High RNAemia Associates with Skewed T-Cell Response in PLWH Hospitalized for COVID-19

Matteo Augello[1], Valeria Bono[1], Roberta Rovito[1], Camilla Tincati[1], Silvia Bianchi[2], Lucia Taramasso[3], Antonio Di Biagio[3,4], Annapaola Callegaro[5], Franco Maggiolo[6], Elisa Borghi[2], Antonella d'Arminio Monforte[1], Giulia Marchetti[1]

[1] *Clinic of Infectious Diseases and Tropical Medicine, San Paolo Hospital, ASST Santi Paolo e Carlo, Department of Health Sciences, University of Milan, Milan, Italy.* [2] *Microbiology and Clinical Microbiology, Department of Health Sciences, University of Milan, Milan, Italy.* [3] *Infectious Diseases Unit, San Martino Policlinico Hospital.* [4] *Department of Health Sciences, University of Genoa, Genoa, Italy.* [5] *Biobank Unit and Microbiology and Virology Laboratory, ASST Papa Giovanni XXIII, Bergamo, Italy.* [6] *Division of Infectious Diseases, ASST Papa Giovanni XXIII, Bergamo, Italy.*

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BACKGROUND

People living with HIV (PLWH) may display an increased risk of severe COVID-19 outcomes[1]. High SARS-CoV-2 RNAemia has emerged as a hallmark of severe disease[2], yet its pathogenic role in the context of COVID-19 in PLWH is unknown. We hereby measured SARS-CoV-2 RNAemia and explored its association with T-cell and humoral responses, inflammation and clinical severity in PLWH.

METHODS

- **Study population**: unvaccinated **PLWH** and **age/sex-matched people living without HIV (PLWOH)** hospitalized for **COVID-19 pneumonia** at a median of **10 days from symptoms onset** (March 2020 – January 2021)
- **SARS-CoV-2 RNAemia**: plasma → *RT-qPCR*
- **T-cell activation** (HLA-DR+CD-38+), **cytotoxic T-cells** [granzyme-B(GRZB)+perforin(PRF)+], **GRZB/PRF production** (MFI) **by cytotoxic T-cells**: PBMCs → *flow cytometry*
- **SARS-CoV-2–specific T-cells**: PBMCs (stimulation with wild type SARS-CoV-2 S+N+M peptides) → *flow cytometry*
- **Anti-RBD antibodies**: plasma → *ELISA*
- **Spike-ACE2 binding inhibition activity**: plasma → *receptor binding inhibition assay*
- **Statistics**: *Mann-Whitney test* and *Spearman's correlation*

RESULTS I

Demographic and clinical characteristics of study participants

	HIV+ (*n*=18)	HIV– (*n*=18)	*P* value*
Age, years [median (IQR)]	60 (49–67)	60 (47–66)	0.7843
Sex [*n* (%)]			>0.9999
Male	14 (77.8)	14 (77.8)	
Female	4 (22.2)	4 (22.2)	
Ethnicity [*n* (%)]			0.0903
Caucasian	15 (83.3)	13 (72.2)	
Latin-American	1 (5.6)	5 (27.8)	
African	2 (11.1)	0 (0)	
Comorbidities [*n* (%)]			
Hypertension	9 (50)	5 (27.8)	0.3053
Chronic heart disease	4 (22.2)	5 (27.8)	>0.9999
Chronic pulmonary disease	1 (5.6)	1 (5.6)	>0.9999
Chronic kidney disease	3 (75)	1 (25)	0.6026
Liver disease	5 (27.8)	1 (5.6)	0.1774
Diabetes	2 (11.1)	6 (33.3)	0.2285
Neurologic disease	4 (22.2)	1 (5.6)	0.3377
History of cancer	5 (27.8)	2 (11.1)	0.4018
P_aO_2/F_iO_2 nadir [median (IQR)]	140 (122–151.5)	207 (156.3–309.3)	**0.0005**
Maximum oxygen therapy [*n* (%)]			0.1756
Low-flow systems	10 (55.6)	5 (27.8)	
CPAP/NIV/OTI	8 (44.4)	13 (72.2)	
Outcome [*n* (%)]			>0.9999
Death	1 (5.6)	0 (0)	
Dismissal	17 (94.4)	18 (100)	

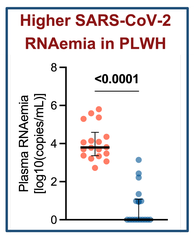
IQR: interquartile range; P_aO_2: arterial partial pressure of oxygen; F_iO_2: fraction of inspired oxygen; CPAP: continuous positive airway pressure; NIV: noninvasive ventilation; OTI: orotracheal intubation.
*Statistical analyses: Mann-Whitney *U* test, Fisher exact test, Chi-square test.

