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SARS-CoV-2 Incidence, Testing Rates, and Severe COVID-19 Outcomes among People with and without HIV: A Population-Based Case-Cohort Study

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Summary:

To assess SARS-CoV-2 outcomes, we matched a municipal COVID-19 registry and clinic rosters from a municipal primary care network containing a large HIV clinic and assessed clinical outcomes by HIV status. The risk of severe COVID-19 was higher among people living with HIV (PLWH; adjusted relative risk=1.84, 95% confidence interval=1.05–3.25), while SARS-CoV-2 incidence was lower despite higher testing rates. SARS-CoV-2 vaccination campaigns should prioritize PLWH to prevent severe COVID-19 disease given potentially higher risk.

Introduction:

Early studies examining the impact of HIV status on COVID-19 clinical outcomes, performed predominantly in hospitalized cohorts, suggested similar or better outcomes for people living with HIV compared (PLWH) to the general population.^[1] However hospitalized cohorts are susceptible to bias, particularly if the threshold for admission among PLWH could be lower than that for people without HIV.^[1–4] More recently, large population-based studies, including one in New York State, have demonstrated increased mortality risk among PLWH from COVID-19.^[2–4] Given the heterogeneity in SARS-CoV-2 susceptibility^[4–6] and clinical COVID-19 outcomes among cohorts of PLWH,^[1] we performed a large population-based study in San Francisco. This study examines the impact of HIV status on COVID-19 outcomes within a municipal primary care health system containing one of San Francisco's largest HIV clinics, Ward 86, over the first year of the COVID-19 pandemic.

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Materials and Methods:

We conducted a population-level match of the COVID-19 registry of the San Francisco Department of Public Health (SFDPH) with the clinic rosters of the San Francisco Primary Care Clinics (SFPC) from February 1, 2020, to March 1, 2021, including individuals with at least one visit in the prior two years. The SFDPH COVID-19 testing registry is a centralized reporting system capturing COVID-19 diagnoses, given that COVID-19 is a reportable illness locally. The SFPC is a safety-net municipal health system administered by the SFDPH comprising 12 adult medicine clinics, including one of the largest HIV clinics in San Francisco, Ward 86. We examined the COVID-19 attack rate and testing rate among the full prospective cohort by HIV status using Poisson mixed models with a random-effects for the individual patient identifier. To examine the severity of COVID-19 clinical outcomes by HIV status we performed a case-cohort study and assessed need for supplemental oxygen, use of a ventilator, and COVID-19-related death through in-depth chart review.^[7] We performed chart review among all PLWH with positive SARS-CoV-2 tests, and randomly sampled 591 adults without HIV with positive SARS-CoV-2 from the two largest adult medicine clinics within the health network. To assess risk of hospitalization, severe COVID-19, and death, we performed binomial relative risk regression, with the inclusion of probability weights and robust standard errors to account for the sampling fraction.^[7]

Results:

Attack and Testing Rate

Overall, there were 22,024 participants examined over 25,630 person-years at risk in the SFPC system, of whom 2,690 were PLWH examined over 3,168 person-years (Table). The SARS-CoV-2 incidence was 79.1 per 1,000 person-years [95% confidence interval (CI): 75.6–83.9] among people without HIV and 34.7 per 1,000 person-years (95% CI 37.0–51.6) among PLWH. When adjusting for age, sex, and race/ethnicity, the rate of SARS-CoV-2 infection was 40% lower among PLWH (adjusted rate ratio (ARR) 0.60; 95% CI: 0.50–0.72). The rate of SARS-CoV-2 infection was 210% higher among Latinx vs. White individuals (ARR 3.10; 95% CI: 2.65–3.63). The rate of SARS CoV-2 testing was 8% higher among PLWH (ARR 1.08; 95% CI: 1.05–1.11) than people without HIV.

