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Original Article

Nationwide Descriptive Epidemiological Study of Patients with COVID-19 Evacuated from Wuhan, China to Japan from January to February, 2020

Hidetoshi Nomoto[1,2], Masahiro Ishikane[1,3]*, Yoshiaki Gu[3,4], Ryosuke Yamamuro[5], Ryosuke Osawa[5], Naoto Hosokawa[5], Toshinori Sahara[6], Fukumi Nakamura-Uchiyama[6,7], Kazuaki Fukushima[8], Noritaka Sekiya[9], Akifumi Imamura[8], Yuji Fujikura[10], Akihiko Kawana[10], Kaoru Nagata[11], Kaku Tamura[12], Satoshi Kutsuna[1,13], and Norio Ohmagari[1,2,3]

[1]Disease Control and Prevention Center and [3]AMR Clinical Reference Center, National Center for Global Health and Medicine, Tokyo; [2]Emerging and Reemerging Infectious Diseases (National Center for Global Health and Medicine), Graduate School of Medicine, Tohoku University, Miyagi; [4]Department of Infectious Diseases, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University, Tokyo; [5]Department of Infectious Diseases, Kameda Medical Center, Chiba; [6]Department of Infectious Diseases, Ebara Hospital, Tokyo Metropolitan Health and Hospitals Corporation, Tokyo; [7]Department of Infectious Diseases, Tokyo Metropolitan Bokutoh General Hospital, Tokyo; [8]Department of Infectious Diseases and [9]Department of Infection Prevention and Control, Tokyo Metropolitan Cancer and Infectious Diseases Center Komagome Hospital, Tokyo; [10]Division of Infectious Diseases and Respiratory Medicine, Department of Internal Medicine, National Defense Medical College, Saitama; [11]Japanese Red Cross Musashino Hospital, Tokyo; [12]Self-Defense Forces Central Hospital, Tokyo; and [13]Department of Infection Control, Graduate School of Medicine, Osaka University, Osaka, Japan

ABSTRACT: We investigated the epidemiological findings regarding the route of coronavirus disease 2019 (COVID-19) and infection prevention and control (IPC) measures among returnees in the emergency evacuation from Wuhan, China to Japan during the COVID-19 outbreak in 2020. A total of 12 of the 14 returnees (median age [range]: 49.5 years [29–65 years]; 9 men [75%]) had confirmed COVID-19. The proportion of returnees with COVID-19 was 12/566 (2.1%) in Flights 1–3 and 2/263 (0.8%) in Flights 4 and 5. Six patients were asymptomatic on admission, while 3 patients developed symptoms thereafter. None of the participants reported a specific history of contact with animals, going to seafood markets, or visiting medical facilities. Two patients were in contact with an individual who was confirmed or suspected of having COVID-19. Most patients resided in hotels in the center of Wuhan City, taking taxis and trains for commute. Patients relatively adhered to IPC measures such as wearing a mask and hand hygiene. However, emphasis on IPC measures such as universal masking and more rigorous avoidance of exposure risk might have been necessary to prevent infection. In addition, forced social distancing due to lockdown might have contributed to the lower infection rates in Flights 4 and 5, compared to Flights 1–3.

INTRODUCTION

Since its emergence in December, 2019, coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has become a severe global concern. The World Health Organization (WHO) declared COVID-19 a public health emergency of international concern (PHEIC) on January 30, 2020 (1). Given that the Wuhan City government initiated lockdown measures in the city on January 23, the Japanese government evacuated citizens from Wuhan to return to Japan, as did the governments of other countries, such as Singapore and Germany (2–7).

