

Clinical Features and Outcomes of COVID-19 in People Living with HIV: A Single-Center, Age-Matched Cohort Study of Hospitalized and Clinic Patients

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Abstract

As we continue to learn the effects of the human immunodeficiency virus-infected with SARS-CoV-2. We describe 7 patients with an age-matched cohort in hospitalized and clinic patients in our hospital health system with a 90 day follow up for these patients. A retrospective, age-matched cohort study with people living with HIV (PWLH) that were diagnosed with COVID-19 in the hospital and on an outpatient basis at our health system. Duration of symptoms in PLWH was noted to be longer (6-49 days); they also had a close follow-up with their primary care physician. PLWH noted to have respiratory symptoms (air hunger, shortness of breath, and productive cough) for a duration of 1-2 months after COVID-19 testing. This case series does not show an increased risk of infection or adverse outcomes in COVID-19 infection when compared with the general population consistent with prior case series. The persistence of respiratory symptoms in PLWH for up to 2 months warrants further research.

Keywords: COVID-19; HIV infection; SARS-CoV-2; Antiretroviral therapy; Follow-up

List of Abbreviations: SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2; HIV: Human Immunodeficiency Virus; PWLH: People Living With HIV; COVID-19: Coronavirus Disease 2019; CD4: Cluster of Differentiation 4 CD4+ T Helper Cells; ART: Antiretroviral Therapy; RT-PCR: Reverse Transcription- Polymerase Chain Reaction; CDC: Centers for Disease Control and Prevention; CHI: Catholic Health Initiatives; PCR: Polymerase Chain Reaction; IRB: Institutional Review Board; EMR: Electronic Medical Record; CABP: Community-Acquired Bacterial Pneumonia; RNA: Ribonucleic Acid

Background

The 2019 novel coronavirus (SARS-CoV-2) causing COVID-19 infection has emerged to become a global pandemic with significant fatality. Studies have demonstrated that older adults and people of any age who have serious underlying medical condition might be at higher risk for severe illness, including people who are immunocompromised [1]. Contrary to the presumption, studies showed that people living with HIV (PLWH) are not at higher risk of contracting COVID-19 compared to those without a diagnosis of HIV [2-8]. The reported incidence of COVID-19 in PLWH in various studies from China, the United Kingdom, and New York City was low at 0.8% to 1% [9-11].

The risk for people coinfecting with COVID-19 and HIV experiencing severe illness was reported to be greatest in PLWH with a low CD4 cell count, and not receiving antiretroviral therapy (ART) [12-14]. On the other hand, the severity of COVID-19 pneumonia/disease in PLWH was similar to the general population [15]. The proposed hypothesis includes a protective effect of ART, immune exhaustion, or defective cellular immunity that prevents the cytokine storm known to create severe illness in those infected with COVID-19.

As we continue to learn about the COVID-19 pandemic and its effects on the HIV community there have been several case reports and case series which evaluated hospitalized patients with SARS-CoV-2 infection in PLWH. We performed a retrospective, age-matched cohort study with PWLH that were diagnosed with COVID-19 confirmed by a positive SARS-CoV-2 RT-PCR test from nasopharyngeal swab specimens that were treated in the hospital and on an outpatient basis at our health system. At pres-

ent, the CDC states that “based on limited data, we believe people with HIV who are on effective HIV treatment have the same risk for COVID-19 as people who do not have HIV.”

Methods

A retrospective, age-matched cohort study with PWLH that were diagnosed with COVID-19 in the hospital and on an outpatient basis at our CHI health system in Omaha, Nebraska. Two providers that care for HIV patients that were alerted to patients with positive COVID-19 PCR testing those that were admitted to a CHI hospital or obtained a COVID-19 PCR test on out patient basis. Patients age 19-95 years who have tested positive for COVID-19 in the CHI Health system from April 1, 2020-July 31, 2020 were eligible for electronic medical record (EMR) review. EMR was used to evaluate follow up with any medical provider within 90 days from first positive COVID-19 PCR test. After all patient information was gathered and entered into the excel spreadsheet, the spreadsheet was locked as per institutional IRB recommendations.

Results and Discussion

PLWH contracting COVID-19 with a comparative age and sex control group found several important findings. (Table 1a) Of the 7 PLWH, only 2/7 patients were noted to have a CD4 count of < 200 cells/mm³, of which only one patient had a detectable viral load on ART [15]. Patients with HIV that were hospitalized received more antibiotics with broader coverage (vancomycin with piperacillin-tazobactam) compared to ceftriaxone with azithromycin and for longer duration when compared to those that did not have HIV for presumed community-acquired bacterial pneumonia (CABP).

