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## Omicron sublineage recombinant XBB evades neutralising antibodies in recipients of BNT162b2 or CoronaVac vaccines

The SARS-CoV-2 omicron variant XBB sublineage, a BA.2.10.1–BA.2.75 recombinant classified as variant under monitoring by WHO, has been found in 35 countries,<sup>1</sup> and has become the dominant strain in Singapore. There is early evidence suggesting that XBB might be associated with a higher risk of reinfection.<sup>2</sup> A previous study using a pseudovirus neutralisation test and sera from individuals who received CoronaVac (Sinovac) found that XBB is the most immunoevasive sublineage.<sup>3</sup>

We assessed the neutralisation of XBB.1 and XBB.3 compared with BA.5.2 (a widely circulating strain since July, 2022) and the ancestral strain, using a live virus neutralisation test.<sup>4,5</sup> XBB.1 differs from XBB.3 due to an extra spike mutation: Gly252Val. We included sera specimens from 30 individuals who received two to four doses of BNT162b2 (Pfizer-BioNtech) or CoronaVac with or without previous SARS-CoV-2 infection (seven [23%] individuals who received two vaccinations and had a previous BA.2 infection; seven [23%] who received three vaccinations and had a previous BA.2 infection; nine [30%] who received three vaccinations and had no previous SARS-CoV-2 infections; and seven [23%] who received four vaccinations and had no previous SARS-CoV-2 infections; appendix p 3). Overall, the geometric mean 50% neutralising antibody titre (NT<sub>50</sub> GMT) was lower for XBB strains (XBB.1, 26.0; XBB.3, 19.4) than the ancestral strain (436.1; XBB.1 16.8-fold, p<0.0001; XBB.3: 22.5-fold, p<0.0001) or BA.5.2 strain (87.4; XBB.1 3.4-fold, p=0.0191; XBB.3 4.5-fold, p<0.0001), but the difference between XBB.1 and XBB.3 was not statistically significant (p=0.17; appendix p 1). All subgroups with different history of vaccination or

infection had a statistically significantly lower GMT against XBB.1 or XBB.3 than those against the ancestral strain (appendix p 1).

Paired acute and convalescent serum specimens were available for one patient with BA.5.2 and two patients with XBB. The patient who had previously had a BA.5.2 infection, had a 16.2 times higher NT<sub>50</sub> GMT against the ancestral strain and a 16.5 times higher GMT NT<sub>50</sub> against BA.5.2 for the convalescent serum than the acute serum, but the acute and convalescent sera had similar NT<sub>50</sub> against XBB.1 or XBB.3 (appendix p 2). The patient who had previously had an XBB.1 infection had an increase in their NT<sub>50</sub> GMT against the ancestral strain by 7.9 times, BA.5.2 by 29.6 times, XBB.1 by 21.3 times, and XBB.3 by 28.1 times (appendix p 2). The patient who had previously had an XBB.3 infection had an increase in their NT<sub>50</sub> GMT against XBB.1 by 10.8 times and XBB.3 by 6.9 times; this patient had a 2.1 times increase in their NT<sub>50</sub> GMT against the ancestral strain and a 3.2 times increase against BA.5.2. In summary, our data showed that both XBB.1 and XBB.3 were much more immunoevasive than ancestral strain and BA.5.2. This immunoevasion is consistently seen in patients with different history of vaccination or infection. Since patients infected with BA.5.2 might not elicit neutralising antibody against XBB sublineage, patients who have been infected with BA.5 or those with bivalent vaccine might have a higher risk of reinfection or vaccine breakthrough infection from XBB sublineage than previous sublineages.

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See Online for appendix