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# Management following the first confirmed case of SARS-CoV-2 in a domestic cat associated with a massive outbreak in South Korea

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Keywords: SARS-CoV-2 COVID-19 Animal transmission Community	Objectives: We analyzed how the virus spreads to local communities, based on the results of an epidemiological investigation of a religious facility in which a large group of patients was infected. Furthermore, we report for the first time in South Korea that a domestic cat was infected with SARS-CoV-2. <i>Methods:</i> An epidemiological investigation was conducted to investigate the group outbreak. In addition, to verify cat–cat or cat–human transmission, we monitored whether exposed cats or humans were infected. Next-generation sequencing (NGS) of the viral full-length genome test was conducted on the positive samples from both owners and the cats. <i>Results:</i> Total number of SARS-CoV-2 cases rose from 78 individuals, who visited a religious facility who were involved in 42 transmitted cases in the community, either through close contact with household members (47.62%) or through a group outbreak (16.67%). We observed an infected cat as well as individuals to which they were exposed. However, neither—further—cat to cat nor cat to human transmission occurred. <i>Conclusions:</i> COVID-19 can be transmitted from humans to animals under certain conditions. Therefore, monitoring and studying the transmission of COVID-19, a novel infectious disease, between humans and animals is necessary through the One Health approach.

# 1. Introduction

The coronavirus disease 2019 (COVID-19) pandemic has spread worldwide since the first reported outbreak was associated with an animal and seafood market in Wuhan, China at the end of December 2019 [1,2]. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spreads from person to person through close contact and has been introduced to local communities through group outbreaks [3,4] such as religious facilities and nursing homes in South Korea [5].

As with severe acute respiratory syndrome coronavirus 1 (SARS-CoV-1) and Middle East respiratory syndrome coronavirus (MERS-CoV), which are two coronaviruses of animal origin, many investigators have speculated that the etiologic agent of COVID-19 is an animal, possibly bats, and that it may have spread to humans through an intermediate host [6]. Just as SARS-CoV-1 was detected in cats and dogs in 2003, SARS-CoV-2, the virus causing COVID-19 in humans, has also been

confirmed in animals; 26 countries have reported infections in animals to date, among which, 15 countries have reported infected cats [7,8]; OIE [9]. The possibility of transmission between humans and animals remains low, but transmission may be possible under certain conditions—similar to the mutual transmission between mink and humans, which was confirmed in Denmark [10].

In this study, we analyzed how the virus spreads to local communities, based on the results of an epidemiological investigation of a religious facility in which a large group of patients was infected. Furthermore, we report for the first time in South Korea that a domestic cat was infected with SARS-CoV-2. In addition, to verify cat-cat or cat-human transmission, we monitored whether exposed cats or humans were infected.

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### 2. Methods

#### 2.1. Outbreak setting

Between January 7th and February 4th, 2021, a large number of confirmed cases occurred in religious facility A where accommodation and boarding were available. This facility accommodated 80 members. A speaker was invited weekly for more than 1 year to host religious services. Four services were held daily at 06:00, 11:00, 15:00, and 20:00, and lasted approximately 2 h each. The facility consisted of a chapel, a dining area, and five accommodations. The chapel seats approximately 144 people who sit separately on each side and consists of two prayer rooms, two bedrooms, and two toilets on each side of the chapel. Accommodations are divided into five buildings, each of which is inhabited by men or by women and includes shared and single rooms. The total capacity of the accommodation is 33 individuals, of which, 29 lived in the accommodation at the time of the outbreak. The dining area has 10 tables: three dining tables accommodate six people, and six dining tables accommodate four people. Thus, it can seat approximately 42 people. Three meals are provided daily. A facility regulation requires participation in worship and requires members to refrain from other conversations or meetings. Many residents were long-term residents, having lodged for more than 1 month. Most visitors lived in the area where the facility was located, but some were from other areas. An epidemiological investigation was conducted to investigate the environment of the group outbreak and to track the source of infection and individuals who came into contact with the virus. In the process, for the first time in Korea, a domestic animal (i.e., a cat) was confirmed as having COVID-19.

