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Sensitivity Analysis in a Dengue Fever Vector-Bias Epidemiological Model

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***Abstract*: Vector-bias model has been formulated and modified by including immigration and disease induced fatality rate. Then for the basic and modified models, basic reproduction ratios have been derived, equations and numerical values have been determined for sensitivity indices of re-breeding ratios with respect to epidemiological parameters. Then by numerical simulations we justified analytical results.**

***Keywords*: Vector-Bias, Sensitivity Index, Re-Breeding Ratio, Epidemiological.**

1. Introduction

Epidemiological history of dengue elucidates that certain part of the world specially tropical and subtropical regions, urban and semi-urban areas where dengue is a large health worry for the population. Female vectors named as Aedes aegypti & Aedes albopictus are communicators of Dengue Virus (DV). DV I-IV are four serotypes of DV. Dengue infecting approximately 50 million people per year. More than 50% world population is at great danger of infection due to living in DV disease present area [6]. Dengue Hemorrhagic Fever (DHF) patients are mostly found in South-East Asia [9]. In the last two decades dengue occurred among people of America in a significant way [2]. In Pakistan Dengue Fever (DF) caused destructive role since 1994 till 27 September 2013 [3, 4]. Khyber Pukhtunkhwa (KPK) of Pakistan is most infective province with DV types DV-II and DV-III [7]. According to Director General Health (DGH) KPK, Pakistan the mortality rate in total infected population was (0.364%: 43/11818) from 14 August 2013 to 27 November 2013. The proposed models consist of collection of parameters corresponding to host and vector populations.

We assumed the unknown parameters as constant. Nevertheless, in a realistic case of any process, some of the parameters may be changed which implicitly depend on various factors. Most of such factors do commonly not exist explicitly in the epidemiological model due to the reason that there is a need of balance between epidemiological model, results and numerical simulations and lack of accurate understanding about them [8].

The remaining sections of the paper are organized as follows: In Section 2 we formulate and develop vector-bias epidemiological model and compute expressions for re-breeding ratios. In Section 3 we derived expressions for sensitivity indices and compute its values. In Section 4 numerical simulations, are presented using epidemiological and entomological parameters values to analyse sensitivity. Section 5 is devoted to discussion. Finally conclusion is given in section 6.

2. Vector Bias Epidemiological Models

The basic model

ODEs governed the model are:

$$\frac{d\hat{S}_H}{dt} = \lambda_H N_H - \left(\frac{\beta_{VH} q \hat{I}_V}{p\hat{I}_H + q\hat{S}_H} + \lambda_H + \sigma_i\right)\hat{S}_H, \quad (1)$$

$$\frac{d\hat{I}_H}{dt} = \left(\frac{\beta_{VH} q \hat{I}_V}{p\hat{I}_H + q\hat{S}_H} + \sigma_i\right)\hat{S}_H - (\lambda_H + \eta)\hat{I}_H, \quad (2)$$

$$\frac{d\hat{R}_H}{dt} = \eta\hat{I}_H - \lambda_H\hat{R}_H \quad (3)$$

$$\frac{d\hat{S}_V}{dt} = \lambda_V N_V - \left(\frac{\beta_{HV} p \hat{I}_H}{p\hat{I}_H + q\hat{S}_H} + \lambda_V + \sigma_e\right)\hat{S}_V, \quad (4)$$

$$\frac{d\hat{I}_V}{dt} = \left(\frac{\beta_{HV} p \hat{I}_H}{p\hat{I}_H + q\hat{S}_H} + \sigma_e\right)\hat{S}_V - \lambda_V\hat{I}_V. \quad (5)$$

Definition of parametric symbols and technical terminologies used in the proposed models:

N_H: indicates total population of hosts (humans),

$\hat{S}_H$: are the numbers of population that are likely to be infected by dengue,

