



Outbreak Report

Coronavirus disease-2019 (COVID-19) outbreak in a long-term care hospital in Korea in early 2021

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SUMMARY

Background: This study describes the outbreak investigations and control measures for a coronavirus disease 2019 (COVID-19) outbreak at a long-term care hospital (LTCH) in Seoul.

Methods: The outbreak occurred from February 24, 2021 to March 2, 2021 at a 228-bed LTCH in Seoul. Monitoring of the outbreak continued until March 16, 2021. The LTCH investigated the outbreak in cooperation with the district public health centre. After approval from the institutional review board, the hospital's COVID-19 outbreak-related data were collected and analysed.

Results: The outbreak commenced when a new caregiver tested positive for COVID-19 in routine employee screening tests. During this outbreak, eight of 342 people including 175 patients and 64 caregivers were positive for the COVID-19 virus SARS-CoV-2. The mean age of the confirmed cases was 75.1 years (range 55–90). Of the eight, four (50%) were males; two (25%) were caregivers; six (75%) were asymptomatic; six (75%) had previously visited a rehabilitation centre, which was located on the basement level; and one visited different hospitals' outpatient clinics. Three of the 22 environmental specimens were test-positive at the corridor's handrail and the bed rails of confirmed patients. The outbreak ended with the immediate transfer of the confirmed cases to hospitals dedicated to infectious diseases and the transfer of close contacts of these cases to designated hospitals which were organised by the health authorities.

Conclusions: We found a potential link between the rehabilitation centre and the outbreak. To prevent future outbreaks at LTCHs, it is necessary to enhance each LTCH's infection control resources and competencies based on its specific requirements, with support from the government.

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Introduction

Coronavirus disease 2019 (COVID-19) caused by the SARS-CoV-2 virus, was found to have a higher mortality rate among

individuals aged over 65 years, patients in long-term care hospitals (LTCHs), and those with underlying medical conditions [1]. LTCHs, especially those for elderly patients are especially vulnerable to COVID-19 [2]. Consequently, COVID-19

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outbreaks in LTCHs have been detected sporadically and repeatedly. From January 20, 2020, to January 19, 2021, outbreaks in LTCHs or nursing homes comprised 12.9% of all recorded major COVID-19 outbreaks in Korea. Outbreaks in these settings had the highest fatality rate, at 12.0% [3]. In the early phase of the COVID-19 pandemic, Korean government mandated once- or twice-weekly screening tests for employees and caregivers in LTCHs, depending on the severity of community transmission trends [4]. Also, the Korea Disease Control and Prevention Agency (KDCA) enforced policies of temporary hospital closure and entire facility cohorting for LTCHs with any confirmed cases of COVID-19 [5]. As a result, 14 LTCHs implemented entire facility cohorting in December 2020, and 996 new cases were reported from these LTCHs [6]. The entire facility cohorting policies for COVID-19 had limitations due to the lack of isolation rooms and healthcare personnel (HCP) in LTCHs [7].

In Korea, LTCHs employ fewer HCP than other types of hospitals [8]. Moreover, in most LTCHs, a nursing department director or a head nurse concurrently took on infection prevention and control (IPC) responsibilities without a full-time IPC specialist, making it challenging to implement thorough IPC measures [9]. Nursing managers at LTCHs reported that the lack of IPC knowledge and the competencies of their nurses hindered effective responses to infectious diseases such as COVID-19 [10]. According to a survey conducted by the Korean National Healthcare-associated Infections Surveillance in 2018, only 53.2% of LTCHs isolated patients who were infected/colonized with multidrug-resistant organisms, and 12.7% were unable to respond to outbreaks of healthcare-associated infections [11]. Therefore, infectious disease outbreaks may not have been appropriately reported or responded to in LTCHs. Few studies have addressed COVID-19 outbreaks at LTCHs in Korea.

A COVID-19 outbreak occurred at the S Hospital, a LTCH in Seoul on February 24, 2021. The outbreak investigation was conducted in collaboration with the district public health centre and concluded on March 16, 2021, following a two-week post-outbreak monitoring period. This study aimed to describe the onset, progression, and resolution of the COVID-19 outbreak at the S Hospital for thorough understanding of the outbreak situation at the LTCH in early 2021.

