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Major Article

A SARS-CoV-2 outbreak associated with vaccine breakthrough in an acute care hospital

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Key Words:
Breakthrough infection
Health care workers
Ventilation
COVID-19 vaccine

Background: We aimed to analyze an outbreak caused by a vaccine breakthrough infection in a hospital with an active infection control program where 91.9% of health care workers were vaccinated.

Methods: We investigated a SARS-CoV-2 outbreak between September 9 and October 2, 2021, in a referral teaching hospital in Korea. We retrospectively collected data on demographics, vaccination history, transmission, and clinical features of confirmed coronavirus disease 2019 (COVID-19) in patients, health care workers, and caregivers.

Results: During the outbreak, 94 individuals tested positive for SARS-CoV-2 using reverse transcription-polymerase chain reaction testing. There were infections in 61 health care workers, 18 patients, and 15 caregivers; 74.5% (70/94) were vaccine breakthrough infections. Most transmissions appeared to be caused by three index cases, which accounted for 86.2% (81/94) of transmissions. Forty-seven (58.0%, 47/81) cases were associated with the hospital staff cafeteria and offices located in the basement. Among health care workers and caregivers, only one required oxygen supplementation. In contrast, among patients, there were four fatal cases (22.2%, 4/18), 3 of which were unvaccinated.

Conclusions: Superspreading infection among fully vaccinated individuals occurred in an acute care hospital while the delta variant was dominant. Given the potential for severe complications, as this outbreak demonstrated, preventive measures including adequate ventilation should be emphasized to minimize transmission in hospitals.

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) Delta variant spread rapidly worldwide and was reported in 185 countries by September 2021.[1] Although vaccination is the cornerstone of protection against SARS-CoV-2, breakthrough infections caused by variant viruses can lead to outbreaks,[2-5] even in countries with high vaccination rates, such as the UK and Israel.[6,7] In Korea, circulation of the Delta variant was first identified in April 2021 and by mid-September the vast majority of cases of coronavirus disease 2019 (COVID-19) were caused by the Delta variant. Although 70% of the population is fully vaccinated in Korea, the number of new confirmed cases has been consistently over 2,000 on a daily basis since August 2021.[8]

The Delta variant is highly contagious with a basic reproduction number ranging from 3.2 to 8 and is more likely to lead to hospitalization compared to the Alpha variant or to the original SARS-CoV-2 virus.[9] The COVID-19 vaccines are effective at preventing hospitalization and death against all variants, including Delta.[10] Nevertheless, concerns about vaccine effectiveness remain. One is the waning of immunity over time.[11] The other is the limited immune response in older adults or immunocompromised individuals.[12] Vaccine breakthrough infections are well recognized but there is limited information about nosocimial COVID-19 outbreaks due to vaccine breakthrough infections.[2-5]

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In this study, we analyzed the transmission of the SARS-CoV-2 Delta variant in health care workers, patients and caregivers at a tertiary care hospital with a well-resourced infection control program (run by 6 infection control nurses and 4 physicians) where 92% of health care workers are vaccinated. We aimed to better understand the nature of SARS-CoV-2 transmissions among vaccinated individuals in acute-care hospital and in so doing suggest better strategies to prevent the spread of SARS-CoV-2 in hospitals.

METHODS

Study institution

The study hospital is a 725-bed referral teaching acute-care hospital in Seoul, Korea. There are 13 wards in three buildings (the main building, the annex, and the maternal and child health center). Wards have of 21-70 beds and the intensive care unit 28 beds. There are 11 negative pressure rooms on the general wards and 4 in the intensive care unit in the annex building. The total number of health care workers in the study institution was 2,107 at the time of this study. Most of them were vaccinated against COVID-19 from March to May 2021. On September 24, 2021, the vaccine uptake was 92% (1,937/2,107). Of the 1,937 vaccinated, 1,728 (89%) received AstraZeneca (ChAdOx1; vaccine efficacy 74.0%[13]), 120 (6%) Moderna (mRNA-1273) (vaccine efficacy 94.1%[14]), 50 (2.6%) Pfizer (BNT162b2; vaccine efficacy 91.3%[15]), 38 (2%) were combination (ChAdOx1 followed by mRNA vaccines) and one Janssen (Ad.26.COV2.S; vaccine efficacy 55.9%[16]).

