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ANALYSIS OF TRANSMISSION MODEL FOR INFLUENZA A(H1N1) VIRUS

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Abstract

An Influenza A (H1N1) causes a respiratory disease to many people. This disease has been occurred in many countries worldwide. It has been continuously announced. The infection can transmit between the people through coughing or sneezing with the virus. In this paper, we formulate the SEIQRS model to describe the transmission of Influenza A(H1N1) virus transmission. We assume that after each person is infected, that person can be infected again. The standard dynamical modeling method is used in this study. The threshold number is obtained to examine the stability of our model. The numerical solutions are shown to support the results. The behaviors of solutions for different threshold numbers are presented. The results of this study should point the new alternative way to reduce the transmission of influenza A(H1N1) virus.

1 Introduction

Influenza virus caused human flu has three types, ie. influenza A, influenza B and influenza C. A respiratory disease caused by influenza virus type A, so called Swine flu. In 2009, There was the outbreak of Swine flu due to infection with H1N1 influenza A and was first observed in Mexico. In 1976, there was an outbreak of swine flu at Fort Dix, New Jersey. This virus is not same as the 2009 outbreak, but it was similar to influenza virus type A. Swine flu also is an Emerging Infectious Disease (EID) because the Swine flu virus has not circulated previously in human; the virus is entirely new [1]. It usually spread

Key words: Influenza, standard dynamical modeling, equilibrium states, basic reproductive number, local stability.

among pigs and is not same as human flu virus. It does not often infect people, and the rare human cases that have occurred in the past have mainly affected people who had direct contact with pigs. But the current Swine flu outbreak is different. It is caused by a new Swine flu virus. It has changed in way of the transmission. The new Swine flu virus can spread from person to person, among people who have not had any contact with pigs. In the beginning of March 2009, An influenza outbreak of 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, 2009, two cases in children were also reported in California near the Mexican border. As of April 27, 2009, the United States Government had reported 40 laboratory confirmed human cases of swine flu, with no deaths. Mexico has reported 26 confirmed human cases of infection with the same virus, including seven deaths. The current outbreak of swine influenza A (H1N1) evolved so rapidly that as on April 29, 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 laboratory confirmed human cases and deaths due to rapidly progressive pneumonia, respiratory failure and acute respiratory distress syndrome (ARDS) [2].World Health Organization (WHO) declared ever 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 November 27, 2009[3]. Updated data on swine flu deaths has reached a total of 16,931 deaths as of March 21, 2010 [4]. Instead of misleading case counts, CDC has estimated the number of cases, hospitalizations, and deaths between April 2009 and April 10, 2010. The CDC has estimated that between 43 million and 89 million cases of 2009 H1N1, between 195,000 and 403,000 H1N1 cases related hospitalizations, and between about 8,870 and 18,300 H1N1 cases related deaths [5]. D. Klinkenberg, A. Everts-van der Wind, et al. [6] 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 and estimate the model parameters from data of the 1997/1998 CSFV epidemic in the Netherlands. In this paper, we study the transmission of Influenza A(H1N1) virus through mathematical modeling. The standard dynamical modeling method is used for analysis the behavior of solutions. In this paper, the formulation of model is presented in section 2. The analytical and numerical results are presented in section 3. Finally, the discussion and conclusion of our model are presented in section 4.

2 Mathematical model

We consider the transmission of influenza A (H1N1) virus between the people. The people are separated into 5 types such that susceptible, exposed, infectious, quarantine and recovered. We suppose that after each person is infected, that person can be infected again. The diagram of the transmission is presented in figure 1

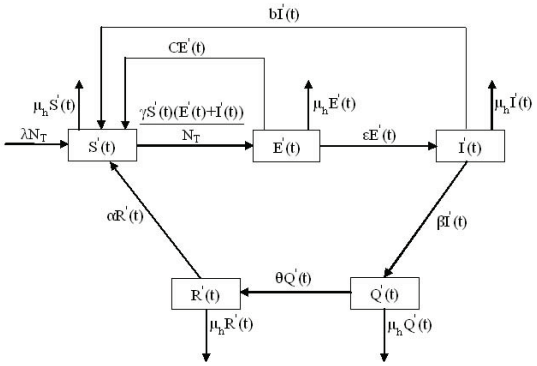


Figure 1: Flow chart of the model.

