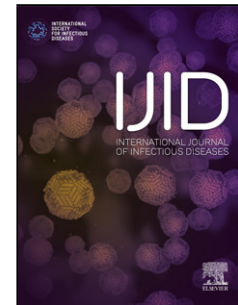


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Title: Transmission potential and severity of COVID-19 in South Korea

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Highlights:

- COVID-19 caused 6,284 cases and 42 deaths in South Korea as of March 8, 2020.
- The mean reproduction number R_t of COVID-19 in Korea was estimated at 1.5.
- The crude case fatality rate is higher among males and increases with age.
- Sustained disease transmission of COVID-19 in the region is indicated.
- Our estimates support the implementation of social distancing measures in Korea.

Abstract:

Objectives: Since the first case of 2019 novel coronavirus (COVID-19) identified on Jan 20, 2020 in South Korea, the number of cases rapidly increased, resulting in 6,284 cases including 42 deaths as of March 6, 2020. To examine the growth rate of the outbreak, we aimed to present the first study to report the reproduction number of COVID-19 in South Korea.

Methods: The daily confirmed cases of COVID-19 in South Korea were extracted from publicly available sources. By using the empirical reporting delay distribution and simulating the generalized growth model, we estimated the effective reproduction number based on the discretized probability distribution of the generation interval.

Results: We identified four major clusters and estimated the reproduction number at 1.5 (95% CI: 1.4-1.6). In addition, the intrinsic growth rate was estimated at 0.6 (95% CI: 0.6, 0.7) and the scaling of growth parameter was estimated at 0.8 (95% CI: 0.7, 0.8), indicating sub-exponential growth dynamics of COVID-19. The crude case fatality rate is higher among males (1.1%) compared to females (0.4%) and increases with older age.

Conclusions: Our results indicate early sustained transmission of COVID-19 in South Korea and support the implementation of social distancing measures to rapidly control the outbreak.

Keywords: coronavirus, COVID-19, Korea, reproduction number

Introduction

A novel coronavirus (SARS-CoV-2) that emerged out of the city of Wuhan, China in December 2019 has already demonstrated its potential to generate explosive outbreaks in confined settings and cross borders following human mobility patterns (Mizumoto et al., 2020). While COVID-19 frequently induces mild symptoms common to other respiratory infections, it has also exhibited an ability to generate severe disease among certain groups including older populations and individuals with underlying health issues such as cardiovascular disease and diabetes (Adler, 2020). Nevertheless, a clear picture of the epidemiology of this novel coronavirus is still being elucidated.

The number of cases of COVID-19 in the province of Hubei, the disease epicenter, quickly climbed following an exponential growth trend. The total number of COVID-19 cases is at 80,859 including 3,100 deaths in China as of March 8, 2020 (WHO, 2020). Fortunately, by February 15, 2020 the daily number of new reported cases in China started to decline across the country although Hubei Province reported 128 cases on average per day in the week of March 2-8, 2020 (WHO, 2020). While the epidemic continues to decline in China, 24,727 COVID-19 cases have been reported in more than 100 countries outside of China including South Korea, Italy, Iran, Japan, Germany, and France (WHO, 2020). In particular, South Korea quickly became one of the hardest hit countries with COVID-19, exhibiting a steadily increasing number of cases over the last few days. Hence, it is crucial to monitor the progression of these outbreaks and assess the effects of various public health measures including the social distancing measures in real time.

The first case in South Korea was identified on January 20, 2020 followed by the detection of one or two cases on average in the subsequent days. However, the number of confirmed cases of SARS-CoV-2 infection started to increase rapidly on February 19, 2020 with a total of 6,284 confirmed COVID-19 cases including 42 deaths reported as of March 6, 2020 according to the Korea Centers for Disease Control and Prevention (KCDC) (KCDC, 2020) (Table 1). The epicenter of the South Korean COVID-19 outbreak has been identified in Daegu, a city of 2.5 million people, approximately 150 miles South East of Seoul. The rapid spread of COVID-19 in South Korea has been attributed to one case linked to a superspreading event that has led to more than 3,900 secondary cases stemming from church services in the city of Daegu (Kuhn, 2020, Ryall, 2020). This has led to sustained transmission chains of COVID-

19, with 55% of the cases associated with the church cluster in Daegu (Bostock, 2020). Moreover, three other clusters have been reported including one set in Chundo Daenam hospital in Chungdo-gun, Gyeongsangbuk-do (118 cases), one set in the gym in Cheonan, Chungcheongnam-do (92 cases), and one Pilgrimage to Israel cluster in Gyeongsangbuk-do (49 cases). These few clusters have become the major driving force of the infection. A total of 33 cases were imported while the four major clusters are composed of local cases as described in Table 2.

