SARS-CoV-2 co-infections across the globe (Table 1). A total of 39,461 cases of co-infections of HIV and SARS-CoV-2 have been reported worldwide out of which 24,452 (~62.0%) were males and 14,987 (~38%) were females. Out of the 39,461 cases, patient severity data on 3,213 (8.14%) were available amongst whom 43.8% cases (n=1409) were severely or critically ill (Figure 2). The severity of the coinfected individuals for their respective countries has been depicted in figure 3a. Two population-based cohort studies from the UK and South Africa reported the largest number of HIV/SARS-CoV-2 coinfections of 27,480 and 3,978 patients respectively (Figure 3, Plate A).[5,11] Single case studies have been reported from Austria, Argentina, Cyprus, South Korea, Morocco, Peru and Uganda where the HIV patients had mild and uncomplicated case of COVID-19 with 100% survival rate (Table 1). An exception to this pattern was observed in Libya where a woman in her 80s on zidovudine died due to acute kidney injury and multi-organ failure, possibly due to COVID-19.[25] Interestingly, all the patients from Argentina, Austria, Cyrus, Japan, Singapore (2 cases) and Uganda were on tenofovir, lamivudine, emtricitabine, and efavirenz therapy (Table 1). From the USA, 28 studies have reported a total of 6712 patients with co-infections of which ~13% were severely afflicted (Table 1; Figure 3, Plate A). Italy and Spain have 321 and 408 confirmed cases of co-infections with 23% and ~45% of patients having severe/critical symptoms respectively (Figure 3, Plate A). Compared to the three leading countries for HIV and SARS-CoV-2 co-infections, China has reported 138 patients for HIV/SARS-CoV-2 co-infections of which ~33% were severely/critically ill (Figure 1; Figure 3, Plate A). Other countries like France, Germany, India, and Turkey have fewer than 45 co-infection cases with the majority of them either mildly symptomatic or asymptomatic for COVID-19 (Table 1, Figure 3, Plate A).

Of the 39,461 reported cases of HIV/SARS-CoV-2 concomitant infections, 952 patients (~2.41%) died. From the total of severe/critical-coinfected cases (n=1409) 952 patients
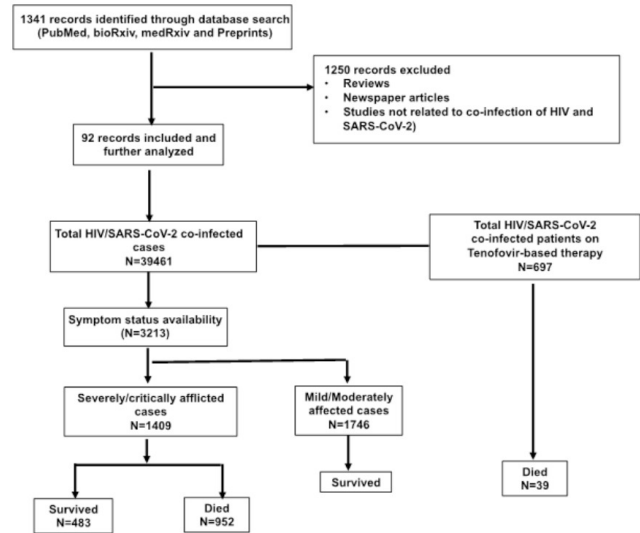

Figure 2. Flow diagram illustrating the selection of study and co-infected cases of HIV/SARS-CoV-2.