Numerous studies have provided insights into the route of infection, clinical presentation, risk factors for severe disease, and prognosis in patients with

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*Corresponding author: Mailing address: Disease Control and Prevention Center, National Center for Global Health and Medicine, 1-21-1 Toyama, Shinjuku-ku, Tokyo 162-8655, Japan. Tel: +81-3-3202-7181, Fax: +81-3-3207-1038, E-mail: ishikanemasahiro@gmail.com

COVID-19 (8-10). Although a previous study suggested early human-to-human transmission of COVID-19 in Wuhan (11), additional evidence regarding the route of infection remains necessary. In late January and early February, 2021, 34 WHO scientists from nations including China, Japan, the United States, and the United Kingdom collaborated to investigate the source of COVID-19 in Wuhan, China. The WHO report on the origins of the COVID-19 pandemic emphasizes the importance of animal markets rather than laboratories (12). Furthermore, although some studies have examined the presence or absence of symptoms in countries that have implemented evacuation measures (2,3), epidemiological evidence regarding the route of infection among travelers in Wuhan, China is scarce.

Therefore, in this study, we investigated epidemiological findings regarding potential routes of COVID-19 infection and use of infection prevention and control (IPC) measures among individuals returning to Japan from Wuhan, China.

MATERIALS AND METHODS

Ethics: This study was approved by the ethics committee of the National Center for Global Health and Medicine (NCGM) (approval no. NCGM-G-003491-00) and conducted in accordance with the Declaration of Helsinki. Patient data were anonymized prior to analysis. Written informed consent was obtained from all participants included in this study.

Study design and participants: This nationwide retrospective cohort study included all Japanese patients with COVID-19 who were evacuated from Wuhan, China to Japan from January to February, 2020. All patients were diagnosed with COVID-19 based on positive quantitative reverse transcription-polymerase chain reaction (qRT-PCR) findings for SARS-CoV-2 in nasopharyngeal swabs in accordance with the protocol recommended by the National Institute of Infectious Diseases (NIID) in Tokyo, Japan (13).

Evacuation procedures: Between January 29 and February 17, all Japanese residents in Wuhan returned to Tokyo International Airport (HND) via 5 flights from Wuhan Tianhe International Airport (WUH) (4–7). The 1st through 5th flights were on January 23, January 30, January 31, February 7, and February 17, respectively. At the HND Quarantine Station, returnees with fever and respiratory symptoms suspected of having COVID-19 were transported to several medical institutions in Tokyo. Returnees who were judged to be asymptomatic at the initial screening were transported to the National Center for Global Health and Medicine (NCGM) in Shinjuku, Tokyo where they underwent body temperature assessments and completed a medical questionnaire concerning contact history and symptoms. Those with any respiratory symptoms indicative of COVID-19 or fever ≥ 37.5 °C were admitted to the NCGM or referred to other hospitals after consultation with infectious disease specialists, depending on the availability of hospital beds. Returnees who did not require hospitalization after consultation at the NCGM were transported to other accommodation facilities and instructed by the government to not leave the room for 14 days. Subsequently, all returnees underwent qRT-PCR testing for SARS-CoV-2 using nasopharyngeal swabs (13). Individuals who developed fever or respiratory symptoms during the 14 days of quarantine at the accommodation were hospitalized for qRT-PCR testing and admitted to an isolation room if the results indicated the presence of a SARS-CoV-2 infection. A second qRT-PCR test for SARS-CoV-2 using pharyngeal swabs was performed on the 13th day after evacuation, and if a series of qRT-PCR tests were negative, returnees were released from isolation at the accommodation facility and returned home (currently, mandated two qRT-PCR-negative results is not used in Japan as a criterion for lifting the isolation of a patient with COVID-19). Those with positive results were isolated in an accommodation facility for follow-up, regardless of symptoms. Asymptomatic patients with positive qRT-PCR results were transported to a medical institution for follow-up and isolation. Because infectious disease laws in Japan at the time indicated that patients with COVID-19 could not be discharged from the hospital until confirmation of two negative PCR tests, PCR tests were performed 24 h after symptom improvement in symptomatic patients and as appropriate following hospitalization in asymptomatic patients.

Data collection: The following data were extracted from medical charts and questionnaires: (i) demographic characteristics, including age, sex, and nationality; (ii) underlying diseases and social history, including smoking and alcohol use; (iii) clinical symptoms; (iv) lifestyle in Wuhan, including residency and workplace, job, accommodations, and transportation; (v) history of contact with patients testing positive for COVID-19 and animals; (vi) history of attending large-scale events or visiting seafood markets; and (vii) frequency of infection prevention and control (IPC) measures within the last 2 weeks in Wuhan.

