Evaluation of Salivary Antibody in Protection from SARS-CoV-2 Infection

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BACKGROUND

The mucosal immune response may have an important role in control of COVID-19 infection and protection from reinfection
The higher levels of mucosal anti-SARS-CoV-2 achieved in people with hybrid immunity could in part explain why natural infection (hybrid immunity) is superior to vaccine only immunity against breakthrough COVID infection.
By extension, if mucosal immunity were stronger or more durable than intramuscular vaccine only immunity, it could provide rationale for development of a mucosal vaccine .

OBJECTIVES:

To determine the IgG and IgA antibody levels in the saliva of a subset of persons participating in a longitudinal observational study of COVID immunity
To compare responses in those with vaccine only and hybrid immunity and assess antibody decay over time.
To determine whether the presence of mucosal IgA protected against reinfection in the subsequent 10 months.

METHODS

A stratified random sample of 51 persons participating in a longitudinal study of antibody responses to COVID vaccines (STOPCoV, n=1286)) were enrolled
They provided salivary samples for analysis in Dec 2022 (baseline) and April 2023 (4 month follow up)
The specimens were assessed for IgG and IgA to spike protein, receptor binding domain to Wuhan ancestral strain and Omicron variant
We compared those with vaccine only (mean 5 doses- no history or prior infection) to those with hybrid immunity (breakthrough in the previous 6 months)

RESULTS

Table 1: Characteristics of cohort compared based on hybrid/vaccine-only immunity up to the baseline visit. BMI: body mass index, IQR: interquartile range, SD: standard deviation.

Variable Value	Hybrid	Vaccine-only	Total	P-value
Total (N)	17 (33.3%)	34 (66.7%)	51	-
Age, n (%)				
30-50	2 (11.8%)	5 (14.7%)	7 (13.7%)	0.7735
70+	15 (88.2%)	29 (85.3%)	44 (86.3%)	
Mean (SD)	71.7 (13.4)	71.9 (12.2)	71.8 (12.5)	0.9444
Median (IQR)	76 (73, 77)	75 (72, 78)	75 (72, 78)	0.8028
Gender				
Female	11 (64.7%)	23 (67.6%)	34 (66.7%)	0.8336
Male	6 (35.3%)	11 (32.4%)	17 (33.3%)	
BMI, n (%)				
Healthy weight	13 (76.5%)	24 (70.6%)	37 (72.5%)	0.6572
Obese	4 (23.5%)	10 (29.4%)	14 (27.5%)	
Mean (SD)	27.1 (3.9)	27.1 (5.6)	27.1 (5.1)	0.9996
Median (IQR)	27 (24, 30)	26 (23, 31)	26 (24, 31)	0.6104
Racial background, n (%)				
Other	4 (23.5%)	2 (5.9%)	6 (11.8%)	0.0652
White	13 (76.5%)	32 (94.1%)	45 (88.2%)	
Smoking status, n (%)				
Never	10 (58.8%)	16 (47.1%)	26 (51.0%)	0.5766
Previous smoker	6 (35.3%)	17 (50.0%)	23 (45.1%)	
Current smoker	1 (5.9%)	1 (2.9%)	2 (3.9%)	
Comorbidities, diabetes or cardiovascular or respiratory or cancer n (%)				
No	6 (35.3%)	9 (26.5%)	15 (29.4%)	0.5145
Yes	11 (64.7%)	25 (73.5%)	36 (70.6%)	
Number of vaccinations up to baseline, n (%)				
Four	8 (47.1%)	3 (8.8%)	11 (21.6%)	0.0066
Five	9 (52.9%)	30 (88.2%)	39 (76.5%)	
Six	0 (0.0%)	1 (2.9%)	1 (2.0%)	
Time from last breakthrough/last vaccine to baseline (days)				
Mean (SD)	87.5 (95.6)	53.8 (29.0)	65.0 (61.1)	0.063
Median (IQR)	60 (32, 75)	48 (34, 75)	48 (32, 75)	0.6674

Hybrid immunity to SARS-COV-2 is associated with increased salivary IgA antibody relative to vaccine only immunity but decays rapidly challenging the role for mucosal vaccines

