



ORIGINAL ARTICLE

Assessment of Intensive Vaccination and Antiviral Treatment in 2009 Influenza Pandemic in Korea

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Abstract

Objectives: We characterized and assessed public health measures, including intensive vaccination and antiviral treatment, implemented during the 2009 influenza pandemic in the Republic of Korea.

Methods: A mathematical model for the 2009 influenza pandemic is formulated. The transmission rate, the vaccination rate, the antiviral treatment rate, and the hospitalized rate are estimated using the least-squares method for the 2009 data of the incidence curves of the infected, vaccinated, treated, and hospitalized.

Results: The cumulative number of infected cases has reduced significantly following the implementation of the intensive vaccination and antiviral treatment. In particular, the intensive vaccination was the most critical factor that prevented severe outbreak.

Conclusion: We have found that the total infected proportion would increase by approximately six times under the half of vaccination rates.

1. Introduction

The worldwide influenza A/H1N1 pandemic in 2009–2010 had a huge impact on the public health system in Korea. The Korean scientists traced the pathogenesis and chronological localization of influenza A/H1N1 [1], and also evaluated and identified strains with antiviral resistance in Korea [2]. Surveillance data on influenza-like illness (ILI) were used to estimate the number of patients with influenza in Korea [3]. Mathematical models were formulated to evaluate the parameters of the existing preparedness plans in Korea [4].

Many pharmaceutical and nonpharmaceutical measures were implemented during an epidemic to delay the peak of the epidemic curve and reduce the casualties [5]. A previous study had demonstrated the effectiveness of nonpharmaceutical measures under certain situations [6], but the timely intervention with pharmaceutical measures using vaccines and antiviral treatment is known to effectively contain or mitigate the impact of an outbreak [7–9]. Public health experts have closely monitored the preventive strategies implemented for recurrent or future epidemics. Recently, many more realistic, tailored mathematical transmission models

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have been developed to answer specific public health questions on an epidemic and their empirical validity have been tested [8,9]. This study aims to investigate how the onset time and the levels of control measures are associated with the effectiveness of intensive vaccination and antiviral treatment. In this study, results from models with full-control measures and models with partial control measures were compared, highlighting the significant differences in model outcomes.

2. Materials and methods

A mathematical influenza transmission model was proposed to investigate the characteristic of the 2009

$$\left\{ \begin{array}{l} \dot{S}(t) = -\beta S(t)[\{bA(t) + I(t)\}/N(t) - u(t)S(t)] \\ \dot{V}(t) = u(t)S(t) - (1 - \sigma)\beta V(t)(\{bA(t) + I(t)\}/N(t)) \\ \dot{E}(t) = \{S(t) + (1 - \sigma)V(t)\}\beta[\{bA(t) + I(t)\}/N(t)] - kE(t) \\ \dot{I}(t) = kpE(t) - (\alpha + \gamma + f)I(t) \\ \dot{A}(t) = k(1 - p)E(t) - \gamma A(t) \\ \dot{H}(t) = \alpha I(t) - (\theta + \delta)H(t) \\ \dot{R}(t) = \gamma[A(t) + I(t)] + fI(t) + \theta H(t) \\ \dot{D}(t) = \delta H(t) \end{array} \right.$$

influenza pandemic and to evaluate the impact of intensive vaccination and antiviral treatment methods implemented in the Republic of Korea. A standard compartment model was used to divide the population into eight compartments with different epidemiological status. The Korean population is integrated to the influenza transmission model, based on data from the 2009 census. Our model classifies individuals as susceptible (S), vaccinated (V), exposed (E), clinically ill and infectious (I), asymptomatic but still infectious (A), hospitalized (H), recovered (R), and dead (D). It is assumed that susceptible individuals become infected at rate:

$$\beta \frac{bA(t) + I(t)}{N(t)}$$

where the total population size is given as follows:

$$N(t) = S(t) + V(t) + E(t) + I(t) + A(t) + H(t) + R(t)$$

Vaccination is administered to susceptible individuals with a vaccination rate $u(t)$. We assumed that the vaccine provides only partial immunity so that vaccinated individuals are less susceptible than unvaccinated individuals, which is modeled by vaccine efficacy (σ). Latently infected individuals proceed to become infectious with a latent period, $1/k$ and a proportion (p) of infected individuals become

symptomatic. We define b as relative infectiousness of asymptomatic cases compared with symptomatic cases. Both symptomatic and asymptomatic individuals recover at the rate γ . Infectious individuals are treated with an antiviral drug at the rate f . Infectious individuals are hospitalized at the rate α and recover at the rate γ . Hospitalized individuals either recover at the rate θ or die from influenza at the rate δ . Recovered individuals are assumed to remain protected for the duration of the epidemic. The baseline values of epidemiological parameters are presented in Table 1. The population is assumed to be completely susceptible at the beginning of the epidemic. The system of differential equations that describes our influenza transmission model is given as follows:

Moreover, the basic reproductive number for the aforementioned system is written as:

$$R_0 = \beta \left[\frac{p}{\gamma} + \frac{(1-p)b}{\gamma} \right]$$

3. Results

Simulation results are generated by numerically solving the given influenza dynamical system. Parameter estimations were carried out using the incidence data of clinically infected, vaccinated, treated, and hospitalized patients during the 2009 influenza pandemic in the Republic of Korea. First, the transmission rate, the vaccination rate, the antiviral treatment rate, and the hospitalized rate were estimated using the least-squares method for the 2009 influenza data, respectively. The estimated range R_0 for the 2009 influenza pandemic is approximately 1.5 using the transmission rate β in Table 1, and the expression for the basic reproductive number R_0 is presented earlier. The estimated vaccination, antiviral treatment, and hospitalized rates are presented in Table 1 and shown in Figure 1E. Next, we explored a baseline pandemic scenario in the context of the 2009 A/H1N1 outbreak in

Table 1. Baseline parameter values calibrated from the 2009 influenza pandemic in the Korea.

Parameter	Description	Value	Reference
β	Transmission rate (days ⁻¹)	0.8	Data fitted
u	Vaccination rate (days ⁻¹)	0–0.006	Data fitted
f	Antiviral treatment rate (days ⁻¹)	0–0.6	Data fitted
A	Diagnostic rate (days ⁻¹)	0–0.08	Data fitted
σ	Vaccine efficacy	0.8	Korea Centers for Disease Control and Prevention
b	Relative infectiousness of asymptomatic cases	0.142	Lee et al [18]
p	Proportion of infected individuals who become symptomatic	0.33	Lee et al [18]
k	Rate of progression from the latent to infected (days ⁻¹)	0.833	Lee et al [18]
γ	Recovery rate for infectious class (days ⁻¹)	0.22	Lee et al [18]
θ	Recovery rate for hospitalized individuals (days ⁻¹)	0.34	Lee et al [18]

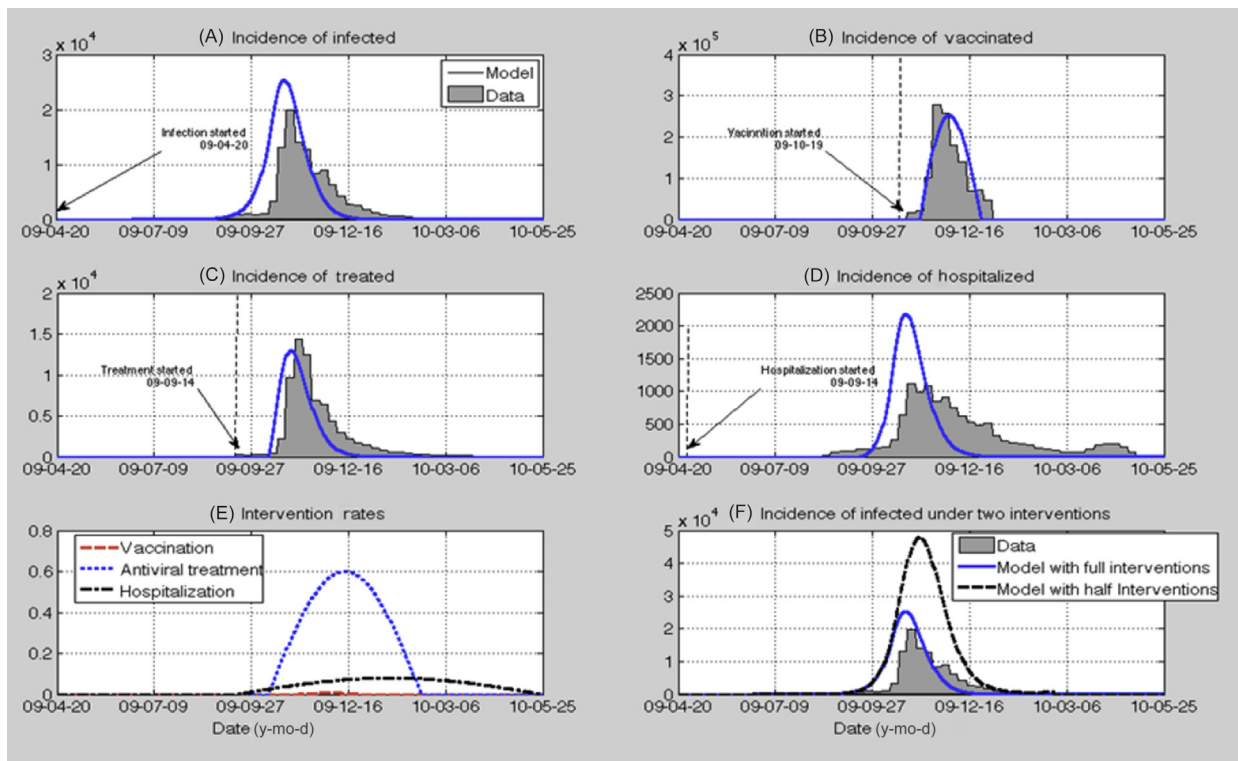


Figure 1. Comparisons of the 2009 influenza data and the model output $R_0=1.5$.

