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Short Communication: Coronavirus Disease 19 Among People Living with HIV in Western India: An Observational Cohort Study

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Abstract

A retrospective cohort study was conducted to assess clinical characteristics and outcomes of coronavirus disease-19 (COVID-19) among people living with HIV (PLHIV) in western India. Out of 86 PLHIV with COVID-19 illness, 19.7% had severe/critical illness and 6 (6.9%) individuals died. Median (interquartile range) age was 51 (47–56) years and 77.6% were male. Eighty-five PLHIV were on antiretroviral treatment with 98% having a viral load <200 copies/mL. Hypertension (HTN) (38.3%) and diabetes mellitus (17.4%) were commonest comorbidities. Fifty-eight percent PLHIV were hospitalized while 6.9% individuals needed intensive care. Presence of medical comorbidity was significantly associated with severe/critical COVID-19, whereas HTN was significantly associated with mortality. Recovery from COVID-19 was documented in 93% PLHIV. In conclusion, PLHIV in western India have similar COVID-19 clinical outcomes as compared with those reported historically among general population. Presence of medical comorbidities rather than HIV-related disease characteristics is associated with severe COVID-19 illness.

Keywords: COVID-19, PLHIV, India, comorbidities

People living with HIV (PLHIV) may have worse coronavirus disease-19 (COVID-19) outcomes due to immune dysregulation and higher prevalence of medical comorbidities in an aging population.[1] Although most data on HIV–COVID-19 coinfection have been published from high-income settings, limited information is available from low- and middle-income countries where burden of HIV infection is high. In a population cohort study from South Africa, HIV infection was independently associated with increased COVID-19 mortality.[2] In non-HIV-infected individual, recovery rates of acute COVID-19 and crude mortality rates of 96.4% and 1.4%, respectively, have been reported from India.[3] Despite a significant HIV and COVID-19 burden in India, clinical characteristics and risk factors for severe COVID-19 have not been well characterized in this population.

We conducted a retrospective cohort study between April 24, 2020, and November 30, 2020, to assess the clinical characteristics of COVID-19 among PLHIV attending a large tertiary private care center in Pune, western India. All individuals accessing care provide an ethics committee approved written informed consent for using routinely collected clinical and laboratory data for research analysis and publication.

All PLHIV with confirmed infection with severe acute respiratory syndrome-coronavirus-2 reverse transcriptase polymerase chain reaction or rapid antigen test were included. Demographics, information on HIV-related variables, and medical comorbidities were abstracted from electronic medical records. Clinical characteristics including presenting symptoms, severity, and outcomes were collected from outpatient and/or hospital records. We used the National Institute of Health definitions to categorize severity of COVID-19 illness.[4]

Data were summarized by COVID-19 disease severity using median and interquartile range (IQR) for continuous variables and frequency and percentages for categorical variables. Continuous and categorical variables were compared across disease severity using Wilcoxon rank test, or Fisher's exact test as appropriate. Univariable and multivariable logistic regression were done to identify independent

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factors associated with COVID-19 disease severity and mortality.

Out of 4,648 PLHIV accessing care during the time period, 86 with confirmed COVID-19 were included in the final analysis. Characteristics of PLHIV with COVID-19 are summarized in Table 1. Median (IQR) age was 51 (47–56) years and 76.7% were male. Median (IQR) duration since HIV diagnosis was 16 (12–18) years. All PLHIV except one were treatment experienced with median (IQR) CD4 count (Antiretroviral Therapy) of 212/mm^3 (74–627) and virologic suppression rate of 98% within 6 months of COVID-19 diagnosis. Only five individuals had severe HIV disease (CD4 ≤ 200/mm^3 and/or plasma viral load >200 copies/mL). Commonest anchor drugs for ART regimens included integrase strand transfer inhibitor (44.7%) and non-nucleoside reverse transcriptase inhibitors (34.1%), whereas 77.8% were on tenofovir-based backbones. At least one medical comorbidity was documented in 52.3% PLHIV with hypertension (HTN) (38.3%) and diabetes mellitus (DM) (17.4%) being the commonest.

