Mathematical model of the symptomatic and asymptomatic infections of Swine flu

P. Pongsumpun*, and I. M. Tang

Abstract—Swine flu (swine influenza) is a respiratory disease caused by type A influenza. This disease is transmitted between the persons through coughing or sneezing with the virus. Persons may also become infected by touching something, contaminated with flu virus and then touching their eyes, nose or mouth. The most common clinical findings are fever, cough, sore throat, malaise, headache, vomiting and diarrhea have also been common, both of which are unusual features of seasonal influenza. In this paper, the transmission of Swine flu is studied through standard dynamical modeling method. The symptomatic and asymptomatic patients are considered with the different transmission rates. The analytical solutions of the model are obtained. The numerical simulations are shown to support the theoretical predictions. The basic reproductive number is produced for introducing the alternative way to decrease the disease outbreak.

Keywords—Asymptomatic, Basic reproductive number, Mathematical model, Swine flu transmission.

I. INTRODUCTION

Swine flu is a highly contagious and rapidly spreading disease occurred by a new strain of type A influenza virus. Swine flu also is an Emerging Infectious Disease (EID) such as SARS, avian influenza and Chikungunya diseases. The swine flu virus has not previously circulated in human; the virus is entirely new [1]. Genetic analysis of swine flu virus showed that its gene segments are similar to influenza virus that circulated among pigs. Beginning in March 2009, an outbreak of influenza in North America was found to be caused by a new strain of influenza virus, designated Influenza H1N1. On April 9, 2009 it became apparent to public health officials in Mexico City that an outbreak of influenza was in progress late in the influenza season. On April 17, two children cases were also reported in California near the Mexican border. The current outbreak of swine influenza A (H1N1) evolved so rapidly. As on 29 April 2009, nine countries officially reported with confirmed cases of swine influenza A/H1N1 infection. Of these, Mexico, United State, Austria, Canada, Germany, Israel, New Zealand, Spain and the United Kingdom have reported from laboratory that confirmed human cases and deaths due to rapidly progressive pneumonia, respiratory failure and acute respiratory distress syndrome (ARDS) [2]. World Health Organization (WHO) declared high stages on its "pandemic" scale-alert 6, designating the Influenza H1N1 2009 a potential threat to worldwide health and declared the outbreak as Public Health Emergency of International Concern (PHEIC) [1]. The total report of swine flu cases worldwide more than 213 countries was 622,482 by 27 November, 2009[3]. Updated data on swine flu deaths has reached a total of 16,931 deaths as of 21 March, 2010 [4]. The most active areas of pandemic influenza virus transmission currently are in parts of Southeast Asia, West Africa, and in the tropical zone of the Americas [4].

Generally, the three types of influenza virus caused human flu are influenza A, influenza B and influenza C. Influenza A virus also infects both pigs and birds, influenza C virus infects pigs but do not infect birds [5]. Pigs can be infected with influenza strains that usually found in pigs, birds and humans. The viruses can be reassortment, a process through two or more influenza viruses can swap genes, produce new and dangerous strains [6]. Swine flu is a reassortment of at least four strains of influenza A virus, strains originated from humans, birds, North America pigs and Eurasian pigs [7]. Over the years, different variations of swine flu viruses have emerged. At this time, there are four main influenza A subtypes that have been isolated in pigs: H1N1, H1N2, H3N2, and H3N1. However, most of the recently isolated influenza virus from pigs are H1N1 virus [8].

Direct transmission of a swine flu virus from pigs to humans is occasionally possible. However, sporadic human infections with swine flu have occurred. Most commonly, these cases occur in persons with direct exposure to pigs [8]. Risk factors that may contribute to swine-to-human transmission include smoking and, especially, not wearing gloves when working with sick animals. Swine influenza viruses are not transmitted by food. Eating properly handled and cooked pork products are safe. Cooking pork to an internal temperature of 160 °F kills the swine flu virus as it does other bacteria and viruses. In the current situation, the swine flu virus appears to be spreading from person to person mainly by infected people coughing and sneezing. The virus spreads when droplets from a cough or sneeze of an infected person are propelled through
the air and deposited on the mouth or nose of people nearby (within approximately one metre). The virus also settles on surfaces in the surrounding environment and can live on a hard surface for up to 24 hours and a soft surface for around 20 minutes. The virus can spread when a person touches droplets on surface and then touches their own mouth or nose before washing their hands. After infection, it usually takes 1 to 4 days before each person becomes ill. Infected adults may be able to transmit the disease to the others people for one day before symptoms appear and up to seven or more days after becoming sick. Children, especially younger children, might be contagious for longer periods [9]. The symptoms of swine flu are similar to influenza-like illness in general. Symptoms include fever, cough, sore throat, muscle pain, headache, runny nose, chills and fatigue. Some people with swine flu also have reported vomiting and diarrhea associated with swine flu. Swine flu may take chronic medical conditions worse [10-14]. D. Klinkenberg, A. Everts-van der Wind, et al. [15] studied the strategy for emergency vaccination during an epidemic of classical swine fever virus (CSFV) and presented a mathematical model of CSFV transmission between pig herds which quantify the effect of control strategies with and without vaccination.