The flowchart depicts the selection of the studies from 1341 records from various online search tools and the selection of the number of patients to be included in the current study.
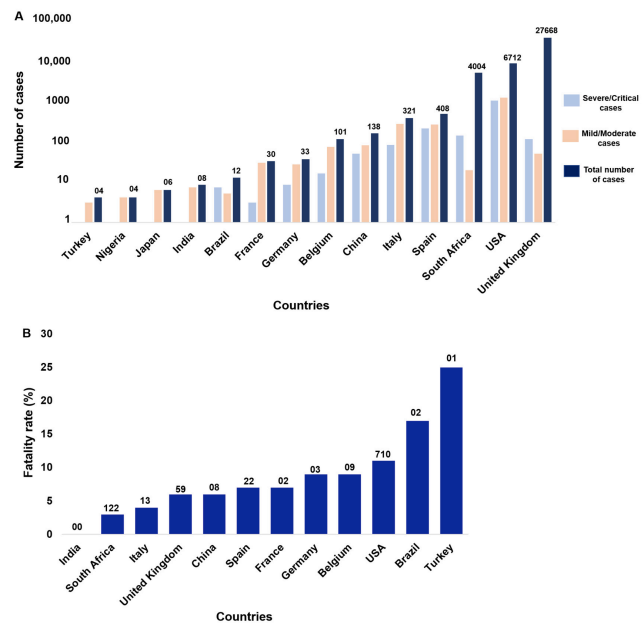

Figure 3. Co-infection cases and deaths of HIV/ SARS-CoV2.

Plate A. Number of co-infected cases of HIV and SARS-CoV2. Argentina, Austria, Cyprus, Japan, Libya, Singapore, and Uganda had single cases for HIV and COVID-19 coinfections so not shown in the graph. The number of mild (either mentioned or if the patient did not require admission to ICU or supplemental oxygen therapy) and severe/critical cases (either mentioned or if the patients were admitted to ICU, required supplemental oxygen/ventilation, or died) are depicted to show the symptomatic status of the patients. The numbers at the top of the histogram show the total number of cases reported for each country.
Plate B. The fatality rate of co-infections of HIV and SARS-CoV-2. The fatality rate was calculated by the number of deaths/total number of cases*100. The numbers on the top of histograms show the total number of deaths/countries.

tients (67.6%) died. It is to be noted that we considered the deceased patients in the severe/critical category for reports that did not specify the severity status of the coin-

Table 1. HIV/SARS-CoV-2 co-infection cases, treatment and outcomes.

Country	No. of reports/cases	Symptom status	Fatality (n)
Argentina	1 report/1 case	Mild	0
Austria	1 report/1 case	Mild	0
Korea	1 report/1 case	Mild	0
Morocco	1 report/1 case	Mild	0
Uganda	1 report/1 case	Mild	0
Peru	1 report/1 case	Severe	1
Libya	1 report/1 case	Severe	1
Panama	1 report/2 cases	50% Mild; 50% Severe	0
Singapore	2 reports/2 cases	50% Mild; 50% Severe	0
Nigeria	1 report/4 cases	100% Mild	0
Turkey	1 report/4 cases	25% Critical; 75% Mild	1
Japan	2 reports/6 cases	100% Mild	0
India	2 reports/8 cases	87.5% Mild; 12.5% Asymptomatic	0
Brazil	4 reports/12 cases	42% Mild; 58.3% Severe	2
France	1 report/30 cases	90% Mild; 10% Severe	2
Germany	1 report/33 cases	76% Mild; 24% Severe/Critical	3
Belgium	1 report/101 cases	21% Asymptomatic; 15% Severe	9
China	14 reports/138 cases	52.2% Severe	8
Italy	9 reports/321 cases	23%Severe/Critical; 73% Mild; 4% Asymptomatic	13
Spain	5 reports/408 cases	44.9% Severe/Critical; 55% Mild	22
South Africa	4 reports/4004 cases	3.04% Severe/Critical	122
United States of America	28 reports/6712 cases	12.6% Severe/Critical	710
United Kingdom	8 reports/27688 cases	0.4% Severe	59

The table illustrates the HIV/SARS-CoV-2 coinfection cases from respective countries, their symptom status, and their outcomes.
Note* People living with HIV received various combinations of ART in multiple studies. The details of the cases for each country have been provided in the Online Supplementary Document, Table S1.

