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The Co-Dynamics of Hepatitis E and HIV

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Abstract. This work investigates the co-dynamics of Hepatitis E and HIV. Initially, we formulate a co-infection dynamics model of Hepatitis E and HIV. Then, we analyze each model and discuss their mathematical results. After that, we investigate the full model and present their basic mathematical results. A bifurcation analysis for full model is investigated. Further, we formulate a mathematical model with five controls. Optimal control model is formulated and the necessary results of the optimal control characterization are presented. Moreover, numerical results with different control strategies are presented. It is shown that each strategy has its own importance but for the disease elimination the combination of all the five controls at the same time can best decrease the disease burden from the community.

1. Introduction

The Hepatitis E is an infectious disease, which is one of the types of Hepatitis. It is self-limiting and sometimes becoming severe and especially in pregnant woman with recorded mortality rate of 20 percent [1]. The middle-aged and especially males are the main targets of HEV in the individuals belong to developed countries [2–5]. The documents show the rapid increase in immunosuppressed transplants patients [6] and hematological malignancies individuals [7]. The co-infection of HIV and HEV is documented in 2009 in UK and France [8, 9]. In 2015, the authors in [10] documented the facts of HIV-HEV co-infection infected people. From 1985-2009, the data reveals the evidence of HEV and HIV co-infection either acute or prior HEV infection is 4 % and 5 % respectively of 194 infected people. It is also shown that among HIV infected individuals the acute Hepatitis individuals is considered one of the causes. In 2015, a study conducted on patients of HIV-HEV infected persons from Italy and it is concluded that the conducted research shows the presence of Hepatitis E in infected patients of HIV with a higher number of circulations, whereas in the general population it is observed a low prevalence of HEV antibodies [11]. In [12], it is documented the co-infection of HIV-HEV among patients in Spain with per year incidence rate in range of 0 % to 0.9 %. In HIV infected patients, the route of HEV acquisition has not been determined yet. An another study showed the presence of Hepatitis E and HIV in patients in Iran [13].

HIV/AIDS are confirmed by many studies that their spread in individuals is 7000 per day [14]. A large number of death from HIV/AIDS is absolutely a life threat to human existence, particular in less developed

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countries like Pakistan, Bangladesh, India, and in sub-Saharan African, where there is a shortage of health facilities. Recent literature shows that more than 30 million people have been killed due to HIV [15]. The HIV has targeted mainly the population of youth, who constitute the working population. It may not be quantified clearly the economic and social burden of HIV/AIDS in many countries. Thus, it is necessary that some serious steps regarding the disease of HIV/AIDS should be taken in order to reduce further the spread of disease. Therefore, mathematical models play an important role in disease epidemiology and biological systems [16–19] to get insight into the disease.

Recent literature shows that the mathematical models have gained much attention regarding the disease dynamics and its role in the spread and control [20, 21]. In [21], the authors investigated the co-dynamics of HIV/AIDS and cryptosporidiosis. Similarly, many researchers investigated the HIV dynamics with prevention and its impact on outbreak and epidemics([22–24]). Since HIV/AIDS is spreading very fast in the communities, and it is noteworthy, that awareness and campaign must be there to get rid the disease. So, in this regard many researchers highlighted this issue through mathematical modeling approach, see ([25–27]). Besides this, HIV/AIDS and many other diseases, a lot of articles have been published to show the dynamics of disease and its burden on the community ([20, 25, 26, 28–33]). In literature, very little attention has been made to investigate the dynamics of Hepatitis E and there is no such model with HIV that describes their co-infection. According to the author's knowledge, no one not paid any attention to study the HIV and Hepatitis E co-infection. So, this paper will briefly explain a mathematical modeling approach to explore the co-infection dynamics of Hepatitis E and HIV/AIDS with different control strategies. The Hepatitis E with optimal control is studied in [34].

The present paper describes the co-infection of Hepatitis E and HIV/AIDS. Both the diseases are very severe and life threaten for the society. Therefore, it is important to formulate a mathematical model on Hepatitis E and HIV. A detailed discussion on both the diseases have been presented in Section 1. The remaining paper can be sectionized as per the following. The model formulation of HIV and Hepatitis E as a co-infection model is investigated in Section 2. The formulation of only Hepatitis E model is given in Section 3 and its mathematical results is investigated. In Section 4, we present only the HIV/AIDS model and show its mathematical results. In Section 5, we discuss the full model of HIV/AIDS and Hepatitis E and present their mathematical results. We formulate the control problem in Section 6 and show the necessary results associated to the model. Numerical results are obtained and discussed with detailed by different control strategies in Section 7 while in Section 8, the work is summarized by a brief conclusion.

2. Model Formulation

This section presents the model formulation of Hepatitis E and HIV/AIDS co-dynamics. Based on the nature of both the diseases, we denote the total population of individuals by $N(t)$ and subdividing into seven different classes; susceptible individuals $S(t)$, individuals exposed to Hepatitis E only $E(t)$, individuals infected with Hepatitis E only $I(t)$, those recovered from Hepatitis E only by $R(t)$, people infected with HIV only $H(t)$, those who infected with AIDS only $A(t)$, individuals infected both from Hepatitis E and HIV, I_{HE}. Besides this, the microbacterium plays an important role in the disease spread of Hepatitis E only, so we also include E_n class in the model. The Hepatitis E only individuals infected through the environment is E_n. Thus, $N = S + E + I + R + H + A + I_{HE}$, so we obtain the following system as per the above discussions:

$$\begin{cases} \frac{d}{dt}S = & \Lambda - dS - (\lambda_1 + \lambda_2)S, \\ \frac{d}{dt}E = & \lambda_1 S - (d+\delta)E, \\ \frac{d}{dt}I = & \delta E - (\pi + d + \psi)I - \lambda_2 I, \\ \frac{d}{dt}R = & \pi I - dR, \\ \frac{d}{dt}E_n = & \theta I - \eta E_n, \\ \frac{d}{dt}H = & \lambda_2 S - (\chi + d + \vartheta)H - \frac{\beta_1 \tau I H}{N} + (1-r)\gamma I_{HE}, \\ \frac{d}{dt}A = & \chi H - (d+\vartheta)A - \frac{\beta_1 \tau I A}{N} + r\gamma I_{HE}, \\ \frac{d}{dt}I_{HE} = & \frac{\beta_1 \tau I(H+A)}{N} + \lambda_2 I - dI_{HE} - \gamma I_{HE}, \end{cases} \tag{1}$$

where

$$\lambda_1 = \frac{\beta_1 \tau I}{S + E + I + R + H + A + I_{HE}} + \alpha_E E_n,$$

$$\lambda_2 = \frac{\beta_2 \xi (H + A)}{S + E + I + R + H + A + I_{HE}}$$

and

$$S(0) = S_0 \geq 0,\ I(0) = I_0 \geq 0,\ R(0) = R_0 \geq 0,\ E_n(0) = E_{n0} \geq 0,\ H(0) = H_0 \geq 0,$$

$$A(0) = A_0 \geq 0,\ I_{HE}(0) = I_{HE(}0) \geq 0. \tag{2}$$

In co-infection model (1), the parameter Λ represents the recruitment rate of the susceptible people, while its natural mortality rate is d. The natural mortality rate of humans due to Hepatitis E only, HIV only and dually infected, are ψ, ϑ and γ respectively. The exposed Hepatitis E individuals are infected with a rate δ. The individuals infected only with Hepatitis E are recovered through the parameter π, and every infected individual from Hepatitis E contributes averagely to the environment by a parameter θ. The HIV infected individuals transfer rate to AIDS class is given by χ. The Hepatitis E virus decays in the environment is given by η. The contact rate of Hepatitis E only is given by β_1, while the contact rate of HIV is given by β_2. The parameters τ and ξ are the contact rates while β_1 and β_2 are the transmission probabilities. The parameter r is the rate of co-infected humans while $r\gamma$ is the proportion to AIDS class while the rate γ defines the death rate of dually infected individuals. The parameter α_E represents the probability of infection through environment.

