Response System for and Epidemiological Features of COVID-19 in Gyeongsangnamdo Province in South Korea

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**Summary:** A response system that enabled the early detection of COVID-19 cases, including asymptomatic and pre-symptomatic cases, and the timely quarantine of these patients and their contacts was the key to curbing disease transmission in Gyeongsangnam-do Province in South Korea.

#### Abstract

**Background:** The South Korean government has been combating COVID-19 outbreak using public information and extensive viral screening. We described the application of the Korean response system in one province and outlined the epidemiological features of COVID-19 in the cohort.

**Methods:** A Rapid Response Team tracked the patients' activities and identified close contacts. A Patient Management Team made decisions regarding the severity of illness, hospital allocation depending on severity, and time of discharge. A national medical center with 155 beds and 4 university-affiliated hospitals with 48 negative-pressure isolation rooms were dedicated for COVID-19 patients.

**Results:** As of April 15, 17 400 residents were tested, of whom 111 were confirmed positive cases. Of the 111 patients, 78 were cured and discharged, 2 recovered after mechanical ventilation, and none died. One healthcare worker at the national center tested positive for SARS-CoV-2. All 412 staff members at the center were tested, but there were no additional infections. Cough (30.0 %) was the most common initial symptom, whereas anosmia and ageusia were the first symptoms in 14.7% and 15.7% of the patients, respectively. Overall, 25 patients (22.5%) reported having no symptoms at admission and 7 (6.3%) remained asymptomatic at discharge.

**Conclusions:** A response system that enabled the early detection of COVID-19 cases, including asymptomatic and pre-symptomatic cases, and timely quarantine of these patients and their contacts, along with efficient allocation of medical resources, was the key to curbing the COVID-19 outbreak in Gyeongsangnam-do Province.

Keywords: COVID-19, Response Team, Asymptomatic patients, Anosmia, Ageusia

#### Introduction

In December 2019, unexplained pneumonia was first reported in Wuhan, China, and on January 7, 2020, the Chinese government officially announced that the pneumonia was caused by the new severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1]. The World Health Organization on March 11 declared the outbreak of coronavirus disease 2019 (COVID-19) a global pandemic. As of April 15, SARS-CoV-2, the etiological agent of COVID-19, was reported to have infected nearly 2 million people in 213 countries, resulting in more than 123 000 deaths [2].

The first confirmed case of COVID-19 in South Korea was announced on January 20. As of April 15, a total of 534 552 residents had been tested, of whom 10 591 were confirmed positive cases and 225 died [3]. While many countries imposed lockdowns and closed their borders to combat COVID-19, South Korea adopted extensive viral screening of the population for patient discovery, isolation of infected people, and quarantine of their close contacts identified through contact tracing [4,5]. We evaluated the application of the Korean response system in one province and analyzed the epidemiological features of COVID-19 in the cohort.

# Methods

## **Response system of Gyeongsangnam-do Province**

Gyeongsangnam-do Province has a population of approximately 3.5 million (as of December 31, 2019). On January 24, a few days after the first travel-associated case of COVID-19 was reported in South Korea, 20 local public health centers and 16 hospitals were designated to screen people for COVID-19. All screening centers were installed outside the medical buildings and followed a tent, container, or drive-through model with a patient flow that did