Transmission of SARS-CoV-2 in Korea has been exacerbated by amplified transmission in confined settings including a hospital and a church in the city of Daegu. The hospital-based outbreak alone involves 118 individuals including 9 hospital staff (News, 2020), which is reminiscent of past outbreaks of SARS and MERS (Chowell et al., 2015). To respond to the mounting number of cases of COVID-19, the Korean government has raised the COVID-19 alert level to the highest (Level 4) on February 23, 2020 to facilitate the implementation of comprehensive social distancing measures including enhanced infection control measures in hospitals, restricting public transportation, cancelling social events, and delaying the start of school activities (Kim, 2020).

While the basic reproduction number, denoted by R_0 , applies at the outset of an exponentially growing epidemic in the context of an entirely susceptible population and in the absence of public health measures and behavior changes, the effective reproduction number (R_t) quantifies the time-dependent transmission potential. This key epidemiological parameter tracks the average number of secondary cases generated per case as the outbreak progresses over time. Steady values of R_t above 1 indicate sustained disease transmission, whereas values of $R_t < 1$ do not support sustained transmission and the number of new cases is expected to follow a declining trend. In this report, using a mathematical model parameterized with cases series of the COVID-19 outbreak in Korea, we investigate the transmission potential and severity of COVID-19 in Korea using early data of local and imported cases reported up until February 26, 2020.

Methods

Data

We obtained the daily series of confirmed cases of COVID-19 in South Korea from January 20, 2020 to February 26, 2020 that are publicly available from the Korea Centers for Disease Control and Prevention (KCDC) (KCDC, 2020). Our data includes the dates of reporting for all confirmed cases, the dates of symptom onsets for the first 28 reported cases, and whether the case is autochthonous (local transmission) or imported. We also summarize the case clusters comprising one or more cases according to the source of infection according to the field investigations conducted by the KCDC (KCDC, 2020).

Accordingly, four major clusters were identified. The total number of confirmed and suspected cases as of March 6, 2020 as well as the crude case and fatality rate distribution by gender and age are presented in Table 1.

Imputing the date of onset

To estimate the growth rate of the epidemic, it is ideal to characterize the epidemic curve according to dates of symptoms onset rather than according to dates of reporting. For the COVID-19 data in Korea, the symptom onset dates are available for only the first 28 reported cases. Moreover, all of the dates of symptoms onset are available for the imported cases. Therefore, we utilize this empirical distribution of reporting delays from the onset to diagnosis to impute the missing dates of onset for the remainder of the cases with missing data. For this purpose, we reconstruct 300 epidemic curves by dates of symptoms onset from which we derive a mean incidence curve of local case incidence and drop the last three data points from the analysis to adjust for reporting delays in our real-time analysis (Tariq et al., 2019).

Estimate of reproduction number from daily case incidence

We assess the effective reproduction number, R_t , which quantifies the time dependent variations in the average number of secondary cases generated per case during the course of an outbreak due to intrinsic factors (decline in susceptible individuals) and extrinsic factors (behavior changes, cultural factors, and the implementation of public health measures) (Anderson and May, 1991, Chowell et al., 2015, Nishiura et al., 2010). Using the Korean incidence curves for imported and local cases, we estimate the evolution of R_t for COVID-19 in Korea. First, we characterize daily local case incidence using the generalized growth model (GGM) (Viboud et al., 2016). This model characterizes the growth profile via two parameters: the growth rate parameter (r) and the scaling of the growth rate parameter (p). The model captures diverse epidemic profiles ranging from constant incidence ($p = 0$), sub-exponential or polynomial growth ($0 < p < 1$), and exponential growth ($p = 1$) (Viboud et al., 2016). The generation interval is assumed to follow a gamma distribution with a mean of 4.41 days and a standard deviation of 3.17 days (Nishiura et al., 2020, You et al., 2020).

