Journal of Advances in Mathematics and Computer Science

23(3): 1-12, 2017; Article no.JAMCS.33955

Previously known as British Journal of Mathematics & Computer Science

ISSN: 2231-0851

Mathematical Model of Dengue Disease Transmission Dynamics with Control Measures

G. R. Phaijoo[1*] and D. B. Gurung[1]

[1] *School of Science, Department of Natural Sciences (Mathematics), Kathmandu University, Dhulikhel, Kavre, Nepal.*

Authors' contributions:

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript

Article Information

DOI: 10.9734/JAMCS/2017/33955

Editor(s):

(1) Dijana Mosic, Department of Mathematics, University of Nis, Serbia.

Reviewers:

(1) Fernando Ariel Genta, Oswaldo Cruz Foundation, Brazil.

(2) Jihad Adnani, University Hassan II Casablanca, Morocco.

Complete Peer review History: http://www.sciencedomain.org/review-history/20052

Original Research Article

Received: 5^{th} ***May*** 2017

Accepted: 6^{th} ***June*** 2017

Published: 14^{th} ***July*** 2017

Abstract

Dengue disease is a mosquito-borne infectious tropical disease caused by the dengue viruses of four serotypes, DEN 1 - DEN 4. It is transmitted between people by the bite of female adult *A*edes mosquitoes. In the present work, we study a vector host epidemic model of dengue disease by considering control measures of the disease. The aim of the study is to observe the effects of control measures on the dengue disease development. Explicit formula for the metric, basic reproduction number R_0 is obtained using Next Generation Matrix method. Stability of the disease free equilibrium and sensitivity analysis of model's parameters are discussed in terms of basic reproduction number. It is observed that the disease free equilibrium is locally and globally stable when $R_0 < 1$ and unstable when $R_0 > 1$. Numerical results are carried out to illustrate the impact of control measures in the disease transmission.

Keywords: Dengue; control measures; basic reproduction number; stability; sensitivity analysis.

2010 Mathematics Subject Classification: 53C25, 83C05, 57N16.

**Corresponding author: E-mail: gangaram@ku.edu.np;*

1 Introduction

Dengue disease is a vector borne infectious disease which is threatening about 2.5 billion people of the world's population especially of tropical and subtropical countries [1]. Four serologically different viruses DEN 1 - DEN 4 cause dengue disease. These viruses are transmitted to humans by the bites of *Aedes* mosquitoes. A person infected by one of the four serotypes of viruses never get infected by that serotype again but loses immunity to other three serotypes of the viruses [2].

Different mathematical models have been proposed and analyzed to understand the transmission dynamics of infectious diseases. In recent years, modeling has become a valuable tool in the analysis of dengue disease transmission dynamics and to determine the factors that influence the spread of disease to support control measures. Many researchers [3] [4] [5] [6] [7] [8] [9] have proposed SIR epidemic model [10] to study the transmission dynamics of dengue disease. Incubation periods in hosts and vectors have a significant influence in transmission dynamics of dengue disease. So, different mathematical studies [11] [12] [13] of dengue disease have been made to study dengue disease transmission dynamics with incubation periods.

There is no specific medicine to cure dengue disease. Awareness programs can be helpful in reducing the prevalence of the disease. Different epidemic models [14] [15] have been proposed to study the impact of awareness in controlling dengue disease. Prevention of mosquitoes bites is one of the ways to prevent dengue disease. The mosquitoes bite humans during day and night when lights are on. So, to get rid of mosquitoes' bite, people can use mosquito repellents and nets. If infected hosts feel they have symptoms of the disease and approach the doctor in time for the supportive treatment, they can recover fast. This type of awareness can help controlling the disease. Another way of controlling dengue is destroying larval breeding sites of mosquitoes and killing them. Spray of insecticides may be applied to control larvae or adult mosquitoes which can transmit dengue viruses.

In the present work, we have considered followings as control measures:

(i) some susceptible hosts use mosquito repellents to avoid mosquitoes' bite; (ii) some infected hosts seek for the supportive treatment timely and recover fast; (iii) some infected hosts use mosquito repellents to avoid mosquitoes' bite; (iv) spray of insecticides is applied to control mosquito population.