Let $S'(t)$ be the number of susceptible human at time t,
$E'(t)$ be the number of exposed human at time t,
$I'(t)$ be the number of infectious human at time t,
$Q'(t)$ be the number of quarantine human at time t,
$R'(t)$ be the number of recovered human at time t.
The dynamical equation for each human can be described as follows:

$$\frac{dS'(t)}{dt} = \lambda N_T - \gamma \frac{S'(t)(E'(t) + I'(t))}{N_T} + cE'(t) + bI'(t) + \alpha R'(t) - \mu_h S'(t) \tag{1}$$

$$\frac{dE'(t)}{dt} = \gamma \frac{S'(t)(E'(t) + I'(t))}{N_T} - (c + \varepsilon + \mu_h)E'(t) \tag{2}$$

$$\frac{dI'(t)}{dt} = \varepsilon E'(t) - (\beta + b + \mu_h)I'(t) \tag{3}$$

$$\frac{dQ'(t)}{dt} = \beta I'(t) - (\theta + \mu_h)Q'(t) \tag{4}$$

$$\frac{dR'(t)}{dt} = \theta Q'(t) - (\alpha + \mu_h)R'(t) \tag{5}$$

with the conditions:
$N_T = S'(t) + E'(t) + I'(t) + Q'(t) + R'(t)$

where
λ = the birth rate of human population,
N_T = the total human population,
γ = the contact rate of H1N1 virus transmission,
c = the rate at which the exposed human become to be susceptible human again,
μ_h = the death rate of human population,
$\varepsilon = 1/\text{IIP}$ where IIP is the intrinsic incubation period of H1N1 virus,
b = the rate at which the infectious human become to be the susceptible human again,
θ = the rate at which the quarantine human become to be the recovered human,
α = the rate at which the recovered human become to be the susceptible human again,
β = the rate at which the infectious human become to be the quarantine human,

The total size of population is assumed to be constant. Thus, the rate of change for each human group equals to zero. We set $\frac{dN_T}{dt} = 0$, then we obtain $\lambda = \mu_h$. We normalize our equations(1)-(5) by letting

$$S(t) = \frac{S'(t)}{N_T}, E(t) = \frac{E'(t)}{N_T}, I(t) = \frac{I'(t)}{N_T}, Q(t) = \frac{Q'(t)}{N_T}, R(t) = \frac{R'(t)}{N_T}$$

then the reduced equations become

$$\begin{aligned}\frac{dS(t)}{dt} &= \mu_h - \gamma S(t)(E(t) + I(t) + cE(t) + bI(t) + \\ &\quad \alpha(1 - S(t) - E(t) - I(t) - Q(t)) \ - \mu_h S(t) \qquad (6)\\ \frac{dE(t)}{dt} &= \gamma S(t)(E(t) + I(t)) - (c + \varepsilon + \mu_h)E(t) \qquad (7)\\ \frac{dI(t)}{dt} &= \varepsilon E(t) - (\beta + b + \mu_h)I(t) \qquad (8)\\ \frac{dQ(t)}{dt} &= \beta I(t) - (\theta + \mu_h)Q(t) \qquad (9)\end{aligned}$$

with the conditions

$$1 = S(t) + E(t) + I(t) + Q(t) + R(t) \qquad (10)$$

3 Analysis of the mathematical model

Analytical results
The steady states are obtained by setting the right hand sides of equations (6) to (9) equals to zero, then the steady states are as follows:

i) Disease free steady state: $E_0 = (1, 0, 0, 0)$.
ii) Disease endemic steady state: $E_1 = (S^*, E^*, I^*, Q^*)$.
where

