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Superior magnitude and durability of hybrid immunity following SARS-CoV-2 infection

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Abstract

Background: The emergence of the SARS-CoV-2 Delta variant necessitated examining hybrid immunity (vaccination-plus-infection) to optimize boosting strategies. We analyzed the kinetics, magnitude, and durability of anti-spike receptor binding domain immunoglobulin G (Anti-sRBD IgG) following Delta infection.

Objective: This study analyzed the kinetics, magnitude, and long-term durability of anti-spike receptor binding domain immunoglobulin G (Anti-sRBD IgG) levels following Delta variant infection across individuals with diverse vaccination histories.

Methods: This observational cohort study monitored 161 patients with varying vaccination histories for up to 16 weeks post-infection. Responses were compared against SARS-CoV-2 naïve controls receiving a two-dose inactivated series plus a heterologous booster. Sub-analyses assessed post-infection booster immunogenicity.

Results: Prior vaccination significantly enhanced humoral responses. Patients with two prior doses achieved the highest median Anti-sRBD IgG peaks, surpassing vaccine-boosted naïve controls. While unvaccinated individuals exhibited delayed primary responses, hybrid immunity demonstrated superior durability with slower antibody decay than vaccine-only immunity. Crucially, while a post-infection booster effectively primed unvaccinated patients, early boosting in previously vaccinated individuals yielded minimal immunological gain.

Conclusions: Hybrid immunity confers superior antibody magnitude and durability, highlighting the synergy between vaccination and natural infection. Early post-infection boosting in previously vaccinated individuals appears to provide limited additional benefit, supporting tailored booster timing strategies.

Key words: COVID-19, hybrid immunity, COVID-19 vaccine, Anamnestic response, durability

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Introduction

Coronavirus disease 2019 (COVID-19) has been a global pandemic since late 2019. Several platforms of the COVID-19 vaccine were developed within a year of the outbreak and were made publicly available in January 2020.[1] The emergence of SARS-CoV-2 and the resulting COVID-19 pandemic necessitated the rapid development of efficacious vaccines, utilizing diverse technological platforms including inactivated (e.g., CoronaVac), viral vector (e.g., AZD-1222), and mRNA (e.g., BNT162b2) technologies, all primarily targeting the viral Spike (S) protein. Initial global vaccination efforts

demonstrated high effectiveness, particularly against severe disease and hospitalization.[2] COVID-19 vaccines provide high protection against symptomatic COVID-19 but not infection, with efficacy ranging from 66% to 95%.[3] Initial global vaccination efforts demonstrated high effectiveness, particularly against severe disease and hospitalization. However, the subsequent emergence and global dominance of Variants of Concern (VOCs), such as the Delta (B.1.617.2) variant that prevailed during the period of this study (late 2021), introduced significant challenges. Specific mutations in the S protein's Receptor-Binding Domain (RBD)—a critical target for neutralizing antibodies—impaired the protective efficacy against infection (sterile immunity) and resulted in numerous breakthrough cases among the vaccinated population.[4,5] This immunological escape, coupled with observed waning immunity, provided the foundational rationale for implementing booster vaccine recommendations worldwide to restore the magnitude and breadth of the humoral response.[6]

In the face of fluctuating vaccine supply and the urgent public health need to enhance protection against the Delta variant, Thailand adopted a national policy of heterologous vaccination, employing mixed platforms (e.g., an inactivated primary series followed by an mRNA or viral vector booster). This strategy, supported by evidence demonstrating a superior immunological profile compared to homologous regimens, has created a complex landscape of acquired immunity within the population.[7] The interplay between prior vaccination and subsequent natural infection gives rise to hybrid immunity (or infection-plus-vaccination immunity), now recognized as a highly robust and durable form of protection. Immunologically, hybrid immunity relies on the principle of anamnestic response, where either vaccination or infection primes the immune system by generating memory B cells, and the subsequent exposure acts as a potent recall stimulus. This process drives a superior germinal center reaction, promoting affinity maturation of memory B cells and the eventual production of plasma cells secreting higher-affinity, often broader, neutralizing antibodies than immunity derived from either exposure alone.[7-9]

Given Thailand's widespread heterologous regimens and the Delta-driven wave of breakthrough infections, distinct patterns of hybrid immunity have emerged but remain poorly characterized. This study aimed to compare the kinetics, peak magnitude, and short-term durability of anti-sRBD IgG after Delta infection across different pre-existing vaccination histories, and to benchmark these responses against naïve heterologous-boosted controls. We hypothesized that complete primary vaccination before infection would confer higher and more sustained post-infection antibody responses than partial or no prior vaccination.

