Stability Analysis of a Transmission Model for Influenza Virus A H1N1

Nguyen Huu Khanh

Abstract— We study a non-linear mathematical model describing the transmission of Influenza virus A H1N1. The model is represented by a system of differential equations depending on parameters. Mathematical analysis shows that dynamics of the spread of the influenza virus is determined by the basic reproduction number R_0. If $R_0 \leq 1$, the disease free equilibrium is globally asymptotically stable, and if $R_0 > 1$, the endemic equilibrium is globally asymptotically stable under some conditions. Lyapunov functional approach is used for proving the global stability of equilibria. A numerical investigation is carried out to confirmthe analytical results.

Index Terms— Influenza virus, disease free equilibrium, endemic equilibrium, basic reproductive ratio, stability, transcritical bifurcation.

1 Introduction

Influenza, also called the flu, is a disease caused by a virus that affects mainly the nose, throat, bronchi and, casionally, lungs.

Many papers have studied mathematical models for influenza virus. In 2003, Neil and coworkers [9] constructed a mathematical model of influenza transmission simulating the effect of neuraminidase inhibitor therapy on infection rates and transmission of drugresistant viral strains. In [12], an estimation of the basic reproduction number R_0 for pandemic influenza A H1N1 was made with the data from initial reports of laboratory confirmed pandemic influenza A H1N1. Recently, Pongsumpun [11], considered the model for the transmission of Swine flu, a new strain of type A influenza virus, with different probability of the patients who have symptomatic and asymptomatic infections.

In this paper, we consider a mode depicting the transmission of influenza virus A H1N1. The model is given by a system of five differential equations depending on parameters. We suppose that the infectious component consistes of symptomatic class and asymptomatic class; and the birth and natural death rates have a common rate μ. By using the method of next generation matrix [4], we found a threshold R_0 called basic reproduction number. In general, when $R_0 \leq 1$, the disease dies out andwhen $R_0 > 1$, the disease persists in the population. If we suppose that the endemic equilibrium also exists for $R_0 < 1$, although it is not true, then the bifurcation occurring in the model can be explained as a transcritical bifurcation. We concentrate our study on the globally stable stability of equilibria. This is obtained by Lyapunov functional approach. A numerical investigation is carried out by Mathematica software and AUTO software package [3] confirming analytic results.

The paper is organized as follows. In the next section, we introduce the structure of the transmission model, equilibria and the basic reproduction number. Section 3 deals with the stability of equilibria by using the Routh-Hurwit criterion and Lyapunov functional approach. Some numerical simulations are given in section 4. Finally, section 5 summarizes this work.

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2 The Model and Its Basic Properties

2.1 The structure of the model

We consider a model for the transmission of pandemic influenza A H1N1. In the model, individuals are classified as susceptible ($S(t)$), exposed ($E(t)$), symptomatic infectious ($I(t)$), asymptomatic and partially infectious ($A(t)$) and recovered ($R(t)$). Hence, the total population at time t is given by $N(t) = S(t) + E(t) + I(t) + A(t) + R(t)$. By rescaling, we can consider with $N(t) = 1$. We assume that the birth and natural death rates have common rate μ. Susceptible individuals in contact with the virus progress to the exposed class at the rate $\beta(E(t) + I(t))/N$, where β is the transmission rate. A proportion $0 < p < 1$ of talent individuals progress to the clinically infectious class $I(t)$ at the rate k while the rest $(1 - p)$ progress to the asymptomatic partially infectious class $A(t)$ at the same rate k. Symptomatic and asymptomatic cases progress to the covered class $R(t)$ at the rates γ_1 and γ_2.

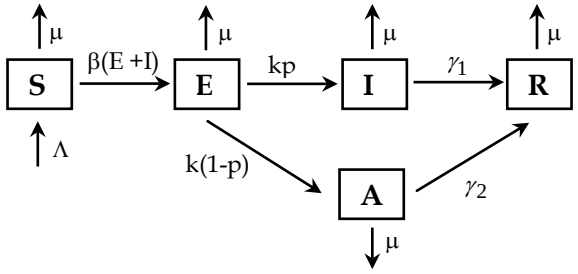

Fig 1. Transfer diagram of the model

The model is given by the following differential equations

$$\begin{aligned}
\frac{dS}{dt} &= \mu - \beta S(t)(E(t)+I(t)) - \mu S \\
\frac{dE}{dt} &= \beta S(t)(E(t)+I(t)) - (kp+\mu)E(t) \\
\frac{dI}{dt} &= kpE(t) - (\gamma_1+\mu)I(t) \\
\frac{dA}{dt} &= k(1-p)E(t) - (\gamma_2+\mu)A(t) \\
\frac{dR}{dt} &= \gamma_1 I(t) + \gamma_2 A(t) - \mu R(t).
\end{aligned} \tag{1}$$