In 2003, Neil M Ferguson and et al [16] used the mathematical model of influenza transmission to simulate the impact of neuraminidase inhibitor therapy on infection rates and transmission of drug-resistant viral strains. Fraser et al modeled the transmission dynamics of influenza A (H1N1) in the human population, but they did not include cross-species transmission [17]. Coburn [18] has recently developed a complex model that tracks influenza transmission of three species (birds, pigs and human). Analysis of his model generated significant insights into the emergence of novel recombinant strains of influenza (such as H1N1), as well as in predicting their epidemic and pandemic potential.

In our model, the transmission of Swine flu is considered with the different probability of the patients who be symptomatic and asymptomatic infections. The simulations of the parameters are presented. The basic reproductive number is shown to introduce the way for reducing the outbreak of the disease.

\[ \frac{dI}{dt} = \frac{hS(I_s + I_a)}{N} - (\beta_s + \beta_a)bE - \mu_hE \]

\[ \frac{dI_s}{dt} = \beta_s bE - \mu_I I_s - cI_s \]

\[ \frac{dI_a}{dt} = \beta_a bE - \mu_I I_a - cI_a \]

\[ \frac{dQ}{dt} = c(I_s + I_a) - (\mu_h + g)Q \]

\[ \frac{dR}{dt} = gQ - \mu_hR \]

with \( N = S + E + I_s + I_a + Q + R \)

where the variables and parameters are defined as follows:

- \( S \) is the number of susceptible persons,
- \( E \) is the number of exposed persons,
- \( I_s \) is the number of symptomatic infectious persons,
- \( I_a \) is the number of asymptomatic infectious persons,
- \( Q \) is the number of Quarantine persons,
- \( R \) is the number of recovered persons,
- \( N \) is the total human population,
- \( \lambda \) is the birth rate of human population,
- \( \mu_h \) is the death rate of human population,
- \( h \) is the transmission rate of swine flu,
- \( \beta_s \) is the transmission probability of swine flu to the human then that person become symptomatic patient,
- \( \beta_a \) is the transmission probability of swine flu to the human then that person become asymptomatic patient,
- \( b = \frac{1}{IIP} \), where IIP is the incubation period of swine flu in human,
- \( c \) is the rate at which the swine flu cases are moved to the quarantine human,
- \( g \) is the recovery rate of the human population.

We introduce the new variables:

\[ s = \frac{S}{N}, e = \frac{E}{N}, i_s = \frac{I_s}{N}, i_a = \frac{I_a}{N}, q = \frac{Q}{N}, r = \frac{R}{N} \]

The system (1) can be rewritten as follows:

\[ \frac{ds}{dt} = \mu_h - hs(i_s + i_a) - \mu_h s \]

\[ \frac{de}{dt} = hs(i_s + i_a) - (\beta_s + \beta_a)be - \mu_h e \]

\[ \frac{di_s}{dt} = \beta_s be - (\mu_h + c)i_s \]

\[ \frac{di_a}{dt} = \beta_a be - (\mu_h + c)i_a \]

\[ \frac{dq}{dt} = c(i_s + i_a) - (\mu_h + g)q \]