Next, to estimate the most recent estimate of R_t , we simulate the progression of incident cases from GGM, and apply the discretized probability distribution (ρ_i) of the generation interval using the renewal equation (H. Nishiura, 2009, Nishiura and Chowell, 2014, Paine et al., 2010) given by

$$R_{t_i} = \frac{I_i}{\sum_{j=0}^i (I_{i-j} + \alpha J_{i-j}) \rho_j}.$$

In the renewal equation we denote the local incidence at calendar time t_i by I_i , and the raw incidence

of imported cases at calendar time t_i by J_i . The parameter $0 \leq \alpha \leq 1$ quantifies the relative contribution of imported cases to the secondary disease transmission (Nishiura and Roberts, 2010). The denominator represents the total number of cases that contribute to the incidence cases at time t_i . Next, we estimate R_t for 300 simulated curves assuming a Poisson error structure to derive the uncertainty bounds around the curve of R_t (Chowell, 2017).

Results

Reconstructed incidence of COVID-19

The reconstructed daily incidence curve of COVID-19 after the imputing the onset dates for the Korean cases is shown in Figure 1. Between January 20 and February 18, 2020 an average of 2 new cases were reported each day, whereas between February 19-26, 2020, 154 new cases were reported on average each day.

Effective reproduction number (R_t) from daily case incidence

Under the empirical reporting delay distribution from early Korean cases with available dates of onset, the intrinsic growth rate (r) was estimated at 0.6 (95% CI: 0.6, 0.7) and the scaling of growth parameter (p) was estimated at 0.8 (95% CI: 0.7, 0.8), indicating sub-exponential growth dynamics of COVID-19 in Korea (Figure 2, Table 3). The mean reproduction number R_t was estimated at 1.5 (95% CI: 1.4, 1.6) as of February 26, 2020. Our estimates of R_t are not sensitive to the changes to the parameter that modulates the contribution of the imported cases to transmission (α).

The crude case fatality rate

The crude case fatality rate is higher among males (1.1%) compared to females (0.4%) and increases with older age, from 0.1% among those 30-39 yrs to 6% among those ≥ 80 yrs as of March 6, 2020.

Transmission clusters

Spatial distribution of the Korean clusters is shown in Figure 3 and the characteristics of each cluster are presented in Table 2 as of March 8, 2020.

Shincheonji Church of Jesus cluster

As of March 8, 2020, 4,482 confirmed cases of COVID-19 are linked to this cluster, according to the KCDC (KCDC, 2020). This largest cluster is associated with Shincheonji Church of Jesus, with the first case (the 31st patient in the country) confirmed on Feb. 18. It is unclear how this case contracted the illness, as she does not present a recent history of travel or contact with another infected patient.

However, this case attended Shincheonji Church of Jesus in Daegu four times before and after becoming a symptomatic case of COVID-19, and visited the hospital in Cheongdo after a car accident. According to the KCDC, the patient had contact with 166 people mostly at Shincheonji Church and the hospital in Cheongdo, who now placed themselves into self-quarantine. The Shincheonji church of Jesus has temporarily closed its facilities and halted the church activities as of February 18, 2020.

Chungdo Daenam hospital cluster

This cluster comprised of 118 local cases and seven deaths is associated with Chungdo Daenam hospital, where South Korea's first coronavirus associated case fatality occurred. Of the 118 cases, 92 were confirmed on Feb 22, 2020 (KCDC, 2020). A 63-year-old man who died of pneumonia at the hospital on Feb 19 was posthumously tested positive for COVID-19. On Feb 21, another patient at Daenam Hospital died from COVID-19, followed by another death on Feb 23. The confirmed cases were mainly from psychiatric ward and includes nine medical staffs. The exact route of the infection is not yet known.

