

COVID-19 Testing, Characteristics, and Outcomes Among People Living With HIV in an Integrated Health System

Jennifer J. Chang, MD,^a Katia Bruxvoort, PhD,^b Lie H. Chen, DrPH,^b Bobak Akhavan, MD,^{a,c} Janelle Rodriguez, MD,^a and Rulin C. Hechter, PhD^{b,d}

Background: Understanding the attributes of COVID-19 clinical severity among people living with HIV (PLWH) compared with those in HIV-uninfected patients is critical for risk stratification and treatment strategies.

Methods: We conducted a retrospective study at Kaiser Permanente Southern California among PLWH aged 18 years or older. We compared the incidence of SARS-CoV-2 molecular testing, COVID-19 diagnosis, and COVID-19 hospitalization among PLWH and HIV-uninfected adults. A chart review was conducted for PLWH with COVID-19 to examine viral suppression of HIV and most recent CD4⁺ counts in the year before COVID-19 diagnosis, known exposures to COVID-19, and clinical presentation.

Results: Between March 1, 2020, and May 31, 2020, the incidence of SARS-CoV-2 molecular testing, COVID-19 diagnosis, and COVID-19 hospitalization was 551.2, 57.0, and 9.3 per 10,000 PLWH, respectively, compared with 268.4, 34.6, and 5.3 per 10,000 HIV-uninfected individuals, respectively. Among those with COVID-19, the distribution of race/ethnicity, smoking status, and comorbidities was similar in PLWH and HIV-uninfected patients; however, PLWH were mostly men, younger, and less obese than HIV-uninfected individuals. Health care utilization regarding emergency care and hospitalizations in the year before COVID-19-related hospitalization was similar between the groups. Overall, HIV was virologically suppressed in >95% of PLWH with COVID-19, and HIV viral load and CD4⁺ status did not differ between hospitalized and nonhospitalized patients.

Conclusions: In this population of patients with well-controlled HIV infection, the incidence of testing, diagnosis, and hospitalization

for COVID-19 was higher in PLWH than that in HIV-uninfected patients.

Key Words: COVID-19, PLWH, PWH, HIV, AIDS

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BACKGROUND

The COVID-19 pandemic has resulted in significant morbidity and mortality, with at least 122 million cases confirmed and more than 2.7 million deaths worldwide, as of March 21, 2021.¹ More than 542,000 deaths have been reported in the United States.² Major risk factors for poor outcomes associated with COVID-19 include older age and preexisting underlying medical conditions such as diabetes mellitus,³ obesity,⁴ cardiovascular disease,⁵ and chronic kidney disease.⁶

Limited reports on the characteristics and outcomes of SARS-CoV-2 infection and subsequent COVID-19 disease in people living with HIV (PLWH) have been published through several case series.^{7–17} One case series of PLWH in New York City reported a particularly high mortality rate (19/72 or 26% of cases) after COVID-19 hospitalization.¹⁴ Two studies reported no significant differences among hospitalized PLWH matched with hospitalized HIV-negative patients in COVID-19 disease severity as measured by intubation and death.^{15,16} Understanding risk factors underlying COVID-19 clinical severity among PLWH is critical for risk stratification and treatment strategies in this population. Modern antiretroviral therapy to treat HIV infection has enabled PLWH who are virally suppressed to significantly extend life expectancy. Within the Kaiser Permanente system, an 8-year life expectancy gap persists.¹⁸ Comorbidities associated with antiretroviral therapy or underlying chronic inflammation in well-controlled HIV may predispose PLWH to more severe COVID-19 outcomes.

In this study, we have described the incidence of testing, diagnosis, and hospitalization for COVID-19 among PLWH and HIV-uninfected patients in a large integrated health care system in California.

METHODS

We conducted a retrospective cohort study among health plan members at Kaiser Permanente Southern California (KPSC) between March 1, 2020, and May 31, 2020.

