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Research Article

Optimal control strategy for dengue transmission with second infection

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Abstract: This paper presents a mathematical model for dengue disease to understand its dynamics by using a set of differential equations to describe the effects between human and mosquito populations. In this model, the human population is divided into five types of individuals: susceptible (S_h), vaccination (V_h), first infectious (I_1), second infectious (I_2), and recovered (R_h) and the mosquitoes population is divided into three types of individuals: larva mosquitoes (A_m), uninfected female mosquitoes (M_s) and infected female mosquitoes (M_i). The epidemic and endemic analysis have also presented along with numerical simulations to verify our model. Our results suggested that the prevention and control of dengue outbreaks can be implemented in an optimal way.

Keywords : Dengue fever, Mathematical model, Equilibrium, Optimal control theory

1. Introduction

The dengue virus is transmitted by female mosquitoes, mainly of the Aedes species and to a lesser extent, Ae. albopictus. The mosquito bites during daytime hours, particularly around the hours of dawn and dusk. DEN 1, DEN 2, DEN 3 and DEN 4. Accordingly to the World Health Organization (WHO) over 2.5 billion people are now at risk for Dengue. Currently, the WHO estimates that there may be 50-100 million Dengue infections worldwide (World Health Organization, 2010). Local transmission of dengue was reported in France and Croatia in 2010 and imported cases were detected in three other European countries. In 2012 an outbreak of dengue on the Madeira Islands of Portugal resulted in over 2000 cases, and imported cases were detected in 10 other countries in mainland Portugal. In 2013, cases have occurred in Florida (USA) and Yunnan (China). Dengue is more common among children, adolescents and adults.

There have been many mathematical models (see, e.g., (Esteya 1998; Bowman, 2005; Rodrigues *et al*., 2012; Singh *et al*., 2014)) to predict the prevalence and transmission dynamics of dengue disease. In this study, they assumed that the human population is constant and the vector population is asymptotically constant (Esteya 1998). In 2011, Helena Sofia Rodrigues, et.al. proposed a model based on two populations, humans and mosquitoes, with insecticide control has been presented. The result shows that a steady insecticide compaign can reduce the number of infected humans and mosquitoes (Bowman, 2005). In 2014, B. Singh, et.al. discussed the effects of vaccination strategies on the dynamic of the dengue disease transmission model with assumption that a random fraction of the recovered host population can loses the immunity and becomes susceptible again (Singh *et al*., 2014). In 2015, Tarig Mohamed, et.al. studied describing the dynamics of dengue fever. The sensitivity index of the basic reproduction number is carried out in order to establish the relative significance of the model parameters in the disease spread (Ali *et al*., 2015).

Furthermore, T. M.Ali (Ali *et al*., 2015), B. Singh (Singh *et al*., 2014) and M. Chairat (Thongtha and Chairat, 2017) have proposed some dengue mathematical model that studied factors that reduced the number of dengue infections. Their studies suggested that by combining the three measures: deployed vaccine, both medical treatments in infected and elimination of egg or larvae can prevent dengue fever outbreaks.

We refer the reader to those articles and the references therein for a detailed epidemiological description of the dengue virus. There have been many purposed mathematical models such as by Esteya (1998), Bowman (2005), Rodrigues et al. (2012), Singh et al. (2014), however, none of the mentioned papers have consider the second infection of the virus. To investigate in this case, we further extend our previous work by including the second stage of the virus infection and use the same parameters to calculate in our model. In this work, we have ideas from the model of dengue fever of M. Chairat (Thongtha and Chairat, 2017). We focus on the second infection of deterministic SEIR model. In the remainder of this paper, we will first present the dengue fever model with control measures incorporated. We will then conduct an equilibrium analysis for the epidemic and endemic dynamics of the system when the controls are constants. Then, we will turn to time-dependent control system and perform an optimal control study for the dengue fever model. Finally we round up the paper by conclusion and discussion.