$\hat{I}_H$: are the numbers of population that are infected by dengue,

$\hat{R}_H$: are recovered people,

N_V: Number of vectors (mosquitos),

$\hat{S}_V$: are the numbers of mosquitos that are likely to be infected by dengue virus,

$\hat{I}_V$: represents infected vectors,

η : recovery rate of humans,

λ_H: natural fatality rate of humans or birth rate,

λ_V: death rate of vector,

σ_i: is intrinsic incubation rate,

σ_e: is extrinsic incubation rate,

$\frac{\beta_{VH} q \hat{S}_H \hat{I}_V}{p\hat{I}_H + q\hat{S}_H}$: is incident function for host,

$\frac{\beta_{HV} p \hat{S}_V \hat{I}_H}{p\hat{I}_H + q\hat{S}_H}$: is incident function for vector,

β_{VH}: indicate dengue virus transmission rate from vector to host,

β_{HV}: represent dengue virus transmission rate from human to mosquito,

p: is the probability of vectors that bite host if the host is infectious,

q: is the probability of bite by vectors if the human is susceptible,

$\frac{q\hat{S}_H}{p\hat{I}_H + q\hat{S}_H}$: is the chance of human to be susceptible after bite of vector,

$\frac{p\hat{I}_H}{p\hat{I}_H + q\hat{S}_H}$: is the chance of human to be infected after bite of vector.

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Where,
$q\hat{S}_H$:is the total susceptible humans bitten by vector,
$p\hat{I}_H$:is the total infectious humans bitten by vector and
$p\hat{I}_H + q\hat{S}_H$:is the total number of hosts bitten by mosquitos.

Assume:
$N_H = \hat{S}_H + \hat{I}_H + \hat{R}_H$ and $N_V = \hat{S}_V + \hat{I}_V$.

Normalized system of equations from (1) to (5) by considering:
$\frac{\hat{S}_H}{N_H} = S_H$, $\frac{\hat{I}_H}{N_H} = I_H$, $\frac{\hat{R}_H}{N_H} = R_H$, $\frac{\hat{S}_V}{N_V} = S_V$, $\frac{\hat{I}_V}{N_V} = I_V$,
$S_H + I_H + R_H = 1$ and $S_V + I_V = 1$.

$$\frac{dS_H}{dt} = \lambda_H - \left(\frac{N_V\beta_{VH}q}{N_H(pI_H+qS_H)} I_V + \lambda_H + \sigma_i\right) S_H, \quad (6)$$
$$\frac{dI_H}{dt} = \left(\frac{N_V\beta_{VH}q}{N_H(pI_H+qS_H)} I_V + \sigma_i\right)S_H - (\lambda_H + \eta)I_H, \quad (7)$$
$$\frac{dR_H}{dt} = \eta I_H - \lambda_H R_H, \quad (8)$$
$$\frac{dS_V}{dt} = \lambda_V - \left(\frac{\beta_{HV}p}{pI_H+qS_H} I_H + \lambda_V + \sigma_e\right)S_V, \quad (9)$$
$$\frac{dI_V}{dt} = \left(\frac{\beta_{HV}p}{pI_H+qS_H} I_H + \sigma_e\right)S_V - \lambda_V I_V. \quad (10)$$

Reduced System of equations from (6) to (10) into: [1]
$$\frac{dI_H}{dt} = \frac{\beta_{VH}N_V}{N_H}[1 - g(I_H)]I_V + \sigma_i[1 - R_H] - [\lambda_H + \sigma_i + \eta]I_H, \quad (11)$$
$$\frac{dI_V}{dt} = \beta_{HV} g(I_H)[1 - I_V] - [\sigma_e + \lambda_V]I_V + \sigma_e, \quad (12)$$
where,
$$g(I_H) = \frac{pI_H}{(p-q)I_H + q(1-R_H)}.$$

Invariant region:
$\Gamma = \{(I_H, I_V) \in R^2 : 0 \le I_H \le 1;\ 0 \le I_V \le 1\}$ in which we studied the properties of system of equations(11) and (12).

