Mathematical modeling of zika virus disease with nonlinear incidence and optimal control

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Mathematical modeling of zika virus disease with nonlinear incidence and optimal control

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Abstract. The Zika virus was first discovered in a rhesus monkey in the Zika Forest of Uganda in 1947, and it was isolated from humans in Nigeria in 1952. Zika virus disease is primarily a mosquito-borne disease, which is transmitted to human primarily through the bite of an infected Aedes species mosquito. However, there is documented evidence of sexual transmission of this disease too. In this paper, a nonlinear mathematical model for Zika virus by considering nonlinear incidence is formulated and analyzed. The equilibria and the basic reproduction number (R_0) of the model are found. The stability of the different equilibria of the model is discussed in detail. When the basic reproduction number $R_0 < 1$, the disease-free equilibrium is locally and globally stable i.e. in this case disease dies out. For $R_0 > 1$, we have endemic equilibrium which is locally stable under some restriction on parameters. Further this model is extended to optimal control model and is analyzed by using Pontryagin's Maximum Principle. It has been observed that optimal control plays a significant role in reducing the number of zika infectives. Finally, numerical simulation is performed to illustrate the analytical findings.

1. Introduction

The Zika virus is a mosquito-borne disease. The infection is transmitted to human population through the bite of infected Aedes mosquitoes. In 1947 in the Zika Forest of Uganda first Zika virus was identified in a rhesus monkey and later in 1952 it was isolated from human population in Nigeria. The general symptoms of Zika virus are conjunctivitis, headache, joint pain, mild fever, muscle and, skin rash, etc. The symptom of the virus is exhibited within two to seven days, [1]. During the infected period of Zika, people should drink plenty of fluids and rest sufficiently. Since 2015, the sexual transmission of the disease and blood transfusion of the infected individual are being investigated in the following nations - Argentina, Canada, Chile, France, Italy, New Zealand, Peru, Portugal, and the United States of America. The first sexually transmitted case of Zika virus disease was diagnosed in France in February 2016.

In April 2007, in the island of Yap, the first outbreak Zika virus was identified which was outside of Africa and Asia. During 2013-14 the largest outbreak of Zika cases estimated to be around 30,000 was reported in the French Polynesia. In 2015, rapid spread of Zika virus was recorded among South

American countries, especially Brazil and Colombia notified PAHO/WHO [2]. In Brazil the Public Health authority detected Zika virus in 14 states and in Colombia out of 98 samples 9 samples were conformed. In Brazil, between October 2015 to February 2016, more than 6000 Zika virus infected cases were recorded including 139 cases of congenital microcephaly. In Colombia, during December 2015 to February 2016, nearly 200 GBS cases were identified with suspected link with Zika infection and in El Salvador nearly 118 GBS cases confirmed as Zika where 5 died [3]. On 1st February 2016, the World Health Organizing (WHO) declared that the Zika virus epidemic as a Public Health Emergency of International Concern (PHEIC) [4].

The transmission dynamics of Zika Virus has been studied and analyzed recently by various researchers [5, 6, 7, 8, 9] using mathematical models as a tool. In [5], authors proposed a mathematical model for transmission dynamics of Zika virus disease and they have shown the control measure of Zika virus through prevention, treatment and insecticides. In [6], authors incorporated the sexual transmission of this disease in the proposed model and computed basic reproduction number and using real data the numerical simulation illustrated the analysis. In [7] authors proposed a new deterministic model introducing vertical transmission of Zika virus and incorporating the cases of new born babies with microcephaly and asymptomatic infected populations. In [8], authors proposed a two patch model for the transmission dynamics of Zika virus to see the effect of short-term dispersal. In [9], authors proposed a mathematical model of Zika virus of the 2013 –14 French Polynesia outbreaks and analyzed using real data. Authors estimated the reproduction number using the real data performed sensitivity analysis.

At present Zika virus is endemic and hence its study is most essential. Here we present a mathematical model for Zika Virus disease by considering standard incidence type interaction for human to human transmission of the disease. Here we assume that the total human population is variable. In this model we introduce the incidence rate $\frac{cI_h}{1+I_h}$, which was also proposed in [10, 11], where cI_h measures infected force of the virus and $\frac{1}{1+I_h}$ measures susceptible individuals when the number of infected individuals increases. Further our proposed mathematical model is extended to optimal control problem. This helps in finding the optimal control strategies to reduce the number of Zika infected cases.

This paper is organized as follows: in Section 2 we formulation our mathematical model; in Section 3 we compute the basic reproduction number and find the existence of equilibria; in Section 4 we present the stability analysis of the model; in Section 5 we illustrate the numerical simulation and results of the model; in Section 6, we study the optimal control model and its analysis; in Section 7 we demonstrate the numerical simulation results of the optimal control model and finally in the Section 8 we conclude our paper.

2. Model formulation:

Here we have proposed a mathematical model for Zika virus disease by considering nonlinear incidence. The model was formulated by considering two populations human and vector (mosquito). In the proposed model the human population has been divided into three independent compartments such as Susceptible individuals (S_h), Infected individuals (I_h) and Recovered individuals (R_h). Also the vector population has been divided into two compartments Susceptible vector (S_v) and Infected vector (I_v). The transmission of the disease is possible between human to human, human to vector and vector to human. In this model we incorporate a nonlinear incidence term for human to human transmission, which is of saturated incidence type. Several authors have considered this type of nonlinear incidence term in their respective model [10, 11, 12].

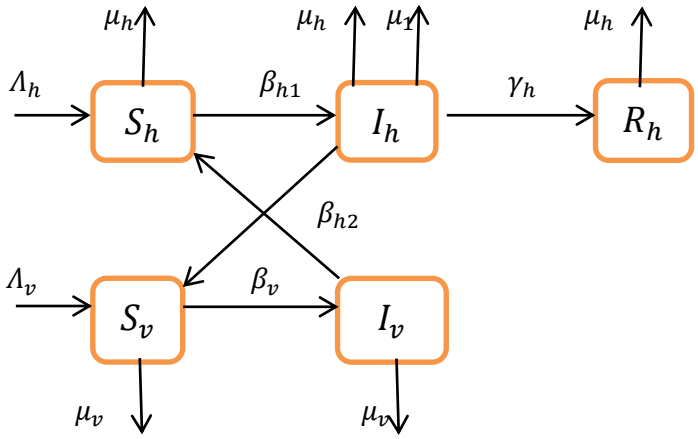

Figure 1: Flow chart for the transmission of Zika virus disease

The proposed mathematical model of Zika virus is as follows:

$$\begin{aligned}
\frac{dS_h}{dt} &= \Lambda_h - \beta_{h1}\left(\frac{cI_h}{1+I_h}\right)S_h - \beta_{h2}\frac{I_v}{N_h}S_h - \mu_h S_h \\
\frac{dI_h}{dt} &= \beta_{h1}\left(\frac{cI_h}{1+I_h}\right)S_h + \beta_{h2}\frac{I_v}{N_h}S_h - (\gamma_h+\mu_h+\mu_1)I_h \\
\frac{dR_h}{dt} &= \gamma_h I_h - \mu_h R_h \\
\frac{dS_v}{dt} &= \Lambda_v - \beta_v\frac{I_h}{N_h}S_v - \mu_v S_v \\
\frac{dI_v}{dt} &= \beta_v\frac{I_h}{N_h}S_v - \mu_v I_v
\end{aligned} \tag{1}$$

where

Λ_h : Recruitment rate of human individuals
Λ_v : Recruitment rate of vector individuals (mosquito)
μ_h : Natural death rate of human individuals
μ_v : Natural death rate of vector individuals (mosquito)
μ_1 : Death rate of human due to infection
β_{h1}: Contact rate between $S_h$and I_h
β_{h2}: Contact rate between $S_h$and I_v
β_v: Contact rate between $S_v$and I_h
γ_h: Recovery rate of infectives (human)

Consider $(S_h, I_h, R_h, S_v, I_v)$ be any solution with positive initial conditions and $N_h(t)$ and $N_v(t)$ be the total human and vector population respectively. Then we have $N_h = S_h + I_h + R_h$ and $N_v = S_v + I_v$. The time derivative of N in the above equation is given by

$$\frac{dN_h}{dt} = \Lambda_h - \mu_h N_h - \mu_1 I_h$$

$$\frac{dN_v}{dt} = \Lambda_h - \mu_v N_v$$

Hence we can rewrite the model in the following form:

$$\begin{aligned}
\frac{dN_h}{dt} &= \Lambda_h - \mu_h N_h - \mu_1 I_h \\
\frac{dI_h}{dt} &= \left(\beta_{h1}\left(\frac{cI_h}{1+I_h}\right) + \beta_{h2}\frac{I_v}{N_h}\right)(N_h - I_h - R_h) - (\gamma_h + \mu_h + \mu_1)I_h \\
\frac{dR_h}{dt} &= \gamma_h I_h - \mu_h R_h \qquad (2) \\
\frac{dN_v}{dt} &= \Lambda_h - \mu_v N_v \\
\frac{dI_v}{dt} &= \beta_v \frac{I_h}{N_h}(N_v - I_v) - \mu_v I_v
\end{aligned}$$

3. Existence of equilibrium and the basic reproduction number

3.1 Disease free equilibrium point E_0 and the basic reproduction number R_0

We consider the system (2) and find the disease free equilibrium point. The disease free equilibrium for this model we have $E_0 = \left(N_h^0, I_h^0, R_h^0, N_v^0, I_v^0\right) = \left(\frac{\Lambda_h}{\mu_h}, 0, 0, \frac{\Lambda_v}{\mu_v}, 0\right)$

Now we find the basic reproduction number R_0 by following the next generation matrix methods as described in [13 - 14]. We find the matrix F and V as follows:

$$\mathcal{F} = \begin{pmatrix} \left(\beta_{h1}\left(\frac{cI_h}{1+I_h}\right) + \beta_{h2}\frac{I_v}{N_h}\right)(N_h - I_h - R_h) \\ \beta_v \frac{I_h}{N_h}(N_v - I_v) \end{pmatrix} \text{ and } \quad \mathrm{V} = \begin{pmatrix} (\gamma_h + \mu_h + \mu_1)I_h \\ \mu_v I_v \end{pmatrix}$$

$$\text{F= Jacobian of } \mathcal{F} \text{ at } E_0 = \begin{pmatrix} \beta_{h1} c N_h^0 & \beta_{h2} \\ \beta_v \frac{N_v^0}{N_h^0} & 0 \end{pmatrix}$$

$$\text{V= Jacobian of } \mathcal{V} \text{ at } E_0 = \begin{pmatrix} \gamma_h + \mu_h + \mu_1 & 0 \\ 0 & \mu_v \end{pmatrix}$$

And it follows that

$$\mathrm{FV}^{-1} = \begin{pmatrix} \beta_{h1} c N_h^0 D_1 & \beta_{h2} D_2 \\ \beta_v \frac{N_v^0}{N_h^0} D_2 & 0 \end{pmatrix},$$

where $D_1 = \frac{1}{\gamma_h + \mu_h + \mu_1}$, $D_2 = \frac{1}{\mu_v}$

The largest eigenvalue of FV^{-1} is called the basic reproduction number R_0 and is obtained as follows:

$$R_0 = \frac{\beta_{h1} c N_h^0 D_1 + \sqrt{(\beta_{h1} c N_h^0 D_1)^2 + 4\beta_{h2}\beta_v \frac{N_v^0}{N_h^0} D_1 D_2}}{2} = \frac{R_{hh} + \sqrt{(R_{hh})^2 + 4R_{hv}}}{2}$$

where

$$R_{hh} = \frac{\beta_{h1} c N_h^0}{\gamma_h + \mu_h + \mu_1} \text{ and } \quad R_{hv} = \beta_{h2}\beta_v \frac{N_v^0}{N_h^0} D_1 D_2.$$

Here R_{hh} denotes the basic reproduction due to human to human transmission by ignoring the transmission due to vectors. Similarly, R_{hv} denotes the basic reproduction due to interactions with vectors in the absence of human to human transmission. The reproduction number R_0 gives the average number of infected individuals generated by the one infected in a fully susceptible population and for our model it is given by above expression of R_0 .

3.2 Existence of endemic equilibrium

The endemic equilibrium point of the model we have $E_1 = (N_h^*, I_h^*, R_h^*, N_v^*, I_v^*)$, where,

$$N_h^* = \frac{\Lambda_h - \mu_1 I_h^*}{\mu_h},$$

$$R_h^* = \frac{\gamma_h I_h^*}{\mu_h},$$

$$N_v^* = \frac{\Lambda_v}{\mu_v},$$

$$I_v^* = \frac{\Lambda_v \mu_h \beta_v I_h^*}{\mu_v \mu_h \beta_v I_h^* + \mu_v^2 (\Lambda_v - \mu_1 I_h^*)}$$

And there is a positive root of I_h^* of the following non-linear equation

$$g(I_h) = [\Lambda_h - (\mu_1 + \mu_h + \gamma_h) I_h] \left[\frac{c\beta_{h1}(\Lambda_h - \mu_1 I_h)}{(1 + I_h)\mu_h} + \frac{\beta_{h2}\Lambda_v \beta_v \mu_h}{\mu_h \mu_v \beta_v I_h + (\Lambda_h - \mu_1 I_h)\mu_v^2} \right]$$

$$-(\Lambda_h - \mu_1 I_h)(\mu_1 + \mu_h + \gamma_h) = 0.$$

Here, we note the following:

$$g(0) = \Lambda_h \left[\frac{c\beta_{h1}\Lambda_h}{\mu_h} + \frac{\beta_{h2}\Lambda_v \beta_v \mu_h}{\Lambda_h \mu_v^2} \right] - \Lambda_h(\mu_1 + \mu_h + \gamma_h) > 0$$

$$g\left(\frac{\Lambda_h}{\mu_1 + \mu_h + \gamma_h}\right) = -\Lambda_h(\mu_h + \gamma_h) < 0$$

$$g\left(\frac{\Lambda_v}{\mu_1}\right) = -\Lambda_h \frac{\mu_h + \gamma_h}{\mu_1} \left[\frac{\beta_{h2}\Lambda_v \beta_v \mu_1}{\Lambda_h \mu_v \beta_v} \right] < 0$$