In Korea, caregivers, including guardians, are allowed to stay in hospitals to help care for patients who require additional assistance. During the pandemic, most hospitals have allowed one caregiver per patient. In the study hospital, patients and caregivers were admitted only if the COVID-19 screening test was negative within 3 days. If the test was positive, the patient would be transferred to a hospital for COVID-19 or to a community treatment center. The follow-up test was performed on the fifth day of admission and repeated weekly. Follow-up tests however were not performed once a patient had completed vaccination against COVID-19. The study hospital conducted symptom monitoring for health care workers using daily text messages, a policy than began in March 2021. In addition, if a health care worker developed a COVID-19 related symptom or sign, they would be requested to get tested through a clinic in the infectious diseases department and were excluded from work until confirmed negative. In the study hospital, it is mandatory that all health care workers and caregivers wear masks or respirators at all times except when eating.

Two central air-conditioning systems exist in the main building of the study hospital. In the annex and the maternal and child health center, there is one central air-conditioning system.. The staff cafeteria is located on the first basement floor of the main building. There are no windows on this floor and ventilation is provided with multi-blade fans. Dining tables are equipped with an acrylic partition, allowing people to sit apart from each other. The number of air exchanges per hour has not been measured.

Definition

Cases of transmission cases were classified into index, secondary, tertiary, and quaternary cases, as well as beyond depending on the transmission links provided by the epidemiological investigation. Epidemiological links were based on WHO and institutional COVID-19 contact tracing guidelines.[17] A contact is defined as a person who has any one of the following exposures to a confirmed case during a potential infectious period: (1) face-to-face contact with a confirmed case within 1 meter and for at least 15 minutes, (2) direct physical contact with a confirmed case, (3) direct care for a patient with confirmed COVID-19 disease without the use of recommended PPE, or (4) other situations as indicated by local risk assessments. The potential infectious period started 2 days before the case's first symptom until the initiation of isolation for symptomatic cases or starting two days before the case's specimen collection date until isolation for asymptomatic cases. For cases where the exposure source and events are clear, the difference between the exposure date and the test date or the symptom start date were calculated as the incubation period. Superspreading events were defined when an index case infected more than 10 secondary cases.[18] For symptomatic cases in this outbreak, the clinical course was described using a modified 6-category ordinal scale.[19]

Data collection

We retrospectively collected data on demographics, vaccination history, transmission order, incubation period, and clinical data (symptoms, signs, and treatment outcomes) of COVID-19 confirmed health care workers and caregivers during the hospital outbreak. The confirmed cases were associated with outbreak events. In cases with uncertain epidemiological links, we assumed that they were outbreak associated and included them. Diagnosis of COVID-19 was confirmed by reverse transcription-polymerase chain reaction (RT-PCR) for the RNA-dependent RNA polymerase (RdRp)/ORF1ab, nucleocapsid (N), and envelope (E) genes of SARS-CoV-2. The initial cycle threshold (Ct) value of the RdRp/ORF1ab gene was collected from the study institution or government.

Statistical analyses

Categorical variables were expressed as counts and frequencies. Continuous variables were expressed in median and interquartile range (IQR) or mean and standard deviation (SD). Proportions for categorical variables were compared using the χ^2 or Fisher's exact test. Variables with a P-value of <.05 were considered statistically significant.

Ethical statement

The Institutional Review Board and Ethics Committee of Soonchunhyang University Seoul Hospital (No. 2021-10-014) approved this study. The board waived the requirement for informed consent.

RESULTS

Case finding and response during COVID-19 outbreak in the hospital

On September 17, 2022, a nurse on the 9th floor of the annex along with an internal medicine resident tested positive for COVID-19. The next day, a technician engineer working in the magnetic resonance imaging (MRI) room and a clerk serving as a secretary in an outpatient clinic were confirmed positive. There were no epidemiological links between these initial four cases. On September 19, another technician engineer in the MRI room was confirmed positive for COVID-19. The first screening tests were conducted for all employees for 3 days (September 20-22) and 32 health care workers were identified to be positive for COVID-19. The heath care worker who first developed symptoms in this outbreak was a patient transport team staff identified during the first set of screening tests on September 20. The onset of symptoms of the patient transport team staff was September 14. The second and third sets of screening tests were conducted on September 27-29 and October 4-6, respectively. In the second set of screening tests, there was five health care

workers were identified as COVID-19. There was no additional case in the third set of tests.