$$I^* = \frac{(R_0 - 1)}{R_0} \frac{(\varepsilon L_3 L_4)}{[L_4(\mu_h L_1 + (\beta + \mu_h)\varepsilon + \alpha(L_1 + \varepsilon)) + \beta\varepsilon\alpha]}, \tag{11}$$

$$S^* = \frac{\mu_h + I^* \left(b + c\frac{L_1}{\varepsilon} + \frac{\alpha\beta\theta}{L_3 L_4} \right)}{\mu_h + I^* \frac{\gamma}{\varepsilon}(L_1 + \varepsilon)}, \tag{12}$$

$$E^* = I^* \left(\frac{L_1}{\varepsilon} \right), \tag{13}$$

$$Q^* = I^* \left(\frac{\beta}{L_4} \right), \tag{14}$$

where

$$R_0 = \frac{\gamma(b + \beta + \varepsilon + \mu_h)}{(b + \beta + \mu_h)(c + \varepsilon + \mu_h)} = \frac{\gamma(L_1 + \varepsilon)}{L_1 L_2}, \tag{15}$$

$$L_1 = b + \beta + \mu_h, \tag{16}$$

$$L_2 = c + \varepsilon + \mu_h, \tag{17}$$

$$L_3 = \alpha + \mu_h \quad \text{and} \tag{18}$$

$$L_4 = \theta + \mu_h. \tag{19}$$

Theorem 1. *The disease free steady state E_0 of equations (6)-(9) is locally asymptotically stable in D if $R_0 < 1$, and is unstable if $R_0 > 1$, where*

$$D = \{(S, E, I, Q) | S \geq 0, E \geq 0, I \geq 0, Q \geq 0, S + E + I + Q \leq 1\}.$$

Proof. To determine the local stable of the disease-free steady state E_0, we evaluate the Jacobian matrix $J(E_0)$ as follows:

$$J_{E_0} = \begin{bmatrix} -\alpha - \mu_h & -\gamma + c - \alpha & -\gamma + b - \alpha & -\alpha \\ 0 & \gamma - (c + \varepsilon + \mu_h) & \gamma & 0 \\ 0 & \varepsilon & -(\beta + b + \mu_h) & 0 \\ 0 & 0 & \beta & -(\theta + \mu_h) \end{bmatrix}$$

The eigenvalues of the above Jacobian matrix are

$$\eta_1 = -L_3, \eta_2 = -L_4, \eta_{3,4} = \frac{1}{2}[(\gamma - L_1 - L_2) \pm \sqrt{\Delta}]$$

where $\Delta = 4\varepsilon\gamma + \gamma^2 + 2\gamma L_1 + L_1^2 - 2\gamma L_2 - 2L_1 L_2 + L_2^2$

If $R_0 < 1$, then we have

$$\gamma L_1 - L_1 L_2 + \gamma\varepsilon < 0.$$

Consider $\Delta = (L_1L_2 - \gamma)^2 + 4(\gamma L_1 - L_1L_2 + \gamma\varepsilon)$
$< (L_1L_2 - \gamma)^2$.

That is

$\sqrt{\Delta} < L_1 + L_2 - \gamma$ when $L_1 + L_2 - \gamma \geq 0$.

$\lambda_3 = \frac{1}{2}[(\gamma - L_1 - L_2) + \sqrt{\Delta}] < \frac{1}{2}[(\gamma - L_1 - L_2) + L_1 + L_2 - \gamma] = 0,$

$\lambda_4 = \frac{1}{2}[(\gamma - L_1 - L_2) + \sqrt{\Delta}] < \frac{1}{2}[(\gamma - L_1 - L_2) - (L_1 + L_2 - \gamma)] \leq 0.$

Therefore all roots of the characteristic equations have negative real parts for $R_0 < 1$. Thus, the disease-free steady state E_0 is locally asymptotically stable for $R_0 < 1$ and unstable for $R_0 > 1$.