It is easy to observe that, $\frac{\Lambda_h}{\mu_1 + \mu_h + \gamma_h} < I_h < \frac{\Lambda_v}{\mu_1}$, $g(I_h)$ is always negative, i.e. there is no change of sign in $g(I_h)$, so there is no root of $g(I_h)$ in the interval $\frac{\Lambda_h}{\mu_1 + \mu_h + \gamma_h} < I_h < \frac{\Lambda_v}{\mu_1}$. Hence we can conclude that there is at least one root of $g(I_h) = 0$ in the interval $0 < I_h < \frac{\Lambda_h}{\mu_1 + \mu_h + \gamma_h}$. Thus under the

following condition, there exists unique positive root of $g(I_h) = 0$ and we name that root as I_h^*. Hence we get our endemic equilibrium point as $E_1 = (N_h^*, I_h^*, R_h^*, N_v^*, I_v^*)$.

$$\frac{dg(I_h)}{dI_h} = -[\Lambda_h - (\mu_1 + \mu_h + \gamma_h)I_h][\frac{c\beta_{h1}\mu_1(1+I_h)+c\beta_{h1}(\Lambda_h-\mu_1 I_h)}{(1+I_h^*)^2\mu_h} + \frac{\beta_{h2}\Lambda_v\beta_v\mu_h(\mu_h\mu_v\beta_v-\mu_1\mu_v^2)}{(\mu_h\mu_v\beta_v I_h+(\Lambda_h-\mu_1 I_h)\mu_v^2)^2}] - (\mu_1 + \mu_h + \gamma_h)[\frac{c\beta_{h1}(\Lambda_h-\mu_1 I_h)}{(1+I_h)\mu_h} + \frac{\beta_{h2}\Lambda_v\beta_v\mu_h}{\mu_h\mu_v\beta_v I_h+(\Lambda_h-\mu_1 I_h)\mu_v^2}] + (\mu_1 + \mu_h + \gamma_h) < 0.$$

4. Stability analysis

4.1 Local stability of disease-free equilibrium

Theorem 4.1.1 When $R_0 < 1$, the disease free equilibrium E_0 is locally asymptotically stable otherwise it is unstable.

The Jacobian matrix of the system (2) at disease free equilibrium point E_0 is obtained as follows:

$$J_0 = \begin{pmatrix} -\mu_h & -\mu_1 & 0 & 0 & 0 \\ 0 & m_{22} & 0 & 0 & \beta_{h2} \\ 0 & \gamma_h & -\mu_h & 0 & 0 \\ 0 & 0 & 0 & -\mu_v & 0 \\ 0 & \beta_v\frac{N_v^0}{N_h^0} & 0 & 0 & -\mu_v \end{pmatrix}$$

Where

$$m_{22} = \beta_{h1}c\left(\frac{\Lambda_h}{\mu_h}\right) - (\gamma_h + \mu_h + \mu_1)$$

Clearly three eigenvalues of the matrix J_0 are $-\mu_h, -\mu_h \; and \; -\mu_v$ and the remaining two roots are obtained by solving the following equation.

$$\lambda^2 + (\mu_v - m_{22})\lambda - (m_{22}\mu_v + \beta_{h2}\beta_v\frac{N_v^0}{N_h^0}) = 0,$$

Where

$$m_{22} = \beta_{h1}c\left(\frac{\Lambda_h}{\mu_h}\right) - (\gamma_h + \mu_h + \mu_1) = \frac{\beta_{h1}c\left(\frac{\Lambda_h}{\mu_h}\right)}{\gamma_h+\mu_h+\mu_1} - 1 = R_{hh} - 1 < 0 \text{ for } R_{hh} < 1.$$

Hence $(\mu_v - m_{22}) > 0$

Now

$$-(m_{22}\mu_v + \beta_{h2}\beta_v\frac{N_v^0}{N_h^0}) = \mu_v(\gamma_h + \mu_h + \mu_1)[1 - (R_{hh} + R_{hv})] > 0 \quad \text{for} \quad R_{hh} + R_{hv} < 1.$$

It is observed that $R_{hh} + R_{hv} < 1$, whenever $R_0 < 1$. Hence the disease free equilibrium is locally asymptotically stable.

4.2 Global stability of disease free equilibrium

To prove the global stability of disease free equilibrium, we are useing the theorem described in [15,16]

Theorem 4.2.1 If the given mathematical model can be written in the form:

$$\frac{dX}{dt} = F(X,Y), \text{and } \frac{dY}{dt} = G(X,Y), \mathrm{G(X,0)} = 0 \qquad (*)$$

where, $X = (N_h, N_v)^T$ *and* $Y = (I_h, I_v)^T$, represent the classes of uninfected and the class of infected individuals respectively. Then the DFE is represented here by $E_0 = (X_{0,}0) = \left(\frac{\Lambda_h}{\mu_h}, \frac{\Lambda_v}{\mu_v}, 0, 0\right)$.

For the global asymptotic stability of E_0 , the condition (H1) and (H2) given below must be satisfied.

H_1: $\frac{dX}{dt} = F(X_{0,}0)$, X_0 is global asymptotically stable,

H_2: $G(X,Y) = AY - \hat{G}(X,Y)$, $\widehat{G}(X,Y) \geq 0$, here $A = D_Y G(X_{0,}0)$ is M- matrix (In M-matrix, all the off diagonal element of matrix are non-negative). If the system (2) satisfies the given condition in (*) then the equilibrium point $E_0 = (X_{0,}0)$ is a global asymptotically stable equilibrium provided $R_0 < 1$.

And for our mathematical model, the result is shown in the next theorem, as given below.

Theorem 4.2.2 The equilibrium point $E_0 = (X_{0,}0)$ is GAS (Global Asymptotically Stable) , provided $R_0 < 1$ and the conditions given in (*) are satisfied.