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From the ^aDepartment of Infectious Diseases, Kaiser Permanente Los Angeles Medical Center, Los Angeles, CA; ^bDepartment of Research and Evaluation, Kaiser Permanente Southern California, Pasadena, CA; ^cDivision of Pulmonary and Critical Care, Cedars-Sinai Medical Center, Los Angeles, CA; and ^dDepartment of Health Systems Science, Kaiser Permanente Bernard J. Tyson School of Medicine, Pasadena, CA.

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Correspondence to: Jennifer J. Chang, MD, Department of Infectious Diseases, Kaiser Permanente at Los Angeles Medical Center, 1505 N. Edgemont Street, 2nd Fl, Los Angeles, CA 90027 (e-mail: Jennifer.Jiwen.Chang@kp.org).

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Study Setting

KPSC has 15 medical centers and 234 medical offices, serving more than 4.6 million members with similar racial/ethnic diversity as the surrounding Southern California population.¹⁹ The comprehensive electronic health record system in KPSC captures all aspects of outpatient care, emergency department visits, and hospitalizations and laboratory tests and pharmacy dispensing records.

Study Population

The underlying study population included all adult (aged 18 years or older) KPSC members by May 31, 2020. HIV status was identified from the KPSC HIV patient registry. PLWH and HIV-uninfected adults aged 18 years or older with at least 1 day of KPSC membership between March 1, 2020, and May 31, 2020, were included in the analysis.

COVID-19 Case Definitions

COVID-19 cases were defined by either (1) a SARS-CoV-2 molecular diagnostic test showing a positive result or (2) a clinical diagnosis with documented ICD-10 codes from health care encounters in outpatient, emergency department, or inpatient settings. COVID-19 hospitalizations were defined as any inpatient admission 14 days before or 30 days after a severe acute respiratory syndrome coronavirus 2 or SARS-CoV-2 test with a positive or clinical diagnosis.

Measures and Chart Review

We compared baseline demographics, comorbidities, and health care utilization among PLWH and HIV-uninfected cohorts. For 57 PLWH with confirmed COVID-19 infection, we also reviewed baseline HIV-specific characteristics and presenting symptoms using the electronic health record, including demographics (age at diagnosis, sex, and race/ethnicity), insurance type, most recent body mass index (BMI), current or former smoking, and health care utilization in the previous year. Preexisting comorbidities were identified by ICD-10 codes in the previous year, including hypertension, diabetes mellitus, ischemic heart disease, peripheral vascular disease, congestive heart failure, cerebrovascular disease, renal failure, chronic obstructive pulmonary disease, asthma, obstructive sleep apnea, and cancer. For PLWH and HIV-uninfected individuals hospitalized for COVID-19, we also assessed admission to intensive care units, need for invasive mechanical ventilation, hospital discharge status, and deaths.

We conducted a manual chart review to describe COVID-19 presentation and clinical course among PLWH, reviewing any symptoms reported within 30 days before COVID-19 diagnosis. Exposure history and occupations were captured from progress notes, where available. Data were captured on HIV-related laboratory tests (ie, most recent HIV viral load and CD4⁺ cell counts in the previous year), exposure history, and clinical characteristics of COVID-19 infection. A detailed chart review was not conducted for HIV-

uninfected patients because it was not feasible to conduct a manual chart review in this large group.

Statistical Analysis

We computed the incidence of testing, diagnosis, and hospitalization for COVID-19 among PLWH and HIV-uninfected individuals in the KPSC population. We compared the demographic and clinical characteristics at COVID-19 diagnosis by HIV status and COVID-19 hospitalization using the χ^2 test or the Fisher exact test for categorical variables and the Kruskal–Wallis test for continuous variables. Among PLWH with COVID-19, we also characterized differences in presenting symptoms and clinical course among hospitalized and nonhospitalized patients.