Methods

Participants

Between 30 July and 1 December 2021, during the Delta-dominant wave in Thailand, 161 patients with RT-PCR–confirmed SARS-CoV-2 infection at Thammasat University Hospital were enrolled in an observational cohort. Demographic data, clinical characteristics, infection history, and vaccination records were collected at presentation to the respiratory infection clinic. Vaccination histories were verified using the national mobile application of the Ministry of Public Health, where all administered doses are mandatorily recorded. All participants provided written informed consent. The study was approved by the Human Research Ethics Committee of Thammasat University (Medicine) (MTU-EC-PE-2-346/64).

Assessment of immunogenicity

The humoral immune response was quantified by measuring anti-spike receptor binding domain Immunoglobulin G (Anti-sRBD IgG) levels using an in-house quantitative anti-SRBD IgG ELISA (detailed in the supplementary document). This critical antibody was examined longitudinally at five time points post-COVID-19 diagnosis: day 0–5, day 14–21, week 8, week 12, and week 16, enabling characterization of the kinetic curve and long-term durability. Alongside these measurements, patient demographics, clinical severity, and complete vaccination history (pre- and post-infection) were recorded for stratification. For comparison against a purely vaccine-induced response, Anti-sRBD IgG levels in the cohort were rigorously contrasted with those from COVID-19-naïve individuals (naïveté confirmed by negative anti-nucleocapsid IgG). These control subjects received a primary series of two doses of CoronaVac followed by a heterologous booster (at least three months later) of either AZD-1222 (AstraZeneca®) or BNT162b2 (Pfizer-BioNTech®) (50 individuals per group). Anti-sRBD IgG in the SARS-COV-2 naïve groups were measured at day 0, 14, 30, and 90 days post-booster (V1, V2, V3, V4), providing the essential reference for purely vaccine-mediated hybrid-style immunity. Surrogate virus neutralization testing (sVNT) against the Delta variant was performed on pooled serum samples stratified by infection–vaccination history and visit time point. Individual participant samples were not directly tested. Neutralization estimates therefore reflect group-level measurements derived from pooled specimens rather than individual-level functional confirmation.

Statistical analysis

Continuous variables were summarized as median (interquartile range), and categorical variables as counts and percentages. Between-group comparisons of anti-sRBD IgG levels at each time point were performed using Kruskal–Wallis tests with appropriate post-hoc pairwise comparisons. For selected sub-analyses, two-way ANOVA was applied to evaluate the interaction between time and vaccination status where distributional assumptions were reasonably met. Missing observations in the longitudinal dataset were handled using complete case analysis; no imputation was performed.

Results

Demographic data of patients were presented in **Table 1**. Demographic characteristics did not differ significantly among the eight groups stratified by vaccination and infection history (**Table 1**).

Anti-sRBD IgG Kinetics, Magnitude, and Durability during post exposure period

The analysis of Anti-sRBD IgG dynamics across the study groups, as detailed in **Table 2** and **Figure 1**, demonstrated that prior vaccination significantly boosted the humoral response. The highest median Anti-sRBD IgG level at the peak response (Visit 2, Day 10–20) was observed in patients who received two vaccine doses prior to infection (median 4,291 BAU/mL), significantly surpassing the peak of the purely vaccine-boosted naïve controls (2SV-PZ, median 3,739 BAU/mL; 2SV-AZ, median 1,779 BAU/mL). Conversely, the "Infection only" group displayed a unique kinetic pattern, where the median antibody level at 90 days (Visit 4, 1,036 BAU/mL) exceeding those observed Visit 2 (139.5 BAU/mL), consistent with a primary immune response. Furthermore, regarding durability, groups with a complete primary vaccination history (e.g., "2 doses - Infection," median 2,785 BAU/mL at Visit 4) maintained significantly higher antibody titers at 90 days compared to those who were unvaccinated or received only one dose of vaccine ("Infection - 1 dose vaccine," median 420.2 BAU/mL at Visit 4), confirming that prior full vaccination confers superior long-term antibody maintenance post-infection.