2.1. Model basic properties

2.2. Solution positivity

The model (1) that shows the population of human, so, it is clear that the variables as well as the parameters are non-negative and it can be shown that for non-negative values, the systems leads to non-negative. Considering the feasible region for the Hepatitis E and HIV/AIDS co-infection model in the following:

$$\bigotimes = \left\{ (S, E, I, R, H, A, I_{HE}) \in R_+^7 : N \leq \frac{\Lambda}{d},\ E_n \in R_+ : E_n \leq \frac{\Lambda\theta}{d\eta} \right\}.$$

Further, we show the positive invariance of $\bigotimes$, where the solutions associated to the system (1) $\forall\ t > 0$ remains in $\bigotimes$. Summing the total population of the model (1) leads to the following:

$$N'(t) = \Lambda - dN - \psi I - \vartheta(H + A) \leq \Lambda - dN.$$

It follows by using a standard comparison method:

$$N(t) \leq N(0)exp(-dt) + \frac{\Lambda}{d}(1 - exp(-dt)).$$

Particularly, $N(t) \leq \frac{\Lambda}{d}$ when $N(0) \leq \frac{\Lambda}{d}$. So, the given region is positively invariant. Thus, we will discuss the co-infection model (1) in $\bigotimes$ which is epidemiologically and mathematically well posed. Next, we present the mathematical analysis of each model in details.

3. Only Hepatitis E model

Here, we only investigate the Hepatitis E model and present its mathematical results. The only Hepatitis E model can be obtained by setting $H = A = I_{HE} = 0$ in model (1), which leads to the following:

$$\begin{cases} \frac{dS}{dt} = \Lambda - \frac{\beta_1 \tau IS}{N} - \alpha_E E_n S - dS, \\ \frac{dE}{dt} = \frac{\beta_1 \tau IS}{N} + \alpha_E E_n S - (d + \delta)E, \\ \frac{dI}{dt} = \delta E - (d + \pi + \psi)I, \\ \frac{dR}{dt} = \pi I - dR, \\ \frac{dE_n}{dt} = \theta I - \eta E_n, \end{cases} \tag{3}$$

where $N = S + E + I + R$.

3.1. Stability results

This subsection determines the basic results associated to the only Hepatitis E model (3). We denote the disease free equilibrium of the Hepatitis E only model (3) shown by P_0^E and can be obtained by

$$P_0^E = \Big(\frac{\Lambda}{d}, 0, 0, 0, 0\Big).$$

First, we obtain an expression for the basic reproduction number of the only Hepatitis E model (3). For only Hepatitis E model (3), the basic reproduction number shown by $\mathcal{R}_0^E$ and is obtained by the following method in [37]. In the computations of $\mathcal{R}_0^E$ involved the necessary matrices

$$F = \begin{pmatrix} 0 & \tau\beta_1 & \frac{\Lambda\alpha_E}{d} \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}, \quad V = \begin{pmatrix} \delta + d & 0 & 0 \\ -\delta & d + \pi + \psi & 0 \\ 0 & -\theta & \eta \end{pmatrix}.$$

For the only Hepatitis E model (3), we finally obtain the basic reproduction number $\mathcal{R}_0^E$ as,

$$\mathcal{R}_0^E = \frac{\delta\left(\beta_1 \eta d\tau + \theta\Lambda\alpha_E\right)}{\eta d(\delta + d)(d + \pi + \psi)}.$$

The following theorem is presented for the local stability of the only Hepatitis E model (3).

Theorem 3.1. *If $\mathcal{R}_0^E < 1$, then, the only Hepatitis E model (3) is locally asymptotically stable (LAS).*

Proof. The only Hepatitis E model (3) at P_0^E is

$$J(P_0^E) = \begin{pmatrix} -d & 0 & -\tau\beta_1 & 0 & -\frac{\Lambda\alpha_E}{d} \\ 0 & -(\delta + d) & \tau\beta_1 & 0 & \frac{\Lambda\alpha_E}{d} \\ 0 & \delta & -(d + \pi + \psi) & 0 & 0 \\ 0 & 0 & \pi & -d & 0 \\ 0 & 0 & \theta & 0 & -\eta \end{pmatrix}.$$

Obviously in $J(P_0^E)$, the two eigenvalues are $-d$, $-d$ are negative. The rest of the values with negative real parts can be obtained by solving the following equation,

$$\lambda^3 + \Phi_1\lambda^2 + \Phi_2\lambda + \Phi_3 = 0,$$

where

$$\begin{aligned}
\Phi_1 &= \delta + \eta + 2d + \pi + \psi,\\
\Phi_2 &= -\beta_1\delta\tau + (d + \psi + \pi)(d + \delta + \eta) + \eta(d + \delta),\\
\Phi_3 &= \eta(\delta + d)(d + \pi + \psi)(1 - \mathcal{R}_0^E).
\end{aligned}$$

Clearly, Φ_1 and Φ_2 are positive and Φ_3 is positive only when $\mathcal{R}_0^E < 1$. Also, it is easy to verify that $\Phi_1\Phi_2 > \Phi_3$, which is the Routh-Hurtwiz conditions. Thus, it is concluded that all the eigenvalues of the only Hepatitis E model (3) at P_0^E have negative real parts. So, the only Hepatitis E model (3) at P_0^E is locally asymptotically stable if $\mathcal{R}_0^E < 1$. □

3.2. Endemic Equilibria

In this subsection, we find the endemic equilibria of the only Hepatitis E model (3) shown by $P_1^E = (S^*, E^*, I^*, R^*, E_n^*)$ and is given by:

$$\begin{cases}
S^* = \frac{\Lambda}{d+\overline{\lambda}},\\
E^* = \frac{\overline{\lambda}\Lambda}{(d+\delta)(d+\overline{\lambda})},\\
I^* = \frac{\delta\overline{\lambda}\Lambda}{(d+\delta)(d+\overline{\lambda})(d+\psi+\pi)},\\
R^* = \frac{\pi I^*}{d},\\
E_n^* = \frac{\theta I^*}{\eta},
\end{cases}$$

where

$$\overline{\lambda} = \frac{\beta_1\tau I^*}{E^* + I^* + R^* + S^*} + \alpha_E E_n^*,$$

satisfies the equation below,

$$P(\overline{\lambda}) = c_0\overline{\lambda}^2 + c_1\overline{\lambda} + c_2, \tag{4}$$

where

$$\begin{aligned}
c_0 &= \eta(d + \delta)(d + \psi + \pi)\Big((d + \pi)\delta + d(d + \psi + \pi)\Big),\\
c_1 &= d\eta(d + \delta)(d + \psi + \pi)\Big(-\beta_1\delta\tau + \psi(2d + \delta) + 2(d + \pi)(d + \delta)\Big) - \alpha_E\delta\theta\Lambda\Big((d + \pi)(d + \delta) + d\psi\Big),\\
c_2 &= d^2\eta(d + \delta)^2(d + \psi + \pi)^2(1 - \mathcal{R}_0^E).
\end{aligned}$$

The coefficient c_0 in (4) is positive clearly while c_2 can be positive if $\mathcal{R}_0^E < 1$ and if $\mathcal{R}_0^E > 1$, then it becomes negative. The positive solution of equation (4) completely depends on the sign of c_1. We can have a unique endemic equilibrium if the condition holds, $c_2 < 0 \iff \mathcal{R}_0^E > 1$. If $c_1 < 0$ and $c_2 = 0$ or their discriminant is zero, then we have a unique endemic equilibrium. We can have two equilibria if $c_2 > 0$, $c_1 < 0$ and their discriminant is positive. Besides, these cases no equilibria exists for the model.

3.3. Global Stability of only Hepatitis E model

Here, we explore the global dynamics of the only Hepatitis E model (3) at the disease free case. For this, we give the following result.