Statistical analysis: Continuous variables are expressed as medians and ranges, while categorical variables are expressed as absolute and relative frequencies. Analyses were conducted to visualize where patients with COVID-19 lived and worked in Wuhan prior to evacuation.

RESULTS

Demographic characteristics and clinical symptoms of returnees: During the study period, 829 returnees were evacuated from Wuhan, China to Japan via 5 flights and screened for SARS-CoV-2 using qRT-PCR. Among them, 14 patients (1.7%) were confirmed to have COVID-19, accounting for 6 of 206 patients (2.9%) on the 1st flight (January 29, 2020), 3 of 210 patients (1.4%) on the 2nd flight (January 30, 2020), 3 of 150 patients (2.0%) on the 3rd flight (January 31, 2020), 1 of 198 patients (0.5%) on the 4th flight (February 7, 2020), and 1 of 65 patients (1.5%) on the 5th flight (February 17, 2020). Epidemiological findings from 12 (85.7%) of the 14 patients with confirmed COVID-19 were analyzed. Two patients who did not provide consent to participate in the study were excluded. The median (range) age of this cohort was 49.5 years (29–65), and nine patients (75.0%) were men. Most patients (10/12 [83.3%]) had no underlying disease. Among the two patients (16.6%) with underlying disease, one

Table 1. Demographic characteristics and clinical symptoms among patients with COVID-19 evacuated from Wuhan to Japan between January and February 2020 (n = 12)

Category	Variables	Data[1)]
Demographics	Age, median (range), years	49.5 (29–65)
	Japanese	12 (100)
	Male sex	9 (75.0)
	Pregnant	0 (0)
Underlying disease	No underlying disease	10 (83.3)
	Asthma	1 (8.3)
	IgA nephropathy	1 (8.3)
	Current alcohol use	9 (75.0)
	Current smoking	6 (50.0)
Clinical symptoms	Asymptomatic on admission	6 (50.0)
	Symptomatic on admission	6 (50.0)
	Symptomatic after admission	3 (25.0)
	Maximum temperature ≥37.5℃	5 (41.7)
	General fatigue	4 (33.3)
	Diarrhea	3 (25.0)
	Cough	2 (16.7)
	Throat pain	2 (16.7)
	Myalgia	2 (16.7)
	Dyspnea	2 (16.7)
	Nausea	2 (16.7)
	Anorexia	2 (16.7)
	Chill	1 (8.3)
	Hemoptysis	1 (8.3)
	Arthralgia	1 (8.3)
	Headache	1 (8.3)
	Nasal discharge	1 (8.3)
	Vomiting	1 (8.3)
	Sputum	0 (0)
	Altered mental status	0 (0)
	Convulsion	0 (0)
	Conjunctivitis	0 (0)
	Chest pain	0 (0)
	Epistaxis	0 (0)
	Abdominal pain	0 (0)

[1)]: Unless otherwise stated, data are presented as n (%).
COVID-19, coronavirus disease 2019.

had IgA nephropathy, while the other had asthma. On admission, six patients (50%) were asymptomatic, while 3 patients developed symptoms after admission. The most common symptom during the study period was fever (5/12 [41.7%]), followed by general fatigue (4/12 [33.3%]) and diarrhea (3/12 [25.0%]) (Table 1).