Theorem 2. *The disease-endemic steady state E_1 of equations (6)-(9) is locally asymptotically stable in D for $R_0 > 1$*

Proof. The Jacobian matrix at E_1 is given by:

$$J_{E_1} = \begin{bmatrix} -\gamma(E^* + I^*) - \alpha - \mu_h & -\gamma + S^* + c - \alpha & -\gamma S^* + b - \alpha & -\alpha \\ \gamma(E^* + I^*) & \gamma S^* - (c + \varepsilon + \mu_h) & \gamma S^* & 0 \\ 0 & \varepsilon & -(\beta + b + \mu_h) & 0 \\ 0 & 0 & \beta & -(\theta + \mu_h) \end{bmatrix}$$

The characteristic equation is

$$\eta^4 + a_3\eta^3 + a_2\eta^2 + a_1\eta + a_0 = 0 \tag{20}$$

where

$$a_3 = \alpha + b + x_4 + \gamma X_h^* + \theta \tag{21}$$

$$\begin{aligned} a_2 = {} & \beta(c + \varepsilon) + \beta E_h^*\gamma + \varepsilon E_h^*\gamma + \beta\gamma I_h^* + \varepsilon\gamma I_h^* + 3\beta\mu_h + 3c\mu_h + 3\varepsilon\mu_h + 3E_h^*\gamma\mu_h \\ & + 3\gamma I_h^*\mu_h + 6\mu_h^2 + \beta\gamma S_h^* + \varepsilon\gamma S_h^* + 3\gamma\mu_h S_h^* + x_3\theta + \gamma X_h^*\theta + b(c + \varepsilon + 3\mu_h \\ & + \gamma X_h^* + \theta) + \alpha(b + x_3 + \gamma X_h^* + \theta) \end{aligned} \tag{22}$$

$$\begin{aligned} a_1 = {} & \mu_h(\mu_h(3(c + \varepsilon) + 4\mu_h) + \gamma(2\varepsilon + 3\mu_h)X_h^* + b(2(c + \varepsilon + \gamma X_h^*) + 3\mu_h \\ & + 2\gamma X_h^*)) + (bm_2 + \mu_h(2(c + \varepsilon) + 3\mu_h) + \gamma(\varepsilon + 2\mu)X_h^*)\theta + \alpha((b + \beta)m_2 \\ & + \mu_h(2(c + \varepsilon) + 3\mu_h) + \gamma(\varepsilon + 2\mu_h)X_h^* + (b + \beta + m_2)\theta) + \beta(\mu_h(2c + 3\mu_h \\ & + 2\gamma X_h^* + (c + 2\mu_h + \gamma X_h^*)\theta + \varepsilon(\gamma(E_h^* + I_h^*) + 2\mu h + \theta)) \end{aligned} \tag{23}$$

$$\begin{aligned} a_0 = {} & (\beta(c\mu_h + m_4(\gamma(E_h^* + I_h^*) + \mu_h) + \gamma\mu_h S_h^*) + \mu_h(b(\varepsilon + m_3) + (c + m_4)\mu_h \\ & + \gamma m_4 X_h^*))(\mu_h + \theta) + \alpha((b(\varepsilon + m_3) + (c + m_4)\mu_h + \gamma m_4 X_h^*)(\mu_h + \theta) \\ & + \beta(m_3(\mu_h + \theta) + \varepsilon(\gamma(E_h^* + I_h^*) + \mu_h + \theta))) \end{aligned} \tag{24}$$

where

$X_h^* = S_h^* + E_h^* + I_h^*, x_3 = \beta + c + \varepsilon + 3\mu_h, x_4 = \beta + c + \varepsilon + 4\mu_h, m_2 = c + \varepsilon + 2\mu_h + \gamma X_h^*,$

