Dynamic model of disease spread with two infection stages

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Abstract. The spread of infectious diseases has always been of concerns and a threat to public health. It has caused serious problems for the survival of human beings and other species. In epidemiology, mathematical models are the basic conceptual tools used to understand epidemic dynamics and to formulate control strategies. A mathematical model of the transmission dynamics of infectious disease is an important theoretical epidemiology method, which has been used to simulate in analyzing and control of infectious diseases. In this paper, we will discuss about disease model with infection-stage structure, where the period of infection is partitioned into two stages: the acute and the chronic stages. The disease-free equilibrium was locally asymptotically stable when \( R_0 < 1 \) and the endemic equilibrium was locally asymptotically stable when \( R_0 > 1 \).

1. Introduction

A disease is any condition of an organism with disturbed functional dynamic homeostasis and inability to perform to a necessary extent the functions providing productive relations with the environment. The spread of infectious diseases has always been of concerns and a threat to public health. In real terms, the outcome of advances in response to infectious disease threats reflects in marked progress in infectious disease control and human health protection [1]. The course of a disease infection can be divided into several distinct stages, namely chronic and acute stage [2]. Infection begins because of the interaction between susceptible individuals with disease seeds that exist in the surrounding environment. After the disease enter the body of a susceptible individual, then the initial infection level begins. When the disease worsens, it indicates that the disease has entered the chronic infection level.

In epidemiology, mathematical models are the basic conceptual tools used to understand epidemic dynamics and to formulate control strategies [3]. A mathematical model of the transmission dynamics of infectious disease is an important theoretical epidemiology method, which has been used to simulate in analyzing and control of infectious diseases [4]. There is a long distinguished history of mathematical models in epidemiology. Most of the models in mathematical epidemiology are compartmental models, with the population being divided into compartments. The first model used was SIR, in which persons in a population are either in three states: “healthy, but susceptible to infection”, “infected by the disease or virus”, and “recovery”. SIR model proposed by Kermack and McKendrick in 1927. This model is often used in cases of diseases that have the possibility of total recovery[5-9]. The SIS disease model is one of the simplest virus infection models, in which persons in a population are either in two states: “healthy, but susceptible to infection” or “infected by the disease or virus and, thus, infectious to neighbors”[10-13]. Junyuan and Fei have investigated of global stability SIS disease model with Lyapunov functional approach [14]. Yukihiko and Gergely have investigated of SIS disease model with a finite infectious period [15]. For diseases with long
infectious periods, it is more appropriate to introduce infection stages or progression stages into the disease models, for example Hepatitis B, schistosomiasis, malaria, gonorrhea and other sexually transmitted diseases [16].

In this paper, we will discuss about disease model with infection-stage structure, where the period of infection is partitioned into two stages: the chronic and the acute stages. Modifications models by adding some parameters and variables that simulate real conditions of the biological epidemical [17]. These tools are used to analyze the overall behavior of a population to an epidemic situation. Then the basic reproduction ratio was determined as well as the existence point of endemic and non-endemic equilibrium. For a compartmental model of the spread of infectious diseases the next-generation matrix is a method used to derive the basic reproduction ratio [10].Then the equilibrium point analysis method is used to determine the stability of the system [14].

2. Research Methods
In this section we consider a disease model with chronic and acute stages. We assume that the infected individuals in the chronic stage are transferred to the acute stage, and individuals in both stages can recover or die. Then we divide the total population into three groups: the susceptibles (S), the infectives in the chronic stage (I_1), and the infectives in the acute stage (I_2). After contacts with infectives, a susceptible is infected and enters the chronic stage, and then progresses to the acute stage. We assume that all the recruits are susceptible for infection. The transmission scheme is given in Figure 1.