#### 2.2. Epidemiologic investigation and response measures

Human Patient #1 (i.e., Index case, human) presented symptoms on January 5th, 2021, and was confirmed as having the virus on January 10th, 2021, through a patient-under-investigation-examination in area B, which was the patient's residence. The distance between the location of religious facility A and area B is approximately 340 km with an approximate travel time of 4 h by car. Investigations revealed that Patient #1 visited the religious facility from January 3-8 for lectures. On January 10, epidemiological surveys and examinations were conducted over the phone with 29 residents of the prayer center. On January 11, 28 of the 29 residents of the prayer center were confirmed as being infected, and both a site and environmental investigation were conducted after closing the facility. In addition, telephone epidemiological surveys and examinations were conducted by securing a list of visitors. In the site and environmental investigation, epidemiological investigators conducted a risk assessment for the facility with the six indicators of "degree of enclosure," "density," "continuity," "clustering," "activity," and "management," based on the guidelines of the Korea Disease Control and Prevention Agency (KDCA; Cheongju, Republic of Korea) [11].

Environmental samples were collected to determine the degree of environmental contamination. The samples were collected by dividing the facility into the front of the chapel, the back of the chapel, and the living areas (i.e., dining area and accommodation). The samples were primarily collected from places where droplets and physical contact were likely to have occurred [12]. Owing to the large number of visitors from other areas, there was a high possibility of transmission to communities other than the area in which religious facility A was located. Therefore, a national emergency disaster message was sent within the region on January 11 and on January 15 to track and examine potentially exposed individuals. The examination candidates were as follows: 1) residents of religious facility A, 2) individuals who visited religious facility A after December 1st, 2020, 3) individuals who came into contact with a person confirmed to be infected, and 4) individuals who were exposed to contact throughout the route of the confirmed patient. The person who came into contact was classified at the discretion of the epidemiological investigator and was defined as a person who had close

contact with the household for more than 15 min or a person who did not wear appropriate protective equipment (Korea Centers for Disease Control & Prevention). The COVID-19 confirmation test for the test candidates was conducted using quantitative real-time reverse transcription PCR (RT-qPCR) assays [12]. Individuals confirmed as "positive," based on the COVID-19 test results, were transferred to a hospital dedicated to infectious diseases, and people who came into contact with the aforementioned individuals were investigated. Among individuals who tested negative, based on the COVID-19 test results, any resident or visitor to religious facility A or individuals who had come into contact with such people were quarantined for 14 days beginning on the final day of exposure. Tests were also conducted when the individuals became symptomatic or at the end of the quarantine period.

A visitor list was obtained, dating from December 1. An inspection was conducted to identify the infection route. In-depth epidemiological investigations were conducted on the three patients who had the earliest symptom onset through a global positioning system, credit card usage details, and in-depth interviews.

During the site investigation on January 11, investigators confirmed that three pets (cats A, B, and C) were living in the accommodation of the religious facility. On January 19, an animal protection organization rescued cats A, B, and C at the request of their owners (i.e., a mother and daughter). Owing to signs such as loose stools, samples were collected by animal protection and public health authorities, using the established criteria [12]. On January 20, samples were collected from the nasal, oropharynx, back (i.e., fur), and forepaw. As signs persisted, additional samples were collected on January 23 (i.e., nasal, oropharyngeal, rectal, and stool samples). Additional samples were collected on January 25 (i. e., stool), and additional samples were collected on February 3, the day before the release from quarantine. The samples were transferred to a local testing institution, and RT-qPCR was conducted. Positive samples were transferred to the KDCA, and a final confirmation test (RT-qPCR) was conducted [13,14].

As part of the public health response, positive samples from the owners (i.e., mother and daughter), which had been collected on January 11, were transferred from a local testing institution to the KDCA. Next-generation sequencing (NGS) of the viral full-length genome test was conducted on the positive samples from both owners and the cats [12,13]. After RNA extraction from the samples, cDNA was amplified using the primer pools (https://artic.network/ncov-2019). Libraries were prepared using the Nextera DNA Flex Library Prep Kit (Illumina, USA) and sequencing was performed on the MiSeq instrument with  $2 \times 150$  base pairs using a MiSeq reagent kit V2 (Illumina, USA) to obtain an average genome coverage greater than  $1000 \times$  for all the samples. The reads were trimmed and mapped to reference genome MN908947.3 using CLC Genomics Workbench version 20.0.3 (CLC Bio, Denmark). All the sequence data were uploaded to NCBI.

The cat that had tested positive and the other cats, which came into contact with the infected cat were isolated and managed by using the Center for Disease Control (CDC) Toolkit (Atlanta, GA, USA) [15]. By referring to established CDC recommendations, the human exposed to the cat testing positive at close proximity for 15 min without appropriate protective equipment is set to contacts #1-#5 [16,17]. For those who were exposed, active monitoring was conducted once daily for 14 days, and RT-qPCR tests were performed on the 5th day and 13th days before quarantine release, based on the average incubation period.