fected patients. Therefore, the exact proportion of severely/critically ill patients who succumbed owing to HIV/SARS-CoV-2 coinfection cannot be validated. We analyzed deaths amongst the co-infected patients, and the highest have been reported from the USA (n=710) giving the fatality rate of ~11%, mostly attributable to several comorbidities (Figure 3, Plate B).[26-45] The second highest number of deaths were reported in South Africa (n=122) but with an overall case fatality rate of only ~3% (Figure 3 Plate B).[5,42,43] A large portion of deceased patients from South Africa also had other co-morbidities like hypertension, diabetes, chronic kidney disease, chronic respiratory disease, and tuberculosis.[5,42,43] Another recent study showed that a large proportion of COVID-19 deceased individuals from nine provinces of South Africa were people living with HIV (13.9% of 3088 total deaths; data not included in the graphs).[46] Another report from New York with 2988 and 2410 cases of HIV/SARS-CoV-2 coinfection showed 7% and ~13% of fatality rate respectively which was much higher than for people with HIV but negative for SARS-CoV-2.[43,46] Similar results were reported from a UK population-based cohort wherein HIV/SARS-CoV-2 coinfected individuals were at a higher risk of fatality than those without HIV.[47]

Interestingly, the study of HIV/SARS-CoV-2 co-infection from India (Pune and Tamil Nadu) showed that all seven patients had mild symptoms of COVID-19 with no reported deaths.[48,49] In countries where single case reports have been reported, no deaths were recorded as all patients had mild symptoms of COVID-19, except in Libya where the reported positive patient died due to multi-organ failure (Figure 2).[25]

POTENTIAL USE OF ANTI-HIV COMPOUNDS AGAINST SARS-COV-2

One of the common multiclass antiretroviral therapy administered in combination (NRTIs and NNRTIs) for HIV patients is tenofovir, lamivudine, and efavirenz. From the analysis presented here, it is clear that a large number of patients with co-infections were on NRTIs (especially tenofovir) (Table 1). Our analysis indicates that a total of 697 people living with HIV were already on tenofovir combination therapies, out of which 39 patients died due to COVID-19 (Online Supplementary Document, Table S2). This suggests that people living with HIV have a survival

rate of 94.4% on the tenofovir-based therapy. Another study has suggested the possibly reassuring role of tenofovir-based therapy for pregnant females in the context of COVID-19 pandemic,[50] but more research is needed in this direction.

DISCUSSION

Our work here consolidates data on treatment and outcomes of individuals co-infected with HIV and SARS-CoV-2. As per our knowledge, this is the first study analyzing a large number of HIV/SARS-CoV-2 coinfected patients with a focus on their treatment regime and related outcomes. We analyzed available data from 92 publications with total of 39,461 HIV/SARS-CoV-2 coinfection cases reported worldwide. Multiple reports across the world show that the HIV patients co-infected with COVID-19 have mild symptoms (~64%) and the majority of them survive.[51] The proportion of deceased HIV/SARS-COV-2 coinfected individuals from our study appears to be around 6% of total co-infected cases. Further, almost all the deceased patients from various studies had several comorbidities already known to aggravate COVID-19 severity.[5,24,26,47,48] The most common morbidity in coinfected individuals was hypertension (n=7258; 18.4%) and diabetes (n=2946; 7.5%) out of 39,461 cases. For chronic respiratory diseases in HIV/SARS-CoV-2 coinfected individuals, we found that only 1901 (4.8%) suffered from it out of 39,461 patients.

Recent studies from the USA, UK, and South Africa have reported a large cohort of patients living with HIV/SARS-CoV-2 coinfections, with higher fatality rates when compared to HIV negative individuals.[5,43,47,52] South Africa also has the most HIV cases (7.5 million) as reported in 2018 so the coinfection of HIV and SARS-CoV-2 is expected.(Table 1) [53] A South African study suggested that people with HIV on tenofovir had a lower risk of COVID-19 related deaths as compared to other antiretrovirals.[5] However, reports from USA and UK have not shown any correlation with tenofovir as the data for ART is not available.[43,47,52] Several other studies have also shown lower risks of patients developing severe symptoms and having higher survival rate on tenofovir against SARS-CoV-2 (Figure 1). On the contrary, a report from New York observed a high mortality rate of 78% in HIV/SARS-CoV-2 co-infection, although the sample size was very low (9 patients).[27] Most of the patients with HIV are currently on ART and several studies claim that tenofovir could improve the symptoms of COVID-19.[54,55]

