Mathematical Model of Dengue Fever Incorporating Public Health Interventions

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ABSTRACT

This paper studies the spread of dengue fever in a mathematical model that incorporates data on public health interventions. In this model, the human population is divided into three types of individuals: Susceptible (S_h), Infected (I_h) and Recovered (R_h). The mosquito population is divided into two types: Susceptible (S_v) and Infected (I_v). We examine the reproduction number (R_0) and provides analysis of epidemic and endemic equilibrium points. Further, using optimal control techniques, we perform a study to investigate cost-effective solutions for time-dependent public health interventions in order to curb disease transmission in epidemic settings. MATLAB software was used for computations.

Keywords: Dengue fever, Mathematical model, Optimal Control, Numerical simulation.

INTRODUCTION

Dengue fever is a mosquito-borne tropical disease caused by the dengue virus. This virus is related to the viruses that cause West Nile infection and yellow fever. The dengue virus is transmitted by female mosquitoes, mainly of the species Aedes aegypti and, to a lesser extent, Ae. albopictus. The mosquito bites during daytime hours, particularly around the hours of dawn and dusk. There are four different strains of the dengue virus: 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. Not only is the number of cases increasing as the disease spreads to new areas, but explosive outbreaks are also occurring. The threat of a possible outbreak of dengue fever now exists in Europe. Local transmission of dengue was reported for the first time 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 Europe apart from mainland Portugal. In 2013, cases have occurred in Florida (USA) and Yunnan (China). Dengue is more common among older children, adolescents and adults. The risk of travelers catching dengue depends on several factors, including: the countries they visit, how long they stay in an endemic area (although even short-term visitors

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may be vulnerable to dengue), the season of travel (since mosquitoes breed in fresh-standing water, such as puddles and collected rainwater), and the intensity of dengue transmission in that area. Growing populations and an increase in global travel have resulted in the transmission of the virus between different populations. Transmission of the dengue virus happens in a cycle. An infected human is bitten by a mosquito, the infected mosquito then bites another human, and the cycle continues. Sometimes, symptoms of dengue are mild and can be mistaken for those of the flu or another viral infection. Younger children and people who have never had the infection before tend to have milder cases than older children and adults. However, serious problems can develop. These include dengue hemorrhagic fever, a rare complication characterized by high fever, damage to lymph and blood vessels, bleeding from the nose and gums, enlargement of the liver, and failure of the circulatory system. The symptoms may progress to massive bleeding, shock, and death. This is called dengue shock syndrome (DSS). Unfortunately, since dengue is a virus, traditionally there has not really been anything doctors can do to 'cure' it. Until recently all the patient could do is rest, take painkillers and drink plenty of water.

Mathematical modeling is a powerful tool which can test and compare different intervention strategies that might be useful in controlling or eliminating dengue. Various mathematical models can help people conceptualize the transmission dynamics in a quantitative way as well as enable the testing of different hypotheses to understand their importance. In 2003, Derouich et al. presented a paper dealing with the succession of two epidemics caused by two different strains of dengue. The dynamics of the disease is studied by a compartmental model involving ordinary differential equations for the human and the mosquito populations. Derouich's model allows for better understanding of the disease dynamics. In 2013, Side and Noorani proposed a SIR (Susceptible-Infected-Recovered) model with the dynamics of vector transmission was included. They investigated the re-breeding parameter value based on the number of reported cases of dengue fever in South Sulawesi (Indonesia) and Selangor (Malaysia). The results showed that the transmission rate between humans and mosquitoes is a very important role in the disease outbreaks in both countries. In 2015, Phaijoo and Gurung, they formulated a multipatch model to investigate the impact of temperature and human movement in the transmission dynamics of dengue fever. The study further explored the dynamics of the disease between humans and mosquitoes. The results suggested that proper management of human movement between patch helps to reduce the spread of dengue fever. Meanwhile, according to the article on website: The Economics Times; "Mathematical model could help predict dengue fever epidemic" points out that the model in the form of Susceptible-Infected-Recovered (SIR) is important to study strategies to control the disease and how a variety of neighbor conditions would affect the spread of the disease.

"The SIR-Network model can be used to predict whether local interventions - like cleaning up standing water in containers - in one or two neighborhoods could affect the prevalence of dengue across the city," said coauthor Daniel Coombs, professor at the University of British Colombia in Canada.

