Serological response to mRNA and inactivated COVID-19 vaccine in healthcare workers in Hong Kong: decline in antibodies 12 weeks after two doses

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To the Editor—We previously reported serological findings of 302 healthcare workers (HCWs) who completed two doses of mRNA (BNT162b2/Comirnaty; Fosun-BioNTech Pharma) and inactivated COVID-19 vaccine (CoronaVac; Sinovac Life Sciences, Beijing, China).[1] Both vaccines were found to be immunogenic in the majority of HCWs. The BNT162b2 resulted in a 11-fold higher level of anti-spike IgG (Abbott SARS-CoV-2 IgG II Quant assay, mean=11572.6 AU/mL vs 1005.2 AU/mL; P<0.001) and a higher surrogate neutralising antibody (sNAb) [GenScript cPass SARS-CoV-2 Surrogate Virus Neutralization Test Kit] positive rate (100% vs 94.4%; P<0.001).

We report week 12 serological data of our cohort. Among 197 CoronaVac and 100 BNT162b2 recipients, baseline characteristics of the two vaccine arms were comparable except sex (60.9% and 38% female in CoronaVac and BNT162b2, respectively) [online supplementary Table 1]. There was no difference in anti-spike immunoglobulin G (IgG) positive rate at week 12 (98.5% in CoronaVac vs 99% in BNT162b2; P=1) [Table 1]. Waning of IgG level was observed in both vaccine arms with a larger magnitude of decline in BNT162b2 (-72% vs -64.6%; P<0.001). Despite the more pronounced decline, the median anti-spike IgG of BNT162b2 remained 11-fold higher than that of CoronaVac at week 12 (2840.25 AU/mL vs 253.60 AU/mL; P<0.001).

Decline in sNAb was also observed in both arms but the magnitude was significantly smaller in BNT162b2 (-28.3% in CoronaVac vs -2.3% in BNT162b2; P<0.001). Using the manufacturer's positive cut-off at 30% signal inhibition or above,

TABLE 1. Antibody levels after vaccination with CoronaVac or BNT162b2*

	Corona Vac			BNT162b2			P value† (CoronaVac vs BNT162b2)			
	After dose 1 (≥2 weeks) "Sample 1"	After dose 2 (≥2 weeks) "Sample 2"	After dose 2 (≥12 weeks) "Sample 3"	After dose 1 (≥2 weeks) "Sample 1"	After dose 2 (≥2 weeks) "Sample 2"	After dose 2 (≥12 weeks) "Sample 3"	Sample 1	Sample 2	Sample 3	
No. of serum samples available for analysis		197			100					
Abbott SARS-CoV-2 IgG										
Antibody positive results	128 (65.0%)	196 (99.5%)	194 (98.5%)	98 (98.0%)	100 (100%)	99 (99.0%)	<0.001	1	1	Fisher's exact test§
Antibody level, AU/mL, median (IQR)‡	84.40 (36.50-161.80)	721.30 (449.20-1142.80)	253.60 (163.70-403.00)	1156.45 (542.88-1816.58)	9704.15 (6187.30-14616.48)	2840.25 (1849.93-4522.68)	<0.0001	<0.0001	<0.0001	Wilcoxon rank-sum test‖
GenScript cPass surrogate neutralising antibody										
Antibody positive results	32 (16.2%)	186 (94.4%)	123 (62.4%)	93 (93.0%)	100 (100%)	99 (99.0%)	<0.0001	0.0182	<0.0001	Fisher's exact test
Antibody level, % signal inhibition, median (IQR)	12.61 (2.43-25.18)	69.30 (52.07-52.07)	35.27 (23.60-51.41)	68.29 (51.59-82.56)	97.34 (95.95-98.87)	95.58 (88.71-97.94)	<0.0001	<0.0001	<0.0001	Wilcoxon rank-sum test

Abbreviations: IgG = immunoglobulin G; IQR = interquartile range; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2

* Data are shown in No. (%), unless otherwise specified

† A P value of <0.05 was considered statistically significant

‡ Mean was used in the previous letter

§ Fisher's exact test's null hypothesis: there is no dependence between positive/negative result and vaccine types

‖ Wilcoxon rank-sum test's null hypothesis: there is no difference in central tendency (median) of the readings between vaccine type

significantly more CoronaVac recipients had lost their sNAb at week 12 (94.4% sNAb positive at week 2, 62.4% at week 12) whereas 99% of BNT162b2 recipients remained sNAb positive. Throughout the three time points, BNT162b2 arm had higher levels of anti-spike IgG and sNAb (P<0.001) [Fig].