$m_3 = c + \mu_h + \gamma X_h^*, m_4 = \varepsilon + \mu_h$

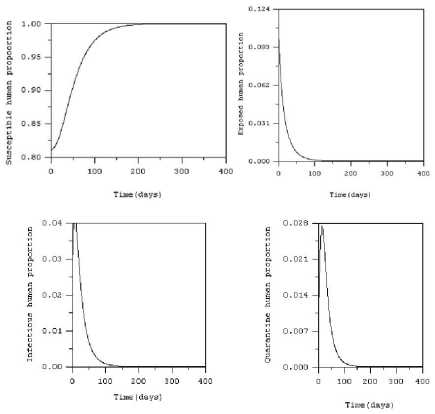
From the Routh-hurwitz criteria, the Disease-endemic steady state is local stability when it satisfied the following conditions:

$$\begin{aligned} &i)a_3 > 0 \\ &ii)a_1 > 0 \\ &iii)a_0 > 0 \\ &iv)a_1a_2a_3 - a_1^2 - a_3^2a_0 > 0 \end{aligned} \tag{25}$$

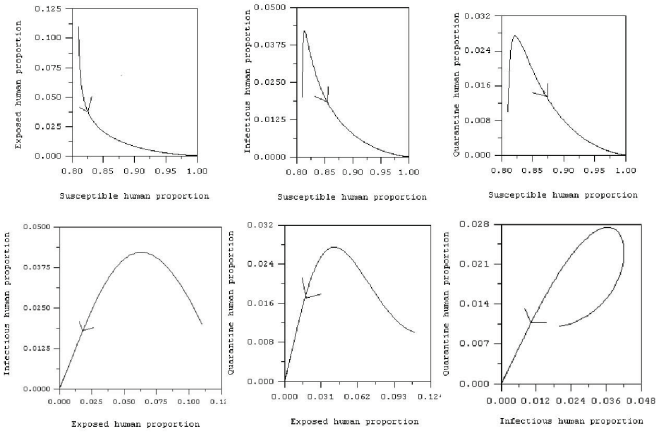
By using MATHEMATICA, the above conditions are satisfied when $R_0 > 1$. Thus, the endemic disease steady state is locally asymptotically stable for $R_0 > 1$.

Numerical results

In this section, we analyze the model given by equations (6)-(9). The parameters are define by $c = \frac{1}{30}$ per day satisfies to the 30 days of the exposed human become to be the susceptible human again, $\mu_h = \frac{1}{365 \times 65}$ per day corresponds to the average life time of 65 years for human population, $\varepsilon = \frac{1}{10}$ per day means the duration of intrinsic incubation of H1N1 is 10 days, $b = \frac{1}{40}$ per day satisfies to the 40 days at which infectious human become to be susceptible human again, $\theta = \frac{1}{6}$ per day corresponds to the 6 days at which quarantine human become to be recovered human, $\alpha = \frac{1}{30}$ per day corresponds to the 30 days at which recovered human become to be susceptible human again, $\beta = \frac{1}{8}$ per day corresponds to the 8 days at which infectious human become to be quarantine human, the contact rate of H1N1 virus transmission (γ) is arbitrarily chosen.The trajectories of solutions when the parameter values will lead to a disease free steady state and when they will lead to an endemic steady state are shown in the following figures.

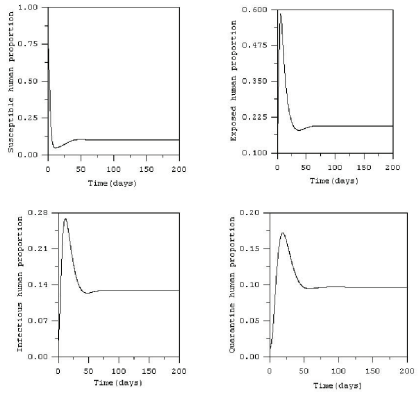


2a)