Table 1. Demographic data of participants.

	Infection only (n = 5)	Infection - 1 dose vaccine (n = 18)	1st dose - Infection - 2nd dose (n = 76)	2 doses - Infection (n = 47)	2 SV-AZ Infection (n = 15)	2SV-AZ (n = 50)	2SV-PZ (n = 50)
Female, n (%)	3 (60)	13 (72.2)	44 (57.9)	23 (48.9)	12 (80)	32 (64)	32 (64)
Age, year (median, range)	58 (43-73)	36 (19-60)	46 (20-75)	41 (19-83)	33 (23-57)	42 (30-56)	36 (21-56)
BMI	24.9 (19.5-35.9)	21.2 (18.4-30)	24.2 (16.4-35.6)	25 (17.3-36.4)	24.2 (17.3-34.7)	22.5 (17.5-33.5)	22.2 (16.4-30.5)
Underlying conditions, n (%)							
• cardiovascular diseases	4 (80)	1 (5.6)	13 (17.1)	7 (14.9)	2 (13.3)	7 (14)	1 (2)
• Chronic obstructive pulmonary disease	0	0	4 (5.3)	3 (6.4)	0	1 (2)	0
• Diabetes	2 (40)	0	8 (10.5)	8 (17.0)	0	1 (2)	0
• Chronic kidney disease	1 (20)	0	0	1 (2.1)	0	0	0
• Cerebrovascular disease	0	0	0	2 (4.3)	0	0	0
• Cancer	0	0	1 (1.3)	1 (2.1)	0	0	0
• Immunosuppressive agents	0	0	0	0	0	0	0

Az: AZD-1222, PZ: BNT162b2, SV: CoronaVac

Table 2. Anti–spike receptor-binding domain (anti-RBD) IgG concentrations following SARS-CoV-2 infection or vaccination. Data are presented as median (interquartile range [IQR]) and expressed in binding antibody units per milliliter (BAU/mL).

	Visit 1 (baseline)	Visit 2 (day 10-20)	Visit 3 (day 30-60)	Visit 4 (day 75-100)	Visit 5 (day > 120)
Infection only (n = 5)	48.53 (23.5 - 56.58)	139.5 (75 - 204)	1,138 (362 - 1,914)	1,036 (131 - 1,940)	713.5 (219.5, 1,208)
Infection - 1 dose vaccine (n = 18)	38.3 (27.08 - 80)	166.6 (81.41 - 471.9)	388 (217.3 - 725.3)	420.2 (334 - 2,850)	3,041 (1,890, 3,804)
1st dose - Infection - 2nd dose (n = 76)	107.2 (55.97 - 687.8)	2,849 (872.3 - 4,128)	2,197 (1,153 - 3,416)	1,825 (730.2 - 2,712)	1,328 (1,102, 2,076)
2 doses - Infection (n = 47)	513.7 (99.87 - 1,102)	4,291 (3,341 - 5,226)	3,510 (2,311 - 4,639)	2,785 (1,879 - 3,793)	2,245 (864.7, 2,428)
2 SV-AZ - Infection (n = 15)	339.2 (176 - 1,865)	4,278 (2,977 - 5,863)	3,636 (3,279 - 4,894)	2,122 (1,216 - 3,671)	2,286 (2,286, 2,286)
2SV-AZ (n = 50)	106.5 (71 - 169.8)	1,779 (1,232 - 2,317)	1,538 (1,203 - 2,226)	925.5 (713.3 - 1,394)	
2SV-PZ (n = 50)	85.5 (65.25 - 137.5)	3,739 (3,318 - 4,236)	2,847 (2,286 - 3,409)	2,223 (1,397 - 3,010)	

