The immunity of public health workers: observation from two waves SARS-CoV-2 Omicron variant endemic in Guangdong province, China

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To the Editor:

In April 2023, Annabel et al report a national prevalence of SARS-CoV-2 antibodies in primary and secondary school children in England [1]. They found high seroprevalence rate of SARS-CoV-2 either in primary or secondary school students. In particular, approximately three fold higher than confirmed infections in unvaccinated children. In late 2022, coronavirus disease 2019 (COVID-19) caused by Omicron variants of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) swept away rapidly throughout China,

especially in Guangdong Province (˜two weeks). Considering the high coverage of COVID-19 vaccines in China [2], the prevention strategies of COVID-19 had been changed from whole population-wide to key and high-risk population [3].

The archived data of COVID-19 vaccine has proved its safety and effectiveness, and has significant effects on preventing virus transmission, reducing disease and death. However, the immune protection effects of vaccination are less durable. The emerging variants of SARS-CoV-2 showed stronger immune escape and transmission ability, and the breakthrough and second infection of COVID-19 have become the biggest challenge for public. This study was designed to investigate the neutralizing antibody (NAb) levels of individuals after first wave rapidly pandemic and the second wave sporadic infection since the end of 2022, and aim to evaluate the cross protection against the latest circulated variants of SARS-CoV-2 in China.

From December 2022 to January 2023, each serum samples was collected from 107 public health workers (adults) at Guangdong Provincial Center for Disease Control and Prevention (GDCDC) who had recovered 4 weeks of first wave COVID-19 pandemic caused by Omicron BA.5 [4]. All participants aged between 22 and 62, including 44 males and 63 females. In July 2023, during the second wave of COVID-19 epidemic caused by Omicron XBB.1.9 in Guangdong Province, 10 (aged 31-57 years old, 10 females) participants reported first or secondary infection, each serum sample were collected accordingly.

The neutralization assay against to SARS-CoV-2 was performed in a biosafety third-level laboratory (BSL-3) of GDCDC. Prototype (2020XN4276) and Omicron sub-lineages (BA.5, GDPCC 2.00303; BQ.1, GDPCC 2.01502; XBB.1.1, GDPCC 2.01503; XBB.1.9, GDPCC 2.01543; XBB.1.16, GDPCC 2.01541) of SARS-CoV-2 clinical isolates were used as target virus, and the titer of each serum sample was determined according to the standard protocol as previously described [5].

For the serum samples from first wave infection participants, we found the NAb titers were significantly decreased against prototype SARS-CoV-2 compared to Omicron variants BA.5, BQ.1 and XBB.1.1. The highest geometric mean titer (GMT) of the samples against prototype was 280, and the GMT for BA.5 was 41 (5.79 fold, P<0.001), BQ.1 and XBB 1.1 was only 8 (BQ.1, 35.86 fold, P<0.001; XBB.1.1, 32.67 fold, P<0.001) (Figure 1A). To investigate the differences in antibody levels among populations with different immunization history, the collected serum samples from first wave infection were divided into three groups, including the primary, the homologous booster and the heterologous booster vaccination group. The GMT in all three groups was higher against prototype than that for BA.5, BQ.1 and XBB.1.1 (Figure 1B-D). In the primary vaccination group, only one serum sample had a higher titer of neutralizing antibodies against BQ.1 than BA.5. The GMT dropped from 152 for prototype to 38 for BA.5 (2.99 fold, P=0.343), 11 for BQ.1 (12.44 fold, P=0.08) and 8 for XBB.1.1 (18.00 fold, P<0.05) (Figure 1B). In the homologous booster vaccination group, the GMT dropped from 286 for prototype to 45 for BA.5 (5.41 fold, P<0.001), 8 for BQ.1 (36.55 fold, P<0.001) and XBB.1.1 (33.53 fold, P<0.001) (Figure 1C). In the heterologous booster vaccination group, the GMT dropped from 287 for prototype, to 22 for BA.5 (11.68 fold, P<0.001), 6 for BQ.1 (44.20 fold, P<0.001), and 8 for XBB.1.1 (32.86 fold, P<0.001) (Figure 1D). In particular, participants from the homologous booster vaccination group had the same titers of neutralizing antibodies against BA.5 and BQ.1.

In addition, the IgG antibody of serum was detected using a commercial SARS-CoV-2 IgG antibody (Magnetic particle chemiluminescence method) test kit (Autobio, Ltd., Co., Shanghai, China). The positive rate of IgG antibody was 98.13% (105/107) (Supplementary Table 1). The median of IgG antibody in homologous booster vaccination group was the highest, at 131.52, followed with the heterologous booster vaccination group, with a median of 127.91 and the primary vacancy group, with 79.72 only (Table 1). There was no correlation between IgG antibody level and the GMT against the prototype virus (r=0.016, P=0.867).

However, for the serum samples from second wave infection participants, we found the highest geometric mean titer (GMT) of the samples against prototype was 362, and the GMT for BA.5 was 119 (2.03 fold, P<0.01), XBB.1.16 was 79 and XBB.1.9 was 69 (XBB.1.16, 3.59 fold, P<0.01; XBB.1.9, 4.28 fold, P<0.01) (Supplementary Figure 1A). The IgG antibody of all participants were detected as positive (10/10), the

median of IgG antibody was 235.09 (Supplementary Table 1 and Supplementary Figure 1B).