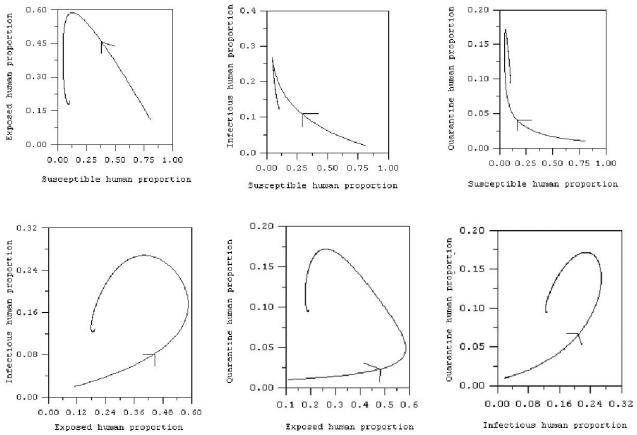


2b)

Figure 2: Behaviors of our model for $R_0 < 1$. The values of parameters are $c = \frac{1}{30}$ per day, $\mu_h = \frac{1}{365 \times 65}$ per day, $\varepsilon = \frac{1}{10}$ per day, $b = \frac{1}{40}$ per day, $\theta = \frac{1}{6}$ per day, $\alpha = \frac{1}{30}$ per day, $\beta = \frac{1}{8}$ per day, $\gamma = 0.05$ and $R_0 = 0.625$. 2a) Time series solutions of susceptible, exposed, infectious and quarantine human proportions, respectively. 2b) The trajectories of solutions projected onto the (S,E), (S,I), (S,Q), (E,I), (E,Q) and (I,Q) planes. The fractions of populations (S^*, E^*, I^*, Q^*) approach to the disease free steady state (1,0,0,0).



3a)



3b)

Figure 3: Behaviors of our model for $R_0 > 1$. The values of parameters are $c = \frac{1}{30}$ per day, $\mu_h = \frac{1}{365 \times 65}$ per day, $\varepsilon = \frac{1}{10}$ per day, $b = \frac{1}{40}$ per day, $\theta = \frac{1}{6}$ per day, $\alpha = \frac{1}{30}$ per day, $\beta = \frac{1}{8}$ per day, $\gamma = 0.8$ and $R_0 = 10$. 3a) Time series solutions of susceptible, exposed, infectious and quarantine human proportions, respectively. 3b) The trajectories of solutions projected onto the (S,E), (S,I), (S,Q), (E,I), (E,Q) and (I,Q) planes. The fractions of populations (S^*, E^*, I^*, Q^*) approach to the endemic disease steady state (0.100043,0.193052,0.128665,0.0964747).

4 Discussion and conclusion

In this study, the mathematical model of H1N1 transmission is analyzed, the threshold number is defined by

$$R_0 = \frac{\gamma(b+\beta+\varepsilon+\mu_h)}{(b+\beta+\mu_h)(c+\varepsilon+\mu_h)}$$

If the threshold number (R_0) is less than one, then the disease free state is local stability. The endemic disease state is local stability for R_0 is greater than one. The bifurcation diagrams are shown in figure 4.