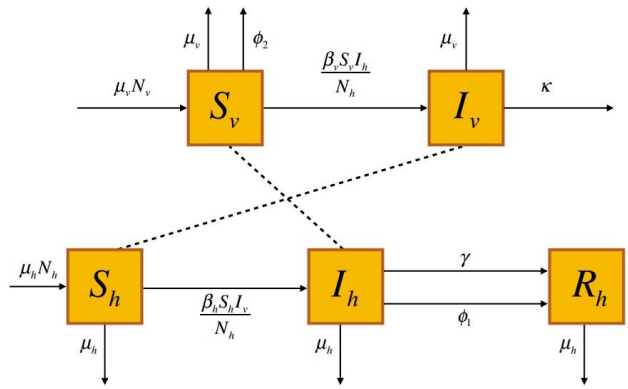
"We give formulae that describe whether an epidemic is possible, in terms of human travel patterns among neighborhoods, mosquito populations and biting rates in each neighborhood," Coombs said.

The researchers applied the SIR-Network model to dengue fever data, which had been updated several times, from the epidemic outbreak of 2007-2008 in various neighborhoods of Rio de Janeiro, Brazil, and soon discovered several interesting features of the epidemic. These constructed models inspired development of this paper's mathematical model of dengue fever by analyzing the (global) stability and using optimal control study.

METHODS AND MAIN RESULTS

1. Model formulation

N_h and N_v represent the population of humans and mosquitoes ("v" for vector"), respectively. The population of mosquitoes is divided into two groups: S_v and I_v, where S_v represents the susceptible mosquitoes and I_v represents the infected mosquitoes with dengue virus. The population of humans is classified into three types: susceptible (S_h), infected (I_h), and recovered (R_h). Note that for the purposes of efficiency in this study, all infected mosquitoes and humans are considered immediately infectious, even though in actuality there is an incubation period between exposure to the disease and the ability to transfer it to other individuals. The natural birth and death rates of humans is considered the same for the purposes of this model and is denoted by μ_h. Similarly mosquito birth and death rates are also treated as equal and denoted by μ_v. β_h and β_v represent the effective human to mosquito contact rate and the effective mosquito to human contact rate, respectively. κ represents the disease related death rate. The recovery rate for the infected population is denoted by γ. The rate at which infected people receive medical treatment for the disease is represented by ϕ_1, and the rate at which infected mosquitoes are eliminated is represented by ϕ_2. Diagram of the model is represented as follows:



The model comprises the following linear system of differential equations:

$$\frac{dS_h}{dt} = \mu_h N_h - \left(\mu_h + \frac{\beta_h I_v}{N_h}\right) S_h, \tag{1}$$

$$\frac{dI_h}{dt} = \frac{\beta_h I_v S_h}{N_h} - (\mu_h + \phi_1 + \gamma) I_h, \tag{2}$$

$$\frac{dR_h}{dt} = (\phi_1 + \gamma) I_h - \mu_h R_h, \tag{3}$$

$$\frac{dS_v}{dt} = \mu_v N_v - \left(\phi_2 + \frac{\beta_v I_h}{N_h} + \mu_v\right) S_v, \tag{4}$$

$$\frac{dI_v}{dt} = \frac{\beta_v S_v I_h}{N_h} - (\kappa + \mu_v) I_v. \tag{5}$$

where $N_h = S_h + I_h + R_h$ and $N_v = S_v + I_v$.

2. Epidemic analysis

The analysis of this model starts with examining the disease-free equilibrium point (DFE) and calculating the basic reproduction number (R_0). By setting $I_h = I_v = 0 = R_h$, the DFE $(\grave{o}_0)$ can be obtained as follows:

$$\grave{o}_0 = (S_h, I_h, R_h, S_v, I_v) = \left(N_h, 0, 0, \frac{\mu_v N_v}{\phi_2 + \mu_v}, 0\right).$$

Note that $S_h + I_h + R_h = N_h$ is a constant which allows us to drop the equation (3) of our system and consider a four-dimensional system to compute the basic reproduction number (R_0) by analyzing the eigenvalues of the Jacobian matrix of the system (1), (2), (4) and (5) as follows:

The Jacobian matrix of the equations (1), (2), (4) and (5) at $\grave{o}_0$ is given by

$$J(\grave{o}_0) = \begin{bmatrix} -\mu_h & 0 & 0 & -\beta_h \\ 0 & -(\mu_h + \phi_1 + \gamma) & 0 & \beta_h \\ 0 & -\dfrac{\beta_v \mu_v N_v}{N_h(\phi_2 + \mu_v)} & -(\phi_2 + \mu_v) & 0 \\ 0 & \dfrac{\beta_v \mu_v N_v}{N_h(\phi_2 + \mu_v)} & 0 & -(\kappa + \mu_v) \end{bmatrix},$$

and the characteristic equation of the matrix $J(\grave{o}_0)$ is

$$0 = det\left(J(\grave{o}_0) - \lambda I\right)$$

$$= (\mu_h + \lambda)\left((\phi_2 + \mu_v) + \lambda\right)\left[\lambda^2 + (\mu_h + \phi_1 + \gamma + \kappa + \mu_v)\lambda + (\mu_h + \phi_1 + \gamma)(\kappa + \mu_v) - \left(\frac{\beta_h \beta_v \mu_v N_v}{N_h(\phi_2 + \mu_v)}\right)\right].$$

The eigenvalues of $J(\grave{o}_0)$ are $\lambda_1 = -\mu_h$, $\lambda_2 = -(\phi_2 + \mu_v)$. The final portion can be put into a quadratic equation of the form $a_0\lambda^2 + a_1\lambda + a_2 = 0$ where

$$a_0 = 1,\ a_1 = \mu_h + \phi_1 + \gamma + \kappa + \mu_v \text{ and } a_2 = (\mu_h + \phi_1 + \gamma)(\kappa + \mu_v) - \left(\frac{\beta_h \beta_v \mu_v N_v}{N_h(\phi_2 + \mu_v)} \right).$$

The Routh-Hurwitz criterion requires $a_1 > 0,\ a_2 > 0$ as the necessary and sufficient conditions for the local asymptotic stability. It can be seen clearly that $a_1 > 0,$ and to see if $a_2 > 0,$ the following inequality can be used:

$$a_2 > 0 \Leftrightarrow (\mu_h + \phi_1 + \gamma)(\kappa + \mu_v) > \left(\frac{\beta_v \mu_v N_v}{N_h(\phi_2 + \mu_v)} \right) \beta_h.$$

Thus $1 > \dfrac{\beta_h \beta_v \mu_v N_v}{N_h(\phi_2 + \mu_v)(\mu_h + \phi_1 + \gamma)(\kappa + \mu_v)}$. Now we define

$$R_0 := \frac{\beta_h \beta_v \mu_v N_v}{N_h(\phi_2 + \mu_v)(\mu_h + \phi_1 + \gamma)(\kappa + \mu_v)}.$$

Theorem 1 When $R_0 < 1,$ the disease-free equilibrium point $(\grave{o}_0)$ is locally asymptotically stable.

To determine the global asymptotic stability of the disease-free equilibrium point, the following lemma is introduced by Castillo-Chavez et al. [7] can be applied.

Lemma 2 Consider a model system written in the form

$$\frac{dX_1}{dt} = F(X_1, X_2),$$
$$\frac{dX_2}{dt} = G(X_1, X_2),\ G(X_1, 0) = 0$$

where $X_1 \in \square^m$ denotes (its components) the number of uninfected individuals and $X_2 \in \square^n$ denotes (its components) the number of infected individuals including latent, infections, etc.; $X_0 = (X_1^*, 0)$ denotes the disease-free equilibrium of the system. Also assume the conditions $(H1)$ and $(H2)$ below:

$(H1)$ For $\dfrac{dX_1}{dt} = F(X_1, 0),\ X_1^*$ is globally asymptotically stable;

$(H2)$ $G(X_1, X_2) = AX_2 - \hat{G}(X_1, X_2),\quad \hat{G}(X_1, X_2) \geq 0$ for $(X_1, X_2) \in \Omega,$ where $A = \dfrac{\partial G}{\partial X_2}(X_1^*, 0)$ is an M-matrix (the off diagonal elements of A are nonnegative) and Ω is the region where the model makes biological sense. Then the DFE $X_0 = (X_1^*, 0)$ is globally asymptotically stable provided that $R_0 < 1.$

Theorem 3 The disease-free equilibrium point $(\grave{o}_0)$ of the model is globally asymptotically stable if $R_0 < 1.$

Proof. To adopt the notations in Lemma 2 and verify the conditions $(H1)$ and $(H2)$, in our ODE system, $X_1 = (S_h, R_h, S_v)$, $X_2 = (I_h, I_v)$ and $X_1^* = (N_h, 0, \frac{\mu_v N_v}{\phi_2 + \mu_v})$.

