1st International Conference on Advance and Scientific Innovation (ICASI)  IOP Publishing

IOP Conf. Series: Journal of Physics: Conf. Series 1175 (2019) 012018  doi:10.1088/1742-6596/1175/1/012018

The Spread of A-H1N1 Swine Flu with Prevention and Healing Efforts in a Mixed Population: Mathematical Model and Dynamical Analysis

Widi Widayanti, Fadilah Ilahi, Elis Ratna Wulan

Department of Mathematics, Faculty of Science and Technology, UIN Sunan Gunung Djati, Bandung, Indonesia

*widihaviana@gmail.com

Abstract. Influenza is a respiratory tract infection caused by a virus. Infection of A-H1N1 influenza virus can cause outbreaks in all countries in the world. The outbreak of A-H1N1 influenza virus occurred in Indonesia in April 2009. This paper develops a mathematical model of the spread of A-H1N1 influenza with prevention and healing efforts for humans in mixed populations. This model is a five-dimensional system of nonlinear differential equations that shows the effect of vaccination and treatment on the spread of A-H1N1 influenza disease. Dynamic simulation provides information about the final results of the condition of the spread of influenza disease in various cases. The sensitivity analysis can be done in two ways, namely by using the sensitivity index of a parameter to a particular variable or by using a graph method.

1. Introduction
On April 21, 2009, the case of swine influenza in humans was first reported in the United States. Swine influenza was caused by H1N1 and infected 2 children (9-10 years old). After a few days, there were seven cases reported in humans infected with H1N1 [1]. Swine influenza is an acute respiratory disease of pigs caused by type A influenza virus [2], [3].

A-H1N1 Influenza is a new strain of influenza A virus infecting humans. A-H1N1 Influenza is different from other influenza virus strains commonly infecting humans and most humans do not have immunity against this virus. Therefore, this virus can easily spread from human to human. Transmission occurs through the air (coughing, sneezing) or through direct contact with patients or contaminated objects. Transmission of this virus can occur quickly especially in young people (10 - 45 years old) [2]–[4].

Symptoms of A-H1N1 influenza are fever, cough, headache, myalgia (muscle pain), joint pain, sore throat, runny nose and sometimes accompanied by vomiting and diarrhea. These symptoms are known as Influenza-Like Illness (ILI) or Flu-like syndrome because it is like the symptoms of flu or other respiratory tract infections commonly experienced by humans [1]–[4]. One of the efforts made to overcome this outbreak is vaccination. Vaccination is given to people who have not been affected with influenza. Vaccination contributes greatly to the reduction in the number of flu patients [5], [6]. In particular circumstances, antiviral is prescribed to increase the efficacy of the vaccination [7].
Several researches previously conducted have proposed mathematical models related to the spread of A-H1N1 influenza, both in pig and in human populations. For example, [4] examines the SIR model in human populations, while [8] examines the SIR model in human populations but the recovered humans may experience a decline in their immune response to disease. [5], [6] examines the SEIR model in pig populations where the outbreak has a latency period. However, [7] examines the SIR model by taking into account the influence of vaccination, quarantine, isolation and antiviral drug therapy

2. Mathematical Model
In this paper, the model formed is a combination of SI model of A-H1N1 influenza in pigs and SIR model of A-H1N1 influenza in humans. The assumptions used are as follows:

a. The population consists of two types of living creatures, namely humans and pigs. The population is assumed to be quite large and closed, therefore, there is no migration in the population.

b. The population is mixed homogeneously, so that each sub-population has the same possibility of making contact with other sub-populations.

c. There is only one type of disease spreading in the population, namely A-H1N1 influenza. The spread only occurs from pigs to pigs and from pigs to humans.

d. Every newborn individual has a chance of being infected with the disease.

e. Birth rates of both humans and pigs are constant.

f. Mortality rates of both humans and pigs are constant. The mortality rate is not only caused by natural death but also affected by deaths due to infection.

g. Prevention and healing efforts of A-H1N1 influenza are only made for humans. The prevention efforts are made on a constant basis through vaccination in susceptible human population, while the healing efforts are made constantly through the provision of antiviral drugs for infected humans.