Theorem 3.2. *The only Hepatitis E model (3) for $\mathcal{R}_0^E < 1$ is globally asymptotically stable.*

Proof. Let us defining the Lyapunov function below,

$$L(t) = \Upsilon_1 E + \Upsilon_2 I + \Upsilon_3 E_n, \tag{5}$$

where Υ_i, for $i = 1, 2, 3$ and to be determined later. The time derivative of equation (5) along the only Hepatitis E model (3), is given by

$$\begin{aligned} L'(t) &= \Upsilon_1[\frac{\beta_1 \tau IS}{N} + \alpha_E E_n S - (d+\delta)E] + \Upsilon_2[\delta E - (d+\pi+\psi)I] + \Upsilon_3[\theta I - \eta E_n] \\ &\leq \Upsilon_1[\beta_1 \tau I + \alpha_E E_n - (d+\delta)E] + \Upsilon_2[\delta E - (d+\pi+\psi)]I + \Upsilon_3[\theta I - \eta E_n] \\ &= [\Upsilon_1\beta_1\tau - \Upsilon_2(d+\pi+\psi) + \Upsilon_3\theta]I + [\Upsilon_2\delta - (d+\delta)\Upsilon_1]E + [\Upsilon_1\alpha_E - \Upsilon_3\eta]E_n \\ &\leq (d+\delta)(d+\pi+\epsilon)(\mathcal{R}_0^E - 1). \end{aligned}$$

The last step is obtained by assigning the value to $\Upsilon_1 = \delta$, $\Upsilon_2 = (\delta + d)$ and $\Upsilon_3 = \frac{\delta\alpha_E}{\eta}$. Thus, $L'[t] \leq 0$ if $\mathcal{R}_0^E < 1$. So, we conclude that the only Hepatitis E model (3) is globally asymptotically stable at P_0^E iff $\mathcal{R}_0^E < 1$. □

4. Only HIV model

Here, we consider the only HIV model and explore its mathematical results. Putting $S = E = I = R = E_n = 0$ in model (1), we can obtain the only HIV model (6), and is given by,

$$\begin{cases} \frac{d}{dt}S = & \Lambda - dS - \lambda_2 S, \\ \frac{d}{dt}H = & \lambda_2 S - (\chi + d + \vartheta)H, \\ \frac{d}{dt}A = & \chi H - (d+\vartheta)A, \end{cases} \tag{6}$$

where $\lambda_2 = \frac{\beta_2\xi(H+A)}{S+H+A}$.

4.1. Stability analysis of HIV only model

This subsection determines the fundamental mathematical results associated to the only HIV model (6). For the only HIV model (6), we denote its disease free equilibrium by E_{H0} and it can be obtained as follows:

$$E_{H0} = (S^0, 0, 0) = \Big(\frac{\Lambda}{d}, 0, 0\Big).$$

To show the stability results of the only HIV model (6), first, we have to obtain the basic reproduction number, denoted by, $\mathcal{R}_{0H}$ for the only HIV model (6). To do this, we follow the technique presented in [37] and obtain $\mathcal{R}_{0H}$, for only HIV model (6), with the following information:

$$F = \begin{pmatrix} \xi\beta_2 & \xi\beta_2 \\ 0 & 0 \end{pmatrix}, \quad V = \begin{pmatrix} d+\chi+\vartheta & 0 \\ -\chi & d+\vartheta \end{pmatrix}.$$

We obtain for the only HIV model (6), the basic reproduction number $\mathcal{R}_{0H}$ is as follows:

$$\mathcal{R}_{0H} = \frac{\beta_2\xi}{d+\vartheta}.$$

To establish the local stability of the only HIV model (6), we present the following theorem:

Theorem 4.1. *The given model (6) is LAS if $\mathcal{R}_{0H} < 1$ and it is unstable when $\mathcal{R}_{0H} > 1$.*

Proof. At E_{H0}, we have

$$J_{0H} = \begin{pmatrix} -d & -\xi\beta_2 & -\xi\beta_2 \\ 0 & -(d+\chi+\vartheta)+\xi\beta_2 & \xi\beta_2 \\ 0 & \chi & -(d+\vartheta) \end{pmatrix}. \tag{7}$$

The characteristics equation associated to J_{0H} is

$$(\lambda + d)(\lambda^2 + \ell_1\lambda + \ell_2\lambda) = 0,$$

where

$$\ell_1 = (d+\chi+\vartheta) + (d+\vartheta)(1-\mathcal{R}_{0H}),$$

$$\ell_2 = (d+\vartheta)(d+\chi+\vartheta)(1-\mathcal{R}_{0H}).$$

Clearly, $-d < 0$ and the remaining can easily be verified from the quadratic equation, when $\mathcal{R}_{0H} < 1$. So, the only HIV model (6) at the equilibrium E_{H0}, when $\mathcal{R}_{0H} < 1$, is locally asymptotically stable. □

4.2. HIV/AIDS model and their endemic equilibria

The endemic equilibrium of the only HIV model (6), given by $E^*_H = (S^*, H^*, A^*)$, and can be obtained by

$$\begin{cases} S^* = \frac{\Lambda}{\beta_2\xi-\vartheta}, \\ H^* = \frac{\Lambda(d+\vartheta)(\mathcal{R}_{0H}-1)}{(\beta_2\xi-\vartheta)(d+\vartheta+\xi)}, \\ A^* = \frac{\chi\Lambda(\mathcal{R}_{0H}-1)}{(\beta_2\xi-\vartheta)(d+\vartheta+\xi)}. \end{cases}$$

For $\mathcal{R}_{0H} > 1$, then the endemic equilibrium of the only HIV model (6) exists.

5. Analysis of the full model

Here, in this section, we present the analysis of the co-infection model (1). The disease free equilibrium of the co-infection model, denoted by E_2, and can be obtained as follows:

$$E_2 = \Big(\frac{\Lambda}{d}, 0, 0, 0, 0, 0, 0, 0\Big).$$

To investigate the stability analysis of the full model (1), we need to obtain the basic reproduction number, denoted by $\mathcal{R}_0$. In order to do this, we use the method presented in [37] on the system (1), and follow their rule to obtain the basic reproduction number $\mathcal{R}_0$. We have

$$F = \begin{pmatrix} 0 & \tau\beta_1 & \frac{\Lambda\alpha_E}{d} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \xi\beta_2 & \xi\beta_2 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix}, \quad V = \begin{pmatrix} \delta+d & 0 & 0 & 0 & 0 & 0 \\ -\delta & d+\pi+\psi & 0 & 0 & 0 & 0 \\ 0 & -\theta & \eta & 0 & 0 & 0 \\ 0 & 0 & 0 & \chi+d+\vartheta & 0 & (r-1)\gamma \\ 0 & 0 & 0 & -\chi & d+\vartheta & -r\gamma \\ 0 & 0 & 0 & 0 & 0 & \gamma+d \end{pmatrix}.$$

Thus,

$$\mathcal{R}_0 = \max\left(\mathcal{R}_0^E, \mathcal{R}_0^H\right) = \Big(\frac{\delta\,(\alpha_E\theta\Lambda + \beta_1\eta d\tau)}{\eta d(\delta+d)(d+\pi+\psi)}, \frac{\beta_2\xi}{d+\vartheta}\Big).$$

Next, we establish the local stability results of the disease free equilibrium E_2 of the full model (1). We have:

Theorem 5.1. *The disease free equilibrium E_2 of the full model (1) is locally asymptotically stable if $\mathcal{R}_0 < 1$.*

Proof. The following Jacobian matrix is obtained at the disease free equilibrium E_2:

$$J = \begin{pmatrix} -d & 0 & -\tau\beta_1 & 0 & -\frac{\Lambda\alpha_E}{d} & -\xi\beta_2 & -\xi\beta_2 & 0 \\ 0 & -(\delta+d) & \tau\beta_1 & 0 & \frac{\Lambda\alpha_E}{d} & 0 & 0 & 0 \\ 0 & \delta & -(d+\pi+\psi) & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \pi & -d & 0 & 0 & 0 & 0 \\ 0 & 0 & \theta & 0 & -\eta & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & -(\chi+d+\vartheta)+\xi\beta_2 & \xi\beta_2 & (1-r)\gamma \\ 0 & 0 & 0 & 0 & 0 & \chi & -(d+\vartheta) & r\gamma \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & -(\gamma+d) \end{pmatrix}.$$