A recent pilot, randomized trial has shown promising results of the tenofovir-based therapy in decreasing the SARS-CoV-2 viral burden in recently infected COVID-19 outpatients.[56] This tenofovir-based combination is reassuring including during pregnancy in COVID-19 patients.[50] Tenofovir-based therapies are already in phase 3 clinical trials for prevention (NCT04334928) and treatment (NCT04712357; NCT04359095; NCT04890626) and possibly might provide an alternative to the current anti-COVID therapies for better survival rates.[11,57] However, it is reasonable to suggest, as by Mirzaei et al, that continued use of ART in people living with HIV does not lead to lower morbidity and mortality from COVID-19 and several studies/

clinical trials point out that NRTIs, NNRTIs, and PI classes of drugs have not shown any significant difference in morbidity and mortality patients with and without COVID-19.[58,59] The impact of the tenofovir-based therapies on HIV and SARS CoV-2 requires a more systematic enquiry and longitudinal follow up either in the form of prospective cohort studies or well planned and executed randomized controlled trials. The evidence is exploratory and provides insight into the possible benefit that can be hypothesized and considered for better-designed studies. Also, the survival benefit of the regimen will need to be presented and adjusted for several factors taking into account disease severity, concomitant comorbidities, demographic factors, compliance to treatment regimens, and access to care, which also varies by setting.

COVID-19 related deaths are associated with immuno-compromised status and are also dependent on several factors like age, comorbidities, healthcare facilities, etc. In the current study, the proportion of patients with HIV appear to have a high incidence of multi-morbidities, severe disease, and a higher proportion of death. We have discussed that a large number of the deceased coinfected HIV/SARS-CoV-2 patients had multiple comorbidities apart from HIV. The large number of people with HIV succumbed to SARS-CoV-2 infections having multiple comorbidities displays that COVID-19 related deaths in people with HIV might also be associated with the current immune status, age, comorbidities, healthcare management, location/country (with better healthcare facilities), and severity of the disease. However, the available data from other countries (India, Nigeria, Uganda, and Brazil) with a high burden of HIV do not indicate that the disease course of COVID-19 differs in people living with HIV than those without HIV.[60]

The current study has a few limitations: 1) some of the countries with a high burden of HIV (India, Nigeria, Uganda, and Brazil) reported only a few studies of co-infections with SARS-CoV-2; 2) the sample size varies across the globe; 3) the healthcare spending and systems of various countries can affect the outcomes of patients; 4) the heterogeneity among the global population is another factor that creates a bias for directly comparing such diverse countries; 5) the variables from the case reports/case series did not provide multiple factors (like RT-PCR validation of the COVID-19 reports, their cytokine profiles, alterations in the CD4+ T cells levels, etc.) and cannot be considered fully reliable. It was not possible to analyze all the variables that were of interest since not all studies mentioned the outcome, severity, and treatment regimen. The evidence generated from these case reports/series or other descriptive studies is weak and aids in generating hypothesis that should be tested by well-designed studies. This can be done through cohort studies or randomized controlled trials with the inclusion of comparison groups. Further, the role of ART on the outcome of HIV/SARS-CoV-2 coinfection has also not been fully investigated. The authors have not factored in these possible biases.

We previously proposed web-based dashboards like PRA-CRITI that can be utilized for predicting effective reproduction number (Rt) of SARS-CoV-2.[61] Similar tools can be used to predict the SARS-CoV-2 transmission in the vulnerable group like people living with HIV to analyze the un-

derlying effects of coinfection in the infected individuals. It is to be noted that HIV/SARS-CoV-2 coinfected patients should continuously monitor their oxygen levels with pulse oximetry for respiratory disease management. The early detection of low oxygen levels can also forewarn patients for 'silent hypoxia' as well and give an indication of deteriorating conditions of HIV/SARS-CoV-2 coinfected individuals.[62] It has been suggested that the levels of vitamins like vitamin D correlate with the outcome of COVID-19 patients [63] while HIV-infected individuals also are vulnerable to low levels of vitamin D.[64] This further highlights the vulnerability of people with HIV that can be coinfected with SARS-CoV-2.