2 Formulation of the Model

In the model, total host (human) population, N_h is divided into four classes: S_h (susceptible), E_h (exposed), I_h (infectious), R_h (recovered) and total vector (mosquito) population, N_v is divided into three classes: S_v (susceptible), E_v (exposed), I_v (infectious). We assume that the fraction u_1 of susceptible hosts use mosquito repellents to avoid mosquitoes' bite. So, the fraction $(1 - u_1)$ of susceptible hosts interact with infectious mosquitoes. The fraction u_2 of infectious hosts seek for the timely supportive treatment and recover fast by the rate $r\gamma_h$ $(r > 1)$. The fraction r_1u_2 (r_1 is the proportionality constant) of infectious hosts use mosquito repellents to avoid mosquitoes' bite. u_3 is a control variable that represents the eradication effort of insecticide spraying. It follows that the recruitment rate of mosquito population is reduced by a factor of $1 - u_3$. Also, it is assumed that the mortality rate of mosquito population increases at a rate r_2u_3 (r_2 is the proportionality constant).

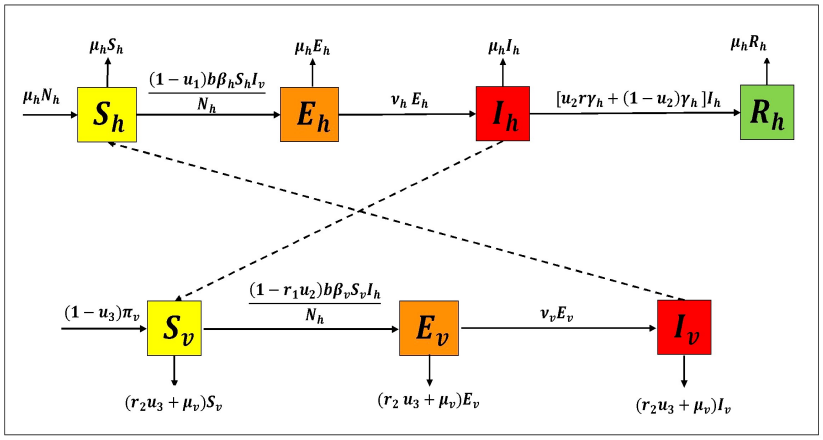

Fig. 1. Flow chart of the model

Fig. 1 describes the dynamics of dengue disease together with control measures. The system of differential equations which describes the present SEIR - SEI vector host model is given by

$$\begin{aligned}
\frac{dS_h}{dt} &= \mu_h N_h - (1-u_1)\frac{b\beta_h}{N_h}S_h I_v - \mu_h S_h \\
\frac{dE_h}{dt} &= (1-u_1)\frac{b\beta_h}{N_h}S_h I_v - (\nu_h+\mu_h)E_h \\
\frac{dI_h}{dt} &= \nu_h E_h - [ru_2\gamma_h + (1-u_2)\gamma_h + \mu_h]I_h \\
\frac{dR_h}{dt} &= [ru_2\gamma_h + (1-u_2)\gamma_h]I_h - \mu_h R_h \\
\frac{dS_v}{dt} &= (1-u_3)\pi_v - (1-r_1u_2)\frac{b\beta_v}{N_h}S_v I_h - (r_2u_3+\mu_v)S_v \\
\frac{dE_v}{dt} &= (1-r_1u_2)\frac{b\beta_v}{N_h}S_v I_h - (r_2u_3+\nu_v+\mu_v)E_v \\
\frac{dI_v}{dt} &= \nu_v E_v - (r_2u_3+\mu_v)I_v
\end{aligned} \tag{2.1}$$

Parameters of the model are described in Table 1.

Table 1. Model parameters and their description

Symbols	Description
μ_h	death rate of host population
ν_h	host's incubation rate
γ_h	recovery rate of host population
β_h	transmission probability from vector to host
π_v	recruitment rate of vector population
μ_v	death rate of vector population
ν_v	vector's incubation rate
β_v	transmission probability from host to vector
b	biting rate of vector

Total host population, $N_h = S_h + E_h + I_h + R_h$, total vector population, $N_v = S_v + E_v + I_v$.

$$\frac{dN_h}{dt} = 0 \text{ and } \frac{dN_v}{dt} = (1-u_3)\pi_v - (r_2u_3+\mu_v)N_v.$$

So, N_h remains constant and N_v approaches the equilibrium $\dfrac{(1-u_3)\pi_v}{(r_2u_3+\mu_v)}$ as $t \to \infty$.

