HHS Public Access

Author manuscript

J Acquir Immune Defic Syndr. Author manuscript; available in PMC 2023 August 15.

Published in final edited form as:

J Acquir Immune Defic Syndr. 2022 August 15; 90(5): e13–e16. doi:10.1097/QAI.0000000000003009.

Effect of HIV Serostatus on ICU Admission and Mortality among Hospitalized Coronavirus Disease 2019 (COVID-19) Patients

Yaa A. Kwapong, MD, MPH[1], **Garima Sharma, MD**[1,5], **Julie K. Shade, PhD**[2], **Damani A. Piggott, MD, PhD**[3], **Todd T. Brown, MD, PhD**[4], **Alborz Soleimanifard**[5], **Katherine C. Wu, MD**[*,1,5], **Allison G. Hays, MD**[*,1,5]

[1]Johns Hopkins Ciccarone Center for the Prevention of Cardiovascular Diseases, Johns Hopkins School of Medicine, Baltimore, MD, USA

[2]Alliance for Cardiovascular Diagnostic and Treatment Innovation (ADVANCE), Johns Hopkins University, Baltimore, 21224, USA

[3]Division of Infectious Diseases, Johns Hopkins University School of Medicine, Baltimore, MD, USA

[4]Division of Endocrinology, Diabetes and Metabolism, Johns Hopkins University School of Medicine, Baltimore, MD, USA

[5]Division of Cardiology, Johns Hopkins University School of Medicine, Baltimore, MD, USA

To the Editors:

INTRODUCTION

With over 5 million deaths globally as of November 2021, coronavirus disease 2019 (COVID-19), caused by SARS-COV-2, continues to be a major public health concern.[1,2] In the general population, several predictors of poor outcomes including mortality in COVID-19 patients have been identified: age, male sex, history of cardiovascular disease and cardiac risk factors.[3] However, less is known about outcomes in immunocompromised patients with COVID-19. An estimated 0.7% of adults worldwide are people living with HIV (PLWH)[4] and the course and predictors of adverse outcomes of COVID-19 in this population need to be better understood. Prior studies have investigated adverse outcomes from COVID-19 among PLWH,[5] with some comparing outcomes in PLWH relative to HIV-negative immunocompetent (HIVneg-ICT) patients.[6-10] However, studies exploring whether PLWH suffer worse outcomes compared to HIV-seronegative immunocompromised (HIVneg-ICS) patients such as those with cancer or solid organ transplant are limited.[11] More complete information is needed regarding risk factors specific to HIV that increase risk of mortality and ICU admission due to COVID-19.

Corresponding author Allison G. Hays, Associate Professor of Medicine, Johns Hopkins University School of Medicine, Division of Cardiology, Medical Director of Echocardiography, 600N Wolfe St, Halstead 565, Baltimore MD 21287, Phone 443-287-6827.
*Co-senior authors. These authors contributed equally to this work.

Part of this data (abstract) was presented at the 23rd International Workshop on Long term complications of HIV and SARS COV 2 held virtually on Dec 6- Dec 9 2021.

Although the higher prevalence of traditional cardiovascular risk factors in PLWH may predispose them to worse outcomes when infected with COVID-19, the lymphopenic state in PLWH and specific combination antiretroviral treatment (cART) regimens may be protective, though studies are inconclusive. [12,13] We sought to evaluate differences in adverse outcomes due to COVID-19 in PLWH relative to HIV-seronegative controls, with and without immunocompromise.

METHODS

We utilized data from the Johns Hopkins Health System Precision Medicine Analytic Platform Registry (JH_CROWN) pulled from the electronic medical records of 5 hospitals in Maryland (Johns Hopkins, Hopkins Bayview, Sibley, Howard County and Suburban Hospital). Adult patients who were diagnosed of COVID-19, confirmed by polymerase chain reaction test, and admitted and died of any cause, or discharged alive between March 1, 2020, and April 4, 2021, were included. Patients with HIV diagnoses were considered PLWH, and age-matched to two HIV-seronegative controls: HIVneg-ICT and HIVneg-ICS. HIVneg-ICS included patients with history of solid organ transplant or cancer (any type) determined by ICD-10 diagnostic codes.

