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Sensitivity of Dengue Fever Transmission Model with respect to Parameters

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Abstract

Dengue is the most common mosquito-borne viral disease in human. Motivated by the failure of current methods to control dengue fever, we study the sensitivity of the dynamics of the dengue transmission model with respect to parameters with aim to identify the most important parameters in order to control dengue. Three dimensional model (consisting susceptible, infective host population and infective vector population) is considered. Deriving the sensitivity equation we study the variation of the host/vector infective population with respect to parameters. Effective contact rates (human to vector and vector to human), death rate of vector population and the probability of susceptible host can permanently be immunized are considered as parameters. Results report that variation of the dynamics of the model with respect to these parameters is significant on the control point of view.

Keywords: *Dengue fever, Mathematical modeling, Sensitivity*

INTRODUCTION

Dengue is a disease which is now endemic in more than 100 countries of Africa, Latin America, Asia and the Western Pacific. It is transmitted to the man by mosquitoes *Aedes aegypti* and exists in two forms: Dengue Fever and Dengue Haemorrhagic Fever. The disease can be contracted by one of the four different serotypes known as DEN1, DEN2, DEN3 and DEN4 [4]. Moreover, immunity is acquired only to the serotype contracted and a contact with a second serotype becomes more dangerous.

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Mortality rate of the dengue infectious disease may reach 40% if the infected person is left untreated [1]. Although almost all of the occurrences of the dengue are in the tropical region, a recent study shows that the dengue may occur in other region too due to the global warming effects [12]. The climate change may convert a region from unsuitable habitat for mosquitoes to live to a new suitable habitat.

Dengue viral infections have been endemic in Sri Lanka since the mid-1960s which was when the first cases of dengue fever/dengue haemorrhagic fever were reported. Since then, there have been regular epidemics in Sri Lanka with increasing numbers of case each year. Figure 1 and 2 show number of dengue cases and deaths due to dengue in Sri Lanka from 1985 to 2005 [8].

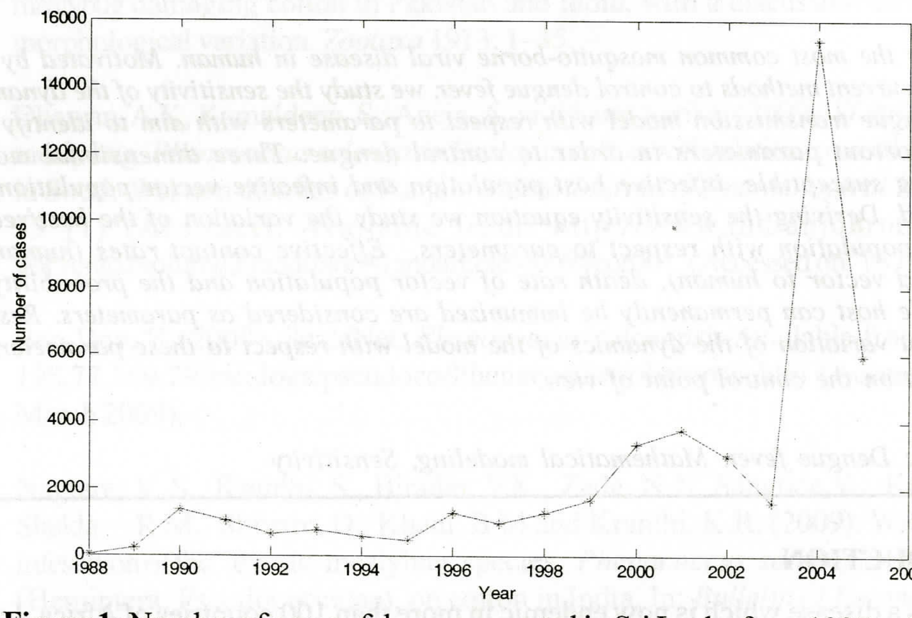

Figure 1: Number of cases of dengue reported in Sri Lanka from 1985 to 2005.

