American Journal of Emergency Medicine 59 (2022) 1–8

Contents lists available at ScienceDirect

American Journal of Emergency Medicine

journal homepage: www.elsevier.com/locate/ajem

Unintended beneficial effects of COVID-19 on influenza-associated emergency department use in Korea

Sola Kim, MD, PhD [a,b], Ju Ok Park, MD, PhD [a,b,*], Hye Ah. Lee, PhD [c], Hang A. Park, MD [a,b], Choung Ah. Lee, MD, PhD [a,b], Soon-Joo Wang, MD, PhD [a,b], Eun Ju Jung, MD [d]

[a] Department of Emergency Medicine, Hallym University Dongtan Sacred Heart Hospital, Hwaseong, Republic of Korea
[b] Department of Emergency Medicine, Hallym University College of Medicine, Chuncheon, Republic of Korea
[c] Clinical Trial Center, Ewha Womans University Mokdong Hospital, Seoul, Republic of Korea
[d] Division of Infectious Diseases, Department of Internal Medicine, Hallym University Dongtan Sacred Heart Hospital, Hwaseong, Republic of Korea

ARTICLE INFO

Article history:
Received 18 January 2022
Received in revised form 5 June 2022
Accepted 21 June 2022

Keywords:
COVID-19
SARS-CoV-2
Influenza
Communicable disease control

ABSTRACT

Background: Non-pharmaceutical interventions, including hand hygiene, wearing masks, and cough etiquette, and public health measures such as social distancing, used to prevent the spread of coronavirus disease 2019 (COVID-19), could reduce the incidence rate of respiratory viral infections such as influenza. We evaluated the effect of COVID-19 on the incidence of influenza in Korea.

Methods: This retrospective study included all patients who visited five urban emergency departments (EDs) during the influenza epidemic seasons of 2017–18, 2018–19, and 2019–20. Influenza was defined as ICD-10 codes J09, J10, and J11, determined from ED discharge records. The weekly incidence rates of influenza per 1000 ED visits during the 2019–20 season, when COVID-19 became a pandemic, were compared with those of 2017–18 and 2018–19. The actual incidence rate of the 2019–20 season was compared with the predicted value using a generalized estimation equation model based on 2017–18 and 2018–19 data.

Results: The weekly influenza incidence rate decreased from 101.6 to 56.6 between week 4 and week 5 in 2020 when the first COVID-19 patient was diagnosed and public health measures were implemented. The weekly incidence rate during week 10 and week 22 of the 2019–20 season decreased most steeply compared to 2017–18 and 2018–19. The actual influenza incidence rate observed in the 2019–20 season was lower than the rate predicted in the 2017–18 and 2018–19 seasons starting from week 7 when a COVID-19 outbreak occurred in Korea.

Conclusions: The implementation of non-pharmaceutical interventions and public health measures for the COVID-19 epidemic effectively reduced the transmission of influenza and associated ED use in Korea. Implementing appropriate public health measures could reduce outbreaks and lessen the burden of influenza during future influenza epidemics.

1. Introduction

The outbreak of coronavirus disease-2019 (COVID-19), which was caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), was reported in Wuhan, China in December 2019, and the first confirmed patient in the Republic of Korea was reported on January 20, 2020 [1-3]. After this first case, the Korea Disease Control and Prevention Agency (KDCA) raised the alert level of the infectious disease crisis from "blue" to "yellow" as more COVID-19 patients were identified, including recommendations that people should wear face masks and practice hand hygiene (Fig. 1) [4]. When there was an outbreak in Daegu metropolitan city, the KDCA raised the infectious disease crisis warning to "red" on February 24, 2020, and began to implement social distancing in public [5,6]. These non-pharmaceutical interventions (NPIs) and public health measures were aimed at preventing the spread of COVID-19 through respiratory droplets. Along with behavioral changes following NPIs and public health measures recommended by the KDCA in the population, these measures were expected to influence the outbreak of other diseases caused by respiratory viruses [7-9].

Abbreviation: COVID-19, coronavirus disease 2019; ED, emergency department; ILI, influenza-like illness; KDCA, Korea Disease Control and Prevention Agency; NDIs, non-pharmaceutical interventions; SARS-CoV-2, severe acute respiratory syndrome coronavirus-2.

* Corresponding author at: 7, Keunjaebong-gil, Hwaseong-si, Gyeonggi-do 18450, Republic of Korea.
E-mail address: juokpark@hallym.ac.kr (J.O. Park).

