Chronic HIV Infection Impacts the Immune Response during Acute SARS-CoV-2

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BACKGROUND

- SARS-CoV-2 infection typically causes self-limited disease, but ~20% experience more severe disease
- Despite effective antiretroviral therapy (ART), people living with HIV (PLWH) experience persistent immune activation and inflammation

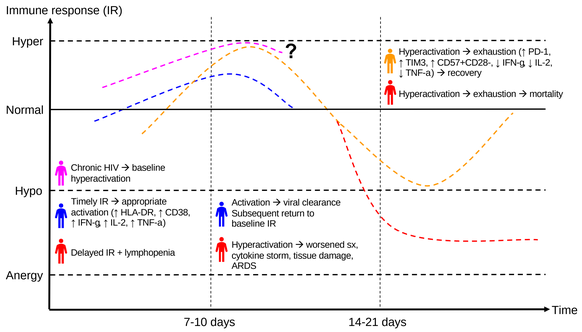


Figure 1. Immune response over time with mild vs severe SARS-CoV-2 infection. Blue – mild disease. Orange – severe disease/recovery. Red – severe disease/mortality. Pink – chronic HIV-infection

There is limited data exploring how immune responses in acute COVID-19 may be altered in PLWH

METHODS

Peripheral blood mononuclear cells isolated and then stained: 1) Immune cell populations 2) Activation/Exhaustion markers 3) Activation-Induced Markers (AIM) 4) Intracellular Cytokine Staining (ICS). For AIM/ICS, cells were stimulated with either a SARS-CoV-2 Spike (S) peptide pool or Membrane/Nucleocapsid/Envelope (M) peptide pool.

Study goal:

Define & compare immune responses during acute COVID-19 in people living with HIV (PLWH) vs HIV-negative individuals, stratified by acute COVID-19 severity

Conclusions:

- PLWH have increased T cell activation & exhaustion and increased classical monocytes compared to HIV-negative presentations of acute COVID-19
- Hospitalized PLWH trended toward decreased T cell activation & exhaustion

	HIV+COVID (n=22)	HIV (n=11)	COVID (n=41)	p value
Age	52 (30-76)	50 (24-72)	65 (25-93)	**0.0007***
Sex				0.4261
Female	11 (50%)	6 (54.5%)	24 (58.5%)	
Male	11 (50%)	5 (45.5%)	17 (41.5%)	
Race				0.3508
AA	14 (63.6%)	8 (72.7%)	26 (63.4%)	
W	8 (36.4%)	2 (18.2%)	15 (36.6%)	
Multiracial	0 (0%)	1 (9.1%)	0 (0%)	
Days post-symptom onset	6 (1-20)		4 (0-16)	0.2157
Clinical Outcome (WHO severity scale)				**0.0136***
(4) No O2 requirement	14 (63.6%)		12 (29.3%)	
(5) Nasal cannula	1 (4.5%)		16 (39%)	
(6) High flow	4 (18.2%)		4 (9.8%)	
(7) Ventilator	2 (9.1%)		3 (7.3%)	
(8) Deceased	1 (4.5%)		6 (14.6%)	
Hospitalization status				**< 0.0001***
Hospitalized	8 (36.4%)		36 (87.8%)	
Non-hospitalized	14 (63.6%)		5 (12.2%)	
Viral Suppression	20 (90.9%)	6 (54.5%)		**0.0274***
CD4				
Percent	31% (13-45%)	29% (10-44%)		0.618
Count	739 (181-1619)	693 (251-1238)		0.8759
ART Regimen				**0.0108***
NRTI	20 (90.9%)	7 (63.6%)		
NNRTI	0 (0%)	3 (27.3%)		
PI	4 (18.2%)	0 (0%)		
INSTI	19 (86.4%)	4 (36.4%)		
Comorbidities				0.8491
Hypertension	18 (81.8%)		34 (82.9%)	
Obesity	10 (45.5%)		21 (51.2%)	
Diabetes	8 (36.4%)		22 (53.7%)	
COPD	6 (27.3%)		8 (19.5%)	
Cancer	5 (22.7%)		8 (19.5%)	

