PLASMA-BASED ANTIGEN PERSISTENCE IN THE POST-ACUTE PHASE OF SARS-COV-2 INFECTION

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BACKGROUND

- The causes of post-acute sequelae of SARS-CoV-2 infection (PASC) remain elusive.
- Persistence of SARS-CoV-2, either as replication-competent virus or viral remnants, has been proposed as one of the underlying mechanisms of PASC.
- Initial use of a plasma-based assay for SARS-CoV-2 antigen revealed that a high fraction of severely affected patients with PASC had circulating antigen.[1]
- It is unknown whether detectable SARS-CoV-2 antigen is specific for PASC or how the assay performs in a broader clinical spectrum of PASC patients.

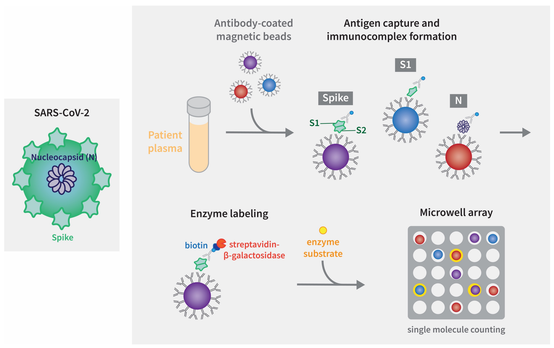
PARTICIPANTS

- Adults with RNA-confirmed SARS-CoV-2 infection enrolled ≥ 3 weeks following initial symptoms.[2]
- Identified via facility- and community-based advertising.
- Examined every 4 months.

MEASUREMENTS

- An interviewer-administered questionnaire ascertained presence of 30 symptoms (new or worse compared to pre-COVID) in the prior 2 days at each exam.
- We used the single molecule array (Simoa) assay to measure spike, S1, and nucleocapsid in plasma collected at the time of assessment (Fig 1.).

Figure 1. Schematic of single molecule array assay for detection of SARS-CoV-2 antigen in plasma samples.



RESULTS

Table 1. Characteristics of participants at enrollment.

Age	46 (37-57)
Female sex at birth	86 (50%)
Race	
White	92 (54%)
Black	8 (5%)
Asian	17 (10%)
Pacific Islander	3 (2%)
Hispanic/Latino	47 (27%)
Comorbid medical conditions	
Diabetes	17 (10%)
Obesity	33 (19%)
Lung disease	30 (17%)
HIV	25 (15%)
Hospitalized with COVID	33 (19%)
Vaccinated prior to enrollment	5 (3%)

Figure 3. Antigen measurements over time in participants with at least one positive antigen.

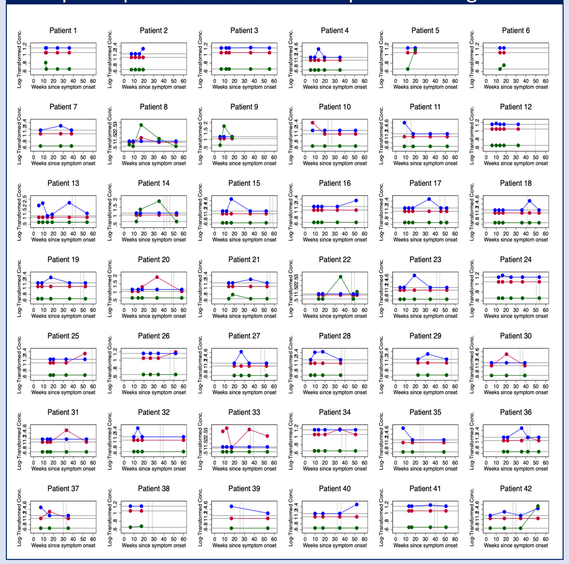
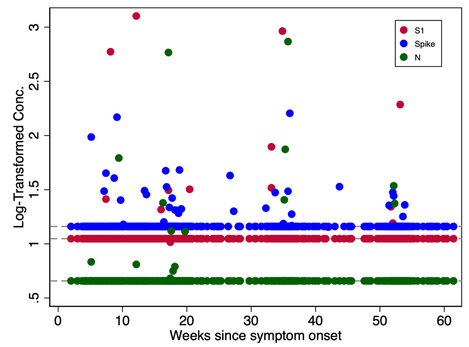


Figure 2. Plasma antigen measurements.