2. Materials and methods

In this section, our main goal in this work is a mathematical model for dengue disease describing the dynamics of this virus DEN1-4. We focus on the second infection of deterministic SEIR model where the population is divided into populations of susceptible humans (S_h), the vaccination (V_h), first infected humans (I_1), second infected humans (I_2), recovered human (R_h). The total human population (N_h) is constant so, $N_h = S_h + V_h + I_1 + I_2 + R_h$. There are also four other state variables related to female, aquatic stage or larva mosquitoes (A_m), uninfected female mosquitoes (M_s), and infected female mosquitoes (M_i). Let a portion σ_i, $0 \le \sigma_i \le 1$ for $i = 1,2$, of newborn host be vaccinated. Assume that the host and vector population has constant with birth and death rate equal to μ_h and μ_v, respectively, c is average daily biting, β_1, β_2 are transmission probability from M_i and β_3, β_4 are transmission probability from I_1, I_2 respectively. $\mu_h N_h$ is human demographics includes a rescruitment term. Q_m is number of eggs at each deposit per capita and K is maximal capacity of larvae $(k \times m)$. λ_m is maturation rate from larvae to adult and natural mortality of larva at a rate μ_A. The recovery rate of the host population is defined by γ. The constant with death rate of first infected I_1 *by* d_1, and the constant with death rate of second infected I_2 *by* d_2. ϕ_1 is the effectiveness of the vaccine, ϕ_2 is an average treatment of I_2, ϕ_4 is an average treatment of I_1, ϕ_3 is an elimination of egg or larvae. k is number of larvae per human and m is female mosquitoes per human. For human population the equations are;

$$\begin{aligned}
\frac{dS_h}{dt} &= \mu_h N_h - \left(c\beta_1 \frac{M_i}{N_h} + c\beta_2 \frac{M_i}{N_h} + \mu_h + \phi_1 \right) S_h, \\
\frac{dV_h}{dt} &= \phi_1 S_h - \left(c\sigma_1\beta_1 \frac{M_i}{N_h} + c\sigma_2\beta_2 \frac{M_i}{N_h} + \mu_h \right) V_h, \\
\frac{dI_1}{dt} &= c\beta_1 \frac{M_i}{N_h} \left(S_h + \sigma_1 V_h \right) - \left(\gamma_1 + d_1 + \phi_2 + \mu_h \right) I_1, \\
\frac{dI_2}{dt} &= c\beta_2 \frac{M_i}{N_h} \left(S_h + \sigma_2 V_h \right) - \left(\gamma_2 + d_2 + \phi_3 + \mu_h \right) I_2, \\
\frac{dR_h}{dt} &= \left(\gamma_1 + \phi_2 \right) I_1 + \left(\gamma_2 + \phi_3 \right) I_2 - \mu_h R_h,
\end{aligned} \tag{1}$$

and for vector population

$$\begin{aligned}
\frac{dA_m}{dt} &= Q_m \left(1 - \frac{A_m}{K} \right) \left(M_s + M_i \right) - \left(\lambda_{ms} + \phi_4 + \mu_A \right) A_m, \\
\frac{dM_s}{dt} &= \lambda_{ms} A_m - \left(c\beta_3 \frac{I_1}{N_h} + c\beta_4 \frac{I_2}{N_h} + \mu_v \right) M_s, \\
\frac{dM_i}{dt} &= \left(c\beta_3 \frac{I_1}{N_h} + c\beta_4 \frac{I_2}{N_h} \right) M_s - \mu_v M_i.
\end{aligned} \tag{2}$$

2.1 Disease-free equilibrium

With constant controls and setting $I_1 = I_2 = R_h = M_i = 0$, the disease-free equilibrium (DFE) of the system (1) and (2) is given by

$$\varepsilon_0 = \left(S_0, V_0, 0, 0, 0, A_0, M_{S0}, 0 \right) \tag{3}$$

where $S_0 = \frac{\mu_h N_h}{\mu_h + \phi_1}$,

$$A_0 = \frac{\lambda_{ms} Q_m K - \mu_v K \left(\lambda_{ms} + \mu_A + \phi_4 \right)}{\lambda_{ms} Q_m},$$

$$V_0 = \frac{\phi_1 N_h}{\mu_h + \phi_1}, \; M_{S0} = \frac{\lambda_{ms} Q_m K - \mu_v K \left(\lambda_{ms} + \mu_A + \phi_4 \right)}{\mu_v Q_m}.$$

$$F = \mathrm{DF}\left(\varepsilon_0\right) = \begin{bmatrix} 0 & 0 & \frac{c\beta_1 \left(S_0 + \sigma V_0 \right)}{N_h} \\ 0 & 0 & \frac{c\beta_2 \left(S_0 + \sigma V_0 \right)}{N_h} \\ \frac{c\beta_3 M_{S0}}{N_h} & \frac{c\beta_4 M_{S0}}{N_h} & 0 \end{bmatrix}, \quad V =$$