On September 19, two caregivers were confirmed positive in different multibed rooms on the 7th floor of the maternal and child health center. Screening tests were then conducted for all caregivers and hospitalized patients. In total, 11 cases were identified on the seventh floor of the maternal and child health center. On September 24, three patients and one caregiver were confirmed positive on a multibed room on the eighth floor of the main building. Then, the second set of screening tests were conducted. In total, 22 cases were identified on the ninth floor of the main building. The last confirmed case was on October 2. On October 8, the outbreak was declared over.

Demographics and transmission features of the outbreak

During the outbreak period, 94 individuals tested positive for SARS-CoV-2. Among them were 61 (64.9%) health care workers and 33 (35.1%) patients or caregivers (18 patients and 15 caregivers). Most health care workers or caregivers were healthy. However, most patients had underlying diseases (Table 1). There were three superspreading events: in the hospital staff cafeteria and offices (n = 47, 50%), on the eighth floor main building (n = 22, 23.4%), and on the seventh floor in the maternal and child health center (n = 12, 12.8%). These superspreading events accounted for 86% (81/94) of transmissions. All super-spreaders had symptoms prior to diagnosis. The health care worker super-spreader had a cough for 6 days before isolation. The other two caregivers were tested for COVID-19 2 (eighth floor main building) and 4 days (seventh floor of the maternal and child health center) after symptom development. Thirteen cases were not associated with the superspreading events (Fig 1). According to the transmission route, the index cases caused 59 (62.8%) secondary infections, 20 cases (21.3%) were tertiary infections and 2 cases (2.1%) were quaternary infections.

There were 70 (74.5%) individuals who completed their vaccinations and one was partially vaccinated. Of the vaccinated individuals, 50 were vaccinated with ChAdOx1, 13 with BNT162b2, 4 with mRNA-1273, one with Ad.26.COV2.S, and one with a combination (first dose with ChAdOx1 and second dose with BNT162b2). Among health care workers, 87% (53/61) completed their vaccinations. The median incubation period was 4 days (range 1-11 days). The median interval between the completion of vaccination and COVID-19 confirmation was 117 days (range, 18-187 days; Table 1).

Superspreading event

The index health care worker in the staff cafeteria completed ChAdOx1 vaccination on May 25 and caused a total of 46 transmissions. The index health care worker spread it to 6 co-workers in the same office and 5 employees in the cooking area adjacent to the staff cafeteria. The fourth transmission was a case in which a health care worker spread it within the office, to the patients, and then to the nurse working in the dialysis room (Fig 2). On the eighth floor of the main building, there was an index caregiver in Room A and it spread to 3 rooms opposite that room (Fig 3A). The index caregiver was unvaccinated and remained on the ward with a cough. The attack rate was 40% (n = 22) among 55 close contacts related to eighth floor of the main building. On the seventh floor of the maternal and child health center, the caregiver in room B was an index case and as a result of epidemiological investigation, it was confirmed that brushing teeth together in the bathroom during the symptom period was the transmission route to other caregivers (Fig 3B). The index caregiver completed ChAdOx1 vaccination on June 24. The attack rate was 19.4% (n = 12) among 62 close contacts related seventh floor in the maternal and child care center. Detailed characteristics of the super-spreaders is presented in Supplemental Table 1.

Clinical manifestation for health care workers, patients, and caregivers

Of the 94 RT-PCR confirmed participants, 28.7% (27/94) were asymptomatic at the time of diagnosis. The median duration of symptom onset and diagnosis was 2 days (range, 1-8 days). The mean Ct value of the RdRp/ORF1ab gene from the upper respiratory tract specimen was 20.61 (SD ± 6.03). There was no significant difference in the mean Ct value of the RdRp/ORF1ab gene between fully vaccinated (mean 20.87, SD ± 6.28) and unvaccinated individuals (mean 19.94, SD ± 5.37, P = .52). Most health care workers were isolated in community treatment centers or homes. Six caregivers were admitted to the hospital for isolation and treatment of COVID-19; however, they did not require supplemental oxygen. There were no fatalities among health care workers or caregivers. Eighteen patients were