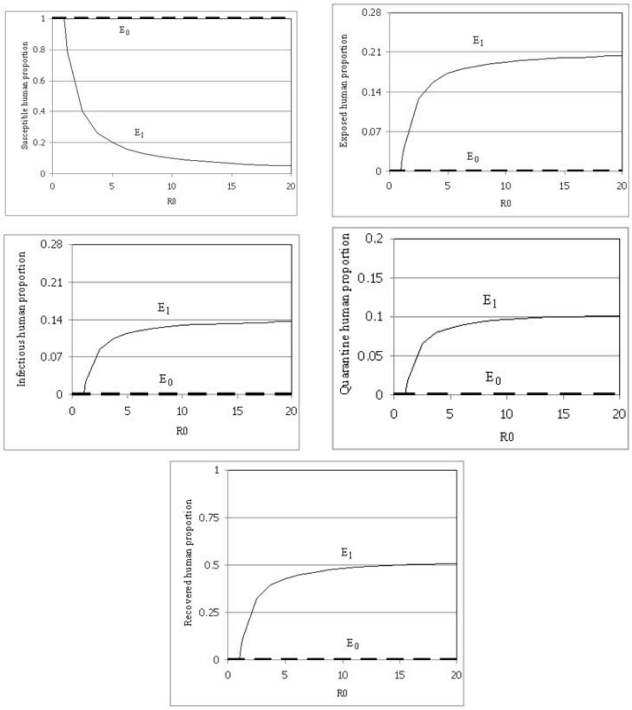


Figure 4: Bifurcation diagram of equations (6)-(9) demonstrate the steady state solutions of susceptible, exposed, infectious, quarantine and recovered human proportions with $c = \frac{1}{30}$ per day, $\mu_h = \frac{1}{365 \times 65}$ per day, $\varepsilon = \frac{1}{10}$ per day, $b = \frac{1}{40}$ per day, $\theta = \frac{1}{6}$ per day, $\alpha = \frac{1}{30}$ per day, $\beta = \frac{1}{8}$ per day. —— represents the stable solutions and - - - - represents the unstable solutions. For $R_0 < 1$, E_0 will be stable. For $R_0 > 1$, E_1 will be stable.

The basic reproductive number is defined by $R = \sqrt{R_0}$ [7]-[8]. It represents the average number of secondary patients that one patient can produce if introduced into a susceptible population. From the bifurcation diagram, if the basic reproductive number is less than or equal to one, then an infective replace itself with less than one new infective, the disease die out. If the basic reproductive number is more than one, then the proportion of susceptible classes decrease and the proportion of infectious classes increase. These behaviors occur because there are enough susceptible human to be infected from H1N1 infectious human.Furthermore, we simulate the behaviors of our solutions for the different threshold numbers as shown in figure 5.

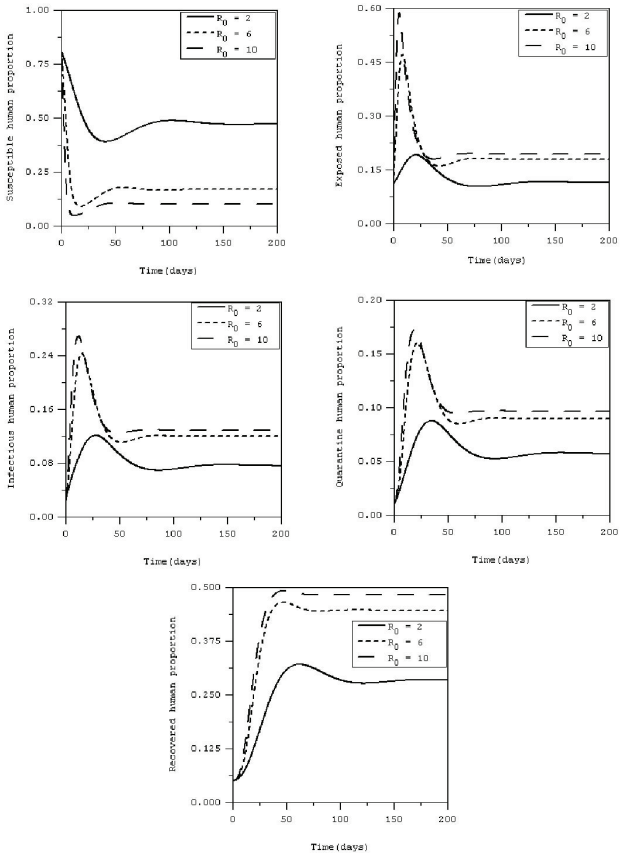


Figure 5: Time series solutions of susceptible, exposed, infectious and quarantine human proportions, respectively, for the different of R_0. The parameters are same as in figure 4.

From figure 5, we can see that if the basic reproductive number is higher, this means that one case can produce the greater number of secondary cases, and then the period of oscillation is shorter. Seasonal influenza occurs every year and the viruses change in each year, but many people have some immunity to the circulating virus that helps limit infections. By contrast, the pandemic swine flu virus was a new virus when it emerged and most people had no or little immunity to it [9]. The basic reproductive numbers are used for reducing the outbreak of many diseases [10-12]. The results of this study should point the way for decreasing the outbreak of this disease.

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