JIDC | THE JOURNAL OF INFECTION IN DEVELOPING COUNTRIES

Coronavirus Pandemic

Effects of vaccination on antibody level and duration of viral shedding in Omicron patients

Zhen Wan[1,2,3 #], Jing Han[1,2 #], Deyin Wang[4,5 #], Yonghui Li[3], Weixiang Zhai[5], Weikang Zhao[1,2], Xiaodong Zhang[3], Yi Xie[1,2]

[1] *Haihe Hospital,Tianjin University, Tianjin, 300350, China*
[2] *Tianjin Institute of Respiratory Diseases, Tianjin, 300350, China*
[3] *Tianjin University, Tianjin, 300072, China*
[4] *Tianjin University of Finance and Economics, Tianjin, 300221, China*
[5] *Tianjin Medical College, Tianjin, 300222, China*

# Authors contributed equally to this work

Abstract

Introduction: We compared the clinical characteristics of vaccinated and non-vaccinated Omicron patients in order to provide a reference for the clinical diagnosis and treatment of coronavirus disease 2019 (COVID-19).

Methodology: This study included 360 patients diagnosed with COVID-19. The serum immunoglobulin G (IgG) and serum immunoglobulin M (IgM) antibody levels of the patients and the duration of virus shedding were analyzed according to age, gender, vaccine dose, and the time from the most recent vaccination to the onset of Omicron infection.

Results: Age (OR = 0.974), days from last vaccination to onset ≤ 180 days (OR = 4.409), and booster dose of the vaccine (OR = 4.999) were protective factors associated with patients who were IgG antibody positive. The duration of virus shedding in IgG -antibody-positive patients was 9 (8-11) days; and this was significantly lower than that in IgG-antibody-negative patients, who had virus shedding duration of 10 (8-12) days ($p < 0.05$).

Conclusions: Booster immunizations could increase IgG-antibody in patients who have already been infected with the Omicron variant and enhance immune protection. In addition, COVID-19 vaccination may shorten the duration of virus shedding.

Key words: COVID-19; vaccination; Omicron; antibody; infectivity.

J Infect Dev Ctries 2024; 18(9.1):S184-S190. doi:10.3855/jidc.19160

(Received 31 August 2023 – Accepted 01 April 2024)

Introduction

The severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) Omicron mutant (Pango lineage B.1.1.529) was first found in South Africa in November 2021 [1]. It subsequently spread quickly around the world and evolved into sublineages such as BA.1 and BA.2 [2,3]. The Omicron variant has caused a large number of infections and deaths and posed a huge threat to global public health security.

Vaccination is one of the most cost-effective and specific interventions for controlling infectious diseases. There has been substantial progress in research on the effectiveness of coronavirus disease 2019 (COVID-19) vaccination worldwide. Studies show that the first-generation COVID-19 vaccines could provide durable protection to prevent disease progression from non-severe to severe outcomes [4-7]. Although previous studies have provided preliminary insights, there are still several gaps in the current literature. This is especially the case with the Omicron variant, where there is insufficient information on the long-term immune response, antibody levels, and virus shedding time of vaccine recipients.

The SARS-CoV-2 virus will continue to mutate into new variants. Therefore, close surveillance of SARS-CoV-2 evolution, immune evasion and vaccination are essential for long-term management of COVID-19. In particular, understanding the immune status of patients after vaccination will be key for policy-makers to implement booster vaccine doses or non-pharmacological interventions. The purpose of this study was to investigate in detail the effects of vaccination on antibody level and duration of viral shedding in patients infected with the Omicron variant.

We evaluated the effectiveness of different vaccination plans in responding to Omicron variants by analyzing changes in individual antibody levels and virus shedding time after vaccination. This study aimed to develop evidence-based vaccination strategies, and thus provide a scientific basis for public health interventions.

Methodology

Study participants

This study was a retrospective cohort study. A total of 429 patients infected with Omicron and admitted to the Tianjin Haihe Hospital from May 13, 2022, to August 5, 2022, were assessed for inclusion in the study. All patients in this study were of the local Chinese ethnicity. The inclusion criteria were as follows: local patients with a positive novel coronavirus nucleic acid test result before admission. The exclusion criteria were as follows: (1) patients who had not been released from centralized isolation as of August 14, 2022 (the date the statistical analysis was conducted); (2) those with missing vaccination and antibody information; and (3) patients aged < 3 years since they did not qualify for vaccination. Among the 429 patients admitted, one patient under isolation restrictions, 60 patients with incomplete information, and 8 patients aged < 3 years were excluded following the exclusion criteria. A total of 360 patients were thus included in this study.

