Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/mjafi

Correspondence/Letter to the Editor

Clinical outcome of patients with HIV/SARS-COV-2 co-infection

Dear Editor,

Corona virus disease 2019 (COVID-19) caused by severe acute respiratory syndrome corona-virus 2 (SARS-CoV-2) was declared as pandemic by WHO on 11 March 2020.[1] Since its first reporting of unusual pneumonia case in Wuhan city of China,[2] this virus spreaded like wild fire to involve the entire world creating unprecedented crisis on existing healthcare facilities. With rising number of cases, human immunodeficiency virus (HIV)/SARS-COV-2 co-infection is also being seen increasingly as reported by various studies.[3–8] The interaction of HIV with SARS-CoV-2 virus at cellular level, clinical manifestations, and course has not been fully studied yet. There is a complex immune dysregulation which has been noticed with a high level of IFNα/β-mRNAs and T cell activation compared to healthy individuals.[8] Theoretically, low CD4 counts with superimposed lymphopenia due to COVID-19 infection in People Living With HIV (PLWH) shall impact their clinical outcomes adversely; but on the contrary, reports from across the globe have not shown any significant increase in mortality.[2–8] However, the number of patients reported so far have been very few and there is a constant need for larger data. With this background, a retrospective study was conducted to know the clinical outcome in previously confirmed patients with HIV who contracted COVID 19 infection and were admitted at one of the largest designated COVID care hospital (Tables 1 and 2).

This retrospective study was conducted on all previously diagnosed HIV patients who were admitted for COVID 19 infection during 13 April 2020 to 31 August 2020 at an advanced COVID 19 designated hospital located in National Capital, New Delhi after ethical clearance. The confirmation of COVID 19 test was based upon real time polymerase chain reaction (RT-PCR E and Rd RP gene) on nasal swab. For statistical analysis of medical data, software packages SPSS (Version 16, Chicago IL, USA) and MS Excel were used. On admission, such patients were investigated for HIV viral load and CD4 count in addition to baseline tests (Complete blood count, C-reactive protein, liver function test, renal function test, blood sugar random and urine analysis). Chest radiograph PA view and inflammatory markers (C-reactive protein, D-dimer, lactate dehydrogenase, serum ferritin, IL-6) were performed when there were features of any underlying systemic illness like pneumonia.

Total 1536 cases were admitted during 13 April to 31 August 2020, out of which 1357 were male (88.3%), 179 (11.7%) were female with median age of 36 years (interquartile range 20 and range 15–94 years). Total mortality due to various causes was 76 (4.96%). Thirteen patients (0.84%) who were known HIV positive were admitted. There were two fatalities in this group which constituted 15.3% of total fatalities. Clinical details, co-morbid conditions, ART regimen, CD4 count, viral load and clinical outcome of patients are depicted in Table 1. Out of thirteen patients, nine patients had mild symptoms of COVID 19 infection while four patients had moderate COVID pneumonia. Patients who recovered fully were on regular ART but had variable (both high and low) HIV viral load. Mortality occurred in a person who had co-morbidities of chronic kidney disease, hypertension and presented with features of urosepsis. Another mortality was noted in a freshly detected case of HIV who had disseminated histoplasmosis at presentation.

With multiple waves of COVID-19 infection hitting various parts of the world and considering limited medical infrastructure, it is imperative for us to figure out the population who are at major risk of severe infection so that a mitigated and targeted response can be undertaken at the right time.

In patients with HIV/SARS-COV-2 co-infection, the greatest concern is the immunological interaction between the two viruses. Diao et al found that the number of total T cells, CD4+ and CD8+ T cells were dramatically reduced in patients with COVID-19, especially those admitted in ICU.[9] Counts of total T cells, CD8+ T cells or CD4+ T cells lower than 800, 300 or 400/μL, respectively, were negatively correlated with patient survival. Study has revealed that T cell lymphopenia, particularly CD 4 cells is common amongst patients infected with COVID 19. Advanced HIV infection along with lymphopenia due to COVID 19 infection could delay the clearance of SARS-CoV2 and promote disease progression.[10] PLWH have significant immune dysregulation which involves predominantly the T cells but studies from various countries have shown that there is no significant increase in the percentage of infection or severe COVID-19 infection in patients with HIV/SARS-COV-2 co-infection.[3–8] Huang et al published the first case of HIV/

Please cite this article as: Singh GK et al., Clinical outcome of patients with HIV/SARS-COV-2 co-infection, Medical Journal Armed Forces India, https://doi.org/10.1016/j.mjafi.2022.09.003

Table 1 – Summary of patients admitted with HIV/SARS-COV-2 co-infection.