Az: AZD-1222, PZ: BNT162b2, SV: CoronaVac

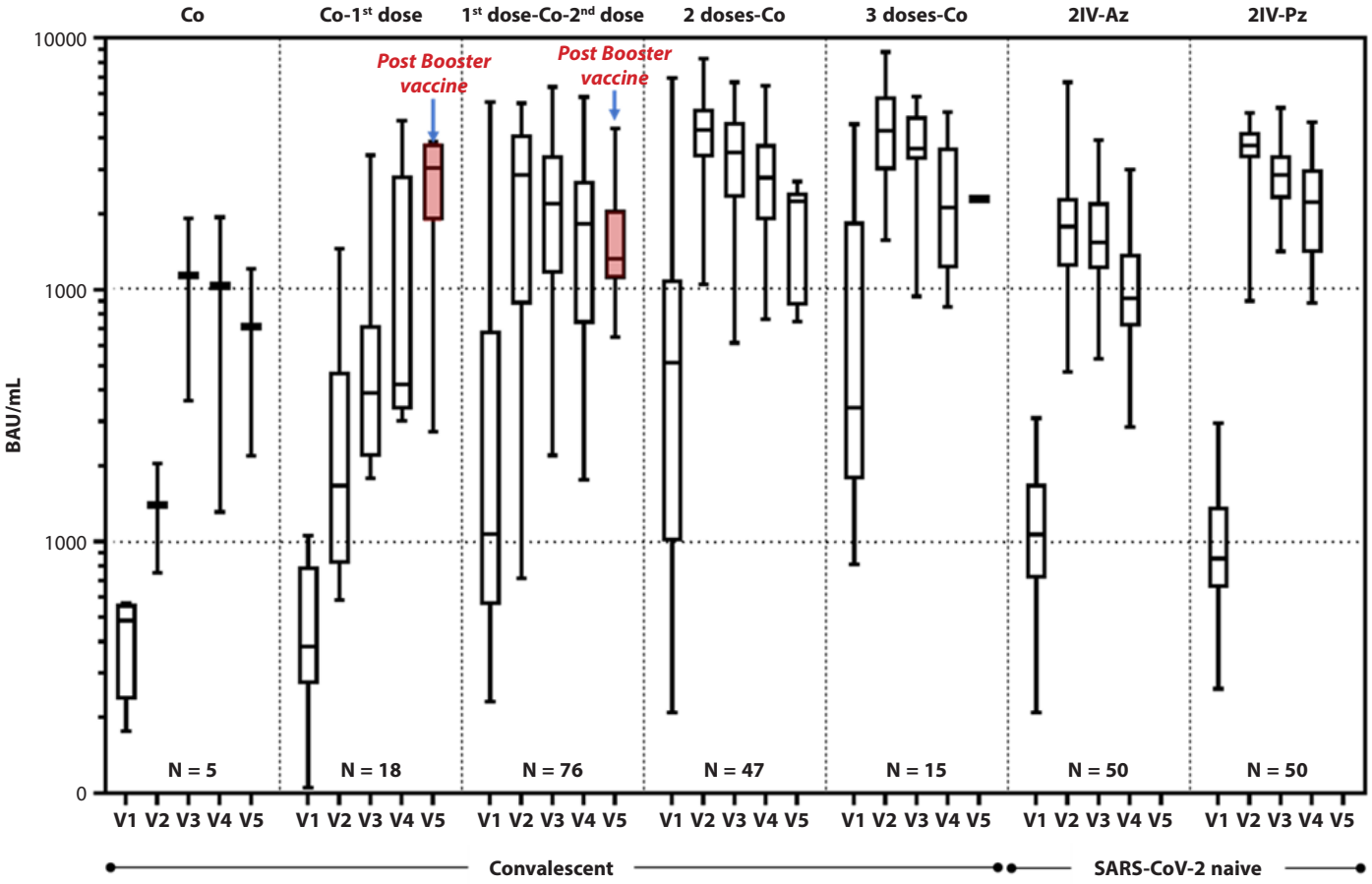


Figure 1. Dynamic of anti-spike-RBD IgG.