Methods

Setting

The S Hospital was a free-standing, 228-bed LTCH with 10 floors and a basement. A cafeteria and a rehabilitation centre were located on the basement level. A reception area, lobbies, and physicians' offices were on the 1st floor. Shared rooms for four or six inpatients were located from the 2nd to the 9th floors. On the 10th floor, there were private patient rooms, a hospital pharmacy, and an outdoor garden. Nursing stations were on the 2nd, 4th, 6th, and 8th floors. The minimum distance between each patient bed in a shared room was 1.5m. Each floor had air conditioning and air circulation systems.

During the outbreak, the hospital had six physicians, 30 nurses, 19 nursing assistants, 10 rehabilitation therapists, a radiologist, two nutritionists, and 14 office workers. On February 24, 2021, 175 patients were hospitalised, with an average age of

79.2 years. Most patients were admitted to the hospital to recuperate and rehabilitate after an acute phase of illness. According to S Hospital regulations, caregivers contracted by the hospital must be present 24 hours a day for patients in shared rooms. For patients in a single room, a private caregiver or a family member should accompany them. On February 24, 2021, 64 caregivers were present at the hospital.

Hospital preparedness for COVID-19

As the number of confirmed COVID-19 cases in Seoul surged rapidly in December 2020, HCP at the hospital were alerted and prepared for potential COVID-19 cases. The hospital's IPC measures for COVID-19 included the following: keeping a non-contact thermometer at the hospital's entrance; strict visitor control and management; COVID-19 screening tests for employees twice a week in compliance with the national guidelines for LTCHs; pre-admission COVID-19 screening tests and quarantine in a single room while awaiting test results; daily fever and symptoms checklist for HCP; supplementing personal protective equipment (PPE) at the wards (HCP were required to wear a N95 mask, a gown, goggles, gloves, and shoe covers when testing suspected patients); strict masking of all (HCP were given KF94 [Korean N95] masks twice a week); restrictions on patients and caregivers leaving the hospital; reinforcement of strict hand hygiene; autoclave sterilisation of reusable devices; daily environmental disinfection of patient rooms and nurses' stations using sodium hypochlorite; and developing and disseminating protocols for any positive COVID-19 cases. All screening tests were conducted using real-time reverse transcription polymerase chain reaction (PCR) to detect SARS-CoV-2 virus. The rapid antigen test was commercially unavailable until the hospital COVID-19 outbreak ended. The COVID-19 PCR assay was performed at a laboratory outside the hospital. The hospital experienced the COVID-19 outbreak despite the preventive measures implemented.

Outbreak investigation and management

For the outbreak investigation, the hospital collaborated with the district public health centre. The district public health centre's epidemic surveillance officers conducted contact tracing by detecting cases based on KDCA definitions at that time and identifying close contacts through interviews with HCP and patients with confirmed COVID-19, as well as closed-circuit television (CCTV) footage. In accordance with the national policy for managing LTCH outbreaks, the district public health centre promptly transferred confirmed cases to hospitals dedicated to infectious diseases. If close contacts were patients, the health authorities relocated them to designated hospitals to ensure they continued receiving appropriate medical care. If not, close contacts were asked to quarantine at home or in designated facilities.

Ethical approval, data collection and analysis

This study reviewed investigation documents containing anonymised personal data after obtaining approval from the institutional review board of Seoul National University (IRB no. 2107/004–016). The document was completed based on electronic medical records, statements from confirmed COVID-19 cases and HCP, and CCTV records. The demographic and

clinical characteristics of the confirmed cases and the COVID-19 transmission in the hospital were analysed descriptively.

Informed consent was not gained from patients involved in this outbreak. All patients were treated according to clinical judgement and IPC practices required to treat them and to control the outbreak according to national guidelines. Patients did not undergo randomisation or intervention for the purpose of this study. Data were analysed and presented anonymously.