In summary, we identified the NAb titer of against prototype and Omicron variants BA.5 were significantly higher than that against Omicron variants BQ.1, XBB.1.1, XBB.1.9 and XBB.1.16 whether primary or secondary infection. The cross protection of neutralizing antibodies induced by prototype and Omicron BA.5 were poor when challenged by BQ.1, XBB.1.1, XBB.1.9 and XBB.1.16 variants, indicating that we should pay attention to the risk of multiple infection of any other novel Omicron variants emerging in near future.

Conflicts of Interest

The authors declare that there are no conflicts of interest.

Author contributions

RYY and HZ conceived and designed the experiments. RYY, LRZ, HZ, LNY, HFL, PPZ and CML performed the experiments. RYY analyzed the data. RYY, LLZ, XZ, ZL, JL, BSL and JFS contributed reagents/materials/analysis tools. RYY wrote the paper.

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Table and Figure Legends

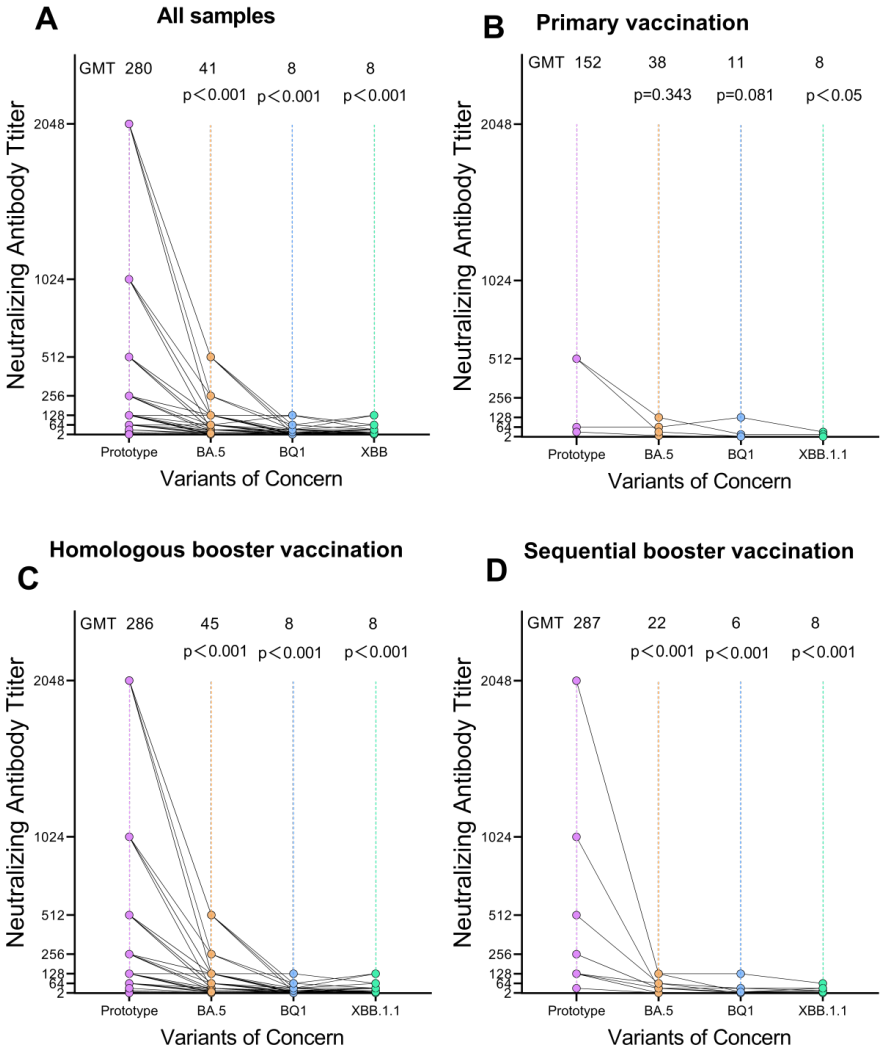

Figure 1 Neutralization experiment results of three variants of SARS-CoV-2: (A) Neutralizing antibody level of all samples; (B) Neutralizing antibody level of primary vaccination group; (C) Neutralizing antibody level of homologous booster group; (D) Neutralizing antibody level of heterologous booster group.

Table 1 Immune status of different vaccination groups

Vaccination group	Prototype	Prototype	IgG (+)	IgG (+)
	N (%)	GMT	N (%)	MEDIAN
primary vaccination	4 (3.74%)	152	4 (3.81%)	79.72
homologous booster	91 (85.05%)	286	89 (84.76%)	131.52
heterologous booster	12 (11.21%)	287	12 (11.43%)	127.91

Supplementary Figure 1 Immune effect of 10 participants during the second wave of COVID-19 epidemic: (A) four variants of SARS-CoV-2 neutralizing antibody level; (B) IgG antibody level.

Supplementary Table 1. Immune status of population in the first and second wave of COVID-19 epidemic in Guangdong province, China.