https://doi.org/10.1016/j.ajem.2022.06.039
0735-6757/

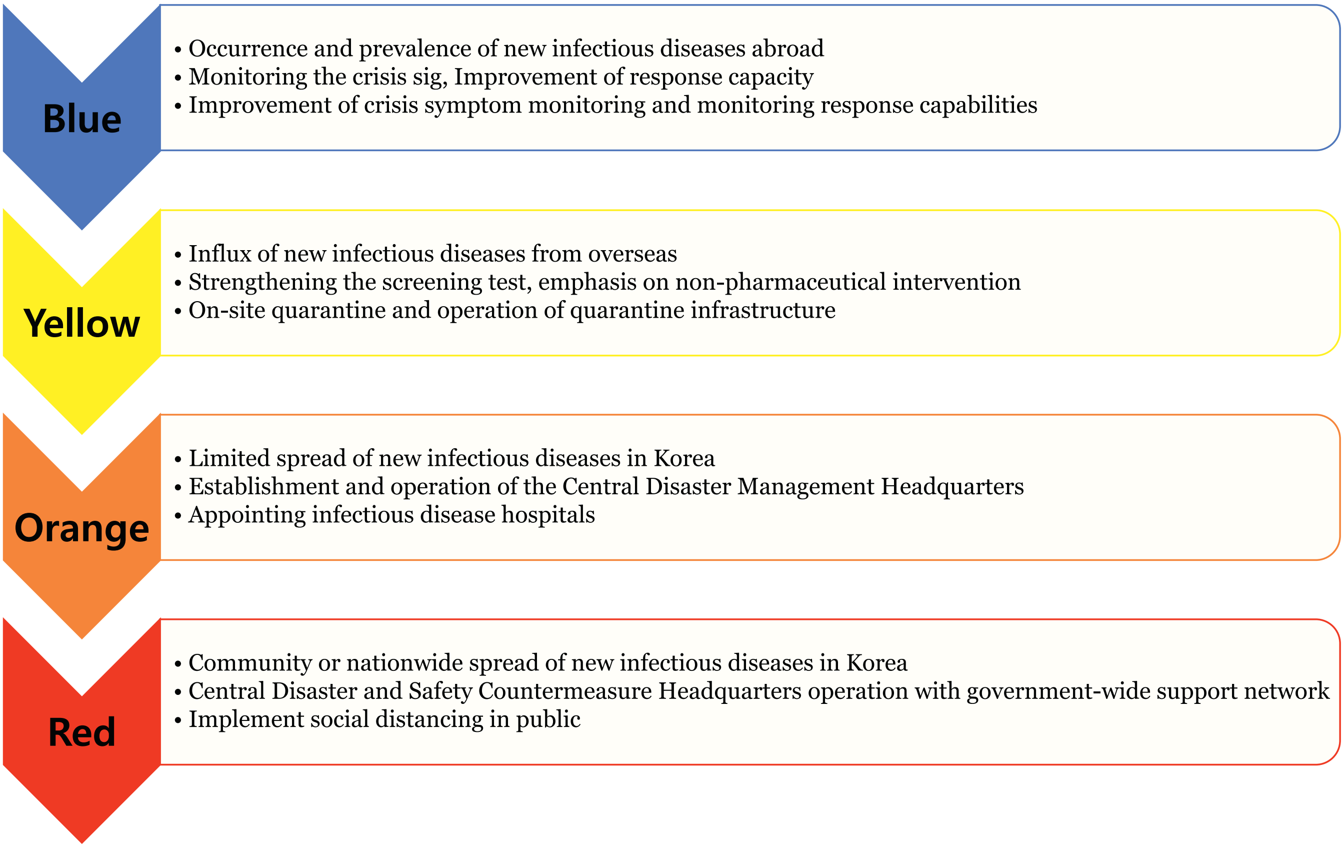

Fig. 1. Alert level of the infectious disease crisis by the Korea Disease Control and Prevention Agency.

Influenza is caused by a respiratory virus that spreads through droplet-based transmission and is highly contagious and prevalent in winter [10]. Influenza is associated with a high mortality rate owing to complications such as pneumonia in high-risk groups including elderly patients aged ≥65 years, pregnant women, and immunosuppressed patients [11-13]. It is estimated that 3–5 million people have a severe influenza infection each year, and 25–50 million people have died from influenza worldwide [14]. In Korea, it is estimated that >23,000 people are hospitalized and >1200 people die from influenza per year [15]. To reduce the burden due to influenza, it is important to establish active prevention policies and infection control measures. NPIs such as hand hygiene, cough etiquette, and use of masks are known to lower the risk of acquiring influenza infection, as well as to delay and reduce the peak of the epidemic [16,17].

Before COVID-19, even though public health agencies had invested physically and financially in promoting NPIs for controlling influenza epidemics, they were not considered mandatory nor widely accepted. However, during the COVID-19 pandemic, the KDCA has mandated mask use and social distancing behaviors, such as closing schools and suspension of mass gathering events. The majority of people implemented NPIs and maintained social distancing. We considered that such a large-scale behavioral change occurring in society could have an unintended effect on other respiratory infectious diseases, such as influenza. Influenza surveillance systems based in primary clinics can monitor influenza-like illnesses (ILIs) but usually do not include severe patients. Meanwhile, influenza surveillance based in the emergency department (ED), which includes severe patients, could be more objective due to the use of diagnostic tests.

We aimed to analyze the beneficial effects of the COVID-19 pandemic related increase in NPIs and public health measures on the incidence of influenza using data from EDs in selected Korean hospitals.

2. Materials and methods

2.1. Study setting and design

This retrospective observational study was conducted in the EDs of five urban teaching hospitals in Korea. The study was approved by the institutional review board of our institution, and the need for informed consent was waived because of the retrospective design of the study (IRB number: 2020–05-017).