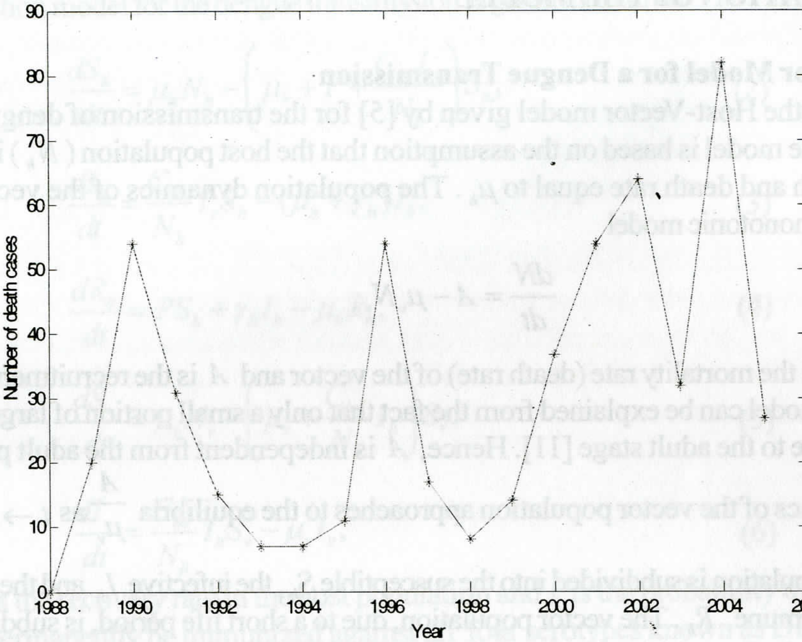

Figure 2: Number of deaths due to dengue in Sri Lanka from 1985 to 2005.

Mathematical modeling became an interesting tool for the understanding of these illnesses and for the proposition of strategies. The formulation of the model and the possibility of a simulation with parameter estimation, allow tests for sensitivity and comparison of conjunctures. To control the dengue effectively, we should understand the dynamics of the disease transmission and take into account all of the relevant details, such as the dynamics of the vector. Several authors [5, 7, 10, 11] developed the models for the dengue disease transmission and included the dynamics of the mosquitoes into a standard SIR (susceptible-infective-recover) epidemic models of a single population. All these available models consist several parameters. These parameters depend on many facts such as the temperature, humidity, rainfalls, vector population and other climatic and environmental conditions. To study the controllability of the dengue transmission, it is necessary requirement that we need to have good understanding about the sensitivity of the dynamics of dengue with respect to parameters. In this study, the sensitivity of a dengue transmission model with respect to parameters is considered.

FORMULATION OF THE MODEL

Host-Vector Model for a Dengue Transmission

We review the Host-Vector model given by [5] for the transmission of dengue fever as follows. The model is based on the assumption that the host population (N_h) is constant, i.e. the birth and death rate equal to μ_h. The population dynamics of the vector N_v are given by a monotonic model

$$\frac{dN}{dt} = A - \mu_v N_v, \tag{1}$$

where μ_V is the mortality rate (death rate) of the vector and A is the recruitment rate. This mosquito model can be explained from the fact that only a small portion of large supply of eggs survive to the adult stage [11]. Hence, A is independent from the adult population. The dynamics of the vector population approaches to the equilibria $\frac{A}{\mu_v}$ as $t \to \infty$.

The host population is subdivided into the susceptible S_h, the infective I_h and the recovered, assumed immune, R_h. The vector population, due to a short life period, is subdivided into the susceptible S_v and the infective I_v. The model supposes a homogeneous mixing of host and vector population so that each bite has an equal probability of being taken from any particular host. Let β_s the average biting rate of susceptible vectors, p_{hv} the average transmission probability of an infectious host to a susceptible vector, the rate of exposure for vectors is given by $\frac{p_{hv} I_h \beta_s}{N_h}$. It is admitted [5] that some infections increase the number of bites by the infected vectors in relation to the susceptible, therefore, we assume that the rate of infected mosquito bites β_i is greater than the one of the susceptible vectors β_s.

Taking p_{vh} as the average transmission probability of an infectious vector to host then the rate of exposure for host is given by $\frac{p_{vh} I_v \beta_i}{N_h}$. We define the adequate contact rate of host to vectors, C_{hv} and the adequate contact rate of vectors to host, C_{vh} and are given by

$$C_{hv} = p_{hv}\beta_s, \quad C_{vh} = p_{vh}\beta_i$$

The interaction model for the dengue transmission is given as follows:

$$\frac{dS_h}{dt} = \mu_h N_h - \left(\mu_h + P + \frac{C_{vh} I_v}{N_h}\right) S_h, \qquad (2)$$

$$\frac{dI_h}{dt} = \frac{C_{vh}}{N_h} I_v S_h - (\mu_h + \gamma_h) I_h, \qquad (3)$$

$$\frac{dR_h}{dt} = PS_h + \gamma_h I_h - \mu_h R_h, \qquad (4)$$

$$\frac{dS_v}{dt} = \mu_v N_v - \left(\mu_v + \frac{C_{hv}}{N_h} I_h\right) S_v, \qquad (5)$$

$$\frac{dI_v}{dt} = \frac{C_{hv}}{N_h} I_h S_v - \mu_v I_v, \qquad (6)$$

where γ_h is the recovery rate in the host population and P is the probability of susceptible host can permanently be immunized against all four serotypes known as DEN1, DEN2, DEN3 and DEN4 [4].