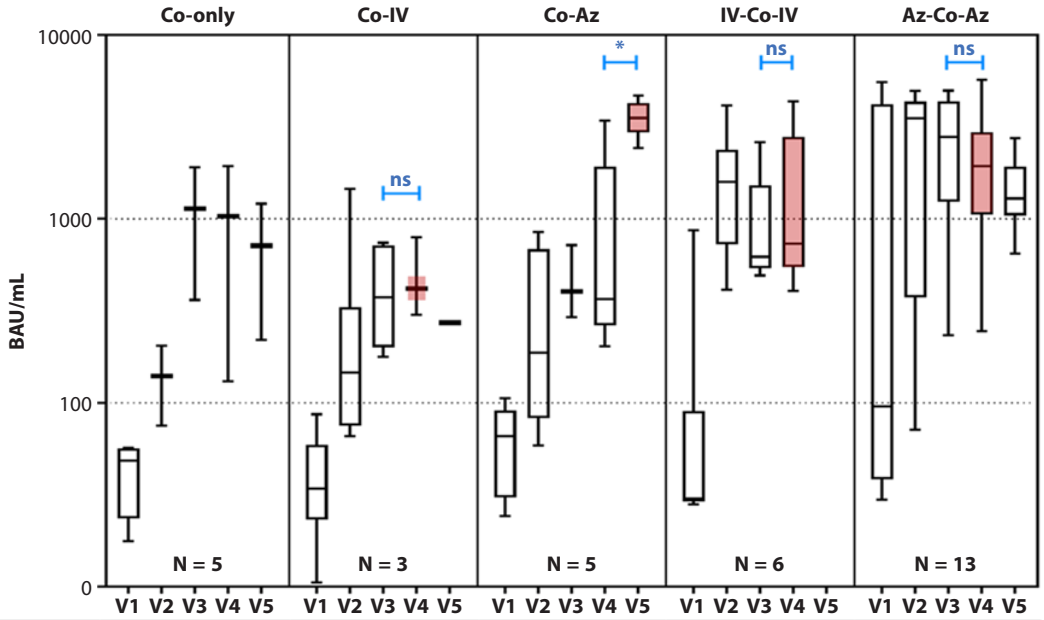
Dynamic of anti-spike-RBD IgG up to 4 months in convalescent individuals and up to 3 months after booster vaccine in individuals who previously received 2 doses of CoronaVac. Anti-spike-RBD IgG was examined at day 0-5 (V1), day 14-21 (V2), week 8 (V3), week 12 (V4), and week 16 (V5) after the diagnosis of COVID-19 infection in convalescences and in SARS-COV-2 naïve groups were measured at day 0, 14, 30, and 90 days (V1, V2, V3, V4), respectively. Anti-spike-RBD IgG at day 14 after infection increased significantly in all groups of convalescences. The highest concentration was found in patients who received complete primary series vaccination with either CoronaVac or AZD-1222. Peak of anti-spike-RBD IgG concentration in unvaccinated patients was at visit 3 (V3; 4 weeks after infection) but still lower than those who were previously vaccinated. In comparison with post booster vaccine, Anti-spike-RBD IgG in previously complete primary series vaccinated ± booster vaccine convalescences (2 doses-Co and 3 doses-Co) were not different from SARS-CoV-2 naïve individuals who received booster vaccine with BNT162b2 following 2 doses of CoronaVac (2IV-Pz) but higher than convalescences who boosted with AZD-1222 (2IV-Az). After days 75 post infection (V4), anti-spike-RBD IgG concentration in previously complete primary series vaccinated convalescences (2 doses-Co) was higher than both day 30 and 90 following booster vaccination with AZD1222 in SARS-CoV2-naïve who primed with 2 doses of CoronaVac (2IV-Az) but comparable with those who received BNT162b2 as booster vaccine (2IV-Pz). In incompletely primary series vaccinated convalescences who received the second dose vaccine (median at 60 days range 48-111 days) after infection (1st dose-Co-2nd dose), post booster vaccination antibody concentration was lower than the previous test at visit 3 while unvaccinated convalescences had higher concentration of antibody after boosted with COVID vaccine (Co-1st dose); median time between infection and vaccination was 89 days (range 53-117 days).