Note that

$$\frac{dX_1}{dt} = F(X_1, 0) = \begin{bmatrix} \mu_h N_h - \mu_h S_h \\ -\mu_h R_h \\ \mu_v N_v - (\phi_2 + \mu_v) S_v \end{bmatrix}.$$

That solution can be found with $S_h(t) = N_h + C_0 e^{-\mu_h t}$, $R_h(t) = C_1 e^{-\mu_h t}$ and $S_v(t) = \frac{\mu_v N_v}{(\phi_2 + \mu_v)} + C_2 e^{-(\phi_2 + \mu_v)t}$. As $t \to \infty$, $S_h(t) \to N_h$, $R_h(t) \to 0$ and $S_v(t) \to \frac{\mu_v N_v}{(\phi_2 + \mu_v)}$.

Thus $X_1^* = (N_h, 0, \frac{\mu_v N_v}{\phi_2 + \mu_v})$ is globally asymptotically stable.

Next, consider

$$G(X_1, X_2) = \begin{bmatrix} \frac{\beta_h I_v S_h}{N_h} - (\mu_h + \phi_1 + \gamma) I_h \\ \frac{\beta_v I_h S_v}{N_h} - (\kappa + \mu_v) I_v \end{bmatrix}, \text{ so } A = \begin{bmatrix} -(\mu_h + \phi_1 + \gamma) & \beta_h \\ \frac{\beta_v \mu_v N_v}{(\phi_2 + \mu_v) N_h} & -(\kappa + \mu_v) \end{bmatrix}$$

where $A = \frac{\partial G}{\partial X_2}(X_1^*, 0)$ with all non-negative off-diagonal elements.

Recall from Lemma 1, the condition $(H2)$,

$$G(X_1, X_2) = AX_2 - \hat{G}(X_1, X_2),$$

this implies that

$$\hat{G}(X_1, X_2) = \begin{bmatrix} \frac{\beta_h I_v}{N_h}(N_h - S_h) \\ \frac{\beta_v I_h}{N_h}\left(\frac{\mu_v N_v}{(\phi_2 + \mu_v)} - S_v\right) \end{bmatrix}.$$

From the equation (1), it can be observed that

$$\begin{aligned} \frac{dS_h}{dt} &= \mu_h N_h - \left(\mu_h + \frac{\beta_h I_v}{N_h}\right) S_h \\ &= \mu_h N_h - \mu_h S_h - \frac{\beta_h I_v S_h}{N_h}. \end{aligned}$$

Since $I_v \geq 0$, we obtain that

$$\frac{dS_h}{dt} \leq \mu_h N_h - \mu_h S_h.$$

We can write

$$\frac{dS_h}{dt} + \mu_h S_h \leq \mu_h N_h. \tag{6}$$

By using the integrating factor technique, let $y := e^{\int \mu_h dt} = e^{\mu_h t}$.

Multiplying on both sides of an inequality (6) with y, thus

$$\left(e^{\mu_h t}\right)\frac{dS_h}{dt}+\left(e^{\mu_h t}\right)\mu_h S_h \le \left(e^{\mu_h t}\right)\mu_h N_h$$

$$\frac{d}{dt}\left(e^{\mu_h t}\cdot S_h\right) \le e^{\mu_h t}\mu_h N_h$$

$$\int \frac{d}{dt}\left(e^{\mu_h t}\cdot S_h\right)dt \le \int e^{\mu_h t}\mu_h N_h dt$$

$$e^{\mu_h t}\cdot S_h \le \frac{e^{\mu_h t}}{\mu_h}\mu_h N_h + C_1$$

$$S_h \le N_h + C_1 e^{-\mu_h t}.$$

As $t\to\infty$, $S_h \to N_h$. Hence $S_h \le N_h$. Similarly, the equation (4)

$$\frac{dS_v}{dt} = \mu_v N_v - \left(\phi_2 + \frac{\beta_v I_h}{N_h} + \mu_v\right)S_v$$

$$= \mu_v N_v - \phi_2 S_v - \frac{\beta_v I_h S_v}{N_h} - \mu_v S_v.$$

Since $I_h \ge 0$, we obtain that

$$\frac{dS_v}{dt} \le \mu_v N_v - \left(\phi_2 + \mu_v\right)S_v. \tag{7}$$

We can write

$$\frac{dS_v}{dt} + \left(\phi_2 + \mu_v\right)S_v \le \mu_v N_v.$$

By using the integrating factor technique, let $z := e^{\int(\phi_2+\mu_v)dt} = e^{(\phi_2+\mu_v)t}$.
Multiplying on both sides of an inequality (7) with z, then