Time Since Symptom Onset (Months)	No. Visits in Bin	Any Antigen Detected	S1 Detected	Spike Detected	N Detected
1-3	175	11 (6%)	2 (1%)	7 (4%)	2 (1%)
4-5	195	22 (11%)	4 (2%)	11 (6%)	8 (4%)
6-7	27	3 (11%)	1 (4%)	2 (7%)	0 (0%)
8-9	107	12 (11%)	4 (4%)	5 (5%)	3 (3%)
10-11	32	4 (13%)	1 (3%)	3 (9%)	0 (0%)
12-13	36	4 (11%)	2 (6%)	2 (6%)	0 (0%)
14-16	91	5 (5%)	1 (1%)	3 (3%)	2 (2%)

Figure 4. Relationship between antigen presence and median symptom count.

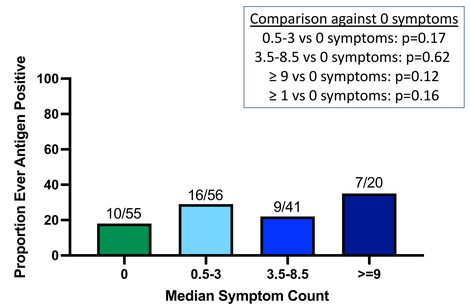
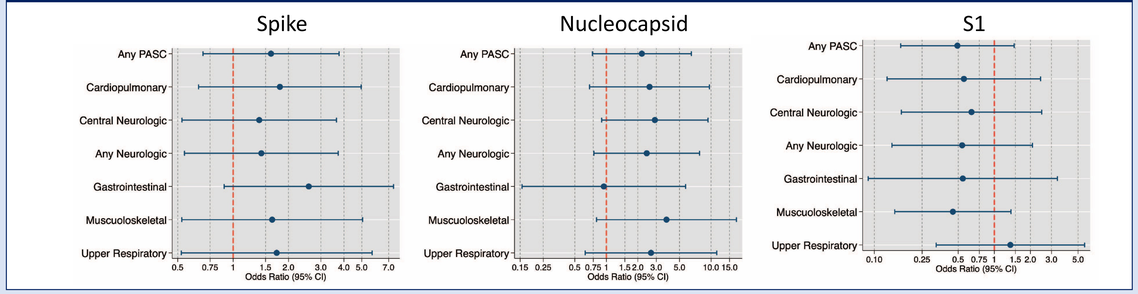


Figure 5. Associations between plasma antigens and symptom clusters.



RESULTS, continued

- 172 participants contributed 667 timepoints from 0.7 to 15.4 months following infection (Table 1).
- 61 of 667 timepoints (9.1%) representing 24% of participants had ≥ 1 detectable SARS-CoV-2 antigen (Fig. 2).
- Most timepoints at which antigen was detected (51/61, 84%) occurred before the participant had ever received a SARS-CoV-2 vaccine (Fig. 3).
- 66% of timepoints featured report of ≥1 symptom.
- Among the 437 timepoints at which ≥ 1 symptom was present, 9.8% had ≥ 1 detectable antigen. This compares to 7.8% of timepoints at which symptoms were absent.
- Compared to participants with persistently no symptoms, those with persistent symptoms had a higher probability of having ≥ 1 timepoint with ≥ 1 detectable antigen (Fig. 4).
- Regarding specific symptoms, participants with gastrointestinal (for spike), neurologic (for N), and musculoskeletal symptoms (for N) had a higher prevalence of detectable antigen compared to participants without any symptoms (Fig. 5).

CONCLUSIONS

- SARS-CoV-2 antigen appears to persist in at least some individuals for at least 14 months following initial infection.
- Presence of SARS-CoV-2 antigen is more frequent in persons with persistent symptoms and some specific symptoms than persons with no symptoms. This suggests but does not prove that antigen is causally related to symptoms.
- That antigen is found in only a fraction of those with PASC indicates either that (1) not all symptoms are driven by antigen, (2) current plasma antigen detection is insensitive relative to tissue, or (3) nominal PASC symptoms are sometimes unrelated to SARS-CoV-2.

REFERENCES

1. Swank et al. Clin Infect Dis 2022.
2. Peluso et al. Open Forum Infect Dis 2022.