Lifestyle, contact/social history, and IPC measures among returnees: The length of stay in Wuhan among patients with confirmed COVID-19 was greater than 1 year in 4 patients (33.3%), between 1 month and 1 year in 3 patients (25.0%), and less than 1 month in 3 patients (25.0%). Favorite shopping locations included supermarkets (10 [83.3%]) and convenience stores (4 [33.3%]). Seven (58.3%) and 3 (25.0%) patients reported outing frequencies of “every day” and “occasionally, respectively. Six (50.0%) patients worked at manufacturing companies. Nine patients (75%) stayed in hotels, while 2 (16.7%) stayed in the workplace. The major routes of transportation were taxis (5 [41.7%]) and trains (5 [41.7%]), followed by buses (3 [25.0%]) and cars (2 [16.7%]). One patient (1 [8.3%]) who attended a large event during the Chinese Lunar New Year had close contact with a patient confirmed to have COVID-19, whereas another (1 [8.3%]) had contact with a patient suspected of having COVID-19 at his workplace. However, none of the other patients reported a specific history of contact with those diagnosed with COVID-19. Furthermore, none of the patients reported contact with animals, going to a seafood market, or visiting medical facilities. During the 2 weeks prior to their return to Japan from Wuhan, 8 patients (66.8%) always wore masks, 11 patients (91.7%) always

Table 2. Lifestyle, contact/social history, and IPC measures among patients with COVID-19 evacuated from Wuhan to Japan between January and February 2020 (n = 12)

Category and Variables		Data[1)]
Lifestyle		
Length of stay in Wuhan	More than 1 year	4 (33.3)
	Between 1 month and 1 year	3 (25.0)
	Less than 1 month	3 (25.0)
	Unknown	2 (16.7)
Pets		0 (0)
Housekeeper		0 (0)
Favorite shopping place[2)]	Supermarket	10 (83.3)
	Convenience store	4 (33.3)
	Mall	1 (8.3)
Frequency of outing	Every day	7 (58.3)
	Occasionally	3 (25.0)
	None	1 (8.3)
	Unknown	1 (8.3)
Job	Manufacturing	6 (50.0)
	Office worker	3 (25.0)
	University	1 (8.3)
	Housewife	1 (8.3)
	Unknown	1 (8.3)
Accommodation	Hotel	9 (75.0)
	Workplace	2 (16.7)
	Home	1 (8.3)
Transportation[2)]	Taxi	5 (41.7)
	Train	5 (41.7)
	Bus	3 (25.0)
	Car	2 (16.7)
	Bicycle	1 (8.3)
Contact history		
Patient with confirmed COVID-19		1 (8.3)
Patient with suspected COVID-19		1 (8.3)
Health care worker		0 (0)
Animal		0 (0)
Visit history		
Large event		1 (8.3)
Seafood market		0 (0)
Medical facility		0 (0)
Frequency of IPC within last 2 weeks in Wuhan		
Mask	Always	8 (66.7)
	Occasionally	3 (25.0)
	None	1 (8.7)
Hand hygiene	Always	11 (91.7)
	Occasionally	1 (8.3)
	None	0 (0)
Gargling	Always	5 (41.7)
	Occasionally	4 (33.3)
	None	3 (25.0)

[1)]: Unless otherwise stated, data are presented as n (%).
[2)]: Multiple answers allowed.
IPC, infection prevention and control; COVID-19, coronavirus disease 2019.

complied with hand hygiene, and 5 patients (41.7%) always gargled with mouth rinses (Table 2).

Areas of residence and workplaces among returnees: Fig. 1 shows the areas of residence and workplaces of patients with COVID-19 evacuated from Wuhan to Japan between January and February 2020. Many returnees resided primarily in the central part of Wuhan and the neighborhood. Six patients (50.0%) stayed in the central areas of Wuhan City, such as Hanvang District and Jinang'an District, while Caiden District represented the most common workplace (3 [25.0%]).