2.2 Next-generation matrix analysis

We start our analysis by determining the basic reproduction number, R_0. R_0 is mathematically defined as the spectral radius of the next-generation matrix. To compute the basic reproduction number, we use the well-known method of van den Driessche and Watmough (Van den Driessche, P. & Watmough, J., 2002). By system (1), I_1, I_2 and M_i are directly related to the infection. We have

$$\begin{bmatrix} \frac{dI_1}{dt} \\ \frac{dI_2}{dt} \\ \frac{dM_i}{dt} \end{bmatrix} = \begin{bmatrix} c\beta_1 \frac{M_i}{N_h} \left(S_h + \sigma V_h \right) \\ c\beta_2 \frac{M_i}{N_h} \left(S_h + \sigma V_h \right) \\ c\beta_3 \frac{I_1}{N_h} M_s + c\beta_4 \frac{I_2}{N_h} M_s \end{bmatrix} - \begin{bmatrix} \left(\gamma_1 + d_1 + \phi_2 + \mu_h \right) I_1 \\ \left(\gamma_2 + d_2 + \phi_3 + \mu_h \right) I_2 \\ \mu_v M_i \end{bmatrix}$$

$$= \mathrm{F} - \mathrm{V},$$

where F denotes the rate of appearance of new infections and V denotes the rate of transfer of individuals into or out of each population set. The next-generation matrix is defined as FV^{-1}, where F and V are the Jacobian matrices given by

$$\left(\varepsilon_0 \right) = \begin{bmatrix} \gamma_1 + d_1 + \phi_2 + \mu_h & 0 & 0 \\ 0 & \gamma_2 + d_2 + \phi_3 + \mu_h & 0 \\ 0 & 0 & \mu_v \end{bmatrix}, \tag{4}$$

where ε_0 is DFE defined in Equation (3). By spectral radius, we have

$$R_0=\sigma\left(FV^{-1}\right)=\sqrt{\frac{c^2\beta_1\beta_3M_{S0}\left(S_0+\sigma V_0\right)\left(\mu_h+\gamma_1+d_1+\phi_2\right)+c^2\beta_2\beta_4M_{S0}\left(S_0+\sigma V_0\right)\left(\mu_h+\gamma_2+d_2+\phi_3\right)}{\mu_vN_h^2\left(\mu_h+\gamma_1+d_1+\phi_2\right)\left(\mu_h+\gamma_2+d_2+\phi_3\right)}}. \quad (5)$$

Consequently, based on the work in the paper proposed by Van Den Driessche and Watmough (Van den Driessche, P. & Watmough, J., 2002)., we immediately have the following result:

Theorem1 The disease-free equilibrium of the model is locally asymptotically stable *if* $R_0<1$, and unstable *if* $R_0>1$.

2.3 Endemic equilibrium

When the disease is presence in the population, $I_1,I_2\neq0$ and $M_i\neq0$, there may be several critical points where $I_1,I_2\neq0$ and $M_i\neq0$, which are the endemic equilibrium points of the model. These points will be denoted as $\varepsilon_1^*=\left(S_h^*,V_h^*,I_1^*,I_2^*,R_h^*\right)\neq0$ and $\varepsilon_2^*=\left(A_m^*,M_s^*,M_i^*\right)\neq0$

2.4 Local stability

Next, we proceed to analyze the stability properties of the endemic equilibrium. First we prove the following result regarding the local stability.

Theorem3 The positive endemic equilibrium ε_1^* and ε_2^* is locally asymptotically stable.