Az: AZD-1222, Co: COVID-19 infection, IV: inactivated vaccine, Pz: BNT162b2, RBD: receptor binding domain

Immunogenicity of Post-Infection Booster Doses

During follow-up, a sub-analysis assessed the impact of a single post-infection booster dose in patients who were previously unvaccinated or incompletely vaccinated. The results, detailed in **Figure 2**, demonstrated a platform-dependent effect, particularly for those who were infection-naïve prior to their COVID-19 diagnosis. In previously unvaccinated patients, receiving a single dose of AZD-1222 (Co-Az) post-infection induced a highly significant boost, with the median Anti-sRBD IgG levels rising by a factor of 10.52. This finding confirms that the natural infection serves as a powerful initial immunological prime, making a single viral vector dose highly effective. However, in other comparable subgroups, the post-infection boost was minimal; for instance, those receiving an inactivated vaccine (Co-IV) post-infection showed negligible increases (median fold rise of 1.07), and generally, post-vaccination levels were not significantly different from pre-vaccination (post-infection) levels in previously vaccinated groups. This observation suggests that the timing and choice of the booster vaccine platform are critical for maximizing the immunological gain after natural infection, especially when compared to the highly potent primary immune priming conferred by the natural SARS-CoV-2 infection itself.

An exploratory surrogate neutralization analysis demonstrated that infection-only participants exhibited modest neutralizing activity, with median sVNT percent inhibition peaking at 55.2% on day 30 and declining to 45.4% by day 120. In contrast, hybrid immunity groups showed substantially higher neutralization levels. Individuals with prior vaccination followed by infection—particularly those with two or three vaccine doses—frequently achieved median inhibition levels of 80–100% at days 14 and 30. Although some decline was observed by day 120, neutralization remained consistently higher than in the infection-only group (supplementary table). Overall, a clear exposure-dependent gradient was observed, with increasing numbers of prior vaccine doses associated with progressively stronger neutralizing responses.



Days between infection and vaccination (median, range)		59 (58-76)	104 (62-198)	63 (56-73)	59.5 (40-83)
Days of antibody testing after vaccination (median, range)		20 (1-27)	31 (16-39)	23 (18-45)	37 (7-48)
Fold rising		1.07 (1.07-1.36)	10.52 (1.37-17.41)	0.87 (0.64-7.834)	0.89 (0.55-3.25)

Figure 2. Dynamic of anti-spike-RBD IgG up to 4 months in convalescent individuals.
Dynamic of anti-spike-RBD IgG up to 4 months in convalescent individuals who either received or not received booster COVID-19 vaccine following SAS-CoV-2 infection. Booster vaccine after infection with AZD-1222 after COVID-19 infection could increase anti-sRBD IgG concentration in unvaccinated convalescences while booster vaccine with CoronaVac as the first or second dose after COVID infection or the second dose of AZD-1222 in convalescences could not increase anti-sRBD IgG concentration. Red bars represent post-booster vaccination anti-sRBD IgG.

Az: AZD-1222, Co: COVID-19 infection, IV: inactivated vaccine, NS: not significant, Pz: BNT162b2, RBD: receptor binding domain

Discussion

Our study confirms that prior vaccination significantly primes the immune system for a vigorous and accelerated humoral response upon subsequent SARS-CoV-2 Delta variant infection, underscoring the immunological superiority of hybrid immunity. The observation that the Anti-sRBD IgG peak magnitude in previously vaccinated individuals surpassed the levels achieved by purely vaccine-boosted naïve controls strongly validates the synergistic effect of combining existing immune memory with a natural antigenic exposure. This heightened response is an anamnestic response, where memory B cells generated by prior vaccination are rapidly and potently recalled by the infection.[10] The finding that the specific platform used for the primary series (inactivated versus viral vector) did not alter the magnitude of this post-infection peak suggests that the presence of established immune memory, rather than the intrinsic potency of the initial prime, is the critical determinant of the robust secondary response.