Introducing the proportions

$$s_h = \frac{S_h}{N_h}, \quad e_h = \frac{E_h}{N_h}, \quad i_h = \frac{I_h}{N_h}, \quad r_h = \frac{R_h}{N_h}, \quad s_v = \frac{S_v}{(1-u_3)\pi_v/(r_2u_3+\mu_v)}$$

$$e_v = \frac{E_v}{(1-u_3)\pi_v/(r_2u_3+\mu_v)}, \quad i_v = \frac{I_v}{(1-u_3)\pi_v/(r_2u_3+\mu_v)}$$

Since $r_h = 1 - s_h - e_h - i_h$ and $s_v = 1 - e_v - i_v$, the system of equations (2.1) can be written as the equivalent five dimensional non-linear system of ODEs:

$$\begin{aligned}
\frac{ds_h}{dt} &= \mu_h(1-s_h) - \alpha s_h i_v \\
\frac{de_h}{dt} &= \alpha s_h i_v - \beta e_h \\
\frac{di_h}{dt} &= \nu_h e_h - \gamma i_h \\
\frac{de_v}{dt} &= \delta s_v i_h - (\epsilon+\nu_v)e_v \\
\frac{di_v}{dt} &= \nu_v e_v - \epsilon i_v
\end{aligned} \tag{2.2}$$

Here,

$\alpha = \dfrac{b\beta_h\pi_v(1-u_1)(1-u_3)}{N_h(r_2u_3+\mu_v)}$, $\beta = \nu_h + \mu_h$, $\gamma = ru_2\gamma_h + (1-u_2)\gamma_h + \mu_h$, $\delta = (1-r_1u_2)b\beta_v$,
$\epsilon = r_2u_3 + \mu_v$.

3 Stability Analysis

3.1 Basic reproduction number

Definition 3.1. Basic reproduction number, R_0 is the expected number of secondary infections caused by a single infectious individual during their entire infectious lifetime.

Mathematical expression for the basic reproduction number is obtained using Next Generation Matrix Method [16] [17]. The basic reproduction number R_0 is obtained as

$$R_0 = \rho(FV^{-1}) = \sqrt{\frac{\alpha\delta\nu_h\nu_v}{\beta\gamma\epsilon(\epsilon+\nu_v)}} \tag{3.1}$$

Here,

$$F = \begin{bmatrix} 0 & 0 & 0 & \alpha \\ 0 & 0 & \delta & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}, \quad V = \begin{bmatrix} \beta & 0 & 0 & 0 \\ 0 & \epsilon+\nu_v & 0 & 0 \\ -\nu_h & 0 & \gamma & 0 \\ 0 & -\nu_v & 0 & \epsilon \end{bmatrix} \tag{3.2}$$

3.2 Equilibrium points of the model

Two possible equilibrium points of the model are $E_0 = (1, 0, 0, 0, 0)$ and $E_1 = (s_h^*, e_h^*, i_h^*, e_v^*, i_v^*)$ where,

$$s_h^* = \frac{(\beta\gamma\epsilon + \delta\mu_h\nu_h)(\epsilon + \nu_v)}{\delta\nu_h[\epsilon\mu_h + (\alpha + \mu_h)\nu_v]}, \quad e_h^* = \frac{\mu_h\beta\gamma\epsilon(\epsilon + \nu_v)(R_0^2 - 1)}{\beta\delta\nu_h[\epsilon\mu_h + (\alpha + \mu_h)\nu_v]}, \quad i_h^* = \frac{\mu_h\beta\gamma\epsilon(\epsilon + \nu_v)(R_0^2 - 1)}{\beta\delta\gamma[\epsilon\mu_h + (\alpha + \mu_h)\nu_v]},$$

$$e_v^* = \frac{\mu_h\beta\gamma\epsilon^2(R_0^2 - 1)}{\alpha\nu_v(\beta\gamma\epsilon + \delta\mu_h\nu_h)}, \quad i_v^* = \frac{\mu_h\beta\gamma\epsilon(R_0^2 - 1)}{\alpha(\beta\gamma\epsilon + \delta\mu_h\nu_h)}$$

Here, the first equilibrium point is disease free equilibrium (DFE) point which always exists in the absence of infective population. The second point if exists is called endemic equilibrium point. This point exists if $R_0 > 1$.