Proof. The jacobian matrix of the system (1) at $x=\varepsilon_1^*$ is given by

$$J\left(S_h^*,\mathrm{V}_h^*,\mathrm{I}_h^*\right)=\begin{bmatrix}-\left(\alpha_1M_i^*+\alpha_2M_i^*+\mu_h+\phi_1\right) & 0 & 0 & 0\\ \phi_1 & -\left(\sigma_1\alpha_1M_i^*+\sigma_2\alpha_2M_i^*+\mu_h\right) & 0 & 0\\ \alpha_1M_i^* & \sigma_1\alpha_1M_i^* & -W_1 & 0\\ \alpha_2M_i^* & \sigma_2\alpha_2M_i^* & 0 & -W_2\end{bmatrix}$$

where $\alpha_1=\frac{c\beta_1}{N_h}$, $\alpha_2=\frac{c\beta_2}{N_h}$,
$W_1=\gamma_1+d_1+\mu_h+\phi_2$ and

$W_2=\gamma_2+d_2+\mu_h+\phi_3$.

The characteristic polynomial of $J\left(\varepsilon_1^*\right)$ is

$$\begin{aligned}0 &= \det\left[J\left(\varepsilon_1^*\right)-\lambda I^*\right]\\ &=\left(-\lambda-(\alpha_1M_i^*+\alpha_2M_i^*+\mu_h+\phi_1)\right)\\ &\quad\left(-\lambda-(\sigma_1\alpha_1M_i^*+\sigma_2\alpha_2M_i^*+\mu_h)\right)\\ &\quad(-\lambda-W_1)(-\lambda-W_2).\end{aligned}$$

Thus $\lambda_1=-\left(\alpha_1M_i^*+\alpha_2M_i^*+\mu_h+\phi_1\right)$,
$\lambda_2=-\left(\sigma_1\alpha_1M_i^*+\sigma_2\alpha_2M_i^*+\mu_h\right)$,
$\lambda_3=-W_1$, $\lambda_4=-W_2$, which all of the eigenvalues are negative numbers. And the jacobian matrix of the system (1) at $x=\varepsilon_2^*$ is given by

$$J\left(A_m^*,M_s^*,M_i^*\right)=\begin{bmatrix}-\left(\frac{Q_m}{K}\left(M_s^*+M_i^*\right)+\lambda_{ms}+\phi_4+\mu_A\right) & 0 & 0\\ \lambda_{ms} & -\left(c\beta_3\frac{I_1}{N_h}+c\beta_4\frac{I_2}{N_h}+\mu_v\right) & 0\\ 0 & c\beta_3\frac{I_1}{N_h}+c\beta_4\frac{I_2}{N_h} & -\mu_v\end{bmatrix}$$

The characteristic polynomial of $J\left(\varepsilon_1^*\right)$ is

$$\begin{aligned}0 &= \det\left[J\left(\varepsilon_2^*\right)-\lambda I^*\right]\\ &=\left(-\lambda-(\frac{Q_m}{K}\left(M_s^*+M_i^*\right)+\lambda_{ms}+\phi_4+\mu_A)\right)\\ &\quad\left(-\lambda-(c\beta_3\frac{I_1}{N_h}+c\beta_4\frac{I_2}{N_h}+\mu_v)\right)\\ &\quad(-\lambda-\mu_{v1})=0.\end{aligned}$$

Thus

$$\lambda_1=-\left(\frac{Q_m}{K}\left(M_s^*+M_i^*\right)+\lambda_{ms}+\phi_4+\mu_A\right),$$
$$\lambda_2=-\left(c\beta_3\frac{I_1}{N_h}+c\beta_4\frac{I_2}{N_h}+\mu_v\right),\quad\lambda_3=-\mu_v,$$

which all of the eigenvalues are negative numbers. Thus, ε_1^* and ε_2^* are locally asymptotically stable. We complete the proof.

3. Results : Optimal control

Now we turn to the more general model with time-dependent controls $\phi_1(t), \phi_2(t), \phi_3(t)$, and $\phi_4(t)$. We consider the system on a time interval [0,T]. The function $\phi_1(t)$, $\phi_2(t)$, $\phi_3(t)$, and $\phi_4(t)$ are assumed to be at least Lebesgue measurable on [0,T]. The control set is defined as

$$\Omega = \left\{ \begin{matrix} \phi_1(t), \phi_2(t), \phi_3(t), \phi_4(t) \\ 0 < \phi_1(t) < \phi_{1\max}, \ 0 < \phi_2(t) < \phi_{2\max}, \\ 0 < \phi_3(t) < \phi_{3\max}, \ 0 < \phi_4(t) < \phi_{4\max} \end{matrix} \right\}$$