Among the 286 HCWs who had positive sNAb after two doses of vaccine, 64 had lost their sNAb while 222 had sustained sNAb at week 12. Sustained sNAb at week 12 were associated with younger age, BNT162b2 and higher antibody at any time point (Table 2). Multivariate logistic regression analysis showed that only higher IgG and sNAb level at 2 weeks after the second dose were significantly associated with sustained sNAb at week 12 (online supplementary Table 2).

These results demonstrate rapid antibody decline after both mRNA and inactivated vaccine with a more durable sNAb in the BNT162b2 arm. However, further studies are needed to clarify the impact of waning antibody on vaccine efficacy and protection against severe infection.

Author contributions

Concept or design: All authors.
Acquisition of data: All authors.
Analysis or interpretation of data: All authors.
Drafting of the manuscript: JST Zee.
Critical revision of the manuscript for important intellectual content: All authors.

All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest

All authors have disclosed no conflicts of interest.

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Ethics approval

This study obtained ethics approval (Ref RC-2021-07) from the Research Ethics Committee of the Hong Kong Sanatorium & Hospital Medical Group.

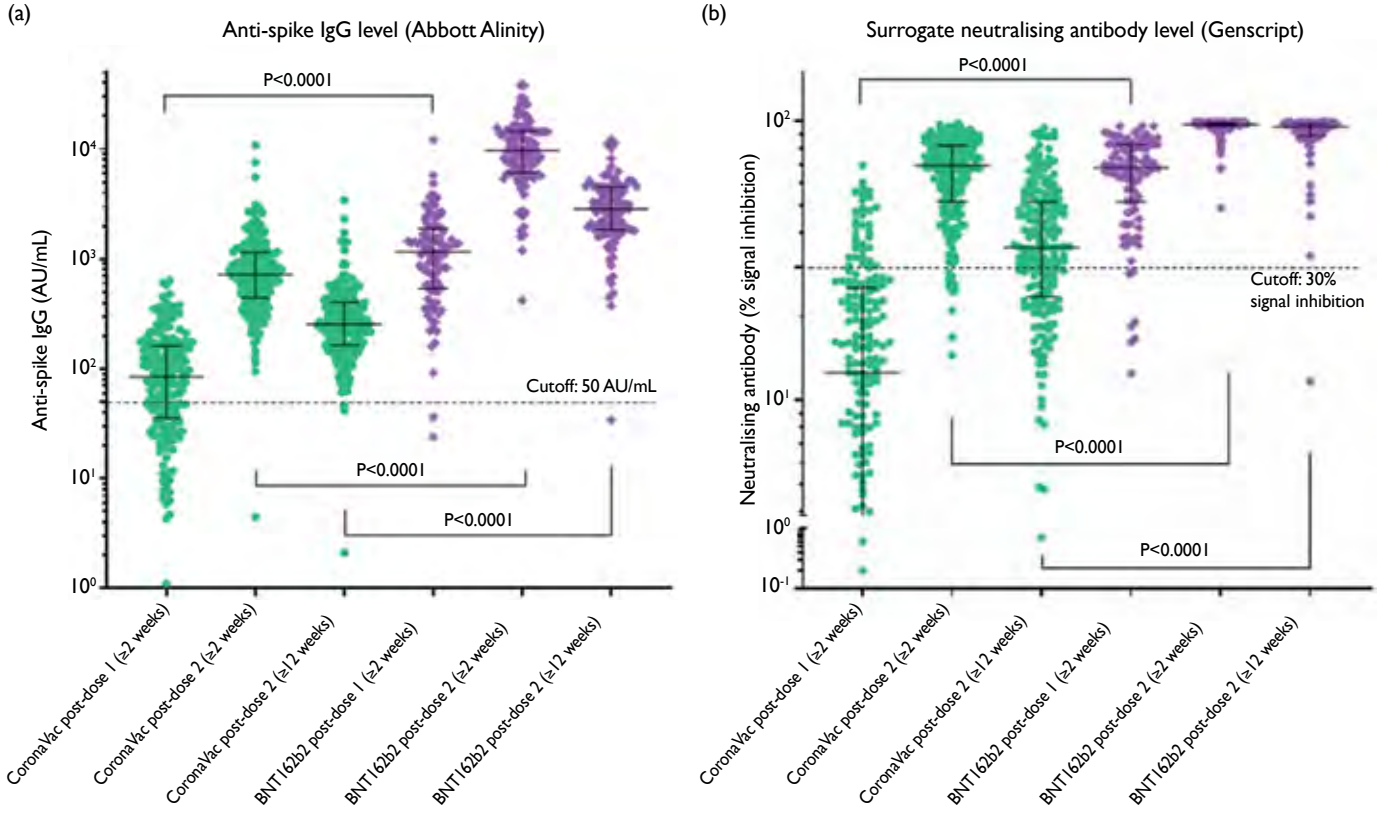

FIG. (a) Anti-spike immunoglobulin G (IgG) level; (b) surrogate neutralising antibody level after dose 1 and 2 of CoronaVac and BNT162b2. Each dot represents the antibody level of a participant after dose 1 or dose 2 of CoronaVac or BNT162b2

TABLE 2. Factors associated with sustained or lost surrogate neutralising antibody (sNAb) at week 12*

	sNAb lost at week 12 (n=64)	sNAb sustained at week 12 (n=222)	P value†
Sex			0.0749
Male	23 (35.9%)	110 (49.5%)	
Female	41 (64.1%)	112 (50.5%)	
Age, y	50.75 ± 10.12	47.21 ± 10.20	0.0154
Vaccine type			<0.0001
CoronaVac	63 (98.4%)	123 (55.4%)	
BNT162B2	1 (1.6%)	99 (44.6%)	
Medical co-morbidites			
No. of medical co-morbidities			0.9386