The annual number of patients treated in each ED ranges from 10,000 to 80,000, which varies from hospital to hospital. From 2017 to 2019, the median number of patients treated in the EDs of the five hospitals was 41,218. The population of the area where two hospitals are located is 9.7 million, and the populations of the area where the other three hospitals are located are 890,000, 550,000, and 280,000, respectively. When patients are discharged from the ED, they are diagnosed based on the International Classification of Diseases (ICD)-10 code. Influenza can be diagnosed through an antigen test using immunochromatographic assay (BD Veritor System for Rapid Detection of Flu A + B) [18]. However, during an influenza epidemic declared by KDCA, it also can be diagnosed based on clinical symptoms only. The influenza epidemic is declared by the KDCA when the average proportion of patients with ILIs is more than two standard deviations from the average proportion of patients in the non-epidemic period over the past 3 years since 2006. The influenza epidemic is declared over by the KDCA after review, if the average proportion of patients with ILIs is below the standard for declaring an epidemic for 3 consecutive weeks. According to declarations by the KDCA, in the winter of 2017–18, the influenza epidemic began at week 48 of 2017, peaked during the first week of 2018, and concluded at week 21 of 2018. In the 2018–19 season, the influenza epidemic began at week 46 of 2018, peaked at week 52 of 2018 and week 16 of 2019, and concluded during week 25 of 2019 [19]. During the 2018–19 epidemic, the first peak was dominantly type A influenza and the second peak was dominantly type B influenza. In the 2019–20 season, when COVID-19 became a pandemic, the influenza epidemic was declared at week 46, peaked at week 52, and concluded at week 13 of 2020.

2.2. Study participants

For convenience, in this study, we included all patients who visited five EDs from week 40 of each year to week 22 of the following year, considering the start and peak of each influenza epidemic period in 2017–18, 2018–19, and 2019–20. We excluded patients who visited the ED only for receiving their medical records. All patients were divided into three phases based on their visiting week. The first phase was defined as patients who visited from weeks 40 to 52 when the number of influenza patients increased; the second phase was defined as patients who visited from weeks 1 to 9 of the following year, wherein the number of patients gradually decreased, and the third phase was defined as patients who visited from weeks 10 to 22 when the second epidemic peak occurred (Fig. 2).

2.3. Variables

Information on patients was extracted anonymously from the electronic records of the hospitals. A diagnosis of influenza was defined as ICD-10 codes J09, J10, and J11, determined from ED discharge records. For body temperature, we used the first measurement taken immediately after the ED visit. Fever was defined as a body temperature of >37.5 °C according to the suspected symptoms of COVID-19 defined by the KDCA. COVID-19 pandemic-related information was collected from announcements made by the KDCA.

2.4. Statistical analysis

The demographic findings for each season were described. Data of categorical variables are reported as counts and percentages, and data of continuous variables are reported as median, first quartile, and third quartile. The weekly incidence rates of influenza per 1000 ED visits were calculated for each season. The analysis was performed according to the phases of the period considered in this study. The difference in the incidence rate between seasons for each phase was expressed as the incidence rate ratio with a 95% confidence interval (95% CI). A generalized estimation equation model with a Poisson distribution was used to compare changes in the weekly incidence rate for each season and to predict the trend of the influenza epidemic in the 2019–20 season based on the data of influenza incidence rates in the 2017–18 and 2018–19 seasons [20]. β means the change in the weekly incidence rate. Since the weekly data that can be evaluated for each phase are short, we estimated changes in weekly incidence rates over time using a linear term for time. All statistical analyses were performed using SAS software (version 9.4; SAS Institute Inc., Cary, NC, USA).

3. Results

During the study period, 463,633 patients visited the ED of the participating hospitals (Table 1). There were 147,295 influenza patients in the 2019–20 season. In the 2018–19 and 2017–18 seasons, there were 162,315 and 154,023 influenza patients, respectively. The distribution of age and sex of patients was similar during each phase. However, in the third phase of the 2019–20 season, wherein the number of COVID-19 patients surged nationwide, the total number of ED visits was lower, and the median patient age was older than that in the previous two seasons. The proportion of patients whose body temperature was >37.5 °C was the lowest (14.7%) in the third phase of the 2019–20 season. Fig. 3 shows the weekly distribution influenza-diagnosed patients by hospital by season.

Fig. 4 shows the weekly incidence rate of influenza per 1000 ED visits by season. In the first phase (weeks 40 to 52), influenza incidence rate increased weekly in every season. In the second phase (weeks 1 to 9), the influenza incidence rate decreased in every season. In particular, in the 2019–20 season, the weekly influenza incidence rate per 1000 ED visits sharply decreased from 101. 6 to 56.6 between weeks 4 and 5. In week 4, the first COVID-19 patient was diagnosed in Korea, and the KDCA raised the alert level from "blue" to "yellow" with emphasis on practicing hand hygiene, following cough etiquette, and wearing masks. When an outbreak of COVID-19 occurred in Daegu metropolitan city in week 9, the KDCA raised the alert level from "orange" to "red" and recommended social distancing such as maintaining a 2-m distance between people, refraining from going out, restricting movement, suspending mass gathering events, and closing schools. After week 9 of 2020, the influenza incidence rate per 1000 ED visits remained below 2, and there was no second epidemic wave, unlike that in the 2018–19 season. The ratio of influenza incidence rate per 1000 ED visits by season was evaluated for the third phase, in which social distancing was emphasized in 2019, to compare the difference in incidence rate by season. Compared with the third phase of the 2018–19 and 2017–18 seasons, the incidence rate ratios of the third phase of the 2019–20