This investigation was a part of a public health response and used public information; therefore, it did not require institutional review board approval or written informed consent by the participants.

# 3. Results

Fig. 1 presents the epidemic curve, based on the onset date of symptoms of group outbreaks related to religious facility A, as well as the timeline of the overall clinical and epidemiological events. A total of 120 patients were exposed between January 10 and February 4 during

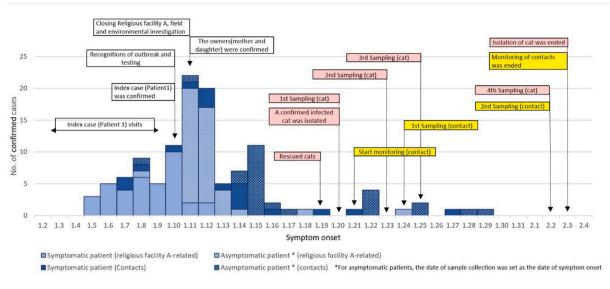


Fig. 1. Epidemic curve based on the date of symptom onset of Outbreak and Timeline of Clinical and Epidemiological events.

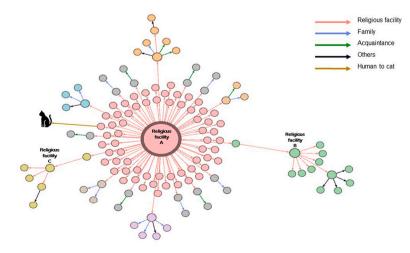
the outbreak. Of the 29 residents, 28 residents were confirmed as having the virus on January 11, and the remaining resident was confirmed as having the virus at the examination before the end of self-quarantine on January 24, thereby resulting in 29 confirmed cases. Therefore, the attack rate for residents at religious facility A was 100%.

Of 189 people on the list of permitted visitors from December 1st, 2020, to January 10th, 2021, examinations were conducted on 138 individuals who were confirmed as having visited the facility. Thus, 131 people were tested (i.e., 94.93% inspection rate); of these, 49 people were confirmed as being infected, which resulted in an attack rate of 37.40%. An additional 42 cases were confirmed through investigations via the 78 confirmed patients who had lived in or visited the religious facility. Two patients who were confirmed with the virus in religious facility A on January 6th and January 7th were reclassified as confirmed cases associated with religious facility A after they had been confirmed as having visited the facility during the epidemiological investigation process. Of the 120 confirmed cases, 66 (55.00%) patients were asymptomatic at diagnosis. Among the residents, 11 (37.93%) of the 29 patients were asymptomatic. Among the visitors, 30 (61.22%) of 49 patients were asymptomatic. Among those who came into contact, 25 (59.52%) of 42 patients were asymptomatic.

Based on the results of visitor tracking to religious facility A from December 1st, 2020, to January 10th, 2021, no transmission to visitors occurred before January 3, 2021. An in-depth epidemiological investigation was conducted on three patients (Patient #1 and two residents) who had the earliest symptom onset date on January 5 to determine the infection route. Two residents, excluding Patient #1, who visited as an outside speaker, had not been to any other places, except the facility.

The risk assessment conducted during the site and environmental investigations had the following results: the chapel was evaluated as having a high overall risk, the accommodation was evaluated as having a moderate overall risk, and the dining area was evaluated as having a moderate overall risk (Appendix 1). In addition, all 19 environmental samples tested positive. The Ct value of the chapel (i.e., front) was significantly lower (p < 0.05) in the three areas (i.e., the viral load was the highest) (Appendix 2).

Fig. 2 shows the results of COVID-19 transmission during the outbreak in the group, established based on the results of the epidemiological investigations. The residents had no particular contact with external factors, other than religious facility A. Therefore, no community spread occurred. Of the 47 visitors to religious facility A, 17 (36.17%) confirmed cases spread 32 new cases to the local community,



\* Same color of circle stands for same subcluster.