RESULTS

Incidence of Testing, Diagnosis, and Hospitalization in PLWH and HIV-Uninfected Patients

The underlying study population included 10,702 PLWH and 3,739,207 HIV-uninfected individuals (Table 1) who were KPSC health plan members between March 1, 2020, and May 31, 2020. Incidence of SARS-CoV-2 molecular testing, COVID-19 diagnosis, and COVID-19 hospitalization was 551.2, 57.0, and 9.3 per 10,000 PLWH compared with 268.4, 34.6, and 5.3 per 10,000 HIV-uninfected individuals, respectively. We observed tests with positive results for 47 PLWH (10.3%) of 590 tested PLWH and 9918 (12.9%) of 100,363 tested HIV-uninfected individuals; an additional 14 PLWH and 3003 HIV-uninfected

TABLE 1. SARS-CoV-2 Testing and COVID-19 Clinical Outcomes Among PLWH and HIV-Uninfected Adults at KPSC, March 1, 2020–May 31, 2020

	HIV-Uninfected Adults	PLWH
Total population (N)	3,739,207	10,702
Tested for SARS-CoV-2 (incidence per 10,000 patients)	10,0363 (268.4)	590 (551.3)
Total COVID-19 cases* (incidence per 10,000 patients)	12,921 (34.6)	61 (57.0)
Positive test result, n (%)	9918 (76.8)	47 (77.0)
Clinical diagnosis, n (%)	3003 (23.2)	14 (23.0)
COVID-19 hospitalizations† (incidence per 10,000 patients)	1975 (5.3)	10 (9.3)
Admitted to ICU, n (%)	494 (25.0)	5 (50.0)
Required mechanical ventilation, n (%)	444 (22.5)	3 (30.0)
Discharged, n (%)	1556 (78.8)	9 (90.0)
Died during hospitalization, n (%)	223 (11.3)	1 (10.0)
Remained hospitalized on May 31, 2020, n (%)	196 (9.9)	0 (0.0)

*Defined as a SARS-CoV-2 molecular diagnostic test showing positive result or a clinical diagnosis for COVID-19.

†Defined as hospitalization 14 days before or 30 days after a SARS-CoV-2 test showing positive result or clinical diagnosis.

individuals had clinical diagnoses only, yielding a total of 61 COVID-19 cases among PLWH and 12,921 COVID-19 cases among HIV-uninfected individuals (Table 1). Ten (16.3%) PLWH were hospitalized with COVID-19, 5 (8.2%) were admitted to the intensive care unit (ICU), 3 (4.9%) required invasive mechanical ventilation, and 1 (1.6%) died from COVID-19. In comparison, for HIV-uninfected patients, 1975 (15.3%) were hospitalized, 494 (3.8%) were admitted to ICU, 444 (3.4%) required invasive mechanical ventilation, and 300 (2.3%) died from COVID-19 (Table 1).

Baseline Characteristics of PLWH and HIV-Uninfected Patients

PLWH with COVID-19 were younger than HIV-uninfected individuals with COVID-19 (20.0% vs. 46.8% aged 60 years or older, respectively, for hospitalized cases and 3.9% vs. 19.3% aged ≥ 60 years or older, respectively, for nonhospitalized cases). PLWH were predominantly men, whereas 53.2% of hospitalized and 42.7% of nonhospitalized HIV-uninfected patients with COVID-19 were men. Slightly higher proportions of hospitalized and nonhospitalized PLWH were White compared with HIV-uninfected individuals (Table 2).

BMI, smoking status, and comorbid conditions did not differ significantly between PLWH and HIV-uninfected individuals for hospitalized and nonhospitalized cases (Table 2). Previous year emergency department and hospitalization utilization was also similar for PLWH and HIV-uninfected individuals who were hospitalized or nonhospitalized.

Exposure History, Symptoms, and Clinical Characteristics of COVID-19 in PLWH

A manual chart review was conducted for 61 PLWH with COVID-19 diagnoses. Of them, 4 were considered not to have COVID-19 based on the chart review; 3 individuals were asymptomatic and showed negative results for SARS-CoV-2 RT-PCR test, and 1 individual had a clinical diagnosis only with no indication of COVID-19 symptoms or testing on the manual chart review. Of the remaining 57 COVID-19 cases, 10 were clinically diagnosed, and 8 of these cases had documentation of a test with positive result outside KPSC.