Cluster related to the gym in Cheonan

In the central cities of Cheonan, 92 COVID-19 patients were associated with to a Zumba dance class after an instructor became the 5th confirmer of Cheonan on February 25, 2020. According to the provincial government of South Chungcheong Province, everyone who attended the class in Cheonan was tested, and 27 cases were confirmed on February 28, 2020, with most of the cases being women in their 30's and 40's (KCDC, 2020). As of March 8, 2020, a total of 92 individuals were infected including Zumba instructors and students as well as their families and acquaintances (KCDC, 2020).

Pilgrimage tour to Israel related

This cluster is comprised of 49 cases as of March 8, 2020. This cluster was identified when 31 Catholic pilgrims visited Israel between February 8, 2020 and February 16, 2020 and were subsequently confirmed for COVID-19 (2020). Amongst these, 11 individuals were diagnosed on February 17, 2020, while 20 others were confirmed positive between February 21-25, 2020 and quarantined immediately. Of the 31 infected pilgrims, 19 belong to the Euseong County, North Gyeongsang Province, while one patient, a tour guide belongs to Seoul. Health authorities have traced multiple contacts from the cases of this cluster, and additional cases were confirmed thereafter, raising concerns about the potential risk of secondary infections.

Discussion

This is the first study to report estimates of the transmission potential of COVID-19 in Korea based on

the trajectory of the epidemic, which was reconstructed by using the dates of onset of the first reported cases in Korea. The estimates of R clearly indicate sustained transmission of the novel coronavirus in Korea and the case fatality rate appears to be higher among males and older populations (Table 1). Moreover, the imported cases contribute little to the secondary disease transmission in Korea, as majority of these cases occurred in the early phase of the epidemic, with the most recent imported case reported on February 9, 2020. These findings support the range of social distancing interventions that the Korean government put in place in order to bring the outbreak under control as soon as possible.

Our estimates of the reproduction number can be compared with earlier estimates reported for the epidemic in China where the estimates of R lie in the range 2-7.1 (Lai et al., 2020, Li et al., 2020, Mizumoto et al., 2020, Read et al., 2020, Special Expert Group for Control of the Epidemic of Novel Coronavirus Pneumonia of the Chinese Preventive Medicine, 2020, Wu et al., 2020, Zhang et al., 2020, Zhou et al., 2020). Moreover, the mean R reached values as high as ~ 11 for the outbreak that unfolded aboard the Princess Cruises Ship during January-February 2020 (Mizumoto and Chowell, 2020). In contrast, a recent study on Singapore's COVID-19 transmission dynamics reported lower estimates for R_t (1.1, 95% CI: 1.1, 1.3) as of February 19th, 2020, reflecting a significant impact of the control interventions that have been implemented in Singapore (Tariq et al., 2020). The estimates of the scaling of growth parameter (p) in our study indicate sub-exponential growth dynamics of COVID-19 in Korea. This aligns well with the sub-exponential growth patterns of COVID-19 in Singapore and all Chinese provinces except Hubei (Roosa et al., 2020, Tariq et al., 2020).

Since the first COVID-19 case was reported on January 20, 2020, the epidemic's trajectory showed a rapid upturn until February 18, 2020, when a super spreader (Case 31) was identified in the Shincheonji Church of Jesus in Daegu cluster. Since then, Korea's confirmed cases have risen tremendously. In fact, 55% of confirmed cases are linked to one cluster of infections, i.e. Shincheonji Church of Jesus in Daegu (KCDC, 2020). Such superspreading events have been reported earlier for the 2015 MERS outbreak in South Korea (Cowling et al., 2015). Amplification of MERS in the hospital setting has been associated with diagnostic delays, which increase the window of opportunity for the generation of secondary cases (Chowell et al., 2015). This underscores the need for rapid testing, case detection and active contact tracing to isolate infectious individuals.

Beyond Korea, substantial COVID-19 transmission has been reported in Italy, Iran, Germany, France, and aboard the Diamond cruise ship (Marcus, 2020, Woods, 2020). While the Chungdo Daenam hospital cluster and the cluster related to the Pilgrimage tour to Israel seem to have stabilized, the other two clusters are still being consolidated. Public health authorities are currently focused on containing

the outbreak in the city of Daegu, the epicenter of the outbreak and North Gyeongsang Province where active contact tracing is being conducted. Nation-wide preventative measures are expected to reduce the community transmission and ultimately bring R_t below one.