Fig. 2. Transmission chains in COVID-19 Religious facility A outbreaks South Korea 2021.

as follows: 15 cases of infection occurred through contact with their family members, 7 cases occurred through small-scale group outbreaks at religious facility B, and 10 cases were spread through other contacts. Of the 32 cases that were first in the community, three (9.38%) cases caused six cases of community transmission, of which four cases were to household contacts and two cases were through other contacts. Four cases of community transmission were caused by two (33.33%) of six cases that were confirmed as a secondary contact, of which one case occurred through household contacts and three cases occurred through other contacts. When transmission occurred, the average number of positive transmissions was 1.91 people. The average number of visitors who transmitted was 1.88 people.

Table 1 shows the clinical and epidemiological characteristics of the owners (i.e., mother and daughter) and cats A, B, and C. The mother and daughter were 54 years old and 21 years old, respectively, and stated that they had lived in religious facility A since August 2020 without particular access to external areas. Both patients were asymptomatic at the time of diagnosis on January 11, 2021, and were discharged from a hospital dedicated to COVID-19 on January 20, 2021, because they met the standards of isolation release for asymptomatic patients.

Cats A, B, and C were transferred to a temporary shelter on January 19, which was the 9th day from the date of separation from the owners. The oropharyngeal swab sample from cat C tested positive for SARS-CoV-2 RNA; it had been collected on January 20. The other samples [i.e., nasal, back (i.e., fur), and forepaw samples] were negative. All samples from cats A and B were negative. All samples from cats A, B, and C, obtained on January 3, January 5, and January 13, were negative.

To confirm where the cats had visited, interviews were conducted with the owners. The owners stated that cats A, B, and C stayed in the room of religious facility A with their owners and that the cats had not visited anywhere else. Cat C was isolated for 14 days from the date of specimen collection, and cats A and B were observed for signs. Cat A was a mother cat, and her exact age was unknown. She was asymptomatic during the monitoring period. Cats B and C were kittens of cat A and were an estimated 3 months old. Cat B continued to have signs of loose stool during the monitoring period and had signs of bloody stool 4 days before the end of the quarantine period. Cat C continued to exhibit loose stool signs during the isolation period. Cats B and C were diagnosed with dehydration and coccidiosis, after undergoing a comprehensive veterinary examination post-quarantine because the signs had persisted. Blood collection for antibody testing was attempted after quarantine but failed due to dehydration from persistent diarrhea in cats B and C. Viral culture could not be attempted because of the insufficient sample volume.

The NGS of the viral full-length genome was conducted for both owners (i.e., mother and daughter) and cat C All three samples were analyzed for the SARS-CoV-2. As the domestic epidemic GH type (B.1.497 lineage, PANGOLIN v.2.3.2), the genomes of the daughter and the cat were 100% identical, and the genomes of the daughter and her mother showed one single nucleotide difference (silent mutant) (Table 2). Five people—two cat rescuers, two people who took the samples, and one caregiver who came into contact with cat C without wearing appropriate protective equipment—were monitored once daily for 14 days from the date of the last contact. None of the five exposed individuals experienced any particular symptoms during this period. In addition, RT-qPCR tests conducted on day 5 (i.e., January 24, 2021) and day 13 (i.e., February 2, 2021) all had negative results.

#### 4. Discussion

In this study, we demonstrated that COVID-19 can be transmitted from humans to animals under certain conditions by analyzing the spread in transmission during the outbreak of COVID-19 among 120 interconnected residents, visitors, and individuals who came into contact with them. The infections had originated from religious facility A. Consistent with previous studies, droplet transmission was assumed, based on the site and environmental investigations [3]. As a result of risk assessment, the highest risk was identified in the chapel, and the results of the environmental samples were also high with a significant difference at the front of the chapel, where numerous droplets spread due to praying aloud (i.e., praying together). Based on the regulations of religious facility A, which encouraged participation in worship and

Table 1

The clinical and epidemiological characteristics of the owners (i.e., mother and daughter) and cats A, B, and C.