Results

Summary of outbreak cases and infection prevention and control (IPC) measures

Caregiver #1 was an index case (Figure 1). On February 18, 2021, she started working as a caregiver in room 505, where six patients were hospitalised. A day prior to her first day of employment, caregiver #1 tested negative for COVID-19 at the district public health centre. On February 24, caregiver #1 was confirmed with COVID-19 during a routine employee screening test. She had no symptoms, including no fever or cough. Immediately, she was isolated in a single room, and the incident was reported to the district public health centre. The hospital restricted movement on the 5th floor, where she had been on duty, distributed PPE, and mandated the use of Level D protection sets for HCP and caregivers. During the early phase of the COVID-19 pandemic, Korean HCP were provided with Level D PPE sets, which included a Level D coverall classified by the Occupational Safety and Health Administration [12], an N95 respirator, gloves, foot covers, a hood, and goggles or a face-shield. Instructional videos were provided to employees and caregivers via smartphones, to enable the hospital to educate them on how to wear and remove PPE. Environmental surfaces in room 505, in the corridor on the 5th floor, and along the route taken through the hospital by caregiver #1 were disinfected. In addition, because Caregiver #1 had accompanied one patient from room 505 to the rehabilitation centre, the hospital closed the rehabilitation centre and directed all therapists to remain at home until they received further instructions from the district public health centre. Following the initial assessment, the district public health centre classified all patients in room 505 (patients #1, 2, 3, 4, 5, and 6) and another caregiver (caregiver #2) as close contacts, and requested PCR tests for all hospital employees, patients, and caregivers. The district public health centre organised a hospital designated for infectious diseases where the index case would be transferred, designated hospitals for close contact patients, and assigned ambulances for transportation.

On February 25, 2021 the next day, patient #1 and another patient (patient #7) on the 8th floor were found to be COVID-19 positive on the SARS-CoV-2 PCR testing. Patients (patient #8, 9, 10, 11, and 12) and caregivers (caregiver #3 and 4) in room 802 were classified as close contacts based on the district public health centre's contact tracing using CCTV recording analysis. The district public health centre provided additional PPE supplies and ordered quarantine for four rehabilitation therapists (therapists #1, 2, 3, and 4) who treated patient #7. In addition, the district public health centre disinfected the rooms of the confirmed patients, corridors on the 5th and 8th floors, and hospital elevators. On the same day, the confirmed patients were transferred to the hospitals designated for infectious

diseases. The S Hospital additionally restricted movement on the 8th floor, and meals were served to patients and caregivers on the 5th and 8th floors using disposable plates. During this response, caregiver #4 resigned and this was reported to the district public health centre.

On February 26, caregiver #5 in room 901, who also visited a rehabilitation centre, tested positive. While identifying close contacts immediately, infection control measures were implemented. In addition, the hospital continued to conduct SARS-CoV-2 PCR tests based on the list provided by the district public health centre to prevent further spread. As patient #12, who had been on the close contact list, tested positive on February 27, patient #16 was classified as a close contact because she received physical therapy in the rehabilitation centre next to patient #12 without wearing a mask on February 23. Also, nursing assistants (assistants #1 and #2) who had close contact with patient #12 were quarantined at home for 14 days from February 27. Patient #17 in room 504 tested positive on February 28.

From the first day of the outbreak, patients were required to wear KF94 masks in their rooms. HCP and caregivers were obliged to wear full-body PPE on the 5th, 8th, and 9th floors. In addition, HCP were required to change PPE completely and perform hand hygiene in a PPE donning and doffing area next to the doors when leaving the rooms for the confirmed patients. Although Korea began its national vaccination program on February 26, 2021 [13], and the study LTCH received COVID-19 vaccines from the KDCA on that day, the LTCH decided to begin vaccinations after the outbreak ended. Consequently, during the post-outbreak monitoring period, employees and caregivers were divided into two groups based on their preferred date and vaccinated on March 6 and 9 2021 (Figure 2). Although vaccination was optional, no employee or caregiver refused the vaccine.

Before the outbreak, SARS-CoV-2 PCR tests were performed twice a week for all employees and caregivers, following the KDCA guidelines. The government covered the expenses of the screening tests. The test was conducted once on Mondays or Tuesdays and once on Wednesdays or Thursdays, for the convenience of shift workers. However, during the outbreak, SARS-CoV2 PCR tests were conducted based on the list provided by the district public health centre. To avoid overlap, routine screening tests for employees were not performed during this period. Since no cases had been confirmed after March 2, 2021 the district public health centre no longer required specific employees and caregivers to be screened. Therefore, people not on the list of the district public health centre underwent routine screening tests, ensuring that all employees and caregivers were tested for COVID-19 at least twice a week (Figure 3).