Obviously, the two eigenvalues of the Jacobian matrix J are negative, *i.e.*, $-d < 0$, $-d < 0$ and $-(\gamma + d) < 0$. The rest of the eigenvalues can be obtained through the following equation:

$$\lambda^5 + \varpi_1\lambda^4 + \varpi_2\lambda^3 + \varpi_3\lambda^2 + \varpi_4\lambda + \varpi_5 = 0, \tag{8}$$

where

$$\begin{aligned}
\varpi_1 &= \chi + \delta + \eta + 3d + \pi + \psi + \vartheta + (d+\vartheta)\left(1 - \mathcal{R}_0^H\right), \\
\varpi_2 &= \eta(\chi + \delta + 3d + \pi + \psi + \vartheta) - \beta_1\delta\tau + (\delta+d)(\chi + 2d + \pi + \psi + \vartheta) \\
&\quad +(\chi + d + \vartheta)(d + \pi + \psi) + (d+\vartheta)(\chi + \delta + \eta + 3d + \pi + \psi + \vartheta)(1 - \mathcal{R}_0^H), \\
\varpi_3 &= -\beta_1\delta\tau\left(-\beta_2\xi + \chi + 2(d+\vartheta)\right) + (\delta+d)(\chi + d + \vartheta)(\eta + d + \pi + \psi) \\
&\quad +\eta(\chi + d + \vartheta)(d + \pi + \psi) + \eta(\delta+d)(d + \pi + \psi)(1 - \mathcal{R}_0^E) + \\
&\quad (d+\vartheta)((\delta+d)(\chi + \eta + 2d + \pi + \psi + \vartheta) + (d + \pi + \psi)(\chi + \eta + d + \vartheta) + \eta(\chi + d + \vartheta))\times \\
&\quad (1 - \mathcal{R}_0^H), \\
\varpi_4 &= (d+\vartheta)(\chi + d + \vartheta)\left(-\beta_1\delta\tau + \eta(\delta+d) + (\delta+d)(d + \pi + \psi) + \eta(d + \pi + \psi)\right)(1 - \mathcal{R}_0^H) \\
&\quad +\eta(\delta+d)(\chi\kappa + 2(d+\vartheta))(d + \pi + \psi)(1 - \mathcal{R}_0^E)(1 - \mathcal{R}_0^H) \\
\varpi_5 &= \eta(\delta+d)(d+\vartheta)(\chi + d + \vartheta)(d + \pi + \psi)(1 - \mathcal{R}_0^E)(1 - \mathcal{R}_0^H).
\end{aligned}$$

Clearly, the coefficient $\varpi_i > 0$ for $i = 1, 2..., 5$ can be shown easily that when $\mathcal{R}_0 < 1$. Further, the Routh-Hurtwiz criteria $\varpi_i > 0$ for $i = 1, 2..., 5$ and the condition given below must be met

$$\begin{pmatrix} \varpi_1 & 1 & 0 & 0 & 0 \\ \varpi_3 & \varpi_2 & \varpi_1 & 1 & 0 \\ \varpi_5 & \varpi_4 & \varpi_3 & \varpi_2 & \varpi_1 \\ 0 & 0 & \varpi_5 & \varpi_4 & \varpi_3 \\ 0 & 0 & 0 & 0 & \varpi_5 \end{pmatrix} > 0. \tag{9}$$

The condition (9) together, with $\mathcal{R}_0 < 1$, ensures, the fulfillment of the Routh-Hurtwiz criteria. So, it can be concluded that the co-infection model described by (1), is locally asymptotically stable if $\mathcal{R}_0 < 1$ and the condition (9) satisfies. □

5.1. Bifurcation analysis of the full model

Here, we present the bifurcation phenomenon of the co-infection model (1) by using the centre manifold theory. In order to investigate the bifurcation analysis of the co-infection model, we consider $\mathcal{R}_0^E = 1$ and $\mathcal{R}_0^H = 1$ if and only if

$$\beta_1 = \beta_1^* = \frac{\delta(\eta d(d+\pi+\psi) - \theta\Lambda\alpha_E) + \eta d^2(d+\pi+\psi)}{\delta\eta d\tau}$$

and

$$\beta_2 = \beta_2^* = \frac{d+\vartheta}{\xi}.$$

Further, we rename the variables of the full model by, $S = y_1$, $E = y_2$, $I = y_3$, $R = y_4$, $E_n = y_5$, $H = y_6$, $A = y_7$ and $I_{HE} = y_8$ and $N = y_1 + y_2 + y_3 + y_4 + y_6 + y_7 + y_8$. Furthermore, employing the vector notation $\overrightarrow{y} = (y_1, y_2, y_3, y_4, y_5, y_6, y_7, y_8)$, then, the co-infection model (1) can be described as in the form $dy/dt = F\overrightarrow{x}$, with $F = (g_1, g_2, g_3, g_4, g_5, g_6, g_7, g_8)^T$ is as follows:

$$\begin{cases} \frac{d}{dt}y_1 = & \Lambda - dy_1 - (\lambda_1 + \lambda_2)y_1, \\ \frac{d}{dt}y_2 = & \lambda_1 y_1 - (d+\delta)y_2, \\ \frac{d}{dt}x_3 = & \delta y_2 - (\pi + d + \psi)y_3 - \lambda_2 y_3, \\ \frac{d}{dt}y_4 = & \pi y_3 - dy_4, \\ \frac{d}{dt}y_5 = & \theta y_3 - \eta y_5, \\ \frac{d}{dt}y_6 = & \lambda_2 y_1 - (\chi + d + \vartheta)y_6 - \frac{\beta_1\tau y_3 y_6}{N} + (1-r)\gamma y_8, \\ \frac{d}{dt}x_7 = & \chi y_6 - (d+\vartheta)y_7 - \frac{\beta_1\tau y_3 y_7}{N} + r\gamma y_8, \\ \frac{d}{dt}y_8 = & \frac{\beta_1\tau y_3(y_6+y_7)}{N} + \lambda_2 y_3 - dy_8 - \gamma y_8, \end{cases} \tag{10}$$

where

$$\lambda_1 = \frac{\beta_1\tau y_3}{N} + \alpha_E y_5$$

and

$$\lambda_2 = \frac{\beta_2\xi(y_6+y_7)}{N}.$$

The evaluation of the Jacobian matrix at E_2 of the system (10), given by J_{HE}, leads to

$$J_{HE} = \begin{pmatrix} -d & 0 & -M_1 & 0 & -\frac{\Lambda\alpha_E}{d} & -d-\vartheta & -d-\vartheta & 0 \\ 0 & -(\delta+d) & M_1 & 0 & \frac{\Lambda\alpha_E}{d} & 0 & 0 & 0 \\ 0 & \delta & -(d+\pi+\psi) & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \pi & -d & 0 & 0 & 0 & 0 \\ 0 & 0 & \theta & 0 & -\eta & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & -\chi & d+\vartheta & (1-r)\gamma \\ 0 & 0 & 0 & 0 & 0 & \chi & -(d+\vartheta) & r\gamma \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & -\gamma-d \end{pmatrix}.$$

where $M_1 = \frac{\eta(d+\pi+\psi)d^2 + \delta(\eta d(d+\pi+\psi) - \theta\Lambda\alpha_E)}{\delta\eta d}$. It is obvious that one of the eigenvalues of the Jacobian matrix J_{HE} is zero, while the rest of have the negative real parts. So, the centre manifold theory is appropriate and can be used to investigate the bifurcation analysis of the co-infection model (1). To proceed further, we

have to compute left and right eigenvectors of J_{HE}, respectively shown by $\overrightarrow{l} = [l_1, l_2, l_3, l_4, l_5, l_6, l_7, l_8]^T$ and $\overrightarrow{m} = [m_1, m_2, m_3, m_4, m_5, m_6, m_7, m_8]$. The following result is then obtained

$$\begin{aligned} l_1 &= -\frac{l_7(d+\vartheta)(\chi+d+\vartheta)}{\chi d} - \frac{l_3\left(\delta d+\delta\pi+\delta\psi+d^2+d\pi+d\psi\right)}{\delta d}, \\ l_2 &= \frac{l_3(d+\pi+\psi)}{\delta},\ l_4=\frac{\pi l_3}{d},\ l_5=\frac{\theta l_3}{\eta}, l_6=\frac{l_7(d+\vartheta)}{\chi}, \\ l_3 &= l_3>0,\ l_7=l_7>0,\ l_8=0. \end{aligned}$$

and

$$\begin{aligned} m_1 &= 0,\ m_2=m_2>0,\ m_6=m_6>0,\ m_3=\frac{m_2(\delta+d)}{\delta},\ m_4=0,\ m_5=\frac{\Lambda\alpha_E m_2}{\eta d}, \\ m_7 &= m_6,\ m_8=\frac{\gamma m_6}{\gamma+d}. \end{aligned}$$