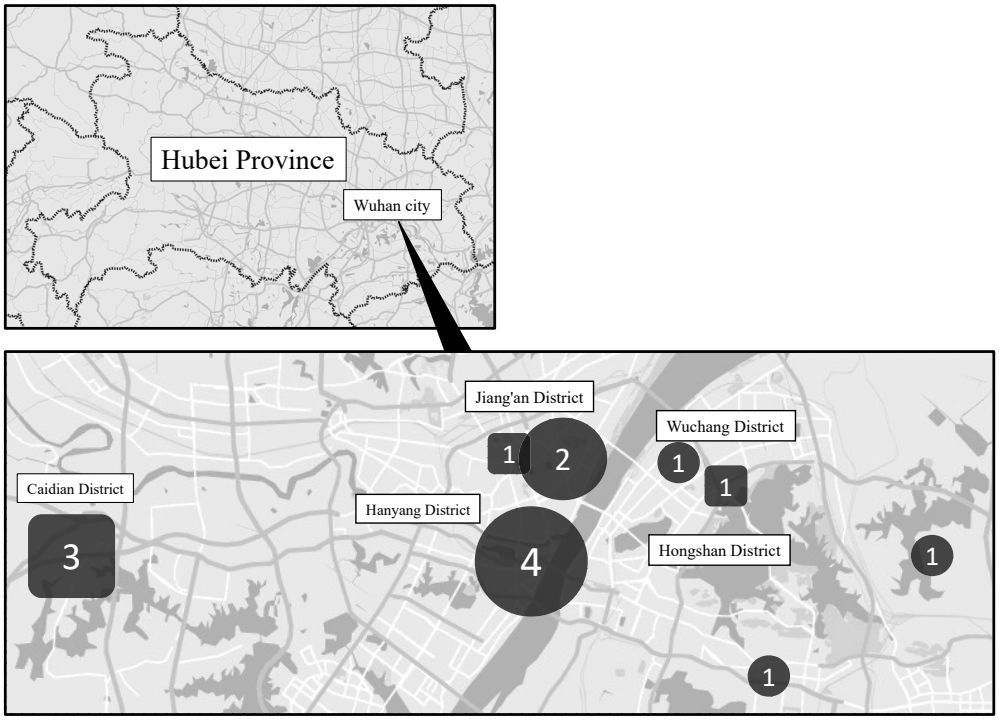

Fig. 1. Areas of residence and workplaces of patients with COVID-19 evacuated from Wuhan to Japan between January and February 2020. The map shows a view of Hubei Province and Wuhan City. Circles indicate places of residence and squares indicate workplaces. The numbers represent the number of patients in each area.

DISCUSSION

We investigated the epidemiological findings of patients with COVID-19 who were evacuated from Wuhan, China to Japan. Avoiding the "three Cs" (crowded places, close-contact settings, and confined and enclosed spaces) was known to be important for preventing infection (14). Most patients were going out every day or occasionally, although one returnee attended a large event. In our study, 2 patients had a history of contact with an individual confirmed and suspected to have COVID-19, respectively, while the remaining 10 patients (83.3%) did not. Although the WHO report on the origins of the COVID-19 pandemic highlighted animal markets as a likely source (12), no patient reported a history of contact with animals or visits to seafood markets. Most patients stayed in hotels in the center of Wuhan City, using taxis and trains for commute, resulting in contact with an unspecified number of people, which may have contributed to the infection. These findings suggest that human-to-human transmission had already been established in Wuhan City when evacuation measures were implemented following the PHEIC declaration by the WHO.

According to the self-reports of returnees, IPC measures such as hand hygiene and wearing a mask within 2 weeks of return seemed to be relatively well implemented based on our results. However, it is difficult to assess the extent to which the IPC measures were complied. The concept of pre-symptomatic infectivity and universal masking for IPC were not prevalent at that time, indicating that infection may have been transmitted by pre-symptomatic or asymptomatic patients. Additionally, it was not recognized at the time that conversations during meals or in enclosed spaces posed a risk of infection, and returnees might not have worn masks in such circumstances. Therefore, there could be a discrepancy between truly effective IPC measures and those perceived by the returnees. Given this background, the lockdown's forcible blocking of people's interactions may contribute to reducing opportunities for exposure to infections, as shown in previous studies (15,16).