This is the first study to estimate the transmission potential and severity of COVID-19 in Korea. Our current findings suggest sustained disease transmission in the region, underscoring the need to implement a wide array of social distancing measures to rapidly contain the outbreak in Korea, mitigate the morbidity and mortality impact of the disease, and stem the number of case exportations to other nations.

Contributions: ES, AT and GC analyzed the data. YS and WC retrieved and managed the data. ES, AT, and GC wrote the first draft of the paper. All authors contributed to the writing of the paper.

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Ethical Approval: Not required.

Conflict of Interest Statement: None

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Figure 1: Reconstructed epidemic curve for the local Korean COVID-19 cases by the dates of onset as of February 26, 2020. The blue triangles represent the local cases, red triangles represent the imported cases and the gray curves correspond to the uncertainty in the local cases because of missing onset dates.

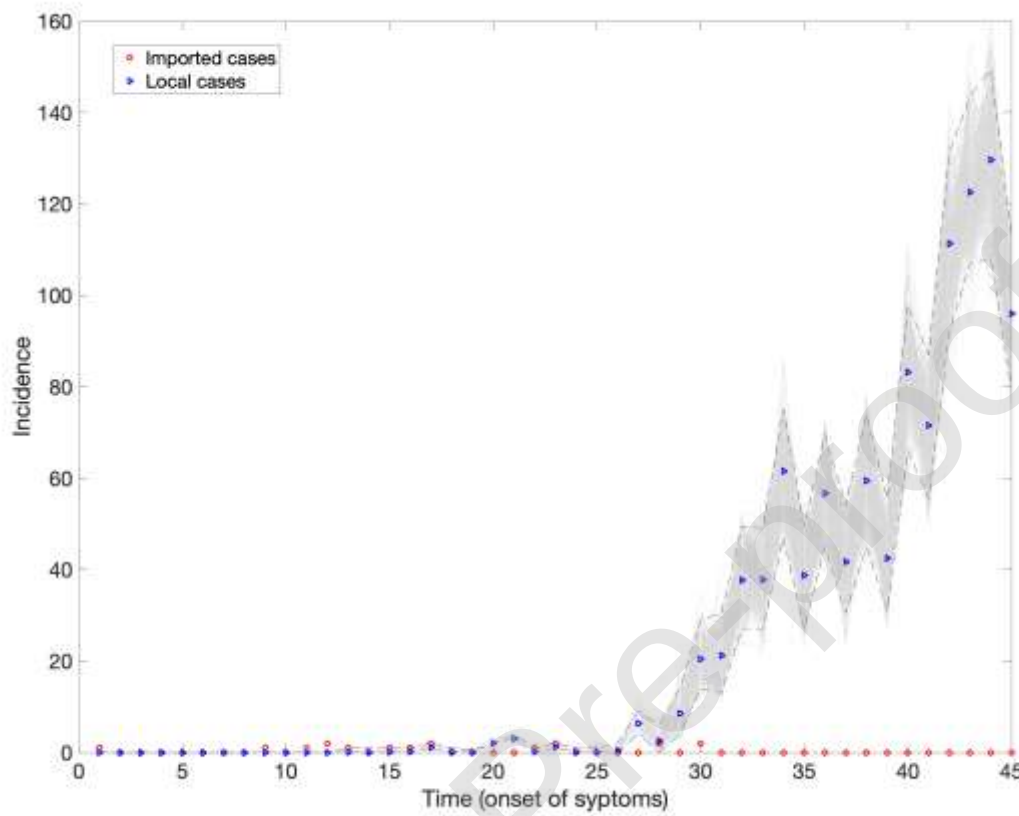


Figure 2: The mean reproduction number with 95% CI estimated by adjusting for the imported cases with $\alpha=0.15$. Estimates for growth rate (r) and the scaling of the growth rate parameter (p) are also provided. The plot at the bottom depicts the fit of the Generalized Growth Model to the Korean data assuming Poisson error structure as of February 26, 2020.