Three Dimensional Simplified Model

Using [5]

$$S_h + I_h + R_h = N_h \quad \text{and } S_v + I_v = N_v$$

three dimensional system can be obtained and by introducing following quantities

$$S_h^* = \frac{S_h}{N_h}, \quad I_h^* = \frac{I_h}{N_h}, \quad I_v^* = \frac{I_v}{N_v}$$

system can be rendered into dimensionless form. Dropping the star, the system reads as

$$\frac{dS_h}{dt} = \mu_h (1 - S_h) - \frac{N_v C_{vh}}{N_h} S_h I_v - PS_h, \qquad (7)$$

$$\frac{dI_h}{dt} = \frac{N_v C_{vh}}{N_h} S_h I_v - (\mu_h + \gamma_h) I_h, \qquad (8)$$

$$\frac{dI_v}{dt} = C_{hv} I_h (1 - I_v) - \mu_v I_v. \qquad (9)$$

Sensitivity Equations

The results of sensitivity analysis have wide-ranging applications in science and engineering, including model development, parameter estimation, model simplification, data assimilation, optimization and optimal control. The basic measures of sensitivity are the partial derivatives

$$\frac{\partial \text{model responses}}{\partial \text{model parameters}},$$

and called the sensitivity coefficients of the model [3,9]. Usually, a given system contains several parameters (like dengue transmission model). But since we are interesting in sensitivities, we can treat one parameter after another while keeping the remaining ones fixed [6]. It is therefore sufficient in the following theory to suppose that system depends only on one scalar parameter. Consider the initial value problem,

$$\frac{dy}{dt} = y' = f(t, y, p), \;\; y(0) = y_0, \tag{10}$$

where p denotes the parameter. When parameter p is replaced in (10) by q another solution can be obtained, which is denoted by $\hat{y}(t)$:

$$\hat{y}' = f(t, \hat{y}, q), \;\; \hat{y}(0) = y_0, \tag{11}$$

Now subtract (10) from (11) and linearize,

$$\begin{aligned} \hat{y}' - y' &= f(t, \hat{y}, q) - f(t, y, p) \\ &= \frac{\partial f}{\partial y}(t, y, p)(\hat{y} - y) + \frac{\partial f}{\partial p}(t, y, p)(q - p) + \rho_1(\hat{y} - y) + \rho_2(q - p) \end{aligned}$$

where ρ_1 and ρ_2 are denoted higher order terms. Introducing sensitivity variable

$$\sigma(t) = \frac{\hat{y}(t) - y(t)}{q - p} = \frac{\partial y}{\partial p}$$

and neglecting higher order terms, sensitivity equations can be obtained:

$$\frac{d\sigma}{dt} = \frac{\partial f}{\partial y}(t, y(t), p) + \frac{\partial f}{\partial p}(t, y(t), p), \;\; \sigma(0) = \frac{\partial y_0}{\partial p}. \tag{12}$$

We study the sensitivity of the dengue fever transmission model with respect to parameters. Effective contact rates (human to vector C_{hv} and vector to human C_{vh}), death rate of vector population (μ_v) and the probability (p) of susceptible host can permanently be immunized are considered as parameters.

NUMERICAL METHODS AND SIMULATION CONDITIONS

Numerics

Both systems (equations (7)-(8) and sensitivity system (12)) were solved using the MATLAB routine ode23. This routine is an implementation of an explicit Runge-Kutta (2, 3) pair [2].

Parameter Values

Table 1 summarizes the simulation conditions and parameter values which we used in the simulation [10].