Proof: By using Theorem (4.2) to mathematical model system, we consider

$$F(X_{0,}0) = \Lambda - \mu S, \qquad G(X,Y) = AY - \hat{G}(X,Y)$$

where,

$$A = \begin{bmatrix} \beta_{h1} c\left(\frac{\Lambda_h}{\mu_h}\right) - (\gamma_h + \mu_h + \mu_1) & \beta_{h2} \\ \beta_v \frac{N_v^0}{N_h^0} & -\mu_v \end{bmatrix}$$

And

$$\hat{G}(X,Y) = \begin{bmatrix} \widehat{G_1}(\mathrm{X},\mathrm{Y}) \\ \widehat{G_2}(\mathrm{X},\mathrm{Y}) \end{bmatrix} = \begin{pmatrix} \left(\beta_{h1}\left(\frac{cI_h}{1+I_h}\right) + \beta_{h2}\frac{I_v}{N_h}\right)(N_h - I_h - R_h) \\ \beta_v \frac{I_h}{N_h}(N_v - I_v) \end{pmatrix}$$

Here we can easily observe that $\widehat{G_1}(X,Y) > 0$, $\widehat{G_2}(X,Y) > 0$, hence $\hat{G}(X,Y) > 0$ for all (X,Y). Also by the definition of M matrix we can say that the matrix A is M matrix. Hence the DFE (E_0) is globally stability.

4.3 Local stability of endemic equilibrium point

Theorem 4.3.1 When $R_0 > 1$ then endemic equilibrium E_1 is locally asymptotically stable under the condition $\left(\frac{N_v^* - I_v^*}{N_h^*}\right) > \frac{\mu_1}{\beta_v}$.

Proof: The jacobian matrix J_1 at the endemic equilibrium point E_1 is given by

$$J_1 = \begin{pmatrix} -\mu_h & -\mu_1 & 0 & 0 & 0 \\ m_{21} & m_{22} & m_{23} & 0 & m_{25} \\ 0 & \gamma_h & -\mu_h & 0 & 0 \\ 0 & 0 & 0 & -\mu_v & 0 \\ m_{51} & m_{52} & 0 & m_{54} & m_{55} \end{pmatrix}$$

where,

$$m_{21} = \beta_{h1}\frac{cI_h^*}{1+I_h^*} + \beta_{h2}\frac{I_v^*(I_h^* + R_h^*)}{N_h^{*2}}$$

$$m_{22} = -\left[\frac{\beta_{h1} c I_h (N_h^* - I_h^* - R_h^*) - \beta_{h1} c (N_h^* - 2I_h^* - R_h^*)(1+I_h^*)}{(1+I_h^*)^2} + \frac{\beta_{h2} I_v^*}{N_h^*} + (\gamma_h + \mu_h + \mu_1)\right]$$

$$m_{23} = -\left(\beta_{h1} \frac{c I_h^*}{1 + I_h^*} + \beta_{h2} \frac{I_v^*}{N_h^*}\right)$$

$$m_{25} = \beta_{h2}\left(1 - \frac{I_h^* + R_h^*}{N_h^*}\right)$$

$$m_{51} = -\beta_v \left(\frac{I_h (N_v^* - I_v^*)}{N_h^{*2}}\right)$$

$$m_{52} = \beta_v \left(\frac{N_v^* - I_v^*}{N_h^*}\right)$$

$$m_{54} = \beta_v \frac{I_h^*}{N_h^*}$$

$$m_{55} = -\left(\beta_v \frac{I_h^*}{N_h^*} + \mu_v\right)$$

Clearly, the two roots of the matrix J_1 are $-\mu_h, -\mu_v$ and the remaining roots are obtained by solving the following equation.

$$\lambda^3 + A\lambda^2 + B\lambda + C = 0$$

where,

$$A = \mu_h - m_{22} - m_{55} > 0$$

$$B = -(\mu_h m_{22} + \mu_h m_{55} - m_{22} m_{55} + \gamma_h m_{23} + m_{23} m_{52} - \mu_1 m_{21}) > 0$$

$$C = (\mu_h m_{22} m_{55} + \gamma_h m_{23} m_{55} - \mu_h m_{25} m_{52} - \mu_1 m_{21} m_{55} + \mu_1 m_{51} m_{25}) > 0$$

Therefore, by Routh Hurwitz's theorem all the three roots of the cubic equation are negative or have negative real parts, provided $AB - C > 0$, we get

$AB - C = \mu_1 \mu_h m_{21} - \mu_h^2 (m_{22} + m_{55}) + \mu_h \left(4 m_{22} m_{55} - \gamma_h m_{23} - m_{23} m_{52} + m_{22}^2 + m_{55}^2 - m_{25} m_{52}\right) + \gamma_h (m_{22} m_{23} + 2 m_{23} m_{55}) + \mu_1 (-m_{21} m_{22} - 2\, m_{21} m_{55} + m_{51} m_{25}) + m_{23} m_{52} (m_{22} + m_{55}) - m_{22} m_{55} (m_{22} + m_{55})$.

which is positive under the condition $\beta_v \left(\frac{N_v^* - I_v^*}{N_h^*}\right) > \mu_1$. Hence, the endemic equilibrium is locally asymptotically stable

5. Numerical simulation:

To support our analytical results, we perform numerical simulation. Here most of the parameters values are taken from the reference [6, 9] and some parameter values are assumed. In the proposed model, all the parameter are in per day. The values of the parameters are listed in the following Table 1.

Table 1. Parameters and their values

Parameter	Value (Day)
Λ_h	20
Λ_v	20(DFE), 40 (EE)
β_{h1}	0.005
β_{h2}	0.4
μ_h	1/ (60*365
μ_v	1/14
γ_h	1/20
β_v	0.5
μ_1	0.04227

To demonstrate the stability of disease-free equilibrium point, we consider Λ_v= 20 and all other parameters as listed in the Table 1. For this set of parameters R_0 = 0.8802 and disease free equilibrium point E_0 is (2100, 0, 0, 600, 0). In the Fig. 2 is demonstrating the stability of disease free equilibrium point E_0. The stability of the endemic equilibrium (E_1) is demonstrated by changing the value of Λ_v from 20 to 30. For this set of parameters, the basic reproduction number R_0 = 2.1347 and equilibrium point E_1 is (97, 200, 68, 100, 250). This is demonstrated in Figure 3. In Figure 4, variation of I_h with time is shown for different values of γ_h.