Figure 1-Salivary IgG and IgA at baseline to Receptor Binding domain and spike ancestral Wuhan and Omicron COVID variants (% positive control and 95% CI)

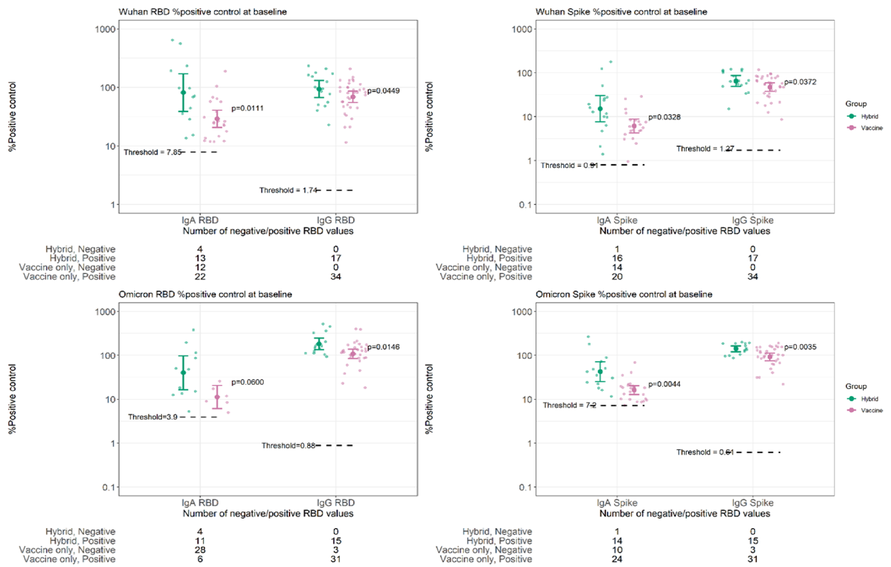


Figure 2_-Decay in salivary antibody between baseline and 4 month follow up (mean , standard error)

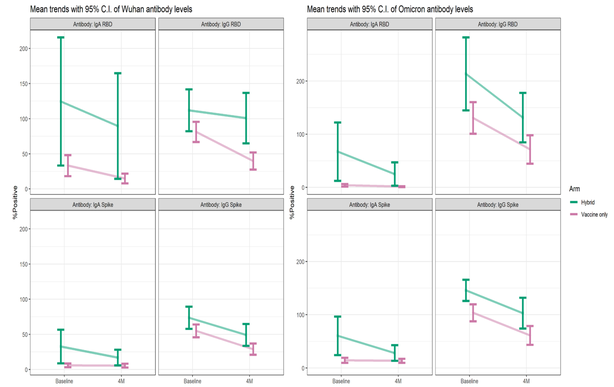
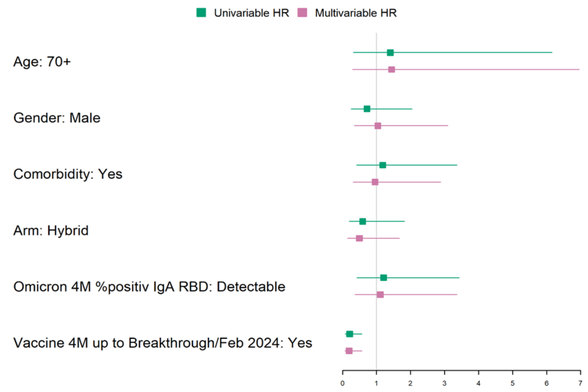


Figure 3: Multivariable Cox proportional hazards model of factors associated with breakthrough COVID infection



CONCLUSIONS

1. **Salivary IgA antibody is increased in persons with hybrid immunity relative to those with vaccine only immunity**
2. **There is rapid decay in salivary IgA over a 4 month period**
3. **Detectable salivary igA to RBD was not associated with protection against a breakthrough COVID infection over the subsequent 10 months**
4. **Receipt of a vaccine booster was protective against a breakthrough infection over the subsequent 10 months**

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