Data collection

We collected clinical and demographic information on each patient, after removing identifying information. The data included age, gender, comorbidities, vaccination, duration of virus shedding, and serum immunoglobulin G/serum immunoglobulin M (IgG/IgM) antibody levels. Following China's healthcare policies, those with COVID-19 were immediately tested for COVID-19 RNA at the risk location determined by professionals. Since the patients were all local, the antibodies were detected within one week of onset for all cases.

The types of vaccines were categorized into inactivated virus vaccines (Sinovac/Sinopharm/Zifivax COVID-19 vaccine) and adenovirus vector vaccines (CanSinoBIO COVID-19 vaccine). The third dose of the inactivated virus vaccine was a booster, while the second dose of the adenovirus vector vaccine was a booster. The two groups of patients based on vaccine type, were further were divided according to the number of days from the last vaccination to the disease onset (≤ 180 days group and > 180 days group).

This study was approved by the Ethics Review Committee of Tianjin Haihe Hospital (approval no. 2022HHWZ-004) and the requirement for informed consent was waived. All methods were carried out in accordance with the relevant guidelines and regulations.

Patient, pathogenic and serological examination

In this study, patients were classified into asymptomatic, mild and ordinary based on clinical characteristics. In the mild type patients, the main symptoms are upper respiratory tract infections, such as dry throat, sore throat, cough, fever, etc., with no

Table 1. IgG and IgM antibody levels in different groups of patients with Omicron infection.

Variable	N	IgG positive	*p*	IgM positive	*p*
Gender					
Male	176	133 (75.6%)	0.391	15 (8.5%)	0.167
Female	184	146 (79.3%)		9 (4.9)	
Age (years)					
< 14	13	12 (92.3%)	0.003	1 (7.7%)	0.835
14–59	287	230 (80.1%)		18 (6.3%)	
> 60	60	37 (61.7%)		5 (8.3%)	
No. of days from the last vaccination to the disease onset (days)					
> 180	222	166 (74.8%)	< 0.001	16 (7.2%)	0.806
≤ 180	123	112 (91.1%)		8 (6.5%)	
Vaccination status					
Unvaccinated	15	1 (6.7%)	< 0.001	0 (0%)	0.256
No booster vaccinated	127	76 (59.8%)		6 (4.7%)	
Booster vaccinated	218	202 (92.7%)[a]		18 (8.3%)	
Type of vaccine					
Adenovirus vectors	40	30 (75%)	0.343	3 (7.5%)	0.749
Inactivated viruses	305	248 (81.3%)		21 (6.9%)	
Comorbidities					
Yes	91	64 (70.3%)	0.058	7 (7.7%)	0.650
No	269	215 (79.9%)		17 (6.3%)	

[a] This difference was statistically significant when compared with the no booster vaccinated group, $p < 0.05$.

manifestations of pneumonia on imaging. Ordinary type patients had fever, respiratory tract symptoms and other typical symptoms. In addition, imaging showed signs of pneumonia.

Upper respiratory tract samples (nasopharyngeal swabs) of patients were collected and SARS-COV-2 was detected by nucleic acid amplification detection. According to the Chinese guidelines for prevention, control, diagnosis and treatment; patients were required to undergo at least two nucleic acid tests before being discharged. The standard for nucleic acid collection was to start collecting nasopharyngeal swabs from asymptomatic patients on the sixth day of admission. For symptomatic patients, nasopharyngeal swabs should be collected at least 3 days after the symptoms improved and the body temperature returned to normal. If the Ct value of *N* gene and *ORF* gene in two consecutive SARS-CoV-2 nucleic acid tests was more than 35 (fluorescent quantitative polymerase chain reaction, PCR, method, the threshold value was 40, and the sampling time interval was at least 24 hours), or the nucleic acid of novel coronavirus was negative in two consecutive tests (fluorescent quantitative PCR method, the threshold value was less than 35, and the sampling time interval was at least 24 hours), the patient could be discharged. The time from the first positive nucleic acid test to patients' discharge was considered the time of virus shedding.

Specific IgM and IgG antibodies were detected in blood samples using SARS-CoV-2 IgM and IgG detection kit and chemiluminescence method. All patients were tested for IgM and IgG within three days of admission to the hospital. The antibody results were expressed as S/CO, where S represents the luminous value of the sample and CO represents the cut-off value. An S/CO value ≥ 1.00 indicated a positive result and an S/CO value < 1.00 indicated a negative result.