$$\left(e^{(\phi_2+\mu_v)t}\right)\frac{dS_h}{dt}+\left(e^{(\phi_2+\mu_v)t}\right)(\phi_2+\mu_v)S_v \le \left(e^{(\phi_2+\mu_v)t}\right)\mu_v N_v$$

$$\frac{d}{dt}\left(e^{(\phi_2+\mu_v)t}\cdot S_v\right) \le e^{(\phi_2+\mu_v)t}\mu_v N_v$$

$$\int \frac{d}{dt}\left(e^{(\phi_2+\mu_v)t}\cdot S_v\right)dt \le \int e^{(\phi_2+\mu_v)t}\mu_v N_v dt$$

$$e^{(\phi_2+\mu_v)t}\cdot S_v \le \frac{e^{(\phi_2+\mu_v)t}}{(\phi_2+\mu_v)}\mu_v N_v + C_2$$

$$S_v \le \frac{\mu_v N_v}{(\phi_2+\mu_v)} + C_2 e^{-(\phi_2+\mu_v)t}.$$

As $t\to\infty$, $S_v \to \frac{\mu_v N_v}{(\phi_2+\mu_v)}$. Thus $S_v \le \frac{\mu_v N_v}{(\phi_2+\mu_v)}$. Hence $\hat{G}(X_1, X_2) \ge 0$. Therefore, the DFE $X_0 = (X_1^*, 0)$ is globally asymptotically stable.

□

3. Endemic analysis

The stability of the DFE determines the short-term epidemics of the disease, whereas its dynamics over a longer of time is characterized by the stability at the endemic equilibrium. This section will analyze the endemic properties of this dengue fever model. The first thing to examine is the existence of the positive endemic equilibrium. The endemic equilibrium of the model is denoted by $\dot{o}^* = (S_h^*, I_h^*, R_h^*, S_v^*, I_v^*)$ which is determined by

$$S_h^* = \frac{\mu_h N_h N_h (\kappa + \mu_v)(\phi_2 N_h + \beta_v I_h^* + \mu_v N_h)}{\mu_h N_h (\kappa + \mu_v)(\phi_2 N_h + \beta_v I_h^* + \mu_v N_h) + \beta_h \beta_v \mu_v N_v I_h^*}, \; I_h^* = \frac{\beta_h I_v^* S_h^*}{N_h(\mu_h + \phi_1 + \gamma)}, \; R_h^* = \frac{(\phi_1 + \gamma) I_h^*}{\mu_h},$$

$$S_v^* = \frac{\mu_v N_v N_h}{(\phi_2 N_h + \beta_v I_h^* + \mu_v N_h)}, \text{ and } I_v^* = \frac{\beta_v \mu_v N_v N_h I_h^*}{N_h(\kappa + \mu_v)(\phi_2 N_h + \beta_v I_h^* + \mu_v N_h)}.$$

Finally, the following can be obtained $I_h^* = \frac{N_h N_h (\kappa + \mu_v)(\phi_2 + \mu_v)\mu_h (R_0 - 1)}{(\mu_h + \phi_1 + \gamma)(\mu_h N_h (\kappa + \mu_v)\beta_v + \beta_h \beta_v \mu_v N_v)}$.

It is clear that $I_h^* > 0$ when $R_0 > 1$. That leads to the result below:

Theorem 4 The positive endemic equilibrium point $(\dot{o}^*)$ of the model exists and is unique if $R_0 > 1$, and if $R_0 < 1$ then there is no positive endemic equilibrium.

The next step is to analyze the stability properties of the endemic equilibrium point. The following result can be verified regarding the local stability.

Theorem 5 When $R_0 > 1$, the endemic equilibrium point $(\dot{o}^*)$ is locally asymptotically stable.