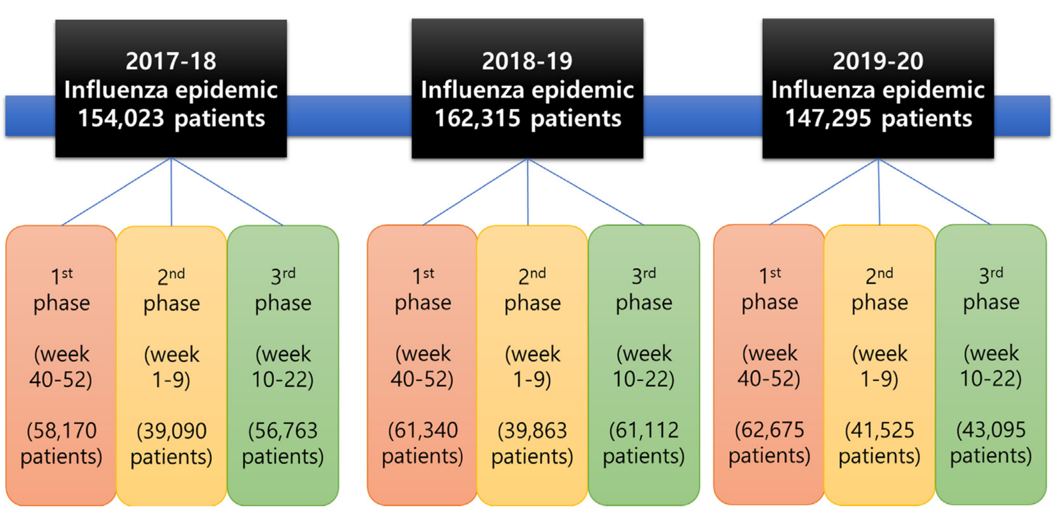

Fig. 2. Numbers of patients during the study period.

Table 1
Demographic characteristics by season and phase

	Total		2017–18 season						2018–19 season						2019–20 season					
			1st phase		2nd phase		3rd phase		1st phase		2nd phase		3rd phase		1st phase		2nd phase		3rd phase	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Total	463,633	100.0	58,170	100.0	39,090	100.0	56,763	100.0	61,340	100.0	39,863	100.0	61,112	100.00	62,675	100.0	41,525	100.0	43,095	100.0
Age																				
Median (Q1-Q3)	36	(12–56)	34	(8–54)	36	(13–56)	33	(8–55)	34	(9–55)	37	(17–57)	35	(11–56)	36	(10–57)	37	(17–58)	41	(24–60)
0 ≤ age < 10	107,778	23.2	15,115	26.0	8993	23.0	15,116	26.6	15,796	25.8	8201	20.6	14,738	24.12	15,105	24.1	8429	20.3	6285	14.6
10 ≤ age < 20	33,958	7.3	4471	7.7	2593	6.6	4580	8.1	4763	7.8	2652	6.7	4926	8.06	4625	7.4	2739	6.6	2609	6.1
20 ≤ age < 30	54,171	11.7	6636	11.4	4722	12.1	6268	11.0	6858	11.2	4970	12.5	7000	11.45	6708	10.7	5301	12.8	5708	13.2
30 ≤ age < 40	59,402	12.8	7447	12.8	5225	13.4	6946	12.2	7686	12.5	5285	13.3	7660	12.53	7662	12.2	5582	13.4	5909	13.7
40 ≤ age < 50	53,741	11.6	6868	11.8	4637	11.9	6356	11.2	6962	11.3	4723	11.8	6564	10.74	7260	11.6	4907	11.8	5464	12.7
50 ≤ age < 60	56,896	12.3	7045	12.1	4809	12.3	6759	11.9	7306	11.9	5114	12.8	7259	11.88	7592	12.1	5053	12.2	5959	13.8
60 ≤ age < 70	41,309	8.9	4571	7.9	3380	8.6	4658	8.2	5242	8.5	3668	9.2	5420	8.87	5669	9.0	4010	9.7	4691	10.9
70 ≤ age < 80	30,424	6.6	3434	5.9	2638	6.7	3444	6.1	3648	5.9	2778	7.0	4092	6.70	4206	6.7	2853	6.9	3331	7.7
80 ≤ age < 90	22,086	4.8	2217	3.8	1795	4.6	2251	4.0	2652	4.3	2110	5.3	2950	4.83	3229	5.2	2213	5.3	2669	6.2
90 ≤ age	3868	0.8	366	0.6	298	0.8	385	0.7	427	0.7	362	0.9	503	0.82	619	1.0	438	1.1	470	1.1
Sex																				
Male	239,166	51.6	30,282	52.1	19,494	49.9	29,262	51.6	31,544	51.4	20,153	50.6	31,933	52.25	32,397	51.7	21,400	51.5	22,701	52.7
Female	224,467	48.4	27,888	47.9	19,596	50.1	27,501	48.4	29,796	48.6	19,710	49.4	29,179	47.75	30,278	48.3	20,125	48.5	20,394	47.3
Body temperature																				
median (Q1-Q3)	37	(36.4–37.2)	37	(36.4–37.2)	37	(36.4–37.3)	37	(36.4–37.2)	37	(36.4–37.3)	37	(36.4–37.1)	37	(36.5–37.2)	37	(36.4–37.2)	37	(36.4–37.3)	37	(36.4–37.1)
fever (≥37.5)	89,285	19.3	10,923	18.8	8502	21.7	10,551	18.6	13,398	21.8	6502	16.3	12,107	19.81	12,132	19.4	8831	21.3	6339	14.7
Influenza																				
diagnosed patients	17,895	3.9	1962	3.4	3515	9.0	438	0.8	3523	5.7	1251	3.1	2079	3.40	2066	3.3	3016	7.3	45	0.1
rate per 1000 ED visits	38.6		33.7		89.9		7.7		57.4		31.4		34.0		33.0		72.6		1.0	
ED visit patients																				
A hospital	78,318	16.9	10,413	17.9	7352	18.8	9906	17.5	10,242	16.7	6967	17.5	9640	15.8	10,169	16.2	6953	16.7	6676	15.5
B hospital	149,551	32.3	18,724	32.2	12,409	31.7	18,404	32.4	20,336	33.2	12,493	31.3	20,346	33.3	19,845	31.7	13,123	31.6	13,871	32.2
C hospital	62,574	13.5	7730	13.3	5144	13.2	7287	12.8	7655	12.5	5122	12.8	8068	13.2	8909	14.2	6322	15.2	6337	14.7
D hospital	18,098	3.9	2794	4.8	2021	5.2	2765	4.9	2926	4.8	1935	4.9	2775	4.5	1299	2.1	800	1.9	783	1.8
E hospital	155,092	33.5	18,509	31.8	12,164	31.1	18,401	32.4	20,181	32.9	13,346	33.5	20,283	33.2	22,453	35.8	14,327	34.5	15,428	35.8