CONCLUSIONS

As per our analysis, it is evident that HIV/SARS-CoV-2 coinfected patients have a higher risk of severity and mortality when compared to those without HIV and other comorbidities as is evident by the large cohort studies. The spread of both viruses coexisting in the vulnerable populace might lead to adverse public health outcomes. Further, people with HIV on a tenofovir regimen if coinfected with SARS-CoV-2 might have a better survival rate than those on other ART regimens. It is a possibility that needs to be tested further that people with HIV already on the antiretroviral regimen (especially tenofovir-based therapy) may display some level of co-protection against SARS-CoV-2 infections and the individuals might develop mild symptoms. In sum, HIV/SARS-CoV-2 co-infection cohorts need to be analyzed across many countries with high HIV burdens with much larger data sets.

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REFERENCES

1. Gutman JR, Lucchi NW, Cantey PT, et al. Malaria and Parasitic Neglected Tropical Diseases: Potential Syndemics with COVID-19? *The American journal of tropical medicine and hygiene*. Published online 2020. doi:10.4269/ajtmh.20-0516

2. Arastehfar A, Carvalho A, van de Veerdonk FL, et al. COVID-19 associated pulmonary aspergillosis (CAPA)—from immunology to treatment. *Journal of Fungi*. Published online 2020. doi:10.3390/jof6020091

3. Rawson TM, Moore LSP, Zhu N, et al. Bacterial and Fungal Coinfection in Individuals With Coronavirus: A Rapid Review To Support COVID-19 Antimicrobial Prescribing. *Clinical Infectious Diseases*. Published online 2020. doi:10.1093/cid/ciaa530

4. Gayam V, Konala VM, Naramala S, et al. Presenting characteristics, comorbidities, and outcomes of patients coinfected with COVID-19 and Mycoplasma pneumoniae in the USA. *Journal of Medical Virology*. Published online 2020. doi:10.1002/jmv.26026

5. Davies MA. HIV and risk of COVID-19 death: a population cohort study from the Western Cape Province, South Africa. *medRxiv*. Published online 2020. doi:10.1101/2020.07.02.20145185

6. Rahi M, Das P, Sharma A. COVID-19 mitigation steps provide a blueprint for malaria control and elimination. *American Journal of Tropical Medicine and Hygiene*. Published online 2020. doi:10.4269/ajtmh.20-0394

7. Kristen Hess SJ, Xiaohong Hu, Jianmin Li, Baohua Wu, Chenchen Yu, Hong Zhu, Chan Jin, Mi Chen, John Gerstle M, Morgan, Michael Friend, Anna Satcher Johnson, Azfar Siddiqi AH. *Diagnoses of HIV Infection in the United States and Dependent Areas, 2017*. Vol 29.; 2018:129.

8. UNAIDS. *Global AIDS Update 2019—Communities at the Centre*.; 2019.

9. Shiau S, Krause KD, Valera P, Swaminathan S, Halkitis PN. The Burden of COVID-19 in People Living with HIV: A Syndemic Perspective. *AIDS and Behavior*. Published online 2020. doi:10.1007/s10461-020-02871-9

10. Bhaskaran K, Rentsch CT, MacKenna B, et al. HIV infection and COVID-19 death: a population-based cohort analysis of UK primary care data and linked national death registrations within the OpenSAFELY platform. *The Lancet HIV*. 2021;8:e24-32. doi:10.1016/S2352-3018(20)30305-2

11. Prevention of SARS-CoV-2 (COVID-19) Through Pre-Exposure Prophylaxis With Tenofovir Disoproxil Fumarate/Emtricitabine and Hydroxychloroquine in Healthcare Personnel: Randomized Clinical Trial Controlled With Placebo. Published online 2020. https://clinicaltrials.gov/ct2/show/NCT04334928

12. A Prospective/Retrospective,Randomized Controlled Clinical Study of Antiviral Therapy in the 2019-nCoV Pneumonia. https://clinicaltrials.gov/ct2/show/NCT04255017?draw=2

13. Efficacy and Safety of Darunavir and Cobicistat for Treatment of COVID-19 (DC-COVID-19). *2020.*

14. Kaplan JE. Antiretrovirals: HIV and AIDS Drugs. Published online July 28, 2020. Accessed August 15, 2021. https://www.webmd.com/hiv-aids/aids-hiv-medication