S.No.	Age	Clinical presentation and course	Antiretroviral regimen	CD4 Count (Cells/mm^3)	Viral Load (Copies/ml)	Co-morbidities	Outcome
1.	58/M	Admitted and being managed for persistent fever, UTI, urosepsis and delirium. While managing he developed LRTI and detected to be COVID positive. Day 6 developed cough, respiratory dis- tress CXR PA view: bilateral pneumonia Day 10: Respiratory distress (Death)	TLE 42 Months	320	<40	Hyperten- sion, Chronic Kidney dis- ease, HIV Neurocognitive disorder	**Fatal**
2.	45/M	Fever, mild URTI	TLE 80 Months	440	<40	Diabetes mellitus	Recovered
3.	55/M	Fever, Mild URTI	TLE 68 Months	386	<40	Diabetes mellitus, hypertension	Recovered
4.	33/M	Fever, mild URTI	TLE 12Months	209	<40	–	Recovered
5.	32/M	Fever, mild URTI	TLE 18 Months	202	<40	–	Recovered
6.	39/M	Severe disseminated histoplasmosis- superimposed COVID Pneumonia Day 8- Respiratory failure Day 10- Death	Not On Treatment	17	1.1×10^5	–	Fatal
7.	39/M	Disseminated histoplasmosis, CMV radiculo neuropathy Fever, URTI	TLE 88 Months	20	2.6×10^5	–	Recovered
8.	32/M	Fever, mild URTI	TLE 60 Months	680	Not detected	–	Recovered
9.	19/M	Fever, mild URTI	TLD 12 Months	461	<20	–	Recovered
10.	34/M	Fever, mild URTI	TLE 40 Months	484	Not detected	–	Recovered
11.	42/M	HIV dementia, avascular necrosis left hip, Fever, mild URTI	ZLD 01 Month	40	6.18×10^6	–	Recovered
12.	54/F	Moderate COVID pneumonia treated with short course of oral glucocorticoid	TLD/r 42 months	422	Not detected	–	Recovered
13.	42/M	Moderate COVID pneumonia treated with short course of oral glucocorticoids	ZL A/r 28 Months	144	7×10^6	–	Recovered

(UTI-urinary tract infection, URTI- upper respiratory tract infection, LRTI- lower respiratory tract infection, CXR PA view-chest X ray posterio-anterior view, TLE-tenofovir/limuvudine/efavirenz, TLD-tenofovir/limivudine/dolutegravir, ZLA/r-ziduvudine/lamivudine/atazanavirritonavir, CMV- cytomegalovirus).

SARS-COV-2 co-infection in an elderly male who developed COVID-19 pneumonia.[2] The patient was managed with good outcome. Nagarakanti et al observed that the HIV infection was well controlled in all patients with HIV/SARS-CoV-2 co-infection except for 3 patients who had presented with acquired immune deficiency syndrome (AIDS).[3] All patients with AIDS were discharged home uneventfully. They found survival between HIV infection and patients with HIV/SARS-COV-2 co-infection to be comparable. Blanco et al observed 543 consecutive patients with SARS-CoV-2 infection who had been admitted to Hospital Clínic Barcelona, Spain, five were HIV positive.[7] None of these five patients died, although they admitted two patients to intensive care due to severe COVID-19 pneumonia. Summary of such studies with their outcomes are illustrated in Table 2. In our study out of 13 HIV/SARS-COV-2 co-infection, we had two fatalities. Prior co-morbid conditions, severe infection like urosepsis and disseminated histoplasmosis respectively at presentation along with COVID pneumonia could have potentiated their fatal outcome. Treatment of such individuals is challenging considering dysregulation of immune system caused by both the viruses. Barring one who was freshly detected HIV patient, all survivors were on adequate ART with well suppressed HIV viral load and good CD4 levels. This may be due to indirect or direct protective effects of ART against SARS-COV-2 infection. Anti-retro- viral drugs have been tried in patients with COVID-19 mono-infection but the results have not been encouraging.[11] Thus, although in our study ART seems to be offering some protection to patients, the results cannot be completely validated.

In such individuals, the use of steroids is also debatable as it can lead to easy establishment of opportunistic infections. However, subsequent experience has shown that judicious use of steroids in moderate to severe disease is as beneficial in co-infected patients as in general population even when weighted against the risk of immunosuppression caused by steroids in this population.

