Analysis of a Dengue Model with Vertical Transmission and Application to the 2014 Dengue Outbreak in Guangdong Province, China

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Abstract

There is evidence showing that vertical transmission of dengue virus exists in *Aedes* mosquitoes. In this paper we propose a deterministic dengue model with vertical transmission in mosquitoes by including aquatic mosquitoes (eggs, larvae and pupae), adult mosquitoes (susceptible, exposed and infectious), and human hosts (susceptible, exposed, infectious and recovered). We first analyze the existence and stability of disease-free equilibria, calculate the basic reproduction number, and discuss the existence of the disease-endemic equilibrium. Then we study the impact of vertical transmission of the virus in mosquitoes on the spread dynamics of dengue. We also use the model to simulate the reported infected human data from the 2014 dengue outbreak in Guangdong Province, China, and carry out sensitivity analysis of the basic reproduction number in terms of the model parameters.

Keywords: Dengue, vertical transmission, mathematical model, basic reproduction number, disease-free and disease-endemic equilibra

1 Introduction

Dengue is regarded as the most prevalent and rapidly spreading mosquito-borne viral disease of humans. It is endemic in more than 100 counties in southeast Asia, the Americas, the western Pacific, Africa and the eastern Mediterranean regions (Guzman & Harris [22]). As many as 400 million people are infected yearly (CDC [7]). Over 2.5 billion people (over 40% of the world's population) are now at risk from dengue (WHO [44]). There are four distinct but closely related serotypes of the dengue virus, DENV-1,2,3,4. *Aedes aegypti* and *Aedes albopictus* are the main vector transmitters of the dengue virus. In tropical and subtropical regions, the disease shows a resurgent pattern with yearly epidemics, which starts typically in the months with heavy rains and heat, peaking about three or four months after the beginning of the rainy season. It is believed that vertical transmission in mosquitoes with a fraction of the eggs remaining infected leads to the re-appearance of dengue in the same regions (Monath & Heinz [31]).

In China, *Aedes albopictus* is the most important mosquito in dengue transmission (Bai et al. [4]). It can breed in various small containers or plants that hold accumulated water (such as tree

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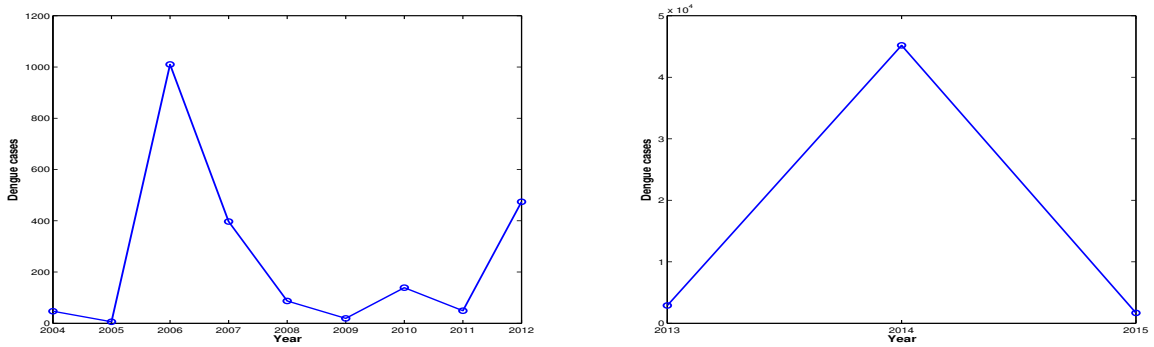
holes, bamboo stems, or leaf axils). Sporadic cases and outbreaks of dengue in the southeast coast regions and the middle and lower reaches of the Yangtze River were documented in the early 1940s, and no cases were reported until 1978 when a sudden outbreak occurred in Foshan, Guangdong Province. Since then all four serotypes of dengue have been recorded (Wu et al. [45]). Before 2010, dengue was characterized as an imported epidemic disease and had not been confirmed to be endemic. From 1978 to 2014, a total of 708,073 human dengue fever cases were reported in Mainland China (Chen & Liu [9]), in southeastern provinces including Guangdong, Hainan, Guangxi, Fujian, Zhejiang and Yunan Provinces. In 2014, a large outbreak of dengue with the most documented human cases occurred in Guangdong Province (HDGD [25]).

In recent years, Guangdong Province has had the highest incidence of dengue in China with cases reported every year, and dengue infections have been reported in Guangdong every year since 2004 (Figure 1). Guangdong Province is located in the southeast of Mainland China, adjacent to Hong Kong and Macao Special Administrative Regions, covering about 179,800 km^2. The average temperature of September of Guangdong Province was 28.1°C in 2014, which was 1.3°C more than usual (GMS [20]). The average temperature of November was 24.8°C in 2014, which was 0.9°C more than usual (GMS [21]). There were more than 101 million visits by international travelers in 2013 (SBGP [38]). *Aedes albopictus* mosquito has been displacing the domestic *Aedes aegypti* mosquito in Guangdong Province to become the major vector of dengue. There was a serious and large-scale outbreak of dengue with 45,129 human cases reported in more than 20 cities of Guangdong Province in 2014, including Guangzhou (37,331 cases), Foshan (3,540 cases), Zhongshan (678 cases), Jiangmen (594 cases), Zhuhai (505 cases), Shenzhen (447 cases), Qingyuan (296 cases), Yangjiang (289 cases), Dongguan (286 cases), Zhaoqing (276 cases), Shantou (245 cases), Zhanjiang (230 cases), and so on (HDGP [24]).



(a) From 2004 to 2012

(b) From 2013 to 2015

Figure 1: The yearly reported dengue cases in Guangdong Province from 2004 to 2015 ([25]).

Various models have been proposed by researchers to study the transmission dynamics of dengue virus investigating different aspects of its spread and behavior, from standard mosquito-borne disease models (Esteva & Vargas [15], Focks et al. [18]) to models incorporating space (Chowell et al. [11], Robert et al. [35]), seasonality and temperature dependence (Bartley et al. [5], Coutinho et al. [12], Katri [28], Stoddard et al. [40]), cross-immunity with multiple strains (Wearing & Rohani [43], Feng & Velasco-Hernandez [17]), and effectiveness of control measures (Chao et al. [8], Pinho et al. [33]). Vertical transmission of dengue virus has been observed in wild *Ae. aegypti* and *Ae. albopictus* mosquitoes (Hull et al. [27], Kow et al. [29], Pherez [32]). Mathematical models have also been proposed to investigate the effect of vertical transmission of dengue virus in mosquitoes (Esteva & Vargas [15], Adams & Boots [1]). Li et al. [30] and Tang

et al. [41] developed mathematical models to characterize the transmission dynamics of the 2014 dengue outbreaks in Guangdong Province.