not overlap with the movement of the general patient population. All patients who had visited the epidemic area, regardless of the presence or absence of respiratory symptoms or fever, were screened at the screening centers. On February 20, the first two cases were confirmed in Gyeongsangnam-do Province. The province's Rapid Response Team (RRT) and Patient Management Team (PMT) were organized according to the Korean government's policy [6]. The RRT investigated each case to determine the patient's recent activities and identify people they have had contact with by interviewing patients, examining medical facility records, tracking mobile phone or credit card data, and checking CCTV footage from 1 day before the appearance of symptoms (2 days since April 2). Any enclosed space that the patient was known to have visited was closed and disinfected and then reopened a day later. The information on a patient's activities was uploaded on the province's website and disseminated through phone alerts to allow other people to determine whether they may have crossed paths with the confirmed patient. Contact persons identified through contact tracing and voluntary notifications were asked to self-isolate at home for 2 weeks, with their COVID-19 symptoms monitored every day. If a contact did not develop any COVID-19 symptoms, he/she was released on the 14<sup>th</sup> day from the last date of contact with the confirmed patient. However, medical workers (including caregivers), residents or staff members of living facilities, students and staff at schools, household contacts, and contacts over the age of 65 were examined on the 13<sup>th</sup> day from the last date of contact and released on the 14<sup>th</sup> day if they tested negative. The province's governor or spokesperson provided COVID-19-related updates through the media and website twice a day (Table 1).

#### Patient care in Gyeongsangnam-do Province

Masan Medical Center (MMC), a national healthcare facility with 155 beds in the province, was prepared for patients with mild to moderate COVID-19 and 4 university-affiliated hospitals with 48 negative-pressure isolation rooms were prepared for patients with severe COVID-19. Infectious disease specialists were dispatched from a university hospital to MMC. All confirmed patients were admitted to MMC or one of the four hospitals according to their severity. Those who were symptom-free and tested negative twice were released. The PMT, consisting of provincial health officers and infectious disease specialists from each hospital, determined a confirmed patient's severity and decided hospital allocation depending on severity. The team shared patients' clinical information 24 hours a day with KakaoTalk (Korean instant messenger service) and reallocated patients from the dedicated national center to one of the four hospitals or vice versa when there was a change in the patients' condition. Patients with impaired consciousness, hypotension, and a respiratory rate of  $\geq$ 25/minute and requiring an O<sub>2</sub> mask to maintain a SpO<sub>2</sub> of  $\geq$  95% were considered as serious patients and transferred to one of the four hospitals as directed by the PMT. An improved patient was transferred back to MMC to free up the negative-pressure isolation rooms for other more serious patients. PMT also decided the discharge date of a patient.

In consultation with the PMT, the MMC formulated detailed plans for safe and effective care of COVID-19 patients (Table 2). All medical personnel could don and doff the personal protective equipment (PPE) in a designated space, enter the ward using a fixed route, and exit after showering. Symptomatic staff could return to work only after testing negative for COVID-19. Although the principle was to allocate 1 room per person, more than 2 patients were allowed to enter the same room when they could maintain a distance of at least 2 meters from each other. On the day of hospitalization, patients underwent portable chest radiography, while additional blood tests were performed for those with fever, underlying comorbidity, or confirmed pneumonia on chest radiographs. These patients were administered medications such as lopinavir/ritonavir or hydroxychloroquine according to MMC's treatment guidelines.

#### Patient data collection

We included a total of 111 patients with confirmed COVID-19 to evaluate the epidemiological and clinical characteristics of the COVID-19 outbreak in Gyeongsangnamdo Province until April 15. A confirmed case of COVID-19 was defined as a positive result on a reverse transcriptase polymerase chain reaction (RT-PCR) assay of SARS-CoV-2 in nasopharyngeal or oropharyngeal swab specimens. Sputum was also collected for the test if possible. Demographic data, information on underlying co-morbidities, clinical features, and laboratory and radiological findings were collected at presentation. Therapeutic data and outcomes were also obtained during admission. The diagnosis of pneumonia was based on radiographic evidence. Patient data was censored at the time of data cutoff, which occurred on April 15, 2020. The Samsung Changwon Hospital's institutional review board approved this study with an authorization agreement from MMC.

### Statistical analysis

Discrete data were presented as frequencies and percentages, and continuous variables were summarized as the mean ± standard deviation or the median and interquartile range after the normality of data was tested using the Shapiro–Wilk normality test. All analyses were conducted with SPSS Statistics 23.0 for Windows (SPSS Inc., Chicago, IL).

