Characteristics and Outcomes of SARS-CoV-2 Infection Among Adults Living With HIV In Delaware: The Story of a Syndemic During the First 12 Months of the SARS-CoV-2 Pandemic

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Background

The intersection of the human immunodeficiency virus (HIV) and severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) pandemics has opened a Pandora's box of unanswered questions within medicine. As of this writing, SARS-CoV-2 has infected 155 million individuals worldwide, including many people living with HIV (PLWH), of whom there are estimated to be 37.9 million individuals at present. Due to the immunosuppressive and inflammatory effects of HIV, concern has emerged over the possibility of worse outcomes in PLWH affected by COVID-19. Worldwide studies have yielded variable associations between HIV and increased risk of morbidity and mortality from SARS-CoV-2/HIV co-infection when compared to people without HIV infection[1-2, 8-9, 10-12, 14-17]. Delaware has been severely affected by overlapping HIV and SARS-CoV-2 pandemics, including our robust statewide panel of PLWH. We hope to better characterize this intersection amongst PLWH in Delaware as captured through the first year of the SARS-CoV-2 pandemic.

Methods

The William J Holloway Community Program serves as the sole Ryan White-funded HIV clinical program in Delaware. The program serves 1754 of the state's 3050 HIV-infected individuals currently accessing care (57.5%), out of a statewide total of 3631. This retrospective descriptive case-series identified PLWH ≥ 18 years old co-infected with SARS-CoV-2 from 1 March 2020 through 9 March 2021 who attended our ambulatory HIV program. Infections were confirmed by SARS-CoV-2 PCR or SARS-CoV-2 IgG antibody following compatible clinical presentation for COVID-19. All results and pre-specified variables were extracted through EMR and external records. The study received ChristianaCare Internal Review Board approval. Chi-Square and t-tests compared categorical and continuous variables respectively between hospitalized and non-hospitalized patients. Logistic regression modeling evaluated co-variates associated with hospitalization.

Results

There were 105 cases of SARS-CoV-2/HIV co-infection with 24 (22.9%) hospitalizations and 4 attributable deaths from COVID-19. Overall, the cohort had high rates of ART utilization (on predominantly INSTI-based regimens with TAF-based NRTI backbone), virologic suppression and robust CD4 counts preceding SARS-CoV-2 co-infection (Table 1). The mean age of hospitalized patients was 59.0 years, a majority were male and African American, and utilized public insurance. Hospitalized patients tended to have less virologic suppression as well as lower proximal and nadir CD4 cell counts, in the setting of high levels of ART resistance; of note, 20/24 (87.0%) of these individuals were historically AIDS-defined and had been living with HIV for a mean duration of 15.8 years (Table 2). Age, BMI >30 kg/m^2, cardiovascular disease, chronic kidney disease and cirrhosis were independently associated with hospitalization by logistic regression (Table 3). A lower rate of hospitalization was seen in individuals with a history of resolved hepatitis B virus infection.

Table 1. Baseline Cohort Characteristics

	Population N = 105 (%)
Sex, biologic	
Male	71 (67.6)
Race	
Black	66 (62.9)
White	26 (24.8)
Hispanic	10 (9.5)
Other	3 (2.9)
Mean Age, years (SD)	50.2 (12.5)
Age Range, years	
18-24	1 (1.0)
25-40	22 (21.0)
41-50	23 (21.9)
51-60	37 (35.2)
> 60	22 (21.0)
Insurance	
None	3 (2.9)
Private	41 (39.4)
Public	60 (57.7)
ART Class[a]	
INSTI	75 (75.0)
INSTI + NNRTI	6 (6.0)
INSTI + PI	6 (6.0)
INSTI + PI + NNRTI	2 (2.0)
NNRTI	3 (3.0)
PI	7 (7.0)
PI + EI[b]	1 (1.0)
Mean Years Living with HIV (SD)	13.3 (9.3)
HIV Viral Load Range, copies/mL	
<200	93 (89.4)
200-1000	1 (1.0)
>1000	4 (3.8)
>5000	6 (5.8)
Mean CD4 Count, cells/mm^3	548.9 (257.2)
CD4 Count ≤ 200 cells/mm^3	10 (9.6)
CD4 Count Nadir Range, cells/mm^3	
<50	20 (19.0)
51-100	11 (10.5)
101-200	18 (17.1)
>200	35 (33.3)
CD4 Count Nadir ≤200 cells/mm^3	49 (46.7)
AIDS-Defined	67 (67.0)
ART Resistance[c]	32 (38.6)
Hepatitis B infection (HBV)	
Chronic HBV	8 (7.6)
Resolved HBV	15 (14.3)
Hepatitis C infection (HCV)	
Chronic HCV	4 (3.8)
Treatment with Cure	9 (8.6)
Spontaneous Clearance	9 (8.6)
Comorbidities	
BMI (mean (SD)), kg/m^2	31.4 (8.1)
Cardiovascular Disease	22 (21.0)
Diabetes	21 (20.0)
Hypertension	53 (50.5)
Dyslipidemia	51 (48.6)
Chronic Kidney Disease	16 (15.2)
Chronic Lung Disease	24 (22.9)
Cirrhosis	7 (6.7)
Hospitalized	24 (22.9)
ICU Admission	9 (13.6)