Beyond the magnitude of the peak, the kinetics of the antibody response provided key insights into the quality of the immune priming. The rapid decay from the high peak observed in all vaccinated groups contrasts sharply with the unique pattern seen in the previously unvaccinated group, where antibody levels continued to rise, reaching their maximum concentration later in the follow-up period. This delayed, sustained rise is the characteristic signature of a primary immune response, indicating the slower process required for the de novo formation of germinal centers, distinguishing it from the rapid recall kinetics seen in primed individuals.[11,12] Our data show that hybrid immunity confers superior durability. Antibody concentrations in groups with a complete vaccination history contracted significantly more slowly, maintaining higher titers at the 90-day mark compared to those with incomplete or no prior vaccination. Furthermore, this slower decline was evident when comparing them to SARS-CoV-2 naïve individuals who were boosted with AZD-1222 following two doses of inactivated vaccine, demonstrating a clear advantage in long-term maintenance of humoral immunity. Fass et al. reported that after booster vaccination with BNT162b2 or mRNA-1273, anti-RBD IgG concentration in previously infected individuals was higher than infection-naïve individuals. The concentration decreased at four months after booster vaccination but stayed steady at seven months in individuals with hybrid immunity.[13] Moore et al. reported a similar trend in which prior infection-induced and maintained the higher concentration of anti-SARS-CoV-2 Spike IgG at one and six months after booster vaccine than infection-naïve individuals.[14] Our findings collectively suggest that natural infection following vaccination can induce a humoral immune response that is both stronger and yields better durability of SARS-CoV-2 specific antibodies than certain vaccine-only regimens, a pattern that has also been documented in Omicron-era studies, although the absolute titers required for protection against Omicron are considerably higher due to its enhanced immune escape.[15-17] This superior long-term maintenance is consistent with previous reports suggesting that the dual exposure drives a more profound process of B-cell affinity maturation and the establishment of long-lived plasma cells (LLPCs), which are crucial for sustained antibody secretion.[12,18,19]

Importantly, our exploratory surrogate neutralization analysis provides supportive functional context to these binding antibody findings, as sVNT-measured ACE2–RBD inhibition has been shown to correlate with variant-specific neutralizing activity. Hybrid immunity groups demonstrated substantially higher Delta sVNT inhibition compared with infection-only participants, consistent with reports that infected–vaccinated individuals exhibit stronger neutralizing responses than vaccination-only or infection-only cohorts. Individuals receiving two or three prior vaccine doses frequently achieved near-complete inhibition at early time points, whereas infection-only participants exhibited modest neutralization that peaked and subsequently declined, mirroring dose- and exposure-dependent neutralization patterns seen in other studies. This exposure-dependent gradient, with increasing numbers of prior vaccine doses associated with progressively stronger neutralizing responses, reinforces the biological plausibility that repeated antigenic stimulation enhances not only antibody quantity but also functional neutralization breadth and potency.[20-22]

The findings related to post-infection booster doses provide crucial, actionable data for public health policy regarding optimal sequencing. The observation that administering a single dose of a viral vector vaccine to a previously unvaccinated patient post-infection induced a highly significant antibody fold rise confirms that the natural infection effectively acts as an immunological prime, making a single subsequent dose highly immunogenic and sufficient to establish strong hybrid immunity in this subgroup. Biologically, this likely reflects differences in antigen presentation and immune priming between platforms. Viral-vector vaccines deliver spike antigen intracellularly, promoting MHC class I and II presentation, stronger $CD4^+$ T-cell help, and $CD8^+$ T-cell activation, thereby supporting germinal center maturation and high-affinity memory B-cell expansion. In contrast, inactivated vaccines rely predominantly on exogenous antigen presentation and may elicit comparatively weaker T-cell priming, potentially limiting the magnitude of secondary recall responses. These mechanistic differences may partly explain the stronger post-infection boosting observed with viral-vector platforms compared with inactivated vaccines.[23-25] However, a significant policy implication arises from the observation that a booster offered too early in the convalescent phase to previously vaccinated individuals resulted in a minimal or insignificant antibody increase. This likely reflects transient immune activation during the early convalescent phase

by the recent infection, and early boosting yields limited immunological gain.[1,26-28] Buckner et al. reported that a booster vaccine given at less than 180 days after infection only elicits a slight increase of SARS-CoV-2 specific IgG followed by the decline of concentration at 60 days after boosting. In contrast, a booster vaccine given at 180 days or later following infection induces a higher level of antibody, which also remains steady at 60 days after boosting.[29] Moreover, the negligible fold increase observed when using an inactivated vaccine as the post-infection booster highlights that the choice of platform remains critical for maximizing the subsequent recall response, even after the immune system has been primed by the natural virus.

