Stability analysis of hand foot and mouth infectious disease model with time delay and non monotonic contact rate

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Abstract: Based on the epidemic characteristics of the hand- foot- mouth disease, using non monotonic contact rate of the dependent variable function K (S) to represent a series of external and internal factors, not in the hand, foot and mouth disease dynamics model introduced in double time delay, and thus establish a touch delay and have not monotonous content, foot and mouth disease model, and then linearized model can be converted to a linear system, discusses the model disease-free equilibrium and the existence and stability of the endemic equilibrium, told of the disease- free equilibrium model is the only, and in 5 cases, the existence of the endemic equilibrium is discussed. Finally, it is found that the disease- free equilibrium is unstable when the basic regeneration number is greater than 1, and the local disease equilibrium is asymptotically stable.

1. Introduction

In the existing research on the model of the foot and mouth disease, the contact rate is monotonous or even saturated. However, in real life, the infection rate of many diseases does not tend to be saturated after monotonous increase due to various factors. At present, patients with hand, foot and mouth disease will be treated with isolation immediately after onset to prevent the disease from spreading again, so the contact rate function is only related to susceptible people, but not to patients. Therefore, in this paper, according to the characteristics of hand, foot and mouth disease in practice, the non-monotonic contact rate function $k(S)=\beta_1+\beta_2 S/1+\delta S^2$ of dependent variable S is used to express the influence of a series of external and internal factors. The introduction of double time lag in the kinetic model of hand, foot and mouth disease, the establishment of a hand, foot and mouth disease model with time lag and non-monotonic contact rate, can better study the impact of disease latency and restorer immune period on the transmission of infectious diseases. Therefore, it is proposed to be closer to the actual prevention and control strategy of infectious diseases.

2. Model establishment

Assuming that the contact rate function is monotonically increasing and then monotonically decreasing, the function $k(S)=\beta_1+\beta_2 S/1+\delta S^2$ can represent the law of hand, foot and mouth disease, which depends on the change of the susceptible person, where β1 refers to the consideration of the inhibitory factor. The constant contact rate before the promotion factor, β2 indicates the coefficient of action of the promoting factor, and δ indicates the coefficient of action of the inhibitor. Some factors will increase the contact rate, and others will reduce the contact rate. This non-monotonic contact rate function monotonically increases in the interval [0, m), monotonically decreasing in the interval [m, +∞), where

$$m = \frac{\sqrt{\beta_1^2\delta^2 + \beta_2^2\delta} - \beta_1\delta}{\beta_2\delta}$$

Based on the above assumptions, the literature [1] studied the following hand, foot and mouth disease models with non-monotonic contact rates.

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$$\begin{cases} \dfrac{dS}{dt} = \Lambda - k(s)IS + \gamma R - \mu S \\ \dfrac{dI}{dt} = k(s)IS + (\alpha + \mu)I \\ \dfrac{dR}{dt} = \alpha I - (\gamma + \mu)R \end{cases} \quad (1)$$

Where S(t), (I t), and R(t) are the number of susceptible, infected, and restored persons at time are external inputs to the population (assuming all are susceptible), and μ is natural death. The rate, α is the natural recovery rate of the infected person, and γ refers to the conversion rate of the individual who lost the immunity and returned to the susceptible person. The parameters Λ, μ, α and γ are positive constants, the parameters β2 and δ Is a non-negative constant.

In order to more realistically describe the infection pattern of hand, foot and mouth disease, and consider the effect of time lag on disease, study the following hand, foot and mouth disease model with time lag and non-monotonic contact rate.

$$\begin{cases} \dfrac{dS(t)}{dt} = \Lambda - \dfrac{\beta_1 + \beta_2 S(t)}{1 + \delta S^2(t)} I(t) + \gamma e^{-\mu\tau} R(t-\tau) - \mu S(t) \\ \dfrac{dE(t)}{dt} = \dfrac{\beta_1 + \beta_2 S(t)}{1 + \delta S^2(t)} I(t) - \dfrac{\beta_1 + \beta_2 e^{-\mu\omega} S(t-\omega)}{1 + \delta S^2(t-\omega)} I(t-\omega) - \mu E(t) \\ \dfrac{dI(t)}{dt} = \dfrac{\beta_1 + \beta_2 e^{-\mu\omega} S(t-\omega)}{1 + \delta S^2(t-\omega)} I(t-\omega) - (\alpha + \mu + d) I(t) \\ \dfrac{dQ(t)}{dt} = \alpha\rho I(t) - (\delta + \mu) Q(t) \\ \dfrac{dR(t)}{dt} = \alpha(I - \rho) I(t) + \delta Q(t) - \gamma e^{-\mu\tau} R(t-\tau) - \mu R(t) \\ N(t) = S(t) + E(t) + I(t) + Q(t) + R(t) \end{cases} \quad (2)$$