Table 1a: Demographics, clinical characteristics at admission, treatment and outcomes of 7 patients with HIV & COVID-19 of hospitalized and clinic patients

	HIV and COVID-19						
	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
Demographics and Baseline HIV status							
Age (years)	38	49	47	50	53	54	56
Race	Hispanic	African American	Hispanic	Caucasian	Caucasian	Caucasian	Caucasian
Gender	Male	Female	Male	Male	Male	Male	Male
HIV risk factor, COVID-19 Exposure	MSM, Unknown	Heterosexual, Unknown	MSM, Partner COVID + Exposure	Unknown, Hospital Employee	MSM, Partner COVID + Exposure	MSM, Unknown	MSM, Unknown
Comorbidities (HTN,DM,cancer, smoking, immunosuppression, chronic inflammatory diseases, cardiac conditions)	Kaposi Sarcoma on chemotherapy	GERD, Obesity	Tobacco Smoker	T2DM, Moderate persistent asthma	Melanoma, HTN	Former Smoker, T2DM, HTN	Kaposi Sarcoma, Syphilis, Hepatitis C

HIV status (values at or before COVID-19 dx)	Positive	Positive	Positive	Positive	Positive	Positive	Positive
Year of HIV diagnosis	2018	2002	2015	2000	1999	2001	2007
CD4 Cell count (cells per μ L)	30	173	1,178	29.8	628	328	874
CD4:CD8 ratio	0.1	0.2	1.5	0.8	0.7	0.4	0.8
HIV viral load at or before admission (copies per mL)	517	Not Detected, <40	Not Detected, <40	Not Detected, <40	Not Detected, <40	Not Detected, <40	Not Detected, <40
ART- regimen before admission	(Biktarvy) BIC/FTC/TAF, Atovaquone	(Biktarvy)BIC/FTC/TAF	(Descovy) FTC/TAF, (Tivicay) DTG	(Triumeq) ABC / DTG / 3TC	(Biktarvy) BIC/FTC/TAF	(Genvoya) EVG/COBI/FTC/TAF	(Genvoya) EVG/COBI/FTC/TAF
BMI	23.57	35.1	30.1	27.5	35	41.3	26.1
Duration of Symptoms (Days)	6	6	Unknown	25	49	29	25
COVID-19 Diagnosis	4/29/20	5/19/20	6/30/20	4/13/20	5/15/20	5/13/20	6/26/20
Symptoms and Vital signs							
Temperature	103 °F	100.3 °F	n/a	100.2 °F	98 °F	96.2 °F	98.2 °F
Symptoms	Nausea, chills, and night sweats	Fever, chills, myalgia, headache, cough, chest pressure, loss of appetite, vomiting after eating or drinking	Fever, fatigue, sore throat, intermittent cough, and generalized body aches	Fever, chills, cough (productive), and Shortness of breath	Pleuritic chest pain	Fatigue, congestion, rhinorrhea, cough, wheezing, weakness, headache, decreased concentration, and increased sleep	Fever, chills, congestion, cough (non-productive), diaphoresis, fatigue, and lack of smell (chronic)
Blood pressure (mm Hg)	136/72	150/82	n/a	116/78	n/a	112/64	132/88
Respiratory Rate (breaths per min)	20	n/a	n/a	22	16	16	n/a
Heart Rate (beats per min)	118	95	n/a	108	71	96	68
Chest X-Ray (CXR) findings or CT chest w/out contrast	CXR: No radiographic evidence of cardiopulmonary findings	n/a	CXR: No active chest disease	CT chest w/out contrast: Patchy foci of ground glass opacities scattered throughout lungs most pronounced in bilateral lower lobes, representing infectious process. Multifocal Pneumonia	n/a	CXR: No acute cardiopulmonary abnormality	CXR: Cardiac silhouette and pulmonary vasculature are normal. No edema or infiltrate. There is a granuloma in the right lung base and left upper lobe. Minor nodularity in the right apex is also unchanged from 2018.
O2 Saturation on room air	99%	95%	ND	98%	88%	96%	97%
PaO2/FiO2 ratio	n/a	452	n/a	n/a	n/a	n/a	n/a
Laboratory Results							
White blood cell count (k/ul)	15.1	ND	ND	3.6	ND	ND	ND
Abs Lymphocyte (k/ul)	1.1	ND	ND	1.3	ND	ND	ND
Platelets (k/ul)	88	ND	ND	113	ND	ND	ND