15. Arts EJ, Hazuda DJ. HIV-1 Antiretroviral Drug Therapy. *Cold Spring Harbor Perspectives in Medicine*. 2012;2(4):a007161-a007161. doi:10.1101/cshperspect.a007161

16. Venkataraman S, Prasad B, Selvarajan R. RNA Dependent RNA Polymerases: Insights from Structure, Function and Evolution. *Viruses*. 2018;10(2):76. doi:10.3390/v10020076

17. Horby PW, Mafham M, Bell JL, et al. Lopinavir–ritonavir in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial. *The Lancet*. 2020;396(10259):1345-1352. doi:10.1016/S0140-6736(20)32013-4

18. WHO discontinues hydroxychloroquine and lopinavir/ritonavir treatment arms for COVID-19. Published online July 2020.

19. De Meyer S, Bojkova D, Cinatl J, et al. Lack of antiviral activity of darunavir against SARS-CoV-2. *International Journal of Infectious Diseases*. Published online 2020. doi:10.1016/j.ijid.2020.05.085

20. Tricco AA, Antony J, Zarin W, et al. A scoping review of rapid review methods. *BMC Medicine*. 2015;13:224.

21. Zhu F, Cao Y, Xu S, Zhou M. Co-infection of SARS-CoV-2 and HIV in a patient in Wuhan city, China. *Journal of Medical Virology*. Published online 2020. doi:10.1002/jmv.25732

22. Zhao J, Liao X, Wang H, et al. Early virus clearance and delayed antibody response in a case of COVID-19 with a history of co-infection with HIV-1 and HCV. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America*. Published online 2020. doi:10.1093/cid/ciaa408

23. Sallard E, Lescure FX, Yazdanpanah Y, Mentre F, Peiffer-Smadja N. Type 1 interferons as a potential treatment against COVID-19. *Antiviral Research*. Published online 2020. doi:10.1016/j.antiviral.2020.104791

24. Louisa SJ, Lin Serene WX, Gollamudi S. A case of HIV and SARS-CoV-2 co-infection in Singapore. *JAIDS Journal of Acquired Immune Deficiency Syndromes*. Published online 2020. doi:10.1097/qai.0000000000002401

25. Elhadi M, Momen AA, Ali Senussi Abdulhadi OM, Msherghi A. Fatal case of HIV and COVID-19. *New Microbes and New Infections*. Published online 2020. doi:10.1016/j.nmni.2020.100742

26. Ridgway JP, Farley B, Benoit JL, et al. A Case Series of Five People Living with HIV Hospitalized with COVID-19 in Chicago, Illinois. *AIDS Patient Care and STDs*. Published online 2020. doi:10.1089/apc.2020.0103

27. Suwanwongse K, Shabarek N. Clinical features and outcome of HIV/SARS-CoV-2 coinfected patients in The Bronx, New York city. *Journal of Medical Virology*. Published online 2020. doi:10.1002/jmv.26077

28. Haddad S, Tayyar R, Risch L, et al. Encephalopathy and seizure activity in a COVID-19 well controlled HIV patient. *IDCases*. Published online 2020. doi:10.1016/j.idcr.2020.e00814

29. Benkovic S, Kim M, Sin E. 4 Cases: HIV and SARS-CoV-2 Co-infection in patients from Long Island, New York. *Journal of Medical Virology*. Published online 2020. doi:10.1002/jmv.26029

30. Shalev N, Scherer M, LaSota ED, et al. Clinical characteristics and outcomes in people living with HIV hospitalized for COVID-19. *Clinical Infectious Diseases*. Published online 2020. doi:10.1093/cid/ciaa635

31. Ho HE, Peluso MJ, Margus C, et al. Clinical outcomes and immunologic characteristics of Covid-19 in people with HIV. *The Journal of infectious diseases*. Published online 2020. doi:10.1093/infdis/jiaa380