where \( S + E + i_s + i_a + q + r = 1 \)
III. ANALYTICAL SOLUTIONS

A. Analytical Results

We use the standard dynamical modeling method to analyze our model. The equilibrium states are obtained by setting the right hand side of (2) equal to zero. The equilibrium states are given as the disease free state and the disease endemic state. The disease free state is \( G_1 = (1,0,0,0,0) \) and the disease endemic state is \( G_2 = (s^*, e^*, i^*_s, i^*_a, q^*) \) where
\[
s^* = \frac{(b(\beta_a + \beta_s) + \mu_h)(c + \mu_h)}{b(\beta_a + \beta_s)}
\]
\[
e^* = \frac{\mu_h(\mu_h(c + \mu_h) + b(\beta_a + \beta_s)(h - (c + \mu_h)))}{b(\beta_a + \beta_s)h(b(\beta_a + \beta_s) + \mu_h)}
\]
\[
i^*_s = \frac{\beta_a\mu_h(\mu_h(c + \mu_h) + b(\beta_a + \beta_s)(h - (c + \mu_h)))}{(\beta_a + \beta_s)h(b(\beta_a + \beta_s) + \mu_h)(c + \mu_h)} \tag{3}
\]
\[
i^*_a = \frac{\mu_h(\mu_h(c + \mu_h) + b(\beta_a + \beta_s)(h - (c + \mu_h)))}{(\beta_a + \beta_s)h(b(\beta_a + \beta_s) + \mu_h)(c + \mu_h)}
\]
\[
q^* = \frac{c \mu_h(\mu_h(c + \mu_h) + b(\beta_a + \beta_s)(h - (c + \mu_h)))}{b(\beta_a + \beta_s) + \mu_h}(c + \mu_h)\log(h + \mu_h).
\]

The local stability of each equilibrium state is determined by the sign of eigenvalues for each equilibrium state. The eigenvalues are obtained by solving the following characteristic equation:
\[
|J - \rho I| = 0 \tag{4}
\]
where \( J \) and \( I \) are the Jacobian matrix and identity matrix, respectively. If the real parts of all eigenvalues \((\rho)\) are negative then that equilibrium state is locally stable.

i) The disease free state \( G_1 = (1,0,0,0,0) \), the characteristic equation is given by
\[
(\rho + \mu_h)^2(\rho + g + \mu_h)(\rho + c + \mu_h)
\]
\[
+ b(\beta_a + \beta_s)(c + \mu_h)(\rho + 2\mu_h) + b(\beta_a + \beta_s)(c + \mu_h) = 0 \tag{5}
\]
The corresponding eigenvalues are given by
\[
\rho_{1,2} = -\mu_h - \mu_h = -2\mu_h
\]
\[
\rho_{3,6} = -\frac{1}{2}(b(\beta_a + \beta_s) + c + 2\mu_h)
\]
\[
\pm \sqrt{(-b(\beta_a + \beta_s) + c + 2\mu_h)^2 + 4b(\beta_a + \beta_s)h(\mu_h + \mu_h)} \tag{6}
\]

It can be seen that the real parts of the eigenvalues \(\rho_1, \rho_2, \rho_3\) and \(\rho_4\) are negative. From our evaluations, the eigenvalues \(\rho_5\) and \(\rho_6\) are negative when \(S_0 < 1\), where
\[
S_0 = \frac{b(\beta_a + \beta_s)h}{(c + \mu_h)(b(\beta_a + \beta_s) + \mu_h)} \tag{7}
\]
Hence, the disease free state is locally stable for \(S_0 < 1\).

ii) The disease endemic state \( G_2 = (s^*, e^*, i^*_s, i^*_a, q^*) \) where \(s^*, e^*, i^*_s, i^*_a, q^*\) are defined in (3), the characteristic equation of the disease endemic state is defined by
\[
\rho^4 + A_3\rho^3 + A_2\rho^2 + A_1\rho + A_0 = 0 \tag{8}
\]
where
\[
A_3 = \frac{\mu_h}{h}[2c^2(1 + \mu_h) + b(\beta_a + \beta_s)(c + \mu_h) + c\mu_h(6 + 5\mu_h)],
\]
\[
+ \mu_h(h + \mu_h(4 + 3\mu_h))]
\]
\[
A_2 = \frac{\mu_h(c + \mu_h)(c + 2\mu_h)}{b(\beta_a + \beta_s) + \mu_h} + \frac{S_0}{h}[c^3 + 5c^2\mu_h + 3\mu_h^2(h + \mu_h)]
\]
\[
+ c\mu_h(2h + 7\mu_h) + b(\beta_a + \beta_s)(c^2 + 2c\mu_h + \mu_h(h + \mu_h))]
\]
\[
A_1 = \mu_h(c + \mu_h)(b(\beta_a + \beta_s) + \mu_h)\left[-1 + \frac{2b(\beta_a + \beta_s) + c + 3\mu_h}{b(\beta_a + \beta_s) + \mu_h}\right]
\]
\[
A_0 = (b(\beta_a + \beta_s) + \mu_h)(c + \mu_h)(S_0 - 1) \tag{9}
\]

The sign of the real part of all eigenvalues can be determined by using the Routh–Hurwitz criteria [19-20]:

i) \(A_3 > 0\)

ii) \(A_4 > 0\)

iii) \(A_5 > 0\)

iv) \(A_6 - A_5^2 - A_4^2 > 0\).