Statistical analysis

IBM SPSS Statistics for Windows (version 22.0; IBM Corp., Armonk, NY, USA) software was used for the statistical analyses. The numerical variables with normal distributions were expressed as mean ± standard deviation (x ± s), and comparisons between the two groups were performed with t tests. Continuous variables were presented as medians (25^{th} percentile, 75^{th} percentile) due to skewed distributions, and categorical variables were presented as n (%). Rate comparisons were performed using the Mann-Whitney U test, and the Kruskal-Wallis test was used for comparisons between groups, as appropriate. Statistical significance was set at p value < 0.05. All variables with $p < 0.2$ in the univariate analysis were included in the multivariate logistic regression model. A Kaplan-Meier curve was used to plot the graph comparing different IgG antibodies and the duration of virus shedding. Multivariate logistic regression was used to evaluate the factors influencing the patients' IgG level. The results were presented as odds ratios (ORs) and 95% confidence intervals (CIs).

Results

A total of 360 patients were included in this study. There were 176 (48.89%) men and 184 (51.11%) women. The average age was 41.69 ± 18.103 years. There were 13 patients (3.6%) aged < 14 years, 287 (79.7%) aged 14-59 years, and 60 (16.7%) aged ≥ 60 years. Among the admitted patients, 228 (63.3%) were asymptomatic, 128 (35.6%) had mild type, and 4 (1.1%) had ordinary type. A total of 25.3% (91) of the patients had one or more comorbidities; the most common of which were hypertension, diabetes, and coronary heart disease (CHD). Fifteen of the patients (4.16%) were not vaccinated. A total of 127 patients (35.28%) did not receive a booster vaccination, while 218 (60.56%) did receive a booster vaccination. Among the 345 patients vaccinated, 222 (64.35%) were in the > 180 days group and 123 (35.65%) were in the ≤ 180 days group. Forty patients (11.59%) received an adenovirus vector vaccine, while 305 (88.41%) received an inactivated virus vaccine. Univariate analysis was conducted for each group of indicators. Significant differences were

Table 2. Multivariate analysis of influencing factors of IgG antibody level.

Variable	β	S.E.	Wald χ^2	p	OR	95% CI	
						Lower	Upper
Age	-0.026	0.009	9.236	0.002	0.974	0.957	0.991
No. of days from the last vaccination to the disease onset							
> 180					1.000		
≤ 180	1.484	0.392	14.340	< 0.001	4.409	2.046	9.502
Vaccination status							
No booster vaccinated					1.000		
Booster vaccinated	1.609	0.446	13.040	< 0.001	4.999	2.087	11.972
Constant	0.747	0.610	1.501	0.221	2.110		

CI: confidence interval; OR: odds ratio; SE: standard error.

Table 3. Comparison of the durations of virus shedding in different groups of patients with Omicron infections.

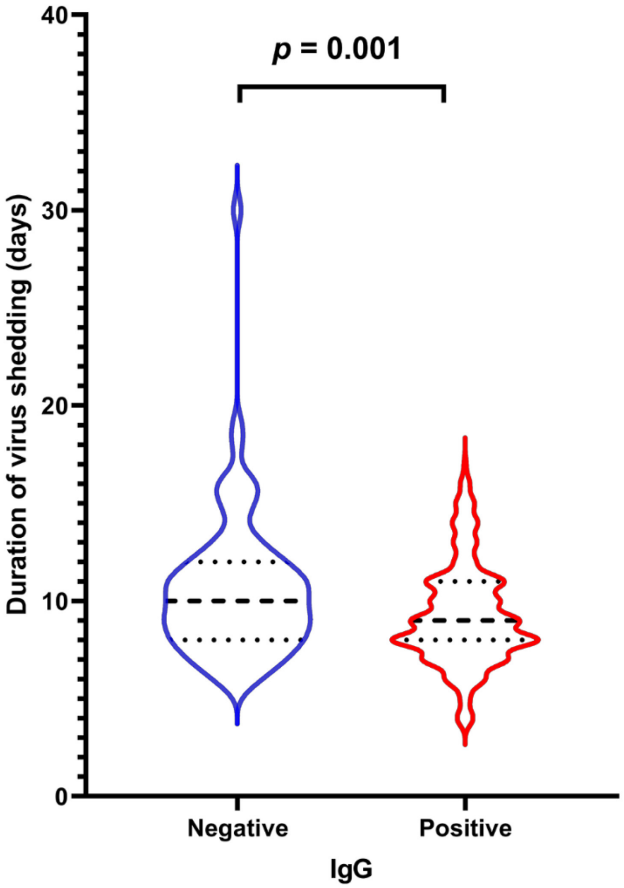
Variable	N	Duration of virus shedding *M* (P_{25}, P_{75})	*H/Z*	*p*
Gender				
Male	176	9 (8,11)	-1.132	0.258
Female	184	9 (8,11)		
Age (years)				
< 14	13	10 (6.5,12)		
14–59	287	9 (8,11)	0.604	0.739
> 60	60	9 (8,11)		
Comorbidities				
Yes	91	9 (8,11)	-0.215	0.830
No	269	9 (8,11)		
IgG				
Negative	81	10 (8,12)	-3.211	0.001
Positive	279	9 (8,11)		