ED = emergency department; Q1 = first quartile; Q3 = third quartile.

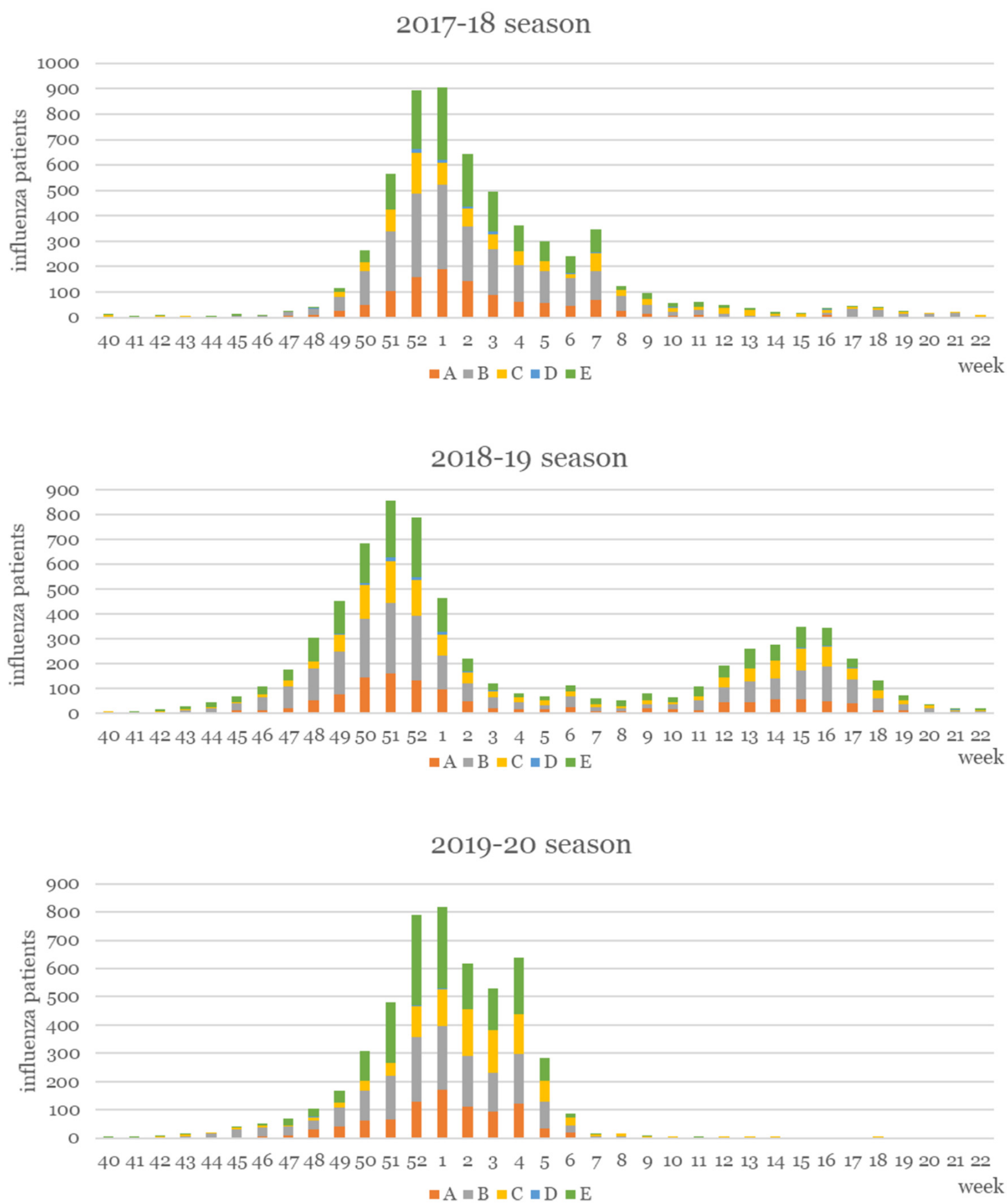

Fig. 3. Influenza epidemic curve by hospital by season.

season were 0.03 and 0.14, respectively, which showed a statistically significant difference ($p < 0.01$).

