Symptoms and Biomarkers of Long COVID in People Living With and Without HIV

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Background

• The incidence of long COVID after SARS-CoV-2 infection is 10% or greater, even in people who were vaccinated prior to infection.

• Living with HIV is a risk factor for severe acute COVID-19, but it is unknown whether living with HIV is a risk factor for long COVID.

Objectives

• To characterize symptoms in the first 12 months after initial SARS-CoV-2 infection in people living with and without HIV as compared to people who never had SARS-CoV-2 infection.

• To identify blood-based biomarkers or immune signatures associated with long COVID symptoms in people living with HIV (PWH).

Study Design & Methods

• We conducted a nation-wide, one year prospective observational cohort study enrolling adults 18+ years old who speak either English or Spanish.

• Fully remote study: all study events could be completed from a location of the participant's choosing, such as their home. Surveys were completed online or by telephone. Blood draws, orthostatic vital signs, height and weight were obtained via mobile phlebotomist.

• Participants living with and without HIV who had their first known SARS-CoV-2 infection within the previous 4 weeks were enrolled. Additionally, participants who believed they had never had SARS-CoV-2 infection (never-COVID) were enrolled. If a never-COVID participant had a positive anti-SARS-CoV-2 nucleocapsid antibody, they were removed from the analyses.

• Symptom surveys were based on the FLU-PRO Plus plus 11 additional symptoms from patient-led long COVID surveys, and participants were asked to name other symptoms. At enrollment, post-COVID participants were asked to recall symptoms in the month prior to SARS-CoV-2 infection.

• 32-plex cytokine panel + cortisol and MSD-platform based multiplex antibody and pseudo-neutralization assays were performed in batches on thawed plasma or serum. Tests performed in the Rush University Hospital clinical laboratory include: CBC w/diff, CD4, HIV antigen/antibody, SARS-CoV-2 anti-nucleocapsid IgG, d-dimer, high sensitivity C-reactive protein, creatine kinase, and lipid panel.

• In unadjusted analyses, PWH were more likely to report 1+ new/worsened symptoms post-COVID at 2 months but not at 4 or 6 months post-COVID compared to HIV-seronegative people.

• MIP-5/CCL19 levels were elevated in PWH post-COVID compared to never-COVID PWH.

• Inflammatory networks remain activated at 1 month post-COVID in all people and at 4 months post-COVID in PWH.

• Preliminary analyses link cortisol, TIM-3, TGF-beta, and C5a levels with specific long COVID symptoms.

	Entry	M1	M2	M4	M6	M12
Surveys	x	x	x	x	x	x
Neurocognitive batteries		x		x		
Blood, height, weight, orthostatic vitals		x[1]		x[2]		

[1]Optional for HIV-seronegative never-COVID (arm 4)
[2]Only post-COVID study arms (arms 1&2)

Figure 1. Study event schedule.

Table 1. Participant characteristics.

	Post-COVID PWH n=73	*Post-COVID HIV seronegative n=121*	*Never-COVID PWH n=78*	*Never-COVID HIV seronegative n=69*
Age (y), median (IQR)	47 (35-58)	35 (26-48)	59 (50-64)	53 (37-62)
Male sex at birth, %	83.6	35.5	59.0	40.6
Transgender, %	1.4	2.5	2.6	0
Hispanic ethnicity, %	19.2	4.1	9.0	8.7
Black/African American race, %	32.9	12.4	57.7	8.7
White race, %	47.9	68.6	37.2	73.9
Asian race, %	4.1	14.0	1.3	10.1
BMI, median (IQR)	26.3 (23.2-31.8)	25.5 (21.7-31.1)	28.3 (23.5-33.8)	23.6 (22.9-31.9)
Recent tobacco use, %	26.0	1.7	32.1	4.4
<1 hour/week exercise, %	19.7	14.9	22.6	10.7
Hypertension, %	11.0	5.8	20.5	7.2
COPD/emphysema, %	2.7	0	10.3	1.5
Diabetes, %	8.2	0.8	24.4	4.4
Chronic kidney disease, %	2.7	0	3.9	0
Asymptomatic COVID, %	8.2	0.8		
Hospitalized for COVID, %	5.5	0.8		
1+ vaccines prior to COVID, %	84.9	95.9		
Self-reported CD4, median (IQR)	586 (379-758)		736 (486-962)	
Reported taking ART, %	98.6		97.4	