None	49 (76.6%)	158 (71.2%)	
1	9 (14.1%)	40 (18%)	
2	4 (6.3%)	15 (6.8%)	
3	2 (3.1%)	8 (3.6%)	
4	0	0	
5	0	1 (0.5%)	
Diabetes mellitus	4 (6.3%)	10 (4.5%)	0.5233
Hypertension	6 (9.4%)	23 (10.4%)	1
Hyperlipidaemia	6 (9.4%)	26 (11.7%)	0.8219
Cardiovascular disease	1 (1.6%)	1 (0.5%)	0.3981
Stroke	0	0	-
Asthma	0	4 (1.8%)	0.5782
Chronic renal disease	0	1 (0.5%)	1
Chronic liver disease or cirrhosis	3 (4.7%)	4 (1.8%)	0.1890
History of malignancy	2 (3.1%)	8 (3.6%)	1
Systemic lupus erythematosus	0	0	-
Other autoimmune disease	1 (1.6%)	6 (2.7%)	1
Medication			
Steroid	0	1 (0.5%)	1
Non-steroid immunosuppressant	0	1 (0.5%)	1
Abbott SARS-CoV-2 IgG (AU/mL)			
After dose 1 (≥2 weeks)	70.50 ± 77.48	232.45 ± 982.83	<0.0001
After dose 2 (≥2 weeks)	454.95 ± 363.50	1952.25 ± 8033.10	<0.0001
After dose 2 (≥12 weeks)	158.45 ± 94.83	654.20 ± 2347.80	<0.0001
GenScript cPass surrogate neutralising antibody (% signal inhibition)			
After dose 1 (≥2 weeks)	7.81 ± 18.64	35.28 ± 52.14	<0.0001
After dose 2 (≥2 weeks)	55.00 ± 23.44	88.53 ± 22.45	<0.0001
After dose 2 (≥12 weeks)	21.57 ± 9.90	70.25 ± 48.17	<0.0001
(CoronaVac only)			
Abbott SARS-CoV-2 IgG (AU/mL)			
After dose 1 (≥2 weeks)	72.10 ± 78.45	115.50 ± 129.55	0.0036
After dose 2 (≥2 weeks)	458.20 ± 364.30	986.20 ± 711.90	<0.0001
After dose 2 (≥12 weeks)	159.50 ± 90.80	356.20 ± 252.60	<0.0001
GenScript cPass surrogate neutralising antibody (% signal inhibition)			
After dose 1 (≥2 weeks)	7.56 ± 18.73	16.16 ± 20.60	0.0052
After dose 2 (≥2 weeks)	55.64 ± 24.17	78.02 ± 18.10	<0.0001
After dose 2 (≥12 weeks)	21.70 ± 9.86	47.55 ± 24.22	<0.0001

Abbreviations: IgG = immunoglobulin G; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; sNAb = surrogate neutralising antibody

* Data are shown as mean ± standard deviation or No. (%), unless otherwise specified

† No. of positive test results was tested using Fisher's exact test or Chi squared test. Means were tested using *t* test. A P value of <0.05 was considered statistically significant

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