The value of a after some rigorous computation leads to

$$a = -\frac{2\left(\eta K_1 d m_6 l_7 + \chi K_2 m_2 l_3(\gamma+d)\right)}{\chi^2\delta\eta\Lambda d(\gamma+d)},$$

where

$$\begin{aligned} K_1 &= 2\beta_2\delta d\xi l_7(\gamma+d)(\chi+d+\vartheta)^2 + \chi l_3\left(\beta_1\delta d\tau(\gamma(-\chi+d+\vartheta)+2\dot{(}d+\vartheta))+\beta_2(\chi+d+\vartheta)\right) \\ &\quad +\chi\xi l_3\Big(\gamma(\delta(d+2\pi)+2d(d+\pi+\psi))+2\dot{(}\delta(d+\pi)+d(d+\pi+\psi))\Big), \\ K_2 &= \chi l_3 l_7\left(\beta_2\eta d^2\xi(\chi(\delta+d)+(2\delta+d)(d+\vartheta))+\beta_1\chi\delta\eta d^2\tau+\delta\theta\Lambda\rho(d+\vartheta)(\chi+d+\vartheta)\right) \\ &\quad +\chi l_3\Big(\beta_1\eta d\tau(\delta(d+\pi)+d(d+\pi+\psi))+\theta\Lambda\rho(\delta+d)(d+\pi+\psi)\Big). \end{aligned}$$

Then, the computation of b leads to:

$$b = \tau m_2 l_3 > 0.$$

The sign of a can best determine the possibility of backward bifurcation in the co-infection model as b is clearly positive.

Theorem 5.2. *The co-infection model will undergo backward bifurcation if the condition a is positive.*

6. Application of optimal control

Models of infectious disease with control analysis are used widely for the possible elimination of disease control and prevention. A variety of articles are published in the literature with control for different infectious diseases such as [38–41]. The optimal control problem is formulated with different controls. We consider five controls for the possible elimination of Hepatitis E and HIV-AIDS from the community. The controls are:

- u_1 : It denotes the possible prevention of individuals infected by Hepatitis E virus.

- u_2 : It shows the efforts made for the prevention of HIV infections.

- u_3: Treatment of prevention efforts or the available treatment for the individuals infected with Hepatitis E.

- u_4 : Treatment or prevention efforts for HIV infected individuals.

- u_5 : Drug efficacy for the treatment of HIV-AIDS and Hepatitis E individuals.

Considering the above assumptions, the optima control problem can be shown through the following system of nonlinear differential equations:

$$\begin{cases} \frac{d}{dt}S = & \Lambda - dS - \Big(\frac{\beta_1\tau I}{N} + \alpha_n E_n\Big)(1-u_1)S - (1-u_2)\Big(\frac{\beta_2\xi(H+A)}{N}\Big)S, \\ \frac{d}{dt}E = & (1-u_1)\Big(\frac{\beta_1\tau I}{N} + \alpha_n E_n\Big)S - (d+\delta)E, \\ \frac{d}{dt}I = & \delta E - (\pi u_3 + d + \psi)I - (1-u_2)\Big(\frac{\beta_2\xi(H+A)}{N}\Big)I, \\ \frac{d}{dt}R = & \pi u_3 I - dR, \\ \frac{d}{dt}E_n = & \theta I - \eta E_n, \\ \frac{d}{dt}H = & (1-u_2)\Big(\frac{\beta_2\xi(H+A)}{N}\Big)S - (u_4\chi + d + \vartheta)H - (1-u_1)\frac{\beta_1\tau IH}{N} + (1-u_5 r)\gamma I_{HE}, \\ \frac{d}{dt}A = & u_4\chi H - (d+\vartheta)A - (1-u_1)\frac{\beta_1\tau IA}{N} + u_5 r\gamma I_{HE}, \\ \frac{d}{dt}I_{HE} = & (1-u_1)\frac{\beta_1\tau I(H+A)}{N} + (1-u_2)\Big(\frac{\beta_2\xi(H+A)}{N}\Big)I - dI_{HE} - u_5\gamma I_{HE}. \end{cases} \tag{11}$$

For the optimal control problem (11), we define the following objective functional:

$$\begin{aligned} J(u_1,u_2,u_3,u_4,u_5) &= \int_0^{T_f} [B_1E + B_2I + B_3H + B_4A + B_5I_{HE} + B_6u_1^2 \\ &\quad + B_7u_2^2 + B_8u_3^2 + B_9u_4^2 + B_{10}u_5^2]dT. \end{aligned} \tag{12}$$

In control problem (11), the Hepatitis E individuals, HIV infection and the co-infection individuals together with associated and the possible treatment and preventions controls, u_i for $i = 1, 2, ..., 5$, are minimized. In objective functional (12), the final time is shown by T_f, while the coefficients, B_i for $i = 1, ..., 10$ denote the weight and the balancing constants for the state and control variables in the objective functionals. We define the control set in the following for our optimal control problem with the defined controls u_i^*, for $i = 1, ..., 5$, such that

$$\begin{aligned} \Sigma &= \{(u_1,u_2,u_3,u_4,u_5)/u_i(t) \textit{ is Lebesgue measurable on } [0,1], \textit{ where} \\ &\quad 0 \le u_i(t) \le 1,\ i = 1, 2...5\}. \end{aligned} \tag{13}$$

Further, we define the Lagrangian L and the Hamiltonian $\mathcal{H}$ for the optimal control problem (11), given by

$$\begin{aligned} L(E,I,H,A,I_{HE},u_1,u_2,u_3,u_4,u_5) &= B_1E + B_2I + B_3H + B_4A + B_5I_{HE} + B_6u_1^2 + B_7u_2^2 \\ &\quad + B_8u_3^2 + B_9u_4^2 + B_{10}u_5^2. \end{aligned}$$

and

$$\begin{aligned} \mathcal{H} &= B_1E + B_2I + B_3H + B_4A + B_5I_{HE} + B_6u_1^2 + B_7u_2^2 + B_8u_3^2 + B_9u_4^2 + B_{10}u_5^2 + \\ &\quad \lambda_S[\Lambda - d_sS - \Big(\frac{\beta_1\tau I}{N} + \alpha_n E_n\Big)(1-u_1)S - (1-u_2)\Big(\frac{\beta_2\xi(H+A)}{N}\Big)S] + \end{aligned}$$

$$\lambda_E[(1-u_1)\Big(\frac{\beta_1\tau I}{N}+\alpha_n E_n\Big)S-(d+\delta)E]+$$
$$\lambda_I[\delta E-(\pi u_3+d+\psi)I-(1-u_2)\Big(\frac{\beta_2\xi(H+A)}{N}\Big)I]+$$
$$\lambda_R[\pi u_3 I-dR]+\lambda_{E_n}[\theta I-\eta E_n]+\lambda_H[(1-u_2)\Big(\frac{\beta_2\xi(H+A)}{N}\Big)S-(u_4\chi+d+\vartheta)H$$
$$-(1-u_1)\frac{\beta_1\tau IH}{N}+(1-u_5 r)\gamma I_{HE}]+$$
$$\lambda_A[u_4\chi H-(d+\vartheta)A-(1-u_1)\frac{\beta_1\tau IA}{N}+u_5 r\gamma I_{HE}]+$$
$$\lambda_{I_{HE}}[(1-u_1)\frac{\beta_1\tau I(H+A)}{N}+(1-u_2)\Big(\frac{\beta_2\xi(H+A)}{N}\Big)I-dI_{HE}-u_5\gamma I_{HE}], \tag{14}$$

where λ_S, λ_E, λ_I, λ_R, λ_{E_n}, λ_H, λ_A and $\lambda_{I_{HE}}$ represent the adjoint variables. The optimal control problem existing is shown by:

Theorem 6.1. *An optimal control $u^*=(u_1^*,u_2^*,u_3^*,u_5^*,u_5^*)$ exists, with*

$$J(u_1^*,u_2^*,u_3^*,u_4^*,u_5^*)=\min J(u_1,u_2,u_3,u_4,u_5),$$

associated to the control system (11) and with initial condition (2).