a = in addition to NRTI backbone (F/TAF in vast majority of patients)
b = entry inhibitor
c = defined as clinically significant resistance to ART in one or more drug class
d = either isolated anti-HBc (with negative HBV DNA) or anti-HBc + anti-HBs

Table 2. Characteristics of Hospitalized and Non-Hospitalized Patients

	Hospitalized N = 24 (%)	Not Hospitalized N = 81 (%)	p-Value
Sex, biologic			
Male	17 (70.8)	54 (66.7)	0.893
Race			0.265
Black	19 (79.2)	47 (58.0)	
White	4 (16.7)	22 (27.2)	
Hispanic	1 (4.2)	9 (11.1)	
Other	0 (0.0)	3 (3.7)	
Mean Age, years (SD)	59.0 (11.3)	47.6 (11.7)	**<0.001**
Age Range, years			**0.006**
18-24	0 (0.0)	1 (1.2)	
25-40	2 (8.3)	20 (24.7)	
41-50	2 (8.3)	21 (25.9)	
51-60	9 (37.5)	28 (34.6)	
>60	11 (45.8)	11 (13.6)	
Insurance			**0.022**
None	0 (0.0)	3 (3.7)	
Private	4 (17.4)	37 (45.7)	
Public	19 (82.6)	41 (50.6)	
ART Class[a]			0.646
INSTI	14 (63.6)	61 (78.2)	
INSTI + NNRTI	2 (9.1)	4 (5.1)	
INSTI + PI	1 (4.5)	5 (6.4)	
INSTI + PI + NNRTI	1 (4.5)	1 (1.3)	
NNRTI	1 (4.5)	2 (2.6)	
PI	3 (13.6)	4 (5.1)	
PI + EI[b]	0 (0.0)	1 (1.3)	
Mean Years Living With HIV (SD)	15.8 (8.7)	12.6 (9.4)	0.165
HIV Viral Load Range, copies/mL			**0.037**
<200	19 (82.6)	74 (91.4)	
200-1000	0 (0.0)	1 (1.2)	
>1000	0 (0.0)	4 (4.9)	
>5000	4 (17.4)	2 (2.5)	
Mean CD4 Count, cells/mm^3 (SD)	444.3 (243.8)	578.6 (254.6)	**0.026**
CD4 Count ≤ 200 cells/mm^3	4 (17.4)	6 (7.4)	0.302
CD4 Count Nadir Range, cells/mm^3			0.053
<50	7 (29.2)	13 (16.0)	
51-100	5 (20.8)	6 (7.4)	
101-200	5 (20.8)	13 (16.0)	
>200 cells/mm^3	3 (12.5)	32 (39.5)	
CD4 Count Nadir ≤200 cells/mm^3	17 (70.8)	32 (39.5)	**0.014**
AIDS-Defined	20 (87.0)	47 (61.0)	**0.039**
ART Resistance[c]	10 (50.0)	22 (34.9)	0.345
Hepatitis B Infection (HBV)			0.417
Chronic HBV	3 (12.5)	5 (6.2)	
Resolved HBV[d]	2 (8.3)	13 (16.0)	
Hepatitis C Infection (HCV)			0.128
Chronic HCV	2 (8.3)	2 (2.5)	
Treatment with Cure	4 (16.7)	5 (6.2)	
Spontaneous Clearance	3 (12.5)	6 (7.4)	
Comorbidities			
BMI (mean (SD)), kg/m^2	30.6 (8.2)	31.6 (8.1)	0.609
Cardiovascular Disease	14 (58.3)	8 (9.9)	**<0.001**
Diabetes	10 (41.7)	11 (13.6)	**0.006**
Hypertension	17 (70.8)	36 (44.4)	**0.041**
Dyslipidemia	14 (58.3)	37 (45.7)	0.391
Chronic Kidney Disease	10 (41.7)	6 (7.4)	**<0.001**
Chronic Lung Disease	7 (29.2)	17 (21.0)	0.575
Cirrhosis	5 (20.8)	2 (2.5)	**0.007**