Finally, we emphasize that our data were generated in the context of Delta variant infection, and extrapolation to Omicron must be cautious given the substantially greater immune escape of Omicron lineages. Although the exploratory sVNT findings support functional neutralization against Delta, neutralization breadth against contemporary Omicron subvariants cannot be inferred.

Our study has several limitations inherent to observational cohort designs, including unequal and, in some subgroups, small sample sizes (e.g., infection-only group), as well as unavoidable attrition during extended follow-up. Small subgroup numbers reduce statistical power, widen confidence intervals, and may have influenced p-values in comparative analyses, increasing the risk of type II error; therefore, findings from these groups should be interpreted cautiously. In addition, individual-level neutralization was not directly measured; sVNT was performed using pooled subgroup samples, providing supportive group-level functional evidence rather than definitive per-participant confirmation. Finally, reliance primarily on quantitative Anti-sRBD IgG limits full functional interpretation, as high binding antibody titers do not inherently guarantee broad neutralization against highly immune-evasive variants such as Omicron, where substantial reductions in neutralization have been documented across vaccine platforms and prior infection histories.

Future research in this cohort and others should therefore extend beyond Anti-sRBD IgG quantification to incorporate variant-specific functional neutralization assays, especially against currently circulating Omicron subvariants, in order to define the quality and protective breadth of hybrid antibodies. In addition, integration of cellular immune profiling—particularly T-cell–mediated responses—is essential. T-cell immunity plays a critical role in protection against severe disease and is generally less affected by spike protein mutations than antibody responses. Comprehensive evaluation of both humoral neutralizing activity and cellular immunity will be necessary to more accurately characterize the durability, breadth, and clinical relevance of hybrid immunity under ongoing viral evolution.

Conclusion

During the Delta-dominant period in a heterologous vaccination setting, hybrid immunity following complete primary vaccination and subsequent breakthrough infection generated stronger, more durable, and functionally supported anti-sRBD IgG responses than vaccination alone or infection alone. Exploratory surrogate neutralization findings further demonstrated an exposure-dependent increase in Delta neutralizing activity among hybrid groups. These results support tailored booster timing suggesting limited incremental benefit from early post-infection boosting in previously vaccinated individuals and highlight the immunogenic efficiency of a single, appropriately timed viral-vector booster after infection in unvaccinated patients when informing national booster strategies.

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Author contributions

- Conception and Design: PS, SN
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- Drafting the Manuscript: SN, PS
- Critical Revision: PS, SN, PJ
- Writing – Review & Editing: All authors
- Visualization: SN
- Funding Acquisition: PS
- Study Supervision: PS, SN

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Supplementary table. Delta surrogate virus neutralization test (sVNT) percent inhibition according to infection–vaccination history and visit time point.

Infection–vaccination history	Visit	Percent inhibition of Delta variant		
		25% Percentile	Median	75% Percentile
Infected only	Visit 1	29.47	30.05	30.24
	Visit 2	30.66	32.15	33.64
	Visit 3	37.29	55.21	73.13
	Visit 4	31.96	52.84	73.73
	Visit 5	34	45.41	56.82
Infected - single dose vaccine	Visit 1	29.56	29.82	30.78
	Visit 2	30.81	32.78	39.83
	Visit 3	33.95	37.89	45.68
	Visit 4	36.64	38.63	86.83
	Visit 5	72.56	94.42	100
1st dose - Infected - Second dose	Visit 1	30.27	31.41	45.31
	Visit 2	49.34	96.41	100
	Visit 3	56.41	82.5	100
	Visit 4	45.79	71.07	91.56
	Visit 5	54.37	59.6	76.87
2 doses - infected	Visit 1	31.24	40.79	54.37
	Visit 2	100	100	100
	Visit 3	82.29	100	100
	Visit 4	72.32	93.23	100
	Visit 5	48.9	80.77	85
3 doses - infected	Visit 1	33	36.76	72
	Visit 2	97.67	100	100
	Visit 3	100	100	100
	Visit 4	57	77.93	90.68
	Visit 5	81.72	81.72	81.72