Proof. For the proof, we follow the results given in [38–41]. The state variables together with control are non-negative. For problem minimizing, the objective functional (12) with the necessary convexity in $u_1(t)$, $u_2(t)$, $u_3(t)$, $u_4(t)$ and $u_5(t)$ is satisfied. Further, by definition, the set of control variables $u_1,u_2,u_3,u_4,u_5\in\Sigma$ is closed and convex. With bounded optimal solution, it guarantees the optimal control existence. Furthermore, in the objective functional, the integrand given by $B_1E+B_2I+B_3H+B_4A+B_5I_{HE}+B_6u_1^2+B_7u_2^2+B_8u_3^2+B_9u_4^2+B_{10}u_5^2$ is convex on Σ. □

Theorem 6.2. *The given optimal controls u_i^* for $i=1,...,5$ and solutions of S,E,I,R,E_n,H,A and I_{HE} of the associated model (11-12) that minimize $J(u_i)$, for $i=1,...,5$ over Σ. Then, λ_i, for $i=S,E,I,R,E_n,H,A,I_{HE}$ satisfy*

$$\frac{-d\lambda_i}{dt}=\frac{\partial H}{\partial i}, \tag{15}$$

where $i=S,E,I,R,E_n,H,A,I_{HE}$ and the transversality conditions,

$$\lambda_S(t_f)=\lambda_E(t_f)=\lambda_I(t_f)=\lambda_R(t_f)=\lambda_{E_n}(t_f)=\lambda_H(t_f)=\lambda_A(t_f)=\lambda_{I_{HE}}(t_f)=0 \tag{16}$$

and

$$u_1^*=\min\left\{1,\max\left(0,\frac{\lambda_1 S[\lambda_E-\lambda_S]+\frac{\beta_1\tau IA}{N}[\lambda_{I_{HE}}-\lambda_A]+\frac{\beta_1\tau IH}{N}[\lambda_{I_{HE}}-\lambda_H]}{2B_6}\right)\right\}, \tag{17}$$

$$u_2^*=\min\left\{1,\max\left(0,\frac{\lambda_2 S[\lambda_H-\lambda_S]+\lambda_2 I[\lambda_{I_{HE}}-\lambda_I]}{2B_7}\right)\right\}, \tag{18}$$

$$u_3^*=\min\left\{1,\max\left(0,\frac{\pi I[\lambda_I-\lambda_R]}{2B_8}\right)\right\}, \tag{19}$$

$$u_4^*=\min\left\{1,\max\left(0,\frac{\chi H[\lambda_H-\lambda_A]}{2B_9}\right)\right\}, \tag{20}$$

and

$$u_5^* = \min\left\{1, \max\left(0, \frac{r\gamma I_{HE}[\lambda_H - \lambda_A] + \gamma I_{HE}\lambda_{I_{HE}}}{2B_{10}}\right)\right\}. \tag{21}$$

Proof. It follows from [42] that leads to the conditions of an optimal control existence, results of the convexity of the integrand of J with respect to u_1, u_2, u_3, u_4 and u_5, the boundedness of the state variables, the fulfillment of the Lipschitz property of the state variables. We obtain, the adjoint equations by using the Hamiltonian and the optimal control problem in connection with optimal control characterization, and is presented by,

$$\begin{aligned}
\frac{d\lambda_S}{dt} &= (1-u_1)\Big[\beta_1\tau I\Big(\frac{N-S}{N^2}\Big) + \alpha_E E_n\Big](\lambda_S - \lambda_E) + (1-u_2)\beta_2\xi(H+A)\Big(\frac{N-S}{N^2}\Big)\times \\
&\quad (\lambda_S - \lambda_H) + (1-u_2)\beta_2\xi\frac{(H+A)}{N^2}(\lambda_{I_{HE}} - \lambda_I) + \frac{(1-u_1)\beta_1\tau IH}{N^2}(\lambda_{I_{HE}} - \lambda_H) \\
&\quad + \frac{(1-u_1)\beta_1\tau IA}{N^2}(\lambda_{I_{HE}} - \lambda_A) + d_s\lambda_S, \\
\frac{d\lambda_E}{dt} &= \frac{(1-u_1)S\beta_1\tau I}{N^2}(\lambda_E - \lambda_S) + (1-u_2)\beta_2\xi S\frac{(H+A)}{N^2}(\lambda_H - \lambda_S) \\
&\quad + (1-u_1)\frac{\beta_1\tau IH}{N^2}(\lambda_{I_{HE}} - \lambda_H) + (1-u_1)\frac{\beta_1\tau IA}{N^2}(\lambda_{I_{HE}} - \lambda_A) \\
&\quad + (1-u_2)\beta_2\xi I\frac{(H+A)}{N^2}(\lambda_{I_{HE}} - \lambda_I) + d\lambda_E + \delta(\lambda_E - \lambda_I) - B_1, \\
\frac{d\lambda_I}{dt} &= (1-u_1)\beta_1 S\tau\frac{(N-I)}{N^2}(\lambda_S - \lambda_E) + (1-u_2)\frac{\beta_2\xi S(H+A)}{N^2}(\lambda_H - \lambda_S) \\
&\quad + (1-u_2)\beta_2\xi(H+A)\frac{(N-I)}{N^2}(\lambda_I - \lambda_{I_{HE}}) + (1-u_1)\beta_1\tau H\frac{(N-I)}{N^2}(\lambda_H - \lambda_{I_{HE}}) \\
&\quad (1-u_1)\beta_1\tau A\frac{(N-I)}{N^2}(\lambda_A - \lambda_{I_{HE}}) + \lambda_I(\pi u_3 + d + \psi) - \pi u_3\lambda_R - \theta\lambda_{E_n} - B_2, \\
\frac{d\lambda_R}{dt} &= (1-u_1)\frac{\beta_1\tau IS}{N^2}(\lambda_E - \lambda_S) + (1-u_2)\beta_2\xi S\frac{(H+A)}{N^2}(\lambda_H - \lambda_S) \\
&\quad + (1-u_1)\frac{\beta_1\tau IH}{N^2}(\lambda_{I_{HE}} - \lambda_H) + (1-u_1)\frac{\beta_1\tau IA}{N^2}(\lambda_{I_{HE}} - \lambda_A) \\
&\quad + (1-u_2)\beta_2\xi I\frac{(H+A)}{N^2}(\lambda_{I_{HE}} - \lambda_I) + d\lambda_R, \\
\frac{d\lambda_{E_n}}{dt} &= (\lambda_S - \lambda_E)(1-u_1)\alpha_E S + \eta\lambda_{E_n}, \\
\frac{d\lambda_H}{dt} &= (1-u_1)\frac{\beta_1\tau IS}{N^2}(\lambda_E - \lambda_S) + (1-u_2)\beta_2\xi S\frac{(N-(H+A))}{N^2}(\lambda_S - \lambda_H) \\
&\quad + (1-u_2)\frac{\beta_2\xi I(N-(H+A))}{N^2}(\lambda_I - \lambda_{I_{HE}}) + (1-u_1)\frac{\beta_1\tau I(N-H)}{N^2}(\lambda_H - \lambda_{I_{HE}}) \\
&\quad + (1-u_1)\frac{\beta_1\tau IA}{N^2}(\lambda_{I_{HE}} - \lambda_A) + \lambda_H(u_4\chi + d + \vartheta) - \lambda_A u_4\chi - B_3, \\
\frac{d\lambda_A}{dt} &= (1-u_1)\frac{\beta_1\tau IS}{N^2}(\lambda_E - \lambda_S) + (1-u_2)\beta_2\xi\frac{(N-(H+A))}{N^2}(\lambda_S - \lambda_H) \\
&\quad + (1-u_2)\beta_2\xi I\frac{(N-(H+A))}{N^2}(\lambda_I - \lambda_{I_{HE}}) + (1-u_1)\frac{\beta_1\tau I(N-A)}{N^2}(\lambda_A - \lambda_{I_{HE}}) \\
&\quad + (1-u_1)\frac{\beta_1\tau IH}{N^2}(\lambda_{I_{HE}} - \lambda_H) + \lambda_A(d + \vartheta) - B_4,
\end{aligned}$$

$$\begin{aligned}\frac{d\lambda_{I_{HE}}}{dt} &= \frac{(1-u_1)\beta_1\tau IS}{N^2}(\lambda_E-\lambda_S)+(1-u_2)\beta_2\xi S\frac{(H+A)}{N^2}(\lambda_H-\lambda_S)\\ &+(1-u_2)\beta_2\xi I\frac{(H+A)}{N^2}(\lambda_{I_{HE}}-\lambda_H)+\frac{(1-u_1)\beta_1\tau IH}{N^2}(\lambda_{I_{HE}}-\lambda_H)\\ &+\frac{(1-u_1)\beta_1\tau IA}{N^2}(\lambda_{I_{HE}}-\lambda_A)+(\dot{+}u_5\gamma)\lambda_{I_{HE}}-\lambda_H(1-u_5r)\gamma\\ &-\lambda_A u_5 r\gamma - B_5. \end{aligned} \tag{22}$$