The variables used for the model are as follows.

| Variable | Description | Interval Value |
|----------|-------------|---------------|
| $S_b$    | The average number of pigs susceptible to A-H1N1 influenza | $S_b \geq 0, S_b \in \mathbb{Z}$ |
| $I_b$    | The average number of pigs infected with A-H1N1 influenza | $I_b \geq 0, I_b \in \mathbb{Z}$ |
| $S_m$    | The average number of humans susceptible to A-H1N1 influenza | $S_m \geq 0, S_m \in \mathbb{Z}$ |
| $I_m$    | The average number of humans infected with A-H1N1 influenza | $I_m \geq 0, I_m \in \mathbb{Z}$ |
| $R_m$    | The average number of humans insusceptible to A-H1N1 influenza | $R_m \geq 0, R_m \in \mathbb{Z}$ |

The parameters used for the model are as follows.

| Parameter | Description | Interval Value |
|-----------|-------------|---------------|
| $\alpha$  | Mobility of pigs susceptible to A-H1N1 influenza | $\alpha \geq 0, \alpha \in \mathbb{Z}$ |
| $\delta$  | Mobility of humans susceptible to A-H1N1 influenza | $\delta \geq 0, \delta \in \mathbb{Z}$ |
| $\beta_1$ | Coefficient of periodic transmission for pigs | $0 \leq \beta_1 \leq 1, \beta_1 \in \mathbb{R}$ |
| $p$       | The chance of success of the average number of pigs susceptible to A-H1N1 influenza due to interacting with other pigs | $0 \leq p \leq 1, p \in \mathbb{R}$ |
| $\beta_2$ | Coefficient of periodic transmission for humans | $0 \leq \beta_2 \leq 1, \beta_2 \in \mathbb{R}$ |
| $\sigma$  | Vaccination rate of humans for every age and time | $0 < \sigma \leq 1, \sigma \in \mathbb{R}$ |
| $q$       | The chance of success of the average number of humans susceptible to A-H1N1 influenza due to interacting with pigs | $0 \leq q \leq 1, q \in \mathbb{R}$ |
| $\theta$  | Healing rate of humans infected with A-H1N1 influenza | $0 < \theta \leq 1, \theta \in \mathbb{R}$ |
| $r$       | The chance of success of the average number of humans infected with A-H1N1 influenza to be insusceptible | $0 \leq r \leq 1, r \in \mathbb{R}$ |
| $\eta$    | Natural mortality rate in a population of pigs | $0 < \eta \leq 1, \eta \in \mathbb{R}$ |
| $\nu$     | Mortality rate of pigs due to infection with A-H1N1 influenza | $0 < \nu \leq 1, \nu \in \mathbb{R}$ |
Natural mortality rate in a population of humans $\mu$ \hspace{1cm} $0 < \mu \leq 1, \mu \in \mathbb{R}$

Mortality rate of humans due to infection with A-H1N1 influenza $\omega$ \hspace{1cm} $0 < \omega \leq 1, \omega \in \mathbb{R}$

Based on the assumptions that have been made, the interaction diagram formed is as follows:

The interaction model formed based on the interaction diagram above is as follows,

$$\frac{dS_b}{dt} = \alpha - p\beta_1 S_b I_b - \eta S_b \hspace{1cm} (1)$$

$$\frac{dI_b}{dt} = p\beta_1 S_b I_b - (\eta + \nu)I_b \hspace{1cm} (2)$$

$$\frac{dS_m}{dt} = \delta - q\sigma S_m - (1-q)\beta_2 S_m I_b - \mu S_m \hspace{1cm} (3)$$

$$\frac{dI_m}{dt} = (1-q)\beta_2 S_m I_b - r\theta I_m - (\mu + \omega)I_m \hspace{1cm} (4)$$