### Results

### Epidemiological characteristics of COVID-19 outbreak in South Gyeongsang Province

As of April 15, 2020, a total of 17 400 residents had been tested, of whom 111 patients were confirmed positive cases: 70 cases were related to travel to Daegu-si or Gyeongsangbuk-do Province, 24 to local outbreaks, 15 to overseas travel, and 2 to travel to Busan-si (Figure 1) [4]. Of the 111 patients, 78 were cured and discharged and 2 patients recovered after undergoing mechanical ventilation; there were no casualties. As of April 15, the province's preliminary case fatality rate was 0% [5]. The oropharyngeal or nasopharyngeal swab test for SARS-CoV-2 became positive again in 3 patients who had been discharged after two consecutively negative results (7, 15, and 16 in Figure 1[B]). On April 2, a healthcare worker at MMC tested positive for SARS-CoV-2. Subsequently, all of the 412 healthcare workers, including 9 contacts were tested for COVID-19, but no additional case was documented (109 in Figure 1[B]). The healthcare worker's son (110 in Figure 1[B]) was the only confirmed patient among the people tested for COVID-19.

# **Clinical characteristics of COVID-19 patients**

The clinical characteristics of the 111 patients in Gyeongsangnam-do Province are provided in Table 3. The mean age of the patients was  $41.3 \pm 19.0$  years, and 51.4% were female. The most prevalent underlying disease was hypertension (18.9%), followed by diabetes (7.2%) and solid tumors (3.6%). Seventy-four patients (66.7%) had clear information regarding the specific date of exposure. The mean incubation period was  $6.5 \pm 4.3$  days (range 0–17). Five patients (7.5%) among patients who develop symptoms did not show symptoms until 14 days after infection. The mean interval from symptom onset to admission was  $5.3 \pm 5.4$  days (range 0–32). Cough (30.0%) was the most common initial symptom, followed by myalgia (26.1%). Only 25.2% of patients complained of fever, whereas anosmia and ageusia were the first symptoms in 14.7% and 15.7% of patients, respectively. A total of 25 patients (22.5%) reported having no symptoms at admission, of whom 18 patients developed symptoms after an average of  $2.6 \pm 1.9$  days (range 1–8), while the remaining 7 (6.3%) remained asymptomatic at discharge. Pneumonia developed 7.0 days after the onset of initial symptoms, on average, in 44.1% of the patients. On admission, lymphopenia (<1 500 mm<sup>3</sup>) was present in 52.2% of the patients, thrombocytopenia in 7.5%, and leukopenia in 25.4%. The mean duration of SARS-CoV-2 RNA detection was 24.0 ± 10.8 days (range 5–58) after symptom onset.

## Discussion

This study described the response system adopted by a South Korean province to control the COVID-19 outbreak and the epidemiological features of COVID-19 in the cohort. The response system, which included the RRT and PMT, and the efficient allocation of medical resources were the key to controlling the outbreak in Gyeongsangnam-do Province. The response system helped in the early detection and quarantine of confirmed patients and their contacts. It made it possible to identify even patients who were asymptomatic or in the early stages.

The Korean government has provided rapid, large-scale diagnostic tests to detect COVID-19 patients. As of April, a total of 5 diagnostic agents were provided fast-track approval, and the maximum daily testing capacity increased from 3 000 people in February to approximately 20 000 people in April [7]. In addition to these large-scale diagnostic tests, the strategy of tracking mobile phone and credit card data and using CCTV footage facilitated rapid and

effective contact tracing. This in turn enabled the RRT to quarantine confirmed patients and their contacts in a timely manner to avoid additional transmission, which could contribute to reducing the overall size of an outbreak or bringing it under control over a longer time period. The RRT also quarantined and disinfected the enclosed spaces that the patients had visited. Aerosols from infected persons may pose an inhalation threat in closed areas, particularly if the ventilation is poor. A recent study showed that experimentally produced aerosols containing SARS-CoV-2 virions remained infectious in tissue-culture assays, with only a slight reduction in infectivity during the 3-hour period of observation [8].