Table 1: Parameter values

Parameter	Notation	Value
Transmission probability of vector to human	p_{hv}	0.75
Transmission probability of human to vector	p_{vh}	0.75
Bites per susceptible mosquito per day	β_s	0.50
Bites per infectious mosquito per day	β_i	1.00
Effective contact rate, human to vector	C_{hv}	0.375
Effective contact rate, vector to human	C_{vh}	0.75
Human life span	$\frac{1}{\mu_h}$	25000 days
Vector life span	$\frac{1}{\mu_v}$	4 days
Host infection duration	$\frac{1}{\mu_h + \gamma_h}$	3 days
Human population	N_h	10,000
Vector population	N_v	20,000

RESULTS

Figure 3 shows dynamics of host and vector population. It shows that the host susceptible (S_h) drops significantly in a relatively small period of time. Both host infective (I_h) and vector infective (I_v) increases significantly during the period of 30 days, and then degrease.

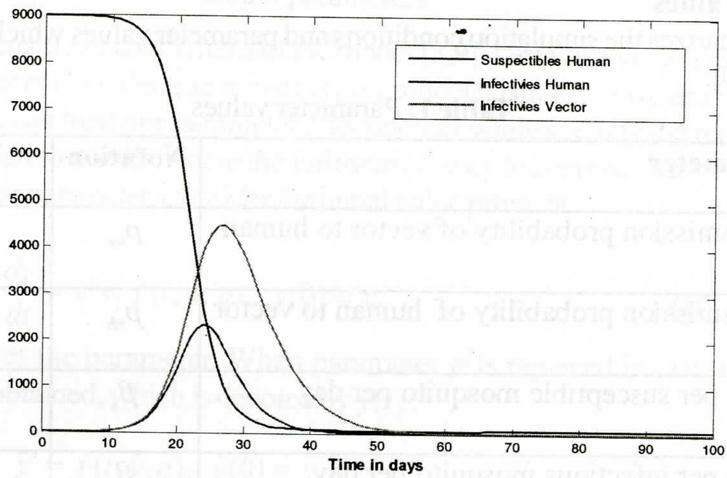

Figure 3: Dynamics of host/vector population.

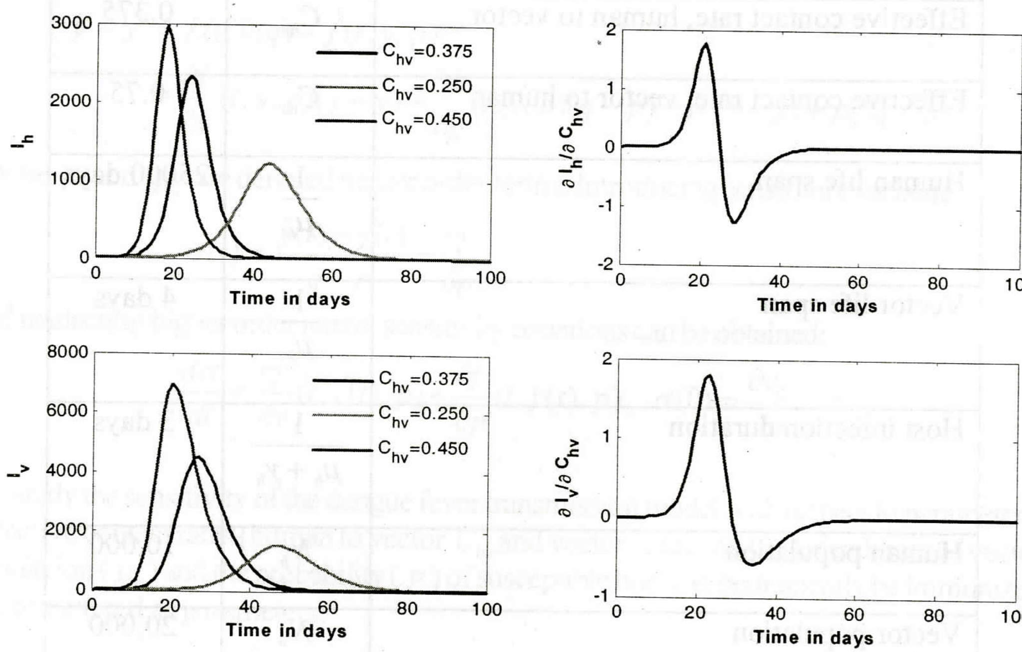

Figure 4: Sensitivity of dynamics of dengue transmission model with respect C_{hv}.