with the condition

$$S(t)+E(t)+I(t)+A(t)+R(t)=1.$$

Because of the absence of the recovered class $R(t)$ in the first four equations, we can study the following reduced system:

$$\begin{aligned}
\frac{dS}{dt} &= \mu - \beta S(t)(E(t)+I(t)) - \mu S \\
\frac{dE}{dt} &= \beta S(t)(E(t)+I(t)) - (kp+\mu)E(t) \\
\frac{dI}{dt} &= kpE(t) - (\gamma_1+\mu)I(t) \\
\frac{dA}{dt} &= k(1-p)E(t) - (\gamma_2+\mu)A(t).
\end{aligned} \tag{2}$$

2.2 Invariant set

We establish the invariant set of the system (1) that is the set

$$D = \{(S(t),E(t),I(t),A(t),R(t)) : S(t),\ E(t),\ I(t),A(t),R(t) \ge 0\}.$$

This means that the solution of the system is still in D for $t > 0$. Hence, for the rest of the paper we only focus on system (1) restricted to D.

2.3 Equilibria

To find equilibria, we set the right-hand side of the system (2) equal to zero. There are two equilibria in the (S, E, I, A) space:

1) The disease free equilibrium $P_0(1, 0, 0, 0)$.

2) The endemic equilibrium $P_1(S^*, E^*, I^*, A^*)$ where

$$S^* = \frac{(\gamma_1+\mu)(kp+\mu)}{\beta(\gamma_1+kp+\mu)},$$

$$E^* = \frac{\mu[\beta(\gamma_1+kp+\mu)-(\gamma_1+\mu)(kp+\mu)]}{\beta(kp+\mu)(\gamma_1+kp+\mu)},$$

$$I^* = \frac{kp\mu[\beta(\gamma_1+kp+\mu)-(\gamma_1+\mu)(kp+\mu)]}{\beta(\gamma_1+\mu)(kp+\mu)(\gamma_1+kp+\mu)},$$

$$A^* = \frac{k(1-p)\mu[\beta(\gamma_1+kp+\mu)-(\gamma_1+\mu)(kp+\mu)]}{\beta(\gamma_1+\mu)(kp+\mu)(\gamma_1+kp+\mu)}.$$

It is seen that the disease free equilibrium P_0 always exists. When $R_0 > 1$ then $\beta(\gamma_1+kp+\mu)-(\gamma_1+\mu)(kp+\mu) > 0$. This implies the endemic equilibrium P_1 exists for $R_0 > 1$.

2.4 The basic reproductive ratio

The dynamics of the model is decided by the basic reproductive ratio R_0, which is defined as the number of newly infected cells that arise from any one cell when almost all cells are uninfected. By using the method of next generating matrix [4], we found that

$$R_0 = \frac{\beta(\gamma_1+kp+\mu)}{(\gamma_1+\mu)(kp+\mu)}.$$

As $R_0 < 1$, the system has an unique equilibrium P_0 and it is stable. For $R_0 > 1$, the system has two equilibria P_0 and P_1, where P_0 is unstable and P_1 is stable.

In the next section, we will show that for $R_0 < 1$ the transmission is extinct whereas for $R_0 > 1$ the virus still remain.

3 Stability of Equilibria

3.1 Local stability of equilibria

Theorem 1. *The disease free equilibrium P_0 is locally asymptotically stable if $R_0 < 1$. Whereas, P_0 is unstable if $R_0 > 1$.*

Proof

The Jacobian matrix at P_0 is given by

$$J_0 = \begin{pmatrix} -\mu & -\beta & -\beta & 0 \\ 0 & \beta-(kp+\mu) & \beta & 0 \\ 0 & kp & -(\gamma_1+\mu) & 0 \\ 0 & k(1-p) & 0 & -(\gamma_2+\mu) \end{pmatrix}$$