identified between the groups for age, number of days from the last vaccination to the disease onset (>180 days or ≤ 180 days), and vaccination status ($p < 0.001$) (Table 1).

In the multivariate regression analysis, age (OR = 0.974; 95% CI 0.957-0.991; $p < 0.05$), days from last vaccination to onset ≤ 180 days (OR = 4.409; 95% CI 2.046-9.502; $p < 0.001$), and booster vaccination (OR = 4.999; 95% CI 2.087-11.972; $p < 0.001$) were statistically significant (Table 2).

Among all 360 patients, the median number of days of virus shedding was 9 (8-11) days. A univariate analysis was conducted after the patients were grouped according to their gender, age, comorbidities, and IgG antibody status (Table 3). The duration of virus shedding was 10 (8-12) days among the IgG-antibody-negative patients and 9 (8-11) days among the IgG-antibody-positive patients (Figure 1). This difference was statistically significant ($p < 0.05$) (Figure 2).

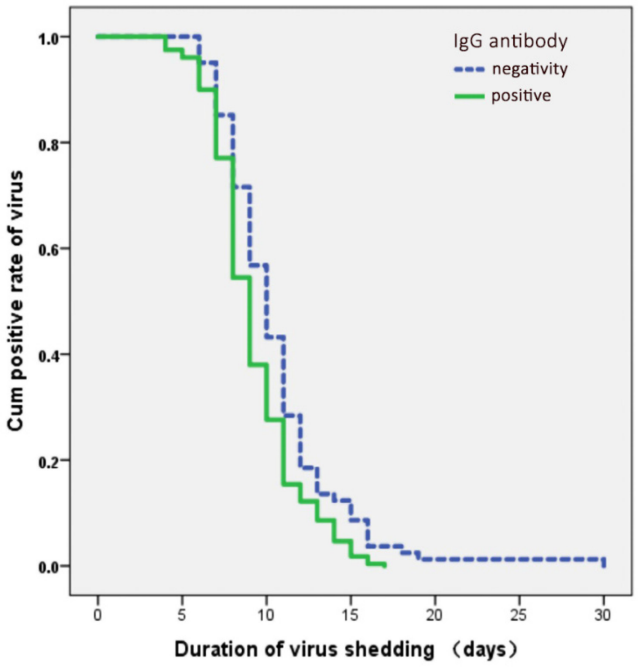
Figure 1. Comparison of the duration of virus shedding grouped by IgG antibody status.



Discussion

A retrospective analysis of the vaccination information of 360 patients with COVID-19 who were

Figure 2. Kaplan-Meier plot for IgG antibody status.



Cum, cumulative

admitted to the Haihe Hospital in Tianjin City was conducted. The results showed that the age, days from last vaccination to onset of ≤ 180 days, and booster vaccination were protective factors for IgG antibodies. The median duration of virus shedding was 9 (8-11) days among the 360 patients. The duration of virus shedding among the IgG-antibody-positive patients was lower than that among the IgG-antibody-negative patients. None of the patients in this study developed any severe symptoms.

