Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

were being monitored by healthcare professionals.[2,3] By Aug 26, the Brazilian health authorities had reported a total of nine cases in pregnancy (four in São Paulo, three in Rio de Janeiro, one in Minas Gerais, and one in Ceará).[2] Eight had monkeypox PCR-confirmed by Sept 1, whereas the woman in Ceará tested negative.[2] On Aug 5, a local newspaper in São Paulo reported that one of the infected pregnant women had passed the transmission phase, with both mother and baby in a stable condition, but there was no information on vertical transmission.[4] In Minas Gerais, the 26-year-old pregnant woman with monkeypox presented to hospital with skin lesions on Aug 4 and gave birth to a healthy infant on Aug 14.[5] She was isolated from her baby after birth and discharged healthy on Aug 17. There was no vertical transmission; the neonate was asymptomatic but remained in hospital when the mother was discharged.

Reassuringly, it appears that, so far, none of the monkeypox infections reported in pregnant women have been severe, and there has been no evidence that pregnant women have more severe disease or worse outcomes than non-pregnant people. There is, however, an urgent need for an international registry or reporting system to better understand the course, management, treatment, and outcomes of monkeypox, as well as the safety and effectiveness of vaccination, in populations at high risk, including the mother–fetus dyad, so that patients worldwide can be provided with accurate advice and evidence-based care. Unfortunately, we are currently having to rely on news outlets providing sparse information that is not externally verifiable. Nevertheless, a higher number of monkeypox infections in pregnancy have now been reported in non-endemic versus endemic countries, highlighting decades of neglect by international communities of such infectious diseases in endemic countries. If there are lessons to be learnt in the current monkeypox outbreak, we are failing to learn them.

AK and PO'B are members of the Royal College of Obstetricians and Gynaecologists' group developing guidance on monkeypox in pregnancy. PO'B is Vice-President of the Royal College of Obstetricians and Gynaecologists. All other authors declare no competing interests.

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Further humoral immunity evasion of emerging SARS-CoV-2 BA.4 and BA.5 subvariants

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SARS-CoV-2 BA.4 and BA.5 lineages have been the dominant strains in most regions worldwide and are continuously gaining mutations in the receptor-binding domain.[1,2] Multiple BA.4 and BA.5 subvariants with Arg346 mutations in the spike glycoprotein have been identified in various countries, such as BA.4.6, BF.7, BA.5.2.6, BA.4.1.9, and BE.1.2 harbouring Arg346Thr; BA.4.7 and BF.13 harbouring Arg346Ser; and BA.5.9 with Arg346Ile mutations (appendix p 4). These subvariants, especially BA.4.6, exhibit growth advantages compared with other variants including the original BA.4 and BA.5 strains.[3] Previous studies have identified Arg346 as an important immunogenic residue because Arg346 mutations would allow the virus to escape neutralisation by a large group of neutralising antibodies.[2] Unlike Arg346Lys carried by BA.1.1, which maintained a similar chemical property, mutations from Arg to either Thr, Ser, or Ile correspond to a much stronger shift in antibody recognition.[4,5] The efficacy of vaccines and neutralising antibody drugs against these BA.4 and BA.5 sublineages needs immediate evaluation.

In this study, we measured the neutralising titres of plasma samples against the SARS-CoV-2 BA.4 and BA.5 subvariants with Arg346 mutations. The plasma samples were obtained from vaccinated

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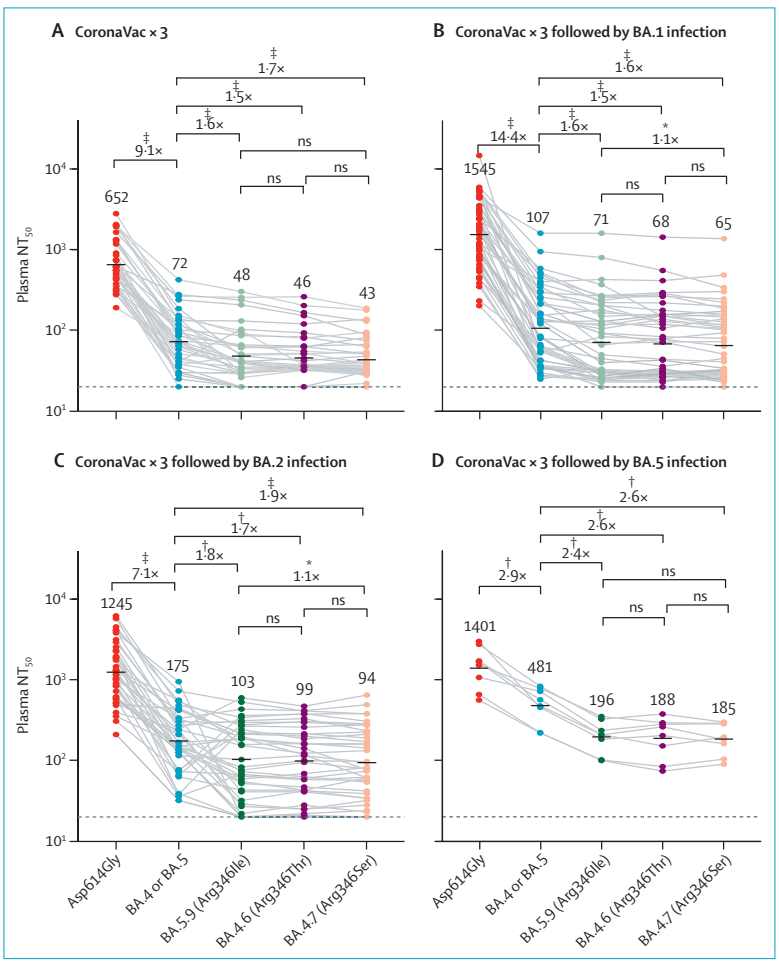