Eigenvalues of the above matrix are

$$\lambda_1 = -\mu,\ \ \lambda_2 = -\gamma_2 - \mu,$$

$$\lambda_3 = -\frac{1}{2}\left(L+\sqrt{L^2+4G}\right),\quad \lambda_4 = -\frac{1}{2}\left(L-\sqrt{L^2+4G}\right)$$

where

$$L = \gamma_1 + kp + 2\mu - \beta,\ \ G = \beta(\gamma_1+kp+\mu) - (\gamma_1+\mu)(kp+\mu).$$

Eigenvalues λ_1, λ_2 and λ_3 are always negative. If $R_0 < 1$, then $G < 0$. It implies $\lambda_4 < 0$. Therefore, P_0 is locally asymptotically stable. Whereas, for $R_0 > 1$ then $\lambda_4 > 0$ and P_0 is unstable. ■

Theorem 2. *The endemic equilibrium P_1 is local asymptotically stable for $R_0 > 1$.*

Proof

The local stability for endemic equilibria is determined by the Jacobian matrix of the system (1) at P_1, which is

$$J=\begin{pmatrix} -\beta(E^*+I^*)-\mu & -\beta S^* & -\beta S^* & 0 \\ \beta(E^*+I^*) & \beta S^*-(kp+\mu) & \beta S^* & 0 \\ 0 & kp & -(\gamma_1+\mu) & 0 \\ 0 & k(1-p) & 0 & -(\gamma_2+\mu) \end{pmatrix}.$$

The characteristic equation is given by

$$\lambda^4+a_3\lambda^3+a_2\lambda^2+a_1\lambda+a_0=0,$$

where

$$a_0=\beta(\gamma_1+\mu)(\gamma_2+\mu)(kp+\mu)(X^*+Y^*),$$

$$a_1=\gamma_2\left(3\mu^2+\beta kp(E^*+I^*-S^*)+2\mu\left(kp+\beta(E^*+I^*-S^*)\right)\right)$$
$$+\ \mu\left(4\mu^2+2\beta kp(E^*+I^*-S^*)+3\mu\left(kp+\beta(E^*+I^*-S^*)\right)\right)$$
$$+\ \gamma_1\left(3\mu^2+\beta kp(E^*+I^*)+2\mu\left(kp+\beta(E^*+I^*-S^*)\right)\right)$$
$$+\ \gamma_1\gamma_2(2\mu+kp+\beta(E^*+I^*-S^*)),$$

$$a_2=6\mu^2+\beta kp(E^*+I^*-S^*)+3\mu\left(kp+\beta(E^*+I^*-S^*)\right)$$
$$+\ \gamma_2\left(3\mu+kp+\beta(E^*+I^*-S^*)\right)+\gamma_1\left(\gamma_2+3\mu+kp+\beta(E^*+I^*-S^*)\right),$$

$$a_3=\gamma_1+\gamma_2+4p+kp+\beta(E^*+I^*-S^*).$$

By using Mathematica software, we can check that the following conditions are satisfied

$$a_0>0,\ \ a_1>0,\ a_3>0 \text{ and } a_1a_2a_3-a_1^2-a_0a_3^2>0.$$

According to the Routh-Hurwit criterion, the endemic equilibrium P_1 is locally stable. ■

3.2 Global stability of equilibria

In this section we use Lyapunov function to prove the global stability of equilibria.

Theorem 3. *If $R_0 \le 1$ then the disease free equilibrium P_0 is globally asymptotically stable in D.*

Proof

We construct the following Lyapunov fuction

$$W(t)=(S-1-\ln S)+E+aI+A.$$

where $\dfrac{\beta}{\gamma_1+\mu}<a<\dfrac{2kp+\mu-\beta-k}{kp}$, $2kp+\mu-\beta-k>0$.

The derivative of $W(t)$ along the curve of (2) is given by

$$W'(t)=\left(1-\frac{1}{S}\right)S'+E'+aI'+A'$$

$$=\left(1-\frac{1}{S}\right)\left(\mu-\beta S(E+I)-\mu S\right)+\left(\beta S(E+I)-(kp+\mu)E\right)$$
$$+\ a\left(kpE-(\gamma_1+\mu)I\right)+\left(k(1-p)E-(\gamma_2+\mu)A\right)$$

$$=-\frac{\mu(1-S)^2}{S}-\left(2kp+\mu-\beta-k-kp\right)E-\left(a(\gamma_1+\mu)-\beta\right)I-(\gamma_2+\mu)A.$$

Because $\dfrac{\beta}{\gamma_1+\mu}<a<\dfrac{2kp+\mu-\beta-k}{kp}$ then we have $a(\gamma_1+\mu)-\beta>0$ and $2kp+\mu-\beta-k-kp>0$.