It is evident that vertical transmission in mosquitoes with a fraction of the eggs remaining infected leads to the re-appearance of dengue in the same regions (Monath & Heinz [31]) and it has been suggested that vertical transmission is one of means by which dengue virus persists. However, it is unclear how widespread vertical transmission is in nature and how important vertical transmission is in the epidemiology and control of dengue. Via mathematical modeling, Esteva & Vargas [15] examined vertical transmission of dengue virus and suggested that vertical transmission favored endemic dengue fever and could be important in areas of low human density. The mathematical models of Coutinho et al. [12] indicated that vertical transmission could help dengue virus to survive through seasons of low adult vector populations. Adams & Boots [1] considered an extensive model to examine the impact of vertical transmission on the epidemiology of dengue virus and concluded that it would be unlikely that vertical transmission was important to the ecological dynamics of dengue virus.

In this paper in order to study the impact of vertical transmission of the virus in mosquitoes on the spread dynamics of dengue between mosquito vectors and human hosts, we propose a deterministic dengue model with vertical transmission in mosquitoes by including aquatic mosquitoes (eggs, larvae and pupae), adult mosquitoes (susceptible, exposed and infectious), and human hosts (susceptible, exposed, infectious and recovered). We first analyze the existence and stability of disease-free equilibria, calculate the basic reproduction number, and discuss the existence of the disease-endemic equilibrium. Then we study the impact of vertical transmission on the dynamics of the model. Finally we use the model to simulate the reported infected human data from the 2014 dengue outbreak in Guangdong Province, China, and carry out sensitivity analysis of the basic reproduction number in terms of the model parameters.

2 Mathematical model

For simplicity, only a single serotype model is considered in this paper. We describe the dynamics of dengue in its three components of transmission: the aquatic mosquitoes (ncluding the eggs, larvae and pupae), the adult mosquitoes and human hosts. We divide the aquatic mosquitoes into susceptible (S_A) and infected aquatic mosquitoes (I_A) subgroups. The incubation period for adult mosquitoes lasts between 10 and 12 days for an average mosquito lifespans raging from 11 to 20 days, and therefore, should not be ignored in the transmission of dengue. The adult mosquitoes are divided into susceptible (A_M), exposed (E_M) and infectious (I_M) subgroups. Similar to the assumption in [12], the mosquito population follows a logistic growth. Evidence shows that vertical transmission of the virus exists in mosquitoes (Buckner et al. [6]), which is described by the term $(1-\nu)\mu_M I_M(1-\frac{N_A}{k_A})$. The human population is divided into susceptible (S_H), exposed (E_H), infectious (I_H) and recovered (R_H) subpopulations. We assume that people are immune after they recover.

We construct the model based on the dengue endemic situation in Guangdong Province of China in 2014. The total population of Guangdong Province was 106.44×10^6 in 2013, the birth rate was 10.71‰, and the newborn population in 2013 was $1,137,300$ (SBGP [39]). Thus, the newborn population per day was $3,116$. The mortality population in 2013 was $498,000$ and the mortality rate was 4.69‰ ([39]). Then, the mortality population per day was $1,364$ and the mortality rate per day was 1.28×10^{-5}. Till October 31, the total reported dengue related deaths in 2014 was 6, which is very small compared with the total of $42,358$ reported infected cases of dengue in Guangdong Province. Therefore, we ignore the disease induced mortality rate of humans, i.e., assume the dengue mortality in humans is 0, and the only loss for humans is natural death with the rate δ_H. The transmissions from mosquitoes to humans and from humans to mosquitoes

are described by $\lambda_H S_H \frac{I_M}{N_M}$ and $\lambda_M S_M \frac{I_H}{N_H}$, respectively.

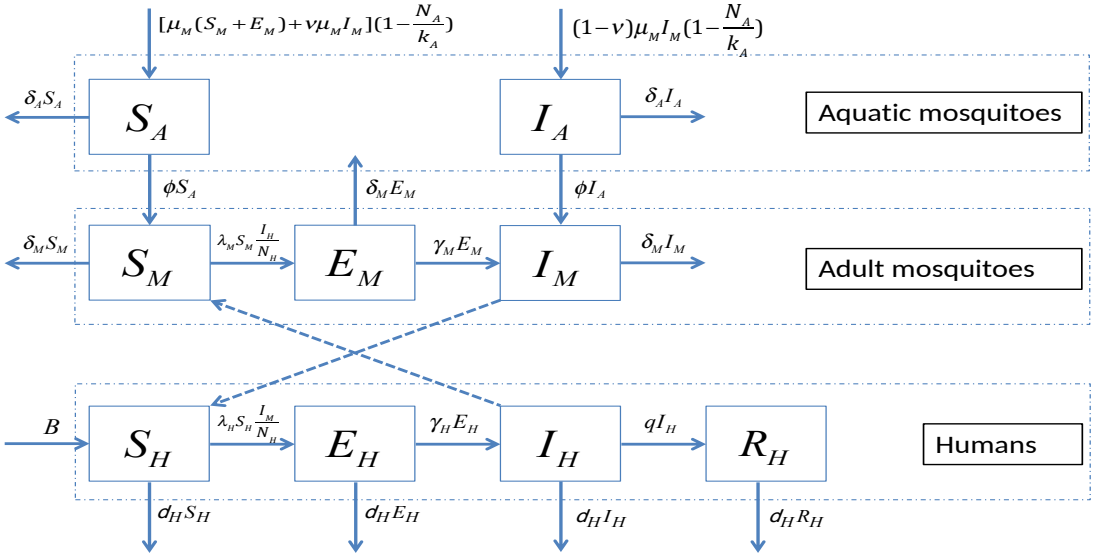


Figure 2: Flowchart of the dengue model (2.1).

The features of transmission are illustrated in Figure 2 and the mathematical model is described by the following ordinary differential equations:

$$\begin{aligned}
\frac{dS_A}{dt} &= [\mu_M(S_M+E_M)+\nu\mu_M I_M](1-\frac{N_A}{k_A})-\phi S_A-\delta_A S_A,\\
\frac{dI_A}{dt} &= (1-\nu)\mu_M I_M(1-\frac{N_A}{k_A})-\phi I_A-\delta_A I_A,\\
\frac{dS_M}{dt} &= \phi S_A - b\beta_{HM} S_M \frac{I_H}{N_H}-\delta_M S_M,\\
\frac{dE_M}{dt} &= b\beta_{HM} S_M \frac{I_H}{N_H}-\gamma_M E_M-\delta_M E_M\\
\frac{dI_M}{dt} &= \gamma_M E_M-\delta_M I_M+\phi I_A,\\
\frac{dS_H}{dt} &= B-b\beta_{MH} I_M \frac{S_H}{N_H}-\delta_H S_H,\\
\frac{dE_H}{dt} &= b\beta_{MH} I_M \frac{S_H}{N_H}-\gamma_H E_H-\delta_H E_H,\\
\frac{dI_H}{dt} &= \gamma_H E_H - qI_H-\delta_H I_H,\\
\frac{dR_H}{dt} &= qI_H-\delta_H R_H.
\end{aligned} \tag{2.1}$$