![Figure 1. The schematic diagram of stage progression](image)

Based on the compartment diagram in Figure 1, the SIS model with two infection stages is given in System (1). The parameter descriptions are given in Table 1.

\[
\begin{align*}
\frac{dS}{dt} &= \mu A - \beta S(I_1 + kI_2) - \mu S + \gamma_1 I_1 + \gamma_2 I_2 \\
\frac{dI_1}{dt} &= \beta S(I_1 + kI_2) - (\alpha_1 + \mu) I_1 - \gamma_1 I_1 - \varepsilon I_1 \\
\frac{dI_2}{dt} &= \varepsilon I_1 - (\alpha_2 + \mu) I_2 - \gamma_2 I_2
\end{align*}
\]

(1)

**Table 1. Definition and parameter values**

| Parameters | Definition |
|------------|------------|
| \(\beta\)  | Transmission rate from individuals at the acute infection level to susceptible |
| \(\mu\)    | Natural birth and death rate |
| \(\alpha_1, \alpha_2\) | Death rate |
| \(\gamma_1, \gamma_2\) | Recovery rate |
| \(\varepsilon\) | Transition rate from acute infection level to chronic infection level |
| \(A\)      | Population size before infection |
| \(k\)      | Effectiveness between susceptible and individuals at chronic infection level |
3. Results and Discussion

The disease-free equilibrium of the System (1) is given by \( T_0 = (A, 0, 0) \). An endemic equilibrium of System (1) satisfies

\[
\begin{align*}
\mu A - \beta S \left( I_1 + kI_2 \right) - \mu S + \gamma_1 I_1 + \gamma_2 I_2 &= 0, \\
\beta S \left( I_1 + kI_2 \right) - \left( \alpha_2 + \mu \right) I_1 - \gamma_1 I_1 - \varepsilon I_1 &= 0, \\
\varepsilon I_1 - \left( \alpha_2 + \mu \right) I_2 - \gamma_1 I_2 &= 0.
\end{align*}
\]

(2) (3) (4)

According to Eq. (3) and Eq. (4), we get

\[
S = \frac{I_1 \left( \mu + \alpha_1 + \gamma_1 + \varepsilon \right)}{\beta \left( I_1 + I_2 \right)}.
\]

(5)

and

\[
I_2 = \frac{\varepsilon I_1}{\left( \mu + \alpha_2 + \gamma_2 \right)}.
\]

(6)

By substituting Eq. (6) to Eq. (5), we get

\[
S = \frac{\left( \mu + \alpha_2 + \gamma_2 \right) \left( \mu + \alpha_1 + \gamma_1 + \varepsilon \right)}{\beta \left( \mu + \alpha_2 + \gamma_2 + k\varepsilon \right)}.
\]

(7)

According to Eq. (2), we get

\[
\beta S \left( I_1 + kI_2 \right) = \mu A - \mu S + \gamma_1 I_1 + \gamma_2 I_2.
\]

(8)

By substituting Eq. (8) to Eq. (3), we get

\[
I_1 = \frac{\mu A - \mu S + \gamma_2 I_2}{\left( \alpha_1 + \mu + \varepsilon \right)}.
\]

(9)

By substituting Eq. (6) and Eq. (7) to Eq. (9), we get

\[
I_1 = \frac{\mu A \left( \mu + \alpha_2 + \gamma_2 \right)}{\left( \mu + \alpha_2 + \gamma_2 \right) \left( \alpha_1 + \mu + \varepsilon \right) - \varepsilon \gamma_2} \left( 1 - \frac{\left( \mu + \alpha_1 + \gamma_1 + \varepsilon \right) \left( \mu + \alpha_2 + \gamma_2 \right)}{\beta A \left( \mu + \alpha_2 + \gamma_2 + k\varepsilon \right)} \right).
\]

When \( I_1 > 0 \), then

\[
\frac{\beta A \left( \mu + \alpha_2 + \gamma_2 + k\varepsilon \right)}{\left( \mu + \alpha_1 + \gamma_1 + \varepsilon \right) \left( \mu + \alpha_2 + \gamma_2 \right)} > 1.
\]

Hence, the basic reproductive ratio of System (1) is given by

\[
R_0 = \frac{\beta A \left( \mu + \alpha_2 + \gamma_2 + k\varepsilon \right)}{\left( \mu + \alpha_1 + \gamma_1 + \varepsilon \right) \left( \mu + \alpha_2 + \gamma_2 \right)}.
\]

(10)