Thus, $W'(t)\le 0$ for $R_0\le 1$. Note that $W'(t)=0$ if and only if $S = 1$, $E = I = A = 0$. Hence, the invariant set $\{(S, E, I, A): W'(t)=0\}$ is the singleton $\{P_0\}$, where P_0 is the disease free equilibrium point. Therefore, by the Salle 's invariance principle [11], P_0 is globally stable in the set D when $R_0\le 1$. This completes the proof. ■

Theorem 4. *If $R_0 > 1$ then the endemic equilibrium P_1 is globally asymptotically stable in D under some conditions of parameters.*

Proof

We construct the following Lyapunov function

$$W(t)=(S-S^*-\ln S)+(E-E^*\ln E)+a(I-I^*\ln I)+b(A-A^*\ln A),$$

where a and b are suitable constants.

The derivative of $W(t)$ along the curve of (2) is given by

$$W'(t)=\left(1-\frac{S^*}{S}\right)S'+\left(1-\frac{E^*}{E}\right)E'+k\left(1-\frac{I^*}{I}\right)I'+\left(1-\frac{A^*}{A}\right)A'$$

$$=\left(1-\frac{S^*}{S}\right)\left(\mu-\beta S(E+I)-\mu S\right)+\left(1-\frac{E^*}{E}\right)\left(\beta S(E+I)-(kp+\mu)E\right)$$

$$+\ a\left(1-\frac{I^*}{I}\right)\left(kpE-(\gamma_1+\mu)E\right)+b\left(1-\frac{A^*}{A}\right)\left(k(1-p)E-(\gamma_2+\mu)\right).$$

By using equations in (2) for P_1 and choosing suitable values for a and b, one can shows that $W'(t)\le 0$ for $R_0>1$. Note that $W'(t)=0$ if and only if $S = S^*$, $E = E^*$, $I = I^*$ and $A = A^*$. Therefore, by the Salle 's invariance principle [11], P_1 is globally stable in the set D when $R_0>1$. This completes the proof. ■

3.3 Bifurcation analysis

The change of local stability of the equilibria P_0 and P_1 can be explained by a transcritical bifurcation. In theory bifurcation, transcritical bifurcation is a local bifurcation in which an equilibrium having an eigenvalue whose real part passes through zero. In transcritical bifurcation, an equilibrium exists for all values of a parameter and is never destroyed. Such an equilibrium interchanges its stability with another equilibrium at bifurcation value, where they collide. In our system, the disease free equilibrium P_0 always exists. It is stable for $R_0 < 1$ and unstable for $R_0 > 1$. The endemic equilibrium P_1 exists for $R_0 > 1$ and it is unstable. If we suppose that P_1 also exists for $R_0 < 1$, although it is not real, then bifurcation in the model (1) can be seen as a form of transcritical bifurcation at $R_0 = 1$.

4 Numerical Simulation

In this section, we carry out a numerical investigation for the system (2) to illustrate the analytic results obtained above.

For $\beta = 0.15$, $\gamma_1 = 0.1$, $\gamma_2 = 0.25$, $k = 0.5$, $p = 0.5$, $\mu = 0.25$ we have $R_0 = 0.1514286 < 1$. In this case, the disease free equilibrium P_0 is globally asymptotically stable. With the condition $E(0) = 0.01$, $E(0) = 0.01$, $I(t) = 0.021$, $A(0) = 0.05$, the component

$E(t)$, $I(t)$ and $A(t)$ tend to 0 as t approaches to $+\infty$ (see Fig 2). This implies that the disease dies out.

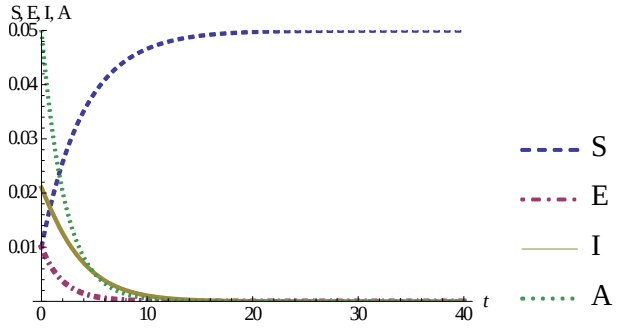

Fig 2. Time series of S, E, I, A for $R_0 < 1$.