The parameters are listed in Table 1 and the variables are described as follows:

$S_A(t) \geq 0$: the number of susceptible aquatic mosquitoes including the susceptible eggs, susceptible larvaes and susceptible pupae at time t;

$I_A(t) \geq 0$: the number of infected aquatic mosquitoes including the infected eggs, infected larvaes and infected pupae at time t;

$N_A(t) = S_A(t) + I_A(t) \geq 0$: the total population of aquatic mosquitoes including the eggs, larvaes and pupae at time t;

$S_M(t) \geq 0$: the number of susceptible adult mosquitoes at time t;

$E_M(t) \geq 0$: the number of exposed adult mosquitoes at time t;

$I_M(t) \geq 0$: the number of infectious adult mosquitoes at time t;

$N_M(t) = S_M(t) + E_M(t) + I_M(t) \geq 0$: the total population of adult mosquitoes at time t;

$S_H(t) > 0$: the number of susceptible humans at time t;

$E_H(t) \geq 0$: the number of exposed humans at time t;

$I_H(t) \geq 0$: the number of infectious humans at time t;

$R_H(t) \geq 0$: the number of recovered humans at time t;

$N_H(t) = S_H(t) + E_H(t) + I_H(t) + R_H(t) > 0$: the total population of humans at time t.

Table 1: Parameter Description

Parameter	Interpretation	Value	Reference
μ_M	the birth rate of mosquitoes	0-11.2 per day	[33]
δ_A	the death rate of aquatic mosquitoes	0.01-0.47 per day	[33]
k_A	the carrying capacity of aquatic mosquitoes		
δ_M	the death rate of adult mosquitoes	0.02-0.09 per day	[33]
ϕ	the maturation rate of aquatic mosquitoes	0-0.19 per day	[33]
ν	the proportion of mosquito eggs laid by an infected female mosquito that is infected and female	11.11%	[6]
β_{HM}	the probability of transmission from humans to mosquitoes		
β_{MH}	the probability of transmission from mosquitoes to humans		
b	biting rate	0.76(bite/mosquito)	[36]
B	recruit for humans	3116 per day	[39]
δ_H	natural mortality rate of humans	1.28×10^{-5}	
γ_M	the progress rate of adult mosquitoes from exposed to infectious	0.1 per day	[34]
γ_H	the progress rate of humans from exposed to infectious	0.125-0.25 per day	[34]
q	the recovery rate of humans	1/6 per day	[23]

From system (2.1), we have the following system of the total populations of aquatic mosquitoes,

adult mosquitoes, and humans

$$\begin{aligned}
\frac{dN_A}{dt} &= \mu_M N_M(1-\frac{N_A}{k_A}) - (\phi+\delta_A)N_A,\\
\frac{dN_M}{dt} &= \phi N_A - \delta_M N_M,\\
\frac{dN_H}{dt} &= B - \delta_H N_H.
\end{aligned} \tag{2.2}$$

Define the net reproductive number for system (2.2) as

$$r_0 := \frac{\mu_M \phi}{\delta_M(\phi+\delta_A)}.$$

Then, we have the following result on the population dynamics of the mosquitoes and humans.

Theorem 2.1 *The equilibrium $(0,0,N_{H0})$ of system (2.2) is locally asymptotically stable if $r_0<1$ and unstable if $r_0>1$. Moreover, if $r_0>1$, one more equilibrium (N_{A0},N_{M0},N_{H0}) of system (2.2) arises, which is locally asymptotically stable if it exists, where*

$$N_{A0}=\frac{k_A(\mu_M\phi-\delta_M\phi-\delta_A\delta_M)}{\mu_M\phi},\ N_{M0}=\frac{k_A(\mu_M\phi-\delta_M\phi-\delta_A\delta_M)}{\mu_M\delta_M},\ N_{H0}=\frac{B}{\delta_H}.$$

Proof. It is easy to see that system (2.2) always has an equilibrium $(0,0,N_{H0})$ with $N_{H0}=B/\delta_H$. Moreover, the equilibrium (N_{A0},N_{M0},N_{H0}) exists if and only if $r_0>1$.

The eigenvalues of the Jacobian matrix for system (2.2) at $(0,0,N_{H0})$ satisfy the following equation

$$(\lambda+\delta_M)(\lambda^2+(\phi+\delta_A+\delta_M)\lambda+(\phi+\delta_A)\delta_M-\phi\mu_M)=0.$$

Thus, if $\mu_M\phi<\delta_A\delta_M+\delta_M\phi$, i.e., $r_0<1$, $(0,0,N_{H0})$ is locally asymptotically stable, while it is unstable if $\mu_M\phi>\delta_A\delta_M+\delta_M\phi$, i.e., $r_0>1$. ∎

3 Existence and stability of equilibria

Since $N_A\geq 0, N_M\geq 0$ and $N_H>0$, system (2.1) always has a disease-free equilibrium $E_{00}=(0,0,0,0,0,N_{H0},0,0,0)$. Moreover, if $r_0>1$, there is one more disease-free equilibrium $E_0=(N_{A0},0,N_{M0},0,0,N_{H0},0,0,0)$, where N_{A0},N_{M0},N_{H0} are stated as above. Biologically, the second disease-free equilibrium E_0 means that the aquatic mosquitoes, adult mosquitoes, and humans persist and are free of infection of dengue virus, which makes more sense and is more interesting.

Firstly, we consider the stability of E_{00} and have the following result.

Lemma 3.1 *The disease-free equilibrium E_{00} is locally asymptotically stable if $r_0<1$ and unstable if $r_0>1$.*

Proof. The eigenvalues of the Jacobian matrix for system (2.1) at E_{00} satisfy the following equation

$$\begin{aligned}
&(\lambda+\delta_H)^2(\lambda+q+\delta_H)(\lambda+\delta_H+\gamma_H)(\lambda+\delta_M+\gamma_M)(\lambda^2+(\delta_A+\delta_M+\phi)\lambda+\delta_A\delta_M+\delta_M\phi\\
&\quad-\mu_M\phi)(\lambda^2+(\delta_A+\delta_M+\phi)\lambda+\nu\mu_M\phi+\delta_A\delta_M+\delta_M\phi-\mu_M\phi)=0.
\end{aligned}$$

Therefore, if $\mu_M\phi<\delta_A\delta_M+\delta_M\phi$, i.e., $r_0<1$, E_{00} is locally asymptotically stable, while E_{00} is unstable if $\mu_M\phi>\delta_A\delta_M+\delta_M\phi$, i.e., $r_0>1$. ∎