Monocyte frequencies

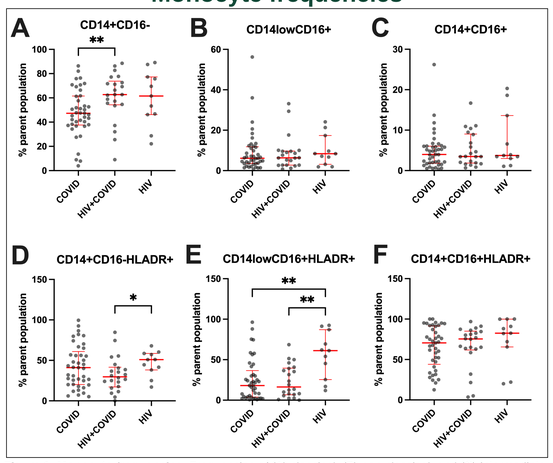


Figure 1. Monocyte frequencies. Frequencies of (A) classical, (B) non-classical, and (C) intermediate monocytes. (D-F) Frequencies of activated monocytes, classified by HLA-DR expression, from the previously mentioned subsets. COVID – HIV-seronegative participants experiencing acute COVID-19. HIV+COVID – HIV-seropositive participants experiencing acute COVID-19. HIV – HIV-seropositive participants without SARS-CoV-2 infection. Red bars denote median and interquartile range. P values determined by Mann Whitney U test are as follows: * p < 0.05, ** p < 0.01.

T cell expression of activation/exhaustion markers

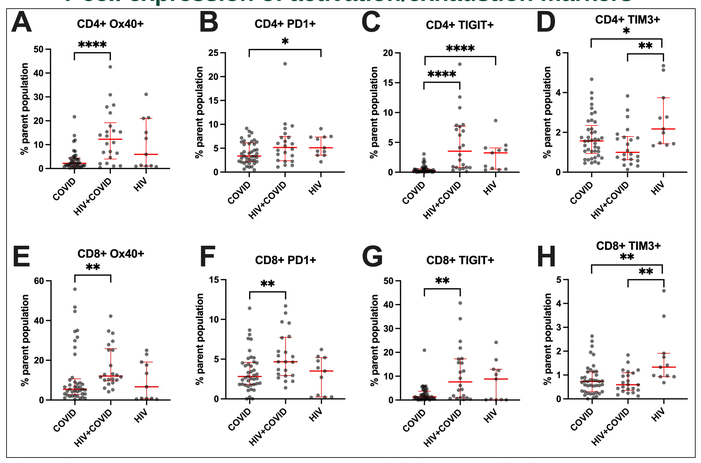


Figure 2. T cell expression of activation and exhaustion markers. (A-D) Frequencies of CD4+ T cells expressing activation markers CD137 and OX40 and exhaustion markers PD1 and TIGIT. (E-H) Frequencies of CD8+ T cells expressing activation markers CD137 and OX40 and exhaustion markers PD1 and TIGIT. COVID – HIV-seronegative participants experiencing acute COVID-19. HIV+COVID – HIV-seropositive participants experiencing acute COVID-19. HIV – HIV-seropositive participants without SARS-CoV-2 infection. Red bars denote median and interquartile range. P values determined by Mann Whitney U test are as follows: * p < 0.05, ** p < 0.01, **** p < 0.0001.