Table 1
Demographics of the study participants

	Health care workers (n = 61)	Patients (n = 18)	Caregivers (n = 15)	*P* value
Male	35 (57.4)	8 (44.4)	4 (26.7)	.92
Age, mean±SD	42.2 ± 18.8	75.6 ± 18.0	54.9 ± 15.1	<.001
Underlying disease/condition				
Hypertension	2 (3.3)	12 (66.7)	3 (20.0)	<.001
Diabetes	0	7 (38.9)	0	<.001
Neurologic disease	0	5 (27.8)	0	<.001
Chronic kidney disease	0	3 (16.7)	0	.009
Cardiovascular disease	0	5 (27.8)	2 (13.3)	<.001
Chronic liver disease	0	2 (11.1)	0	.06
Malignancy	0	4 (22.2)	0	.001
None	58 (95.1)	4 (22.2%)	11 (73.3)	<.001
Vaccination	53 (86.9)	8 (44.4)	9 (60.0)	<.001
ChAdOx1 (Oxford AstraZeneca)	48 (78.7)	1 (5.6)	2 (13.3)	
BNT162b2 (BioNTech Pfizer)	1 (1.6)	7 (38.9)	5 (33.3)	
mRNA-1273 (Moderna)	4 (6.6)	0	0	
Ad.26.COV2.S (Janssen)	0	0	1 (6.7)	
Combination	0	0	1 (6.7)*	
Partially or unvaccinated	8 (13.1)	10 (55.6)	6 (40.0)	
Interval of vaccination and infection, median, days (IQR)	118.0 (104.5, 121.0)	119.5 (82.5, 139.8)	70.0 (24.0, 94.0)	.26

Data are presented as number (%), unless otherwise indicated.
IQR, interquartile range; SD, standard deviation.
*The first dose was ChAdOx1 and the second dose was BNT162b2.

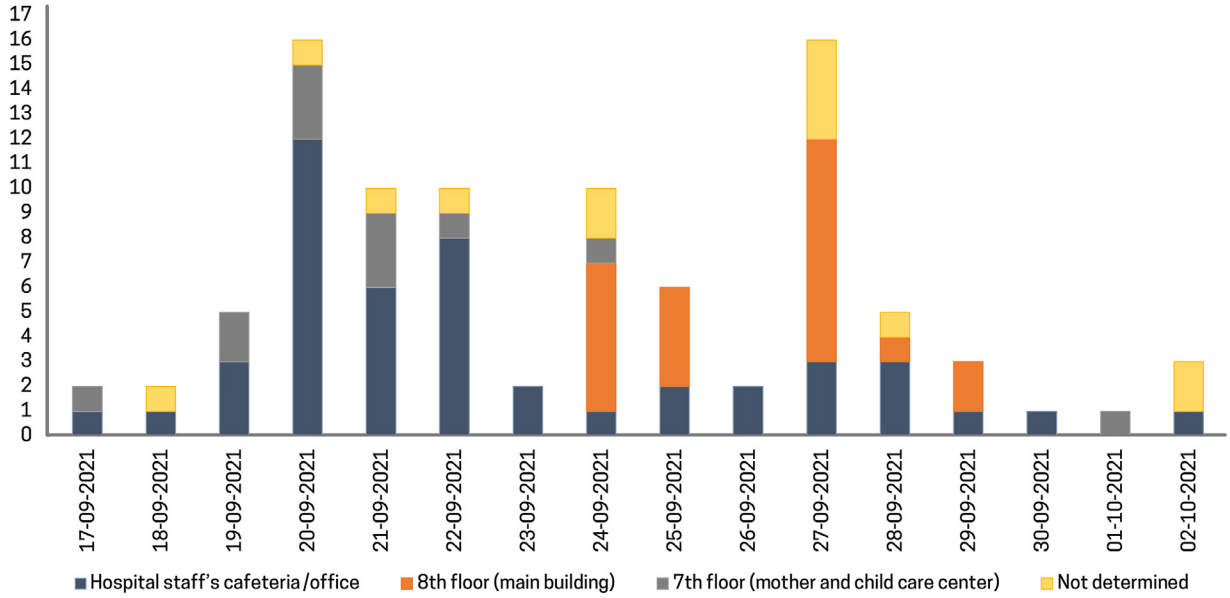

Fig 1. Epidemic curve of COVID-19 according to the main superspreading event.

admitted to the hospital for the treatment of COVID-19. Among them, 61.1% (11/18) required supplemental oxygen. The in-hospital mortality rate was 22.2% (4/18): 3 of these patients were unvaccinated (Table 2). The time between the diagnosis of COVID-19 and death for the four fatal cases were 4, 8, 18, and 18 days, respectively.