The Linearization matrix for system of equations (11) & (12) is written as:
$$L(I_H, I_V) = \begin{pmatrix} l_{11} & l_{12} \\ l_{21} & l_{22} \end{pmatrix} \quad (13)$$
where,
$$l_{11} = -\left(\frac{\beta_{VH}N_V}{N_H} g'(I_H) I_V + (\lambda_H + \eta + \sigma_i)\right),$$
$$l_{12} = \frac{\beta_{VH}N_V}{N_H}(1 - g(I_H)),$$
$l_{21} = \beta_{HV} g'(I_H)(1 - I_V)$ and
$$l_{22} = -(\beta_{HV} g(I_H) + (\sigma_e + \lambda_V))$$
such that,
$$g'(I_H) = \frac{pq(1-R_H)}{[(p-q)I_H + q(1-R_H)]^2}. \quad (14)$$

Consider disease free equilibrium (DFE) $E_0 = (0, 0)$ and time dependent state variable $R_H = 0$, equation(13) become
$$L(0,0) = \begin{pmatrix} -(\lambda_H + \eta + \sigma_i) & \frac{\beta_{VH}N_V}{N_H} \\ \frac{p\beta_{HV}}{q} & -(\sigma_e + \lambda_V) \end{pmatrix}, \quad (15)$$
$\det[L(0,0)] = (\sigma_e + \lambda_V)(\lambda_H + \eta + \sigma_i)(1 - R_0)$,
where, $R_0 = \frac{pN_V\beta_{HV}\beta_{VH}}{qN_H(\sigma_e+\lambda_V)(\lambda_H+\eta+\sigma_i)}$, (16)
is the re-breeding ratio or basic reproduction ratio for the basic model.

The modified model

We modify the basic model to include fatality rate due to disease (θ_d) and immigration of hosts (Λ_H).

State equations governed the model are:
$$\frac{d\hat{S}_H}{dt} = \Lambda_H - \left(\frac{\beta_{VH}q\hat{I}_V}{p\hat{I}_H+q\hat{S}_H} + \lambda_H + \sigma_i\right)\hat{S}_H, \quad (17)$$
$$\frac{d\hat{I}_H}{dt} = \left(\frac{\beta_{VH}q\hat{I}_V}{p\hat{I}_H+q\hat{S}_H} + \sigma_i\right)\hat{S}_H - (\lambda_H + \eta + \theta_d)\hat{I}_H, \quad (18)$$
$$\frac{d\hat{R}_H}{dt} = \eta\hat{I}_H - \lambda_H\hat{R}_H, \quad (19)$$
$$\frac{d\hat{S}_V}{dt} = \lambda_V N_V - \left(\frac{\beta_{HV}p\hat{I}_H}{p\hat{I}_H+q\hat{S}_H} + \lambda_V + \sigma_e\right)\hat{S}_V, \quad (20)$$
$$\frac{d\hat{I}_V}{dt} = \left(\frac{\beta_{HV}p\hat{I}_H}{p\hat{I}_H+q\hat{S}_H} + \sigma_e\right)\hat{S}_V - \lambda_V\hat{I}_V, \quad (21)$$