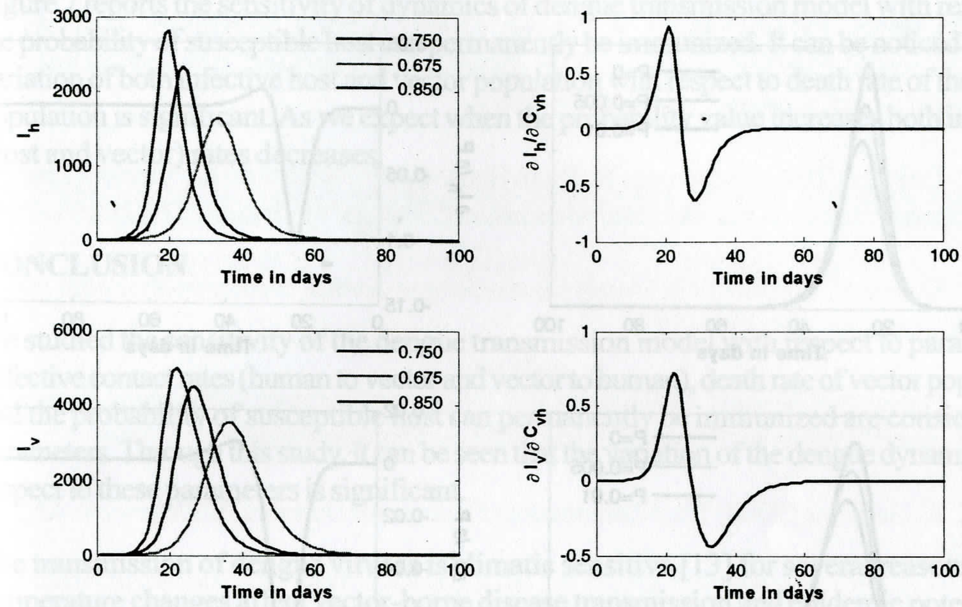

Figure 5: Sensitivity of dynamics of dengue transmission model with respect to C_{vh}.

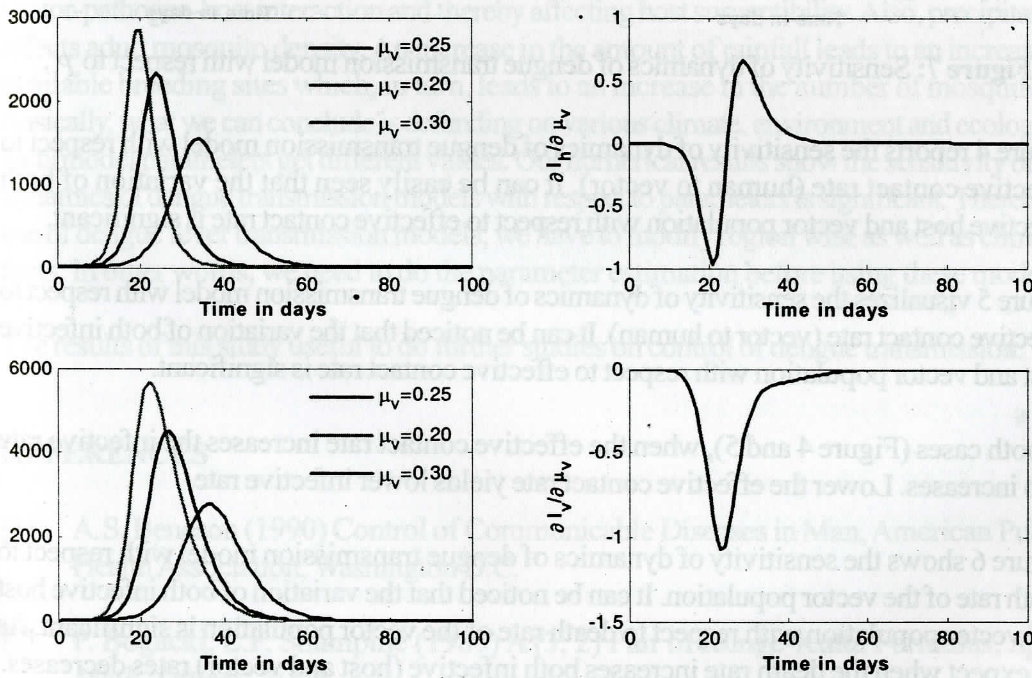

Figure 6: Sensitivity of dynamics of dengue transmission model with respect to μ_v.