The results of evaluating the weekly change in the incidence rate during the second phase by season show that the weekly incidence rate decreased by $\beta = -0.21$ (95% CI -0.22, -0.19) in 2017–18, by $\beta = -0.27$ (95% CI -0.29, -0.24) in 2018–19, and most steeply by $\beta = -0.33$ (95% CI -0.35, -0.31) in 2019–20 (Fig. 5). The results of testing showed a statistically significant difference in the change in weekly incidence rate in the second phase by season ($p < 0.001$). During the third phase, the weekly incidence rate in the 2019–20 season decreased most steeply by $\beta = -0.12$ (95% CI -0.09, -0.15). The weekly incidence rate in 2017–18 decreased by $\beta = -0.10$ (95% CI -0.09, -0.11), and the weekly incidence rate in 2018–19 decreased by $\beta = -0.14$ (95% CI -0.06, -0.23). The change in weekly incidence rate in the second phase by season was not a statistically significant difference. The p-value for the 2017–18 and 2019–20 seasons, and the 2018–19 and 2019–20 seasons were 0.59 and 0.32 respectively.

The weekly incidence rate of the 2019–20 season in the second phase was predicted based on the trend of incidence rates in the 2017–18 and 2018–19 seasons. For this purpose, a generalized estimation equation model was used (Fig. 6). The bar of predicted weekly influenza incidence rate in Fig. 6 indicates the confidence interval. From week 7, the actual influenza incidence rate observed in the 2019 season was lower than the value predicted in the 2017–18 or 2018–19 seasons.

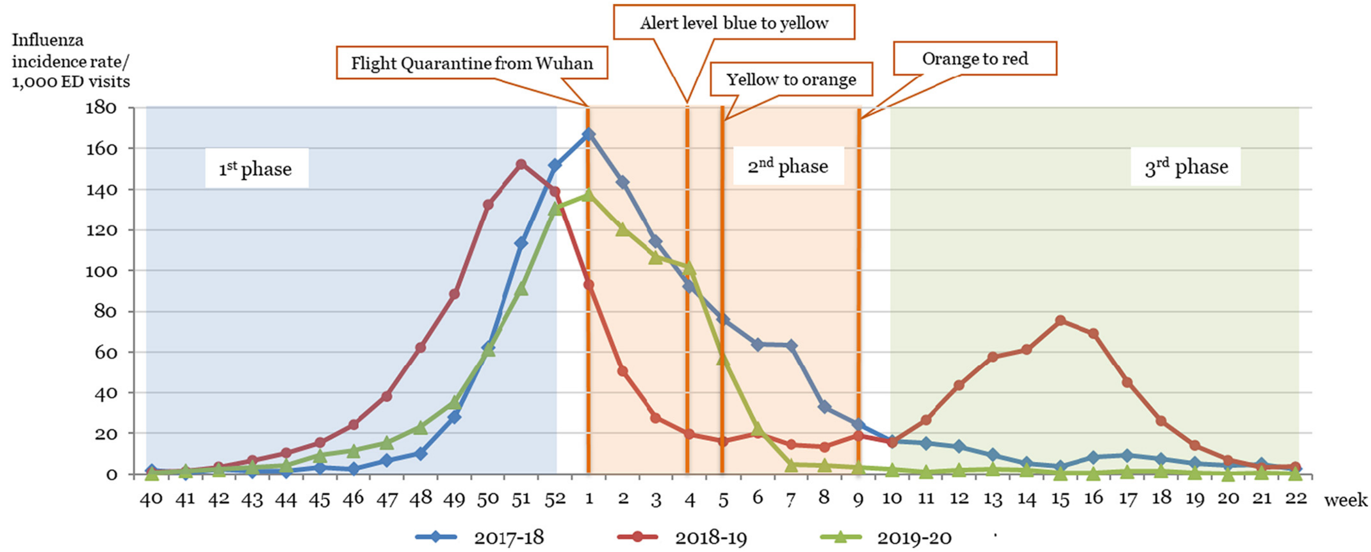

Fig. 4. Weekly influenza incidence rates per 1000 emergency department visits by season.

4. Discussion

We investigated the effect of the COVID-19 epidemic on reducing the incidence of influenza-associated ED use by analyzing ED-based data, comparing the changes in the weekly incidence rate and predicting the trend of the influenza epidemic. The weekly influenza incidence rate per 1000 ED visits decreased sharply after the change in the alert level announced by the government. The weekly change in the incidence rate in the second phase was the most dramatic in the 2019–20 season compared to that in the 2018–19 and 2017–18 seasons. From week 7 of 2020, the actual influenza incidence rate observed was lower than the incidence rate predicted by the 2017–18 or 2018–19 seasons.

Our findings suggest that public health measures, including social distancing and the use of personal protective measures, are associated with a reduced spread of influenza. When the KDCA raised the level of infectious disease crisis alert, they recommended and implemented a change in the behavior of the population and social distancing policy. The government emphasized mandatory use of masks in public places, following cough etiquette, practicing hand hygiene, staying at home after the onset of respiratory symptoms, refraining from nonessential social activities, and postponing school and preschool openings. Fig. 7 shows the COVID-19 incidence, ED visits and population mobility derived from data published by Statistics Korea based on mobile big data analysis [21]. Population mobility defined as visiting a city other than the one in which the person lives and staying there for >30 min by using telecommunication-based mobility data. The population mobility started to decline from week 8, when the number of confirmed COVID-19 cases surged and the government raised the alert level of the infectious disease. The ED use also declined when the number of confirmed COVID-19 cases surged. This shows that people were influenced by government policies and quarantine rules. The official influenza epidemic period of the 2019 season as defined by the KDCA ended 12 weeks earlier than that of the previous season [19]. During 2020–2021, the KDCA did not declare the influenza epidemic [19]. These findings support our results.