Then, the endemic equilibrium of the System (1) is \( T_1 = \left( S^*, I_1^*, I_2^* \right) \) with

\[
S^* = \frac{\left( \mu + \alpha_2 + \gamma_2 \right) \left( \mu + \alpha_1 + \gamma_1 + \varepsilon \right)}{\beta \left( \mu + \alpha_2 + \gamma_2 \right)},
\]

\[
I_1^* = \frac{\mu A \left( \mu + \alpha_2 + \gamma_2 \right)}{\left( \mu + \alpha_2 + \gamma_2 \right) \left( \alpha_1 + \mu + \varepsilon \right) - \varepsilon \gamma_2} \left( 1 - \frac{1}{R_0} \right),
\]

\[
I_2^* = \frac{\varepsilon I_1^*}{\left( \mu + \alpha_2 + \gamma_2 \right)}.
\]

The endemic equilibrium \( T_1 \) exists if and only if \( R_0 > 1 \).

**Theorem 1.** The disease-free equilibrium of System (1) is locally asymptotically stable if and only if \( R_0 < 1 \).

**Proof.** The corresponding Jacobian matrix of \( T_0 \) is as follows
where
\[ m = \mu + \gamma_1 + \alpha_1 + \varepsilon \]
\[ n = \mu + \gamma_2 + \alpha_2. \]

Eigenvalues of \( J_{(r_i)} \) are
\[ \lambda_1 = -\mu, \]
\[ \lambda_{2,3} = -\frac{b_3 \pm \sqrt{b_3^2 - 4c_1}}{2}, \]
where
\[ b_3 = m + n - \beta A, \]
\[ c_1 = mn - \beta A(n + k\varepsilon). \]

It can be observed that all of the eigenvalues of \( J_{(r_i)} \) are negative if and only if \( R_0 < 1. \)

**Theorem 2.** The endemic equilibrium of System (1) is locally asymptotically stable if and only if \( R_0 > 1. \)

**Proof.** The corresponding Jacobian matrix of \( T_1 \) is as follows
\[
J_{(r_i)} = \begin{pmatrix}
-\mu & -\beta A + \gamma_1 & -\beta kA + \gamma_2 \\
0 & \beta A - m & \beta kA \\
0 & \varepsilon & -n
\end{pmatrix},
\]
where
\[ m = \mu + \gamma_1 + \alpha_1 + \varepsilon \]
\[ n = \mu + \gamma_2 + \alpha_2. \]

The characteristic polynomial of the matrix is \( \lambda^3 + a_2\lambda^2 + b_2\lambda + c_2 = 0, \) where
\[ a_2 = \mu + n + \frac{\beta I^*_1(n + k\varepsilon)}{n} + \frac{mk\varepsilon}{(n + k\varepsilon)} \]
\[ b_2 = \frac{\beta I^*_1(n + k\varepsilon)}{n}(m - \gamma_1) + \beta I^*_1(n + k\varepsilon) + \mu n + \frac{mn^2 + mk\varepsilon}{(n + k\varepsilon)} \]
\[ c_2 = \frac{\beta I^*_1(n + k\varepsilon)[(\mu + \alpha_1)n + (n - \gamma_2)\varepsilon]}{n}. \]

Therefore, by Routh-Herwitz criteria, we conclude that the eigenvalues of \( J_{(r_i)} \) are all negative when \( R_0 > 1. \)

Based on the equilibrium points, we will illustrate the dynamics of the diseases with different stages of infection for controlling Hepatitis B. It is performed by analyzing the effect of basic reproduction ratio to transmission rate from individuals at the acute infection level to susceptible. The values of the parameters and the initial conditions are given in Table 2 [10].
Table 2. Initial condition and parameter values

| Symbols | Value | Dimension |
|---------|-------|-----------|
| $S(0)$ | 1300  | human     |
| $I_1(0)$ | 150   | human     |
| $I_2(0)$ | 50    | human     |
| $t$     | [0,40] | year      |
| $\mu$   | 0.06  | day$^{-1}$|
| $\alpha_1$ | 0.08 | day$^{-1}$|
| $\alpha_2$ | 0.15 | day$^{-1}$|
| $\gamma_1$ | 0.22 | day$^{-1}$|
| $\gamma_2$ | 0.12 | day$^{-1}$|
| $\epsilon$ | 0.175 | day$^{-1}$|
| $A$     | 1500  | human     |
| $k$     | 2     | -         |