where $\phi_{1\max}$, $\phi_{2\max}$, $\phi_{3\max}$ and $\phi_{4\max}$ denote the upper bounds for the effort of vaccination, treatment of first infected, treatment of second infected and elimination rate of egg or larvae, respectively. The bounds reflect practical limitation on the maximum rate of control in given time period. The presence of time-dependent controls makes the analysis of our system difficult. In fact, the disease dynamics now depend on the evolution of control. In what follows we perform an optimal control study on this problem. We aim to minimize the total number of infections and the costs of control over the time interval $[0, T]$; i.e.,

$$\min_{\phi_{1,4} \in \Omega} \int_0^T \left[\begin{matrix} I_1(t) + I_2(t) + c_{11}\phi_1(t) S_h(t) + c_{12}\phi_1^2(t) + c_{21}\phi_2(t) I_1(t) + c_{22}\phi_2^2(t) \\ + c_{31}\phi_3(t) I_2(t) + c_{32}\phi_3^2(t) + c_{41}\phi_4(t) A_m(t) + c_{42}\phi_4^2(t) \end{matrix} \right] dt \quad (6)$$

Here, the parameters c_{11}, c_{12}, c_{21}, c_{22}, c_{31}, c_{32}, c_{41}, and c_{42} with appropriate units, define the appropriate costs associated with these controls. Quadratic terms are introduced to indicate nonlinear costs potentially arising at high intervention level. The minimization process is subject to the differential equation of our system, which are now referred to as the state equations. Correspondingly, the unknows S_h, I_1, I_2 and M_i are now called the state variables, in contrast to the control variables $\phi_1(t), \phi_2(t), \phi_3(t)$, and $\phi_4(t)$. Our goal is to determine the optimal controls $\phi_1^*(t), \phi_2^*(t), \phi_3^*(t)$ and $\phi_4^*(t)$, so as to minimize the objective functional in (6).

Let us first define the adjoint functions

$\lambda_{S_h}, \lambda_{V_h}, \lambda_{I_1}, \lambda_{I_2}, \lambda_{A_m}, \lambda_{M_s}$ and λ_{M_i} associated with the state equations for $S_h, V_h, I_1, I_2, A_m, M_s$ and M_i respectively. We then form the Hamitonian, H, by multiplying state equation, and adding each of these products to the integrand of the objective functional. As a result, we obtain

$$\begin{aligned} H &= I_1(t) + I_2(t) + c_{11}\phi_1(t) S_h(t) + c_{12}\phi_1^2(t) \\ &+ c_{21}\phi_2(t) I_1(t) + c_{22}\phi_2^2(t) + c_{31}\phi_3(t) I_2(t) \\ &+ c_{32}\phi_3^2(t) + c_{41}\phi_4(t) A_m(t) + c_{42}\phi_4^2(t) \\ &+ \lambda_{S_h}\left(\mu_h N_h - \left(c\beta_1 \frac{M_i}{N_h} + c\beta_2 \frac{M_i}{N_h} + \mu_h + \phi_1 \right) S_h \right) \\ &+ \lambda_{V_h}\left(\phi_1 S_h - \left(c\sigma_1\beta_1 \frac{M_i}{N_h} + c\sigma_2\beta_2 \frac{M_i}{N_h} + \mu_h \right) V_h \right) \\ &+ \lambda_{I_1}\left(c\beta_1 \frac{M_i}{N_h}(S_h + \sigma_1 V_h) - (\gamma_1 + d_1 + \phi_2 + \mu_h) I_1 \right) \\ &+ \lambda_{I_2}\left(c\beta_2 \frac{M_i}{N_h}(S_h + \sigma_2 V_h) - (\gamma_2 + d_2 + \phi_3 + \mu_h) I_2 \right) \\ &+ \lambda_{A_m}\left(Q_m\left(1 - \frac{A_m}{K}\right)(M_s + M_i) - (\lambda_{ms} + \phi_4 + \mu_A) A_m \right) \\ &+ \lambda_{M_s}\left(\lambda_{ms} A_m - \left(c\beta_3 \frac{I_1}{N_h} + c\beta_4 \frac{I_2}{N_h} + \mu_v \right) M_s \right) \\ &+ \lambda_{M_i}\left(\left(c\beta_3 \frac{I_1}{N_h} + c\beta_4 \frac{I_2}{N_h} \right) M_s - \mu_v M_i \right) \end{aligned}$$