a = in addition to NRTI backbone (F/TAF in vast majority of patients)
b = entry inhibitor
c = defined as clinically significant resistance to ART in one or more drug class
d = either isolated anti-HBc (with negative HBV DNA) or anti-HBc + anti-HBs

Table 3. Logistic Regression Model of Hospitalization

Variable	Odds Ratio	95% Confidence Interval	p-Value
Age, years	1.12	[1.01;1.23]	**0.029**
Male sex	0.15	[0.02;1.38]	0.092
Black race	0.86	[0.11;6.63]	0.885
BMI >30 kg/m^2	7.36	[0.99;54.79]	0.051
Cardiovascular Disease	26.30	[2.73;253.53]	**0.004**
Diabetes	1.21	[0.16;8.91]	0.854
Hypertension	0.28	[0.03;2.46]	0.250
Chronic Kidney Disease	44.96	[2.75;735.55]	**0.007**
Cirrhosis	61.36	[1.81;2081.76]	**0.022**
AIDS-Defined	0.17	[0.02;1.61]	0.122
INSTI-Based ART	0.79	[0.11;5.51]	0.808
HIV Viral Load ≤ 200 copies/mL	0.41	[0.02;7.04]	0.541
Public Insurance	2.22	[0.25;20.00]	0.472

Conclusions & Discussion

Our cohort data is the first to capture the experience of patients co-infected with HIV/SARS-CoV-2 in Delaware. In keeping with previously published data, increasing age and presence of well-defined co-morbidities in the setting of HIV/SARS-CoV-2 co-infection are independently associated with higher odds of hospitalization[6,10,13,16]. Patients' immunologic profiles and HIV-specific histories (including nadir CD4 count, virologic suppression, AIDS-defined status and known ART resistance) were not found to be independently associated with hospitalization. However, from an immunological perspective, we observed that AIDS-defined individuals were over-represented amongst PLWH hospitalized with SARS-CoV-2 co-infection, and historical nadir CD4 counts as well as proximal CD4 counts were lower in hospitalized than non-hospitalized SARS-CoV-2 cases. These observations, along with high rates of ART resistance and significant time living with HIV amongst hospitalized patients, altogether buttress the idea that cumulative lifetime immunosuppression and/or HIV viremia, with the expected associated changes in the underlying immunologic profiles of these patients, may be associated with higher rates of progression to severe COVID-19 in PLWH.

Furthermore, our data highlight the seeming risk of underlying chronic inflammation that is either a direct result of HIV itself and/or multi-morbidity[3,5,6,18]. We hypothesize that this increased, underlying, chronic inflammation amongst hospitalized co-infected patients may contribute to a more severe presentation of COVID-19.

Although not reaching statistical significance, we identified high rates of resolved HBV infection amongst non-hospitalized co-infected patients and postulate there may be an underlying immunologic mechanism to this hypothesis-generating observation[4,7].

While our descriptive analysis is potentially suggestive of wider trends, our analysis was limited by a small sample size, incomplete historical data for some variables, and wide confidence intervals. Larger studies are needed to further investigate the roles of long-term immunosuppression and inflammation, burden of comorbidities, and early and late immunologic responses in COVID-19 outcomes amongst PLWH.

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