$$\frac{dR_m}{dt} = q\sigma S_m + r\theta I_m - \mu R_m \hspace{1cm} (5)$$

3. Analysis Dynamic

This section discusses the analysis of the existence and stability of the equilibrium point of the model and seeks to determine the basic reproduction number ($R_0$). The equilibrium point of A-H1N1 influenza model with prevention and healing efforts for humans in mixed population will be obtained when the rate conditions of $S_b, I_b, S_m, I_m, \text{and } R_m$ are constant, namely

$$\frac{dS_b}{dt} = \frac{dI_b}{dt} = \frac{dS_m}{dt} = \frac{dI_m}{dt} = \frac{dR_m}{dt} = 0 \hspace{1cm} (6)$$

forming two equilibrium points, namely
\[ \begin{align*}
\lambda_1 &= \frac{ap\beta_1 - \eta(\eta + v)}{\eta} \\
\lambda_2 &= -\eta \\
\lambda_3 &= -(q\sigma + \mu) \\
\lambda_4 &= -(r\theta + \mu + \omega) \\
\lambda_5 &= -\mu.
\end{align*} \]

Based the eigenvalues obtained, we know that \( E_1 \) is stable under a condition that \( ap\beta_1 < \eta(\eta + v) \).

b. By substituting the endemic equilibrium point \( (E_2) \) on the Jacobi matrix, the following eigenvalues are obtained.
\[ \begin{align*}
\lambda_1 &= -\frac{1}{2} \left( \frac{ap\beta_1}{\eta + v} + \sqrt{\left( \frac{ap\beta_1}{\eta + v} \right)^2 - 4 \left( ap\beta_1 - \eta(\eta + v) \right)} \right) \\
\lambda_2 &= -\frac{1}{2} \left( \frac{ap\beta_1}{\eta + v} - \sqrt{\left( \frac{ap\beta_1}{\eta + v} \right)^2 - 4 \left( ap\beta_1 - \eta(\eta + v) \right)} \right) \\
\lambda_3 &= -(\beta_2(1-q)(ap\beta_1 - \eta(\eta + v)) + \mu + q\sigma) \\
\lambda_4 &= -(r\theta + \mu + \omega) \\
\lambda_5 &= -\mu.
\end{align*} \]

Based the eigenvalues obtained, we know that \( E_2 \) is stable under a condition that \( ap\beta_1 > \eta(\eta + v) \).
The basic reproductive number \( R_0 \) represents the average number of cases in which infected individuals in the infectious period cause susceptible populations. If \( R_0 < 1 \), the virus of A-H1N1 influenza is gone so that the population becomes disease-free because the population of infected individuals goes near zero. If \( R_0 > 1 \), it indicates the existence of the virus of A-H1N1 influenza in a population, causing the disease to become endemic because the population of infected individuals is more than zero. The basic reproductive number \( R_0 \) can be determined using \textit{Next Generation Matrix} (NGM) method. \textit{Next Generation Matrix} (NGM) can be obtained from \( I_b \) and \( I_m \) as follows:

\[
I_b = \phi((S_b, S_m, R_m), I_b) - \psi((S_b, S_m, R_m), I_b)
\]

\[
I_m = \phi((S_b, S_m, R_m), I_m) - \psi((S_b, S_m, R_m), I_m)
\]

with

\[
\phi = \left[ \frac{p \beta_1 S_b I_b}{(1-q) \beta_2 S_m I_b} \right],
\]

\[
\psi = \left[ \frac{(\eta + \nu) I_b}{(r \theta + \mu + \omega)} \right].
\]

Then, forming the Jacobian matrix for \( \phi \) and \( \psi \), namely:

\[
F = \begin{bmatrix}
\frac{\alpha p \beta_1 S_b}{\eta} & 0 \\
(1-q) \beta_2 S_m & 0 \\
\alpha p \beta_1 & 0 \\
\end{bmatrix},
\]

\[
V = \begin{bmatrix}
\frac{\eta + \nu}{\eta + \nu} & 0 \\
0 & r \theta + \mu + \omega \\
\end{bmatrix}
\]