To obtain expression for u_i^* for $i = 1, ...5$, subject to the conditions given, we can obtain the optimal control characterization (16-20). So,

$$\frac{\partial\mathcal{H}}{\partial u_1}=\frac{\partial\mathcal{H}}{\partial u_2}=\frac{\partial\mathcal{H}}{\partial u_3}=\frac{\partial\mathcal{H}}{\partial u_4}=\frac{\partial\mathcal{H}}{\partial u_5}=0,$$

and we have the following results:

$$\begin{aligned} u_1^* &= \min\left\{1,\max\left(0,\frac{\lambda_1 S[\lambda_E-\lambda_S]+\frac{\beta_1\tau IA}{N}[\lambda_{I_{HE}}-\lambda_A]+\frac{\beta_1\tau IH}{N}[\lambda_{I_{HE}}-\lambda_H]}{2B_6}\right)\right\},\\ u_2^* &= \min\left\{1,\max\left(0,\frac{\lambda_2 S[\lambda_H-\lambda_S]+\lambda_2 I[\lambda_{I_{HE}}-\lambda_I]}{2B_7}\right)\right\},\\ u_3^* &= \min\left\{1,\max\left(0,\frac{\pi I[\lambda_I-\lambda_R]}{2B_8}\right)\right\},\\ u_4^* &= \min\left\{1,\max\left(0,\frac{\chi H[\lambda_H-\lambda_A]}{2B_9}\right)\right\},\\ u_5^* &= \min\left\{1,\max\left(0,\frac{r\gamma I_{HE}[\lambda_H-\lambda_A]+\gamma I_{HE}\lambda_{I_{HE}}}{2B_{10}}\right)\right\}. \end{aligned} \tag{23}$$

□

7. Numerical simulations

This section describes the numerical simulation of the optimal control model together and without control problem. The optimal control problem varied with u_i for $i = 1, 2, ..., 5$ and make different strategies for the early elimination of disease. The numerical results are obtained by using the numerical technique Runge-Kutta order four backward scheme. The optimal control system together with adjoint equations as well as the optimal control characterization and the system without control are solved numerically and presented the graphical results with different control strategies. The time level is chosen in unit of 200 days. The optimal control model and control characterization are obtained. In Table 1, we gave the parameters' values used in the numerical solution. The other parameters, we consider in the numerical simulation are given by $B_1 = 20$, $B_2 = 28$, $B_3 = 10$, $B_4 = 69$, $B_5 = 2$ and $B_6 = 20$, $B_7 = 40$, $B_8 = 11$, $B_9 = 10$, $B_{10} = 10$. The parameters considered in numerical simulation of the optimal control problem are given in Table 1. In the simulations, we represent the control and without control system by dashed line and solid line respectively.

Parameter	Description	value	Ref
Λ	Birth rate	0.05 day^{-1}	[35]
d	Natural death rate in each class	0.000039 day^{-1}	[36]
ψ	Disease related death rate due to Hepatitis E	0.00095 day^{-1}	Assumed
α_E	Prob. of infection through environment	0.005 day^{-1}	Assumed
δ	Progression of infection from Hepatitis E	0.08 day^{-1}	Assumed
β_1	Hepatitis E transmission probability rate	0.05day^{-1}	Assumed
θ	Hepatitis E infected contribution to the environment	0.7 day^{-1}	Assumed
τ	Hepatitis contact rate	0.123 day^{-1}	Assumed
ξ	HIV contact rate	0.025 day^{-1}	[21]
β_2	HIV infection transmission probability rate	0.05 day^{-1}	[35]
χ	Rate of progression to AIDS stage	0.000548 day^{-1}	[35]
π	Recovery rate from Hepatitis E	0.0238-0.1429 day^{-1}	[43]
η	Microbes mortality rate	0.033 day^{-1}	Assumed
ϑ	HIV/AIDS related death	0.00913 day^{-1}	[21]
r	Rate of co-infected humans	0.08 day^{-1}	[21]
γ	Modification parameter	0.08 day^{-1}	[21]

Table 1: Parameters and variables used in simulation.

7.1. Strategy 1

In this strategy, we activate the control variables $u_1 = u_4 \neq 0$ and the rest of the three control variables are set to be zero and optimize the objective functional given in (12). We obtained the graphical results for this strategy given in Figure 1 with subgraphs (a-f). The number of infected individuals with Hepatitis E only, with HIV-AIDS only and the co-infected individuals decrease. The Hepatitis E exposed and infected individuals decrease well in Figure 1(a-b) for the control system. The viral load in the environment given in Figure 1(c) for the control system decreases after day 100. The HIV infected individuals only (see Figure 1(d)) decrease after day 150. The AIDS infected individuals only (see Figure 1(e)) and the co-infected individuals (see Figure 1(f)) decrease respectively after days 20 and 30. This strategy is useful for the infection elimination of Hepatitis E exposed individuals only, infected with Hepatitis E only, AIDS infected only and co-infected only.

7.2. Strategy 2

In this strategy, we activate the control variables $u_2 = u_4 \neq 0$ and the rest of the three control variables are set to be zero and optimize the objective functional given in (12). We obtained the graphical results for this strategy given in Figure 2 with subgraphs (a-f). In Figure 2 subgraphs (a-b), the number of exposed and infected individuals due to only Hepatitis E decreases the same as in Strategy 1. The viral load in the environment after day 100 decreases, see Figure 2(c). The individuals infected due to HIV infection only increase, see Figure 2(d), comparing to the Strategy 1, which is not suitable for the minimization of infection only HIV individuals but for the case of only AIDS infected individual. There can be seen a decrease after day 20, see Figure 2(e). Further, in Figure 2(f), the co-infected individuals decrease little.

7.3. Strategy 3

In this strategy, we activate the control variables $u_1 = u_2 \neq 0$ and set the rest of the three control inactive and optimize the objective functional given in (12). We obtained the graphical results for this strategy given in Figure 3 with subgraphs (a-f). In Figure 3 subgraphs (a-b), the number of exposed and infected individuals due to only Hepatitis E decreases. The viral load in the environment after day 100 decreases, see Figure 3(c). Comparing to the Strategy 2, the same effect of only HIV infected individuals are observed, see Figure 3(d). Further, the only AIDS infected individuals decrease after day 20 and the co-infected individuals increase. It can be seen from these three strategies, the strategies 2 and 3 are not much suitable for the minimization of HIV and co-infected individuals but can be useful up to some extent for the minimization of exposed due to Hepatitis E only, infected due to only Hepatitis E and infected due to only AIDS.

7.4. Strategy 4

In this strategy, we activate the control variables $u_3 = u_4 \neq 0$ and set the rest of the three controls inactive and optimize the objective functional given in (12). We obtained the graphical results for this strategy given in Figure 4 with subgraphs (a-f). In Figure 4 subgraphs (a-b), the results are almost the same that is observed for the exposed and infected individuals due to only Hepatitis E in Strategies 1, 2 and 3. The viral load in the environment after day 100 decreases, see Figure 4(c), the same like Strategies 1, 2 and 3. The same effect on only HIV infected individuals and the co-infected individuals is observed, that is the increase in the individuals of the HIV infected only and the co-infected individuals like Strategies 2 and 3, see Figure 4(d-f). The number of only AIDS infected individuals decreases after day 20, which is considered effective strategies for this. It can be seen from these three strategies, the Strategies 2, 3 and 4 are not much suitable for the minimization of HIV and co-infected individuals but can be useful up to some extent for the minimization of exposed due to only Hepatitis E, infected due to only Hepatitis E and infected due to only AIDS but not suitable for the other classes of individuals.

7.5. Strategy 5

It can bee seen in the above mentioned strategies with different sets of controls that there is a possible minimization of the infection in Hepatitis E, HIV and their co-infection. A combination of different set of controls is used to optimize the objective functional. In each of these strategies discussed above, it may or may not give the useful results that are required. But here, we activate all the available controls and optimize the objective functional J. The corresponding results associated to this strategy are depicted in Figure 5 with subgraphs (a-f). One can observe that this strategy is useful for the minimization of all the infected and exposed due to only Hepatitis E, infected due to HIV-AIDS only and at the same time the viral load in the environment. A significant decrease can bee seen in Hepatitis E exposed and infected individuals only as shown in Figure 5(a-b), and viral load in the environment Figure 5(c), HIV-AIDS and co-infected individuals Figure 5(d-f). Thus, we conclude that the Strategy 5, could be the best strategy for the minimization of infected individuals due to Hepatitis E, HIV-AIDS and co-infected individuals.