Substituting parameter values on Table 2 to Eq. (10), we get

$$R_0 = 5777.40017 \beta.$$  \hspace{1cm}(11)

Substituting $R_0 = 1$ to Eq. (11), we get $\beta = 0.00017$. The simulation is divided into two cases, i.e. $R_0 < 1$ and $R_0 > 1$. Based on Figure 2, shown that $R_0 < 1$ fulfilled if $0 < \beta < 0.00017$. Based on Eq. (11), shown that $R_0 > 1$ fulfilled if $\beta > 0.00017$. These cases illustrated in Figure 2 below.

![Figure 2](image)

**Figure 2** (a) Simulation of case $R_0 < 1$, (b) Simulation of case $R_0 > 1$

Based on Table 3 below, shown that the number of *Hepatitis B* cases decreases significantly when the transmission rate from individuals at the acute infection level to susceptible ($\beta$) is reduced.
4. Conclusion

A dynamical model for transmission of about disease with infection-stage structure was developed in this study. In this model, the population is divided into three compartments, ie susceptible individuals, infected individuals at the chronic infection level, and infected individuals at acute infection level. The basic reproduction ratio and equilibrium points, i.e. the disease-free and the endemic equilibrium of the model, were obtained. The disease-free equilibrium was locally asymptotically stable when \( R_0 < 1 \) and the endemic equilibrium was locally asymptotically stable when \( R_0 > 1 \). Numerical simulation Hepatitis B cases decreases significantly when the transmission rate from individuals at the acute infection level to susceptible is reduced. For computations and plots, the Maple packages were used.

References

[1] Nii-Trebi N I 2017 *Biomed Res. Int* **13**(1) 1
[2] Cohen J, Powderly W G and Opal S M 2017 *Infectious Diseases* 4th Edition (New York: Elsevier Inc)
[3] Mahmudah D E A, Suryanto and Trisilowati 2013 *Appl. Math. Sci.* **7**(99) 4919–4927
[4] Liang P, Zu J and Zhuang G 2018 *J. Epidemiol.* **28**(5) 221
[5] Zhou A, Sattayatham P and Jiao J 2016 *Adv. Differ. Equ.* **2016**(140) 1
[6] Barro M, Guiro A and Ouedraogo D 2018 *CUBO A Math. J.* **20**(2) 53
[7] Hussin A, Omar A, and Hasan Y A 2013 *Sci. Asia* **39**(1) 42
[8] Han Q and Wang Z 2015 *Adv. Differ. Equations* **333**(2015) 1
[9] Muroya Y 2013 *Nonlinear Anal. Real World Appl.* **14**(2013) 1693
[10] Tassier T 2013 *The Economics of Epidemiology* (New York: Springer)
[11] Brauer F, van den Driessche P, and Wu J 2000 *Mathematical Epidemiology* (New York: Springer)
[12] Diekmann O and Heesterbeek J 2000 *Mathematical Epidemiology of Infectious Diseases, Model Building, Analysis and Interpretation* (Chichester: John Wiley and Son).
[13] Bichara D, Kang Y, Horan R, and Perrings C 2015 *Bull. Math. Biol.* **77**(11) 2004
[14] Yang J and Xu F 2018 *J. Franklin Inst.* **355**(14) 6763
[15] Nakata Y and Röst G 2018 *Differ. Integr. Equations* **31**(3) 161
[16] Ma Z and Li J 2019 *Dynamical Modeling and Analysis of Epidemics*. (Singapore: World Scientific Publishing)
[17] Cantó B, Coll C, and Sánchez E 2017 *Adv. Differ. Equ.* **2017**(33) 1

Table 3. The number of Hepatitis B cases based on transmission rate

| \( \beta \) | \( S(t) \) | \( I_1(t) \) | \( I_2(t) \) |
|---------|--------|----------|----------|
| 0.00085 | 1500   | 0        | 0        |
| 0.00017 | 1350   | 20       | 15       |
| 0.001   | 260    | 297      | 158      |