This study found that the level of IgG antibodies was higher in patients who were vaccinated with booster vaccine before infection. Patients with positive IgG antibody had a shorter virus infection duration. This suggests that vaccination can effectively help the body clear the virus quicker, reduce the rate of severe COVID-19, and even help prevent severe disease and/or death. While it is clear that vaccination cannot completely prevent the invasion of viruses and eliminate infection, it has a significant effect on the body's resistance to the virus. Previous research has shown that after the vaccine booster dose, the antibody level increases rapidly [8]. The antibody level begins to rise after three days and increases even more after seven days. By day 14, the antibody level has been found to be approximately 10-30 times the original level. Although the antibody level decreases again by six months after the booster vaccination, the lowest level still exceeds the peak of the previous two doses of the vaccination. Many reports have indicated that the positive conversion rate of serum neutralizing antibodies produced by COVID-19 vaccines against Omicron variants is high. For example, healthy adults who received three doses of the COVID-19 mRNA vaccine or inactivated virus vaccine against an Omicron mutant (including BA. 1 ~ BA. 5 and other subtype mutants) by homologous vaccination, have been found to have 3.3% to 80% higher levels of serum antibodies against Omicron variants compared to the unvaccinated individuals [9-16]. Lu *et al.* also found that one year later, the sera of 135 patients with COVID-19 treated with one dose of mRNA vaccine (BNT162b2), one dose of inactivated virus vaccine (CoronaVac), and two doses of inactivated virus vaccine (CoronaVac), showed levels of positive neutralizing antibodies that were 90.6%, 21.7%, and 85.7%, respectively, all of which were higher than the 12.3% in the unvaccinated group [17].

The results also showed that the level of IgG antibody positivity in patients in the ≤ 180 days group was higher than that in the patients who were in > 180 days group. Other studies have also shown that the level of antibodies to COVID-19 virus generally decrease within 6 to 12 months after vaccination [18-20]. Gaebler *et al*. also found that the antibody level decreases over time and the virus continues to mutate [21]. Breakthrough infections have often occurred in individuals who are fully vaccinated, which has prompted experts to widely recommend booster vaccinations to combat the decline of immunity and COVID-19 variations [22].

Our study found that the duration of virus shedding in IgG-antibody-positive patients was shorter than that in IgG-antibody-negative patients. Wang *et al.* showed that the IgG antibody level has the greatest impact on the efficacy of neutralization; therefore, IgG levels can be used to assess the body's resistance to COVID-19 infections [23]. Many studies have shown that vaccination can reduce the symptoms of COVID-19 and shorten the course of the disease [9,24-25]. Vaccination has also been shown to provide a protective effect and help establish an immune barrier against COVID-19. Xu *et al.* found that inactivated vaccines can shorten viral RNA shedding in breakthrough infected patients who have mild-to-moderate illness and may improve the ability of the host to generate specific antibodies against the infection [26]. There were no severe cases among the patients we studied. Therefore, we could not determine the relationship between disease severity and vaccine. We intend to conduct multi-center and large-scale research on the severity of COVID-19 in the future.

Conclusions

The COVID-19 booster vaccine significantly increased the IgG antibody level in patients with Omicron infections, strengthening their immune protection. In addition, COVID-19 vaccination shortened the duration of virus shedding. Therefore, booster vaccinations are an important means of controlling the COVID-19 pandemic.

Acknowledgements

We thank all our colleagues who helped us during the current study. We would like to thank Editage (www.editage.com) for English language editing.

Funding

This work was funded by Tianjin Key Medical Discipline (Specialty) Construction Project TJYXZDXK-067C, "Project + Team" Key Training Fund of Tianjin (XC202041), Tianjin Science and Technology Plan Project (20YFZCSN01110), and Science Technology Planning

Project of Tianjin Municipal Education Commission (2022YGYB14).

Ethics approval

Given the retrospective nature of this study, the Ethics Review Board at our institution waived the requirement for informed patient consent.

Availability of data and material

Data used to support the findings of this study are available from the corresponding author upon request.

Authors' contributions

Conception and design of study: XZ, JH, YX, DW; literature search, ZW, YL; data collection, WZ, YL, ZW; data analysis, JH, YX; data interpretation, XZ, JH, YX, WZ, ZW. All authors read and approved the final manuscript. ZW, JH, and DW contributed equally to this work.

