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Protection afforded by previous infection, vaccination, and hybrid immunity against symptomatic Omicron BA.1 and BA.2 infections

Heba N. Altarawneh, MD[1,2,3], Hiam Chemaitelly, PhD[1,2,3], Laith J. Abu-Raddad, PhD[1,2,3,4*], and National Study Group for Covid-19 Epidemiology in Qatar

[1]Infectious Disease Epidemiology Group, Weill Cornell Medicine-Qatar, Cornell University, Doha, Qatar; [2]World Health Organization Collaborating Centre for Disease Epidemiology Analytics on HIV/AIDS, Sexually Transmitted Infections, and Viral Hepatitis, Weill Cornell Medicine–Qatar, Cornell University, Doha, Qatar; [3]Department of Population Health Sciences, Weill Cornell Medicine, Cornell University, New York, USA; [4]Department of Public Health, College of Health Sciences, QU Health, Qatar University, Doha, Qatar

Weill Cornell Medicine-Qatar

Background

- Qatar experienced five SARS-CoV-2 epidemic waves dominated sequentially by the original virus, Alpha, Beta, Omicron BA.1 and BA.2 subvariants in addition to a prolonged low-incidence phase dominated by Delta
- The Omicron wave started on December 19, 2021 and was first dominated by the Omicron BA.1 subvariant followed by the Omicron BA.2 subvariant
- The Omicron BA.1 and BA.2 subvariants of concern harbor mutations that can mediate immune evasion

Objective

- To establish the protection conferred by previous pre-omicron infection, vaccination, or a hybrid of both against symptomatic Omicron BA.1 and BA.2 infections and against severe, critical, or fatal Covid-19

Methods

- Ten national, matched, test-negative case-control studies were conducted in Qatar from January 18, 2021, through February 21, 2022, on a sample of 511,981 PCR-positive tests and 4,028,739 PCR-negative tests
- We estimated the effectiveness of BNT162b2 (Pfizer-BioNTech) vaccine, mRNA-1273 (Moderna) vaccine, natural immunity due to previous pre-omicron infection, and hybrid immunity from previous pre-omicron infection and vaccination against symptomatic Alpha, Beta, Delta, Omicron BA.1 and BA.2 infections and against severe, critical, or fatal Covid-19

Results

- Effectiveness of previous pre-omicron infection alone against symptomatic Omicron BA.2 infection was 46.1% (95% CI: 39.5-51.9%)
- Effectiveness of two-dose BNT162b2 vaccination alone against symptomatic Omicron BA.2 infection was negligible at -1.1% (95% CI: -7.1-4.6), but nearly all individuals received their second dose >6 months earlier
- Effectiveness of three-dose BNT162b2 vaccination alone against symptomatic Omicron BA.2 infection was 52.2% (95% CI: 48.1-55.9%)
- Effectiveness of hybrid immunity of previous pre-omicron infection and two-dose BNT162b2 vaccination against symptomatic Omicron BA.2 infection was 55.1% (95% CI: 50.9-58.9%)
- Effectiveness of hybrid immunity of previous pre-omicron infection and three-dose BNT162b2 vaccination against symptomatic Omicron BA.2 infection was 77.3% (95% CI: 72.4-81.4%)
- Similar results were observed in analyses of effectiveness against Omicron BA.1 infection and of vaccination with mRNA-127
- Effectiveness of previous pre-omicron infection, BNT162b2 vaccination, and hybrid immunity against symptomatic Alpha, Beta, and Delta infections was robust (most at approximately 90%)
- Previous pre-omicron infection, BNT162b2 vaccination, and hybrid immunity all showed strong effectiveness against severe, critical, or fatal COVID-19 regardless of variant

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Results … Continued

Table 1. Effectiveness of previous pre-omicron infection, vaccination with BNT162b2, and hybrid immunity against symptomatic Alpha, Beta, Delta, Omicron BA.1 and BA.2 infections and against severe, critical, or fatal Covid-19