Normalized system of equations from (17) to (21) by considering:
$\frac{\hat{S}_H}{N_H} = S_H$, $\frac{\hat{I}_H}{N_H} = I_H$, $\frac{\hat{R}_H}{N_H} = R_H$, $\frac{\hat{S}_V}{N_V} = S_V$, $\frac{\hat{I}_V}{N_V} = I_V$.
$$\frac{dS_H}{dt} = \frac{\Lambda_H}{N_H} - \left(\frac{N_V\beta_{VH}q}{N_H(pI_H+qS_H)} I_V + \lambda_H + \sigma_i\right)S_H, \quad (22)$$
$$\frac{dI_H}{dt} = \left(\frac{N_V\beta_{VH}q}{N_H(pI_H+qS_H)} I_V + \sigma_i\right)S_H - (\lambda_H + \eta + \theta_d)I_H, \quad (23)$$
$$\frac{dR_H}{dt} = \eta I_H - \lambda_H R_H, \quad (24)$$
$$\frac{dS_V}{dt} = \lambda_V - \left(\frac{\beta_{HV}p}{pI_H+qS_H} I_H + \lambda_V + \sigma_e\right)S_V, \quad (25)$$
$$\frac{dI_V}{dt} = \left(\frac{\beta_{HV}p}{pI_H+qS_H} I_H + \sigma_e\right)S_V - \lambda_V I_V \quad (26)$$

Assuming that $\hat{S}_H + \hat{I}_H + \hat{R}_H = N_H$ and $\hat{S}_V + \hat{I}_V = N_V$. System of equations from (17) to (21) can be reduced into:
$$\frac{d\hat{S}_H}{dt} = \Lambda_H - \left(\frac{\beta_{VH}q\hat{I}_V}{p\hat{I}_H+q\hat{S}_H} + \lambda_H + \sigma_i\right)\hat{S}_H, \quad (27)$$
$$\frac{d\hat{I}_H}{dt} = \left(\frac{\beta_{VH}q\hat{I}_V}{p\hat{I}_H+q\hat{S}_H} + \sigma_i\right)\hat{S}_H - (\lambda_H + \eta + \theta_d)\hat{I}_H, \quad (28)$$
$$\frac{d\hat{I}_V}{dt} = \left(\frac{\beta_{HV}p\hat{I}_H}{p\hat{I}_H+q\hat{S}_H} + \sigma_e\right)\hat{S}_V - \lambda_V\hat{I}_V. \quad (29)$$

Assume:
$$\Gamma = \left\{(\hat{S}_H, \hat{I}_H, \hat{I}_V) : 0 \le \hat{S}_H, \hat{I}_H \le \frac{\Lambda_H}{\lambda_H + \sigma_i}, 0 \le \hat{I}_V \le N_V\right\}$$
is an invariant region and we study properties of system of equations (27) to (29) in it.

Consider left hand side of system of equations from (27) to (29) equal to zero and solved for DFE we get $E_0 = \left(\frac{\Lambda_H}{\lambda_H + \sigma_i}, 0, 0\right)$.

Jacobian matrix for system of equations from (27) to (29) can be determined as:
$$J(\hat{S}_H, \hat{I}_H, \hat{I}_V) = \begin{pmatrix} j_{11} & j_{12} & j_{13} \\ j_{21} & j_{22} & j_{23} \\ j_{31} & j_{32} & j_{33} \end{pmatrix}, \quad (30)$$
where,
$$j_{11} = -\left(\lambda_H + \sigma_i + \frac{\beta_{VH}pq\hat{I}_H\hat{I}_V}{(p\hat{I}_H+q\hat{S}_H)^2}\right), j_{12} = \frac{\beta_{VH}pq\hat{S}_H\hat{I}_V}{(p\hat{I}_H+q\hat{S}_H)^2},$$
$$j_{13} = \frac{-\beta_{VH}q\hat{S}_H}{(p\hat{I}_H+q\hat{S}_H)}, j_{21} = \sigma_i + \frac{\beta_{VH}pq\hat{I}_H\hat{I}_V}{(p\hat{I}_H+q\hat{S}_H)^2},$$
$$j_{22} = -\left((\lambda_H + \theta_d + \eta) + \frac{\beta_{VH}pq\hat{S}_H\hat{I}_V}{(p\hat{I}_H+q\hat{S}_H)^2}\right),$$
$$j_{23} = \frac{\beta_{VH}q\hat{S}_H}{(p\hat{I}_H+q\hat{S}_H)}, j_{31} = -\frac{\beta_{HV}pq\hat{I}_H(N_V-\hat{I}_V)}{(p\hat{I}_H+q\hat{S}_H)^2},$$
$$j_{32} = \frac{\beta_{HV}pq\hat{S}_H(N_V-\hat{I}_V)}{(p\hat{I}_H+q\hat{S}_H)^2}, j_{33} = -\left(\lambda_V + \sigma_e + \frac{\beta_{HV}p\hat{I}_H}{(p\hat{I}_H+q\hat{S}_H)}\right).$$