References

1. World Health Organization (2021) Classification of Omicron (B.1.1.529): SARS-CoV-2 variant of concern. Available: https://www.who.int/news/item/26-11-2021-classification-of-omicron-(b.1.1.529)-sars-cov-2-variant-of-concern. Accessed: 14 September 2023.
2. Khandia R, Singhal S, Alqahtani T, Kamal MA, El-Shall NA, Nainu F, Desingu PA, Dhama K (2022) Emergence of SARS-CoV-2 Omicron (B.1.1.529) variant, salient features, high global health concerns and strategies to counter it amid ongoing COVID-19 pandemic. Environ Res 209: 112816. doi: 10.1016/j.envres.2022.112816.
3. Islam MdR, Hossain MdJ (2022) Detection of SARS-CoV-2 Omicron (B.1.1.529) variant has created panic among the people across the world: what should we do right now? J Med Virol 94: 1768–1769. doi: 10.1002/jmv.27546.
4. Wu Q, Wang H, Cai J, Ai J, Li Y, Zhang H, Wang S, Sun F, Wu Y, Zhou J, Wang Y, Yu H, Zhang W (2023) Vaccination effects on post-infection outcomes in the Omicron BA.2 outbreak in Shanghai. Emerg Microbes Infect 12: e2169197. doi: 10.1080/22221751.2023.2169197.
5. McMenamin ME, Nealon J, Lin Y, Wong JY, Cheung JK, Lau EHY, Wu P, Leung GM, Cowling BJ (2022) Vaccine effectiveness of one, two, and three doses of BNT162b2 and CoronaVac against COVID-19 in Hong Kong: a population-based observational study. Lancet Infect Dis. 22: 1435–1443. doi: 10.1016/S1473-3099(22)00345-0.
6. Yang B, Wong IOL, Xiao J, Tsang TK, Liao Q, Cowling BJ (2022) Effectiveness of CoronaVac and BNT162b2 vaccines against severe acute respiratory syndrome coronavirus 2 Omicron BA.2 infections in Hong Kong. J Infect Dis. 226: 1382–1384. doi: 10.1093/infdis/jiac360.
7. Huang Z, Xu S, Liu J, Wu L, Qiu J, Wang N, Ren J, Li Z, Guo X, Tao F, Chen J, Lu D, Sun X, Wang W (2022) Effectiveness of inactivated and Ad5-nCoV COVID-19 vaccines against SARS-CoV-2 Omicron BA. 2 variant infection, severe illness, and death. BMC Med. 20: 400. doi: 10.1186/s12916-022-02606-8.
8. Abbasi J (2022) Studies suggest COVID-19 vaccine boosters save lives. JAMA 327: 115. doi: 10.1001/jama.2021.23455.
9. Yu X, Qi X, Cao Y, Li P, Lu L, Wang P, Feng Y, Yang J, Wei H, Guo L, Sun M, Liu Q, Lv J, Feng Y (2022) Three doses of an inactivation-based COVID-19 vaccine induces cross-neutralizing immunity against the SARS CoV-2 Omicron variant. Emerg Microbes Infect 11: 749–752. doi: 10.1080/22221751.2022.2044271.
10. Wang K, Jia Z, Bao L, Wang L, Cao L, Chi H, Hu Y, Li Q, Zhou Y, Jiang Y, Zhu Q, Deng Y, Liu P, Wang N, Wang L, Liu M, Li Y, Zhu B, Fan K, Fu W, Yang P, Pei X, Cui Z, Qin L, Ge P, Wu J, Liu S, Chen Y, Huang W, Wang Q, Qin C-F, Wang Y, Qin C, Wang X (2022) Memory B cell repertoire from triple vaccinees against diverse SARS-CoV-2 variants. Nature 603: 919–925. doi: 10.1038/s41586-022-04466-x.