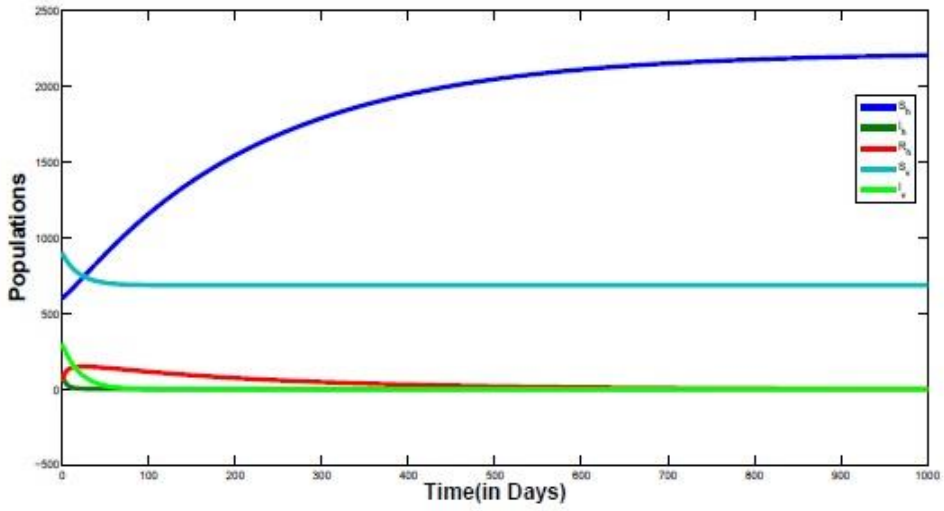

Figure2: Variation of S_h, I_h, R_h, S_v, I_v with time showing the stability of disease-free equilibrium point.

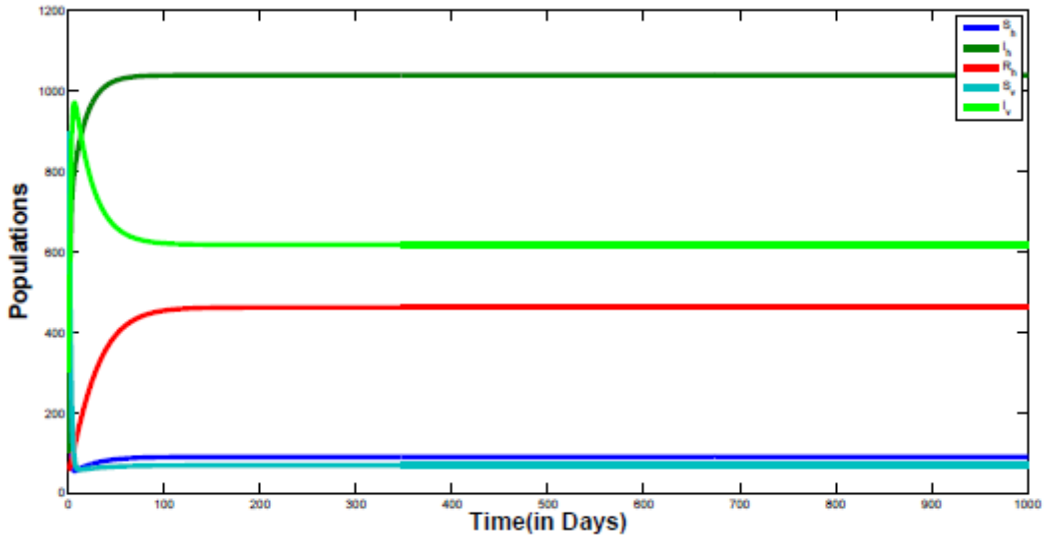

Figure3: Variation of S_h, I_h, R_h, S_v, I_v with time showing the stability of endemic equilibrium point.

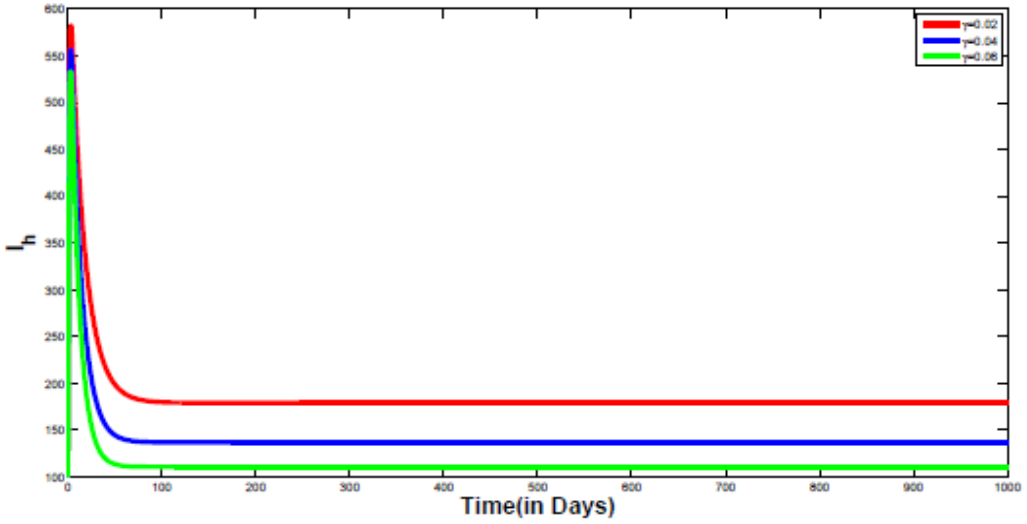

Figure4: Variation of I_h with time for different values of γ_h .

6. Optimal control model

In this section we have extended the mathematical model (2) to optimal control problem by including two optimal control parameters u_1 and u_2. If u_1 and u_2 are equal to zero, then there is no effort being placed in these controls at time t and if they are equal to one then maximum effort is applied. The control variable u_1 represents the use of insecticide-treated bed nets and the use of mosquito repulsive lotions and electronic devices, to reduce mosquito biting rate. The control variable u_2 corresponds to additional death rate of mosquitoes due to control efforts. Based on the above assumptions, the optimal control model as follows:

$$\frac{dS_h}{dt} = \Lambda_h - \beta_{h1}\left(\frac{cI_h}{1+I_h}\right)S_h - (1-u_1(t))\beta_{h2}\frac{I_v}{N_h}S_h - \mu_h S_h$$

$$\frac{dI_h}{dt} = \beta_{h1}\left(\frac{cI_h}{1+I_h}\right)S_h + (1-u_1(t))\beta_{h2}\frac{I_v}{N_h}S_h - (\gamma_h+\mu_h+\mu_1)I_h \qquad (3)$$

$$\frac{dR_h}{dt} = \gamma_h I_h - \mu_h R_h$$

$$\frac{dS_v}{dt} = \Lambda_v - (1-u_1(t))\beta_v\frac{I_h}{N_h}S_v - (\mu_v+u_2(t))S_v$$

$$\frac{dI_v}{dt} = (1-u_1(t))\beta_v\frac{I_h}{N_h}S_v - (\mu_v+u_2(t))I_v$$

6.1 The optimal control problem

Here, with the help of optimal control theory we analyze the behavior of our system. The objective functional for fixed time t_f is given below:

$$J = \int_0^{t_f}[(A_1I_h + A_2(S_v+I_v) + \frac{1}{2}A_3u_1^2 + \frac{1}{2}A_4u_2^2]\,dt$$

Here the parameter $A_1 \geq 0, A_2 \geq 0, A_3 \geq 0, A_4 \geq 0$, and they represent the weight constants.