32. Ridgway JP, Schmitt J, Friedman E, et al. HIV Care Continuum and COVID-19 Outcomes Among People Living with HIV During the COVID-19 Pandemic, Chicago, IL. *AIDS and Behavior*. Published online 2020. doi:10.1007/s10461-020-02905-2

33. Patel RH, Pella PM. COVID-19 in a patient with HIV infection. *Journal of Medical Virology*. Published online 2020. doi:10.1002/jmv.26049

34. Sigel K, Swartz T, Golden E, et al. Covid-19 and People with HIV Infection: Outcomes for Hospitalized Patients in New York City. *Clinical Infectious Diseases*. Published online 2020. doi:10.1093/cid/ciaa880

35. Byrd KM, Beckwith CG, Garland JM, et al. SARS-CoV-2 and HIV coinfection: clinical experience from Rhode Island, United States. *Journal of the International AIDS Society*. Published online 2020. doi:10.1002/jia2.25573

36. Okoh AK, Bishburg E, Grinberg S, Nagarakanti S. COVID-19 pneumonia in patients with HIV – A Case Series. *JAIDS Journal of Acquired Immune Deficiency Syndromes*. Published online 2020. doi:10.1097/qai.0000000000002411

37. Gudipati S, Brar I, Murray S, McKinnon JE, Yared N, Markowitz N. Descriptive Analysis of Patients Living with HIV Affected By COVID-19. *Journal of acquired immune deficiency syndromes (1999)*. Published online 2020. doi:10.1097/QAI.0000000000002450

38. Karmen-Tuohy S, Carlucci PM, Zervou FN, et al. Outcomes among HIV-positive patients hospitalized with COVID-19. *JAIDS Journal of Acquired Immune Deficiency Syndromes*. Published online 2020. doi:10.1097/qai.0000000000002423

39. Modi AR, Koval CE, Taege AJ, et al. Coronavirus disease 2019 in an orthotopic liver transplant recipient living with human immunodeficiency virus. *Transplant Infectious Disease*. Published online 2020. doi:10.1111/tid.13351

40. Mahmood K, Rashed ER, Oliveros E, et al. Predisposition or Protection? COVID-19 in a Patient on LVAD Support with HIV/AIDS. *JACC: Case Reports*. Published online 2020. doi:10.1016/j.jaccas.2020.05.015

41. Yousaf B HADI M, ; Syeda F Z NAQVI M, ; Justin T KUPEC M, SARWARI ; Arif R, MD, MSc M. Characteristics and outcomes of COVID-19 in patients with HIV: a multi-center research network study. *AID*. Published online 2020. doi:10.1097/QAD.0000000000002666

42. Stoeckle K, Johnston CD, Jannat-Khah DP, et al. COVID-19 in Hospitalized Adults Living with HIV. *Open Forum Infectious Diseases*. Published online 2020. doi:10.1093/ofid/ofaa327

43. Braunstein SL, Lazar R, Wahnich A, Daskalakis DC, Blackstock OJ. COVID-19 infection among people with HIV in New York City: A population-level analysis of linked surveillance data. *Clinical Infectious Diseases*. Published online 2020:cia1793. doi:10.1093/cid/ciaa1793

44. Sachdev D, Mara E, Hsu L, et al. COVID-19 Susceptibility and Outcomes Among People Living With HIV in San Francisco. *Journal of acquired immune deficiency syndromes (1999)*. 2021;86(1):19-21. doi:10.1097/QAI.0000000000002531

45. Nagarakanti SR, Okoh AK, Grinberg S, Bishburg E. Clinical outcomes of patients with COVID-19 and HIV coinfection. *Journal of Medical Virology*. Published online 2020. doi:10.1002/jmv.26533

46. Pillay-Van Wyk V, Bradshaw D, Groenewald P, et al. COVID-19 deaths in South Africa: 99 days since South Africa's first death. *South African Medical Journal*. 2020;110(11):1093-1099. doi:10.7196/SAMJ.2020.v110i11.14667

47. Bhaskaran K, Rentsch CT, MacKenna B, et al. HIV infection and COVID-19 death: a population-based cohort analysis of UK primary care data and linked national death registrations within the OpenSAFELY platform. *The Lancet HIV*. 2021;8:e24-32. doi:10.1016/S2352-3018(20)30305-2