LDH (U/L)	278	ND	ND	176	ND	ND	ND
C-reactive protein (mg/dL)	41.9	ND	ND	27.3	ND	ND	ND
D-dimer (ng/mL)	0.9	ND	ND	0.34	ND	ND	ND
Ferritin (ng/mL)	452	ND	ND	314	ND	ND	ND
Procalcitonin (ng/mL)	0.55	ND	ND	<0.05	ND	ND	ND
Severity of the infection at admission (mild/mod/severe)	Mild	Mild	Mild	Moderate/Severe	Mild	Mild	Moderate
ART (mention the full regimen)	ART at admission maintained	Not admitted inpatient but continued on ART therapy	Not admitted inpatient but continued on ART therapy	ART at admission maintained	Not admitted inpatient but continued on ART therapy	Not admitted inpatient but continued on ART therapy	Not admitted inpatient but continued on ART therapy
Other antiviral treatments	None	None	None	None	None	None	None
Other antibiotics	Vancomycin, Cefepime, Flagyl, Fluconazole/ Miconazole (14 days), Cefdinir (7 days), Doxycycline (7 days)	None	None	Vancomycin, Zosyn, Azithromycin (5 days), Hydroxychloroquine (5 days)	None	Azithromycin	Ceftriaxone, Doxycycline, Azithromycin
Admitted to intensive care unit	No	No	No	No	No	No	No
Invasive or non-invasive ventilation	No	No	No	No	No	No	No
Corticosteroids or Tocilizumab	No	No	No	Methylprednisolone 40mg IV once then Prednisone 40mg (5days)	No	Triamcinolone Acetonide 40mg IM once	No
Length of hospital stay (days)	4	0	0	6	0	0	0
Length of home quarantine (days)	14	14	14	10	14	14	14
Outcomes	Discharged home	Discharged home	Unknown	Discharged home	Discharged home	Discharged home	Discharged home
Repeat COVID19 Testing done	No	No	No	Yes, after 5 months negative	No	No	No
Seen in hospital for admission within 30,60,90 days	2 ED visits after 60 days for rash and skin abscesses	Seen in ED after a month for constipation. No respiratory symptoms	Seen by PCP after 2 weeks having air hunger and productive cough, improved by the end of 1 month	Required 2 rounds of antibiotics for Bronchitis with doxycycline and Levaquin, continue to have shortness of breath till about 58 days out from diagnosis	Required albuterol inhaler for 2 months to help breath better	No	No

COVID-19 - Coronavirus disease 2019, MSM - Men who have sex with men, n/a - Not available, GERD - Gastroesophageal reflux disease, T2DM - Type 2 Diabetes Mellitus, ESRD - End Stage Renal Disease, HTN - Hypertension, HLD- Hyperlipidemia, BIC - Bicitgravir, TAF - Tenofovir alafenamide, FTC - Emtricitabine, DDTG - Dolutegravir, ABC - Abacavir, 3TC - Lamivudine, EVG - Elvitegravir, COBI - Cobicistat, ART - Antiretroviral therapy, LDH, ED-Emergency department, PCP - Primary care physician.

Table 1b: Demographics, clinical characteristics at admission, treatment and outcomes of 7 patients with COVID-19 age matched cohort of hospitalized and clinic patients

	COVID-19						
	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
Demographics and Baseline HIV status							
Age (years)	38	39	45	50	53	53	59
Race	African American	Hispanic	Asian	Caucasian	Caucasian	Caucasian	African American