Evacuation from Wuhan, China to Japan was divided into two periods, with Flights 1–3 occurring between January 29 and 31 and Flights 4–5 occurring between February 7 and February 17. As of February 17, 2020 a total of 58282 cases were confirmed in the Hubei province (17). The proportion of returnees with confirmed COVID-19 in each period was 12/566 (2.1%) and 2/263 (0.8%), respectively. Previous research has indicated that the median incubation period for COVID-19 is 5.1 days (95% confidence interval [CI], 4.5–5.8 days), and that 97.5% of patients develop symptoms within 11.5 days (95% CI, 8.2–15.6 days) (18). Wuhan was locked-down on January 23, 2020. Therefore, the lower positivity rate in the second period, when the fourth and fifth flights were conducted, might reflect the impact of the lockdown in the city. However, previous studies have indicated that the behavioral restrictions enforced in Wuhan might have decreased the number of cases and delayed the onset of the epidemiological peak, both inside and outside Wuhan (19,20). Many countries that experienced huge outbreaks since the Wuhan lockdown adopted social distancing measures to prevent contact between individuals and reduce transmission (21). In addition,

Wuhan's local government required the wearing of masks in public places since just before the lockdown (22). Such strict adherence to IPC measures might reduce the opportunities of exposures to infections. However, it is unclear whether people voluntarily practiced IPC measures, including wearing masks, before the announcement. Therefore, it is difficult to determine the effectiveness of the mask mandate at that time.

The 12 returnees with COVID-19 were relatively young, and 10 (83.3%) had no underlying diseases. According to a systematic review and meta-analysis of asymptomatic patients with COVID-19, asymptomatic patients were more likely to be relatively younger and without underlying diseases than older with underlying diseases (23). On admission, half of the patients (6 [50.0%]) were diagnosed as asymptomatic, three of whom became symptomatic during hospitalization. Based on data from Japanese citizens returning from Wuhan, Nishiura et al. reported that the proportion of asymptomatic COVID-19 cases was 30.8% (95% CI: 7.7–53.8) (24). In contrast, a statistical model based on data from 3,711 passengers on the Diamond Princess cruise ship developed by Mizumoto et al. estimated the proportion of asymptomatic cases to be 17.9% (95% CI: 15.5–20.2) (25). In our study, 25% (3/12) of patients with COVID-19 were discharged as asymptomatic. Asymptomatic cases of COVID-19 have also been reported in individuals evacuated to other countries (2,3). For example, among 94 individuals returning to Singapore, 8 were symptomatic, while one was asymptomatic (2). Among 126 individuals returning to Germany, 2 (1.6%) were identified as infected, both of whom were asymptomatic on initial symptom-based screening (3). Although the contribution of asymptomatic patients to the spread of COVID-19 remains debatable, the identification of asymptomatic patients in epidemiological studies is a matter of public health concern, highlighting the need for similar IPC measures in both symptomatic and asymptomatic cases.

The present study had some limitations. First, because our study was a retrospective cohort study that utilized medical charts and questionnaires, some data such as relationships between patients (family, friends, or colleagues) and detailed contact information not included in the medical charts and questionnaires were unknown. In addition, the data might have been inaccurate given the subjective nature of these assessments. Further, some participants did not respond to any survey items. However, we believe that these limitations did not significantly alter our conclusions. Second, the participants in our cohort were relatively young, healthy individuals; their symptoms may not reflect those of other populations. Therefore, our study cannot represent the whole picture of COVID-19 in Wuhan, China. Third, returnees were required to wait in hotels and airports before their flights. Although the duration of the waiting period was unknown, we could not exclude the possibility that returnees were exposed to infection in this group setting. It may be necessary to pay attention to IPC measures in settings that require group behavior. Finally, we were unable to collect information on compliance with IPC measures during the flights and could not examine the involvement of compliance with these in-flight measures and the subsequent COVID-19 infection. Therefore, we were unable to evaluate the possibility of transmission during flight (26).

In conclusion, we conducted a nationwide descriptive epidemiological study of evacuees from Wuhan, China to Japan. Many returnees were infected with COVID-19 despite no clear exposure to COVID-19 and self-reported compliance with IPC measures. Emphasis on IPC measures, such as universal masking and more rigorous avoidance of exposure risk, such as avoidance of having meals with others, might have been necessary to prevent infection. In addition, forced social distancing due to lockdown might have contributed to the lower infection rates in Flights 4 and 5, compared to Flights 1–3.

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Conflicts of interest None to declare

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