Results

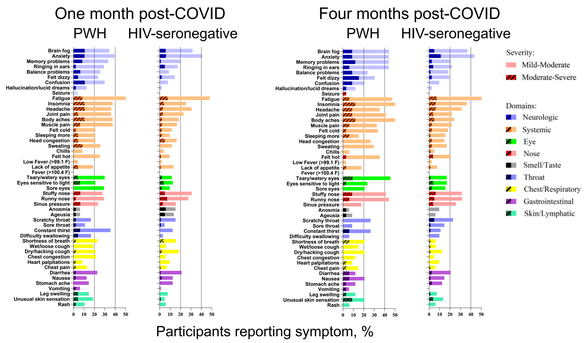

Figure 2. Post-COVID symptom prevalence by HIV serostatus.

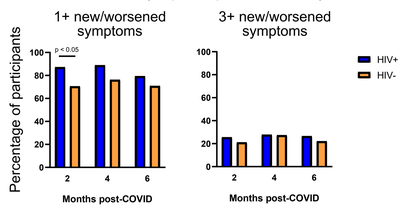

Figure 3. Participants with new or worsened symptoms by HIV serostatus.

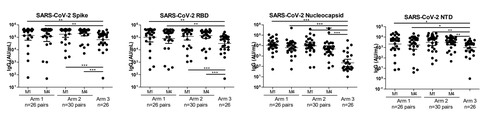

Figure 4. No differences in SARS-CoV-2 antibody titers post-COVID by HIV serostatus.

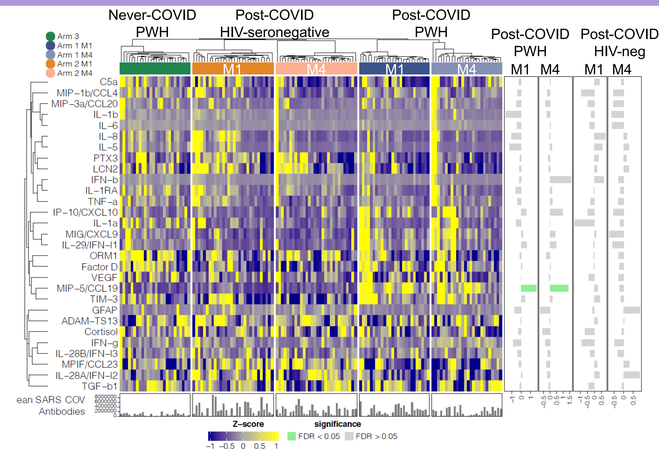

Figure 5. Hierarchical cluster analysis applied to cytokine levels identifies increased MIP-5/CCL19 levels in PWH post-COVID. Right panels indicate log2 fold changes from each group versus never-COVID PWH (arm 3).

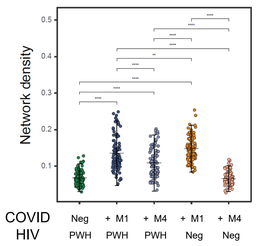

Figure 6. The network density of correlations between cytokines is depicted and suggests that inflammatory networks remain activated 1 month after COVID in PWH and HIV-seronegative people.

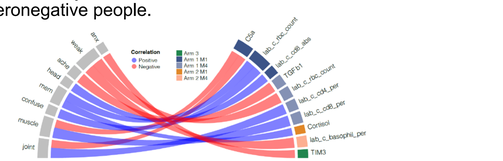

Figure 7. Chord diagram showing associations between specific symptoms and biomarkers within each group.

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