Here we aim to find the optimal controls parameters u_1^* and u_2^* ,such that

$$J(u_1^*, u_2^*) = \min_{u_1,u_{2\in\Omega}} J(u_1,u_2),$$

Where, $\Omega = \{u_1,u_2 : measurable\ and\ 0 \leq u_1,u_2 \leq 1\} and\ t \in [0,t_f]$

The Lagrangian of this problem is defined as:

$$L(I_h,S_v,I_v,u_1,u_2) = A_1I_h + A_2(S_v+I_v) + \tfrac{1}{2}A_3u_1^2 + \tfrac{1}{2}A_4u_2^2$$

The Hamiltonian of this problem defined as:

$$H = L(I_h,S_v,I_v,u_1,u_2) + \lambda_1\frac{dS_h}{dt} + \lambda_2\frac{dI_h}{dt} + \lambda_3\frac{dR_h}{dt} + \lambda_4\frac{dS_v}{dt} + \lambda_5\frac{dI_v}{dt}$$

where λ_i are adjoint variables and $i = 1\ to\ 5$ and the adjoint variables in the form of differential equations are given as follows:

$$\frac{d\lambda_1}{dt} = \lambda_1\mu_h + \beta_{h1}\left(\frac{cI_h}{1+I_h}\right)(\lambda_1-\lambda_2) + (1-u_1)\beta_{h2}\frac{I_v}{N_h}(\lambda_1-\lambda_2) + (1-u_1)\beta_{h2}\frac{I_v}{N_h^2}S_h(\lambda_2-\lambda_1) + (1-u_1)\beta_vS_v\frac{I_v}{N_h^2}(\lambda_5-\lambda_4)$$

$$\frac{d\lambda_2}{dt} = -A_1 + \beta_{h1}S_h\frac{1}{1+{I_h}^2}(\lambda_1-\lambda_2) + (1-u_1)\beta_{h2}\frac{I_v}{N_h^2}S_h(\lambda_1-\lambda_2) + \gamma(\lambda_2-\lambda_3) + (\mu_h+\mu_1)\lambda_2 + (1-u_1)\beta_vS_v\frac{N_h-I_h}{N_h^2}S_h(\lambda_5-\lambda_4)$$

$$\frac{d\lambda_3}{dt} = \lambda_3\mu_h + (1-u_1)\beta_{h2}S_v\frac{I_v}{N_h^2}S_h(\lambda_5-\lambda_4) + (1-u_1)\beta_h S_v\frac{I_v}{N_h^2}S_h(\lambda_5-\lambda_4)$$

$$\frac{d\lambda_4}{dt} = -A_2 + \lambda_4(\mu_h+u_2) + (1-u_1)\beta_v\frac{I_v}{N_h}(\lambda_4-\lambda_5)$$

$$\frac{d\lambda_5}{dt} = -A_2 + \lambda_5(\mu_h+u_2) + (1-u_1)\beta_{h2}\frac{S_h}{N_h}(\lambda_1-\lambda_2)$$

Let $\widetilde{S_h}$, $\widetilde{I_h}$, $\widetilde{R_h}$,$\widetilde{S_v}$, $\widetilde{I_v}$, be the optimum values of $S_h, I_{h,}R_{h,}S_v, I_v$ reprehensively, and the solution of the system (3) be $\lambda_1, \lambda_2, \lambda_3, \lambda_4, \lambda_5$.

*Theorem 6.1.**1*** The given optimal controls $u_1^*, u_2^* \in \Omega$ such that $J(u_1^*, u_2^*) = \min J(u_1, u_2)$ subject to system (3).

Proof: To prove this theorem we follow the method described in Lenhart et al.[17] and Pontryagin [18]. Here the state variables and the controls are positive. For this minimizing problem, the necessary convexity of the objective functional in (u_1, u_2) is satisfied. The control variable set $u_1, u_2 \in \Omega$ is also convex and closed by the definition. The integrand of the functional $A_1I_h + A_2(S_v + I_v) + \frac{1}{2}A_3u_1^2 + \frac{1}{2}A_4u_2^2$ is convex on the control set **Ω** and the state variables are bounded.

Since there exist optimal controls for minimizing the functional subject to equations (3), we use Pontryagin's maximum principle [18] to derive the necessary conditions to find the optimal solutions as follows:

If (x,u) is an optimal solution of an optimal control problem, then there exist a non-trivial vector function $\lambda = \lambda_1, \lambda_2, \lambda_3, \ldots\ldots, \lambda_n$ satisfying the following equalities

$$\frac{dx}{dt} = \frac{\partial H(t,x,u,\lambda)}{\partial\lambda}$$

$$0 = \frac{\partial H(t,x,u,\lambda)}{\partial\lambda}$$

$$\frac{d\lambda}{dt} = \frac{\partial H(t,x,u,\lambda)}{\partial\lambda}$$

Theorem 6.1.2 The given optimal controls (u_1^*, u_2^*) which minimizes J over the region **Ω** given by

$$u_1^* = \min\{1, \max(0, \widetilde{u_1})\}$$

$$u_2^* = \min\{1, \max(0, \widetilde{u_2})\}.$$

Proof: To prove the theorem we use Pontryagin's maximum principle [18]
Using optimally condition:

$$\frac{\partial H}{\partial u_1} = 0\,, \qquad \frac{\partial H}{\partial u_2} = 0$$

we get,

$$\frac{\partial H}{\partial u_1} = A_3u_1 + \beta_{h2}S_h^*\frac{I_h^*}{N_h^*}(\lambda_1-\lambda_2) + \beta_v S_v^*\frac{I_v^*}{N_h^*}(\lambda_4-\lambda_5) = 0$$

This implies $$u_1 = \frac{\beta_{h2} S_h^* \frac{I_v^*}{N_h^*}(\lambda_1 - \lambda_2) + \beta_v S_v^* \frac{I_v^*}{N_h^*}(\lambda_4 - \lambda_5)}{A_3}$$

And $$\frac{\partial H}{\partial u_2} = A_4 u_2 - S_v^* \lambda_4 - I_v^* \lambda_5 = 0$$

This implies $$u_2 = \frac{S_v^* \lambda_4 + I_v^* \lambda_5}{A_4}$$

Again lower and upper bounds for these controls are 1 and 0 respectively. i.e. $u_1 = u_2 = 0$ if $u_1 < 0$ and $u_2 < 0$, and$u_1 = u_2 = 1$ if $\widetilde{u_1} > 1$ and $\widetilde{u_2} > 1$, otherwise $u_1 = \widetilde{u_1}$ and $u_2 = \widetilde{u_2}$. Hence for these controls u_1^*, u_2^* we get optimum value of the function J.

