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Letter to the Editor

Detection of the Omicron BA.2.75 subvariant in Japan

Letter to the Editor

In this journal, we previously reported that the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) Omicron subvariant BA.2 replaces BA.1.1.[1] After the successive emergence and predominance of SARS-CoV-2 subvariants Omicron BA.1, BA.1.1 and BA.2, several other subvariants, e.g., BA.2.12.1, BA.4, and BA.5, emerged,[2,3] among which BA.5 became predominant. There is now concern that incidences of the newly emerged Omicron BA.2.75 subvariant may increase in the future. BA.2.75 has nine new mutations (K147E, W152R, F157L, I210V, G257S, G339H, G446S, N460K, and R493Q [a reversion mutation towards the ancestral variant]) compared with BA.2, which may be related to immune escape and resistance to antibody therapies.[4] The World Health Organization (WHO) has designated BA.2.75 as a variant under monitoring.[5]

BA.2.75 was first identified in a specimen from India collected on January 7, 2022 (EPI_ISL_13804325); its detection frequency gradually increased near the end of May, after which detection of this variant expanded to other countries.[6] As of August 2, 870 entries containing sequencing data for BA.2.75 from 27 countries had been loaded in GISAID (Supplemental materials).[7] By country, the most entries were from India (n = 614), followed by the United States of America (n = 51), Singapore (n = 42), Canada (n = 29), the United Kingdom (n = 27), and Japan (n = 20) (Table 1). The number of BA.2.75 detections has remarkably increased in India (Fig. 1A) and began rising in Singapore after the first BA.2.75 identification on July 18, 2022 (Fig. 1B).

As of August 2, 2022, two cases of BA.2.75 (Accession ID: EPI_ISL_13762812, EPI_ISL_13762799) had been confirmed in Yamanashi Prefecture, Japan (one each on July 1 and July 7, 2022). The two affected individuals were non-vaccinated six- and three-year-old children. Their parents also tested positive for SARS-CoV-2, indicating that familial transmission occurred in both cases. The family member had no history of overseas travel.

These children presented to the outpatient fever clinic and were diagnosed as SARS-CoV-2 positive by PCR and quantitative antigen testing.[8] In the 6-year-old child, the nasopharyngeal swab viral load and antigen level were 3.2 $\log_{10}$ copies/ml (Ct = 27) and 13.4 pg/ml, respectively. Their symptoms included fever (39 °C), cough, sputum, and fatigue, but not sore throat, nausea, vomiting, or taste disorder. The infection route was unknown, as the patient had not been out of the prefecture or traveled abroad in recent months. Six days later, a 3-year-old child presented to the outpatient clinic with fever (38.6 °C), diarrhea, and fatigue. Their viral load was 5.9 log10 copies/ml (Ct = 19), and their antigen level was 3732 pg/ml.

Using nucleic acids extracted from the nasopharyngeal swab specimens, we performed SARS-CoV-2 classification by TaqMan Assay.[9] The presence of Spike mutations Q493R (found in the BA.2 subvariant) and Δ69–70 (found in the BA.4 and BA.5 subvariants) were assessed by TaqMan Assay, but they were not detected in these isolates, suggesting that these viruses were a subvariant other than BA.2, BA.4, or BA.5. We then performed a whole genome sequencing analysis and identified them as BA.2.75.

To search for the origin of these BA.2.75 isolates, an evolutionary phylogenetic tree including BA.2.75 identified in Japan was created using Ultrafast Sample placement on Existing tRees (UShER).[10] It revealed that our identified viruses were genetically close to an ancestral virus (Accession ID: EPI_ISL_13950041) detected from a person who had traveled history to Nepal on June 23, 2022 at the airport quarantine station in Japan (Fig. 1C). Compared with this ancestral virus, two new mutations, ORF1ab D1532N and Spike S408R, were present in our isolates. Therefore, a BA.2.75 influx from overseas may have been infecting people via unknown infection routes. Future work should closely monitor the spread of BA.2.75 infection in Japan.

Table 1
Number of BA.2.75-positive samples reported in each country.

No	Country	Total number of BA.2.75
1	India	614
2	USA	51
3	Singapore	42
4	Canada	29
5	United Kingdom	27
6	Japan	20
7	Nepal	16
8	Australia	15
9	Denmark	12
10	Indonesia	8
11	Germany	6
12	Israel	5
13	Luxembourg	4
14	New Zealand	4
15	South Korea	3
16	France	2
17	Thailand	2
18	Austria	1
19	Cambodia	1
20	China	1
21	Italy	1
22	Martinique	1
23	Netherlands	1
24	Peru	1
25	Slovakia	1
26	Slovenia	1
27	Turkey	1

Abbreviations: SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; Ct, threshold cycle; ORF, open reading frame.