Of the 61 health care workers, 5 (8.2%) remained asymptomatic until discharge or release from isolation. For the remaining 56 health care workers, the median duration of symptoms was 6 days (interquartile range [IQR] 4-10 d). Cough (62.5% [35/56]) was the most common symptom, followed by sore throat (58.9% [33/56]), loss of smell (53.6% [30/56]), loss of taste (42.9% [24/56]), and fever (33.9% [19/56]; Supplemental Table 2).

DISCUSSION

In this study, we found that even in a hospital with a high health care worker vaccination rate, and with a well-trained infection control team, a large-scale outbreak can occur because of breakthrough infections among health care workers. Most of the transmissions were related to the particular super-spreaders. We found that inter-employee infections were mainly related to poorly ventilated hospital staff cafeterias and offices. Infections on the wards were related to resident caregivers. The infected health care workers and caregivers did not progress to severe illness. However, 4 (22%) patients died, and 3 of them were unvaccinated.

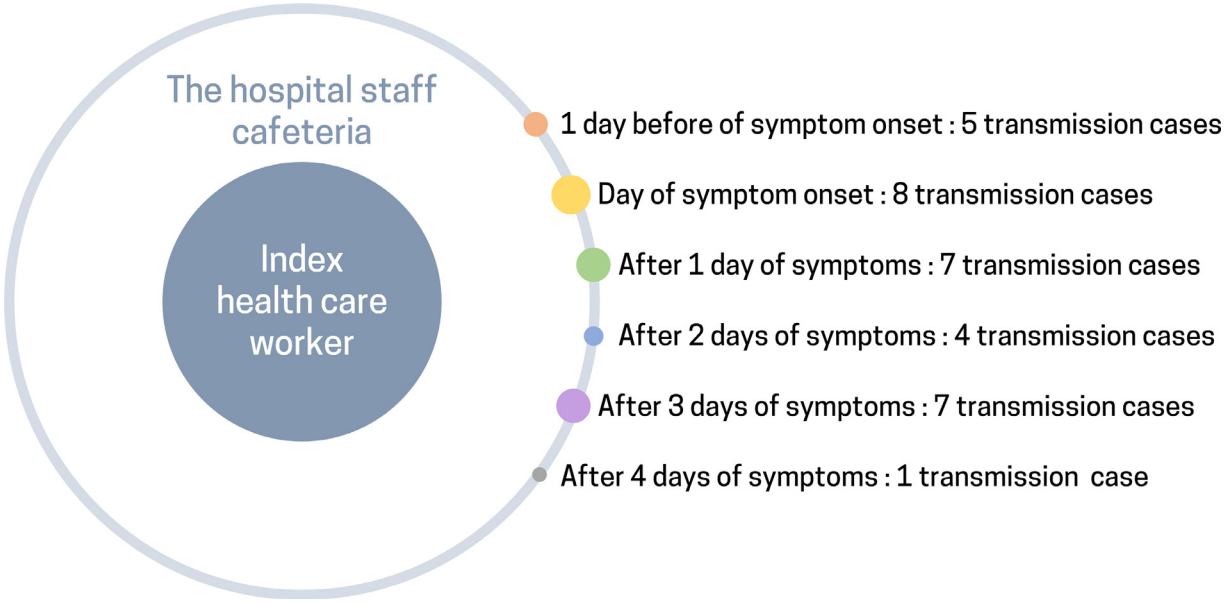

Fig 2. Transmission pattern according to the symptom period in the cafeteria staff.