Differences in patient characteristics were assessed using chi-squared test for categorical variables and student's t test for continuous variables. Logistic regression models were performed: univariate models to assess predictors of ICU admission and death, and multivariate models to investigate the association of ICU admission and death by HIV serostatus. Model 1 was unadjusted. Model 2 was adjusted for age, gender and race. Model 3 was additionally adjusted for hypertension, diabetes, and body mass index. Model 4 was further adjusted for chronic heart failure, chronic renal failure, chronic pulmonary disease, and hepatitis C virus infection, which were significant on univariate analysis. HIV subgroup analyses on CD4 count, viral load (VL) and cART regimen -nucleoside reverse transcriptase inhibitors(NRTI), non-nucleoside reverse transcriptase inhibitors(NNRTI), protease inhibitors and integrase strand transfer inhibitors(INSTI) were performed. All analyses were performed with Stata version 16 (StataCorp, College Station, TX), and a 2-sided alpha (α) level of <0.05 was considered significant.

RESULTS

A total of 463 patients (mean age 53±14 years) hospitalized for COVID-19 were included: PLWH(n=151), HIVneg-ICT(n=185) and HIVneg-ICS(n=127). PLWH were more likely to be current smokers (21.2% vs 15.1% vs 7.9%, p=0.009), users of recreational drugs (28.5% vs 9.2% vs 15.0%, p<0.001) and had higher prevalence of chronic pulmonary disease (44.4% vs 26.5% vs 37.0%, p=0.003), liver disease (35.5% vs 13.5% vs 22.8%, p<0.001) and hepatitis C virus infection (24.5% vs 3.7% vs 7.1%, p<0.001) compared to HIVneg-ICT and HIVneg-ICS patients respectively. (Table 1) Most PLWH (88.5%) had HIV VL suppression with mean CD4 count of 264.5 cells/mm^3(SD 202.7). PLWH were receiving NRTI (76.2%), NNRTI (9.3%), protease inhibitors (12.6%) and INSTI (72.8%).

PLWH had higher odds of ICU admission, compared to HIV neg-ICT in the unadjusted model (odds ratio, OR: 1.59; 95%CI: 1.03-2.45) and after adjusting for age, gender, and race (aOR: 1.64, 95%CI:1.04 −2.59) but when further adjusted for comorbidities in models 3 and 4, the odds of ICU admission were 61% higher but not statistically significant and point estimates were similar (Model 3 aOR: 1.61, 95%CI: 0.99-2.60, p=0.05; model 4 aOR: 1.61, 95%CI: 0.96-2.69, p =0.07). The odds of ICU admission in PLWH did not significantly differ from HIVneg-ICS adults before and after adjustment(model 4 aOR: 1.19, 95%CI:0.68-2.07). HIV VL and CD4 count were not significantly associated with ICU admission (HIV VL: OR:0.96; 95%CI:0.87-1.07; CD4 count: OR:1.00, 95%CI:0.99-1.00) or death (HIV VL: OR:1.02; 95%CI:0.81-1.27; CD4 count: OR:1.00; 95%CI: 0.99-1.00). There was a higher risk of ICU admission in PLWH who were not on NRTI versus those taking NRTI (OR:9.4, 95%CI:1.18-75.24). Hypertension and diabetes predicted ICU admission in all groups. Additionally, among PLWH, liver disease was strongly predictive of ICU admission (OR:2.41, 95%CI:1.19-4.89).

There were no significant differences in the odds of death in PLWH compared to HIVneg-ICT (aOR:0.97, 95%CI:0.32-2.88) or HIVneg-ICS patients (aOR:0.63; 95%CI: 0.23-1.75).

DISCUSSION

In our study of hospitalized COVID-19 patients, we found that PLWH had a higher risk of ICU admission, but not mortality than HIVneg-ICT adults. However, the odds of ICU admission and mortality were similar between PLWH and HIVneg-ICS adults. Although traditional cardiovascular risk factors predicted adverse outcomes in all groups, we additionally identified that liver disease predicted ICU admission in PLWH, but not in the controls. Our study is unique in that it highlights differences in comorbidities and predictors of adverse outcomes in PLWH and two age-matched HIV-seronegative controls, with and without immunocomprise.

Our findings of similar mortality rates in PLWH and HIV-negative controls are consistent with prior publications.[7,15] Although recent meta-analyses of global outcomes in COVID-19 revealed a modest but significant increase in mortality in PLWH vs. HIV-negative individuals[16,17], when subgroup analysis was performed by region, in North America mortality did not differ between groups. This may be due to better access to cART for PLWH in the U.S, compared to Africa and Asia where risk for COVID-19 related mortality was particularly high,[16] although this merits further study.