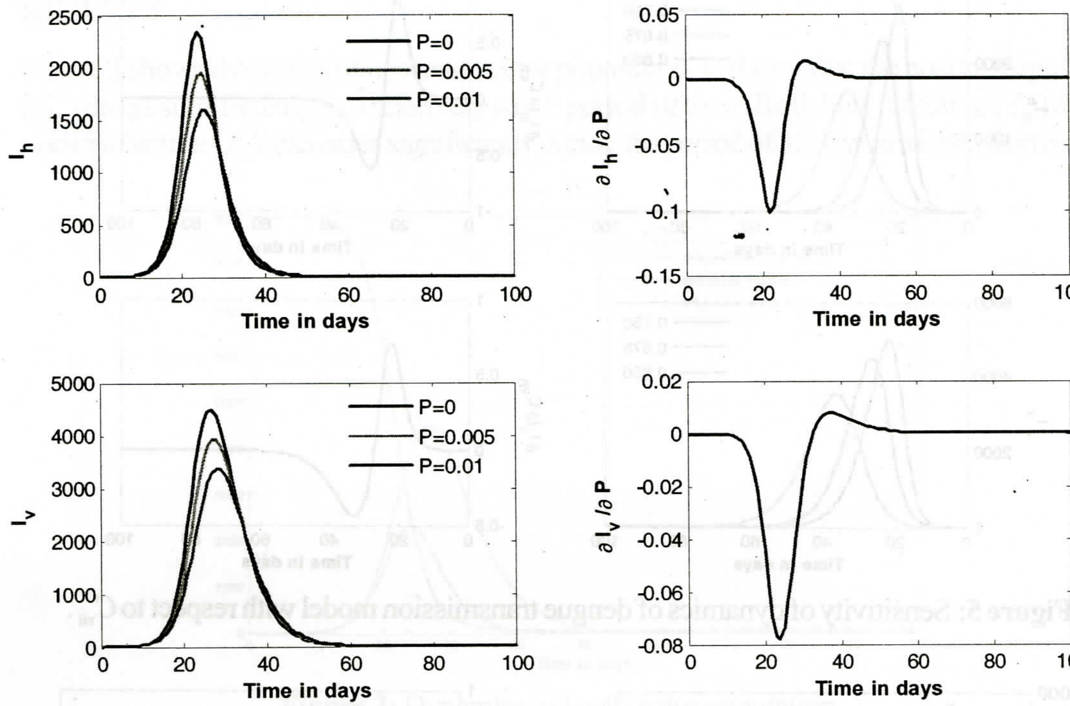

Figure 7: Sensitivity of dynamics of dengue transmission model with respect to p .

Figure 4 reports the sensitivity of dynamics of dengue transmission model with respect to effective contact rate (human to vector). It can be easily seen that the variation of both infective host and vector population with respect to effective contact rate is significant.

Figure 5 visualizes the sensitivity of dynamics of dengue transmission model with respect to effective contact rate (vector to human). It can be noticed that the variation of both infective host and vector population with respect to effective contact rate is significant.

In both cases (Figure 4 and 5), when the effective contact rate increases the infective rate also increases. Lower the effective contact rate yields lower infective rate.

Figure 6 shows the sensitivity of dynamics of dengue transmission model with respect to death rate of the vector population. It can be noticed that the variation of both infective host and vector population with respect to death rate of the vector population is significant. As we expect when the death rate increases both infective (host and vector) rates decreases.

Figure 7 reports the sensitivity of dynamics of dengue transmission model with respect to the probability of susceptible host can permanently be immunized. It can be noticed that the variation of both infective host and vector population with respect to death rate of the vector population is significant. As we expect when the probability value increases both infective (host and vector) rates decreases.

CONCLUSION

We studied the sensitivity of the dengue transmission model with respect to parameters. Effective contact rates (human to vector and vector to human), death rate of vector population and the probability of susceptible host can permanently be immunized are considered as parameters. Through this study, it can be seen that the variation of the dengue dynamics with respect to these parameters is significant.

The transmission of dengue viruses is climatic sensitive [13] for several reasons. First, temperature changes affect vector-borne disease transmission and epidemic potential by altering vector's reproductive rate, biting rate, the extrinsic incubation period of the pathogen, by shifting a vector's geographical range or distribution and increasing or decreasing vector-pathogen-host interaction and thereby affecting host susceptibility. Also, precipitation affects adult mosquito density. An increase in the amount of rainfall leads to an increase in available breeding sites which, in turn, leads to an increase in the number of mosquitoes. Basically, what we can conclude is defending on various climate, environment and ecological facts model parameters get different values. Our numerical results show the sensitivity of the dynamics of dengue transmission models with respect to parameters is significant. Therefore, use of dengue fever transmission models; we have to modify region wise as well as climatic facts. In other words, we need to do the parameter estimation before using these models.

The results of this study useful to do further studies on control of dengue transmission.

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