Findings from the outbreak

In total, eight COVID-19 cases were confirmed between February 25 and March 16, 2021, including patient #13, who was confirmed on March 9 after being transferred to the designated hospital as a close contact. Four positive cases (patient #1, 2, 12 and 13) were from 30 close contacts, which included 19 patients, five caregivers, four physical therapists, and two nursing assistants. No physician or nurse was identified as a confirmed case or close contact. The average age of the confirmed cases was 75.1 years (range: 55–90; Table I). Four (50%) of the eight confirmed cases were males, and two (25%) were caregivers. Seven (87.5%) had underlying diseases, and six (75%) were asymptomatic. The two symptomatic patients had a fever only with underlying

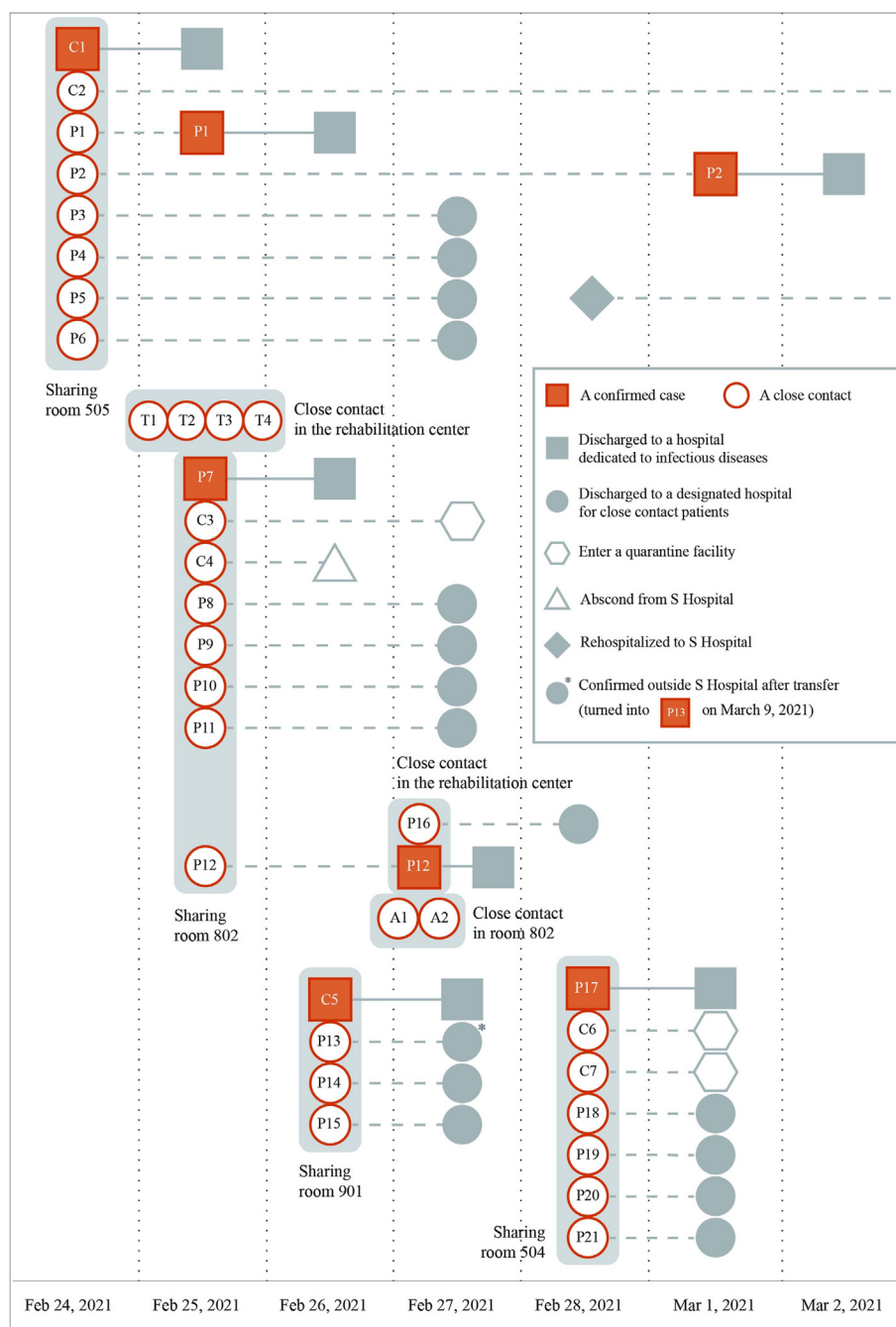


Figure 1. Timeline of the COVID-19 outbreak among epidemiologically linked confirmed cases and close contacts in S Hospital. Note. A, nursing assistant; C, caregiver; P, patient; T, physical therapist.