Next we discuss the stability of the disease-free equilibrium E_0 when it exists. From Diekmann et al. [13, 14] and van den Driessche and Watmough [42], we obtain that

$$F = \begin{pmatrix} 0 & 0 & \frac{(1-\nu)\delta_M(\delta_A+\phi)}{\phi} & 0 & 0 \\ 0 & 0 & 0 & 0 & \frac{b\beta_{HM}k_A\delta_H(\mu_M\phi-\delta_M\phi-\delta_A\delta_M)}{B\delta_M\mu_M} \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & b\beta_{MH} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}$$

and

$$V = \begin{pmatrix} \phi+\delta_A & 0 & 0 & 0 & 0 \\ 0 & \gamma_M+\delta_M & 0 & 0 & 0 \\ -\phi & -\gamma_M & \delta_M & 0 & 0 \\ 0 & 0 & 0 & \gamma_H+\delta_H & 0 \\ 0 & 0 & 0 & -\gamma_H & q+\delta_H \end{pmatrix}.$$

The principal eigenvalue of FV^{-1} satisfies the following equation

$$\lambda^2 - C_1\lambda + C_0 = 0, \tag{3.1}$$

where

$$C_0 = \frac{b^2k_A\beta_{HM}\beta_{MH}\gamma_H\gamma_M\delta_H(\delta_A\delta_M + (\delta_M-\mu_M)\phi)}{B(q+\delta_H)(\gamma_H+\delta_H)\delta_M^2(\gamma_M+\delta_M)\mu_M}, \;\; C_1 = 1-\nu.$$

Thus, let

$$R_{01} = \frac{1}{2}(C_1 + \sqrt{C_1^2 - 4C_0}).$$

Following van den Driessche and Watmough [42], we have the following lemma.

Lemma 3.2 *When $r_0 > 1$, the disease-free equilibrium E_0 exists, and it is asymptotically stable if $R_{01} < 1$, while it is unstable if $R_{01} > 1$.*

Define the basic reproduction number as

$$R_0 := \frac{b^2k_A\beta_{HM}\beta_{MH}\gamma_H\gamma_M\delta_H\mu_M\phi}{b^2k_A\beta_{HM}\beta_{MH}\gamma_H\gamma_M\delta_H\delta_M(\delta_A+\phi) + B(q+\delta_H)(\gamma_H+\delta_H)\delta_M^2(\gamma_M+\delta_M)\mu_M\nu}.$$

We have the following results.

Theorem 3.3 *There is one locally asymptotically stable disease-free equilibrium of system (2.1) either E_{00} or E_0, if $R_0 < 1$ and $r_0 \neq 1$. Both disease-free equilibria E_{00} and E_0 are unstable if $R_0 > 1$.*

Proof. From Lemma 3.1, we know that E_{00} is asymptotically stable if $r_0 < 1$. If $\mu_M\phi > \delta_A\delta_M + \delta_M\phi$, E_{00} is unstable and E_0 exists. Moreover, the conditions

$$\begin{cases} r_0 > 1, \\ R_{01} < 1, \end{cases} \tag{3.2}$$

are equivalent to

$$\begin{cases} r_0 > 1, \\ R_0 < 1, \end{cases} \tag{3.3}$$

which guarantee that E_0 is asymptotically stable by Lemma 3.2. Therefore, if either $r_0 < 1$ or (3.3) holds, i.e., $R_0 < 1$ and $r_0 \neq 1$, then there is one asymptotically stable disease-free equilibrium. Furthermore, when $R_0 > 1$, we have $r_0 > 1$ and $R_{01} > 1$, which imply that both E_{00} and E_0 are unstable. ∎

Next, we discuss the endemic equilibria of system (2.1). Note that $N_A = S_A + I_A$, $N_M = S_M + E_M + I_M$ and $N_H = S_H + E_H + I_H + R_H$. Thus, system (2.1) is equivalent to the following system:

$$\begin{aligned}
&\frac{dN_A}{dt} = \mu_M N_M(1 - \frac{N_A}{k_A}) - (\phi + \delta_A)N_A,\\
&\frac{dI_A}{dt} = (1-\nu)\mu_M I_M(1 - \frac{N_A}{k_A}) - \phi I_A - \delta_A I_A,\\
&\frac{dN_M}{dt} = \phi N_A - \delta_M N_M,\\
&\frac{dE_M}{dt} = b\beta_{HM}(N_M - E_M - I_M)\frac{I_H}{N_H} - \gamma_M E_M - \delta_M E_M\\
&\frac{dI_M}{dt} = \gamma_M E_M - \delta_M I_M + \phi I_A,\\
&\frac{dN_H}{dt} = B - \delta_H N_H.\\
&\frac{dS_H}{dt} = B - b\beta_{MH} I_M \frac{S_H}{N_H} - \delta_H S_H,\\
&\frac{dE_H}{dt} = b\beta_{MH} I_M \frac{S_H}{N_H} - \gamma_H E_H - \delta_H E_H,\\
&\frac{dI_H}{dt} = \gamma_H E_H - qI_H - \delta_H I_H.
\end{aligned} \tag{3.4}$$

We obtain the existence of the disease-endemic equilibrium.

Theorem 3.4 *$E^* = (N_{A0}, I_A^*, N_{M0}, E_M^*, I_M^*, N_{H0}, S_H^*, E_H^*, I_H^*)$ is the unique disease-endemic equilibrium of system (3.4), which exists if and only if $R_0 > 1$, where*

$$\begin{aligned}
&N_{A0} = \tfrac{k_A(\mu_M\phi - \delta_M\phi - \delta_A\delta_M)}{\mu_M\phi},\\
&I_A^* = \tfrac{(1-\nu)I_M^*\delta_M}{\phi},\\
&N_{M0} = \tfrac{k_A(\mu_M\phi - \delta_M\phi - \delta_A\delta_M)}{\mu_M\delta_M},\\
&E_M^* = \tfrac{I_M^*\delta_M\nu}{\gamma_M},\\
&I_M^* = \tfrac{b^2\beta_{HM}\beta_{MH}\delta_H\gamma_H\gamma_M k_A(\delta_M(\phi+\delta_A) - \mu_M\phi) + B\delta_M^2(\gamma_M+\delta_M)(\gamma_H+\delta_H)(q+\delta_H)\mu_M\nu}{\mu_M\delta_M b\beta_{MH}(b\beta_{HM}\delta_H\gamma_H(\delta_M\nu+\gamma_M) + \delta_M(\gamma_M+\delta_M)(\gamma_H+\delta_H)(q+\delta_H))}\\
&N_{H0} = \tfrac{B}{\delta_H},\\
&S_H^* = \tfrac{1}{\delta_H(B + b\beta_{MH}I_M^*)},\\
&E_H^* = \tfrac{Bb\beta_{MH}I_M^*}{(\gamma_H+\delta_H)(B+b\beta_{MH}I_M^*)}\\
&I_H^* = \tfrac{\gamma_H Bb\beta_{MH}I_M^*}{(\gamma_H+\delta_H)(q+\delta_H)(B+b\beta_{MH}I_M^*)}.
\end{aligned}$$