Wearing masks showed protective effects against influenza in randomized controlled studies of community and health care facilities [22,23]. Hand hygiene demonstrated a preventive effect in laboratory settings [24,25]. A meta-analysis showed reduction in the incidence

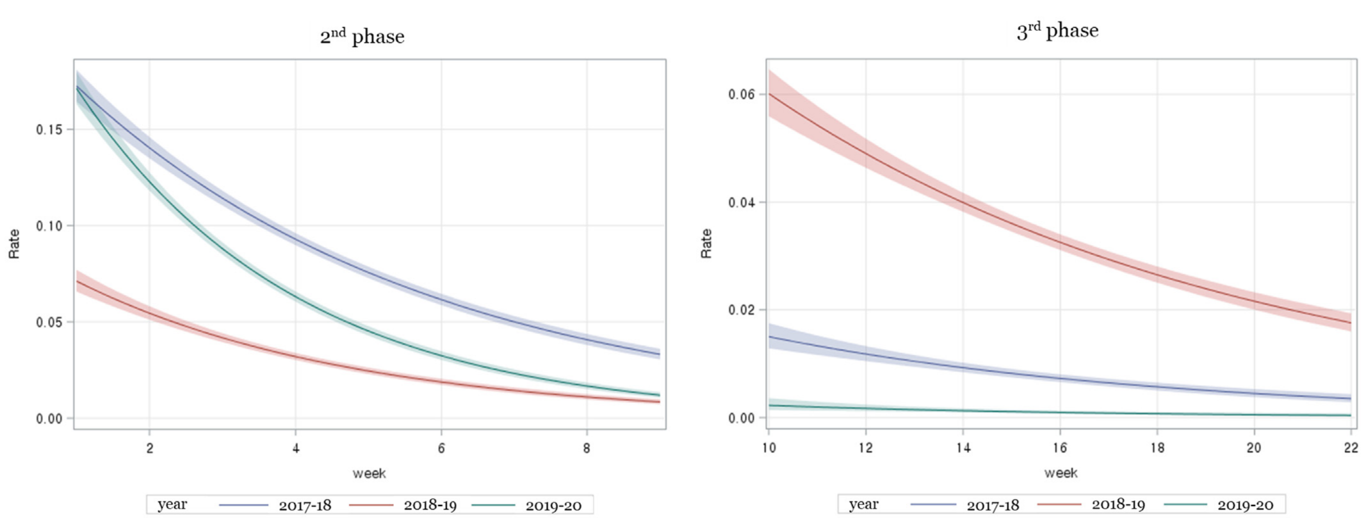

Fig. 5. Trend of weekly change in influenza incidence rates by season: (A) second phase, (B) third phase.

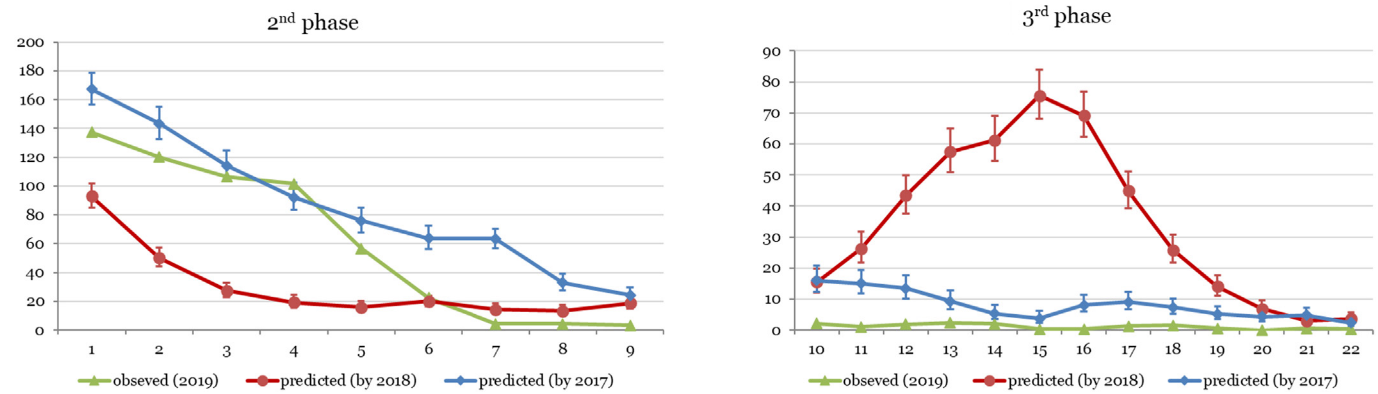

Fig. 6. Prediction of the weekly influenza incidence rates of the 2019–20 season based on that of 2017–18 and 2018–19.

rate of respiratory illness by practicing hand hygiene [26]. In these previous studies, the effectiveness of NPIs in reducing the incidence of influenza was similar to the results of our study, but they were conducted in laboratory or small community settings. In Texas, United States, closing schools showed potential benefits during the influenza epidemic [27]. Social distancing measures in workplaces delayed and reduced the peak influenza attack rate, and were more effective when combined with NPIs as shown in a meta-analysis [28].