respiratory diseases. Notably, patient #1 exhibited a fever on February 23, one day before the onset of the outbreak. Six (75%) had visited the rehabilitation centre. Patient #7 visited different hospitals' outpatient clinics on January 5 and February 4 for a prostate ultrasonography and a video-fluoroscopic swallowing test, which were unavailable at S Hospital. Each time, patient #7 traveled 30 minutes from S Hospital to the outpatient clinics and returned approximately 4 hours later.

Despite the hospital's efforts, some cases revealed vulnerabilities and challenges at the LTCH during the outbreak situation. Patient #2, a 90-year-old elderly male patient with pneumonia and fever, had behavioural problems due to

Alzheimer's disease. Arranging a designated hospital to accept this patient as close contact was difficult. Although he was classified as a close contact on February 24, due to this difficulty, he continued to stay at S Hospital. He was finally confirmed with COVID-19 and transferred on March 2 to a hospital designated for infectious diseases. In another case, patient #5, who had been transferred to a designated hospital as close contact, returned to S Hospital. Not only was the patient unable to adapt to the new environment because of his Alzheimer's disease, but the designated hospital was unable to provide specialized care for his hemiplegia. Moreover, caregiver #4 was classified as a close contact, but she left the

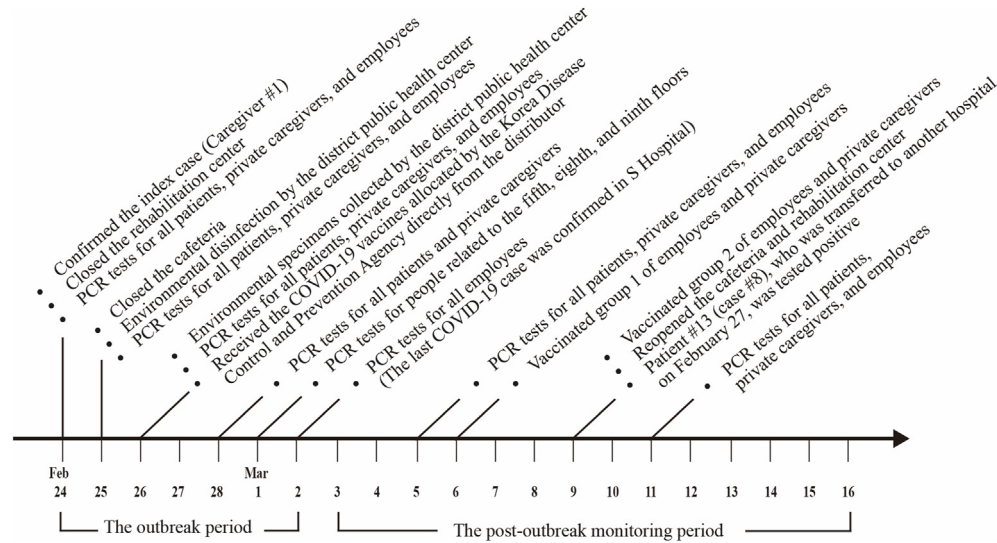


Figure 2. Major events during the COVID-19 outbreak and response measures for infection control by date, February 24 to March 16, 2021.