Thus, we have Theorem 3.1:

Theorem 3.1 (Existence of Equilibrium Points)**.** *System of equations* (2.2) *always has a disease free equilibrium point. If* $R_0 > 1$*, the system of equations* (2.2) *has a unique endemic equilibrium point.*

Theorem 3.2 (Local Stability of DFE)**.** *The DFE of the system of equations* (2.2) *is locally asymptotically stable if* $R_0 < 1$ *and unstable if* $R_0 > 1$*.*

Proof. The Jacobian matrix of the system of equation (2.2) about DFE is obtained as the block structure

$$J = \begin{bmatrix} A & B \\ 0 & F - V \end{bmatrix}$$

Matrix J is triangular matrix. So, the stability of the system of equations (2.2) depends on the matrices on diagonal, $A = [-\mu_h]$ and $F - V$. Matrix A has the eigenvalue $-\mu_h < 0$. Matrix F is non-negative matrix, V is non-singular $M-$ matrix [18]. Spectral abscissa of the matrix $F - V$, $s(F - V) < 0 \Leftrightarrow \rho(FV^{-1}) < 1$ [17]. But, $R_0 = \rho(FV^{-1})$. Therefore, all the eigenvalues lie in the left half plane if $R_0 < 1$. Hence, DFE of the system of equations (2.2) is locally asymptotically stable if $R_0 < 1$.

If $R_0 > 1$ then $s(F - V) > 0$ showing that at least one eigenvalue lies in the right half plane. So, DFE of the system of equations (2.2) is unstable if $R_0 > 1$. □

Theorem 3.3 (Global Stability of DFE)**.** *The DFE of the system of equations* (2.2) *is globally asymptotically stable if* $R_0 < 1$*.*

Proof. In the present model, $s_h \leq 1$ and $s_v \leq 1$. So, from the system of equations (2.2), for the dynamics of infective population

$$\begin{aligned} \frac{de_h}{dt} &\leq \alpha i_v - \beta e_h \\ \frac{de_v}{dt} &\leq \delta i_h - (\epsilon + \nu_v)e_v \\ \frac{di_h}{dt} &= \nu_h e_h - \gamma i_h \\ \frac{di_v}{dt} &= \nu_v e_v - \epsilon i_v \end{aligned} \tag{3.3}$$

Corresponding linear system of equations of (3.3) is

$$\begin{aligned} \frac{de_h}{dt} &= \alpha i_v - \beta e_h \\ \frac{de_v}{dt} &= \delta i_h - (\epsilon + \nu_v) e_v \\ \frac{di_h}{dt} &= \nu_h e_h - \gamma i_h \\ \frac{di_v}{dt} &= \nu_v e_v - \epsilon i_v \end{aligned} \tag{3.4}$$

The system of linear equations (3.4) can be written as

$$\frac{d\vec{u}}{dt} = K\vec{u} \tag{3.5}$$

where $K = F - V$ and $\vec{u} = [e_h,\ e_v,\ i_h,\ i_v]^T$.

If $R_0 = \rho(FV^{-1}) < 1$, then $s(F - V) < 0$ [17], thus each positive solution of (3.4) satisfies $\lim_{t\to\infty} e_h = 0$, $\lim_{t\to\infty} e_v = 0$, $\lim_{t\to\infty} i_h = 0$ and $\lim_{t\to\infty} i_v = 0$. DFE of the system of equations (3.4) is globally asymptotically stable since the system is linear. Since all the variables in the system of equations (2.2) are nonnegative, the use of a comparison theorem [19] [20] leads to $\lim_{t\to\infty} e_h = 0$, $\lim_{t\to\infty} e_v = 0$, $\lim_{t\to\infty} i_h = 0$, $\lim_{t\to\infty} i_v = 0$ and $\lim_{t\to\infty} s_h = 1$. Hence, the DFE, $(1, 0, 0, 0, 0)$ is globally asymptotically stable if $R_0 < 1$. □

4 Sensitivity Analysis

Sensitivity analysis is performed to determine the importance of each parameter to the transmission dynamics of dengue disease. The analysis helps to measure the relative change in a variable when a parameter changes. Such information is very important to study transmission dynamics of the disease and to optimize control measures of the disease. In order to decide the most influential parameter among the control measures in the present model, we have taken the base line values displayed in Table 2.