Figure: **Efficacy of convalescent plasma against BA.4 and BA.5 subvariants with mutations on spike Arg346**

NT_{50} against SARS-CoV-2 Asp614Gly, BA.4 or BA.5, BA.5.9 (BA.4 or BA.5 + Arg346Ile), BA.4.6 (BA.4 or BA.5 + Arg346Thr), BA.4.7 (BA.4 or BA.5 + Arg346Ser) pseudovirus by plasma samples from individuals who received three doses of CoronaVac (N=40; A), and those who received three doses CoronaVac followed by BA.1 breakthrough infection (N=50; B), BA.2 breakthrough infection (N=39; C), or BA.5 breakthrough infection (N=8; D). Geometric mean titres are annotated above each group. NT_{50}=50% neutralisation titres. ns=not significant. *p<0·05; †p<0·01; ‡p<0·001. P-values are calculated by two-tailed Wilcoxon singed-rank test of paired samples.

individuals that received three doses of an inactivated vaccine (CoronaVac) without SARS-CoV-2 infection or with BA.1, BA.2, or BA.5 breakthrough infection (appendix pp 7–9). Plasma from breakthrough infections were obtained 3 to 5 weeks after a positive PCR test for SARS-CoV-2. Vesicular stomatitis virus-based pseudoviruses were used in the neutralisation assays.

Plasma samples from individuals who received three doses of CoronaVac without infection showed a 1·5–1·7-fold decrease in 50% neutralisation titres (NT_{50}) against BA.4 or BA.5 sublineages with Arg346Ile (BA.5.9), Arg346Thr (BA.4.6), and Arg346Ser (BA.4.7), compared with the NT_{50} against BA.4 or BA.5 (figure A). A similar reduction in neutralisation titres was also observed in plasma from BA.1 or BA.2 breakthrough infection convalescents (figures B and C). Importantly, BA.4 or BA.5 sublineages with Arg346Ile, Arg346Thr, or Arg346Ser mutations could significantly evade neutralisation by plasma samples from BA.5 breakthrough infection, exhibiting a 2·4–2·6-fold decrease in NT_{50} (figure D). In contrast, the antibody-escaping capability of BA.1.1 that harbours a Arg346Lys mutation is similar to BA.1, as expected (appendix p 5). These results indicate the strong humoral immunity evasion capability of BA.4 and BA.5 sublineages with Arg346 mutations, suggesting that these sublineages, including BA.4.6, BA.4.7, BA.5.9, BF.7, BA.5.2.6, BA.4.1.9, BE.1.2, and BF.13 might gain an advantage in transmissibility under the global background of the pandemic caused by BA.4 and BA.5 sublineages. Of note, BA.5 convalescent plasma shows higher neutralisation titres against BA.5 than BA.1 and BA.1.1, but due to immune imprinting, or so-called original antigenic sin, convalescent plasma from omicron (including BA.1, BA.2, and BA.5) breakthrough infection is more effective against the ancestral strain with Asp614Gly compared with the respective infected strain.[2,6]

We then evaluated the pseudovirus-neutralising activities of the approved neutralising antibody drugs, including 11 monoclonal antibodies and four cocktails, against the Arg346-mutated BA.4 and BA.5 sublineages (appendix p 6). Cilgavimab did not affect BA.4 and BA.5 sublineages with Arg346Ile, Arg346Thr, or Arg346Ser mutations, resulting in the complete loss of efficacy of Evusheld (tixagevimab with cilgavimab)[7] against BA.4.6, BA.4.7, BA.5.2.6, and BA.5.9 sublineages. The neutralising activity of REGEN-COV (casirivimab with imdevimab)[8] was also reduced due to decreased reactivity of imdevimab against Arg346-mutated sublineages. Furthermore, the potency of sotrovimab[9] was further reduced. Of note, bebtelovimab[10] remained highly potent and was the only neutralising antibody drug approved by the US Food and Drug Administration.

