Effect of hybrid immunity on the neutralizing antibody response to emerging variants and in people living with HIV

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Background

Immunity to SARS-CoV-2 may be elicited from infection, vaccination, or result from both infection and vaccination, termed hybrid immunity. COVID-19 vaccines became available to South Africans in February 2021. However, only 31% of the population is currently vaccinated. Given the widespread SARS-CoV-2 infection in South Africa, we asked whether immunity from vaccination in addition to infection confers additional benefit in terms of neutralizing antibodies, especially in people living with HIV who may have an element of immunosuppression if their HIV infection is not completely suppressed by antiretroviral therapy.

Methods

- Blood samples from adults with a PCR-confirmed SARS-CoV-2 infection was obtained from participants enrolled into a longitudinal prospective cohort study
- ACE2 expressing H1299-E3, human lung cell line was used to isolate virus
- A live virus assay was used to test for neutralizing antibodies from human plasma

Table 1: Characteristics of infected and vaccinated (Ad26.CoV2.S) participants

	Infected Unvaccinated			Infected Vaccinated			Vaccinated Only		
	All	HIV-	HIV+	All	HIV-	HIV+	All	HIV-	HIV+
	62	28 (45.2%)	34 (54.8%)	67	49 (73.1%)	18 (26.9%)	32	24 (75.0%)	8 (25.0%)
Age years	44 (39 - 57)	57 (46 - 64)	41 (35 - 45)	46(40 - 52)	46 (40 - 52)	47 (42 - 51)	45 (39 - 52)	48 (42 – 55)	39 (36 - 42)
Days post-infection	188 (120 - 278)	192 (108 - 279)	187 (122 - 277)	235 (141 - 306)	230 (134 - 303)	304 (187 - 333)	-	-	-
Days post vaccination	-	-	-	48 (34 - 81)	48 (34 - 80)	51 (34 - 86)	74 (50 – 84)	74 (44 - 85)	74 (61 - 82)
Male sex	12 (19.4%)	5 (17.9%)	7 (20.6%)	2 (3.0%)	2 (4.1%)	0 (0.0%)	1 (3.1%)	0 (0.0%)	1 (12.5%)
Number HIV viremic	-	-	10 (29.4%)	-	-	1 (5.6%)	-	-	0 (0.0%)
HIV viral load	-	-	3060 (1224–30160)			3219			
Years ART	-	-	11 (5 – 15)	-	-	7 (5 – 12)	-	-	5 (4 – 11)
CD4 count cells/μL	792 (513 - 1027)	991 (807 - 1179)	581 (328 - 794)	967 (784 - 1325)	1033 (877 - 1424)	852 (730 - 1184)	1199 (853 - 1368)	1215 (1101 - 1413)	735 (458 - 863)
CD4/CD8 ratio	1.1 (0.7 – 1.2)	1.6 (1.3 – 2.1)	0.8 (0.4 – 1.1)	1.6 (1.1 – 2.2)	1.7 (1.4 – 2.3)	1.1 (0.8 – 1.2)	1.8 (1.2 – 2.1)	1.9 (1.2 – 2.3)	1.1 (0.4 – 1.2)

Table 2: Characteristics of Omicron infected participants

	All 39	**Vaccinated** 15 (38%)	**Unvaccinated** 24 (62%)
Age (years)	35 (27-55)	37 (32-60)	31.5 (26-49)
Female (number, percentage)	25 (64%)	9 (60%)	16 (67%)
Days post vaccination to sample (days)	-	139 (120-178)	-
Symptom onset to sample (days)	6 (3-9)	4 (3-6)	7.5 (3-9)
Required supp. O_2	7 (18%)	2 (13%)	5 (21%)
Hospitalized	27 (69%)	8 (53%)	19 (79%)
HIV	14 (36%)	6 (40%)	8 (33%)