At DFE E_0 Jacobian matrix given in equation(30) become:
$$J(E_0) = \begin{pmatrix} -(\lambda_H + \sigma_i) & 0 & -\beta_{VH} \\ \sigma_i & -(\lambda_H + \theta_d + \eta) & \beta_{VH} \\ 0 & \frac{\beta_{HV}pN_V(\lambda_H+\sigma_i)}{q\Lambda_H} & -(\lambda_V + \sigma_e) \end{pmatrix}, \quad (31)$$

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equivalent to

$$J(E_0)=\begin{pmatrix} -(\lambda_H+\sigma_i) & 0 & -\beta_{VH} \\ 0 & -(\lambda_H+\theta_d+\eta) & \frac{\beta_{VH}\lambda_H}{\lambda_H+\sigma_i} \\ 0 & \frac{\beta_{HV}pN_V(\lambda_H+\sigma_i)}{q\Lambda_H} & -(\lambda_V+\sigma_e) \end{pmatrix}, \quad (32)$$

$$\det[J(E_0)]=-(\lambda_H+\sigma_i)(\lambda_H+\theta_d+\eta)(\lambda_V+\sigma_e)(1-R_0),$$

where, $R_0 = \frac{\beta_{VH}\beta_{HV}\lambda_H pN_V}{q\Lambda_H(\lambda_H+\theta_d+\eta)(\lambda_V+\sigma_e)}$, (33)

is the basic reproduction ratio for the modified model.

3. Sensitivity Analysis

By sensitivity analysis, we know about the importance of each parameters used in the model and its tell us about how necessary each parameter for disease communicability [5]. Normalize forward sensitivity index of reproduction ratio can be mathematically defined as:

$$\Psi_P^{R_0}=\frac{dR_0}{dP}\times\frac{P}{R_0} \quad (34)$$

Where P indicates parameter and R_0 is re-breeding ratio. As formulas for re-breeding ratios given in equation (16) and equation(33) are explicit, so one can conveniently find expressions for sensitivity of basic reproduction ratios at indicated parameters as:

$\Psi_P^{R_0}$ with respect to equation(16) for the basic model:

$$\Psi_{\beta_{VH}}^{R_0}=\Psi_{\beta_{HV}}^{R_0}=1,$$

$$\Psi_{\lambda_H}^{R_0}=-\frac{\lambda_H}{\lambda_H+\eta+\sigma_i},\ \Psi_{\sigma_i}^{R_0}=-\frac{\sigma_i}{\lambda_H+\eta+\sigma_i},$$

$$\Psi_{\eta}^{R_0}=-\frac{\eta}{\lambda_H+\eta+\sigma_i},\ \Psi_{\sigma_e}^{R_0}=-\frac{\sigma_e}{\sigma_e+\lambda_V} \text{ and}$$

$$\Psi_{\lambda_V}^{R_0}=-\frac{\lambda_V}{\sigma_e+\lambda_V}.$$

$\Psi_P^{R_0}$ with respect to equation(33) for the modified model:

$$\Psi_{\beta_{VH}}^{R_0}=\Psi_{\beta_{HV}}^{R_0}=1,$$

$$\Psi_{\lambda_H}^{R_0}=\frac{\theta_d+\eta}{\lambda_H+\theta_d+\eta},\ \Psi_{\theta_d}^{R_0}=-\frac{\theta_d}{\lambda_H+\theta_d+\eta},$$

$$\Psi_{\eta}^{R_0}=-\frac{\eta}{\lambda_H+\theta_d+\eta},\ \Psi_{\sigma_e}^{R_0}=-\frac{\sigma_e}{\sigma_e+\lambda_V} \text{ and}$$

$$\Psi_{\lambda_V}^{R_0}=-\frac{\lambda_V}{\sigma_e+\lambda_V}.$$

Table 1.Baseline epidemiological parameters used in the basic model and modified model