PLWH had no difference in risk for ICU admission compared to HIVneg-ICS, suggesting a similar degree of COVID-19 disease severity in adults with immunosuppression regardless of the reason (HIV, transplant, or cancer). Compared to HIVneg-ICT patients, PLWH had significantly increased risk for ICU admission even after adjusting for age, sex, and race. After adjusting for comorbidities, although there was a trend towards increased risk in PLWH, the significance did not persist, possibly due to over-adjustment of confounders in the setting of an intermediate sample size. Other earlier studies reported no significant difference in ICU admission between PLWH and HIVneg-ICT. However, they were limited by a small sample size of PLWH (N<30 PWLH in each study).[8,18] Our study of 151 PLWH

compared to matched controls suggest that immunocompromised patients (whether due to HIV or other causes) are at higher risk of ICU admission relative to immunocompetent patients.

Given the longevity from ART, PLWH often have higher prevalences of traditional cardiovascular risk factors than the general population [19-21] which may predispose them to severe COVID-19 disease. HIV was generally well-controlled in this cohort, and most were on cART, with HIV VL suppression and mean CD4 count of 264 cells/ml. Notably, PLWH who were not taking NRTI, which is considered standard cART, were more likely to be admitted to the ICU compared to those on background NRTI therapy. This suggests that a lack of effective ART may predispose PLWH to more severe COVID-19 requiring ICU admission, however this merits further study. We did not observe an increased risk of death or ICU admission in PLWH with higher VLs or lower CD4 counts, however the sample size was modest and larger studies are needed to ascertain whether greater degrees of immunocompromise among PLWH predispose to worse outcomes.

Interestingly, liver disease was not only more common in PLWH but was also an independent risk factor for ICU admission in HIV. The increased risk for severe COVID-19 associated with liver disease in PLWH may be due to clotting abnormalities and microthromboses that are well described in COVID-19[22] which may be accentuated in the setting of liver dysfunction, and merits further study. Furthermore, PLWH are in a chronic inflammatory state which may affect the immune response to COVID-19. However, we detected no significant difference in degree of systemic inflammation measured by c-reactive protein and D-dimer levels between groups.

Our study had several limitations. The number of deaths in our cohort was low (<12 in each group), limiting detailed analysis of mortality and adjustment for confounding variables. Outcomes were limited to those occurring during hospitalization for COVID-19, and longer term outcomes after hospital discharge were not available. Registry outcomes were based on medical record data (ICD-10 codes), however, we chose objective outcomes of interest to avoid issues related to inaccurate coding. Use of ICD-10 codes to identify patients with cancer does not distinguish between those with prior treated vs active disease.

CONCLUSION

Our study suggests that immunocompromised patients with COVID-19 regardless of underlying cause of immunosuppression, are at higher risk for ICU admission relative to immunocompetent individuals. Larger studies in PLWH are needed to explore the extent to which HIV disease severity markers influence long-term outcomes following COVID-19 infection.

Conflicts of Interest/Sources of Funding

Todd T Brown is supported in part by **K24AI120834**

Allison G. Hays is supported in part by NHLBI: 1R01HL147660

All the other authors have no conflicts of interest.

ABBREVIATIONS

COVID-19	Coronavirus Disease 2019
HIV	human immunodeficiency virus
PLWH	People living with HIV
HIVneg-ICT	HIV negative immunocompetent
HIVneg-ICS	HIV negative immunocompromised
aOR	adjusted odds ratio
VL	viral load
cART	combination antiretroviral therapy
NRTI	Nucleoside reverse transcriptase inhibitor
NNRTI	non-nucleoside reverse transcriptase inhibitor
INSTI	Integrase strand transfer inhibitor