11. Lusvarghi S, Pollett SD, Neerukonda SN, Wang W, Wang R, Vassell R, Epsi NJ, Fries AC, Agan BK, Lindholm DA, Colombo CJ, Mody R, Ewers EC, Lalani T, Ganesan A, Goguet E, Hollis-Perry M, Coggins SA, Simons MP, Katzelnick LC, Wang G, Tribble DR, Bentley L, Eakin AE, Broder CC, Erlandson KJ, Laing ED, Burgess TH, Mitre E, Weiss CD (2022) SARS-CoV-2 BA.1 variant is neutralized by vaccine booster-elicited serum but evades most convalescent serum and therapeutic antibodies. Sci Transl Med 14: eabn8543. doi: 10.1126/scitranslmed.abn8543.
12. Evans JP, Zeng C, Qu P, Faraone J, Zheng Y-M, Carlin C, Bednash JS, Zhou T, Lozanski G, Mallampalli R, Saif LJ, Oltz EM, Mohler PJ, Xu K, Gumina RJ, Liu S-L (2022) Neutralization of SARS-CoV-2 Omicron sub-lineages BA.1, BA.1.1, and BA.2. Cell Host Microbe 30: 1093–1102.e3. doi: 10.1016/j.chom.2022.04.014.
13. Arora P, Zhang L, Krüger N, Rocha C, Sidarovich A, Schulz S, Kempf A, Graichen L, Moldenhauer A-S, Cossmann A, Dopfer-Jablonka A, Behrens GMN, Jäck H-M, Pöhlmann S, Hoffmann M (2022) SARS-CoV-2 Omicron sublineages show comparable cell entry but differential neutralization by therapeutic antibodies. Cell Host Microbe 30: 1103–1111.e6. doi: 10.1016/j.chom.2022.04.017.
14. Bartsch YC, Tong X, Kang J, Avendaño MJ, Serrano EF, García-Salum T, Pardo-Roa C, Riquelme A, Cai Y, Renzi I, Stewart-Jones G, Chen B, Medina RA, Alter G (2022) Omicron variant spike-specific antibody binding and Fc activity are preserved in recipients of mRNA or inactivated COVID-19 vaccines. Sci Transl Med 14: eabn9243. doi: 10.1126/scitranslmed.abn9243.
15. Tuekprakhon A, Nutalai R, Dijokaite-Guraliuc A, Zhou D, Ginn HM, Selvaraj M, Liu C, Mentzer AJ, Supasa P, Duyvesteyn HME, Das R, Skelly D, Ritter TG, Amini A, Bibi S, Adele S, Johnson SA, Constantinides B, Webster H, Temperton N, Klenerman P, Barnes E, Dunachie SJ, Crook D, Pollard AJ, Lambe T, Goulder P, Paterson NG, Williams MA, Hall DR, Conlon C, Deeks A, Frater J, Frending L, Gardiner S, Jämsén A, Jeffery K, Malone T, Phillips E, Rothwell L, Stafford L, Fry EE, Huo J, Mongkolsapaya J, Ren J, Stuart DI, Screaton GR (2022) Antibody escape of SARS-CoV-2 Omicron BA.4 and BA.5 from vaccine and BA.1 serum. Cell 185: 2422–2433.e13. doi: 10.1016/j.cell.2022.06.005.
16. Clemens SAC, Weckx L, Clemens R, Mendes AVA, Souza AR, Silveira MBV, Guarda SNF da, Nobrega MM de, Pinto MI de M, Gonzalez IGS, Salvador N, Franco MM, Mendonça RN de A, Oliveira ISQ, Souza BS de F, Fraga M, Aley P, Bibi S, Cantrell L, Dejnirattisai W, Liu X, Mongkolsapaya J, Supasa P, Screaton GR, Lambe T, Voysey M, Pollard AJ, Bittaye M, Woods D, Davies S, Smith H, Ulaszewska M, Sanders H, Mabette R, Vernon S, Valliji Z, Mead G, Tejpal C, Park J,