The early detection and quarantine of both confirmed patients and their contacts helped identify patients who were asymptomatic or in the early stages, which may have resulted in the lower case fatality rate. Of the 111 patients in Gyeongsangnam-do Province, only 2 patients had received intensive care and none had died as of April 15. In Chinese studies, the overall case fatality rate was 1.3%–2.3% [9-11]. However, the patient outcome differed markedly among geographic regions, highlighting the magnitude of the surge in cases and ease of access to hospitalization [9-11]. In our study, 66.7% of the patients were identified through the contact investigation or examination of the symptoms during self-isolation. A previous study have shown that asymptomatic carriers identified from close contacts were prone to be mildly ill during hospitalization [12]. In addition, the PMT's monitoring of information on patient severity on a daily basis prevented severely ill patients from awaiting hospitalization. Therefore, early identification of patients and appropriate access to medical care when infected is vital for improving chances of survival.

Detecting asymptomatic or early-stage patients allowed us to describe the natural history and diverse initial symptoms of the disease. COVID-19 can cause mild flu-like symptoms, including fever, cough, dyspnea, myalgia, and fatigue, whereas more serious forms can cause

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severe pneumonia, acute respiratory distress syndrome, septic shock, and organ failure, which can be fatal [9-11,13]. A study from 552 hospitals in 30 provinces of China covering 1 099 patients with laboratory-confirmed COVID-19 showed that the most common symptoms were fever (43.8% on admission and 88.7% during hospitalization) and cough (67.8%) [9]. In our study, cough (30.0%) and myalgia (26.1%) were the most common initial symptoms. Only 25.2% of patients complained of fever as an initial symptom of COVID-19. Intriguingly, anosmia and ageusia occurred as an initial symptom in 14.7% and 15.7% of patients, respectively. These findings are in line with the results of a previous cross-sectional survey on the prevalence of olfactory and taste disorders in COVID-19 patients [14]. In that study, 33.9% reported at least one taste or olfactory disorder and 18.6% both. In addition to anosmia and ageusia, one patient presented conjunctivitis in our study. A previous study reported that conjunctivitis developed in 0.8% of the study population [9]. Interestingly, our study found a higher proportion of patients requiring 14 days or more to develop symptoms (7.5%) than previous studies (1-5%) [9,11,15]. Therefore, additional research on mild cases is needed to understand the initial epidemiological characteristics of COVID-19 for early detection and quarantine to control onward transmission of COVID-19.

Notably, a total of 25 patients (22.5%) in our study reported having no symptoms at admission, of whom 18 patients developed symptoms after the mean duration of  $2.6 \pm 1.9$  days (range 1–8) and 7 patients (6.3%) remained asymptomatic until discharge. This finding is consistent with that of a previous study, in which 56% (n=27) of residents who tested positive reported having no symptoms at the time of diagnosis in a skilled nursing facility. Some of them (24/27) developed symptoms subsequently, and 17 of the 24 specimens had viable virus by culture 1 to 6 days before the development of symptoms [16]. Several studies have confirmed the high level of SARS-CoV-2 shedding in the upper respiratory tract even

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before symptom development [15,17]. Recent reports have also suggested that patients might be infectious 1 to 3 days before symptom onset and that up to 40–50% of cases may be attributable to transmission from asymptomatic or pre-symptomatic people [18,19]. Because asymptomatic cases would continue to contribute to transmission, symptom-based screening alone is not enough to control transmission in a COVID-19 outbreak as a high proportion of infectious cases would go undetected. In Gyeongsangnam-do Province, mass screening was performed in highly vulnerable facilities, such as nursing hospitals and nursing homes. These facilities restricted the entry of visitors and non-essential personnel and made it obligatory for all staff members, residents, and visitors to wear a facial mask. These response measures may have helped control onward transmission of COVID-19.