To achieve the optimal control, the adjoint functions must satisfy $\frac{d\lambda_{S_h}}{dt} = -\frac{\partial H}{\partial S_h}$,

$$\frac{d\lambda_{V_h}}{dt} = -\frac{\partial H}{\partial V_h}, \ \frac{d\lambda_{I_1}}{dt} = -\frac{\partial H}{\partial I_1}, \ \frac{d\lambda_{I_2}}{dt} = -\frac{\partial H}{\partial I_2},$$

$$\frac{d\lambda_{A_m}}{dt} = -\frac{\partial H}{\partial A_m}, \ \frac{d\lambda_{M_s}}{dt} = -\frac{\partial H}{\partial M_s}$$

and $\frac{d\lambda_{M_i}}{dt} = -\frac{\partial H}{\partial M_i}$ with transversality conditions (or final time conditions): $\lambda_{S_h}(T) = 0, \ \lambda_{V_h}(T) = 0,$ $\lambda_{I_1}(T) = 0, \ \lambda_{I_2}(T) = 0, \ \lambda_{A_m}(T) = 0, \ \lambda_{M_s}(T) = 0 \ \ \lambda_{M_i}(T) = 0.$ and $\lambda_{M_i}(T) = 0.$ The characterization of the optimal control $\phi_1^*(t), \phi_2^*(t), \phi_3^*(t)$ and $\phi_4^*(t)$ are based on the conditions

$\frac{\partial H}{\partial \phi_1} = 0, \ \frac{\partial H}{\partial \phi_2} = 0, \ \frac{\partial H}{\partial \phi_3} = 0, \frac{\partial H}{\partial \phi_4} = 0,$ respectively, subject to the constraints $0 \le \phi_1 \le \phi_{1\max}, \ 0 \le \phi_2 \le \phi_{2\max}, \ 0 \le \phi_3 \le \phi_{3\max}$ and $0 \le \phi_4 \le \phi_{4\max}.$ Specifically, we have

have $\phi_1^*(t) = \max\left(0, \min\left(\phi_1(t), \phi_{1\max}\right)\right),$

$\phi_2^*(t) = \max\left(0, \min\left(\phi_2(t), \phi_{2\max}\right)\right),$

$\phi_3^*(t) = \max\left(0, \min\left(\phi_3(t), \phi_{3\max}\right)\right)$ and

$\phi_4^*(t) = \max\left(0, \min\left(\phi_4(t), \phi_{4\max}\right)\right)$

where $\phi_1(t) = \left((\lambda_{S_h} - \lambda_{V_h} - c_{11}) S_h(t)\right) / 2c_{12},$

$\phi_2(t) = \left(\left(\lambda_{I_1} - c_{21}\right) I_1(t)\right) / 2c_{22},$

$\phi_3(t) = \left(\left(\lambda_{I_2} - c_{31}\right) I_2(t)\right) / 2c_{32},$ and

$\phi_4(t) = \left(\lambda_{A_m} A_m(t) - c_{41} A_m(t)\right) / 2c_{42}.$

Due to the presence of both initial conditions (for the state equations) and final time conditions (for the adjoint equations), and the fact that most models of our interest are nonlinear, the optimal control system has to be solved numerically. We will use the Forward-Backward Sweep Method to conduct the numerical simulation.

The initial conditions for the problem were:

$S_{h0} = N_h - V_{h0} - I_{10} - I_{20}, \ N_h = 10^5, \ V_{h0} = 0, \ I_{10} = 500, \ I_{20} = 250,$ $R_{h0} = 0, \ A_{m0} = kN_h, \ K = kN_h, \ S_{m0} = mN_h.$ The simulations were carried out using the following values:

Table1 Dengue fever model parameters.