Mild/moderate and severe/critical COVID-19 illness was seen in 80.2% and 19.7%, respectively. The commonest clinical symptoms were fever (62.3%), cough (45.1%), shortness of breath (33.3%), and fatigue (21.5%). Other symptoms included muscle ache (16.1%), loss of taste/smell (13.9%), sore throat (5.3%), and diarrhea (4.3%). Median (IQR) C-reactive protein was lower among PLHIV with mild/moderate illness (6.5 mg/dL, 3.0–28.0) as compared with severe/critical illness (21.1 mg/dL, 11.8–39.2), although this difference was not statistically significant ($p = .07$). Median D-Dimer (ng/mL) was significantly higher among PLHIV with severe/critical as compared with mild/moderate illness (657 vs. 309, $p = .04$).

Forty-two percent PLHIV were isolated at home, whereas remaining were either admitted to isolation facilities (7.5%) or hospitalized (50.5%). Among severe/critical patients, 82.3% received oxygen, with all critical patients receiving mechanical ventilation (MV). Treatments prescribed included hydroxychloroquine (9.6%), azithromycin (12.9%), remdesivir (12.9%), favipiravir (24.7%), and steroids (8.6%). All critical patients died with a crude case fatality ratio of 6.9% [95% confidence interval (CI): 2.6–14.5].

Table 1 summarizes risk factors associated with COVID-19 severity. On univariate analysis, age >50 years [odds ratio (OR): 3.6, 95% CI: 1.1–12.7, $p = .03$] and presence of any medical comorbidity (OR: 5.7, 95% CI: 1.5–21.7, $p = .01$) was associated with higher odds of severe/critical disease, whereas male gender and longer duration since HIV diagnosis had higher odds of severe/critical COVID-19, although this was not statistically significant. On multivariate analysis only presence of medical comorbidity was associated with severe/critical COVID-19 (OR: 4.3, 95% CI: 1.1–17.4, $p = .04$). All PLHIV who died were males with comorbidities.

Table 1. Clinical Characteristics and Risk Factors for Severe/Critical Coronavirus Disease-19 Illness Among People Living with HIV

		COVID-19 disease severity		*Univariable analysis*		*Multivariable analysis*	
Characteristics	*Overall,* n *(%)*	*Mild/moderate,* n *(%),* N = *69*	*Severe/critical,* n *(%),* N = *17*	*OR (95% CI)*	p	*OR (95% CI)*	p
Gender							
Female	20 (23.2)	18 (26.0)	2 (12)	Ref.	—	Ref.	—
Male	66 (76.7)	51 (74.0)	15 (88)	2.6 (0.6–11.7)	0.22	2.5 (0.5–12.7)	0.3
Age (years) >50	45 (52.3)	32 (46.3)	13 (76)	3.6 (1.1–12.7)	0.03	2.3 (0.6–8.4)	0.2
Duration of HIV diagnosis >10 years	68 (79.0)	52 (75.3)	16 (94.1)	5.2 (0.6–42.4)	0.12	Not included	
CD4 ≤ 200	4 (4.6)	3 (4.3)	1 (5.8)	1.7 (0.30–9.7)	0.55	Not included	
HIV VL >200 (within 12 months)	1 (1.1)	1 (1.4)	0	1.02 (0.1–9.7)	>0.95	Not included	
Severe HIV disease (CD4 ≤ 200 and/or VL >200)	5 (5.8)	4 (5.7)	1 (5.8)	1.02 (0.1–9.7)	>0.95	Not included	
ARV regimes (backbone drugs)						Not included	
TAF/TDF	67 (78.8)	56 (81.1)	11 (64.7)	0.52 (0.1–2.3)	0.39		
Other	11 (12.9)	8 (11.5)	3 (17.6)	Ref.			
ARV regimes (anchor drugs)						Not included	
INSTI	38 (44.7)	31 (44.9)	7 (41.1)	Ref.	—		
NNRTIs	29 (34.1)	25 (36.2)	4 (23.5)	0.7 (0.2–2.7)	0.61		
PI/r or INSTI + PI/r	18 (21.1)	12 (17.3)	6 (35.2)	2.2 (0.6–7.9)	0.22		
Presence of any comorbidity	45 (52.3)	31 (44.9)	14 (82.3)	5.7 (1.5–21.7)	0.01	4.3 (1.1–17.4)	0.04
Diabetes	15 (17.4)	11 (15.9)	4 (23.5)	1.6 (0.4–5.9)	0.46	Not included	
Hypertension	33 (38.3)	24 (34.7)	9 (52.9)	2.1 (0.7–6.2)	0.17	Not included	

ARV, antiretroviral; CI, confidence interval; COVID-19, coronavirus disease-19; INSTIs, integrase-strand transfer inhibitors; NNRTIs, nonnucleoside reverse transcriptase inhibitors; OR, odds ratio; PI/r, protease inhibitor/low dose ritonavir; Ref., reference; TAF, tenofovir alafenamide; TDF, tenofovir disoproxyl fumarate; VL, viral load.