For $\beta = 0.5$, $\gamma_1 = 0.1$, $\gamma_2 = 0.15$, $k = 1.5$, $p = 0.5$, $\mu = 0.15$ we have $R_0 = 2.222226 > 1$. In this case, the endemic equilibrium P_1 is globally asymptotically stable. With the condition $E(0) = 0.01$, $E(0) = 0.01$, $I(t) = 0.4$, $A(0) = 0.02$, the exposed component $E(t)$ tends to 0.052, the infectious component $I(t)$ tends to 0.185 and the asymptomatic infectious component $A(t)$ tends to 0.168 as t approaches to $+\infty$ (see Fig 3). This means that the disease remains in populations .

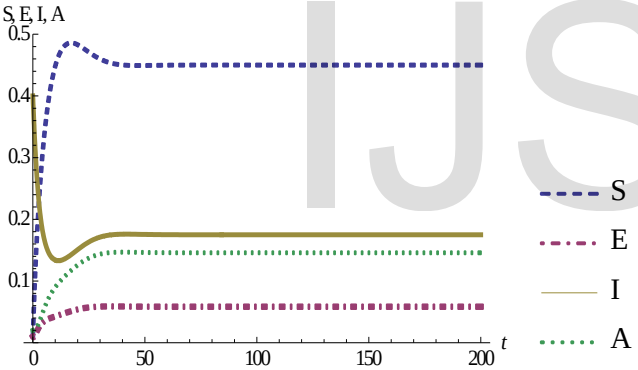

Fig 3. Time series of S, E, I, A for $R_0 > 1$

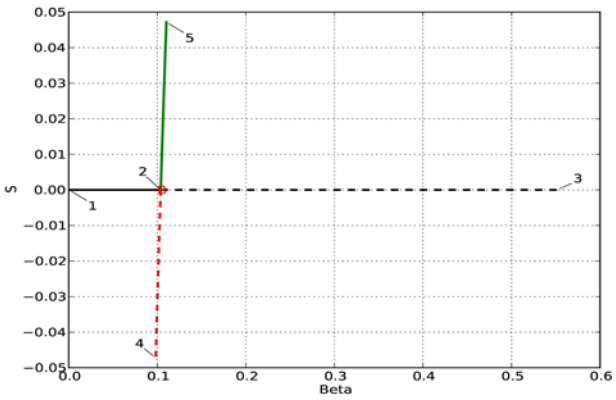

Fig 4. Bifurcation diagram of the system (2) in the plane (S, β)

By using AUTO software package [3], one can detect the transcritical bifurcation in the model.

For $p = 0.0155$, $k = 0.5$, $\gamma_1 = 0.025$, $\gamma_2 = 0.135$, $\mu = 0.1$, and let β vary then we get a transcritical bifurcation occurring at the value $\beta = 0{:}1038$. The bifurcation diagram for this case is given in Figure 4. In this figure, the line passing through the solution 1, 2 and 3 is the curve of disease free equilibrium, and the line containing the solution 4, 2 and 5 is the curve of endemic equilibrium. The solid line is for stable equilibria and the dashed line is for unstable equilibria. Transcritical bifurcation occurs at the solution 2, corresponding to $R_0 = 1$. We also obtain the same bifurcation when other parameters are varied.

5 Conclusion

In this paper, a new type of model for infectious diseases of influenza A H1N1 is introduced and studied. The basic reproduction number, R_0, of system (2) has been found by the method of the next generation matrix. The global stability of system (2) has been proved by using the Lyapunov function. When $R_0 \leq 1$, the system has only a disease free equilibrium P_0 which is globally stable. It implies that the disease dies out eventually. When $R_0 > 1$, the system has a unique endemic equilibrium P_1, which is globally stable under some conditions. This shows that the disease persists in the population and tends to a steady state. The local bifurcation, occurring at $R_0 = 1$, is explained by the transcritical bifurcation. As results indicate that the spread of disease is very sensitive to contact parameter β. The transmission will slow down if the value of β is decreasing. The obtained results show the way to reduce the transmission of the disease.

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