Parameter	Value	Reference	Parameter	Value	Reference
N_h	10^5	Estimated	d_1	2×10^{-8}	Estimated
C	1	(Rodrigues et al., 2012)	d_2	2×10^{-5}	Estimated
β_1	0.03	Estimated	Q_m	400	(Rodrigues *et al*., 2012)
β_2	0.02	Estimated	λ_{ms}	0.08	(Rodrigues *et al*., 2012)
$1/\mu_h$	71×365	(Rodrigues et al., 2012)	β_3	0.04	Estimated
σ_1	$1/3$	(Rodrigues et al., 2012)	β_4	0.02	Estimated
σ_2	$1/3$	(Rodrigues et al., 2012)	μ_A	0.25	(Bowman et al., 2005)
γ_1	0.04	Estimated	μ_v	1/11	(Bowman et al., 2005)
γ_2	0.025	Estimated	m	3	(Bowman et al., 2005)
k	6	(Bowman et al., 2005)			

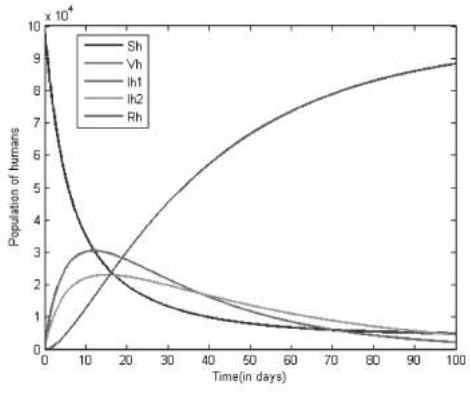

Figure 1 : Dengue infectious population without controls, $\phi_{1,2,3,4}=0.$

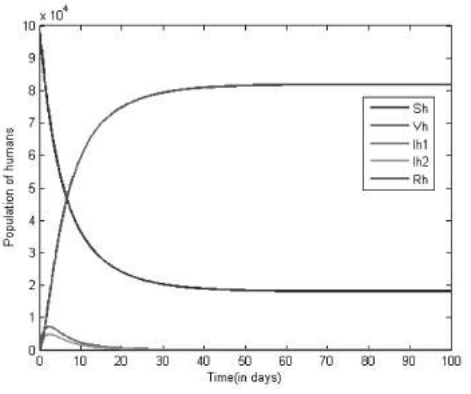

Figure 2 : Dengue infectious population with controls $\phi_1=0, \phi_{2,3,4}=0.7.$

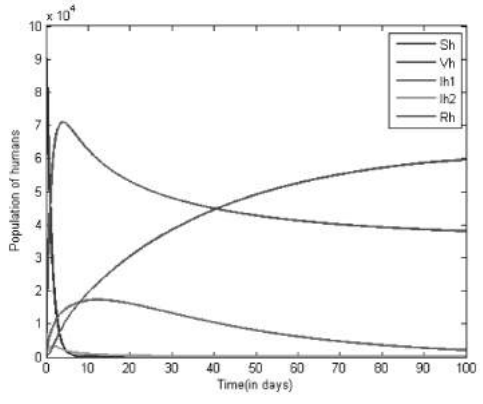

Figure 3 : Dengue infectious population without controls, $\phi_2=0, \phi_{1,3,4}=0.7.$

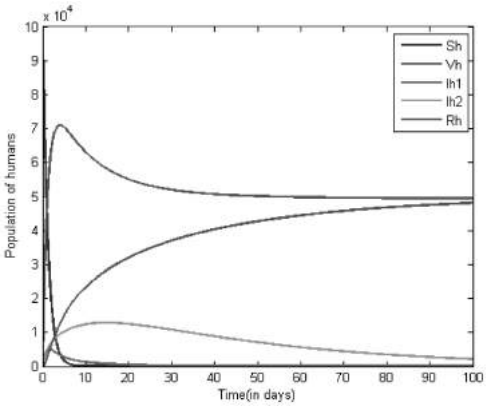

Figure 4 : Dengue infectious population with controls, $\phi_3=0, \phi_{1,2,4}=0.7.$

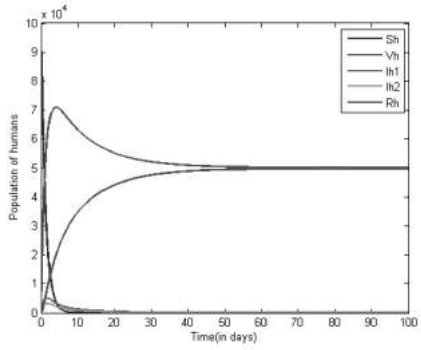

Figure 5 : Dengue infectious population without controls. $\phi_{1,2,3}=0.7,\ \phi_4=0.$