7. Simulation of optimal control:

The optimal control model is simulated using MATLAB by considering the set of parameters which corresponds to the stability of endemic equilibrium point of the model (2). The weight constants are taken as follows:

$$A_1 = 1, A_2 = 1, A_3 = 55, A_4 = 75.$$

The time interval is considered as [0,150]. The system (3) is solved by iterative method with the help of forward and backward difference approximation. Here Figures 5-6 are showing the control profiles of the controls u_1 and u_2 respectively. Finally, to see the effects of optimal controls, in 'figure 7' and 'figure 8', the infected human and infected vectors I_h and I_v are plotted against time with and without control. It is easy to observe that optimal control is very much effective in reducing the number of infectives in the desired interval of time.

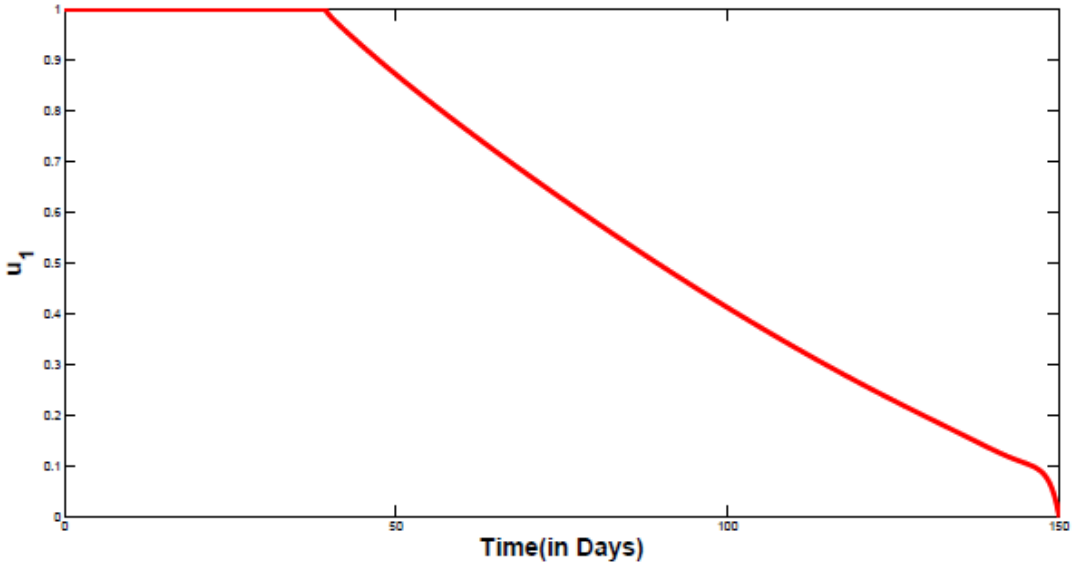

Figure 5 : The control profile of u_1 (t).

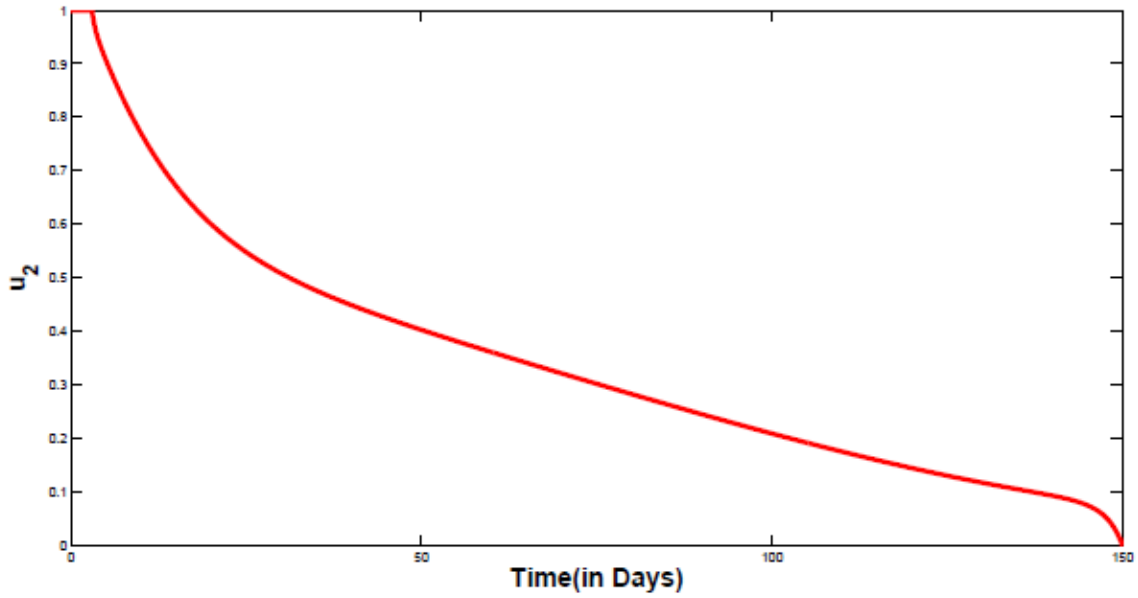

Figure 6: The control profile of $u_2(t)$.

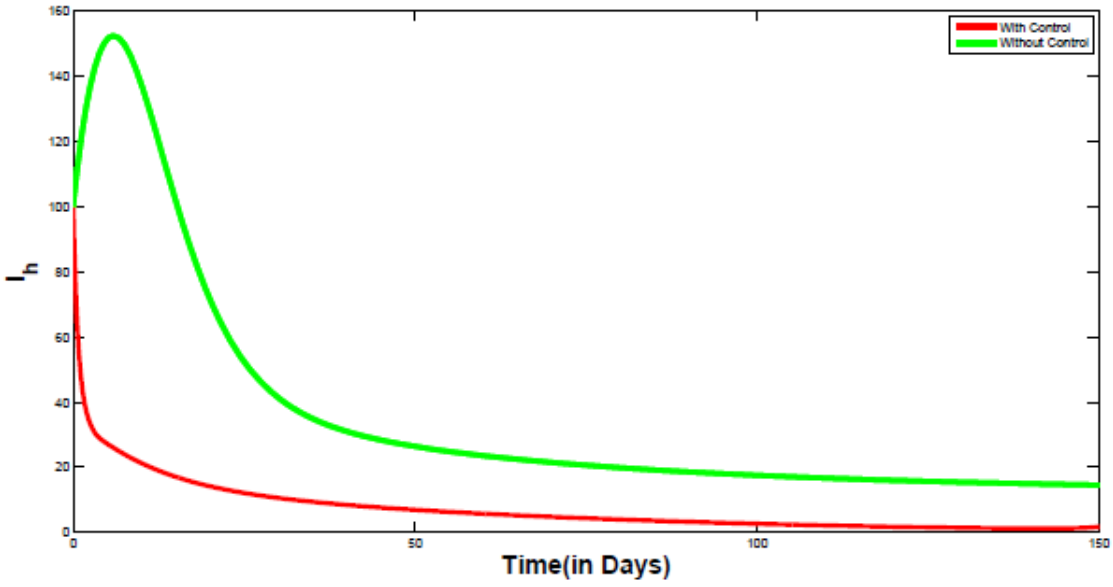

Figure 7: The variation of infected human against time with and without control.