the Republic of Korea in the presence of these estimated vaccination and antiviral treatments. Figure 1 illustrates the incidence curves of the model output (solid curves) and the incidence data (gray bars) for the infected (Figure 1A), vaccinated (Figure 1B), treated (Figure 1C), and hospitalized (Figure 1D) individuals. As shown in Figure 1, the peak size and time and epidemic duration gave a good agreement between the model output and the data. In addition, Table 2 presents the comparisons of the data and model output of the total proportion of infected, vaccinated, treated, and hospitalized patients.

Table 2. Comparisons of the 2009 influenza data and model output.

	Full intervention scenario	Half intervention scenario	Data
Total proportion in population			
Infected	0.0200	0.1347	0.0157
Vaccinated	0.1675	0.0820	0.1690
Treatment	0.0079	0.0183	0.0102
Hospitalized	0.0015	0.0032	0.0018

We evaluated the impact of these intensive vaccination and antiviral treatments on the dynamics of influenza pandemics by comparing the results using the full interventions and the ones under less than half of vaccination and antiviral treatment coverage. The incidence curves of infected patients under the full interventions (solid curve) and the less than half interventions (broken curve) are shown in Figure 1F. It is worth noting that the total proportion of infected individuals had significantly increased from 0.02 to 0.1347 in Table 2. Particularly, the intensive vaccination was found to be the most critical factor that prevents severe outbreak. We also found that the total infected proportion would increase by approximately six times under the half of vaccination rates.

4. Discussion

Previous studies have focused on the effectiveness of a timely introduction of vaccination to reduce the peak of the epidemic curve and delay the epidemic curve [9–13]. In a study that evaluated the effect of vaccination in Korean military camps, the H1N1pdm09 vaccine, administered in January 2010, had approximately 50% effectiveness against the H1N1pdm09 outbreak that occurred in December 2010. The magnitude of vaccination effectiveness was robust with no substantial difference, even when multivariate analysis and various ILI definitions were used. The magnitude of vaccine effectiveness was <70% effectiveness achieved during the 2009–2010 H1N1pdm09 season in previous studies, but the rate was similar to the effectiveness achieved during the 2010–2011 season. Studies that evaluated the vaccination effectiveness 1 year after a vaccination program have indicated that the vaccination effectiveness was not persistent because there were no statistically significant results [14]. However, it was shown that there was still statistically significant vaccination effectiveness 1 year after the vaccination. This was immunologically consistent with the results of an existing antigenicity study in which the vaccination effectiveness was persistent 1 year after the seasonal influenza vaccination, although the antibody titer decreased [15]. Previous studies have evaluated antiviral treatment and showed its limitation in public health measures [16–18].

Simulation results show that the full intervention scenario showed rates close to the 2009 influenza data in the total infected proportion, vaccinated proportion, treatment proportion, and hospitalized proportion in Table 2. This shows that the 2009 pandemic countermeasures in Korea had an excellent effectiveness. The estimated vaccination, antiviral treatment, and hospitalized rates are presented in Table 1 and shown in Figure 1F. Four curves (A–C, and E) in Figure 1 had a fair match with real data with the exception of the

hospitalization proportion (Figure 1D). This can be interpreted as follows: with the introduction of mass vaccination in early September, the patients were more likely treated at their homes. Figure 1E shows the rates of vaccination, antiviral treatment, and hospitalization. The curves simply show the rate of each category. It is different from those numbers presented in Table 2 in that the proportions presented are total proportions of the population, whereas each curve in Figure 1 shows the rate of time-dependent function in the differential equations in our model.

We evaluated the impact of these intensive vaccination and antiviral treatments on the dynamics of influenza pandemics by comparing the results under the full interventions scenario and the ones under less than half of vaccination and antiviral treatment coverage in Figure 1F. The difference is not huge between full intervention and real data in each proportion presented in Table 2. Surprisingly enough, the proportion of infected persons in real data (0.1257) is less than that of the full intervention scenario (0.02). This might warrant some discussion, but it is worthwhile to give full credit to Korean public health workers for their efforts during the 2009–2010 influenza pandemic. Lastly, the intensive vaccination was the single most critical factor that prevents a severe outbreak. We have found that the total infected proportion would increase by approximately six times under the half of vaccination rates.

This study has shown a unique approach to evaluate the effectiveness of mass vaccination in Korea. This evaluation would provide a valuable insight for public health officials and scientists to prepare for the next possible pandemic in Korea.

Conflicts of interest

None to declare.

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