

Geographic correlation between the number of COVID-19 cases and the number of overseas travelers in Japan, Jan-Feb, 2020

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Summary

Since the coronavirus disease 2019 (COVID-19) emerged in Wuhan, China, in December 2019, it has rapidly spread around the world, the number of patients is also increasing in Japan. The number of COVID-19 cases in Japan in the early stage was not uniform and were largely concentrated in several prefectures. The distribution of the COVID-19 cases and the number of foreign travelers as well as Chinese travelers at prefectural level showed a strong positive correlation coefficient of 0.68 ($P < 0.0001$) and 0.60 ($P < 0.0001$), respectively. Moreover, phylogenetic tree analysis revealed that the all of the registered SARS-CoV-2 detected in from January 23 and through February 29, 2020 belonged to the Chinese lineage, while those detected in March 2020, belonged to American and European lineages. Only 14 (20.3%) were infected outside of Japan, but the majority of the cases (79.7%) were infected domestically. To conclude, higher number of COVID-19 cases were found in prefectures with more Chinese travelers, supporting the importance of enforcing policies to restrict entry of overseas travelers to control COVID-19 spread. These findings highlight the risk of secondary transmission in the community caused by apparent or silent imported cases.

Text

An outbreak of coronavirus disease 2019 (COVID-19) occurred in Wuhan, China, in December 2019, and has since spread worldwide (1, 2). In Japan, the first COVID-19 case was reported on January 16, 2020, by the Ministry of Health, Labor and Welfare (MHLW) (3). The patient had visited Wuhan, China, where he became febrile on January 3 and returned to Japan on January 6, 2020.

Since then, the number of cases have been increasing, until on February 21, 2020 (4), two academic societies in Japan (the Japanese Association for Infectious Diseases and the Japanese Society for Infection Prevention and Control), announced that the domestic phase was shifting from border control to the epidemic phase (5). The number of cases in all areas was not uniform and were largely concentrated in Tokyo, Kanagawa, Aichi, and Hokkaido prefectures. We analyzed the geographic association between the number of overseas travelers, especially from mainland China, and the number of COVID-19 cases in 47 prefectures during the first month after the outbreak started in Japan.

Overall, 69 cases were reported by the Japanese government between January 16 and February 21, 2020. We selected data from the official reports of the MHLW and supplemented this information with data from press releases from each prefecture,

including broadcast and paper media. The passengers and crew of the cruise ship, Diamond Princess and evacuation flights from Wuhan were excluded from this analysis.

For each case, the date of report, date of symptom onset, age, travel and behavioral histories were collected from these public sources. The data revealed cases in the Tokyo Metropolitan area (17), Kanagawa (10), Aichi (9), Hokkaido (7), and Okinawa (3), which were more than in other prefectures (**Fig. 1A**). The onset dates for these cases ranged from January 3 through February 19, 2020. The majority (40/69, 57.9 %) of the patients were aged 40–69 years old, whereas the highest prevalence (17/69, 24.6%) was in the age group 60–69; no cases were reported for age groups below 20 years.

On the basis of travel and behavioral histories, 12 patients were infected in China, 2 in the United States (US), and 27 in Japan with known epidemiologic links; 28 had unknown or undisclosed domestic exposure history. Of the 27 patients with known epidemiologic links, 6 were close contacts of COVID-19 patients, 6 were infected during work as they were taxi drivers, 4 on sightseeing buses, 6 during the quarantine operation in the cruise ship the Diamond Princess, and the remaining 5 patients were infected during social events (e.g., parties or festivals).

According to the Japan National Tourism Organization (6), the number of overseas travelers at the prefectural level from January to November 2019 was highest in Tokyo, Osaka, Hokkaido, Kyoto, and Okinawa prefectures. Likewise, the highest number of travelers from China were in Tokyo, followed by Osaka, Hokkaido, Chiba, Kyoto, and Aichi (**Fig. 1B and C**).