Where N(t) is the total population at time t, and S, E, I, Q, and R are the number of susceptible, latent, infected, hospitalized, and restorative individuals, respectively, and Λ is the constant input rate. 11 is the constant contact rate before considering the promoting factors and inhibitors, β2 is the promoting factor, δ is the inhibitory factor, γ is the conversion rate of the susceptible person who loses immunity and becomes susceptible, μ is the natural mortality rate, and d is the disease Mortality, α is the conversion rate of the latent to the infected person and the hospitalized isolate, ρ is the proportion of the total number of patients who are infected but does not need hospitalization, σ is the recovery rate of the hospitalized isolate, w is the disease latency, τ The immune period for the restorer to the disease.

Note that the system (2) does not contain E(t) except for the second equation, so in this project, the system (2) is converted to study the following subsystems.

$$\begin{cases} \dfrac{dS(t)}{dt} = \Lambda - \dfrac{\beta_1 + \beta_2 S(t)}{1 + \delta S^2(t)} I(t) + \gamma e^{-\mu\tau} R(t-\tau) - \mu S(t) \\ \dfrac{dI(t)}{dt} = \dfrac{\beta_1 + \beta_2 e^{-\mu\omega} S(t-\omega)}{1 + \delta S^2(t-\omega)} I(t-\omega) - (\alpha + \mu + d) I(t) \\ \dfrac{dQ(t)}{dt} = \alpha\rho I(t) - (\delta + \mu) Q(t) \\ \dfrac{dR(t)}{dt} = \alpha(I - \rho) I(t) + \delta Q(t) - \gamma e^{-\mu\tau} R(t-\tau) - \mu R(t) \\ N(t) = S(t) + E(t) + I(t) + Q(t) + R(t) \end{cases} \quad (3)$$

3. Qualitative analysis

3.1 The existence of balance points

The disease-free equilibrium point of the model is the constant solution of the system (3). Obviously, the system (3) has the only disease-free equilibrium point E0=(N0,0,0). According to the method of [2], the basic regeneration number is defined as

$$R_0 = \frac{e^{-\mu\omega}(\beta_1 N_0 + \beta_2 N_0^2)}{(\alpha+\mu+d)(1+\delta N_0^2)} \tag{4}$$

In order to find the endemic balance point of the system (3),

$$\Delta = \beta_1^2 e^{-2\mu\omega} - 4(\alpha+\mu+d)(\delta(\alpha+\mu+d) - \beta_2 e^{-\mu\omega}) \tag{5}$$

$$A = e^{\mu\omega}(\alpha+\mu+d) - \frac{\gamma e^{-\mu\tau}}{\gamma e^{-\mu\tau}+\mu}(\alpha(1-\rho) + \frac{\delta\alpha\rho}{\mu+\delta}) \tag{6}$$

According to the system (3), it is calculated

$$I^+ = \frac{\Lambda - \mu S^+}{A},\quad Q^+ = \frac{\alpha\rho}{\alpha+\mu},\quad R^+ = \frac{1}{\gamma e^{-\mu\tau}+\mu}(\alpha(1-\rho) + \frac{\delta\alpha\rho}{\mu+\delta}) \tag{7}$$

S^+ is determined by the following equation

$$(\delta(\alpha+\mu+d) - \beta_2 e^{-\mu w})S^{+2} - \beta_1 e^{-\mu w} S^+ + \alpha+\mu+d = 0 \tag{8}$$

In order to analyze the positive solution of the system (3), that is, the existence of the disease-free equilibrium point of the system (3), the above equations are discussed below.

(1) $\beta_2 e^{-\mu\omega} = \delta(\alpha+\mu+d)$ .System (3) has only one positive solution $S_1 = \frac{\alpha+\mu+d}{\beta_1 e^{-\mu\omega}}$, then there is $I_1 = \frac{\Lambda - \mu S_1}{A} > 0$.

(2) $\beta_2 e^{-\mu\omega} > \delta(\alpha+\mu+d)$ .At this time, Δ>0, system (3) has only one positive solution $S_2 = \frac{\beta_1 e^{-\mu\omega} + \sqrt{\Delta}}{2(\delta(\alpha+\mu+d) - \beta_2 e^{-\mu\omega})}$,Just make sure that $I_2 = \frac{\Lambda - \mu S_2}{A} > 0$ is true, and you can ensure that the balance point is positive, then there is $S_2 < N_0$, ie

$$2N_0(\delta(\alpha+\mu+d) - \beta_2 e^{-\mu\omega}) < \beta_1 e^{-\mu\omega} + \sqrt{\beta_1^2 e^{-2\mu\omega} - 4(\alpha+\mu+d)(\delta(\alpha+\mu+d) - \beta_2 e^{-\mu\omega})} \tag{9}$$

In this case, it is actually equivalent to $R_0 > 1$.