CONCLUSIONS

- PWLH had increased expression of activation and exhaustion markers and increased classical monocytes
- There were limited SARS-CoV-2-specific responses detected in early infection with a bias toward TNF-α
- Future studies include expanding upon our findings by examining plasma and tissue-specific immune responses, as well as analyzing the impact of infection duration on the immune response

ACKNOWLEDGEMENTS

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T cell activation/exhaustion by hospitalization status

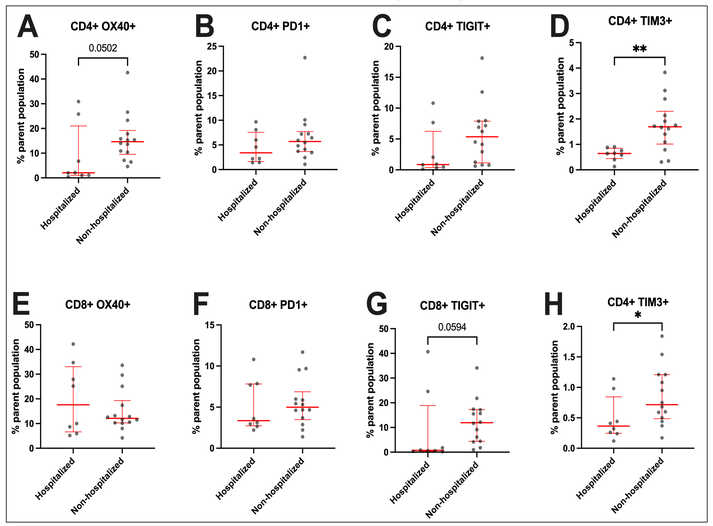


Figure 3. T cell expression of activation and exhaustion markers by hospitalization status from participants in the HIV+COVID cohort. (A-D) Frequencies of CD4+ T cells expressing activation markers CD137 and OX40 and exhaustion markers PD1 and TIGIT. (E-H) Frequencies of CD8+ T cells expressing activation markers CD137 and OX40 and exhaustion markers PD1 and TIGIT. Red bars denote median and interquartile range. P values determined by Mann Whitney U test.

AIM & ICS results

AIM	COVID (n=41)	HIV+COVID (n=22)	p value
S pool			
CD4+OX40+CD137	2 (4.9%)	4 (18.2%)	0.1714
CD8+CD69+CD137	0 (0%)	0 (0%)	1
M pool			
CD4+OX40+CD137	2 (4.9%)	4 (18.2%)	0.1714
CD8+CD69+CD137	0 (0%)	0 (0%)	1

HIV+COVID: Days post-symptom onset

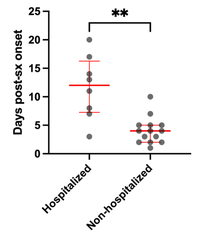


Figure 4. Days post-symptom onset markers by hospitalization status from participants in the HIV+COVID cohort. Red bars denote median and interquartile range. P value determined by Mann Whitney U test. ** p < 0.01

ICS	COVID (n=41)	HIV+COVID (n=22)	p value
S pool			
CD4+ IFN	0 (0%)	0 (0%)	1
CD4+ IL-2	2 (4.9%)	5 (22.7%)	**0.0449***
CD4+ IL-17A	1 (2.4%)	0 (0%)	1
CD4+ TNFa	23 (56.1%)	9 (40.9%)	1
CD4+ ICS total	23 (56.1%)	12 (54.5%)	1
CD8+ IFN	1 (2.4%)	1 (4.5%)	1
CD8+ IL-2	0 (0%)	2 (9.1%)	0.1183
CD8+ TNFa	0 (0%)	3 (13.6%)	**0.0388***
CD8+ ICS total	1 (2.4%)	4 (18.2%)	**0.0464***
M pool			
CD4+ IFN	0 (0%)	0 (0%)	1
CD4+ IL-2	4 (9.8%)	4 (18.2%)	0.4338
CD4+ IL-17A	4 (9.8%)	2 (9.1%)	1
CD4+ TNFa	24 (58.5%)	9 (40.9%)	0.1991
CD4+ ICS total	26 (63.4%)	11 (50%)	0.4213
CD8+ IFN	0 (0%)	0 (0%)	1
CD8+ IL-2	0 (0%)	0 (0%)	1
CD8+ TNFa	0 (0%)	1 (4.5%)	0.3492
CD8+ ICS total	0 (0%)	1 (4.5%)	0.3492