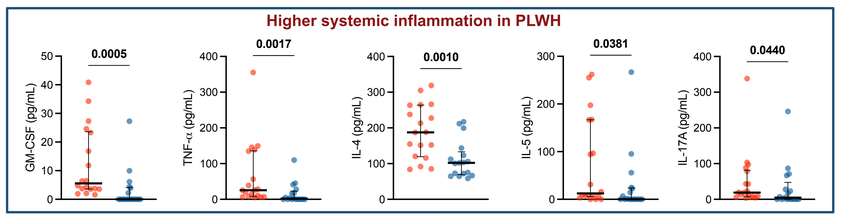
PLWH hospitalized for acute COVID-19 pneumonia feature ***high SARS-CoV-2 RNAemia***, which is associated with ***greater systemic inflammation***, ***skewed T-cell responses*** despite preserved humoral immunity, and ***worse disease severity***

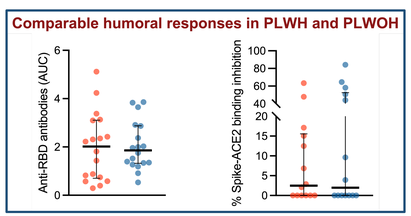
RESULTS II

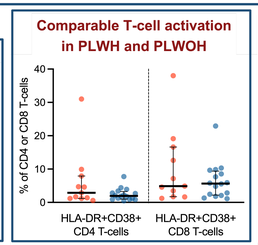
HIV-related characteristics of PLWH

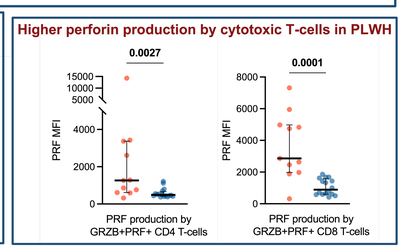
Immunologic parameters [median (IQR)]	
CD4 T-cell count nadir, cells/μL	59 (12.5–331.3)
Current CD4 T-cell count, cells/μL	361.5 (210.3–653.5)
Current CD4/CD8 ratio	0.4 (0.11–1.1)
Current plasma HIV-RNA [*n* (%)]	
Undetectable (<50 copies/mL)	15 (83.3)
Previous AIDS diagnosis [*n* (%)]	5 (27.8)
Time from HIV diagnosis, years [median (IQR)]	18 (6.25–34.5)
Current cART regimen [*n* (%)]	
INSTI-based	9 (50)
PI-based	3 (16.7)
INSTI+PI-based	1 (5.6)
NNRTI-based	3 (16.7)
None (cART-naïve)	2 (11)

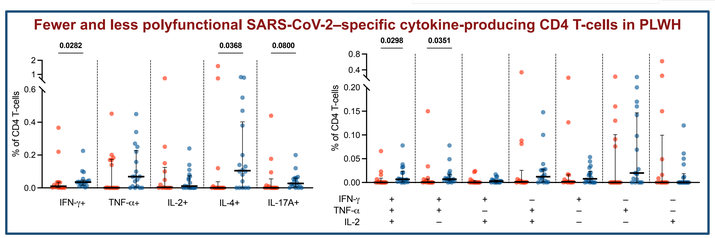


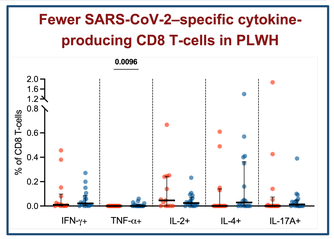








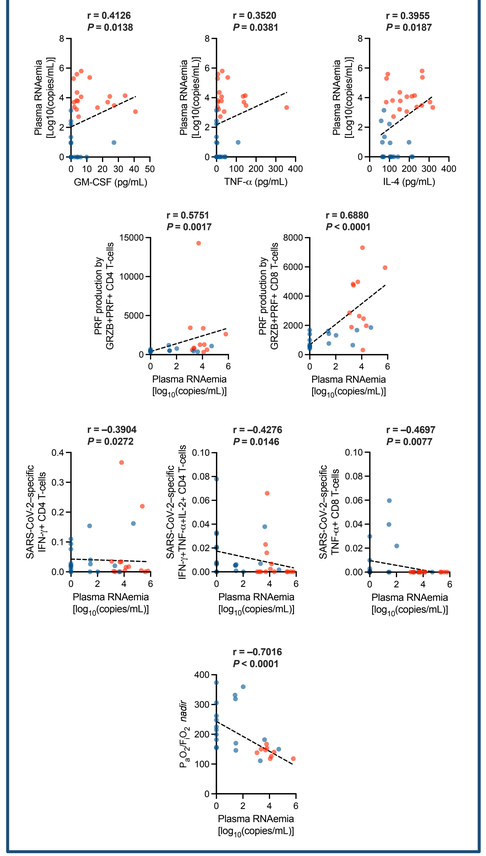




HIV+ HIV–

RESULTS III

SARS-CoV-2 RNAemia correlates positively with plasma inflammatory cytokines and perforin production by cytotoxic T-cells, and negatively with SARS-CoV-2–specific T-cells and P_aO_2/F_iO_2 *nadir*



CONCLUSIONS

As compared to PLWOH, **PLWH hospitalized for COVID-19 pneumonia** feature **high SARS-CoV-2 RNAemia** which is linked to **elevated plasma cytokines**, **skewed T-cell responses** and **worse parameters of respiratory function**. Our data suggest a link between HIV-related T-cell dysfunction and poor control over circulating SARS-CoV-2 that may in turn fuel systemic inflammation and influence COVID-19 severity in PLWH.

ADDITIONAL KEY INFORMATION

Author contact: matteo.augello@unimi.it. **References**: [1] Augello et al., *Curr HIV/AIDS Rep*, 2023; [2] Rovito et al., *Sci Rep*, 2022.