Clinical Outcomes

Overall, there were 1,915 cases of SARS-CoV-2 infection during this time-period, of which all PLWH were sampled (136) and a random sub-cohort which included 591 people without HIV. After adjusting for age, sex, and race/ethnicity, the risk of hospitalization among those with SARS-CoV-2 was 90% higher among PLWH [adjusted relative risk (ARR) 1.90; 95% CI: 1.21–2.98], while the risk of severe COVID-19 infection requiring supplemental oxygen was 84% higher among PLWH (ARR 1.84, 95% CI: 1.05–3.25). The ARR for requiring a ventilator among PLWH was 1.58 (95% CI: 0.52–4.83) and for death it was 1.90 (95% CI: 0.37–9.69). Among the 136 PLWH with SARS-CoV-2 infection, 29 were admitted, 16 required supplemental oxygen, 4 required a ventilator, and 3 died from COVID-19. The risk of severe COVID-19 requiring supplemental oxygen was 30% lower for each 100 CD4+ cell

increase in CD4+ count (RR 0.70; 95% CI: 0.49–0.99), while those with CD4+ counts <200 had a 150% higher risk (RR 2.50; 95% CI: 1.01–6.19). The RR for requiring supplemental oxygen with a detectable vs undetectable viral load was 1.3 (95% CI: 0.51–3.40).

Discussion:

In a population-based study of primary care patients over the first year following known SARS-CoV-2 community transmission within San Francisco, the risk of hospitalization and severe COVID-19 was higher among PLWH with SARS-CoV-2 than those without HIV. These results echo large, population-based studies within New York State, Western Cape, South Africa, and in the United Kingdom.^[2–4] Severe clinical outcomes appear most concentrated among PLWH with low CD4+ counts, presumably related to suppressed or a dysregulated immune response to respiratory infection among PLWH.^[2, 4, 8] SARS-CoV-2 vaccination is expected to attenuate this risk among PLWH.^[9]

SARS-CoV-2 incidence was lower among PLWH despite somewhat greater testing rates in this group, and is similar to the difference estimated via a prior seroprevalence study within a subset of these populations.^[10] This finding may reflect lower exposure to SARS-CoV-2 among PLWH, potentially related to greater adherence to non-pharmaceutical interventions such as physical distancing due to self-perception of higher SARS-CoV-2 risk.^[10] As vaccine distribution was just beginning at the end of the study period, it is unlikely that these results are influenced by differential vaccination rates.

Limitations of this analysis include our inability to adjust for other comorbid medical conditions impacting severe COVID-19. Higher testing rates among PLWH could also potentially lead to greater detection of asymptomatic infections among PLWH. However, greater detection of asymptomatic infections would not be expected to qualitatively impact our results, as this bias would lead to an underestimation of COVID-19 disease severity among PLWH and an overestimation of the SARS-CoV-2 attack rate. Finally, our results should be considered reflective of individuals engaged in primary care within the SFPCC and may not reflect individuals in San Francisco not engaged in primary care.

The higher attack rate among Latinx individuals within this cohort reflects the known epidemic dynamics within San Francisco, influenced by underlying health disparities.^[11] Outreach and prioritization campaigns for SARS-CoV-2 vaccination should target the populations disproportionately impacted by COVID-19, as well as populations with potentially higher risk of severe outcomes, including PLWH.

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Table 1:

Population Characteristics and Clinical Outcomes among People Diagnosed with COVID-19

	Overall Population (n=22,024)	Diagnosed with COVID-19 (n=1,915)	p-value
Median Age (IQR)	47 (36–60)	52 (40–63)	p<0.0001
Female Sex % (n)	50% (11,036)	56% (1,074)	p<0.0001
Race/ethnicity:			
American Indian % (n)	1% (273)	1% (27)	
Asian % (n)	21% (4,515)	10% (186)	
Black % (n)	12% (2,749)	8% (147)	
Latinx % (n)	41% (8,955)	68% (1298)	
White % (n)	20% (4,308)	10% (189)	
Pacific Islander % (n)	1% (266)	2% (29)	
Mixed/Other % (n)	4% (958)	2% (44)	p<0.0001
People living with HIV (PLWH) % (n)	12% (2,690)	7% (136)	p<0.0001
COVID-19 Incident Infection:			
Adjusted Rate Ratio ¹ (95% CI) for COVID-19 infection for PLWH	0.60 (95% CI: 0.50–0.72)		p<0.0001
Severe COVID-19: ¹			
Living with HIV % (n) ³	-	12% (16) ³	
Without HIV % (n) ³		7% (38) ³	
Adjusted Relative Risk ⁴ for severe disease (95% CI) for PLWH	1.84 (95% CI: 1.05–3.25)		p=0.01

IQR: interquartile range; CI: Confidence Interval

¹Adjusted for age, sex, and race/ethnicity²Defined as hypoxia with oxygen saturation at 2 readings requiring supplemental oxygen³Among all 136 PLWH and 591 people without HIV randomly sampled for in-depth chart review