We use the normalized sensitivity index following [21].

Definition 4.1. The normalized forward sensitivity index of a variable u that depends on a parameter p is defined as $\Upsilon_u^p = \dfrac{\partial p}{\partial u} \times \dfrac{u}{p}$. In the present work, we take $p = R_0$ and $u = u_1$, u_2, u_3, r, r_1, r_2.

Negatives signs of sensitivity indices in Table 2 shows that values of basic reproduction number, R_0 get decreased with the increase in the level of control measures u_1, u_2, u_3, r, r_1, r_2. The table shows that more influential control measures are u_1 (use of mosquito repellents to avoid mosquitoes' bite), u_3 (control variable that represents the eradication effort of insecticide spraying) and r (recovery rate improving factor). The greatest value of sensitivity index shows that the control measure, u_3 is the most sensitive control measure. So, u_3 is the most influential measure in controlling the disease.

Table 2. Sensitivity analysis of control measures

Parameters →	u_1	u_2	u_3	r	r_1	r_2
Baseline Values→	0.1	0.1	0.1	1.1	0.1	0.1
Sign →	-ve	-ve	-ve	-ve	-ve	-ve
Sensitivity Indices→	0.056	0.009	0.337	0.054	0.005	0.281

5 Numerical Results and Discussion

In the present work, we have used SEIR - SEI epidemic model with control measures. The simulations are carried out in order to explore the impacts of control measures on the dengue disease dynamics. Following parameter values are used in the model for simulation purpose

$N_h = 5071126$, $\pi_v = 2500000$, $\nu_h = 0.1667$, $\mu_h = 0.0045$, $\mu_v = 0.02941$, $\gamma_h = 0.328833$, $b\beta_h = 0.75$, $b\beta_v = 0.375$, $\nu_v = 0.1428$ [13].

Fig. 2 shows that many susceptible humans remain uninfected over a time when control measures are implemented. When human becomes aware of control measures such as: using mosquito repellents, applying insecticides, seeking doctor for timely treatment and avoiding mosquitoes' bite, only few humans get infected of the disease (Fig. 3). From Fig 2 and Fig. 3 , we see that many hosts can be saved from being infected of the disease when control measures are implemented properly.

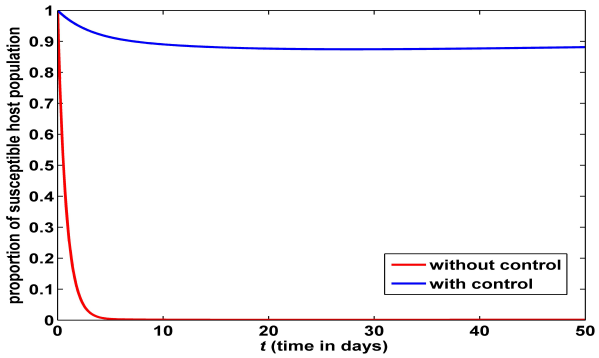

Fig. 2. Dynamics of susceptible hosts with and without implementation of control measures

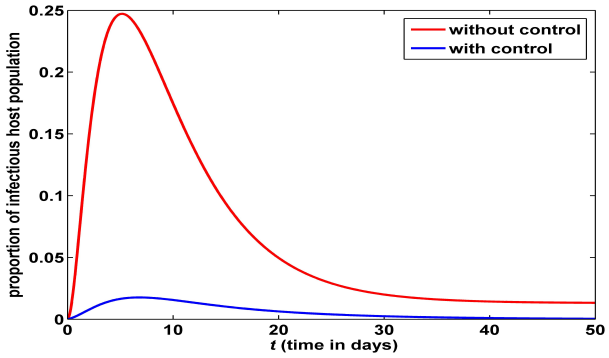

Fig. 3. Dynamics of infectious hosts with and without implementation of control measures

Basic reproduction number, R_0 is a metric which tells that the disease dies out if $R_0 < 1$ and the disease takes hold if $R_0 > 1$. Figs. 4-6 are simulated to study the impact of control measure in determinig the value of R_0. The figures show that R_0 decreases with the increase in level of control measures. That means, the prevalence of disease can be reduced with the implementation of control measures. Sufficient increase in level of control measures causes the basic reproduction number to be less than unity.