Parameters	Values
N_H	100000
β_{VH}	1.125day−1
β_{HV}	1.125day−1
p	0.8
q	0.2
λ_H	0.0000411day−1
λ_V	0.055
σ_i	0.126
σ_e	0.11
η	0.166
N_V	50000
θ_d	0.000035
Λ_H	1000

Table 2.Sensitivity indices of R_0 for the basic model evaluated at the baseline parameter values given in table 1

Parameters	Sensitivity index
β_{VH}	+1
β_{HV}	+1
λ_H	−0.000141
λ_V	−0.33
σ_i	−0.43
σ_e	−0.67
η	−0.57

Table 3.Sensitivity indices of R_0 for the modified model evaluated at the baseline parameter values given in table 1

Parameters	Sensitivity index
β_{VH}	+1
β_{HV}	+1
λ_H	+0.9998
λ_V	−0.33
θ_d	−0.0002107
σ_e	−0.67
η	−0.9994

In table 2 Sensitivity indices equal to +1 indicated that decreases (or increases) the parameters by 10%, decrease (or increase) in R_0 always 10% and the most non positive sensitive parameters with values −0.67, −0.57 and −0.43 means that by increasing (or decreasing) the corresponding parameters by 10% then there is 6.7% , 5.7% and 4.3% decrease (or increase) in R_0.

In table 3 Sensitivity indices is equal to +1 and + 0.9998 indicated that decrease (or increase) the parameters by 10% always gives 10% and 9.998% decrease (or increase) in R_0 and the most non positive sensitive parameter with value −0.9994 means that by increasing (or decreasing) the corresponding parameter by 10% then there is 9.994% decrease (or increase) in R_0.

4. Numerical Simulation

To analyse sensitivity numerically, we use Matlab ODE23s for the system of equations from (6) to (10) for the basic model & system of equations from (22) to (26) for the modified model.

Consider final time equal to 140 days, initially we take $\hat{S}_H=N_H-\hat{I}_H=100000-3$ and $\hat{I}_H=3$, then by normalizing we have $S_H=0.99997$ and $I_H=0.00003$ to find $\frac{\beta_{VH}q}{pI_H+qS_H}$ and $\frac{\beta_{HV}p}{pI_H+qS_H}$ which are necessary parts of incident functions.

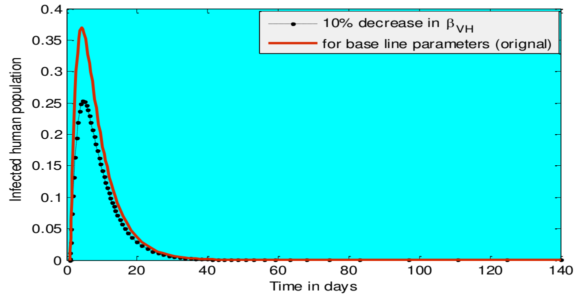

Fig.1. (a) Change in β_{VH} effect on I_H

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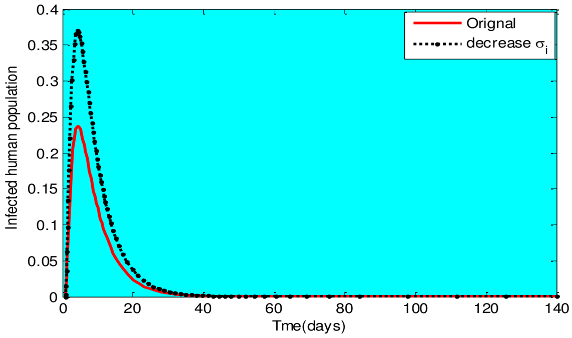

