Seroprevalence of SARS-CoV-2 neutralising antibodies and cross-reactivity to JN.1 one year after the BA.5/BF.7 wave in China

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To The Editor: The SARS-CoV-2 variant JN.1 (BA.2.86.1.1), a subvariant of BA.2.86, has raised concerns due to its heightened transmissibility and capacity to evade immunity.[1–4] It is currently the fastest spreading variant among the circulating variants in the Americas, Europe, and the Western Pacific region.[1,5] China experienced its initial outbreak in mid-December 2022 and a subsequent surge between April and June 2023.[6–8] However, the extent of population immunity since these two waves remain poorly understood. Therefore, we conducted a population-based serosurvey to estimate the prevalence of SARS-CoV-2 antibodies and cross-reactivity to JN.1.

Between November 9 and December 9, 2023, 1472 participants were enrolled in the study. Of these, 753 (51.2%) were male, 10.6% were under 18 years, and 13.2% were over 69 years. Overall, 93.8% of the participants had received primary or booster COVID-19 vaccination, while 67 (6.2%) had not been vaccinated, including 40 children and 27 adults. Among all participants, 89.7% reported an infection during the BA.5/BF.7 wave in China in late 2022, 8.4% reported an additional infection after the BA.5/BF.7 wave, and 1.8% reported no history of infection (Table S1). Using a pseudovirus neutralization assay, neutralising antibodies against D614G, BA.5, XBB.1.5, EG.5.1 and JN.1 were measured (Supplemental Methods). The overall seroprevalence of neutralising antibodies against the D614G (98.2%, 95% CI 97.3%–98.7%), BA.5 (97.0%, 95% CI 96.0%–97.8%), XBB.1.5 (89.1%, 95% CI 87.4%–90.6%), and EG.5.1 (80.9%, 95% CI 78.8%–82.8%) variants was significantly higher than the prevalence against the JN.1 variant (76.3%, 95% CI 98.7%–97.3%) (Fig. 1A). Moreover, the geometric mean titres (GMTs) against D614G (1557, 95% CI 1450–1673), BA.5 (801.1, 95% CI 739.2–868.1), XBB.1.5 (362.8, 95% CI 329.2–399.8), and EG.5.1 (247, 95% CI 222.8–273.8) were significantly higher than those against the JN.1 variant (106.2, 95% CI 98.0–115.2) (Fig. 1A).

Upon further sub-analysis by age group, we observed that the seroprevalence of neutralising antibodies against D614G, BA.5, EG.5.1, and JN.1 was comparable across age groups. However, the seroprevalence of neutralising antibodies against XBB.1.5 in the 50–59 age group was significantly lower than in the 30–39 and 40–49 age groups (Fig. 1A). Notably, individuals aged ≥80 years had a relatively high seroprevalence of neutralising antibodies against JN.1 (88.6%, 95% CI 74.0%–95.5%), although this difference was not significant. Regarding neutralising antibody titres, we observed significantly lower GMTs against D614G in the 0–5 age group than in the other age groups; however, GMTs in the 6–11 age group were significantly higher than those in the 30–39, 40–49, 50–59, 60–69, and 70–79 age groups, and the GMTs in the 50–59 age group were significantly lower than those in the 6–11, 12–17, 18–29, and 40–49 age groups. In contrast, neutralising antibody titres against the other tested variants were similar (Fig. 1A). While the overall seroprevalence of neutralising antibodies against D614G was similar between males and females, there was a higher seroprevalence of neutralising antibodies in females than in males in the