Gender	Male	Male	Male	Male	Male	Female	Male
HIV risk factor, COVID-19 Exposure	n/a, Work	n/a, unknown (Costco employ)	n/a, unknown (work?)	n/a, unknown	n/a, waterfall tourist destination in Eastern Iowa	n/a, unknown	n/a, Works at Nebraska beef
Comorbidities (HTN,DM,cancer, smoking, immunosuppression, chronic inflammatory diseases, cardiac conditions)	HTN, DM, ESRD, Anemia, tobacco use, hx of alcohol abuse	GERD, Hypertension, Severe sleep apnea	None	T2DM, HTN, HLD, Sleep apnea	T2DM	None	None
HIV status (values at or before COVID-19 dx)	Presumed Negative	Presumed Negative	Presumed Negative	Presumed Negative	Presumed Negative	Presumed Negative	Presumed Negative
Year of HIV diagnosis	n/a	n/a	n/a	n/a	n/a	n/a	n/a
CD4 Cell count (cells per μ L)	n/a	n/a	n/a	n/a	n/a	n/a	n/a
CD4:CD8 ratio	n/a	n/a	n/a	n/a	n/a	n/a	n/a
HIV viral load at or before admission (copies per mL)	n/a	n/a	n/a	n/a	n/a	n/a	n/a
ART- regimen before admission	n/a	n/a	n/a	n/a	n/a	n/a	n/a
BMI	23.61	47	23.9	36.6	39.7	30.1	23
Duration of Symptoms (Days)	1	2	10	5	Several days	n/a	4
COVID-19 Diagnosis	6/9/20	7/9/20	6/14/20	6/26/20	7/17/20	7/20/20	6/2/20
Symptoms and Vital signs							
Temperature	98.9 °F	99.4 °F	98.4 °F	100.2 °F	97.9 °F	n/a	99 °F
Symptoms	Dizzy and weak	Fever and shotness of breath	Fevers at night, cough, loss of taste, and loss of appetite	Fever, sore throat, cough, and shortness of breath	Fever, cough, clear rhinorrhea, mild posterior nasal drainage, mild fatigue, and subjective chills	n/a	Fevers, mild cough, fatigue, and myalgias
Blood pressure (mm Hg)	153/89	157/91	120/67	172/103	150/99	n/a	168/124
Respiratory Rate (breaths per min)	20	20	20	18	20	n/a	20
Heart Rate (beats per min)	84	98	67	94	102	n/a	77
Chest X-Ray (CXR) findings or CT chest w/out contrast	CXR:No acute cardiopulmonary process. No evidence of pulmonary tuberculosis	CT angio Chest:Minimal diffuse interstitial prominence, suggests mild pulmonary congestion. Patchy opacities in the right perihilar region and possibly in the right lower lobe, may reflect multifocal pneumonia. Covid pneumonia should be excluded.	CXR:Bilateral multifocal groundglass opacifications consistent with atypical pneumonia versus pleuritis.	CXR:No acute cardiopulmonary process.	n/a	n/a	n/a

O2 Saturation on room air	96%	98%	97%	97%	96%	n/a	95%
PaO2/FiO2 ratio	428	>500	>500	>500	>500	n/a	>500
Laboratory Results							
White blood cell count (k/ul)	6.3	4.1	3.5	3.7	n/a	n/a	n/a
Abs Lymptocyte (k/ul)	1.1	0.8	0.7	1.3	n/a	n/a	n/a
Platelets (k/ul)	146	204	134	184	n/a	n/a	n/a
LDH (U/L)	n/a	229	n/a	n/a	n/a	n/a	n/a
C-reactive protein (mg/dL)	n/a	61	n/a	n/a	n/a	n/a	n/a
D-dimer (ng/mL)	n/a	0.57	n/a	n/a	n/a	n/a	n/a
Ferritin (ng/mL)	n/a	290	n/a	n/a	n/a	n/a	n/a
Procalcitonin (ng/mL)	n/a	<0.05	n/a	n/a	n/a	n/a	n/a
Severity of the infection at admission (mild/mod/severe)	Mild	Moderate	Mild	Mild	Mild	Mild	Mild
ART (mention the full regimen)	None	None	None	None	None	None	None
Other antiviral treatments	None	None	None	None	None	None	None
Other antibiotics	None	Ceftriaxone and Azithromycin	None	None	None	None	None
Admitted to intensive care unit	No	No	No	No	No	No	No
Invasive or non-invasive ventilation	No	No	No	No	No	No	No
Corticosteroids or Tocilizumab	No	Dexamethasone	No	1 dose of dexamethasone	No	No	No
Length of hospital stay (days)	6	6	0	0	0	0	0
Length of home quarantine (days)	n/a	n/a	n/a	14	n/a	n/a	n/a
Outcomes	Discharged home	Discharged home	Discharged home from ED	Discharged home from ED	Discharged home from ED	Only lab test	Discharged home
Repeat COVID19 Testing done	Yes, outside facility noted to be positive for 1 month	7/16/2020 & 11/9/2020 +ve	No	No	No	No	Yes, 6/16/2020 negative
Seen in hospital for admission within 30,60,90 days	No	No	No	No	After 10 days admitted for 5 day and received Remdesivir and dexamethasone.	No	No

COVID-19 - Coronavirus disease 2019, MSM - Men who have sex with men, n/a – Not available, GERD - Gastroesophageal reflux disease, T2DM – Type 2 Diabetes Mellitus, ESRD – End Stage Renal Disease, HTN - Hypertension, HLD- Hyperlipidemia, BIC – Bictegravir, TAF - Tenofovir alafenamide, FTC – Emtricitabine, DTG – Dolutegravir, ABC – Abacavir, 3TC – Lamivudine, EVG – Elvitegravir, COBI – Cobicistat, ART – Antiretroviral therapy, LDH, ED-Emergency department, PCP – Primary care physician.