	Sex/	Symptom	Exposure history	Rt-pcr result			
	Age (y)			Date of sample collection: January 10, 2021			
Owner (mother)				Positive (RdRp (Ct) is 20.14 and E (Ct) is 21.41)			
Owner (daughter)	F/21	Asymptomatic	Resided in the religious facility A since August 2020 No outside entry	Positive (RdRp (Ct) is 18.74 and E (Ct) is 19.53)			
	Sex/ Age (y)	Symptom	Exposure history	Date of sample collection: January 20, 2021	Date of sample collection: January 23, 2021	Date of sample collection: February 3, 2021	
Cat A (mother cat)	F/??	Asymptomatic	Resided in the residence of the owners (mother and daughter) of religious facility A. Environmental sample testing result (the doorknob of the owners' residence): RdRp (Ct) is 27.86 and E (Ct) is 28.39	N: negative OP: negative Back (fur): negative Forepaw: negative	N: negative OP: negative Rectal: negative Stool: negative (1/ 23)/Negative (1/25)	None	
Cat B (kitten)	M/3 mo	Loose stool and bloody stool		N: negative OP: negative Back (fur): negative Forepaw: negative	N: negative OP: negative Rectal: negative Stool: negative (1/ 23)/negative (1/25)	N: negative OP: negative Stool: negative	
Cat C (kitten)	M/3 mo	Loose stool		N: negative OP: positive 1st: RdRp (Ct) is 24.53 E (Ct) is 25.27 2nd: RdRp (Ct) is 25.57 E (Ct) is 26.23 Back (fur): negative Forepaw: negative	N: negative OP: negative Rectal: negative Stool: negative (1/ 23)/negative (1/25)	N: negative OP: negative Stool: negative	

N: nasal; OP: oropharynx.

#### Table 2

The comparison of SARS-CoV-2 genomes of the owners (i.e., mother and daughter) and cat C.

Sample	Gene/Nucleotide	Total reads	Mapped reads	Consensus	Depth of coverage	Genome coverage (%)	SRA number
Owner (mother)	ORF1ab/C2881A	819,022	796,669	29,674	3996	99.2%	SRR13994120
Owner (daughter)	ORF1ab/C2881	846,846	820,676	29,844	4117	99.8%	SRR13994119
Cat C	ORF1ab/C2881	893,414	826,308	29,283	4145	97.9%	SRR13994121

restricted conversations and meetings in spaces other than the chapel, most of the transmission to residents and visitors presumedly occurred in the chapel.

The main transmission route into the community and society was through household contacts, and the proportion of people who did not cause the spread was higher than the proportion of people who caused the spread, which was consistent with the findings of previous studies [4,18–20]. Transmission spread to an average of 1.88 individuals, and another outbreak occurred concerning the outbreak from the religious facility A.

Therefore, to control the spread of COVID-19 outbreaks, the following procedures should be followed. First, if the source of infection is unclear when the first confirmed case occurs, the case must be investigated in association with a group outbreak. Second, if the transmission is confirmed, then contact tracing from the confirmed patient should be conducted more proactively, while keeping in mind the potential that another transmission may have occurred [20,21].

In this case, the virus was confirmed to be transmitted from human to animal through close contact in a specific environment—similar to human-to-human asymptomatic transmission. Therefore, an asymptomatic transmission is possible from humans to animals (i.e., domestic pets such as cats) [22–24]. The exact period of transmission from the owners to the cats is unknown, but the fact that viral shedding stopped within 3 days after the initial positive confirmation (on day 10 after separation from the owners [i.e., mother and daughter]) is similar to the results of previous studies [25,26]. Moreover, samples from the back (i. e., fur) and forepaws of the cats were collected and tested while considering the overall environmental contamination of religious facility A during the initial examination; however, all samples had negative test results.

The oropharynx in cats, unlike the oropharynx in dogs, primarily tests positive, and the possibility of cat-to-cat transmission rather than dog-to-dog transmission may be related to grooming, a characteristic of Felidae, which requires further research [25,27-29]. We observed infected cats, cats, and humans who were exposed to the virus for 14 days. We also conducted additional tests. However, no further transmission from cat to cat or cat to human occurred. However, if a specific environment exists (e.g., a group outbreak, close contact, environmental contamination), the transmission may occur from cat to human, similar to the case of the mink farms group outbreak [10,30]. Therefore, management measures to prevent and monitor the transmission from animals to humans will also be needed [15,16]. In addition, because cat-tocat transmission is possible, as evident in previous cases, it is also necessary to isolate and manage cats confirmed to have the virus or cats that have been exposed to the virus to prevent incidents such as those of the mink farms [9,26].

There are several limitations to our epidemic investigation and

research. First, the exact chain of infection is unknown because the source of infection of the outbreak and the exact route of transmission were not identified. Second, error due to limitations in tracing exposed individuals may exist because the research relied on investigation and personal memories and statements. Third, the sample from the cat that tested positive could not be verified as a viable virus through viral culture. Fourth, whether the infection of the cat that tested positive was a true infection was not possible to determine because an antibody test could not be conducted.