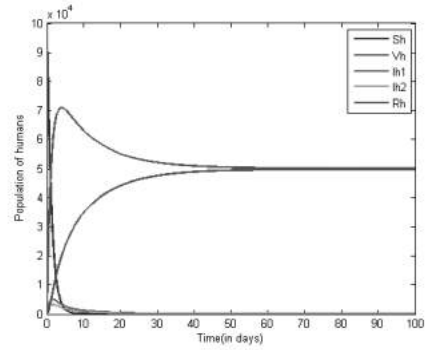

Figure 6 : Dengue infectious population with controls, $\phi_{1,2,3,4}=0.7.$

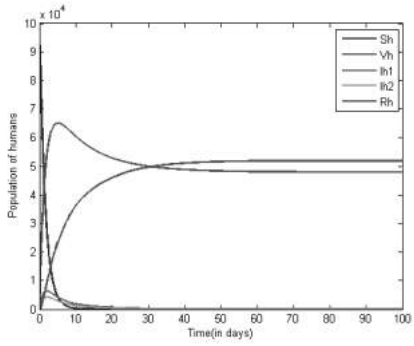

Figure 7 : Dengue infectious population with controls, $\phi_{1,2,3,4}=0.5.$

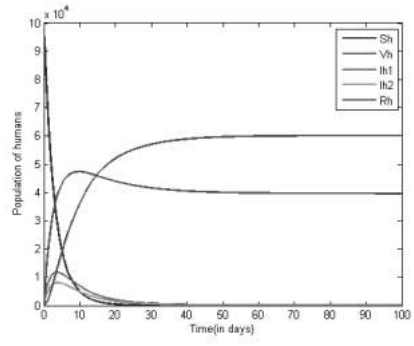

Figure 8 : Dengue infectious population with controls, $\phi_{1,2,3,4}=0.2.$

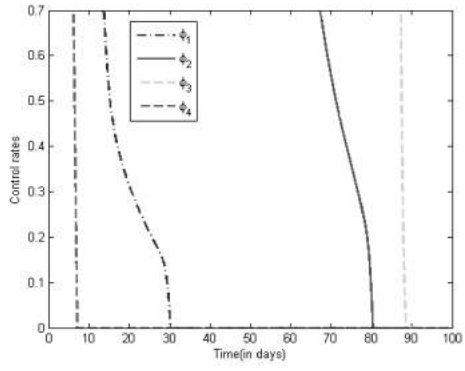

Figure 9 : Rate of controls $(\phi_1,\phi_2,\phi_3,\phi_4=0.7).$

First set of parameters, let $c_{11}=1.0,\ c_{12}=2.0,\ c_{21}=15.0,$ $c_{22}=4.0,\ c_{31}=10.0,\ c_{32}=2.0,\ c_{41}=0.000001,\ c_{42}=0.05,$ $\phi_{\max 1}=0.7,\ \phi_{\max 2}=0.7,\ \phi_{\max 3}=0.7,$ and $\phi_{\max 4}=0.7$.. Figure 1 - Figure 6, represents population without controls and population with controls. Is a comparison of the values of control with vaccination, medical treatment of both infection and elimination of egg or larvae of mosquitoes. We can see that if there is not control with treatment in first infected and second infected humans. It is clearly seen that the infection level has been increase the number of people infected with dengue hemorrhagic fever in first infected and second infected humans. The comparison of $\phi_{\max}$ values can be compared from Figure 2,7 and 8. We can see that the greater the value of $\phi_{\max}$, the less the number of people infected with dengue fever. Figures 9 shows the optimal control proflierd of Figures 2. These plots are very useful to plan for deployments of the treatment in order to control dengue fever outbreaks.

4. Discussion

We have presented a mathematical model of dengue fever with second infection and controls. The equilibria analysis has been conducted. The stability of epidemic and endemic points are controlled by the threshold number. If R_0 is less than one, then the disease dies out and the disease-free equilibrium is stable. If R_0 is greater than one, then the disease persists and the disease-free equilibrium

is unstable. We have deployed vaccine, both medical treatments and elimination of egg or larvae to investigate strategies to reduce numbers of infectious people by using optimal control theory. In conclusion, numerical simulations along with theories have provided and shown that with strategically deployed vaccination, medical treatment and elimination of egg or larvae of mosquitoes can reduce the number of infectious dengue fever people significantly.

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