Beveridge A, Eldawi A, Felle S, Fraga M, Martins TM, Medrado CLM, Matos LJ de AC (2022) Heterologous versus homologous COVID-19 booster vaccination in previous recipients of two doses of CoronaVac COVID-19 vaccine in Brazil (RHH-001): a phase 4, non-inferiority, single blind, randomised study. Lancet 399: 521–529. doi: 10.1016/S0140-6736(22)00094-0.

17. Lu L, Chen L-L, Zhang RR-Q, Tsang OT-Y, Chan JM-C, Tam AR, Leung W-S, Chik TS-H, Lau DP-L, Choi CY-C, Fong CH-Y, Cai J-P, Tsoi H-W, Choi CY-K, Zhang X, Abdullah SMU, Chan BP-C, Chan K-H, Yuen K-Y, Hung IF-N, To KK-W (2022) Boosting of serum neutralizing activity against the Omicron variant among recovered COVID-19 patients by BNT162b2 and CoronaVac vaccines. eBioMedicine 79: 103986. doi: 10.1016/j.ebiom.2022.103986.
18. Sabino EC, Buss LF, Carvalho MPS, Prete CA, Crispim MAE, Fraiji NA, Pereira RHM, Parag KV, Peixoto P da S, Kraemer MUG, Oikawa MK, Salomon T, Cucunuba ZM, Castro MC, Santos AA de S, Nascimento VH, Pereira HS, Ferguson NM, Pybus OG, Kucharski A, Busch MP, Dye C, Faria NR (2021) Resurgence of COVID-19 in Manaus, Brazil, despite high seroprevalence. Lancet 397: 452–455. doi: 10.1016/S0140-6736(21)00183-5.
19. Chia WN, Zhu F, Ong SWX, Young BE, Fong S-W, Bert NL, Tan CW, Tiu C, Zhang J, Tan SY, Pada S, Chan Y-H, Tham CYL, Kunasegaran K, Chen MI-C, Low JGH, Leo Y-S, Renia L, Bertoletti A, Ng LFP, Lye DC, Wang L-F (2021) Dynamics of SARS-CoV-2 neutralising antibody responses and duration of immunity: a longitudinal study. Lancet Microbe 2: e240–e249. doi: 10.1016/S2666-5247(21)00025-2.
20. Widge AT, Rouphael NG, Jackson LA, Anderson EJ, Roberts PC, Makhene M, Chappell JD, Denison MR, Stevens LJ, Pruijssers AJ, McDermott AB, Flach B, Lin BC, Doria-Rose NA, O'Dell S, Schmidt SD, Neuzil KM, Bennett H, Leav B, Makowski M, Albert J, Cross K, Edara V-V, Floyd K, Suthar MS, Buchanan W, Luke CJ, Ledgerwood JE, Mascola JR, Graham BS, Beigel JH (2021) Durability of responses after SARS-CoV-2 mRNA-1273 vaccination. N Engl J Med 384: 80–82. doi: 10.1056/NEJMc2032195.
21. Gaebler C, Wang Z, Lorenzi JCC, Muecksch F, Finkin S, Tokuyama M, Cho A, Jankovic M, Schaefer-Babajew D, Oliveira TY, Cipolla M, Viant C, Barnes CO, Bram Y, Breton G, Hägglöf T, Mendoza P, Hurley A, Turroja M, Gordon K, Millard KG, Ramos V, Schmidt F, Weisblum Y, Jha D, Tankelevich M, Martinez-Delgado G, Yee J, Patel R, Dizon J, Unson-O'Brien C, Shimeliovich I, Robbiani DF, Zhao Z, Gazumyan A, Schwartz RE, Hatziioannou T, Bjorkman PJ, Mehandru S, Bieniasz PD, Caskey M, Nussenzweig MC (2021) Evolution of antibody immunity to SARS-CoV-2. Nature 591: 639–644. doi: 10.1038/s41586-021-03207-w.
22. Omer SB, Malani PN (2022) Booster vaccination to prevent COVID-19 in the era of Omicron: an effective part of a layered public health approach. JAMA 327: 628–629. doi: 10.1001/jama.2022.0892.
23. Wang Z, Lorenzi JCC, Muecksch F, Finkin S, Viant C, Gaebler C, Cipolla M, Hoffmann H-H, Oliveira TY, Oren DA, Ramos V, Nogueira L, Michailidis E, Robbiani DF, Gazumyan A, Rice CM, Hatziioannou T, Bieniasz PD, Caskey M, Nussenzweig MC (2021) Enhanced SARS-CoV-2 neutralization by dimeric IgA. Sci Transl Med 13: eabf1555. doi: 10.1126/scitranslmed.abf1555.
24. Fan Y-J, Chan K-H, Hung IF-N (2021) Safety and efficacy of COVID-19 vaccines: a systematic review and meta-analysis of different vaccines at phase 3. Vaccines 9: 989. doi: 10.3390/vaccines9090989.
25. Feikin DR, Higdon MM, Abu-Raddad LJ, Andrews N, Araos R, Goldberg Y, Groome MJ, Huppert A, O'Brien KL, Smith PG, Wilder-Smith A, Zeger S, Knoll MD, Patel MK (2022) Duration of effectiveness of vaccines against SARS-CoV-2 infection and COVID-19 disease: results of a systematic review and meta-regression. Lancet 399: 924–944. doi: 10.1016/S0140-6736(22)00152-0.
26. Xu C, He Z, Lei W, Chen L, Shen D, Wang X, Xu D, Xu Y, Huang J (2022) Comparison of the duration of viral RNA shedding and anti-SARS-CoV-2 spike IgG and IgM antibody titers in COVID-19 patients who were vaccinated with inactivated vaccines or not: a retrospective study. BMC Infect Dis 22: 831. doi: 10.1186/s12879-022-07808-2.

Corresponding authors

Yi Xie, M. Med.

Haihe Hospital,Tianjin University,

890 Jingu Road, Jinnan District, Tianjin, China
Tel: +86-18920180091
Fax: +86-18920180091
Email: xieyi1223@163.com

Xiaodong Zhang, MD.
Tianjin University, 92 Weijin Road,
Nankai District, Tianjin, China.
Tel: +86 022 27406852
Fax: +86 022 27406852
Email: xiaodongzhang@tju.edu.cn

Conflict of interests: No conflict of interests is declared.