Together, our findings suggest that significant humoral immune

evasion, especially against convalescents from BA.4 and BA.5 breakthrough infection, contributes to the emergence and rapid spread of multiple Arg346-mutated BA.4 and BA.5 sublineages. The decreased neutralisation titres of plasma samples from BA.5 breakthrough-infection convalescents indicate worrisome potential reinfection of BA.4.6 after the recovery from BA.4 or BA.5 infection. Importantly, individuals that received Evusheld as long-term prophylaxis, especially those that are immunodeficient or exhibit high-risk comorbidities, are at particular risk of those subvariants. Also, BA.4 and BA.5-based vaccine boosting strategies should be evaluated in light of the prevalence of these BA.4 and BA.5 subvariants.

YC and XSX are co-founders of Singlomics Biopharmaceuticals and inventors of patents associated with SARS-CoV-2 neutralising antibodies. All other authors declare no competing interests. FJ and YY contributed equally.

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Lung cell entry, cell–cell fusion capacity, and neutralisation sensitivity of omicron sublineage BA.2.75

The SARS-CoV-2 omicron (B.1.1.529) variant evades antibody-mediated neutralisation with high efficiency, challenging efforts to contain the COVID-19 pandemic through vaccination. Several omicron sublineages evolved since January, 2022, with some displaying elevated neutralisation resistance over early sublineages like BA.1, BA.1.1, and BA.2.[1,2] Recently, the novel omicron sublineage BA.2.75, which has a unique constellation of spike protein mutations (appendix p 2), was identified in India and the proportion of infections due to BA.2.75 is steadily increasing.[3]

We investigated the host cell entry and neutralisation sensitivity of BA.2.75 using pseudovirus particles (pp), which adequately model SARS-CoV-2 host cell entry and its neutralisation.[4] Particles bearing BA.2.75 spike ($BA.2.75_{pp}$) entered Calu-3 human lung cells more efficiently than $BA.2_{pp}$ (1·6× increase) but similarly to $BA.4/BA.5_{pp}$ and less efficiently than $B.1_{pp}$, which represents the virus circulating early in the pandemic (January–May, 2020; 1·7× reduction). For the remaining cell lines, entry efficiency of $BA.2_{pp}$, $BA.2.75_{pp}$, and $BA.4/BA.5_{pp}$ were similar (appendix p 2).

The ability of the SARS-CoV-2 spike protein to fuse cells and cause the formation of multinucleated giant cells is believed to contribute to pathogenesis.[5] In our quantitative fusion assay, cell–cell fusion capacity of BA.2.75 spike was higher than BA.2 spike (1·5× increase), similar to BA.4/BA.5 spike, and lower than B.1 spike (1·2× reduction) and the delta (B.1.617.2) variant spike (1·6× reduced; appendix p 2).

Next, we assessed BA.2.75 neutralisation by monoclonal antibodies for COVID-19 treatment. Three of ten antibodies did not neutralise $BA.2.75_{pp}$, and seven antibodies showed reduced neutralisation compared with $B.1_{pp}$ (3·7–922× reduction), with bebtelovimab and cilgavimab neutralising $BA.2.75_{pp}$ most efficiently (appendix p 2).

Finally, we investigated BA.2.75 neutralisation by antibodies induced after vaccination or breakthrough infection during the delta (October, 2021, to January, 2022) or early omicron (February–May, 2022, dominated by BA.1 and BA.2) waves in Germany. While the two-dose BNT162b2 primary immunisation schedule did not induce robust neutralising activity against $BA.2_{pp}$, $BA.2.75_{pp}$, or $BA.4/BA.5_{pp}$, a third dose of the vaccine strongly increased omicron sublineage neutralisation. However, neutralisation of $BA.2.75_{pp}$ and $BA.4/BA.5_{pp}$ was moderately reduced compared with $BA.2_{pp}$ (2·1× reduction for $BA.2.75_{pp}$ and 2·2× reduction for $BA.4/BA.5_{pp}$), and breakthrough infection during the delta wave induced substantially less neutralising activity against all three omicron sublineages as compared

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For **geographic distribution and other data by SARS-CoV-2 strain** see https://cov-spectrum.org