Proof. The first step, we split to consider the endemic equilibrium point as $\dot{o}_1^* = (S_h^*, I_h^*, R_h^*)$ and $\dot{o}_2^* = (S_v^*, I_v^*)$. Note that $S_h + I_h + R_h = N_h$ is a constant which allows us to drop the equation (3) of our system. The Jacobian matrix of the equations (1)-(2), the human population at $x = \dot{o}_1^*$ is given by

$$J(S_h^*, I_h^*, R_h^*) = \begin{bmatrix} -\left(\mu_h + \frac{\beta_h I_v^*}{N_h}\right) & 0 \\ \frac{\beta_h I_v^*}{N_h} & -(\mu_h + \phi_1 + \gamma) \end{bmatrix},$$

and the characteristic equation of the matrix $J(\dot{o}_1^*)$ is

$0 = det\left(\lambda I - J(\dot{o}_1^*)\right) = \left(\lambda + \mu_h + \frac{\beta_h I_v^*}{N_h}\right)\left(\lambda + (\mu_h + \phi_1 + \gamma)\right)$. We obtain $\lambda_1 = -\left(\mu_h + \frac{\beta_h I_v^*}{N_h}\right)$ and $\lambda_2 = -(\mu_h + \phi_1 + \gamma)$ which both of the eigenvalues are negative.

Next, the Jacobian matrix of the equations (4)-(5), the mosquito population at $x = \dot{o}_2^*$ is given by

$$J(S_v^*, I_v^*) = \begin{bmatrix} -\left(\phi_2 + \frac{\beta_v I_h^*}{N_h} + \mu_v\right) & 0 \\ \frac{\beta_v I_h^*}{N_h} & -(\kappa + \mu_v) \end{bmatrix},$$

and the characteristic equation of the matrix $J(\dot{o}_2^*)$ is

$0 = det\left(\lambda I - J(\dot{o}_2^*)\right) = \left(\lambda + \phi_2 + \frac{\beta_v I_h^*}{N_h} + \mu_v\right)\left(\lambda + (\kappa + \mu_v)\right)$. Then $\lambda_3 = -\left(\phi_2 + \frac{\beta_v I_h^*}{N_h} + \mu_v\right)$ and $\lambda_4 = -(\kappa + \mu_v)$ which both of the eigenvalues are negative. By using the stability properties of a linear system theorem, it can be concluded that the endemic equilibrium point $\dot{o}^* = (\dot{o}_1^*, \dot{o}_2^*)$ is locally asymptotically stable. □

4. Optimal control

Now to the general model (1)-(5), time-dependent control profiles $\phi_1(t)$ and $\phi_2(t)$ are added. The system is considered with a time interval of [0,T]. The functions $\phi_1(t)$ and $\phi_2(t)$ are assumed to be at least Lebesgue measurable on [0,T]. The control set is defined as

$$\Omega = \left\{(\phi_1(t), \phi_2(t)) \mid 0 < \phi_1(t) < \phi_{1\max}, 0 < \phi_2(t) < \phi_{2\max}\right\}$$

where $\phi_{1\max}$ and $\phi_{2\max}$ denote the upper bounds of successful treatment on infected humans and elimination rate of infected mosquitoes, respectively. The bounds reflect practical limitation on the maximum rate of control in given time period. This optimal control aims to minimize the total number of infections and the costs of controlling the disease over the time interval $[0, T]$; i.e.,

$$\min_{(\phi_1,\phi_2)\in\Omega} \int_0^T [I_h(t) + c_{11}\phi_1(t)I_h(t) + c_{12}\phi_2(t)S_v(t) + c_{21}\phi_1^2(t) + c_{22}\phi_2^2(t)]\, dt$$

where c_{11}, c_{12}, c_{21} and c_{22} are appropriate units that define the appropriate costs associated with the control. First the adjoint functions are defined as $\lambda_{S_h}, \lambda_{I_h}, \lambda_{S_v}$ and λ_{I_v} is associated with the state equations for S_h, I_h, S_v and I_v, respectively. Hamiltonian, H, can be obtained by multiplying each adjoint function with the right-hand side of its corresponding state equation, and adding each of these products to the integrand of the objective function. As a result, the following is obtained:

$$H = I_h(t) + c_{11}\phi_1(t)I_h(t) + c_{12}\phi_2(t)S_v(t) + c_{21}\phi_1^2(t) + c_{22}\phi_2^2(t) + \lambda_{S_h}\left[\mu_h N_h - (\mu_h + \frac{\beta_h I_v}{N_h})S_h\right]$$
$$+ \lambda_{I_h}\left[\frac{\beta_h I_v S_h}{Nh} - (\mu_h + \phi_1 + \gamma)I_h\right] + \lambda_{S_v}\left[\mu_v N_v - (\phi_2 + \frac{\beta_v I_h}{N_h} + \mu_v)S_v\right] + \lambda_{I_v}\left[\frac{\beta_v S_v I_h}{N_h} - (\kappa + \mu_v)I_v\right].$$