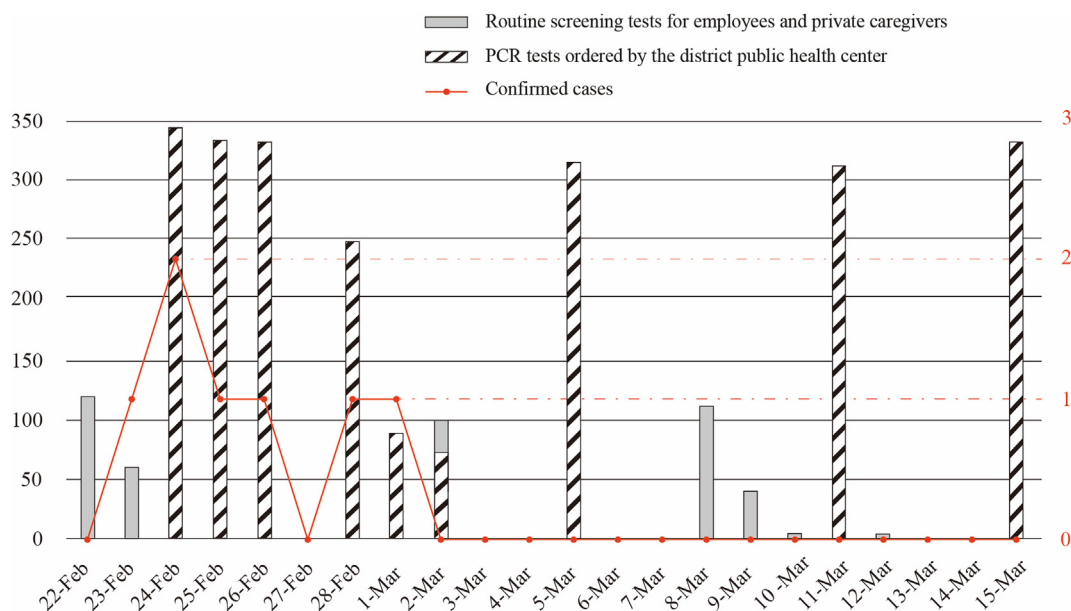


Figure 3. Number of SARS-CoV-2 PCR tests performed on employees, caregivers, and patients by date.

hospital immediately out of fear of contracting COVID-19. This was reported to the district public health centre.

On February 27, the district public health centre collected 22 environmental samples from the elevators, rehabilitation centre, beds of confirmed cases, corridors, and restrooms on the 5th, 8th, and 9th floors as part of the outbreak investigation. Three specimens were positive for COVID-19, taken from the 5th-floor corridor's handrail and the bed rails of patients #1 and #17, both of whom tested positive (see X marks in Figure 4).

This study discovered a potential link between the rehabilitation centre and the hospital's outbreak spread. From 9:00 a.m. to 5:30 p.m., patients' rehabilitation therapies were scheduled every 30 minutes. The rehabilitation centre was 157 m² in size and employed 10 therapists. On February 22, two days before the index case was reported, the largest

number of people (21 in total: 11 patients and 10 therapists) were present during the centre's busiest hours (Figure 5). Confirming how many caregivers accompanied patients was impossible; however, the presence of caregivers indicates that up to an estimated 30 people might have been in the area simultaneously, posing a potential risk for the spread of COVID-19 to other floors. After the rehabilitation centre's closure on February 24, it reopened on March 9, and no subsequent confirmed cases were reported during the post-outbreak monitoring period.

Discussion

This study reported the epidemiologic and clinical characteristics of confirmed COVID-19 cases in the LTCH outbreak

Table I

Clinical and epidemiological characteristics of the confirmed cases of COVID-19 in S Hospital

Characteristics	Confirmed cases								Summary
	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8 ^a	
	Caregiver #1	Patient #1	Patient #7	Caregiver #5	Patient #12	Patient #17	Patient #2	Patient #13	
Sex	F	M	M	F	M	F	M	F	M (50%), F (50%)
Age (yr)	60	85	63	55	82	86	90	80	Mean 75.1
Underlying disease related to the respiratory system	-	COPD	COPD	-	-	-	Pneumonia	-	37.5%
Comorbidity	HTN	AD, HTN, DM, CKD	HTN, Arrhythmia, cerebral hemorrhage, prostatic hyperplasia	-	AD, HTN, DM, cerebral infarction, hemiplegia	AD, HTN, hypothyroidism, femur fracture	AD, prostatic cancer, epidural hemorrhage	HTN, paraplegia, myelopathy	AD (50%), HTN (75%), DM (25%)
Date of confirmation ^b	02/24/2021 ^c	02/25/2021	02/25/2021	02/26/2021	02/27/2021	02/28/2021	03/02/2021	03/09/2021	
Date of symptom onset	-	02/23/2021	-	-	-	-	03/02/2021	-	
Symptoms	-	Fever up to 38.0°C	-	-	-	-	Fever up to 38.2°C	-	
Related room	505	505	802	901	802	504	505	901	
Rehabilitation centre visit	Y	N	Y	Y	Y	Y	N	Y	75%

AD, Alzheimer's disease; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; F, female; HTN, hypertension; M, male; N, no; Y, yes.