REFERENCES

1. Home - Johns Hopkins Coronavirus Resource Center. Accessed November 23, 2021. https://coronavirus.jhu.edu/
2. WHO Coronavirus (COVID-19) Dashboard | WHO Coronavirus (COVID-19) Dashboard With Vaccination Data. Accessed November 23, 2021. https://covid19.who.int/
3. Figliozzi S, Masci PG, Ahmadi N, et al. Predictors of adverse prognosis in COVID-19: A systematic review and meta-analysis. Eur J Clin Invest. 2020;50(10). doi:10.1111/ECI.13362
4. HIV/AIDS. Accessed November 23, 2021. https://www.who.int/data/gho/data/themes/hiv-aids
5. Dandachi D, Geiger G, Montgomery MW, et al. Characteristics, comorbidities, and outcomes in a multicenter registry of patients with HIV and coronavirus disease-19. Clin Infect Dis 2021;73(7) doi:10.1093/cid/ciaa1339
6. Sigel K, Swartz T, Golden E, et al. Coronavirus 2019 and People Living With Human Immunodeficiency Virus: Outcomes for Hospitalized Patients in New York City. Clin Infect Dis 2020;71(11):2933–2938. doi:10.1093/CID/CIAA880 [PubMed: 32594164]
7. Durstenfeld MS, Sun K, Ma Y, et al. Association of Human Immunodeficiency Virus Infection with Outcomes among Adults Hospitalized with COVID-19, AIDS. doi:10.1097/QAD.0000000000003129
8. Nagarakanti SR, Okoh AK, Grinberg S, Bishburg E. Clinical outcomes of patients with COVID-19 and HIV coinfection. J Medical Virol. 2021;93(3):1687–1693. doi:10.1002/JMV.26533
9. Diez C, Romero-Raposo D, Mican R et al. , COVID-19 in hospitalized HIV-positive and HIV-negative patients: A matched study. HIV Med 2021.doi:10.1111/hiv.13145
10. Stoeckie K, Johnston CD, Jannat-Khah DP et al. COVID-19 in Hospitalized Adults with HIV. Open Forum Infect Dis 2020 Aug; 7(8):ofaa327. Doi:10.1093/0fid/ofaa327 [PubMed: 32864388]
11. Sun J, Patel RC, Zheng Q et al. COVID-19 Disease Severity among People with HIV infection or Solid Organ Transplant in the United States: A Nationally-representative, Multicenter, Observational Cohort Study, MedRxiv 2021 July 28;2021.07.26.21261028. doi:10.1101/2021.07.26.21261028. preprint
12. Mascolo S, Romanelli A, Carleo MA, Esposito V. Could HIV infection alter the clinical course of SARS-CoV-2 infection? When less is better. J Medical Virol. 2020;92(10):1777–1778. doi:10.1002/JMV.25881

13. Del Amo J, Polo R, Moreno S et al. Incidence and Severity of COVID-19 in HIV-positive Persons Receiving Antiretroviral Therapy: A cohort study. Ann Intern Med 2020 Oct 6;173(7):536–541. Doi:10.7326/M20-3689 [PubMed: 32589451]

14. Lix L, Smith M, Pitz M et al. Cancer Data Linkage in Manitoba: Expanding the Infrastructure for Research 2016 http://mchp-appserv.cpe.umanitoba.ca/reference/Candata_web_final.pdf#Page=96

15. Flannery S, Schwartz R, Rasul R, et al. A comparison of COVID-19 inpatients by HIV status. Int J STD AIDS. 2021;32(12):9564624211023016–9564624211023016. doi:10.1177/09564624211023015

16. Wang Y, Feng R, Xu J, Shi L, Feng H, Yang H. An updated meta-analysis on the association between HIV infection and COVID-19 mortality. AIDS. 2021;35(11):1875–1878. doi:10.1097/QAD.0000000000002968 [PubMed: 34397487]

17. Mellor MM, Bast AC, Jones NR, et al. Risk of adverse coronavirus disease 2019 outcomes for people living with HIV. AIDS. 2021;35(4):F1–F10. doi:10.1097/QAD.0000000000002836 [PubMed: 33587448]

18. Karmen-Tuohy S, Carlucci PM, Zervou FN et al. Outcomes among HIV-positive patients hospitalized with COVID-19 J Acquired Immune Defic Syndr 2020 doi:10.1097/QAI.0000000000002423

19. Shah ASV, Stelzle D, Ken Lee K, et al. Global burden of atherosclerotic cardiovascular disease in people living with HIV systematic review and meta-analysis. Circulation. 2018;138(11):1100–1112. doi:10.1161/CIRCULATIONAHA.117.033369 [PubMed: 29967196]

20. Grand M, Bia D, Diaz A. Cardiovascular Risk Assessment in People Living With HIV: A Systematic Review and Meta-Analysis of Real-Life Data. Curr HIV Res. 2020;18(1):5–18. doi:10.2174/1570162X17666191212091618 [PubMed: 31830884]

21. Brown LB, Spinelli MA, Gandhi M. The interplay between HIV and COVID-19: summary of the data and responses to date. Curr Opin HIV AIDS 2021; 16:63–73. doi:10.1097/COH.0000000000000659 [PubMed: 33186229]

22. Lowenstein CJ, Solomon SD. Severe COVID-19 is a Microvascular Disease Circulation 2020;142(17):1609–1611. doi:10.1611/CIRCULATIONAHA.120.050354 [PubMed: 32877231]

Table 1:

Comparison of Patient Demographics and Comorbidities of PLWH, HIV-negative Immunocompetent and HIV-negative Immunocompromised Patients Hospitalized for COVID-19.