We examined the geographic correlations between the number of COVID-19 cases at the prefectural level in Japan and overseas travelers using the Pearson's correlation test. The correlation with overall foreign travelers showed a strong positive coefficient of 0.68 ($P < 0.0001$), whereas the correlation with Chinese travelers showed a coefficient of 0.60 ($P < 0.0001$) (**Fig. 1**). Spearman's rank correlation also supported the higher number of overseas foreign travelers and that of Chinese travelers correlated positively with the number of COVID-19 cases in each prefecture (coefficient of 0.57, $P < 0.0001$, and coefficient of 0.65, $P < 0.0001$, respectively). These results indicate that in prefectures with more overseas and Chinese travelers, the number of COVID-19 cases was higher than those in prefectures without travelers.

To support the transmission path of COVID-19 from overseas travelers to Japan, we performed a phylogenetic tree analysis on 27 complete genomes of severe acute respiratory

syndrome coronavirus 2 (SARS-CoV-2) detected in Japan from January 20 and through March 12, 2020. The data were retrieved from Global Initiative on Sharing All Influenza Data (GISAID) EpiCoV™ database (www.gisaid.org), excluding the viruses detected from the outbreak of the cruise ship, Diamond Princess during February and March 2020. In addition, the strains from China (15), Italy (1), France (1), Brazil (1), Canada (1), and US (1) from December 2019 to March 2020 were included in the analysis for the comparison. The analysis was conducted using MEGA v.6.0 software (7), using a maximum-likelihood method.

Phylogenetic tree analysis revealed that all of the registered SARS-CoV-2 detected in Japan from January 20 and through February 29, 2020 belonged to the Chinese lineages, clades B (*L*), B (*O*), and A (*S*) in GISAID classification (8, 9), while those detected in March 2020, belonged to American and European lineages, clades B.1 (*G*), B.1 (*GH*), B.1.1 (*GR*), and B.1.36 (*GH*) (**Fig. 2**). Although the results of the phylogenetic analysis did not encompass all 69 cases and it was not distinguishable between the primary imported cases and the secondary local infections by the information from the database, this analysis supported that the early stages of COVID-19 outbreak in Japan highlights an independent introduction mediated by strains of Chinese origin.

To date, 16,851 cases have been reported in Japan (as of May 31, 2020), except for the COVID-19 outbreak on the cruise ship (10, 11). Initially, border measurement in Japan was applied only to those who arrived from Hubei Province from February 1. Eventually, the ban was extended to Zhejiang Province from February 13 until finally, entry from whole of China was restricted starting on March 16, 2020. Furthermore, from January to February, the reverse transcription polymerase chain reaction (RT-PCR) testing was performed only for patients with fever (≥ 37.5 °C), respiratory symptoms, and a travel history related to the banned areas in China, or a history of close contact with COVID-19 positive patients. These measurements allowed the entry of the SARS-CoV-2 viruses and the secondary transmission in the community.

In Italy, community transmission began in the north, where Chinese travelers were more likely to visit (12, 13). In contrast, Taiwan promptly stopped Chinese travelers to prevent community transmission (14). As border screening is not fully effective, stopping the entry of travelers from infected countries is essential in preventing COVID-19 community transmission (4, 15). It is challenging to balance the economy and infection rate, and strong policies are needed to control highly contagious diseases such as COVID-19.

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Conflict of interest

None to declare.

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Figure legends

Fig. 1. Geographic distribution of the number of COVID-19 cases at the prefectural level in Japan and the number of overseas travelers.

A) Map of the number of COVID-19 cases at the prefectural level in Japan as of February 21, 2020 (N=69). B) Map of the total number of overseas travelers at the prefectural level in Japan, January–November, 2019. C) Map of the number of overseas travelers at the prefectural level in Japan from mainland China, January–November, 2019. The unit values in panel A are cases, and B and C are patients. The original map was generated using ArcMap v.10.6 (ESRI Inc., USA).

Fig. 2. Phylogenetic tree of SARS-CoV-2 strains.

The tree was inferred the maximum-likelihood analysis based on the best-fit nucleotide substitution model for each gene. The strains detected in Japan are indicated by closed triangles, and strain originated from Wuhan, China is indicated by closed circle. Japanese strains detected between January and February, 2020 are shown in bold font. The Chinese lineage is denoted as clades B (*L*), B (*O*), and A (*S*), while the American and European lineages is clades B.1 (*G*), B.1 (*GH*), B.1.1 (*GR*), and B.1.36 (*GH*) in GISAID

classification (8, 9). The bootstrap values were determined for 1,000 interactions. Only values of $\geq 70\%$ are shown.

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