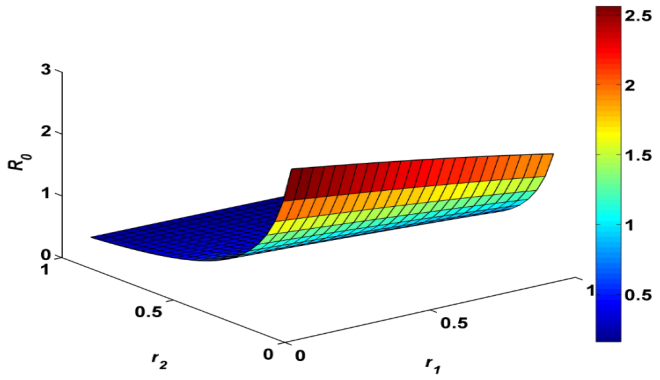

Fig. 4. Basic reproduction number, R_0 against control measures, r_1 and r_2

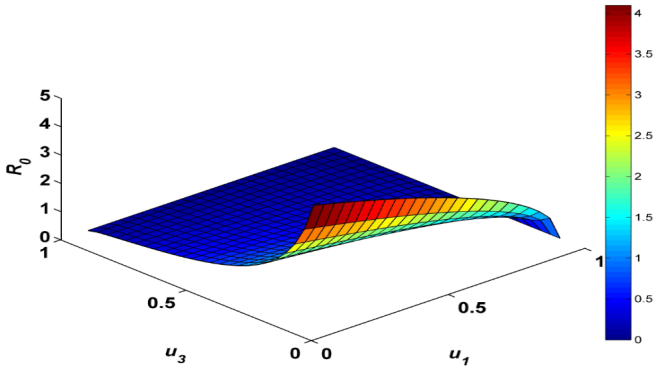

Fig. 5. Basic reproduction number, R_0 against control measures, u_1 and u_3

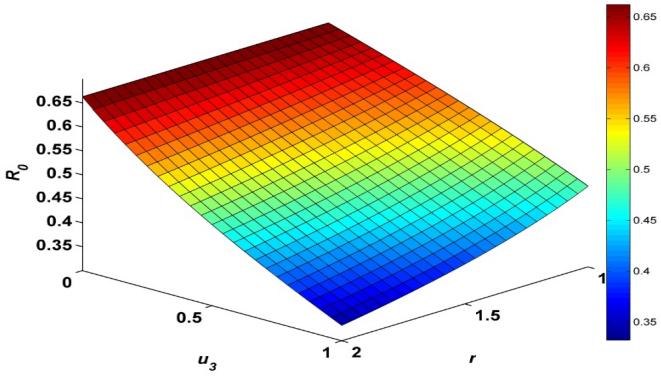

Fig. 6. Basic reproduction number, R_0 against control measures, r and u_3

Figs. 7-10 are simulated to describe the sensitivity of the control measures on the transmission dynamics of dengue disease. The figures show the change in the population of infectious hosts with the change in level of control measures. Among all control measures, the control measures r, u_1, u_3 are seen more sensitive to the disease transmission. Fig. 10 shows that the most sensitive control measure is u_3 (control variable that represents the eradication effort of insecticide spraying).