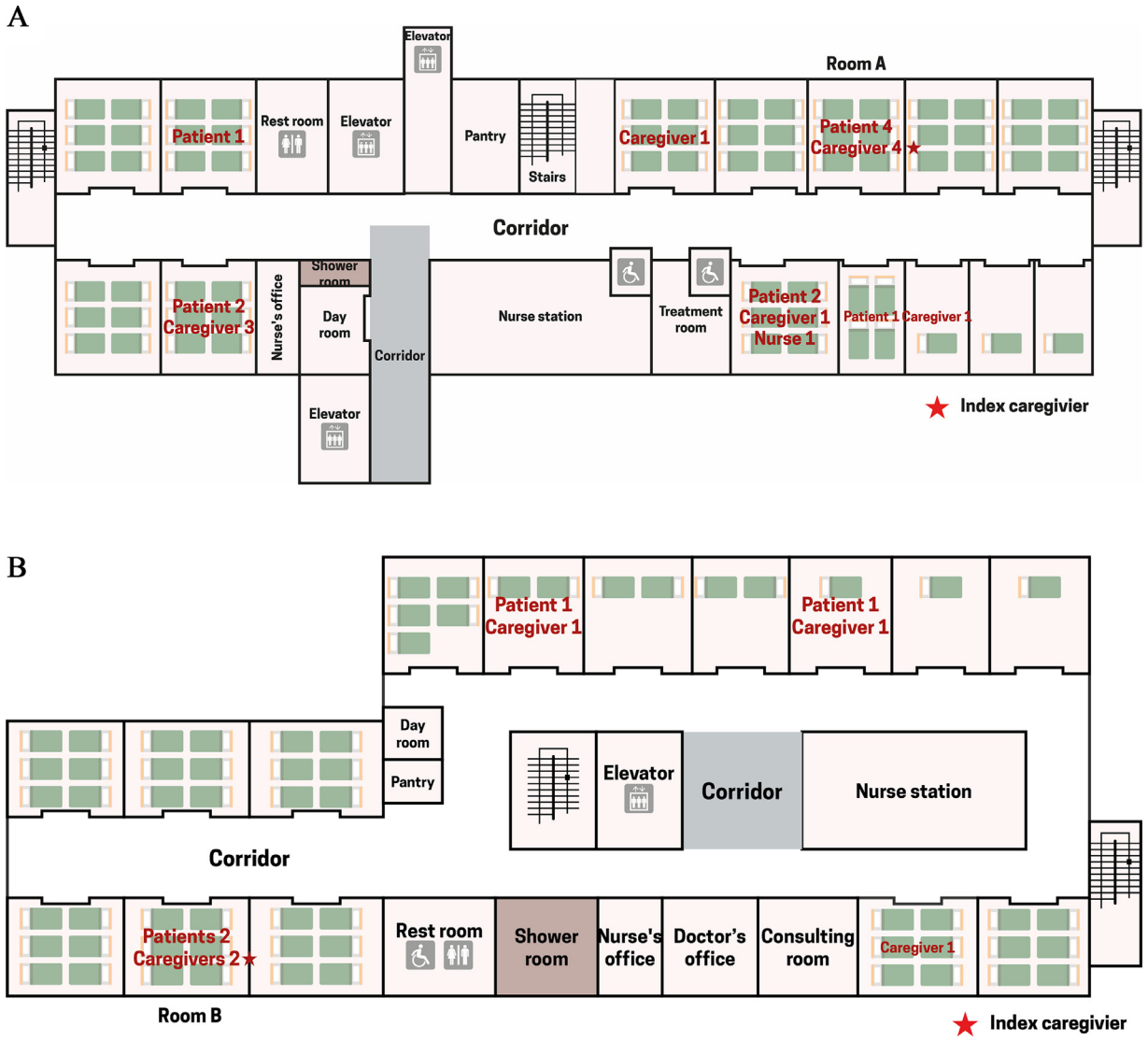

Fig. 3. (A) Distribution of COVID-19 infection on the eighth floor of the main building. (B) Distribution of COVID-19 infection on the seventh floor in the maternal and child health center.

Regardless of the level of circulation of COVID-19 in the community outside the hospital, the occurrence of 2 or more COVID-19 infections among health care workers or patients/caregivers should be carefully investigated. During this outbreak, some cases were initially classified as community-acquired; however, after meticulous epidemiological investigations, they were linked to hospital clusters. In this study, superspreading events were responsible for the in-hospital transmissions. This is in keeping with previous epidemiological studies of healthcare-associated transmission of Middle East Respiratory Syndrome and COVID-19.[20-22] Individual transmission of SARS-CoV-2 between vaccinated persons has been previously described.[23] Our report adds to current knowledge by the description of superspreading events between vaccinated persons. Previous reports of health care workers with breakthrough infection describe lower titers of neutralizing and IgG antibodies, however no cases of secondary transmission were described.[5] In contrast, in our study, among three superspreading events, two were caused by fully vaccinated health care worker and caregiver. The high vaccination rates among health care workers did not prevent secondary transmissions during superspreading events. Therefore, rigorous preventive measures, especially within hospital areas including all nonhealthcare area should be emphasized.