Studies	Case Participants with Symptomatic Infection (PCR-Positive)†		Controls (PCR-Negative)†		Effectiveness against Symptomatic Infection (95% CI)	Case Participants with Severe, Critical, or Fatal Covid-19‡		Controls (PCR-Negative)‡		Effectiveness against Severe, Critical, or Fatal Covid-19 (95% CI)
	Exposed	Unexposed§	Exposed	Unexposed§		Exposed	Unexposed§	Exposed	Unexposed§	
Alpha infection										
Previous infection and no vaccination	43	7,812	759	14,429	89.7 (86.0 to 92.5)	0	484	128	1,997	100.0 (97.1 to 100.0)¶
Two doses and no previous infection	18	7,812	293	14,429	89.9 (83.6 to 93.7)	1	484	99	1,997	96.8 (76.7 to 99.6)
Two doses and previous infection	0	7,812	19	14,429	100.0 (78.6 to 100.0)¶	0	484	7	1,997	100.0 (30.6 to 100.0)¶
Three doses and no previous infection	0	7,812	0	14,429	-	0	484	0	1,997	-
Three doses and previous infection	0	7,812	0	14,429	-	0	484	0	1,997	-
Beta infection										
Previous infection and no vaccination	150	19,595	1,814	31,296	87.0 (84.6 to 89.0)	1	1,553	343	4,746	99.1 (93.7 to 99.9)
Two doses and no previous infection	1,252	19,595	7,581	31,296	81.6 (80.1 to 82.9)	29	1,553	1,964	4,746	97.3 (95.9 to 98.2)
Two doses and previous infection	14	19,595	631	31,296	97.6 (95.9 to 98.6)	0	1,553	184	4,746	100.0 (98.0 to 100.0)¶
Three doses and no previous infection	1	19,595	7	31,296	81.1 (-54.7 to 97.7)	0	1,553	1	4,746	100.0 (-3,800.0 to 100.0)¶
Three doses and previous infection	0	19,595	2	31,296	100.0 (-432.5 to 100.0)¶	0	1,553	0	4,746	-
Delta infection										
Previous infection and no vaccination	56	4,469	727	6,303	90.4 (87.4 to 92.8)	0	211	52	299	100.0 (92.6 to 100.0) ¶
Two doses and no previous infection	3,090	4,469	6,805	6,303	57.7 (54.3 to 60.9)	71	211	757	299	93.0 (89.4 to 95.4)
Two doses and previous infection	65	4,469	1,106	6,303	94.7 (93.1 to 96.0)	0	211	136	299	100.0 (97.3 to 100.0)¶
Three doses and no previous infection	29	4,469	238	6,303	91.7 (87.3 to 94.5)	0	211	40	299	100.0 (90.3 to 100.0)¶
Three doses and previous infection	1	4,469	45	6,303	98.4 (88.6 to 99.8)	0	211	6	299	100.0 (15.1 to 100.0)¶
Omicron BA.1 infection										
Previous infection and no vaccination	149	1,738	255	1,536	50.2 (38.1 to 59.9)	0	12	6	11	100.0 (15.1 to 100.0)¶
Two doses and no previous infection	3,449	1,738	2,762	1,536	−4.9 (−16.4 to 5.4)	5	12	39	11	96.8 (71.1 to 99.6)
Two doses and previous infection	402	1,738	688	1,536	51.7 (43.5 to 58.7)	1	12	8	11	96.2 (37.7 to 99.8)
Three doses and no previous infection	479	1,738	892	1,536	59.6 (52.9 to 65.3)	2	12	20	11	97.5 (71.7 to 99.8)
Three doses and previous infection	47	1,738	131	1,536	74.4 (63.4 to 82.2)	0	12	7	11	100.0 (30.6 to 100.0)¶
Omicron BA.2 infection										
Previous infection and no vaccination	565	6,051	895	5,372	46.1 (39.5 to 51.9)	3	43	17	50	73.4 (0.2 to 92.9)
Two doses and no previous infection	10,880	6,051	8,846	5,372	−1.1 (−7.1 to 4.6)	41	43	168	50	76.8 (58.0 to 87.1)
Two doses and previous infection	1,160	6,051	2,108	5,372	55.1 (50.9 to 58.9)	1	43	41	50	97.8 (82.6 to 99.7)
Three doses and no previous infection	1,884	6,051	2,983	5,372	52.2 (48.1 to 55.9)	3	43	98	50	98.2 (91.9 to 99.6)
Three doses and previous infection	153	6,051	489	5,372	77.3 (72.4 to 81.4)	0	43	23	50	100.0 (82.6 to 100.0)¶