Fig.1. (b)Change in σ_i effect on I_H

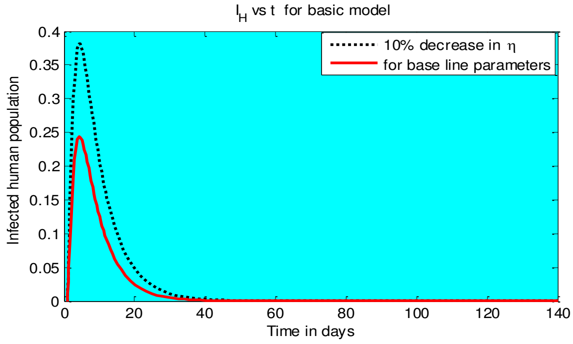

Fig.1. (c)Change in η effect on I_H

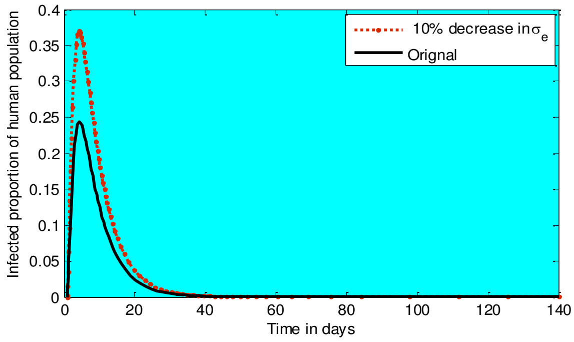

Fig.1. (d)Change in σ_e effect on I_H

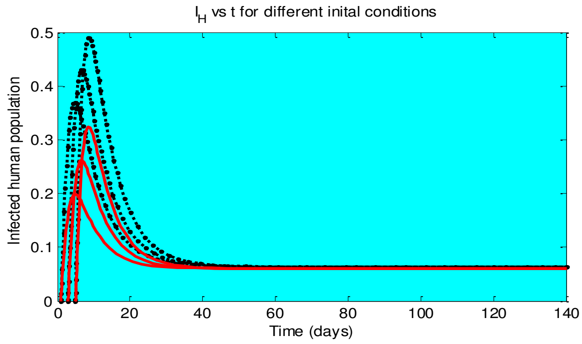

Fig.1. (e)Effect on I_H due to decrease in all parameters by 10%

Fig.1. Infected proportion of human population with 10% decreases in the value of parameters given in table 1 corresponding to sensitivity indices given in table 2 for the infected human population for normalized system of equations from (6) to (10), with the representation that solid line for baseline parameters and dashed lines for variational parameters.