Furthermore, substituting the disease-free equilibrium point \( (E_1) \) on the equation system (1)-(5) forms

\[
K = FV^{-1} = \begin{bmatrix}
\frac{\alpha p \beta_1}{\eta(\eta + \nu)} & 0 & \frac{1}{\eta + \nu} & 0 \\
\frac{(1-q) \beta_2 \delta}{q \sigma + \mu} & 0 & \frac{1}{r \theta + \mu + \omega} & 0 \\
\frac{\alpha p \beta_1}{\eta(\eta + \nu)} & 0 & \frac{(1-q) \beta_2 \delta}{(q \sigma + \mu)(\eta + \nu)} & 0 \\
\end{bmatrix}
\]

According to the NGM, the eigenvalues obtained are as follows.

\[
\lambda = \frac{\alpha p \beta_1}{\eta(\eta + \nu)}, \quad \lambda = 0
\]

Therefore, it can be determined that:

\[
R_0 = \frac{\alpha p \beta_1}{\eta(\eta + \nu)}
\]

4. Sensitivity Analysis

This section shows dynamic simulation and sensitivity analysis of a parameter to a variable. In this case, the dynamic simulation is carried out four times in different cases. Each simulation is tested for three initial values with each \( S_b, I_b, S_m, I_m \), and \( R_m \) namely NA1 = (17, 15, 10, 22, 18), NA2 = (20, 22, 18, 15, 10), and NA3 = (15, 19, 20, 20, 17).
Table 3. List of parameter values in each simulation

| Parameter | Simulation 1 | Simulation 2 | Simulation 3 | Simulation 4 |
|-----------|--------------|--------------|--------------|--------------|
| $\alpha$  | 2            | 2            | 2            | 0            |
| $\delta$  | 4            | 4            | 4            | 4            |
| $\beta_1$ | 0.45         | 0.2          | 0            | 0.45         |
| $\beta_2$ | 0.25         | 0.2          | 0.2          | 0.35         |
| $\sigma$  | 0.3          | 0.4          | 0.8          | 0.24         |
| $\rho$    | 0.2          | 0.2          | 0.8          | 0.12         |
| $\theta$  | 0.3          | 0.4          | 0.3          | 0.64         |
| $\tau$    | 0.4          | 0.6          | 0.24         | 0.36         |
| $\eta$    | 0.15         | 0.5          | 0.51         | 0.15         |
| $\nu$     | 0.1          | 0.5          | 0.45         | 0.35         |
| $\mu$     | 0.24         | 0.5          | 0.25         | 0.52         |
| $\omega$  | 0.3          | 0.4          | 0.14         | 0.14         |

According to the parameter values in Table 1, the following presents the dynamic simulation of $S_b$, $I_b$, $S_m$, $I_m$, and $R_m$ toward $t$ in each simulation.
In Simulation 1, the initial value given meets the existence condition of $E_2$. This is because the number of pigs born ($\alpha$) and the number of pigs becoming infected ($p$ and $\beta_1$) are greater than the number of pigs died ($\eta$ dan $\nu$) making the human population have a greater chance of becoming infected with the disease. It shows that in a mixed population of pigs and humans, there will always be some infected pigs ($I_b \neq 0$) that will cause some humans to be susceptible. Simulation 1 is stable toward $E_2$ at the point of $(S_b, I_b, S_m, I_m, R_m) = (4, 5.33, 2.34, 3.83, 4.08)$ and has an epidemic threshold of $R_0 = 6$ which means that the A-H1N1 influenza is endemic in the population. Therefore, the condition of the spread of A-H1N1 influenza in the mixed population is endemic.