On univariate analysis (data not shown), presence of HTN was the only variable associated with mortality (OR: 11.4, 95% CI: 1.27–102.8, $p = .03$). Owing to small number of mortality events, multivariate analyses were not performed.

In this largest retrospective cohort study on HIV–COVID-19 coinfection from India, majority had mild/moderate COVID-19 illness although crude mortality rate (6.9%) was marginally higher than the historically reported general population in India. As of January 12, 2021, India has reported ~10 million COVID-19 patients with recovery rate and crude mortality ratio of 96.4% and 1.4%, respectively.[3] We documented a similar recovery rate of 93% (95% CI: 85.4–97.4) in our cohort. Other hospital-based non-HIV cohorts from India have reported crude mortality rate of 2%–4%.[5,6] Higher mortality rates among HIV–COVID-19 coinfected individuals as compared with those without HIV infection have been reported in several large population-based studies across the world.[2,7,8] A standardized mortality ratio of COVID-19 death associated with HIV was reported to be 2.39 in a large study from South Africa.[2]

There is conflicting data on the frequency of severe COVID-19 among PLHIV as compared with those without HIV infection. Many studies have failed to show association of HIV infection with need for intensive care unit (ICU) admissions and MV.[9,10] However, some reports have demonstrated increased need for ICU care and MV among PLHIV.[11,12] In our cohort, ~50% PLHIV were hospitalized although this is an overestimate, as during initial days of the pandemic in India, even mild/moderate cases were hospitalized for isolation purposes. However, it would be prudent to assume that 19.7% of the severe/critical cases needed hospitalization.

Factors associated with higher risk of severe COVID-19 and mortality among PLHIV are still unclear. These include HIV related (degree of immune suppression), demographics (aging population), and higher prevalence of medical comorbidities.[1] In our study, we found that presence of at least one medical comorbidity was the only factor significantly associated with severe COVID-19, whereas HTN was significantly associated with mortality. Higher risk of severe COVID-19 and mortality has been reported among individuals with comorbidities such as DM and HTN even in the absence of HIV infection, both globally and in India.[13,14] Almost all of our patients had virologic suppression before COVID-19 diagnosis, with optimal CD4 reconstitution making it difficult to assess the role of immune suppression on COVID-19 severity. Higher risk of COVID-19 severity has been reported among PLHIV with CD4 count $<200/mm^3$ or unsuppressed viral load (VL).[15,16] However, neither CD4 counts $\leq 200/mm^3$ (OR: 1.7, 95% CI: 0.3–9.7, $p = .55$) or VL >200 copies/mL (OR: 1.02, 95% CI: 0.1–9.7, $p > .95$) was significantly associated with severe/critical COVID-19 in our study.

Apart from absence of controls, there are few limitations of the study. Asymptomatic COVID-19 was not ruled out for all PLHIV seeking care. This would likely bring down the rate of severe illness and mortality. However, this is also true of the general population and infection fatality ratio is difficult to determine for individuals with or without HIV infection. Only PLHIV who accessed care during this time period were evaluated as compared with the entire clinic cohort. Disruption in follow-ups was common and it is likely some PLHIV with COVID-19 may not have reported to the clinic.

In conclusion, PLHIV with COVID-19 in India have excellent recovery rate, mirroring that in the general population. However, mortality may be marginally higher with comorbidities being an important associated risk factor.

Authors' Contributions

S.P. designed the study, recruited patients, and drafted the article; S.G. recruited patients; A.C. abstracted data from electronic records; D.D. performed laboratory tests; and K.J. and V.B. performed statistical analysis. All authors commented on the draft article and approved the final article.

Author Disclosure Statement

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