Among PLWH with COVID-19, last recorded HIV-1 quantitative viral load demonstrated that $\geq 95\%$ achieved viral suppression in both hospitalized ($n = 10$, 100.0%) and nonhospitalized patients ($n = 47$, 95.7%). There were no significant differences in recent CD4⁺ levels within the previous year between hospitalized and nonhospitalized patients ($P = 0.168$).

The most common presenting symptoms in PLWH with COVID-19 were cough ($n = 44$, 77.2%), fever ($n = 38$, 66.7%), and shortness of breath ($n = 24$, 42.1%). Nine of 57 (15.8%) PLWH were workers in health care settings; of them, 3 (5.2%) worked in long-term care facilities. By exposure history, in 28 (49.1%) cases, no known exposures were documented. Eleven (19.2%) patients reported at least 1 household contact showing a positive result for COVID-19. Thirteen (22.8%) patients reported exposure to community

members outside their home with a COVID-19 diagnosis. Six (10.5%) patients reported exposure to colleagues or patients with COVID-19.

Treatment and Complications of COVID-19 in PLWH

Substantial variability in treatment patterns existed within the KPSC system for COVID-19 because of evolving practice guidelines and a lack of evidence-based treatment within the study period. The most commonly prescribed anti-infective drugs were antibiotics. Hydroxychloroquine was prescribed to more than half ($n = 6$, 60%) of the hospitalized patients. Three of the 10 (30.0%) hospitalized patients received remdesivir.

Two patients who were hospitalized developed methicillin-susceptible *Staphylococcus aureus* hospital-acquired pneumonia during hospitalization. No patients who survived hospitalization developed myocardial infarction, thromboembolism, other vascular complications, or death within 30 days of discharge.

DISCUSSION

In this population of patients with well-controlled HIV, the incidence of COVID-19, hospitalization, and need for ICU level care as a measure of severity was higher in PLWH than in HIV-uninfected individuals. Comorbidities did not differ significantly between PLWH and HIV-uninfected populations, although PLWH were significantly younger than HIV-uninfected patients with COVID-19.

We found a higher incidence of testing ordered for PLWH (551 per 10,000 patients) than that for HIV-uninfected patients (268 per 10,000 patients). This may be attributed to PLWH being designated as a potential risk group at KPSC during the study period, where prioritization for testing was given to patients in vulnerable populations, including HIV, organ transplantation, pregnancy, malignancy, or elderly populations. Of note, because of national and local limitations in testing capacity, testing policies at KPSC during this period restricted laboratory testing to symptomatic patients at highest risk of hospitalization. Most of the asymptomatic patients were not evaluated for infection during the study period.

Incidence of COVID-19 disease in this study was 57.0 per 10,000 PLWH and 34.6 per 10,000 HIV-uninfected individuals or a 1.6-times higher incidence of COVID-19 in PLWH. It is possible that COVID-19 was underdiagnosed in HIV-uninfected populations because mildly symptomatic patients who were HIV-uninfected without other risk may not have been tested in the early months of the pandemic to conserve testing supplies and prioritize testing for critically ill patients. In addition, a higher incidence of COVID-19 disease in PLWH may also have been attributed to home, community, or occupational risk factors not examined in the HIV-uninfected population.

PLWH in general experience a greater risk of multiple comorbidities associated with aging than HIV-uninfected patients.²⁰ In our study, prevalence of comorbidities was similar between groups in both hospitalized and

TABLE 2. Baseline Characteristics of COVID-19 Cases by HIV Status and Hospitalization, March 1, 2020, to May 31, 2020