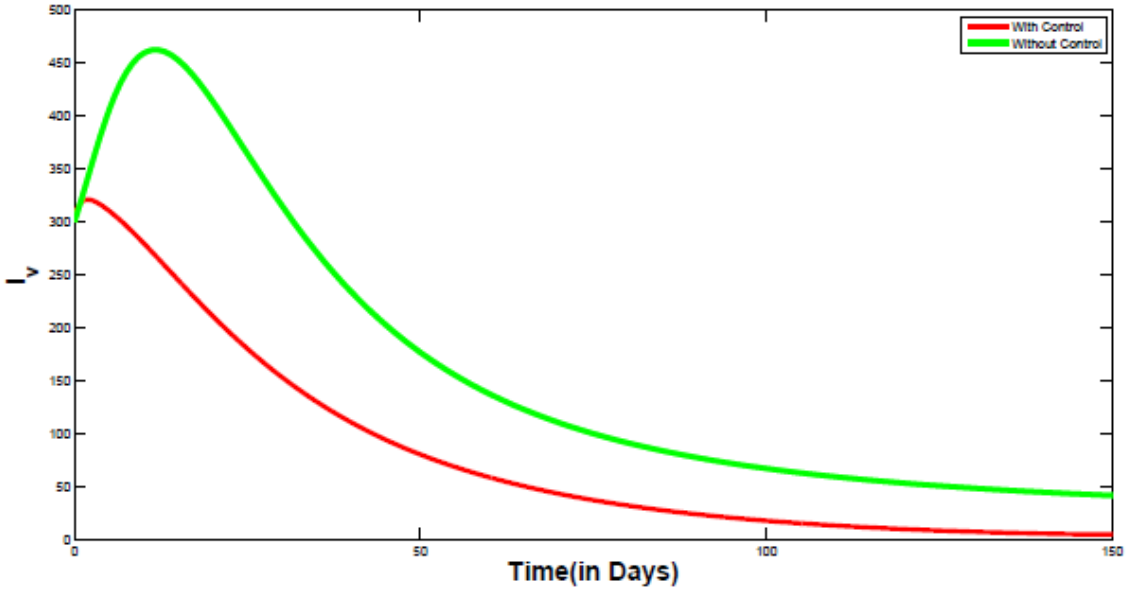

Figure 8: The variation of infected mosquito against time with and without control.

8. Conclusion

In this paper, we have proposed and analyzed a mathematical model for Zika virus disease. The existence of disease free equilibrium and endemic equilibrium are discussed in details. The basic reproduction number R_0 of the proposed model is computed. The disease free equilibrium is globally asymptotically stable whenever the basic reproduction number $R_0 < 1$. The endemic equilibrium point is locally asymptotically stable under some restriction on parameters. Further we extend our model to optimal control problem. Numerical simulations of original model and the optimal control problem suggest that optimal control strategies are the best in reducing the number of infectives in desired interval of time.

References

[1] Shapshak P et al. 2015 Zika virus. in Global Virology I - Identifying and Investigating Viral Diseases *Springer*, 477500 (New York).

[2] World Health Organization (WHO), WHO statement on the first meeting of the International Health Regulations (2005) Emergency Committee on Zika virus and observed increase in neurological disorder sandneo natalmal for mations, February1, 2016. *http://www.who.int/mediacentre/news/statements/2016/1st-emergencycommittee-zika/en/*, Accessed on February 26, 2016

[3] Centers for Disease Control and Prevention (CDC), CDC Emergency Operations Center moves to highest level of activation for Zika response, Febraury 3, 2016. *http://www.cdc.gov/media/releases/2016/s0208-zika-eocaactivation.html*, Accessed on February 26, 2016

[4] Pan American Health Organization (PAHO), Zika virus infection. *http://www.paho.org/hq/index.php?option=com_content & view= article & id = 11585 & Itemid = 41688 & lang = en.* ,Accessed on May 16, 2016

[5] Ebenezer B and Kazeem O O 2016, Mathematical modeling of Zika virus, *Asian Pac J Trop Dis*; **6**(9): 673-679.

[6] Daozhou G, Yijun L, Daihai H, Travis C P, Yang K, Gerardo C and Shigui R 2016 Prevention and Control of Zika as a Mosquito-Borne and Sexually Transmitted Disease: A

Mathematical Modeling Analysis, *http:// www.nature.com/scientificreports, Scientific Reports* — **6**:28070 — DOI: 10.1038/srep28070.

[7] F B Agusto, S bewick and W F Fagan 2017 Mathematical model od Zika virus with vertical transmission, *Infectious Disease Modelling*, KeAi **2**, 244-267.

[8] Victor M M, Baltazar E, Derdei B, Susan A H and Carlos C C 2016 Role of short-term dispersal on the dynamics of Zika virus in an extreme idealized environment, *Infectious Disease Modelling* **2** (2017) 1-14.

[9] Adam J K, Sebastian F, Rosalind M E, Henri-Pierre M, W John Edmunds and Eric J N 2016 Transmission Dynamics of Zika Virus in Island Populations : A Modelling of the 2013–14 French Polynesia Outbrea *PLOS Neglected Tropical Diseases*, DOI:10.1371/journal.pntd.0004726

[10] Buonomo B and Lacitignola D 2011 On the backward bifurcation of a vaccination model with nonlinear incidence, *Nonlinear Analysis: Modelling and Control*, Vol.16, No.1, 30–46

[11] Shigui R and Wendi W 2003 Dynamical behavior of an epidemic model with a nonlinear incidence rat, *J. Differential Equations* **188**, 135–163

[12] Xiao D and Ruan S 2007 Global Analysis of an Epidemic Model with Non monotone Incidence Rate, *Mathematical Biosci*ences, **208**, pp.419–429.

[13] Castillo-Chavez C, Feng Z and Huang W 2002 On the computation of R_0 and its role on global stability, in : Mathematical Approaches for For Emerging and Reemerging Infectious Diseases. *Springer-Verlag*, pp, 229-250.

[14] Driessche P V and Watmough J 2002 Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission *Mathematical Biosciences*, **180**, 29-48

[15] Li M and Muldowney J S 1996 A geometric approach to global stability problems. *SIAM J Math Anal* **27**(4):1070–1083

[16] Srivastav A K and Ghosh M 2016 Modeling and analysis of the symptomatic and asymptomatic infections of swine flu with optimal control, *Model.Earth Syst. Environ., Springer International Publishing Switzerland*, **2**:177, DOI 10.1007/s40808-016-0222-7

[17] Lenhart S and Workman J T 2007 *Optimal control applied to biological models. Crc Press.*

[18] Pontryagin L S, Boltyanskii V G, Gamkrelidze R V and Mishchenko E F 1962 *The Mathematical theory of optimal processes. Interscience Publishers*.