CI denotes confidence interval, Covid-19 coronavirus disease 2019, and PCR polymerase chain reaction.
†A symptomatic infection was defined as a PCR-positive nasopharyngeal swab specimen that was obtained because of the presence of symptoms consistent with a respiratory tract infection. Effectiveness was estimated with the use of a test-negative, case–control study design. The widths of the confidence intervals have not been adjusted for multiplicity and should not be used to infer definitive differences among exposure groups. Severity, criticality, and fatality were defined according to World Health Organization guidelines.
‡Case participants and controls were exactly matched in a 1:2 ratio according to sex, 10-year age group, nationality, calendar week of PCR test, and comorbidity count in the Alpha, Beta, and Delta analyses. Case participants and controls were exactly matched in a 1:1 ratio according to sex, 10-year age group, nationality, and calendar week of PCR test in the Omicron B.A.1 and BA.2 analyses.
‡Case participants and controls were exactly matched in a 1:5 ratio according to sex, 10-year age group, nationality, calendar week of PCR test, and comorbidity count in the Alpha, Beta, and Delta analyses. Case participants and controls were exactly matched in a 1:5 ratio according to sex, 10-year age group, nationality, and calendar week of PCR test in the Omicron B.A.1 and BA.2 analyses.
§Unexposed was defined as no previous pre-omicron infection and no vaccination.
¶The confidence interval was estimated with the use of McNemar's test for matched pairs.

Figure 1. Effectiveness of previous pre-omicron infection, vaccination with BNT162b2, and hybrid immunity against symptomatic Alpha, Beta, Delta, Omicron BA.1 and BA.2 infections

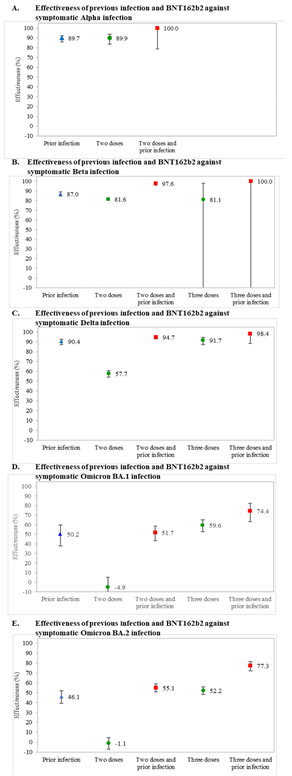
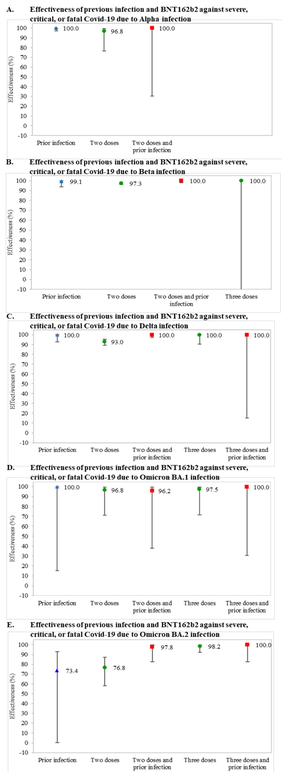


Figure 2. Effectiveness of previous pre-omicron infection, vaccination with BNT162b2, and hybrid immunity against severe, critical, or fatal Covid-19



Conclusions

- Effectiveness of previous pre-omicron infection, vaccination, and hybrid immunity against symptomatic infection with Omicron BA.1 and BA.2 subvariants was lower than that against earlier SARS-CoV-2 variants
- There are no discernable differences between Omicron BA.1 and BA.2 in the effects of previous pre-omicron infection, vaccination, and hybrid immunity
- Vaccination enhances the protection of those with a previous pre-omicron infection regardless of variant
- Hybrid immunity resulting from previous pre-omicron infection and recent booster vaccination conferred the strongest protection against infection
- All five forms of immunity were associated with strong and durable protection against Covid-19–related hospitalization and death across all SARS-CoV-2 variants