(3) $\beta_2 e^{-\mu\omega} > \delta(\alpha+\mu+d)$ .Assuming $\Delta \geq 0$, the system (3) can easily find 2 positive solutions, ie

$$S_2 = \frac{\beta_1 e^{-\mu\omega} - \sqrt{\Delta}}{2(\delta(\alpha+\mu+d) - \beta_2 e^{-\mu\omega})},\quad S_3 = \frac{\beta_1 e^{-\mu\omega} + \sqrt{\Delta}}{2(\delta(\alpha+\mu+d) - \beta_2 e^{-\mu\omega})}, \tag{10}$$

(4)But $I_i = \frac{\Lambda - \mu S_i}{A} > 0$, i = 2, 3, that is, $S_i < N_0$, must be discussed. The existence of I_2 and I_3 is now discussed in two cases.

- Case 1 Δ>0

When $I_2 > 0$ and $I_3 < 0$, you can get

$$2N_0(\delta(\alpha+\mu+d) - \beta_2 e^{-\mu\omega}) - \sqrt{\Delta} < \beta_1 e^{-\mu\omega} < 2N_0(\delta(\alpha+\mu+d) - \beta_2 e^{-\mu\omega}) + \sqrt{\Delta} \tag{11}$$

This contains

$$2N_0(\delta(\alpha+\mu+d)-\beta_2 e^{-\mu\omega})-\sqrt{\Delta}<\beta_1 e^{-\mu\omega}<2N_0(\delta(\alpha+\mu+d)-\beta_2 e^{-\mu\omega}) \quad (12)$$

Let's assume that the above formula is true.

$$\beta_1 e^{-\mu\omega}<2N_0(\delta(\alpha+\mu+d)-\beta_2 e^{-\mu\omega}) \quad (13)$$

$$2N_0(\delta(\alpha+\mu+d)-\beta_2 e^{-\mu\omega})-\beta_1 e^{-\mu\omega}\le\sqrt{\Delta} \quad (14)$$

And also contains

$$2N_0(\delta(\alpha+\mu+d)-\beta_2 e^{-\mu\omega})\le\beta_1 e^{-\mu\omega}<2N_0(\delta(\alpha+\mu+d)-\beta_2 e^{-\mu\omega})+\sqrt{\Delta} \quad (15)$$

Let's assume that the above formula is true.

$$\beta_1 e^{-\mu\omega}-2N_0(\delta(\alpha+\mu+d)-\beta_2 e^{-\mu\omega})<\sqrt{\Delta} \quad (16)$$

Therefore

$$2N_0(\delta(\alpha+\mu+d)-\beta_2 e^{-\mu\omega})-\sqrt{\Delta}<\beta_1 e^{-\mu\omega}>2N_0(\delta(\alpha+\mu+d)-\beta_2 e^{-\mu\omega})+\sqrt{\Delta} \quad (17)$$
$$\Leftrightarrow R_0>1$$

When $I_2>0$ and $I_3>0$,Can get the following conclusions

$$\beta_1 e^{-\mu\omega}<2N_0(\delta(\alpha+\mu+d)-\beta_2 e^{-\mu\omega})-\sqrt{\Delta}\Leftrightarrow R_0<1 \quad (18)$$

- Case 2 $\Delta=0$

When $I_2=I_3>0$, according to $S_i<N_0$, $\beta_1 e^{-\mu\omega}<2N_0(\delta(\alpha+\mu+d)-\beta_2 e^{-\mu\omega})$ can be obtained, so that

$$\begin{aligned}&\beta_1 e^{-\mu\omega}<2N_0(\delta(\alpha+\mu+d)-\beta_2 e^{-\mu\omega})\\&\Leftrightarrow \beta_1 e^{-\mu\omega}<2N_0(\delta(\alpha+\mu+d)-\beta_2 e^{-\mu\omega})-\sqrt{\Delta}\\&\Leftrightarrow R_0<1\end{aligned} \quad (19)$$

Based on the above discussion, the following conclusions are made:

(1) If $\beta_2 e^{-\mu w}=\delta(\alpha+\mu+d)$, when $R_0>1$, $E_1=(S_1, I_1, Q_1, R_1)$ is the only endogenous equilibrium point of system (3), when $R_0\le1$, system (3) has no endemic balance point, at this time

$$S_1=\frac{\alpha+\mu+d}{\beta_1 e^{-\mu\omega}}$$

$$I_1=\frac{\Lambda-\mu S_1}{A},\quad Q_1=\frac{\alpha\rho}{\alpha+\mu},\quad R_1=\frac{1}{\gamma e^{-\mu\tau}+\mu}(\alpha(1-\rho)+\frac{\delta\alpha\rho}{\delta+\mu})I_1$$

(2) If $\beta_2 e^{-\mu w}>\delta(\alpha+\mu+d)$, when $R_0>1$, $E_2=(S_2, I_2, Q_2, R_2)$ is the only endogenous equilibrium point of system (3), when $R_0\le1$, system (3) has no endemic balance point, at this time

$$S_2=\frac{\beta_1 e^{-\mu\omega}-\sqrt{\Delta}}{2(\delta(\alpha+\mu+d)-\beta_2 e^{-\mu\omega})}$$

$$I_2=\frac{\Lambda-\mu S_2}{A},\quad Q_2=\frac{\alpha\rho}{\alpha+\mu}I_2,\quad R_2=\frac{1}{\gamma e^{-\mu\tau}+\mu}(\alpha(1-\rho)+\frac{\delta\alpha\rho}{\delta+\mu})I_2$$

(3) If $\beta_2 e^{-\mu w}<\delta(\alpha+\mu+d)$, when $R_0<1$ and $\Delta>0$ are simultaneously established, system (3) has two endemic equilibrium points $E_2=(S_2, I_2, Q_2, R_2)$ And $E3=(S_3, I_3, Q_3, R_3)$, at this time

$$S_3=\frac{\beta_1 e^{-\mu\omega}+\sqrt{\Delta}}{2(\delta(\alpha+\mu+d)-\beta_2 e^{-\mu\omega})}$$

$$I_3 = \frac{\Lambda - \mu S_3}{A},\ Q_3 = \frac{\alpha\rho}{\alpha+\mu} I_3,\ R_3 = \frac{1}{\gamma e^{-\mu\tau} + \mu}(\alpha(1-\rho) + \frac{\delta\alpha\rho}{\delta+\mu}) I_3$$

(4) If $\beta_2 e^{-\mu w} < \delta(\alpha+\mu+d)$, when $R_0>1$ and $\Delta>0$ are simultaneously established , $E_2 = (S_2, I_2, Q_2, R_2)$ is the only endogenous balance point of system (3).

(5) There is also a special case where， If $\beta_2 e^{-\mu w} < \delta(\alpha+\mu+d)$， when $R_0 < 1$ and $\Delta=0$ are simultaneously established ,Then E_2, E_3 merge into a double root of the system (3), ie

$$E_* = (\frac{S_2+S_3}{2}, \frac{I_2+I_3}{2}, \frac{R_2+R_3}{2})$$

3.2 Stability of the balance point

- Stability of disease-free equilibrium

(1) It is calculated that the function H(S(t)) about S(t) monotonically increases on [0, $\frac{\beta_2 + \sqrt{\beta_2^2, \beta_1^2\delta}}{\beta_1\delta}$), and $\frac{\beta_2 + \sqrt{\beta_2^2, \beta_1^2\delta}}{\beta_1\delta}$ is H (S (t)) = $\frac{\beta_2 + \sqrt{\beta_2^2, \beta_1^2\delta}}{\beta_1\delta}$ maximum value, respectively discuss $R_0 > 1$ and $R_0 \le 1$ and $N_0 \le \frac{\beta_2 + \sqrt{\beta_2^2, \beta_1^2\delta}}{\beta_1\delta}$ At the time, the stability of the disease-free equilibrium point of the system (20) $\frac{\beta_2 + \sqrt{\beta_2^2, \beta_1^2\delta}}{\beta_1\delta}$. It can be obtained from the theorem 3.1 in the literature [2-5] that the disease-free equilibrium point E0 of the system (3) is in the system (3) when $R \le 1$ and $N_0 \le \frac{\beta_2 + \sqrt{\beta_2^2, \beta_1^2\delta}}{\beta_1\delta}$ are simultaneously established. The positive invariant concentration is locally stable.