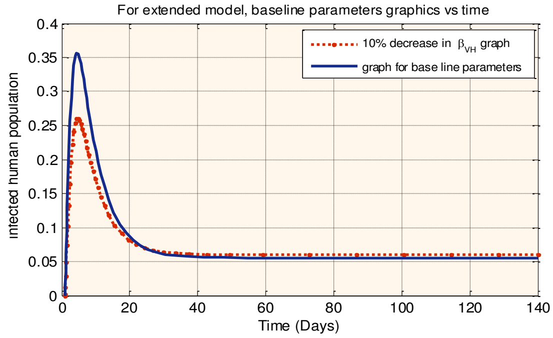

Fig.2. (a) Effect on I_H due to change in β_{VH}

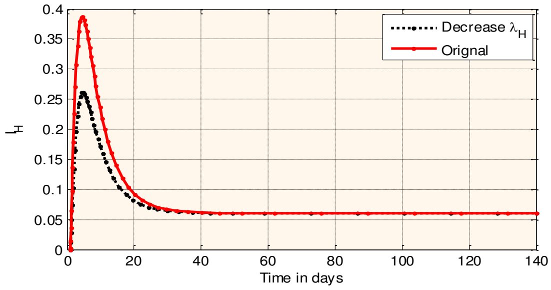

Fig.2.(b) Effect on I_H due to change in λ_H

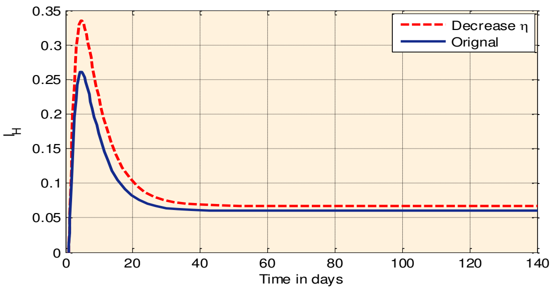

Fig.2.(c) Effect on I_H due to change in η

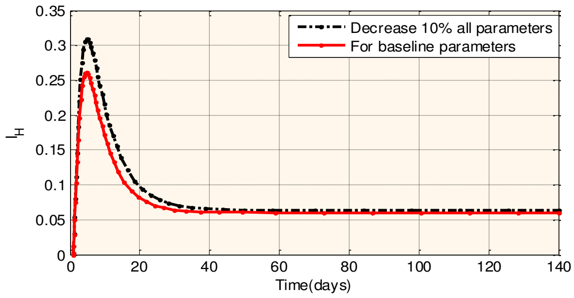

Fig.2.(d) Effect on I_H due to decrease in all parameters by10%

Fig.2. Effect on infected proportion of human population by 10% decrease in the value of parameters given in table 1 corresponding to sensitivity indices given in table 3 for normalized system of equations from (22) to (26).

5. DISCUSSION

Depiction in figure 1 and figure 2 elucidate the effect on dengue infective hosts due to decrease of 10% in baseline parameters in table 1. Some parameters like $\lambda_H$and $\lambda_V$having small and below average sensitivity indices with

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minor and below average amount of influence on $R_0$and also $\lambda_V$is not included in respective system of equationsfrom (6) to (10), for Basic model and the variations are not sketchily perceptible. Similarly, for system of equations from (22) to (26), we neglect to sketch graphics for some parameters.For $\beta_{HV} = \beta_{VH}$ and its influence on hosts is equal,the graphic is neglected. The most positive sensitive parameter is β_{VH} with sensitivity index $\Psi^{R_0}_{\beta_{VH}} = +1$ for Basic and Modified models respectively (see figures 1(a) & 2(a)). Figure 2(b) show same result as previous one. The most non positive sensitive parameter is η of Modified model with $\Psi^{R_0}_{\eta} = -0.9994$ (see figure 2(c)), Figure 1(b), 1(d) and 1(c) with respect to parameters σ_i ,σ_e& η with sensitivity indices $\Psi^{R_0}_{\sigma_i} = -0.43$, $\Psi^{R_0}_{\sigma_e} = -0.67$ &$\Psi^{R_0}_{\eta} = -0.57$ shows same behaviors as figure 2(c). Figure 1(e) reflect different picks values of infected human population with different initial conditions with the aim to compare infected human graphics by considering baseline parameters and all the parameters decreased by 10%. Figure 2(d) shows the actual graph and the graph when all the parameters are decreased by 10%.

6.Conclusion

Sensitivity has been analyzed for R_0 with respect to epidemiological and entomological parameters and proved that $R_0$is most sensitive with respect to epidemiological parameters (that is,β_{VH},β_{HV}, η, σ_e, σ_i). It is recommended that threshold quantity R_0 can be reduced if we control over the parameters.

Such informative findings gives reasonable and sound information to Public health experts and officials who are dealing with the reality of contagious diseases. We are sure that the research outcomes are beneficial to the society affected by dengue.

Acknowledgment

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