Public health measures were adopted for reducing the incidence of COVID-19 and several studies have investigated the effects of these measures on influenza at a national or regional level using a national influenza surveillance database. In Hong Kong, NPIs resulted in 44% reduction in transmissibility [7]. Compared with the three preceding seasons, Singapore recorded a decline in the daily influenza cases and influenza positivity in the 2019–20 season and China showed a reduced rate of influenza transmission during the 2019–2020 season after implementing NPIs [8,29]. Olsen et al. also reported reduction in the positivity of influenza tests in the United States and decreased influenza activity in Australia, Chile, and South Africa [30]. In Korea, two studies used a surveillance system database and reported an early end of the influenza epidemic and decreased peak rate of influenza activity and influenza hospitalization cases [31,32]. Korea had recommended NPIs and implemented a social distancing policy, including postponing school opening and suspension of mass gathering events, after the start of the COVID-19 epidemic. Our study shows statistically significant reduction in the influenza incidence rate observed in the 2019–20 season compared with that predicted by the previous two seasons.

Our study has a few limitations. COVID-19 could have affected healthcare-seeking behaviors. The government encouraged people with respiratory symptoms to visit a hospital. Patients with mild disease became reluctant to visit the hospital because of concerns about contact with confirmed COVID-19 patients. Because this study used ED-based data, the change in hospital visits could also indicate the change in ED visits. People may have visited primary clinics or outpatient clinics other than EDs. This change could affect the incidence rate of influenza among ED visits. To reduce the effect of this decrease in ED visits, when analyzing the incidence rate and associated trend, we used the number of influenza patients per 1000 ED visits, not the number of influenza patients diagnosed in the ED. In our study, it was difficult to determine whether the practice of influenza testing used in the five participating EDs was consistent from year to year. In particular, it is not known whether influenza testing practices have changed since the start of the COVID-19 epidemic. However, even after the COVID-19 epidemic began, the guidelines for conducting influenza testing by participating hospitals and the standards set by the government for diagnosing influenza have not changed. Because this was an observational study, we could not identify which measures were potentially effective in reducing the incidence of influenza. We were unable to ascertain how well

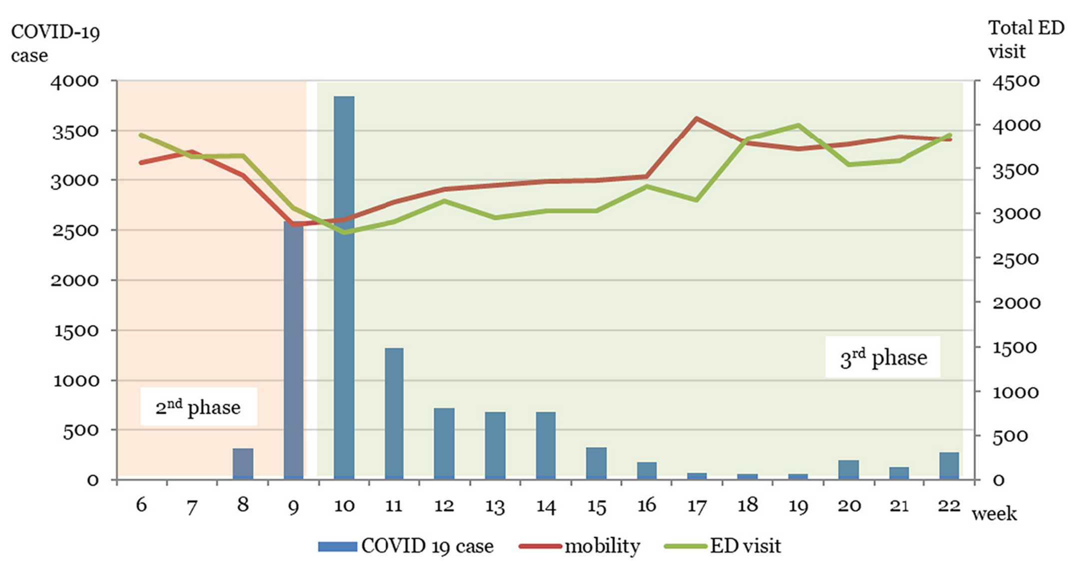

Fig. 7. Weekly COVID-19 incidence rates, population mobility, and ED visits in Korea.

social distancing or behavioral changes were actually performed; this would require further research.

5. Conclusions

Our study suggests that implementing NPIs and public health measures to control the spread of COVID-19 had a substantial impact on reducing influenza and related ED use in Korea. Implementing appropriate NPIs and public health measures could reduce outbreaks and lessen the burden of influenza during future influenza epidemics.

Funding

This research was supported by the Hallym University Research Fund 2020 (HURF-2020-31). The sponsor of this study was not involved in the data collection, analysis and interpretation of data; nor in the writing of the manuscript and in making the decision to submit the manuscript for publication.

Conflicts of interest

The authors have no potential conflicts of interest to disclose.

CRediT authorship contribution statement

Sola Kim: Conceptualization, Formal analysis, Funding acquisition, Methodology, Resources, Visualization, Writing – original draft, Writing – review & editing. **Ju Ok Park:** Conceptualization, Formal analysis, Methodology, Project administration, Supervision, Writing – review & editing. **Hye Ah. Lee:** Data curation, Formal analysis, Software, Validation. **Hang A. Park:** Data curation, Methodology. **Choung Ah. Lee:** Investigation, Methodology. **Soon-Joo Wang:** Investigation, Resources. **Eun Ju Jung:** Supervision, Writing – review & editing.

Acknowledgments

The sponsor of this study was not involved in the data collection, analysis and interpretation of data, writing of the manuscript, or making the decision to submit the manuscript for publication.

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