Interestingly, 3 recovered patients tested positive again using RT-PCR for SARS-CoV-2. These patients had been asymptomatic at first diagnosis and taken no medication. A computed tomography of the chest had been performed during previous admission and immediately after readmission, images of which did not report any abnormal finding. It remains uncertain whether recovered COVID-19 patients who test positive again using RT-PCR can transmit the infection to others through close contact. Investigations are underway to understand this aspect.

This study has several limitations. First, we described the demographic characteristics of the 111 COVID-19 patients, but we could not compare the characteristics with those of individuals who tested negative. Comparative research involving people with negative results is needed to obtain better information on the demographic characteristics of COVID-19 patients. Second, not all close contacts were confirmed to be negative for SARS-CoV-2 before their release from quarantine, which suggests that the strategy could have missed some asymptomatic infections among the contacts. For efficient use of the limited diagnostic

capacity, we focused on several groups, including high risk groups for mass outbreak, groups with high infection rate, and groups showing poor outcomes, such as medical workers (including caregivers), residents or staff members of living facilities, students and staff at schools, household contacts, and contacts over the age of 65. Finally, although our response system was used only as an auxiliary tool to rapidly track confirmed COVID-19 cases in compliance with legal provisions and limitations, the disclosure of a patient's whereabouts and activities for public benefit violate the patient's privacy. In South Korea, people have agreed that infectious disease information should be disclosed in a transparent and timely manner. Following the Middle East respiratory syndrome outbreak in 2015, the Korean government was legally allowed to collect mobile phone, credit card, and other data from patients to reconstruct their recent whereabouts [20]. This strategy has been continually modified, but it is still needed constant efforts to protect privacy. Whether South Korea's contact tracing strategy can be generalized to other locations worldwide would depend on their legal systems and public consensus.

The at-scale diagnostic capacity resulted in early detection and quarantine of confirmed patients and their contacts, and the efficient allocation of medical resources resulted in lower case fatality rates. This response system may have helped us identify asymptomatic or pre-symptomatic patients and control onward transmission of COVID-19. The government continued to advise people to wear masks at all times in public, wash their hands, avoid crowds and meetings, and maintain a 2-meter distance from each other. The response system implemented in Gyeongsangnam-do will be successful only with public cooperation.

# NOTES

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**Conflict of Interest:** None to declare

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Table 1. Response system of Gyeongsangnam-do Province			
Teams or Centers in charge	Members	Major roles	
Rapid Response Team	Province's health officers	Trace a patient's recent whereabouts and activities	
		Investigate patients' contacts	
		Quarantine and disinfect the enclosed spaces that the patients had visited	
Public Communication	Province's officers, Media	Disclose a patient's recent whereabouts and activities to the public through the	
Team		website or phone alerts system	
		Provide COVID-19-related updates through the media and website twice a day	
Local public health centers	20 local public health centers	Serve as COVID-19 screening centers	
	N XO	Control of contacts	
		Responsible for patient transfer	
Patient Management Team	Province's health officers,	Determination of patient's severity	
	Infectious disease	Hospital allocation depending on patient's severity	
	physicians, Attending	Hospital reallocation when there is a change in the patients' condition	
		1	

physicians (3 public medical	Decision on patient's discharge
institutions with 390 beds	
and 4 hospitals with 48	
negative-pressure isolation	
rooms)	
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Table 2. Detailed plans fo	or a dedicated national medical center
Team in charge	Major roles
Executives	Organize new teams and relocate staff for COVID-19 care
Facility Team	Review and adjust heating, ventilation, and air conditioning systems
	Divide area into clean and dirty zones by means of walls, partitions, or barriers
	Separate the paths for staff and patients with dedicated corridors and elevators
Education team	Train medical and non-medical personnel on donning and doffing personal protective equipment (PPE)
	Supervise medical staff members participating in patient's care regarding the wearing and removal of PPE
	Check medical staff for fever or respiratory symptoms before and after work
Patient admission team	Control a patient's path from ambulance to ward