The most important cause of this outbreak was the delay in diagnosis (6 days) in the index health care workers after onset of symptoms. The transmission occurred in the hospital staff cafeteria, where masks are removed at mealtime. Since the virus spread several days before the onset of symptoms, a large number of employees were infected for more than 8 days.[24–26] In the case of breakthrough infection, the symptoms may be milder, so it is important to diligently monitor for symptoms and actively test.[5,25] Moreover, in hospital staff cafeterias where masks are typically removed for meals, a system that can monitor symptoms (fever, medical examination, etc.) should be in place. In addition, for densely populated areas such as hospital staff cafeterias, we recommend maximum ventilation using natural/mechanical methods and depopulate the dining area. Following this outbreak, an air handling unit has been installed in the basement cafeteria.

On the eighth floor of the main building, we suspected internal transmission, since the additional confirmed cases occurred mainly between rooms facing each other. During the outbreak, most of the

Table 2
Clinical course and outcome of the study participants

	Health care workers (n = 61)	Patients (n = 18)	Caregivers (n = 15)	*P* value
Place of isolation				<.001
Community treatment center	52 (85.2)	0	9 (60.0)	
Hospital	6 (9.8)	18 (100.0)	6 (40.0)	
Home	3 (4.9)	0	0	
Duration of hospitalization/isolation, days	9 (8-10)	13 (9-19)	9 (6-11)	.01
Clinical course				<.001
Not hospitalized, no limitations of activities	53 (86.9)	0	9 (60.0)	
Not hospitalized, limitation of activities	1 (1.6)	0	0	
Hospitalized, not requiring supplemental oxygen	6 (9.8)	7 (36.8)	6 (40.0)	
Hospitalized, requiring any supplemental oxygen	1 (1.6)	6 (33.3)	0	
Hospitalized, requiring noninvasive ventilation or HFNC	0	1 (5.6)	0	
Hospitalized, receiving invasive MV or ECMO	0	0	0	
In hospital mortality	0	4 (22.2)	0	.001

Data are presented as number (%), unless otherwise indicated.
ECMO, extracorporeal membrane oxygenation; HFNC, high-flow nasal cannula; MV, mechanical ventilation.

rooms had their doors open despite continuous efforts of staff to keep them closed. Therefore, it is possible that aerosol particles spread across corridors, depending on the indoor and outdoor ventilation conditions (wind, pressure difference). Recently, a hospital COVID-19 outbreak study showed that airborne transmission could be a possible cause of nosocomial outbreaks.[22] In hospitalized patients, compliance with mask-wearing is difficult to implement. Therefore, ventilation strategies to prevent nosocomial outbreaks are important. In contrast, in the maternal and child health center (seventh floor of a different building), the virus spread to several rooms regardless of location. We suspect that this transmission occurred via public areas, such as shower rooms and toilets.

Delta variant breakthrough infections are highly contagious.[10,27] When transmission occurs in a hospital, full recovery is more likely in staff that are young and have no underlying disease. However, in hospitalized patients, complications are more common. In our study, at least two-thirds of patients required oxygen therapy and 22% died. All four deaths in this study occurred among patients, and only one had completed vaccination. A meta-analysis of studies conducted before the emergence of the Omicron variant showed that COVID-19 vaccine efficacy against severe disease remained above 70% after full vaccination, with minimal decrease to 6 months.[28] Vaccine effectiveness to prevent death and respiratory failure during Omicron circulation was 90% overall.[29] Therefore, encouraging vaccination among patients with comorbidities is still very important.

There is a limitation in this study. We did not investigate the titers of neutralizing and IgG antibodies of index patients including superspreaders, therefore, we could not investigate the association of antibody titers and transmission.

CONCLUSIONS

Large outbreaks due to the delta variant can occur through superspreading events, even in hospitals with high employee vaccination rates and regular screening of patients/caregivers and symptom monitoring of health care workers. Although health care workers and caregivers with vaccine breakthrough infections recovered, infections in patients led to poorer outcomes, including death. In hospitals, efforts to minimize transmission through meticulous screening of COVID-19 related symptoms or signs in health care workers and caregivers as well as the use of better ventilation systems for preventing outbreaks via respiratory pathogens is required. Moreover, COVID-19 vaccination is strongly recommended for patients with comorbidities.

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SUPPLEMENTARY MATERIALS

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