Proof. To discuss the disease-endemic equilibrium, we consider the positive solutions of the following algebraic equations:

$$\mu_M N_M(1 - \frac{N_A}{k_A}) - (\phi + \delta_A)N_A = 0, \tag{3.5a}$$

$$(1-\nu)\mu_M I_M(1 - \frac{N_A}{k_A}) - \phi I_A - \delta_A I_A = 0, \tag{3.5b}$$

$$\phi N_A - \delta_M N_M = 0, \tag{3.5c}$$

$$b\beta_{HM}(N_M - E_M - I_M)\frac{I_H}{N_H} - \gamma_M E_M - \delta_M E_M = 0, \tag{3.5d}$$

$$B - \delta_H N_H = 0, \tag{3.5e}$$

$$B - b\beta_{MH} I_M \frac{S_H}{N_H} - \delta_H S_H = 0, \tag{3.5f}$$

$$b\beta_{MH} I_M \frac{S_H}{N_H} - \gamma_H E_H - \delta_H E_H = 0, \tag{3.5g}$$

$$\gamma_H E_H - q I_H - \delta_H I_H = 0. \tag{3.5h}$$

From equations (3.5a), (3.5c) and (3.5e), we know that the positive solutions satisfy $N_A = N_{A0}$, $N_M = N_{M0}$ and $N_H = N_{H0}$, where N_{A0}, N_{M0} and N_{H0} are given in Section 2. Substituting N_{A0}, N_{M0} and N_{H0} into the equations and solving (3.5b), (3.5e) (3.5f), (3.5g) and (3.5h), we obtain that

$$\begin{aligned}
I_A &= \frac{(1-\nu)\mu_M I_M}{\eta_1}(1 - \frac{N_{A0}}{k_A}) = \frac{(1-\nu) I_M \delta_M}{\phi}, \\
E_M &= \frac{I_M}{\gamma_M}(\delta_M - \frac{\phi(1-\nu)\mu_M}{\eta_1}(1 - \frac{N_{A0}}{k_A})) = \frac{I_M \delta_M \nu}{\gamma_M}, \\
S_H &= \frac{B N_{H0}}{N_{H0}\delta_H + b\beta_{MH} I_M}, \\
E_H &= \frac{B b \beta_{MH} I_M}{\eta_3 (N_{H0}\delta_H + b\beta_{MH} I_M)}, \\
I_H &= \frac{\gamma_H B b \beta_{MH} I_M}{\eta_4 \eta_3 (N_{H0}\delta_H + b\beta_{MH} I_M)},
\end{aligned}$$

where $\eta_1 = \phi + \delta_A$, $\eta_2 = \gamma_M + \delta_M$, $\eta_3 = \gamma_H + \delta_H$ and $\eta_4 = q + \delta_H$. Substituting E_M, I_H and E_M into (3.5d), we have the following equation

$$\begin{aligned}
&\{N_{M0} + I_M(\frac{\phi(1-\nu)}{\gamma_M \eta_1}\mu_M(1 - \frac{N_{A0}}{k_A}) - 1 - \frac{\delta_M}{\gamma_M})\}\frac{\gamma_H B b^2 \beta_{HM}\beta_{MH} I_M}{\eta_4 \eta_3 (N_{H0}\delta_H + b\beta_{MH} I_M)} \\
&-\frac{\eta_2 I_M}{\gamma_M}(\delta_M - \frac{\phi}{\eta_1}(1-\nu)\mu_M(1 - \frac{N_{A0}}{k_A})) = 0.
\end{aligned}$$

Since we only consider the positive solutions, the equation is reduced into a linear equation

$$c_0 + c_1 I_M = 0, \tag{3.6}$$

where

$$\begin{aligned}
c_0 &= \frac{B}{\mu_M \delta_M \delta_H}(b^2 \beta_{HM}\beta_{MH}\delta_H \gamma_H \gamma_M k_A(\delta_M \eta_1 - \mu_M \phi) + B\delta_M^2 \eta_2 \eta_3 \eta_4 \mu_M \nu), \\
c_1 &= \frac{b\beta_{MH} B}{\delta_H}(b\beta_{HM}\delta_H \gamma_H(\delta_M \nu + \gamma_M) + \delta_M \eta_2 \eta_3 \eta_4).
\end{aligned}$$

Clearly, $c_1 > 0$. There is only one solution of equation (3.6) $I_M = -c_0/c_1$, which is positive if and only if $c_0 < 0$. Moreover, $c_0 < 0$ if and only if $R_0 > 1$. Therefore, there is a unique disease equilibrium E^* of system (3.4), which exists if and only if $R_0 > 1$. ∎

The results in the theorems and lemmas in this section are summarized in Table 3.

4 The impact of vertical transmission in mosquitoes

In this section, we discussion the impact of vertical transmission of virus in mosquitoes. Firstly, we consider the case of blocking the transmission between mosquitoes and humans, i.e., assume $b = 0$. Then, $R_{01} = C_1 = 1 - \nu < 1$. Therefore, there is always one asymptotically stable disease-free equilibrium of system (2.1).

Table 2: Conditions for the existence and stability of equilibria

Conditions of R_0	Conditions of r_0	Equilibria & stability
$R_0 < 1$	$r_0 < 1$	E_{00} stable
	$r_0 > 1$	E_{00} unstable E_0 stable
$R_0 > 1$	$r_0 > 1$	E_{00} unstable E_0 unstable E^*

In fact, for this case, instead of system (2.1), we can discuss the two subsystems separately for mosquitoes

$$\begin{cases} \frac{dS_A}{dt} = [\mu_M(S_M + E_M) + \nu\mu_M I_M](1 - \frac{N_A}{k_A}) - \phi S_A - \delta_A S_A, \\ \frac{dI_A}{dt} = (1-\nu)\mu_M I_M(1 - \frac{N_A}{k_A}) - \phi I_A - \delta_A I_A, \\ \frac{dS_M}{dt} = \phi S_A - \delta_M S_M, \\ \frac{dE_M}{dt} = -\gamma_M E_M - \delta_M E_M \\ \frac{dI_M}{dt} = \gamma_M E_M - \delta_M I_M + \phi I_A \end{cases} \tag{4.1}$$

and humans

$$\begin{cases} \frac{dS_H}{dt} = B - \delta_H S_H, \\ \frac{dE_H}{dt} = -\gamma_H E_H - \delta_H E_H, \\ \frac{dI_H}{dt} = \gamma_H E_H - qI_H - kI_H - \delta_H I_H, \\ \frac{dR_H}{dt} = qI_H - \delta_H R_H. \end{cases} \tag{4.2}$$