In Simulation 2, 3, and 4, the initial value given meets the existence condition of $E_1$. This is because the number of pigs born ($\alpha$) and the number of pigs becoming infected ($p$ and $\beta_1$) are less than the number of pigs died ($\eta$ dan $\nu$) making the human population have a smaller chance of being infected with the disease. It shows that over time, in a mixed population of pigs and humans, with or without interaction between pigs and pigs or between pigs and humans, there will be a decrease toward zero (there is no infected pig nor human populations). Moreover, there are differences in each simulation, namely in simulation 2 there is a transmission from susceptible to infected pigs ($\beta_1 > 0$) as well as an increase in the number of pigs ($\alpha > 0$) but does not meet the existence condition of $E_2$, whereas in simulation 3 there is no transmission from susceptible to infected pigs ($\beta_1 = 0$) so that the number of susceptible pigs becoming infected decreases, meanwhile in simulation 4 there is no increase in the number of susceptible pigs ($\alpha = 0$) so that the number of pigs susceptible becoming infected decreases as well. Simulation 2, 3 and 4 are all stable toward $E_1$ at the point of $(S_b, I_b, S_m, I_m, R_m) = (4, 0, 6.9, 0, 1.10), (3.9, 0, 4.49, 0, 11.51), \text{and} (0, 0, 7.29, 0, 0.40)$ respectively. As for the epidemic threshold ($R_0$), it is 0.16, 0, and 0 respectively which means that the condition of the spread of A-H1N1 influenza in the mixed population is disease-free.

Sensitivity analysis is performed for $\alpha$, $p$, $\beta_1$, $\eta$, and $\nu$ parameters to the basic reproduction number ($R_0$). This sensitivity analysis can be done by using a graph or by determining the value of the Normalized sensitivity index. Normalized sensitivity index itself is obtained with the normalized sensitivity index of $V$ variable differentiated from $P$ parameter, defined as follows.

$$C_p^V = \frac{\partial V}{\partial P} \times \frac{P}{V} \quad (18)$$

Note: $V$ is the variable to be analyzed and $P$ is the parameter [2], [11], [12].

Some initial values for each parameter are assumed, namely $\alpha = 10, p = 0.4, \beta_1 = 0.5, \eta = 0.4,$ and $\nu = 0.3$, obtaining the value of $R_0 = 7.1428571$. Based on the equation of $R_0$ in (17), the sensitivity index of variables $R_0$ to $\alpha$ is as follows:

$$C_{\alpha}^{R_0} = \frac{\partial R_0}{\partial \alpha} \times \frac{\alpha}{R_0}$$

$$= \frac{p\beta_1}{\eta (\eta + \nu)} \times \frac{\alpha \eta (\eta + \nu)}{\alpha p \beta_1}$$

$$= 1$$

Furthermore, the same thing is done for variable $R_0$ to $p$, $\beta_1$, $\eta$, and $\nu$. The results obtained can be seen in the following table.

| Parameter ($P$) | Sensitivity Index | $R_0$ Value |
|-----------------|------------------|-------------|
|                 |                  | $P - 40\%$ | $P - 20\%$ | $P + 20\%$ | $P + 40\%$ |

Table 4. The changes in the $R_0$ value based on changes in values of each parameter.
The sensitivity analysis can be seen graphically in Figure 3 below.

Based on the results of the sensitivity index, it can be seen that $\alpha$, $p$, and $\beta_1$ parameters have a positive relation to $R_0$, meaning that if $\alpha$, $p$, and $\beta_1$ increase, $R_0$ increases as well, and vice versa if $\alpha$, $p$, and $\beta_1$ decrease, $R_0$ decreases as well. In addition, $\eta$ and $\nu$ have a negative relation to $R_0$ so that if $\eta$ and $\nu$ increase, $R_0$ decreases, and vice versa if $\eta$ and $\nu$ decrease, $R_0$ increases. This condition can be seen from the decrease or increase in the $R_0$ value based on changes in values of each parameter presented in Table 4 and Figure 3.