Results

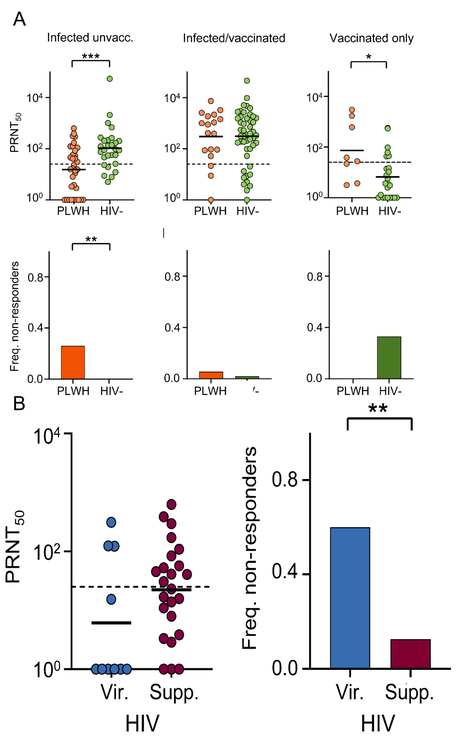

Figure 1: **(A)** Effect of HIV status on neutralization capacity elicited by Ad26.CoV2.S. **(B)** Effect of HIV viremia on neutralization capacity in infected unvaccinated participants

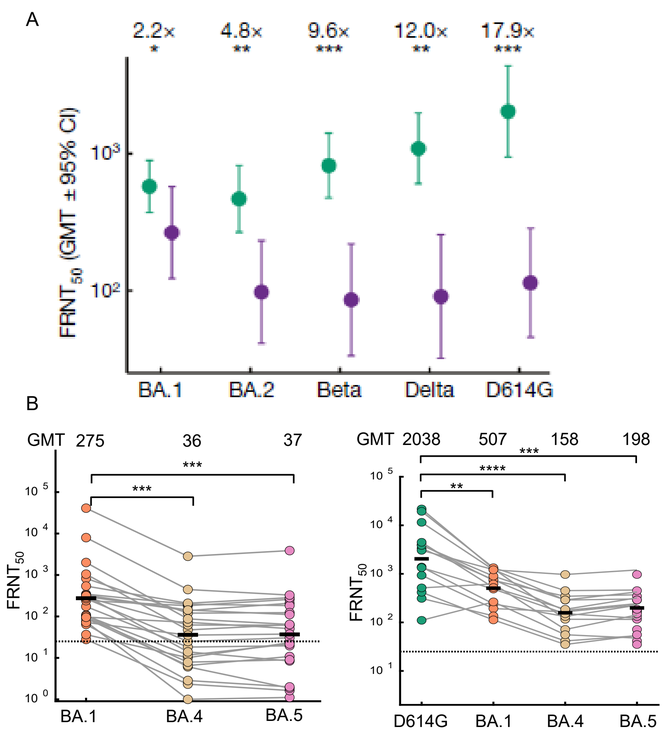

Figure 2: **(A)** Gap in neutralizing immunity between vaccinated and unvaccinated participants infected with Omicron BA.1. **(B)** Escape of BA.4 and BA.5 from BA.1 elicited immunity in unvaccinated and vaccinated infected participants

- We assessed the ability of the Ad26.CoV2.S vaccine to elicit neutralizing antibody activity against the Delta variant in PLWH relative to HIV negative individuals
- Neutralization response of the Delta variant following Ad26.CoV2.S vaccination in people with well controlled HIV was not inferior to HIV negative participants, irrespective of past SARS-CoV-2 infection
- Unvaccinated individuals infected with SARS-CoV-2, and HIV-viremic showed a reduction in neutralization capacity of SARS-CoV-2
- With the emergence of Omicron, the extent to which a new variant provided immunity was unknown. We assed neutralization capacity of participants infected with Omicron BA.1 against previous SARS-CoV-2 variants
- The vaccinated infected group was able to mount a better response over time to Omicron BA.1 in comparison to the unvaccinated infected group.
- Unvaccinated participants displayed a lower neutralization capacity against ancestral SARS-CoV-2, Beta, Delta, and Omicron BA.2, indicating hybrid immunity is effective at eliciting cross protection.
- Omicron evolved into subvariants BA.4 (22A) and BA.5 (22B). Against Omicron BA.4 and BA.5 considerable escape was observed in the unvaccinated infected group infected with BA.1, however this was reduced in the vaccinated infected group

Discussion and Conclusion

- Hybrid immunity consisting of vaccination and infection elicits a stronger and broader neutralizing antibody response to emerging variants relative to infection alone and this difference is more marked in PLWH
- Given the currently low vaccination rate, future immunity may be elicited primarily from infection alone, and not provide sufficient cross-protection from emerging variants or to individuals with a reduced capacity to elicit a potent neutralizing antibody responses

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