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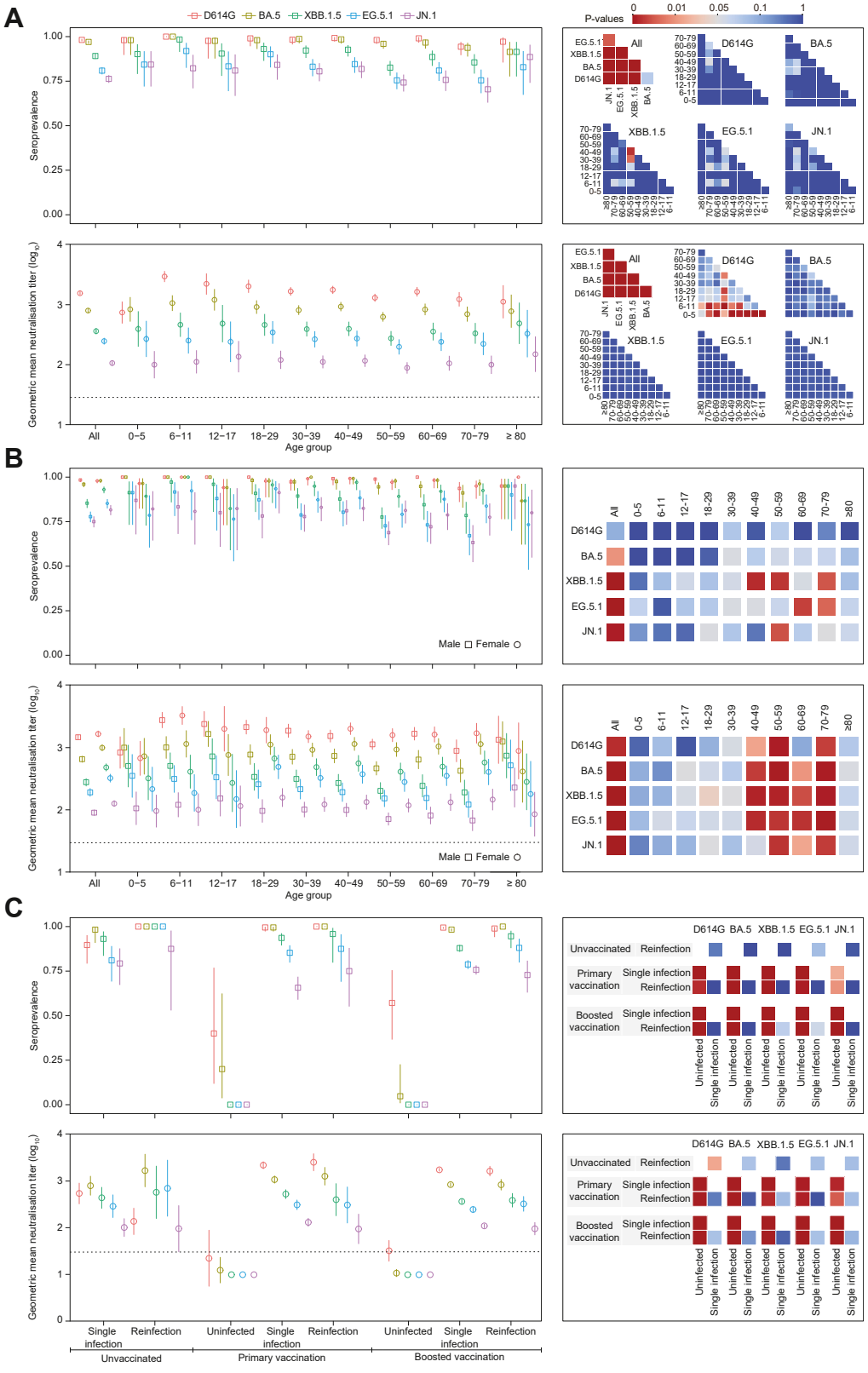
A
B
C
D614G
BA.5
XBB.1.5
EG.5.1
JN.1
Seroprevalence
Geometric mean neutralisation titer (log10)
Age group
All
0–5
6–11
12–17
18–29
30–39
40–49
50–59
60–69
70–79
≥ 80
Male
Female
P-values
0
0.01
0.05
0.1
1
Unvaccinated
Primary vaccination
Boosted vaccination
Single infection
Reinfection
Uninfected

40–49, 50–59, and 70–79 age groups for XBB.1.5, 60–79 age groups for EG.5.1, and 50–59 age group for JN.1 (Fig. 1B). In addition, higher neutralising antibody titres against these variants were observed in females in participants aged 40–79 years (Fig. 1B). In the sub-analysis by vaccination and infection status, only one participant in the unvaccinated group was not infected; therefore, the data of the participant was excluded from further analysis. Overall, regardless of vaccination status, the uninfected groups had a low seroprevalence or absence of neutralising antibodies against D614G, BA.5, XBB.1.5, EG.5.1, or JN.1 (Fig. 1C). In contrast, the single infection and reinfection groups had a high seroprevalence of neutralising antibodies against D614G, BA.5, XBB.1.5, EG.5.1, and JN.1, which were significantly higher than in uninfected groups, regardless of being unvaccinated, primary vaccinated, or booster vaccinated. The GMTs against the tested variants also demonstrated a trend similar to the seroprevalence (Fig. 1C).

In conclusion, our findings revealed that more than 70% of individuals displayed neutralising activity against JN.1. However, the neutralising antibody titres against JN.1 were relatively low, suggesting a lack of effective community immunity against JN.1 variant. It should be noted that we used a pseudotyped virus for the neutralization assay instead of a live virus, which may not fully recapitulate infectious SARS-CoV-2. Despite the extremely low prevalence of the JN.1 variant in China and the high seroprevalence of neutralising antibodies, the potential for a resurgence of COVID-19 caused by JN.1 is increasing due to the low levels of population immunity to JN.1. These findings are crucial for optimizing public health interventions and vaccination programs.

Contributors

M.-J.M. and G.D. conceived and supervised the study. X.-D.S., G.-J.Y., X.-L.J., Y.-W.Z., J.W., and L.-X.Z. collected the blood samples. X.-D.S. and G.-J.Y., X.-J.W., M.-M.W., R.-R.C., and X.-J.H produced pseudoviruses and conducted pseudovirus neutralization experiments. X.-D.S., G.-J.Y., and M.-J.M. analyzed the data and produced the figures. M.-J.M. drafted the manuscript. All authors contributed to data interpretation, critically reviewed the first draft and approved the final version of the manuscript. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Data sharing statement

All data reported in this article are available within the article and its online supplemental materials. The individual-level data reported in this article are not publicly available. Any additional information required to reanalyse the data reported in this article is available from the corresponding author upon reasonable request.

Declaration of interests

We declare no competing interests.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.lanwpc.2024.101040.

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***Fig. 1:* Seroprevalence and geometric mean titre of neutralising antibodies against D614G, BA.5, XBB.1.5, EG.5.1, and JN.1 in the general population of China, November 9–December 9, 2023.** Seroprevalence and geometric mean titre of neutralising antibodies against the ancestral D614G, as well as BA.5, XBB.1.5, EG.5.1, and JN.1 by age (A), sex (B), and vaccination and infection status (C) category. The left panels of graphs A, B, and C depict the seroprevalence rates (up) and geometric mean titre of neutralising antibodies (down), while the corresponding heatmaps on the right show p values from pairwise comparisons of the relative seroprevalence of two variants or age groups (A), male and female (B), and vaccination and infection status (C). The square and/or circle in the graph represent the seroprevalence or geometric mean titre of neutralising antibodies, and the vertical bars represent 95% confidence intervals.