^a Case 8 (patient #13) was transferred to another hospital on February 27, 2021, and was confirmed on March 9, 2021.^b The date of the polymerase chain reaction (PCR) test is one day before the date on which COVID-19 was confirmed.^c She started working on February 18, 2021, after testing negative for COVID-19 at the district public health centre.



Figure 4. Floor plans of the basement, fifth, eighth, and ninth floors of the study hospital with disposition of the confirmed cases and close contacts, and sites of positive environmental specimens (X marks). Note. C, caregiver; P, patient.

and the hospital's measures in response to the outbreak. The hospital lacked a specialised isolation room and a full-time IPC specialist. However, early detection of the infected person through routine employee screening tests and close cooperation with the district public health service prevented the further spread of COVID-19. Another investigation into the Korean LTCH's COVID-19 outbreak in December 2021

reported challenges related to HCP shortage and difficulties with ventilation. It also reported that 91.0% of the individuals in the LTCH (297 out of 300, most of whom were vaccinated) were confirmed in the month after the first confirmed case [14]. In contrast to that report [14], actions implemented at the S Hospital included immediate transfer of confirmed patients and their contacts to other designated hospitals,

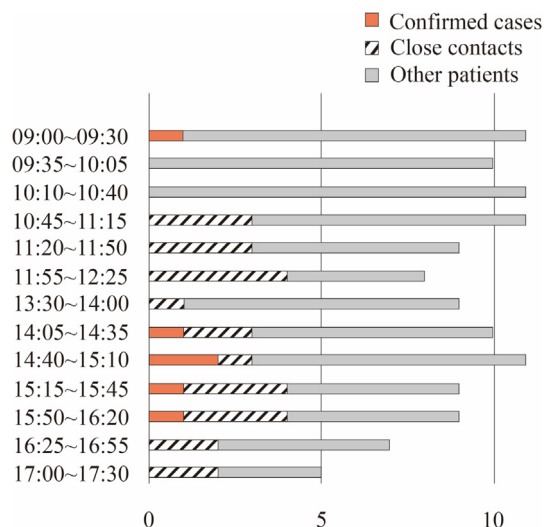


Figure 5. The rehabilitation therapy schedule of COVID-19 cases, close contacts, and other patients on February 22, 2021.

maintaining a minimum distance of 1.5m between patient beds, and installation of a PPE donning/doffing zone in front of the room of a confirmed COVID-19 patient case to enable changing the PPE upon exiting, in addition to all the preventive measures described as part of the hospital preparedness as described in the methods.

Despite all preventive measures, the abrupt onset of the outbreak at the study hospital was unavoidable [15]. One hypothesis regarding the source of the outbreak was developed after reviewing and analysing the data. It was hypothesised that caregiver #1 was likely infected before employment and may have been in the incubation period during the negative pre-employment screening test. She showed no symptoms, even after testing positive for COVID-19. Therefore, COVID-19 may have spread while she cared for six patients alongside another caregiver.

During the review and analysis process, we identified a potential gap in the screening test strategy intended to prevent the introduction of the COVID-19 virus into the hospital. Patient #7, who had visited other hospitals for tests unavailable at the study hospital 20 days before the outbreak, did not have a COVID-19 screening test. Caregivers and patients were generally restricted from leaving the LTCH during the pandemic. However, in an exceptional case like this, patients who needed to visit other hospitals should have had a screening test a, considering the incubation period, even in the absence of symptoms.

As the proportion of asymptomatic COVID-19 cases ranged from 20 to 70% [16], 75% of the confirmed cases in this study were asymptomatic. Moreover, two patients with fever symptoms had pre-existing respiratory diseases. Asymptomatic or atypical COVID-19 symptoms may be associated with elderly patients or other comorbidities, which can mask the infection and potentially results in the development of severe illness particularly in the elderly [17]. It was found that the hospital did not perform COVID-19 PCR tests for patient #2, whose fever started on February 23, 2021, the day prior to the onset of the COVID-19 outbreak. The HCP may have thought that fever was a symptom of the patient's underlying medical condition because outbreaks in LTCHs were uncommon at that time, despite the prevalence of COVID-19 across the country. To

reduce the risk of an outbreak in a LTCH, especially during a pandemic, the HCP need to carefully assess the symptoms of infection in elderly patients and actively perform screening tests.