It can be seen that \(A_3, A_4\) and \(A_5\) satisfy condition (i) to (iii) for \(S_0 > 1\). We consider
\[
A_3A_4 - A_5^2 - A_6 > 0
\]

All of the parameters in (10) are always positive. Hence, the term \(A_3A_4 - A_5^2 - A_6 > 0\) is greater than zero. So condition (iv) is satisfied. Therefore the endemic disease state is local stability for \(S_0 > 1\).

The basic reproductive number of the disease is evaluated by the averaging of the number of secondary patient that one case can produce if introduced into a susceptible human. This number is represented as \(R_0 = \sqrt{S_0}\).

B. Numerical Simulations

In this study, the transmission of Swine flu is considered with the different rate of transmission for virus to be symptomatic and asymptomatic infections. The value of the parameters used in this study are as follows:
\[
\mu_h = 1/(65 * 365), \beta_a = 0.25, \beta_s = 0.75, b = 1/2.5, c = 1/5, g = 1/14, S_0 = 0.9.
\]

The above parameters satisfy the real life observations; The life expectancy of the human is 65 years. The transmission
probability of swine flu to the human then that person become symptomatic patient is assumed to be 25%. The transmission probability of swine flu to the human then that person become asymptomatic patient is assumed to be 75%. The incubation period of swine flu in the human equals 2.5 days. The duration of the swine flu cases are moved to be the quarantine human equals 5 days. The duration of recovery equals 14 days. The other parameters are arbitrarily chosen.

Fig. 1 Numerical solutions of (2) for $R_0\lessgtr 1$ with $
\mu_b = 1/(65 \times 365), h = 0.2, \beta_s = 0.25, \beta_a = 0.75, b = 1/2.5, 
\alpha = 1/5, g = 1/14, S_0 = 0.9$. 

We can see from fig.1 that the numerical solutions converge to the disease free state.
The numerical solutions oscillate to the endemic disease state.

C. Unrealistic Parameter values

For finding the parameters to make a Hopf bifurcation is possible, we have selected a set of parameter values:

\[ \mu_h = 1/(65 \times 365), h = 0.45, \beta_s = 0.25, \beta_a = 0.75, b = 1/2.5, c = 1/5, g = 1/14, S_0 = 2.25. \]

The numerical solutions are shown in figure 3.
From our simulations, we can see that the limit cycle behavior can occur only for unrealistic parameters. This is impossible in the real life.

IV. DISCUSSION AND CONCLUSION

The basic reproductive number of the disease \( S_0 \) is represented as the geometric mean of \( S_0 \), where

\[
S_0 = \frac{b(\beta_a + \beta_s)h}{(c + \mu_h)(b(\beta_a + \beta_s) + \mu_h)}.
\]

The fractions of all populations for the different basic reproductive number are shown in the following figures:
Fig. 4 Bifurcation diagrams of (2) demonstrate the steady state solutions of susceptible, exposed, symptomatic infectious, asymptomatic infectious and quarantine human fractions for the different values of $S_0$. For $S_0 < 1$, $G_1$ will be stable. For $S_0 > 1$, $G_2$ will be stable.

If the threshold number is greater than one, the fraction of susceptible population decreases. The fractions of exposed, symptomatic infectious, asymptomatic infectious and quarantine populations increase. This subsequent characteristic occurs because there are enough susceptible persons to be infected from infectious persons.

Fig. 5 Time series solutions for symptomatic infectious and asymptomatic infectious human for the different values of the transmission probability of swine flu to the human then that person become symptomatic patient.
Fig. 6  Time series solutions for symptomatic infectious and asymptomatic infectious human for the different values of the transmission probability of swine flu to the human then that person become asymptomatic patient.

From fig.5 and fig.6, if the transmission probability of swine flu to the human and that person become symptomatic/asymptomatic patient is higher, then the fraction of symptomatic/asymptomatic patients is higher and the outburst of epidemic is longer. The results of this study shows the alternative way for decreasing the outbreak of the disease.

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