Patient characteristics	PLWH N=151	HIV-negative immunocompetent N=185	HIV-negative Immunocompromised N=127	P-value
Demographics				
Age on admission, years Mean (SD)	52.7(13.8)	52.7(14.2)	54.8(13.8)	0.34
Days admitted, Mean (SD)	6.3 (12.3)	5.7(15.3)	5.7(11.0)	0.89
Gender, n (%)				0.45
Female	54(35.8)	65(35.1)	53(41.7)	
Male	97(64.2)	120(64.9)	74(58.3)	
Race, n (%)				0.83
White	10(6.6)	12(6.5)	8(6.3)	
Black	131(86.8)	160(86.5)	111(87.4)	
Asian	0(0)	1(0.5)	0(0)	
Other	10(6.6)	12(6.5)	7(5.5)	
Ethnicity, n (%)				0.59
Hispanic	11(7.3)	14(7.6)	8(6.3)	
Not Hispanic	140(92.7)	171(92.4)	118(92.9)	
Patient declined	0(0)	0(0)	1(0.8)	
Comorbidities				
Hypertension, n (%)				0.03 *
No	47 (31.1)	70(37.8)	30(23.6)	
Yes	104(68.9)	115(62.2)	97(76.4)	
Diabetes Mellitus, n (%)				0.003 *
No	96(63.6)	113(61.1)	57(44.9)	
Yes	55(36.4)	72(38.9)	70(55.1)	
Renal failure, n (%)				<0.001 *
No	106(70.2)	157(84.9)	73(57.5)	
Yes	45(29.8)	28(15.1)	54(42.5)	
Chronic Heart failure, n (%)				0.11
No	129(85.4)	158(85.4)	98(77.2)	
Yes	22(14.6)	27(14.6)	29(22.8)	
Current smoker, n (%)				0.009 *
No	119(78.8)	157(84.9)	117(92.1)	
Yes	32(21.2)	28(15.1)	10(7.9)	
Body Mass Index, n (%)				0.03 *
<30	92(60.9)	90(48.6)	62(48.8)	
≥ 30	57(37.8)	85(46.0)	63(49.6)	
missing	2(1.3)	10(5.4)	2(1.6)	

Patient characteristics	PLWH N=151	HIV-negative immunocompetent N=185	HIV-negative Immunocompromised N=127	P-value
Chronic pulmonary disease, n (%)				0.003 *
No	84(55.6)	136(73.5)	80(63.0)	
Yes	67(44.4)	49(26.5)	47(37.0)	
Drug use, n (%)				<0.001 *
No	108(71.5)	168(90.8)	108(85.0)	
Yes	43(28.5)	17(9.2)	19(15.0)	
Liver disease, n (%)				<0.001 *
No	98(64.9)	160(86.5)	98(77.2)	
Yes	53(35.1)	25(13.5)	29(22.8)	
Alcohol use disorder, n (%)				0.22
No	130(86.1)	169(91.4)	116(91.3)	
Yes	21(13.9)	16(8.7)	11(8.7)	
Hyperlipidemia, n (%)				0.14
No	122(80.8)	138(74.6)	86(67.7)	
Yes	29(19.2)	47(25.4)	41(32.3)	
Coronary Artery Disease, n (%)				
No	146(96.7)	174(94.1)	115(90.5)	0.23
Yes	5(3.3)	11(5.9)	12(9.5)	
Stroke, n (%)				0.16
No	144(95.4)	172(93.0)	112(88.2)	
Yes	7(4.6)	13(7.0)	15(11.8)	
CABG_PCI[a], n (%)				N/A
No	151(100)	185(100)	127(100)	
Yes	0(0)	0(0)	0(0)	
Hepatitis C Virus Infection, n (%)				<0.001 *
No	114(75.5)	178(96.3)	118(92.9)	
Yes	37(24.5)	7(3.7)	9(7.1)	
Vaccination Status				
Received 2 doses of Moderna or Pfizer prior to COVID-19 admission, n	16	4	5	-

PLWH- People living with HIV

[a] CABG-PCI – Coronary artery Bypass Graft-Percutaneous Coronary Intervention

* p-value <0.05- significant