	Hospitalized			P	Not Hospitalized			P
	HIV-Uninfected Adults 0 (N = 1975)	PLWH 1 (N = 10)	Total (N = 1985)		HIV-Uninfected Adults 0 (N = 10,946)	PLWH 1 (N = 51)	Total (N = 10,997)	
Age, yr				0.080				<0.001
18–39	349 (17.7%)	1 (10.0%)	350 (17.6%)		4168 (38.1%)	16 (31.4%)	4184 (38.1%)	
40–59	701 (35.5%)	7 (70.0%)	708 (35.7%)		4662 (42.6%)	33 (64.7%)	4695 (42.7%)	
≥60	925 (46.8%)	2 (20.0%)	927 (46.7%)		2116 (19.3%)	2 (3.9%)	2118 (19.3%)	
Median (IQR)	58 (25.0)	54 (10.0)	58 (25.0)		45 (24.0)	49 (18.0)	46 (24.0)	
Sex				0.002				<0.001
Women	925 (46.8%)	0 (0%)	925 (46.6%)		6272 (57.3%)	2 (3.92%)	6274 (57.1%)	
Men	1050 (53.2%)	10 (100%)	1060 (53.4%)		4673 (42.7%)	49 (96.1%)	4722 (42.9%)	
Race/ethnicity				0.166				0.095
White	348 (17.6%)	5 (50.0%)	353 (17.8%)		1559 (14.2%)	12 (23.5%)	1571 (14.3%)	
Hispanic	1106 (56.0%)	4 (40.0%)	1110 (55.9%)		6521 (59.6%)	28 (54.9%)	6549 (59.6%)	
Black	195 (9.9%)	0 (0%)	195 (9.8%)		747 (6.8%)	6 (11.8%)	753 (6.9%)	
Asian	266 (13.5%)	1 (10%)	267 (13.5%)		1253 (11.5%)	4 (7.8%)	1257 (11.4%)	
Other/unknown	60 (3.00%)	0 (0%)	60 (3.0%)		866 (7.9%)	1 (2.0%)	867 (7.9%)	
BMI, kg/m ²				0.241				0.006
≤18.5	29 (1.5%)	0 (0%)	29 (1.5%)		55 (0.5%)	1 (2.0%)	56 (0.5%)	
18.5 to <25	322 (16.3%)	3 (30.0%)	325 (16.4%)		1533 (14.0%)	8 (15.7%)	1541 (14.0%)	
25 to <30	558 (28.3%)	5 (50.0%)	563 (28.4%)		2948 (26.9%)	21 (41.2%)	2969 (27.0%)	
≥30	976 (49.4%)	2 (20.0%)	978 (49.3%)		4315 (39.4%)	19 (37.3%)	4334 (39.4%)	
Missing	90 (4.6%)	0 (0%)	90 (4.5%)		2095 (19.1%)	2 (3.9%)	2097 (19.1%)	
Smoking status				0.627				0.678
Current	64 (3.2%)	0 (0%)	64 (3.2%)		525 (4.8%)	3 (5.9%)	528 (4.8%)	
Former	462 (23.4%)	1 (10.0%)	463 (23.3%)		1490 (13.6%)	9 (17.7%)	1499 (13.6%)	
Never	1300 (65.8%)	9 (90.0%)	1309 (65.9%)		7941 (72.6%)	34 (66.7%)	7975 (72.5%)	
Unknown	149 (7.5%)	0 (0%)	149 (7.5%)		990 (9.0%)	5 (9.8%)	995 (9.1%)	
Comorbidities								
Hypertension	967 (48.9%)	3 (30.0%)	970 (48.9%)	0.344	2421 (22.1%)	10 (19.6%)	2431 (22.1%)	0.667
Diabetes mellitus	573 (29.0%)	2 (20.0%)	575 (29.0%)	0.733	1155 (10.6%)	4 (7.8%)	1159 (10.5%)	0.530
Ischemic heart disease	138 (7.0%)	0 (0%)	138 (7.0%)	1.000	171 (1.6%)	1 (2.0%)	172 (1.6%)	0.553
PVD	427 (21.6%)	0 (0%)	427 (21.5%)	0.132	540 (4.9%)	1 (2.0%)	541 (4.9%)	0.518
CHF	145 (7.3%)	0 (0%)	145 (7.3%)	1.000	130 (1.2%)	0 (0%)	130 (1.2%)	1.000
Cerebrovascular disease	141 (7.1%)	1 (10%)	142 (7.2%)	0.525	179 (1.6%)	0 (0%)	179 (1.6%)	1.000
Renal disease	345 (17.5%)	1 (10.0%)	346 (17.4%)	1.000	366 (3.3%)	3 (5.9%)	369 (3.4%)	0.244
COPD	346 (17.5%)	1 (10.0%)	347 (17.5%)	1.000	1228 (11.2%)	3 (5.9%)	1231 (11.2%)	0.228
Asthma	467 (23.7%)	1 (10.0%)	468 (23.6%)	0.468	1518 (13.9%)	6 (11.8%)	1524 (13.9%)	0.665
Obstructive sleep apnea	150 (7.6%)	0 (0%)	150 (7.6%)	1.000	416 (3.8%)	3 (5.9%)	419 (3.8%)	0.445
Cancer	102 (5.16%)	1 (10.0%)	103 (5.2%)	0.418	176 (1.6%)	0 (0%)	176 (1.6%)	1.000
Health care utilization in the year before COVID-19 diagnosis								
Inpatient visits				1.000				0.637
0	1533 (77.6%)	9 (90.0%)	1542 (77.7%)		10,470 (95.7%)	51 (100.0%)	10,521 (95.7%)	
1	285 (14.4%)	1 (10.0%)	286 (14.4%)		377 (3.4%)	0 (0%)	377 (3.4%)	
2+	157 (8.0%)	0 (0%)	157 (7.9%)		99 (0.9%)	0 (0%)	99 (0.9%)	
Emergency department visits				0.200				0.646
0	1186 (60.1%)	8 (80.0%)	1194 (60.2%)		8596 (78.5%)	39 (76.5%)	8635 (78.5%)	
1	460 (23.3%)	0 (0%)	460 (23.2%)		1630 (14.9%)	7 (13.7%)	1637 (14.9%)	
2+	329 (16.7%)	2 (20.0%)	331 (16.7%)		720 (6.6%)	5 (9.8%)	725 (6.6%)	
Outpatient visits				0.215				<0.001
0	240 (12.15%)	0 (0%)	240 (12.1%)		2240 (20.5%)	2 (3.9%)	2242 (20.4%)	
1	238 (12.05%)	2 (20.0%)	240 (12.1%)		1990 (18.2%)	4 (7.8%)	1994 (18.1%)	
2–4	552 (27.95%)	5 (50.0%)	557 (28.1%)		3612 (33.0%)	16 (31.4%)	3628 (33.0%)	
5+	945 (47.85%)	3 (30.0%)	948 (47.8%)		3104 (28.4%)	29 (56.9%)	3133 (28.5%)	

CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; PVD, peripheral vascular disease.

nonhospitalized patients perhaps because a greater proportion of HIV-uninfected patients were older than PLWH. In addition, obesity is a significant risk factor of poorer outcomes associated with COVID-19.⁴ PLWH in this sample were significantly less obese than HIV-uninfected patients (Table 2), which may have been a protective factor.

Our study had several strengths and limitations. We used population-level data for PLWH and HIV-uninfected individuals in a large integrated health care system to assess the incidence of testing, diagnosis, and hospitalization outcomes for COVID-19. Data were inclusive of patients who exhibited mild illness and did not require hospitalization, which adds to literature describing case series of hospitalized patients with HIV.^{7,9,10,13,14,16,17,21}

Analyses were limited by relatively small numbers of PLWH with COVID-19 during the early months of the pandemic. In addition, 4 cases in PLWH with COVID-19 were excluded of an initial 61 identified by ICD-10 diagnostic codes and laboratory results because of incorrect diagnoses. We were unable to manually review all cases of clinically diagnosed COVID-19 in HIV-uninfected patients, potentially overestimating the incidence of diagnosis in HIV-uninfected patients.

In the United States, only 62.7% of all PLWH are virally suppressed, as defined by an HIV viral load of <200 copies/mL.²² As such, our findings may not be generalizable to all PLWH because both hospitalized and nonhospitalized PLWH in our study exhibited >95% virologic suppression, with very few cases where CD4⁺ counts were ≤200 cells/mm³.

In this cohort of PLWH with largely well-controlled HIV, we found that both incidence of testing and incidence of diagnosed COVID-19 were higher in PLWH than in HIV-uninfected patients. Hospitalizations were observed to be proportionally higher in PLWH than in HIV-uninfected patients in our study sample.

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