5. Conclusion
According to the results of the analysis, there are several factors that influence the condition of the spread of A-H1N1 influenza in a mixed population, determining whether it is disease-free or endemic, namely $\alpha$, $p$, $\beta_1$, $\eta$, and $\nu$. If the values of $\alpha$, $p$, and $\beta_1$ is higher than the values of $\eta$ and $\nu$, the disease of A-H1N1 influenza will be endemic in pig population. Biologically, it means that the number of pigs born and the number of pigs becoming infected are greater than the number of pigs died, making the human population have a greater chance of being infected with the disease. Therefore, the condition of the spread of A-H1N1 influenza in the mixed population is epidemic. On the other hand, if the values of $\alpha$, $p$, and $\beta_1$ are less than the values of $\eta$ and $\nu$, the population will be free from the disease of A-H1N1 influenza. Biologically, it means that the number of pigs born and the number of pigs becoming
infected are less than the number of pigs died, making the human population have a smaller chance of being infected with the disease. Therefore, in the mixed population, the condition is disease-free.

References
[1] N. S.-O. I. A. (H1N1) V. I. Team, “Emergence of a novel swine-origin influenza A (H1N1) virus in humans,” *N. Engl. J. Med.*, vol. 360, no. 25, pp. 2605–2615, 2009.
[2] T. M. E. Govaert, C. Thijs, N. Masurel, M. J. W. Sprenger, G. J. Dinant, and J. A. Knottnerus, “The efficacy of influenza vaccination in elderly individuals: a randomized double-blind placebo-controlled trial,” *Jama*, vol. 272, no. 21, pp. 1661–1665, 1994.
[3] W. F. Carman *et al.*, “Effects of influenza vaccination of health-care workers on mortality of elderly people in long-term care: a randomised controlled trial,” *Lancet*, vol. 355, no. 9198, pp. 93–97, 2000.
[4] P. Gonzaga Ospina and A. Munoz, “A Simulation Model Including Vaccination and Seasonality for Influenza A-H1N1 Virus,” *Appl. Math. Sci.*, vol. 10, no. 26, pp. 1269–1276, 2016.
[5] M. Kharis, “Model Seir Untuk Epidemi Flu Babi Pada Populasi Babi Dengan Laju Kontak Jenuh,” *J. MIPA*, vol. 35, no. 1, 2012.
[6] M. Kharis, “Model Deterministik untuk Epidemi Flu Babi Pada Populasi Babi,” *Kreano, J. Mat. Kreat.*, vol. 1, no. 2, pp. 95–105, 2010.
[7] F. Octavianti, “Kesetimbangan model penyebaran virus influenza a H1N1 menggunakan model Susceptible Infected-Recovered (SIR).”
[8] M. Kharis and A. N. Cahyono, “Pemodelan Matematika Pada Epidemi Influenza Dengan Strategi Vaksinasi,” *J. MIPA*, vol. 38, no. 2, pp. 176–185, 2015.
[9] L. Nurjanah, F. Ilahi, and D. Suandi, “Analisis Kestabilan Global dengan Menggunakan Fungsi Lyapunov pada Model Dinamik Epidemi SIR,” *Kubik*, vol. 3, no. 1, pp. 68–76, 2018.
[10] N. Nurhalimah, F. Ilahi, and E. R. Wulan, “Analisis Kestabilan Model Matematika SIA (Susceptible, Infected, AIDS Cases) untuk Penyakit AIDS,” *Kubik*, vol. 3, no. 1, pp. 83–87, 2018.
[11] A. H. Angi, “Tinjauan Struktur Genetik Serta Tingkat Keganasan Virus Influenza H1n1,” *Partner*, vol. 17, no. 2, pp. 181–187, 2010.
[12] J. C. Kwong, S. Maaten, R. E. G. Upshur, D. M. Patrick, and F. Marra, “The effect of universal influenza immunization on antibiotic prescriptions: an ecological study,” *Clin. Infect. Dis.*, vol. 49, no. 5, pp. 750–756, 2009.