48. Marimuthu J, Kumar BS, Aravind Gandhi P. HIV and SARS CoV-2 co-infection: A retrospective, record based, case series from South India. *Journal of medical virology*. 2020;(135):0-3. doi:10.1002/jmv.26271

49. Pujari S, Gugale P, Shah D, et al. Pulmonary tuberculosis masquerading as coronavirus disease 2019 in an HIV-infected individual with advanced immune suppression. *AIDS (London, England)*. 2020;34:2165-2168. doi:10.1097/QAD.0000000000002676

50. Hernandez-Diaz S, Bateman BT, Straub L, et al. Safety of Tenofovir Disoproxil Fumarate (TDF) for Pregnant Women facing the COVID-19 Pandemic. *American Journal of Epidemiology*. 2021;kwab109.

51. Cooper TJ, Woodward BL, Alom S, Harky A. Coronavirus disease 2019 (COVID-19) outcomes in HIV/AIDS patients: a systematic review. *HIV Medicine*. Published online 2020. doi:10.1111/hiv.12911

52. Tesoriero JM, Swain CAE, Pierce JL, et al. Elevated COVID-19 outcomes among persons living with diagnosed HIV infection in New York State: Results from a population-level match of HIV, COVID-19, and hospitalization databases. *medRxiv*. Published online 2020. doi:10.1101/2020.11.04.20226118

53. Global AIDS Update 2020. https://www.unaids.org/en

54. Chien M, Anderson TK, Jockusch S, et al. Nucleotide Analogues as Inhibitors of SARS-CoV-2 Polymerase, a Key Drug Target for COVID-19. *Journal of proteome research*. Published online 2020:3-9. doi:10.1021/acs.jproteome.0c00392

55. Vizcarra P, Pérez-Elías MJ, Quereda C, et al. Description of COVID-19 in HIV-infected individuals: a single-centre, prospective cohort. *The Lancet HIV*. Published online 2020. doi:10.1016/S2352-3018(20)30164-8

56. Parienti J jacques, Prazuck T, Peyro-Saint-Paul L, et al. Effect of Tenofovir Disoproxil Fumarate and Emtricitabine on nasopharyngeal SARS-CoV-2 viral load burden amongst outpatients with COVID-19: A pilot, randomized, open-label phase 2 trial. *EClinicalMedicine*. 2021;100993.

57. National Institute of Health (NIH). Randomized Clinical Trial for the Prevention of SARS-CoV-2 Infection (COVID-19) in Healthcare Personnel (EPICOS)-NCT04334928. *ClinicalTrials.gov*. Published online April 6, 2021. Accessed August 10, 2021. https://clinicaltrials.gov/ct2/show/NCT04334928

58. Livingston E, Bucher K. Coronavirus Disease 2019 (COVID-19) in Italy. *JAMA*. Published online 2020. doi:10.1001/jama.2020.4344

59. Mirzaei H, McFarland W, Karamouzian M, Sharifi H. COVID-19 Among People Living with HIV: A Systematic Review. *AIDS and Behavior*. Published online 2020. doi:10.1007/s10461-020-02983-2

60. *Interim Guidance for COVID-19 and Persons with HIV*. AIDSinfo.

61. Ravinder R, Singh S, Bishnoi S, et al. An adaptive, interacting, cluster-based model for predicting the transmission dynamics of COVID-19. *Heliyon*. 2020;6(12):e05722. doi:10.1016/j.heliyon.2020.e05722

62. Singh A, Kataria S, Das P, Sharma A. A proposal to make the pulse oximetry as omnipresent as thermometry in public health care systems. *Journal of Global Health*. 2020;10(2):0203102.

63. Mohan M, Cherian JJ, Sharma A. Exploring links between Vitamin D deficiency and covid-19. *PLoS Pathogens*. 2020;16(9):e1008874. doi:10.1371/journal.ppat.1008874

64. Lake JE, Adams JS. Vitamin D in HIV-Infected Patients. *Curr HIV/AIDS Rep*. 2011;8(3):133-141. doi:10.1007/s11904-011-0082-8

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