Duration of symptoms in PLWH was noted to be longer (range of 6-49 days). It is unclear if this is due to COVID-19 infection alone. Symptoms in PLWH were dramatically longer compared to the control cohort (Table 1b), with symptom duration range in the control cohort of 1-10 days. In the immunocompetent host, SARS-CoV-2 could present as an asymptomatic infection with mild symptoms all the way to severe disease, with the resolution of the infection within 1–3 weeks after the onset of symptoms [16]. Immunocompromised patients may harbor the infection for a longer duration up to 9 weeks [17]. Unfortunately, due to limitations in testing and inconsistent follow up we were not able to obtain a negative test in all patients. Only 4/14 patients from both cohorts underwent repeat SARS-CoV-2 testing, with only one HIV patient getting tested 5 months out from the initial diagnosis.

PLWH did appear to get closer follow up with their primary care physician. Thirty, 60, and 90 days follow up for PLWH found to have respiratory symptoms (air hunger, shortness of breath, and productive cough) for a duration of 1-2 months after COVID-19 testing. Carfi, *et al.* found fatigue and dyspnea up to 60 days after diagnosis in patients recovering from COVID-19 [18]. Fortunately, no PLWH required admission to the hospital. Interesting to note that the control group did not have the same level of follow-up or did not appear to have accessed our health care system for any further respiratory complaints. Unclear if respiratory symptoms persist in PLWH for a longer duration due to HIV.

The majority of control patients displayed mild COVID-19 disease, and 2/7 PLWH patients had moderate or moderate/severe illness. Fever/elevated temperature over 100 F was noted in 3/7 of PLWH. Other studies show a similar presentation in PLWH with COVID-19, with fever as a common symptom [2,4,8,22,23]. Partner exposure in 2/7 was noted to be the primary COVID-19 exposure in PLWH while 5/7 acquired it from work/community in the control group.

Forty three percent of PLWH were receiving bicitegravir, emtricitabine & tenofovir alafenamide (BIC/FTC/TAF), 29% received elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide fumarate (EVG/COBI/FTC/TAF), 14% received emtricitabine & tenofovir alafenamide (FTC/TAF), with dolutegravir (DTG) and 14% received abacavir, lamivudine, dolutegravir (ABC/DTG /3TC). Only one patient-patient#4 in HIV group did not have TAF in their ART regimen and was noted to be the only moderate to severe case of COVID-19. This patient required intravenous methylprednisolone and oral prednisone with progressive acute respiratory failure with an oxygen requirement of 2 liters of oxygen on discharge after a 6-day hospitalization.

This patient was hospitalized early in the pandemic and also received hydroxychloroquine and broad-spectrum antibiotics. This was the longest hospitalization and most severe case despite undetectable viral load but a CD4 count of 29/uL. The low CD4 count, likely could be responsible for the severity of symptoms [21]. Type 2 diabetes mellitus and moderate persistent asthma also placed the patient at higher risk. Tenofovir blocks the critical RNA-dependent RNA polymerase of SARS-CoV-2, and it is structurally related to remdesivir thus possibly providing a protective effect [5,21,22]. Several studies note a protective effect of immunosuppression although most patients have been on ART and appear to be well-controlled with a similar outcome as patients without HIV.

In PLWH, reported studies show little difference in hospitalized outcome for COVID-19 [2,5,6,8,19,25-27]. Only 2 studies (Suwanwongse, *et al.* and Boule *et al.*) demonstrated worsening mortality in this population [28,29]. Taking into account the racial and gender disparities, comorbidities, and lower socio-economic background likely contributed to the worsening mortality in these two studies [30].

As with previous case series, there are several limitations. First, this was a small retrospective and case-controlled series with inpatient and outpatient cases that were identified only after having symptoms. Second, laboratory information was not obtained from those that were treated on an outpatient basis. Third, the follow-up information was obtained on review of the patient's medical records, thus the severity or exact duration of symptoms is not available especially in the control group.

Conclusion

In conclusion, PLWH does not appear to have an increased risk of infection or adverse outcomes in COVID-19 infection when compared with the general population. While partner exposure was noted to be the primary cause of contracting COVID-19 while the age-matched cohort appeared to be from the community. The protective effect of tenofovir also warrants further evaluation. In our case series, PLWH and COVID-19 were noted to have symptoms that last for up to 2 months whether this is protective or detrimental is difficult to interpret at present, and warrants further research.

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