Patient care team	Care for patients by telephone or in person
Patient management team (PMT)	Determine patient's severity and decide on patient's discharge in conjunction with central PMT daily
	Create and update guidelines
Supply team	Take stock of and supply PPE daily
Environmental cleaning team	Clean all hospital environment
	Handle quarantine waste
	cepted
	21

	Total (n=111)
Age, year	$41.3 \pm 19.0 \text{ (range 1-77)}$
Age $\geq 65$ years, n (%)	11 (9.9)
Female, $n(\%)$	57 (51.4)
Underlying diseases, n (%)	29 (26.1)
Hypertension	21 (18.9)
Diabetes	8 (7.2)
Solid tumor	4 (3.6)
Cerebrovascular diseases	2 (1.8)
Cardiovascular diseases	1 (0.9)
Chronic pulmonary diseases	1 (0.9)
Liver cirrhosis	1 (0.9)
BMI	$24.0 \pm 4.2$ (range 18.1–36.1)
Documented contact history, n (%)	74 (66.7)
Incubation period, days (n=66)	$6.5 \pm 4.3$ (range 0–17)
Time from symptom onset to admission, days	$5.3 \pm 5.4$ (range 0–32)
Initial presentation, n (%)	
Fever	28 (25.2)
Chill	13 (11.7)
Myalgia	29 (26.1)
Cough	40 (30.0)
Sputum	21 (18.9)
Dyspnea	2 (1.8)
Rhinorrhea	6 (5.4)
Nasal congestion	13 (11.7)
Sore throat	28 (25.2)
Chest pain	1 (0.9)
Nausea/vomiting	2 (1.9)
Diarrhea	5 (4.5)
Abdominal pain	2 (1.8)
Headache	6 (5.4)
Anosmia $(n = 102)$	15 (14.7)
Ageusia (n = $102$ )	16 (15.7)
Conjunctival congestion	1 (0.9)
Asymptomatic at diagnosis, n (%)	25 (22.5)
Time from diagnosis to symptom	$2.6 \pm 1.9$ (range 1-8)
development (n=18), days	-
Asymptomatic at discharge, n (%)	7 (6.3)
Laboratory finding at admission (n=67)	
WBC, /mm <sup>3</sup>	5475.2 ± 1897.1 (range 548–12220)
$WBC < 4000/mm^3$	17 (25.4)
Lymphocyte, /mm <sup>3</sup>	1584.7 ± 767.1 (range 245.0–4842.5)
Lymphocyte < 1500/mm3	35 (52.2)

Table 3. Characteristics of the patients with COVID-19

Neutrophil, /mm <sup>3</sup>	$3344.0 \pm 1761.2$ (range 266.9–10333.4)
Neutrophil < 1500/mm3	3 (4.5%)
Hemoglobin, g/dl	$13.9 \pm 1.8$ (range 10.4–18.1)
Platelet, 10 <sup>3</sup> /mm <sup>3</sup>	$215.5 \pm 64.3$ (range 67–413)
Platelet, $< 150000/\text{mm}^3$	5 (7.5)
CRP, mg/dL	$1.8 \pm 5.3$ (range 0–32.8)
AST, IU/L	$29.7 \pm 17.1$ (range 10–114)
ALT, IU/L	$29.4 \pm 27.4$ (range 7–184)
BUN, mg/dl	$12.6 \pm 4.9$ (range 6.5–37.3)
Creatinine, mg/dl	$0.8 \pm 0.2$ (range 0.25–1.24)
Pneumonia at admission, n (%)	21 (18.9)
Pneumonia at discharge, n (%)	49 (44.1)
Time from symptom onset to pneumonia,	7.0 ± 5.5 (1–32)
days (n=48)	
Oxygen support, n (%)	, j
Nasal O2	10 (9.0)
Mask O2	2 (1.8)
Noninvasive mechanical ventilation	1 (0.9)
Invasive mechanical ventilation*	1 (0.9)
ECMO*	1 (0.9)
Medication, n (%)	
Lopinavir/ritonavir or HCQ use	72 (64.8)
Lopinavir/ritonavir use	42 (37.8)
HCQ use	41 (36.9)
Azithromycin use	20 (18.0)
Antibiotics use	46 (41.4)
Steroid use	3 (2.7)
Camostat or Nafamostat use	19 (17.1)
Angiotensin II receptor blocker use	17 (15.3)
Time from symptom onset to	
Last PCR $(+)$ $(n=62)$	$24.0 \pm 10.8$ (range 5–58)
Last PCR (-) (n=100)	$24.4 \pm 10.8$ (range 5–60)