Clearly, the disease-free equilibrium $E_{0H} = (B/\delta_H, 0, 0, 0)$ is the unique equilibrium of (4.2), which is always asymptotically stable. For subsystem (4.1), there is a unique equilibrium $(0, 0, 0, 0, 0)$ which is asymptotically stable if $\mu_M\phi < \delta_A\delta_M + \delta_M\phi$. When $\mu_M\phi > \delta_A\delta_M + \delta_M\phi$, the disease-free equilibrium $(0, 0, 0, 0, 0)$ is unstable and another disease-free equilibrium $(S_{A0}, 0, S_{M0}, 0, 0)$ exists, where S_{A0} and S_{M0} have the same expressions as those in Section 3. Furthermore, the eigenvalues of the Jacobian matrix of (4.1) satisfy the equation

$$\begin{aligned}&(\lambda + \phi + \delta_A)(\lambda + \delta_M)(\lambda + \delta_M + \gamma_M)(k_A\lambda^2 + (\delta_A k_A + \delta_M k_A + k_A\phi + \mu_M S_{M0})\lambda \\ &\quad + k_A\mu_M\phi - k_A\delta_A\delta_M - k_A\delta_M\phi) = 0.\end{aligned}$$

It implies that every eigenvalue has a negative real part and the equilibrium $(S_{A0}, 0, S_{M0}, 0, 0)$ is asymptotically stable. Moreover, there is no disease-endemic equilibria of (4.1).

Therefore, if we can block the transmission between mosquitoes and humans, the disease dengue will be eliminated not only in humans but also in mosquitoes, even if there is vertical transmission within mosquitoes. However, $b = 0$ is a limit case, which is difficult to be achieved. Next, we will discuss the impact of ν (the proportion of mosquito eggs laid by an infected female mosquito that is infected and female) on the transmission of dengue virus when $b \neq 0$, i.e., the impact of ν on the basic reproduction number R_0. Clearly, $R_0 < 1$ is equivalent to

$$\mu_M\phi - \delta_M(\delta_A + \phi) < \frac{B\eta_2\eta_3\eta_4\delta_M^2\mu_M}{b^2k_A\beta_{HM}\beta_{MH}\gamma_H\gamma_M\delta_H}\nu. \tag{4.3}$$

When $r_0 < 1$, i.e., $\mu_M\phi - \delta_M(\delta_A + \phi) < 0$, (4.3) holds for any $\nu \geq 0$. When $r_0 \geq 1$, (4.3) is equivalent to

$$\nu > \frac{(\mu_M\phi - \delta_M(\delta_A + \phi))b^2 k_A \beta_{HM}\beta_{MH}\gamma_H\gamma_M\delta_H}{B(q + \gamma_H)(\gamma_H + \delta_H)(\gamma_M + \delta_M)\delta_M^2\mu_M} \geq 0. \tag{4.4}$$

Note that $0 \leq \nu \leq 1$. The solution of ν for (4.6) is an empty set if

$$\frac{(\mu_M\phi - \delta_M(\delta_A + \phi))b^2 k_A \beta_{HM}\beta_{MH}\gamma_H\gamma_M\delta_H}{B(q + \gamma_H)(\gamma_H + \delta_H)(\gamma_M + \delta_M)\delta_M^2\mu_M} \geq 1,$$

i.e.,

$$b^2\beta_{HM}\beta_{MH} \geq \frac{B(q + \gamma_H)(\gamma_H + \delta_H)(\gamma_M + \delta_M)\delta_M^2\mu_M}{(\mu_M\phi - \delta_M(\delta_A + \phi))k_A\gamma_H\gamma_M\delta_H}. \tag{4.5}$$

Therefore, under the condition (4.5), $R_0 > 1$ for any $0 \leq \nu \leq 1$. We conclude the following results:

Theorem 4.1 *If* $r_0 \geq 1$ *and*

$$b^2\beta_{HM}\beta_{MH} < \frac{B(q + \gamma_H)(\gamma_H + \delta_H)(\gamma_M + \delta_M)\delta_M^2\mu_M}{(\mu_M\phi - \delta_M(\delta_A + \phi))k_A\gamma_H\gamma_M\delta_H},$$

then $R_0 < 1$ *is equivalent to*

$$\nu > \frac{(\mu_M\phi - \delta_M(\delta_A + \phi))b^2 k_A \beta_{HM}\beta_{MH}\gamma_H\gamma_M\delta_H}{B(q + \gamma_H)(\gamma_H + \delta_H)(\gamma_M + \delta_M)\delta_M^2\mu_M}. \tag{4.6}$$

Otherwise, if $r_0 < 1$, *then* $R_0 < 1$ *for any* $0 \leq \nu \leq 1$*; and if*

$$b^2\beta_{HM}\beta_{MH} \geq \frac{B(q + \gamma_H)(\gamma_H + \delta_H)(\gamma_M + \delta_M)\delta_M^2\mu_M}{(\mu_M\phi - \delta_M(\delta_A + \phi))k_A\gamma_H\gamma_M\delta_H} > 0,$$

then $R_0 > 1$ *for any* $0 \leq \nu \leq 1$.

It indicates that the value of ν affects R_0 only if the birth rate of mosquitoes is large enough and the transmissions between mosquitoes and humans are small enough but not vanishing.

5 Numerical simulations and sensitivity analysis

In this section, we first use the model to simulate the reported human data from the 2014 dengue outbreak in Guangdong Province. Then we will perform some sensitivity analysis to demonstrate how the basic reproduction number R_0 depends on the parameters and how the solutions, especially the number of infetious humans $I_H(t)$, depend on some parameters.

During the dengue outbreak in 2014, the Department of Health of Guangdong Province reported daily data from September 22 to October 30, which were the dates with most infected human cases. Assume that every clinically ill individual was eligible to look for medical help and was reported to sanitary authorities; that is, the reported daily data reflects the daily infectious human dengue cases. Based on our model with parameters in Table 1, we simulate the daily infectious human cases from September 22 to October 30 as shown in Figure 3.

Figure 4 shows that R_0 increases as either β_{HM} or β_{MH} or b increases. $R_0 < 1$ requires that both $\beta_{HM} < 0.1$ and $\beta_{MH} < 0.1$. Thus, mosquito bites precaution is the direct method to prevent the transmission of dengue.