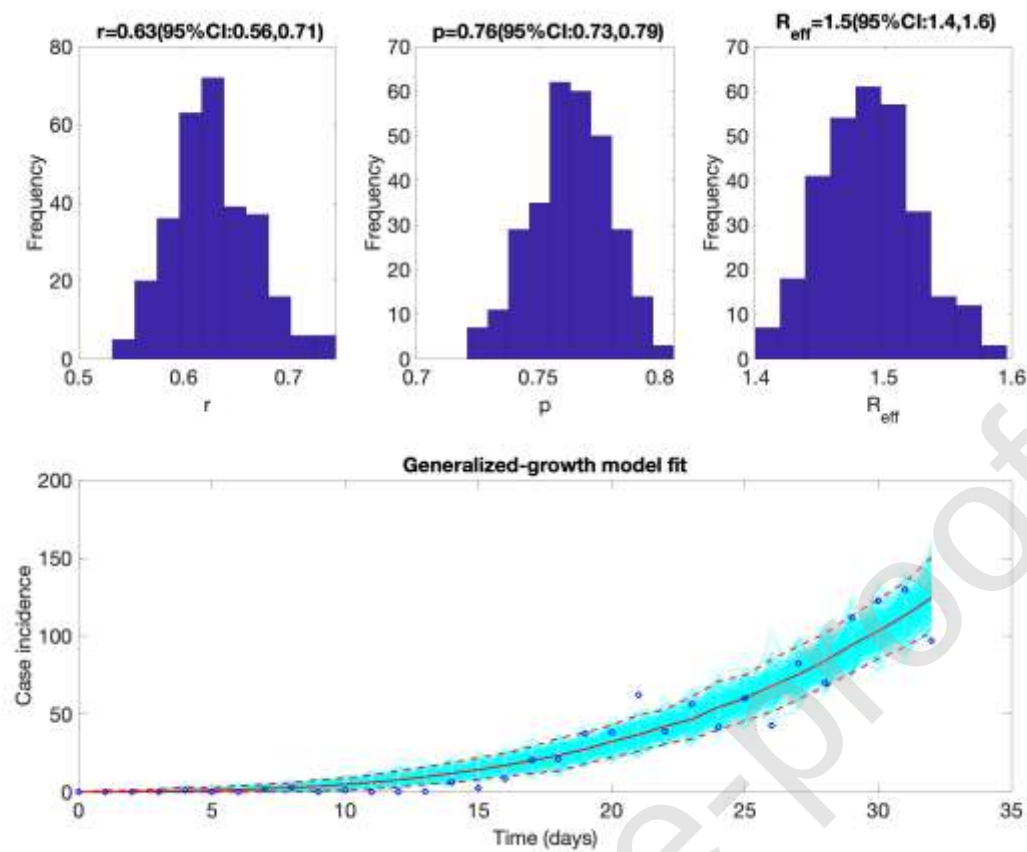


Figure 3: Map depicting the spatial distribution of the four largest clusters of COVID-19 in Korea as of March 8, 2020.