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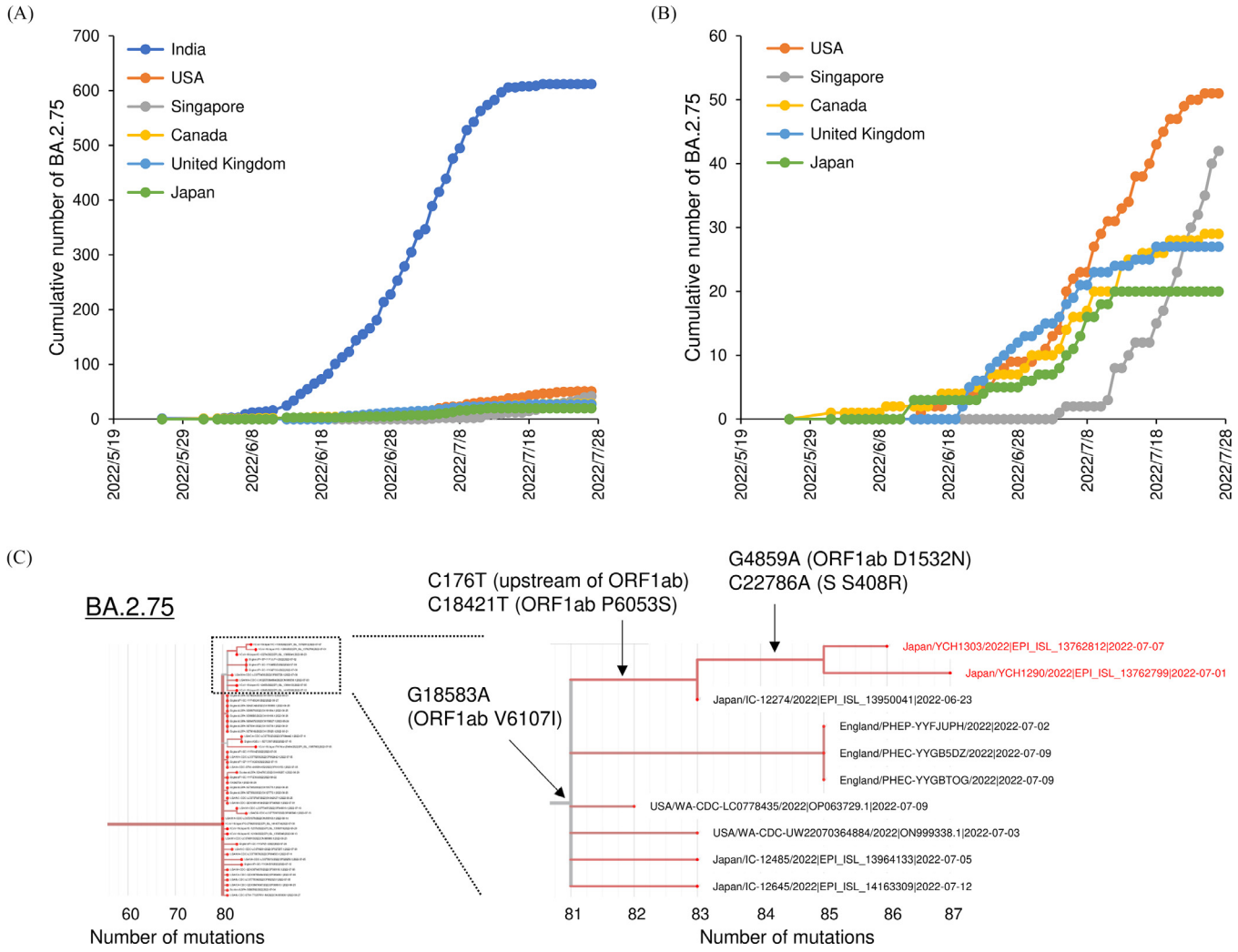

Fig. 1. *Trends in the number of cases of Omicron BA.2.75 infection and evolutionary phylogenetic tree.* (A, B) Cumulative number of detected cases of infection with SARS-CoV-2 Omicron BA.2.75 subvariant in each country, according to information registered in GISAID. (A) Cumulative number of cases of infected individuals in the top six countries with the highest number of reported cases (India, the United States of America, Singapore, the United Kingdom, Canada, and Japan). (B) Cumulative numbers displayed by expanding the data from (A) for countries other than India. (C) Phylogenetic analysis of the Omicron BA.2.75 subvariant conducted by UShER. Mutations noted in the branches of the phylogenetic tree indicate newly acquired mutations. The data shown in red in the right panel are derived from two samples identified in Yamanashi Prefecture, Japan. Abbreviations: ORF, open reading frame; S, spike.

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Declaration of Competing Interest

None.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jinf.2022.08.038.

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