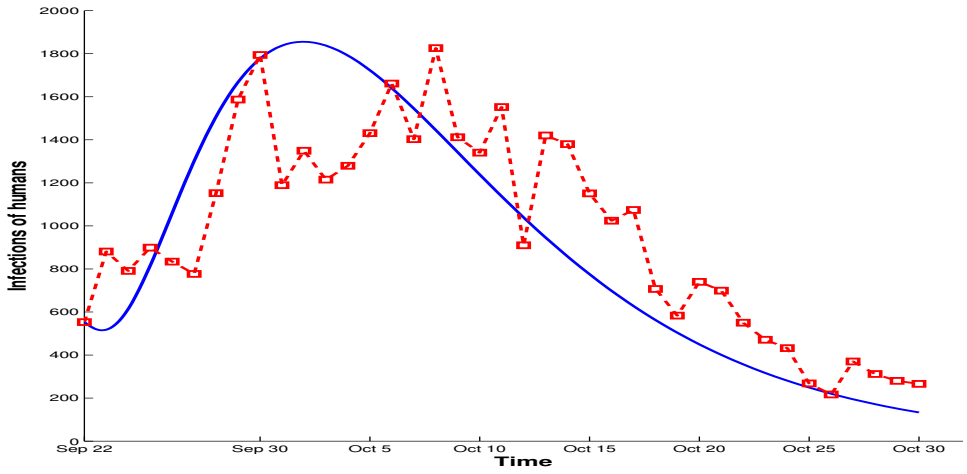
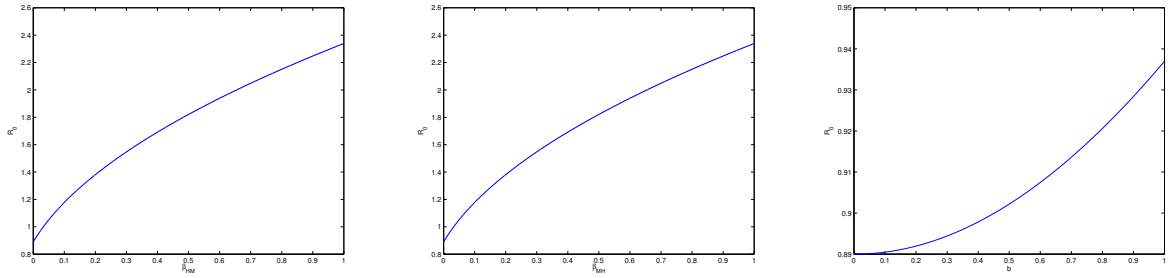


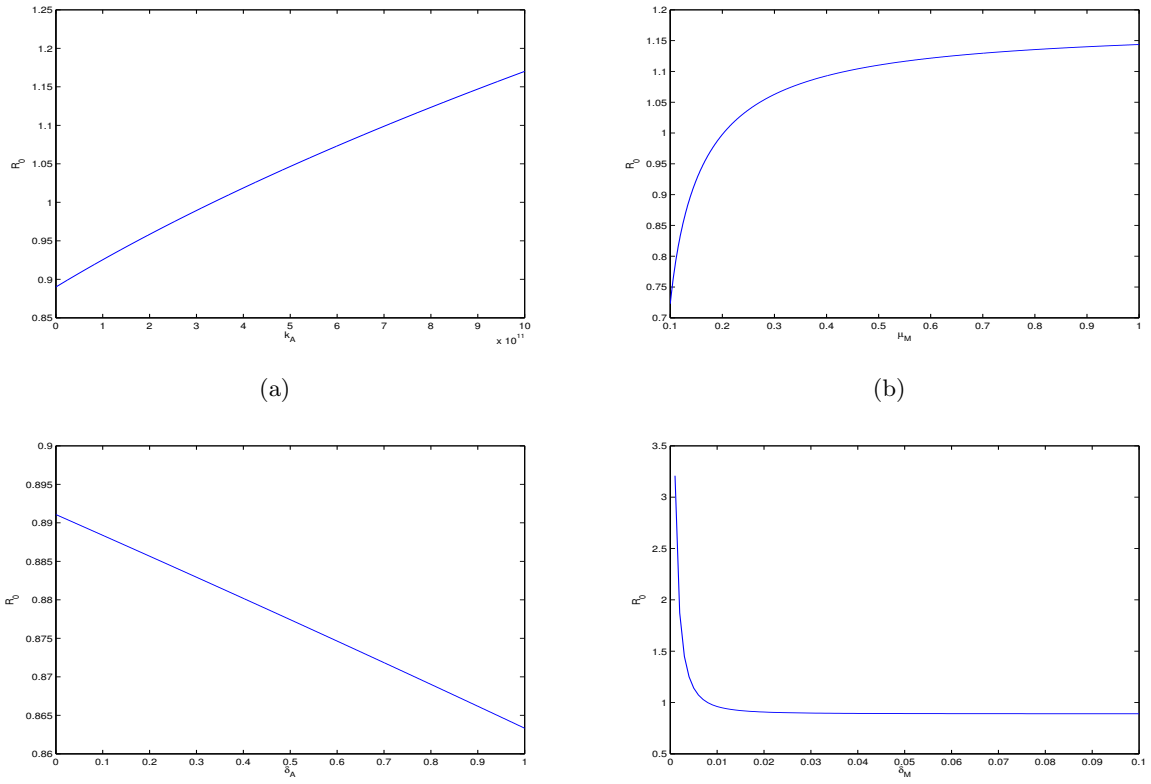
Figure 3: Simulation of the data on reported dengue infected human cases in Guangdong Province from September 22 to October 30, 2014 using model (2.1). The solid curve represents the solution $I_H(t)$ (the number of infectious humans) of model (2.1).



(a) (b) (c)

Figure 4: Plots of the basic reproduction number R_0 in terms of (a) β_{HM} (the probability of transmission from humans to mosquitoes), (b) β_{MH} (the probability of transmission from mosquitoes to humans), and (c) b (biting rate).

Figure 5 (a) shows that R_0 increases as the carrying capacity of aquatic mosquitoes k_A increases. Moreover, if k_A is larger than 3×10^{11}, which is much more than the human population (1.5×10^8), then the basic reproduction number $R_0 > 1$. Compare 5(a) with 5(b), (c) and (d), k_A influences R_0 more than μ_M, δ_A and δ_M do. Therefore, cleaning gathered water, which can reduce k_A effectively, is useful for reducing R_0.



(a) (b)

(c) (d)

Figure 5: Plots of the basic reproduction number R_0 in terms of the parameters. (a) k_A (the carrying capacity of aquatic mosquitoes), (b) μ_M (the birth rate of mosquitoes), (c) δ_A (the death rate of aquatic mosquitoes), and (d) δ_M (the death rate of adult mosquitoes).

Furthermore, Figure 6 shows that $I_H(t)$ depends sensitively on k_A, μ_M, δ_A and δ_M. That is, both cleaning gathered water and killing mosquitoes can prevent the spread of dengue from mosquitoes to human hosts.