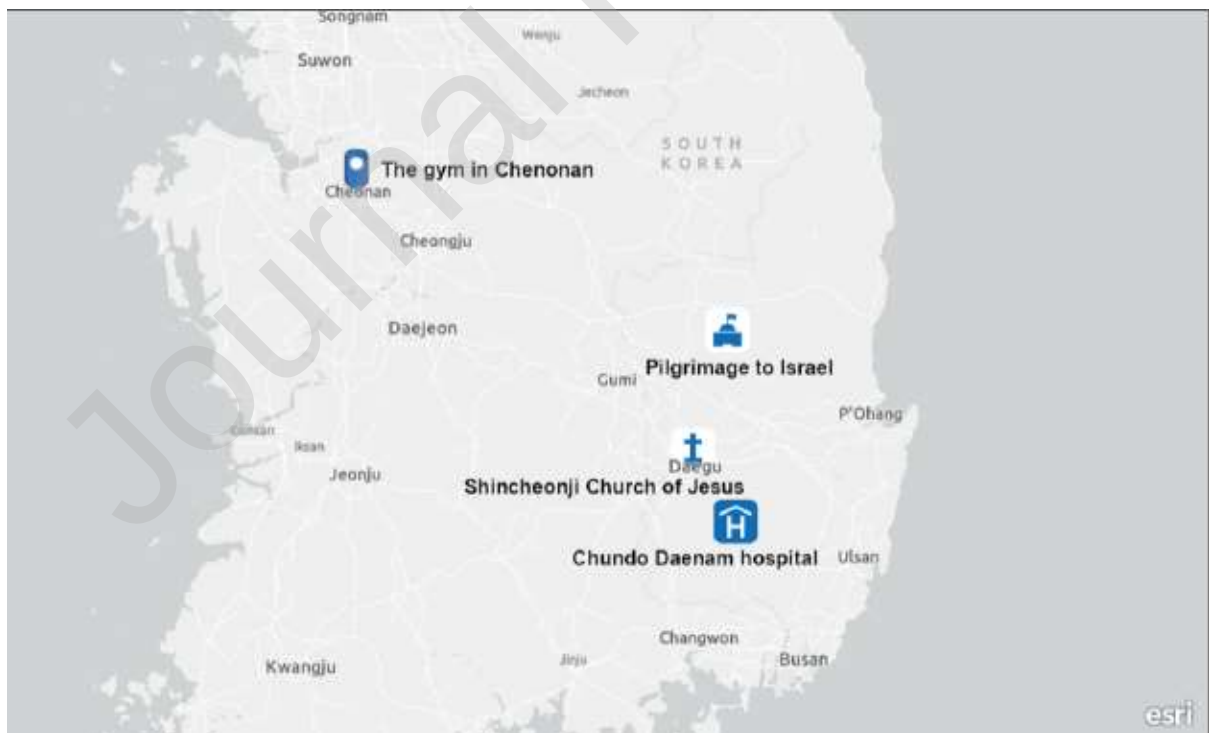


Table 1. The total number of confirmed and suspected cases as of March 6, 2020 as well as the case and fatality rate distribution by gender and age are presented (KCDC, 2020).

Total	Confirmed cases				Suspected cases		
	Subtotal	Discharged	isolated	Deceased	Subtotal	Being tested	Tested negative
164,740	6,284	108	6,134	42	158,456	21,832	136,624
Classification		Cases (%)		Deaths (%)		Fatality rate (%)	
Total		6,284 (100)		42 (100)		0.7	
Sex	Male	2,345 (37.3)		25 (59.5)		1.1	
	Female	3,939 (62.7)		17 (40.5)		0.4	
Age	0-9	45 (0.7)		-		-	
	10-19	292 (4.6)		-		-	
	20-29	1,877 (29.9)		-		-	
	30-39	693 (11.0)		1 (2.4)		0.1	
	40-49	889 (14.1)		1 (2.4)		0.1	
	50-59	1,217 (19.4)		5 (11.9)		0.4	
	60-69	763 (12.1)		11 (26.2)		1.4	
	70-79	340 (5.4)		14 (33.3)		4.1	
	Above 80	168 (2.7)		10 (23.8)		6.0	

Table 2. Characteristics of the largest COVID-19 clusters in South Korea as of March 8, 2020.

Cluster name	Cluster location	Cluster size	Reporting date for the first case linked to cluster	Reporting date for the last case linked to cluster
Shinchunji Church of Jesus	81, Daemyeong-ro, Nam-gu, Daegu, Republic of Korea	4482	2/18/2020	3/08/2020
Chundo Daenam hospital	79-7, Cheonghwa-ro, Hwayang-eup, Cheongdo-gun, Gyeongsangbuk-do, Republic of Korea	118	2/20/2020	2/29/2020
Cluster related to the gym in Cheonan	667, Dujeong-dong, Seobuk-gu, Cheonan-si, Chungcheongnam-do, Republic of Korea	92	2/25/2020	3/08/2020
Pilgrimage to Israel	31, Guncheong-gil, Uiseong-eup, Uiseong-gun, Gyeongsangbuk-do, Republic of Korea	49	2/22/2020	3/02/2020

Table 3: Mean estimates and the corresponding 95% confidence intervals for the effective reproduction number, growth rate and the scaling of growth parameter during the early growth phase as of February 26, 2020.

Parameters	Estimated values
Reproduction number	1.5 (95% CI:1.4,1.6)
Growth rate, r	0.6 (95% CI:0.6,0.7)
Scaling of growth parameter, p	0.8 (95% CI:0.7,0.8)