To achieve the optimal control, the adjoint functions must satisfy $\frac{d\lambda_{S_h}}{dt}=-\frac{\partial H}{\partial S_h}$, $\frac{d\lambda_{I_h}}{dt}=-\frac{\partial H}{\partial I_h}$, $\frac{d\lambda_{S_v}}{dt}=-\frac{\partial H}{\partial S_v}$ and $\frac{d\lambda_{I_v}}{dt}=-\frac{\partial H}{\partial I_v}$ with final-time conditions $\lambda_{S_h}(T)=0$, $\lambda_{I_h}(T)=0$, $\lambda_{S_v}(T)=0$ and $\lambda_{I_v}(T)=0$. The characterizations of the optimal controls $\phi_1^*(t)$ and $\phi_2^*(t)$ are based on the conditions $\frac{\partial H}{\partial \phi_1}=0$ and $\frac{\partial H}{\partial \phi_2}=0$, respectively, subject to the constraints $0\le\phi_1\le\phi_{1\max}$ and $0\le\phi_2\le\phi_{2\max}$. We obtain that $\phi_1^*(t)=\max\left(0,\min\left(\phi_1(t),\phi_{1\max}\right)\right)$ and $\phi_2^*(t)=\max\left(0,\min\left(\phi_2(t),\phi_{2\max}\right)\right)$ where $\phi_1(t)=\left(\lambda_{I_h}I_h-c_{11}I_h\right)/2c_{21}$ and $\phi_2(t)=\left(\lambda_{S_v}S_v-c_{12}S_v\right)/2c_{22}$. The optimal control system, consisting of the state equations, the adjoint equations and the optimality conditions, has to be solved numerically. Numerical simulations have been conducted using various choices of cost parameters and time intervals, and a unique solution has been observed in each case. The numerical results clearly demonstrate that optimal control strategies can significantly bring down the number of infected individuals and infected mosquitoes. Some typical results are presented below.

Table 1: Symbols and Parameter values.

Parameter	Value	Reference	Parameter	Value	Reference
N_h	10,100	Estimated	γ	0.3201	Estimated
N_v	18,000	Estimated	κ	0.19	Estimated
μ_h	3.139×10^{-3}(per day)	[4]	β_h	0.0075	[4]
μ_v	1/14	[4]	β_v	0.00375	[4]
c_{11}	2	Estimated	c_{12}	0.01	Estimated
c_{21}	8	Estimated	c_{22}	2	Estimated

5. Numerical simulation

In this section, numerical simulations were performed using Euler's method with MATLAB.

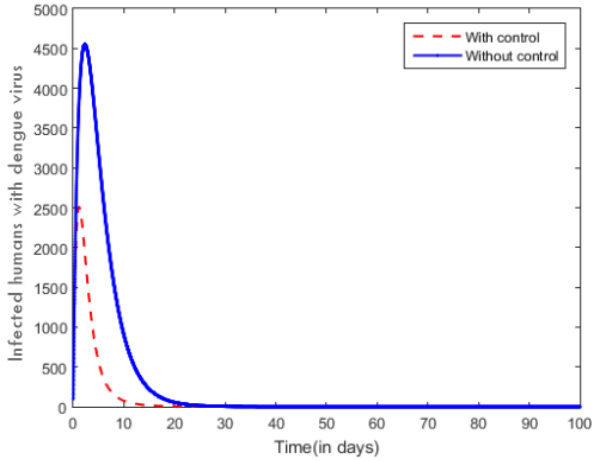


Figure 1: the infected humans with medical treatment for the dengue disease (dashed line) and without medical treatment for the dengue disease (solid line).

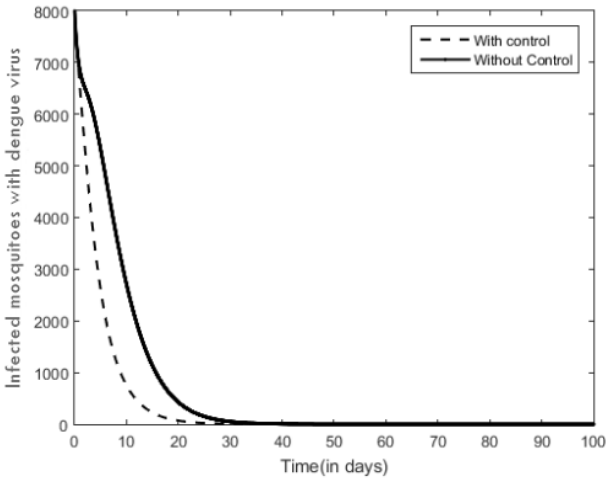


Figure 2: the infected mosquitoes with elimination (dashed line) and without elimination (solid line).