Consistent with of findings of previous studies, this case also provided grounds to state that SARS-CoV-2 is transmitted through close contact with household members or through group outbreaks, and that overall environmental contamination can occur in the process [3,4,24]. The findings also confirmed that COVID-19 can be transmitted from humans to animals under certain conditions such as close contact, outbreaks, and overall environmental contamination [9,26–30]. Therefore, monitoring and studying the transmission of COVID-19 between humans and animals is necessary, which will help track the origin of COVID-19 [31]. Lastly, as the contact between humans and animals gradually increases through methods such as raising domestic pets or livestock, a new infectious disease appearing post-COVID-19 that will emerge from human–animal interactions is highly possible [31,32]. Therefore, research on the emergence and the observation of new infectious diseases and zoonosis is needed, using the One Health Approach [31,32].

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# **Declaration of Competing Interest**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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# Appendix A. Appendix 1

The results of religious facility A risk assessments, which were conducted during both site and environmental investigations

Site	Risk factor	Assessment	Reason
Chapel	The degree of enclosure The degree of density The degree of continuity The degree of clustering	Moderate High High High	Ventilation is possible through windows and doors The distance between seats is $<1$ m Four times a day; stay for $>1$ h on average 144 Seats, 60–100 visitors in the visitors' book records (continued on next page)

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#### (continued)

Site	Risk factor	Assessment	Reason
	The degree of activities	High	Singing and shouting prayers
	The degree of management Overall risk	Low High	No mask; visitors' book record is inaccurate
	The degree of enclosure	Moderate	Ventilation is possible through windows and doors
	The degree of density	High	The distance between beds is $<1$ m; use of public toilets
	The degree of continuity	High	Accommodation facility, stay for $>1$ h on average
Accommodation (multi-person room)	The degree of clustering	Low	Less than 10 people
	The degree of activities	Moderate	Casual conversation
	The degree of management	Low	No mask; no sanitary facilities, except for toilets
	Overall risk	Moderate	
	The degree of enclosure	Moderate	Ventilation is possible through windows and doors
	The degree of density	High	Face-to-face placement; no protective film; the distance between seats is <1 m
	The degree of continuity	Moderate	Stay for <1 h on average
Dining area	The degree of clustering	Moderate	Up to 60 people, separated into two spaces
-	The degree of activities	Low	The notice of "no conversation"
	The degree of management	Low	No visitors' book record; no sanitary facility
	Overall risk	Moderate	·

The degree of enclosure: possibility of nature ventilation; the degree of density: social distancing status; the degree of continuity: average length of stay; the degree of clustering: number of people using at the same time; the degree of activities: amount of droplet occurrence; the degree of management: compliance with quarantine rules, which was evaluated by field epidemiologic intelligence service.

#### Appendix B. Appendix 2

Environmental samples and results of reverse transcriptase PCR conducted during site/field and environmental investigation on January 11, 2021

Environmental sample	RdRp (ct value)	E (ct value)
Chapel (front)		
Doorknob of the room	29.33	30.33
Main pulpit (surface)	23.81	24.57
Mike (rt and lt)*	27.54	28.31
Subpulpit (surface)	25.88	26.56
Chair in the chapel (front)	29.34	29.99
Doorknob of the prayer room	26.79	27.65
Average ct value	27.18	27.96
Chapel (back)		
Donation table	29.40	30.09
Air conditioner	30.20	31.70
Water purifier (surface)	32.97	34.75
Water purifier (inlet)	32.12	33.51
Circuit breaker button	31.97	32.32
Ventilation shaft	28.77	29.56
Average ct value	30.91	31.99
Living space (dining area and accommodation)		
Doorknob of the women's multiperson room	28.07	28.73
Doorknob of the cat owners residence	27.86	28.39
Dressing table of the women's multiperson room	33.61	33.23
Washbasin faucet of the women's multiperson room	27.03	27.92
Chair in the dining area	30.03	30.87
Food stand	33.76	33.70
Average ct value	30.06	30.48
P-value (<0.05)	0.03	0.02

ANOVA: analysis of variance; Ct: cycle threshold; mike: microphone; PCR: polymerase chain reaction.

<sup>\*</sup> The mike (Rt and Lt) RdRp is the average value of mike(Rt) RdRp:26.87 and mike(Lt) RdRp:28.21, The mike (Rt and Lt) E is mike(Rt) E:27.68 and mike(Lt) E:28.93. Statistical analysis/validation was conducted using one-way ANOVA.

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