Our observation in HIV/SARS-COV-2 co-infection has shown that increase in mortality or severe disease in PLWH is usually associated with other severe co-morbidities just like

Please cite this article as: Singh GK et al., Clinical outcome of patients with HIV/SARS-COV-2 co-infection, Medical Journal Armed Forces India, https://doi.org/10.1016/j.mjafi.2022.09.003

Table 2 – Summary of various studies on HIV/SARS-COV-2 co-infection.

Sr No	Studies on co-infection	Country of study	Number of patients with co-infection	Clinical course/outcome
1	Huang C et al.[2]	China	One	Patient developed COVID pneumonia Had a good outcome
2	Nagarakanti SR et al.[3]	Israel	Twenty-three	Three deaths, Two patients required invasive ventilation and two patients were managed in ICU
3	Akyala AI et al.[4]	Nigeria	Four	Mild clinical course with fever and LRTI but with good outcome
4	Karmen-Tuohy S et al.[5]	United States of America	Twenty-one	Three patients died but all three had superimposed bacterial infection. Rest had increase frequency of chest radiograph abnormality and longer hospital stay.
5	Byrd KM et al.[6]	United States of America	Twenty- seven	One patient died, Total nine patients were hospitalised. Overall twenty-six patient had a mild course of the disease.
6	Blanco JL et al.[7]	Spain	Five	Two patients had URTI, three patients had COVID pneumonia. One required invasive mechanical ventilation
7	d'Ettorre G et al.[8]	Italy	One	Severe COVID pneumonia but had a good outcome

the general population. However, small number of such patients were limitation of the study and not enough to derive statistically significant conclusions. There is requirement of larger studies with control population and long-term follow-up to understand the true interaction and association between the two viruses and their clinical outcome.

REFERENCES

1. Internet Coronavirus Disease (COVID-19)-Events as They Happen. *Rolling Updates on Coronavirus Disease (COVID-19)*. World Health Organization; 2020. Available from: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/events-as-they-happen [last accessed on 27 Jul 2021].
2. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. 2020 Feb;395(10223):497–506.
3. Nagarakanti SR, Okoh AK, Grinberg S, Bishburg E. Clinical outcomes of patients with COVID-19 and HIV coinfection. *J Med Virol*. 2021;93(3):1687–1693.
4. Akyala AI, Iwu CJ. Novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) co-infection with HIV: clinical case series analysis in North Central Nigeria. *Pan Afr Med J*. 2020;37:47.
5. Karmen-Tuohy S, Carlucci PM, Zervou FN, et al. Outcomes among HIV-positive patients hospitalized with COVID-19. *J Acquir Immune Defic Syndr*. 2020;85(1):6–10.
6. Byrd KM, Beckwith CG, Garland JM, et al. SARS-CoV-2 and HIV coinfection: clinical experience from Rhode Island, United States. *J Int AIDS Soc*. 2020;23(7), e25573.
7. Blanco JL, Ambrosioni J, Garcia F, et al. COVID-19 in patients with HIV: clinical case series. *Lancet HIV*. 2020;7(5):e314–e316.
8. d'Ettorre G, Recchia G, Ridolfi M, et al. Analysis of type I IFN response and T cell activation in severe COVID-19/HIV-1 coinfection: a case report [published correction appears in Medi- cine (Baltimore). 2020 Oct 16;99(42):e22949]. *Medicine (Baltim)*. 2020;99(36), e21803.
9. Diao B, Wang C, Tan Y, et al. Reduction and functional exhaustion of T cells in patients with coronavirus disease 2019 (COVID-19). *Front Immunol*. 2020;11:827.
10. Gatechompol S, Avihingsanon A, Putcharoen O, et al. COVID-19 and HIV infection co-pandemics and their impact: a review of the literature. *AIDS Res Ther*. 2021;18:28.
11. Costanzo M, De Giglio MAR, Roviello GN. SARS-CoV-2: recent reports on antiviral therapies based on lopinavir/ritonavir, darunavir/umifenovir, hydroxychloroquine, remdesivir, favipiravir and other drugs for the treatment of the New coronavirus. *Curr Med Chem*. 2020;27(27):4536–4541.

G.K. Singh
Associate Professor, (Dermatology), Base Hospital, Delhi Cantt, India

Sumit Arora
Associate Professor, (Medicine), Base Hospital, Delhi Cantt, India

Kuldeep Ashta
Senior Advisor, (Medicine), Base Hospital, Delhi Cantt, India

Teghveer Singh*
Senior Resident (Dermatology), 167 Military Hospital, Pathankot, India

*Corresponding author.
E-mail address: tegveersingh@gmail.com

1 February 2022
Available online xxx

0377-1237/$ – see front matter

https://doi.org/10.1016/j.mjafi.2022.09.003