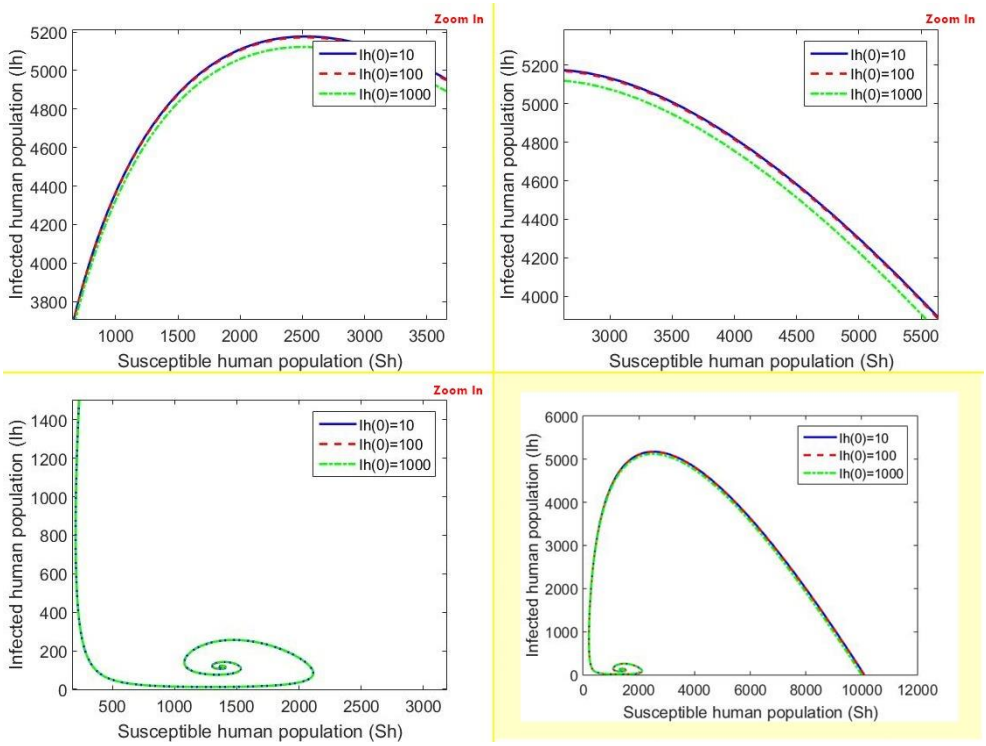


Figure 3 shows three phase portraits for the model with different initial conditions, and $R_0>1$, I_h vs. S_h of human populations.

As results above show that the infected humans with dengue virus have been reduced when received the medical treatment as the Figure 1 and the infected mosquitoes with dengue virus have approached to zero more quickly when there is the mosquito abatement as the Figure 2. Finally, the Figure 3 shows that all curves converge to the endemic equilibrium point with $I_h^* \approx 116.46$, $S_h^* \approx 1376.17$. This guarantees that the specific endemic equilibrium point $\left(\mathfrak{Q}_1^* = (S_h^*, I_h^*, R_h^*)\right)$ is locally (asymptotically) stable.

CONCLUSIONS

This study has presented a mathematical model of dengue fever which takes into account and analyzes both mosquito and human populations. This model has been constructed using both theoretical and numerical methods. In order to uncover the effects of the mosquito elimination rate and the medical treatment of infected humans on the spread of the disease, and in order to find ways to control the outbreak of dengue fever, an optimal control study was carried out. The stability of the disease-free equilibrium point and the endemic equilibrium point are controlled by the threshold number (R_0). If R_0 is less than one, then the disease dies out and the disease-free equilibrium point is stable. If R_0 is greater than one, then the

disease persists and the disease-free equilibrium point is unstable. In conclusion, the numerical simulations and theories are presented here have shown that attentive treatment of infected people and thorough elimination of mosquitoes can significantly reduce the number of infected humans with dengue fever.

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