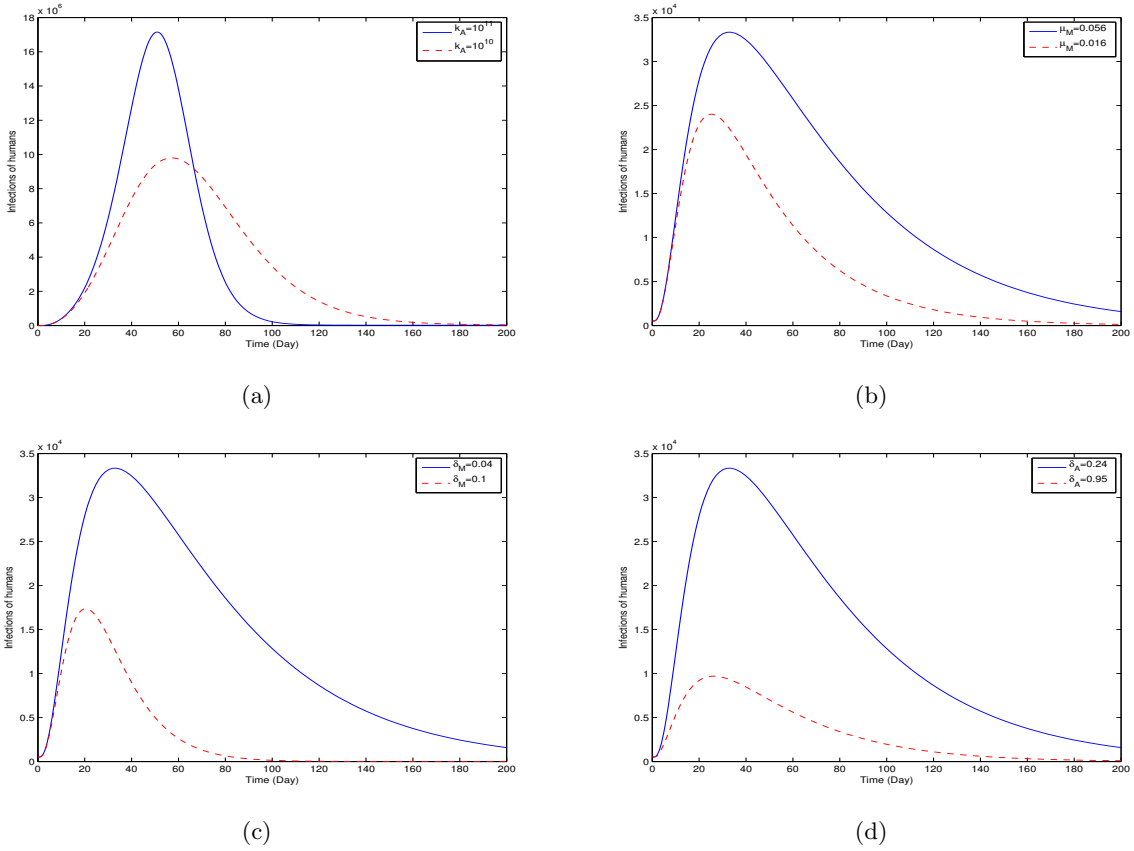


Figure 6: The dependence of the solution of the number of infectious humans $I_H(t)$ as a function of time on different parameter values. (a) k_A; (b) μ_M; (c) δ_M; and (d) δ_A.

6 Discussion

In this paper in order to study the impact of vertical transmission of the virus in mosquitoes on the spread dynamics of dengue between mosquito vectors and human hosts, we proposed a deterministic dengue model with vertical transmission in mosquitoes by including aquatic mosquitoes (eggs, larvae and pupae), adult mosquitoes (susceptible, exposed and infectious), and human hosts (susceptible, exposed, infectious and recovered). We first analyzed the existence and stability of disease-free equilibria, calculated the basic reproduction number, and discussed the existence of the disease-endemic equilibrium. From the stability of the first disease-free equilibrium E_{00}, we know that when r_0 is small enough (< 1), E_{00} is stable and mosquitoes will die out. That is, if we can control the growth of the mosquito population then dengue could be eliminated. There are several methods to control r_0. The first and most effective one is to reduce the birth rate of mosquitoes and increase the death rate of adult mosquitoes. When μ_M is small enough and δ_M is large enough such that $\mu_M - \delta_M < 0$, then $r_0 < 1$ holds. If it fails, i.e., $\mu_M - \delta_M > 0$, the second

measure is either decreasing the growth rate ϕ such that

$$\phi < \frac{\delta_M \delta_A}{\mu_M - \delta_M},$$

or increasing the death of immature mosquitoes δ_A, such that

$$\delta_A > \frac{(\mu_M - \delta_M)\phi}{\delta_M}.$$

Both measures can reduce r_0 to be less than 1.

If it fails to control r_0, then the mosquito population persists, the key point to control the transmission of dengue is to to control R_0 so that it is less than the unity. This can be achieved by controlling the transmission between mosquitoes and humans. We also discussed the impact of vertical transmission on the dynamics of the model. From the analysis in Section 4, if we can block the transmissions between humans and mosquitoes, the disease will be eliminated even vertical transmission of virus in mosquitoes exists. We notice that Theorem 4.1 shows that when the transmissions between humans and mosquitoes exist but small, a large enough vertical transmission rate in mosquitoes can increase R_0. That is, under certain conditions, increase of vertical transmission in mosquitoes could lead to the endemic state of dengue.

The average temperature in Guangdong Province is 21.8°C. The coldest in January is 13.3°C (GMS [19]). The temperature is suitable for the survival of mosquitoes. That is, $r_0 > 1$ in Guangdong Province. Our study shows that vertical transmission in mosquitoes affects the transmission of dengue virus in this case. We believe that this is one of the reasons why dengue virus has existed in Guangdong Province for years as shown in Figure 1, and it is difficult to eliminate the virus.

The large outbreak of dengue in Guangdong Province, China, in 2014 has inspirited a number of studies on the driving force, characteristics, epidemiology, and transmission dynamics of this outbreak. It has been suggested that high temperature, drenching rain, rapid urbanization, pandemic of dengue in Southeast Asia (Shen et al. [37]), higher number of imported cases in May and June (Cheng et al. [10]), delayed mosquito control program and transmission of asymptomatic infections (Li et al. [30]), etc. were responsible for the large outbreak. We used the model to simulate the reported infected human data from the 2014 dengue outbreak in Guangdong Province, China, and carried out sensitivity analysis of the basic reproduction number in terms of the model parameters. We believe that the warmer temperature and heavier rain in Guangdong Province in the spring increased the mosquito population dramatically, as well as more vertical transmission in mosquitoes. After the importation of dengue cases from Southeast Asia, the large mosquito population made the transmission rates between mosquitoes and humans and the vertical transmission rate in mosquitoes usually high and caused the large scale outbreak of dengue fever in Guangdong Province.

Moreover, the monthly reported human dengue cases of Guangdong Province changes periodically, with the highest incidence in September and October, while the lowest in January (HDGP[24]). It is related to the seasonal change in the populations of mosquitoes. Therefore, some parameters should depend on time t when we consider the transmission monthly. We leave it for future work.

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