Note: ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; BMI, body mass index; BUN, Blood urea nitrogen; CRP, C-reactive protein; HCQ, Hydroxychloroquine; NEWS, National Early Warning Score; ECMO, Extracorporeal membrane oxygenation;

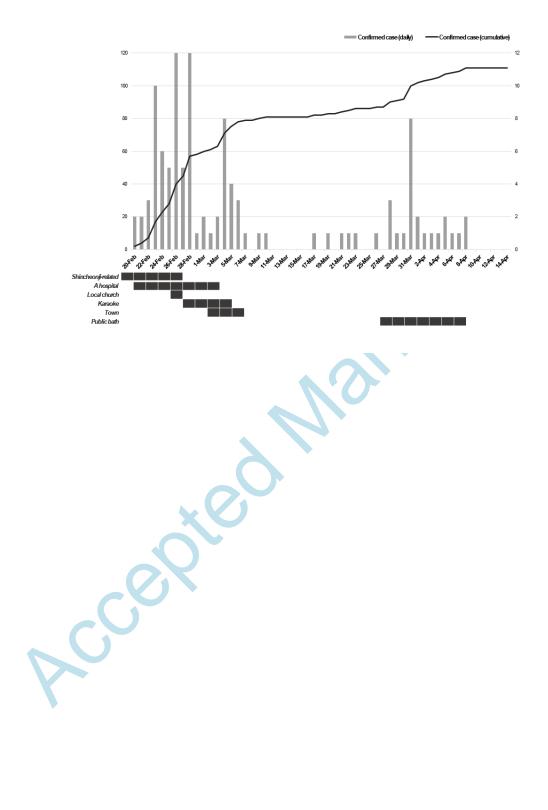
PCR, Polymerase Chain Reaction; WBC, White blood cells

\*One patient received both mechanical ventilation and ECMO

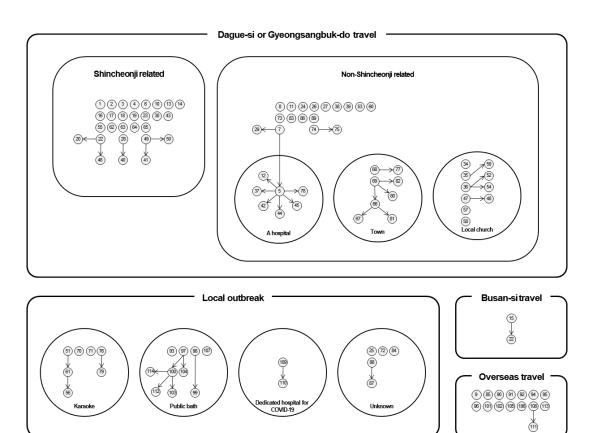
Figure 1. Epidemiological characteristics of COVID-19 outbreak in Gyeongsangnam-do Province (A) COVID-19 cases by date of diagnosis and (B) Transmission map of COVID-19 outbreak in Gyeongsangnam-do Province

Accepted Manuschi

Figure 1 A







Received