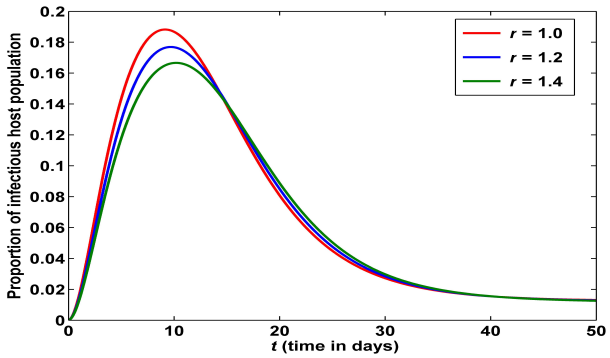

Fig. 7. Dynamics of infectious hosts with various values of control measure, r

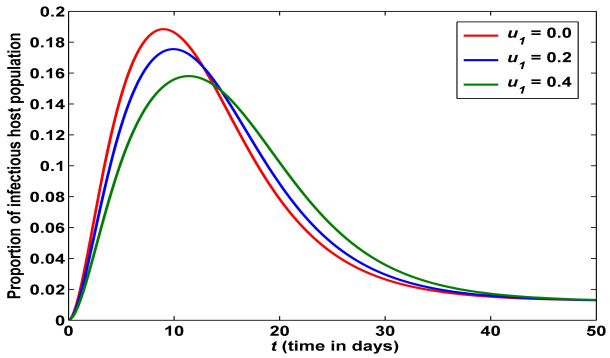

Fig. 8. Dynamics of infectious hosts with various values of control measure, u_1

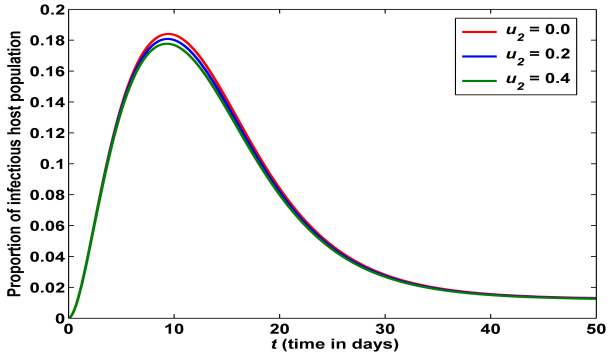

Fig. 9. Dynamics of infectious hosts with various values of control measure, u_2

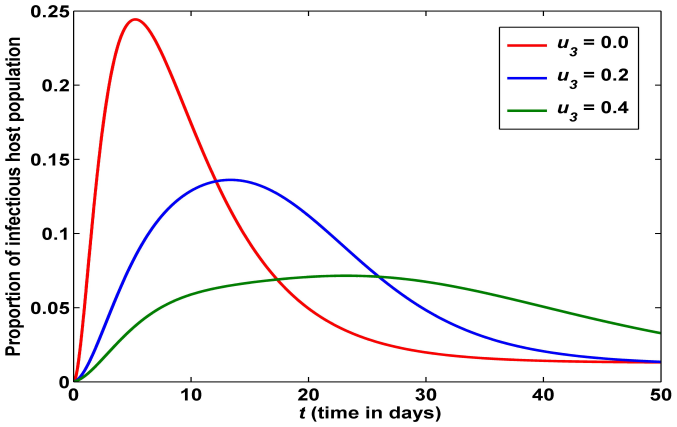

Fig. 10. Dynamics of infectious hosts with various values of control measure, u_3

6 Conclusion

Dengue disease is becoming more prevalent worldwide and spreading in new areas. So, there is an urgent need to develop mosquito management strategies and control strategies of the disease. In the present study, we have used SEIR-SEI epidemic model to study the influence of control measures in transmission dynamics of dengue disease. There is no effective treatment of dengue disease. So, we have introduced some control measures in the model which can help in reducing of burden of the disease.

Basic reproduction number is a metric, which determines whether the disease comes under control or becomes more prevalent. Results in the present work show that DFE of the model is locally and globally stable when $R_0 < 1$; unstable and endemic equilibrium point exists when $R_0 > 1$. Value of basic reproduction number can be reduced by increasing the level of control measures. Also, the simulated results show that very few hosts get infected of the disease in the presence of control measures. That means prevalence of the disease get decreased with the proper implementation of control measures.

Sensitivity analysis is made to identify the more influential control measures among the control measures used against the disease. In the present case, the eradication effort of insecticide spraying is found to be the most influential control measure to decrease the prevalence of the disease and to bring the disease under control.

Competing Interests

Authors have declared that no competing interests exist.

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