(2) Next, discuss the stability of the disease-free equilibrium point when $R_0>1$. To facilitate the study of the system (3), turn it into a linearization system: let x (t) = S (t) - A/μ , y (t) =I (t),z (t) =Q (t),u (t) =R (t), and the corresponding feasible domain is {(x, y, z, u) ｜ $x \ge N_0$, $y \ge 0$, $z \ge 0$, $x + y + z \le 0$}. Then the linearization system of the system (3) is

$$\begin{cases} \frac{dx(t)}{dt} = -\frac{\beta_1 N_0 + \beta_2 N_0^2}{1+\delta S^2(t)} y(t) + \gamma e^{-\mu\tau} u(t-\tau) - \mu(x)t \\ \frac{dy(t)}{dt} = \frac{\beta_1 e^{-\mu\omega} N_0 + \beta_2 e^{-\mu\omega} N_0^2}{1+\delta N_0^2} y(t-\omega) - (\alpha+\mu+d) y(t) \\ \frac{dz(t)}{dt} = \alpha\rho y(t) - (\delta+\mu) z(t) \\ \frac{du(t)}{dt} = \alpha(I-\rho) y(t) + \delta z(t) - \gamma e^{-\mu\tau} u(t-\tau) - \mu u(t) \end{cases} \quad (20)$$

After MATLAB calculation, the characteristic equation of the system is obtained as

$$f(\lambda)(\lambda+\mu)(\lambda+\delta+\mu)(\lambda+\gamma e^{-\mu\tau} e^{-\lambda\tau} + \mu) = 0$$

When R0>1, there is (f 0)<0, and when $\lambda \to +\infty$, (f λ)$\to +\infty$. Therefore, there must be a λ(λ>0), so that (f λ)=0, that is, the system must have a eigen root of the positive real part, so the disease-free equilibrium point is unstable when $R_0>1$.

- Stability of endemic equilibrium

For convenience of writing, $E^+ = (S^+, I^+, Q^+, R^+)$ is used to represent all local disease balance points E_i (i = 1, 2, 3, *). Let $x(t)=S(t)=S(t)-S^+$, $y(t)=I(t)-I^+$,$z(t)=Q(t)-Q^+$,$u(t)=R(t)-R^+$, after translational transformation, the system can be transformed into the following system

$$\begin{cases} \dfrac{ds(t)}{dt} = -a_1 x(t) - a_2 y(t) + a_3 u(t-\tau) \\ \dfrac{dy(t)}{dt} = b_1 x(t-w) + b_2 y(t-w) - b_3 y(t) \\ \dfrac{dz(t)}{dt} = c_1 y(t) - c_2(t) \\ \dfrac{du(t)}{dt} = d_1 y(t) + d_2 z(t) - d3_1 u(t) - d_4 u(t-\tau) \end{cases} \tag{21}$$

Among them

$$a_1 = \mu + \frac{\beta_1 + 2\beta_2 S^+ - \beta_1 \delta S^{+^2}}{(1+\delta S^{+^2})^2}, a_2 = \frac{\beta_1 S^+ + \beta_2 S^{+^2}}{1+\delta S^{+^2}},$$

$$a_3 = \gamma e^{-\mu\tau}$$

$$b_1 = e^{-\mu\omega}\frac{\beta_1 + 2\beta_2 S^+ - \beta_1 \delta S^{+^2}}{(1+\delta S^{+^2})^2}, b_2 = e^{-\mu\omega}\frac{\beta_1 S^+ + \beta_2 S^{+^2}}{1+\delta S^{+^2}},$$

$$b_3 = \alpha + \mu + e + d$$

$$c_1 = \alpha\rho, c_2 = \delta + \mu, d_1 = \alpha(1-\rho), d_2 = \delta, d_3 = \mu, d_4 = \gamma e^{-\mu\tau}$$

The local stability of the systemic (3) endemic equilibrium point Ei = (i = 1, 2, 3, *) is equivalent to the global stability of the zero solution of the system (21). According to the inference 3.1 in the literature [2-5], the zero solution of the system (21) is globally asymptotically stable, that is, the endemic equilibrium point of the system (3) is locally asymptotically stable.

4. Conclusion

In this paper, the existence and stability of the disease-free balance point and the endemic disease balance point of the hand-foot-mouth disease model with time-delay and non-monotonic contact rate are discussed. It is known that the model has the only disease-free balance point, and in 5 cases The existence of the endemic equilibrium point E0=(N0,0,0,0) is discussed. Finally, it is found that the disease-free equilibrium point is unstable when the basic regeneration number is greater than 1, and the endemic disease equilibrium point is globally asymptotically stable. The existence and stability of the model equilibrium point discussed in this paper is only a theoretical discussion. In order to make the conclusion more convincing, what needs to be done is to numerically simulate the model and verify the conclusion. This is the next step. issues that need resolving.

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