COVID-19 spreads via direct contact, droplets, and aerosols [18,19]. The Centers for Disease Control and Prevention reported that if an infectious person engages in physical activities such as exercising and singing for more than 15 minutes in a closed space with inadequate ventilation, the COVID-19 could spread to those who are present or who subsequently visit the space [20]. Droplets and aerosols might have been the primary mode of transmission in this outbreak at the rehabilitation centre, located in a basement with poor air circulation and usually crowded. Because of the adherence to using masks and rigorous surface disinfection, there was no transmission among the therapists and no positive environmental sample. Nonetheless, some patients seemed to contract COVID-19 while receiving therapy because they had difficulty wearing masks constantly due to the cognitive or behavioural issues associated with their illness. COVID-19 transmission to other floors may have been possible through these patients. Contact transmission through the surface seems less likely because environmental tests at the rehabilitation centre and elevators were negative. In addition, COVID-19 could have been transmitted between caregivers waiting for their patients in front of the rehabilitation centre. Large-scale COVID-19 transmission from basement facilities has been reported [21,22]. The establishment of policies for basement facilities in LTCHs, such as ventilation or maximum capacity by size, is required to prevent future outbreaks. Alternative rehabilitation therapy methods, such as bedside rehabilitation treatment [23] to reduce close contact among patients during an outbreak should also be considered.

Most elderly patients in LTCHs require assistance with basic activities of daily living. Maintaining physical distance from patients with dementia or Alzheimer's disease during a pandemic is impossible. These patients cannot comprehend public health measures like using masks, and their psychological symptoms may deteriorate due to restrictions on anxiety-relieving activities such as wandering and family visits [24]. Furthermore, since LTCHs in Korea rarely have well-equipped

isolation rooms and do not employ full-time IPC specialists [25], health authorities ordered the immediate transfer of confirmed patients from LTCHs to hospitals dedicated to infectious diseases in the early phases of the COVID-19 pandemic. Nonetheless, this study reported that the S Hospital had difficulties even when transferring elderly patients with Alzheimer's disease. Patients may have developed close relationships with the HCP and caregivers in the S Hospital, given that the average length of hospitalisation was approximately 175 days. Therefore, patients could have experienced severe anxiety or worsening symptoms with the new environment and HCP who may not have fully understood their needs at the hospitals which were dedicated to infectious diseases. This immediate transfer policy helped to prevent the broader spread of COVID-19 in the LTCH. However, providing individualised and high-quality care to elderly patients became challenging. To improve the quality of nursing care at hospitals dedicated to infectious diseases for the preparation of future infectious disease outbreaks, further studies are necessary to assess how these hospitals managed the influx of patients during the pandemic and to supplement the staffing and facilities for better accommodations. In a previous study that examined the treatment preferences of patients with dementia, their families, the HCP, and the public for long-term care services, treatment provided by the consistent HCP and a broader range of care coordination activities were highly rated [26]. Given the demanding medical conditions of patients in LTCHs and their preferences for consistent treatment, establishing each hospital's infection control infrastructure is required to continue providing care in the current facility during a pandemic. To prevent future outbreaks at LTCHs, it is necessary to enhance their preparedness by installing well-equipped isolation rooms and employing full-time IPC specialists who can provide education to improve HCP's infection control knowledge and skills, tailored to their specific conditions, with support from the government.

This study had several limitations. First, this outbreak investigation included a relatively small number of confirmed cases that occurred in a short time. Second, data from the district public health centre could not be obtained because of confidentiality. In addition, further inspection after reviewing the hospital's investigation records was impractical. Nevertheless, this study provides comprehensive insights into the COVID-19 outbreak in the LTCH and the hospital's infection control measures in early 2021 in Korea, which can serve as valuable evidence for informing policies and support necessary to prepare for potential future outbreaks in LTCHs.

CRediT authorship contribution statement

Eun Jo Kim: Conceptualization, Formal analysis, Methodology, Project administration, Visualization, Writing – original draft, Writing – review & editing. **JaHyun Kang:** Conceptualization, Formal analysis, Methodology, Visualization, Writing – original draft, Writing – review & editing. **HyeonSuk Byeon:** Data curation, Formal analysis, Writing – review & editing.

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Ethical approval

Approval from the Institutional Review Board of Seoul National University (IRB no. 2107/004–016).

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Conflicting of interest statement

The Author(s) declare(s) that there is no conflict of interest.

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