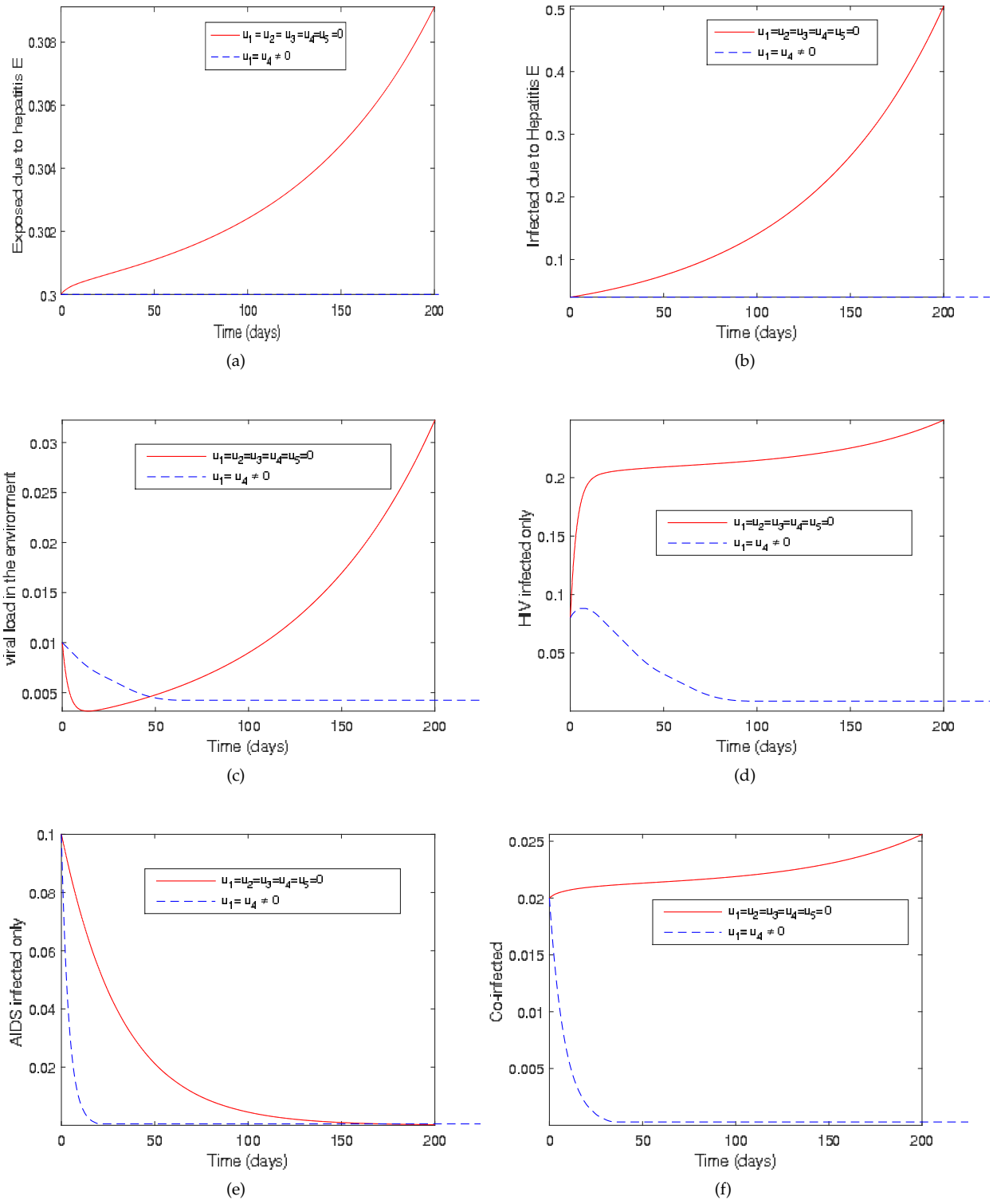

Figure 1: The plot shows the combination of the controls $u_1 = u_4 \neq 0$.

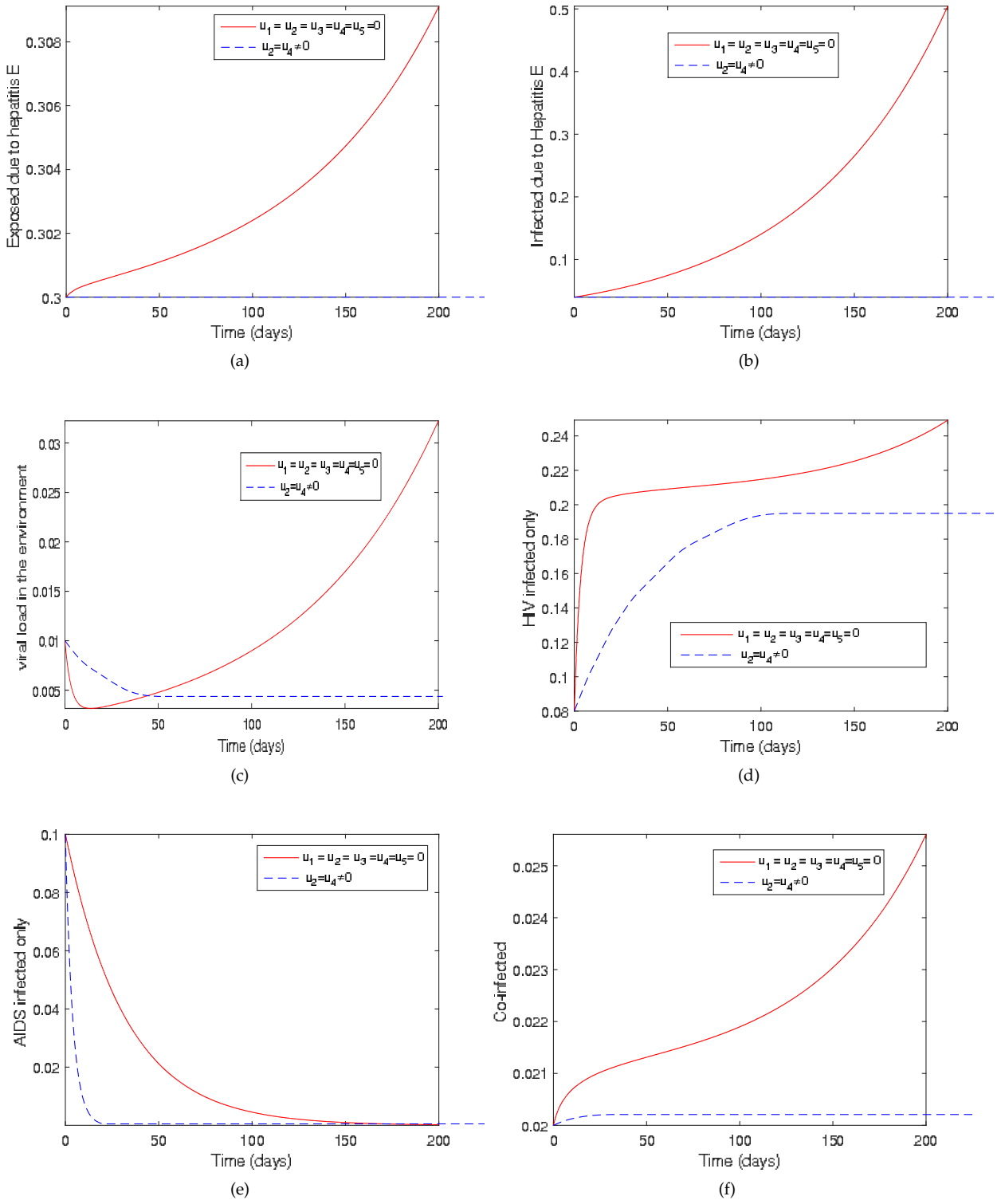

Figure 2: The plot shows the combination of the controls $u_2 = u_4 \neq 0$.

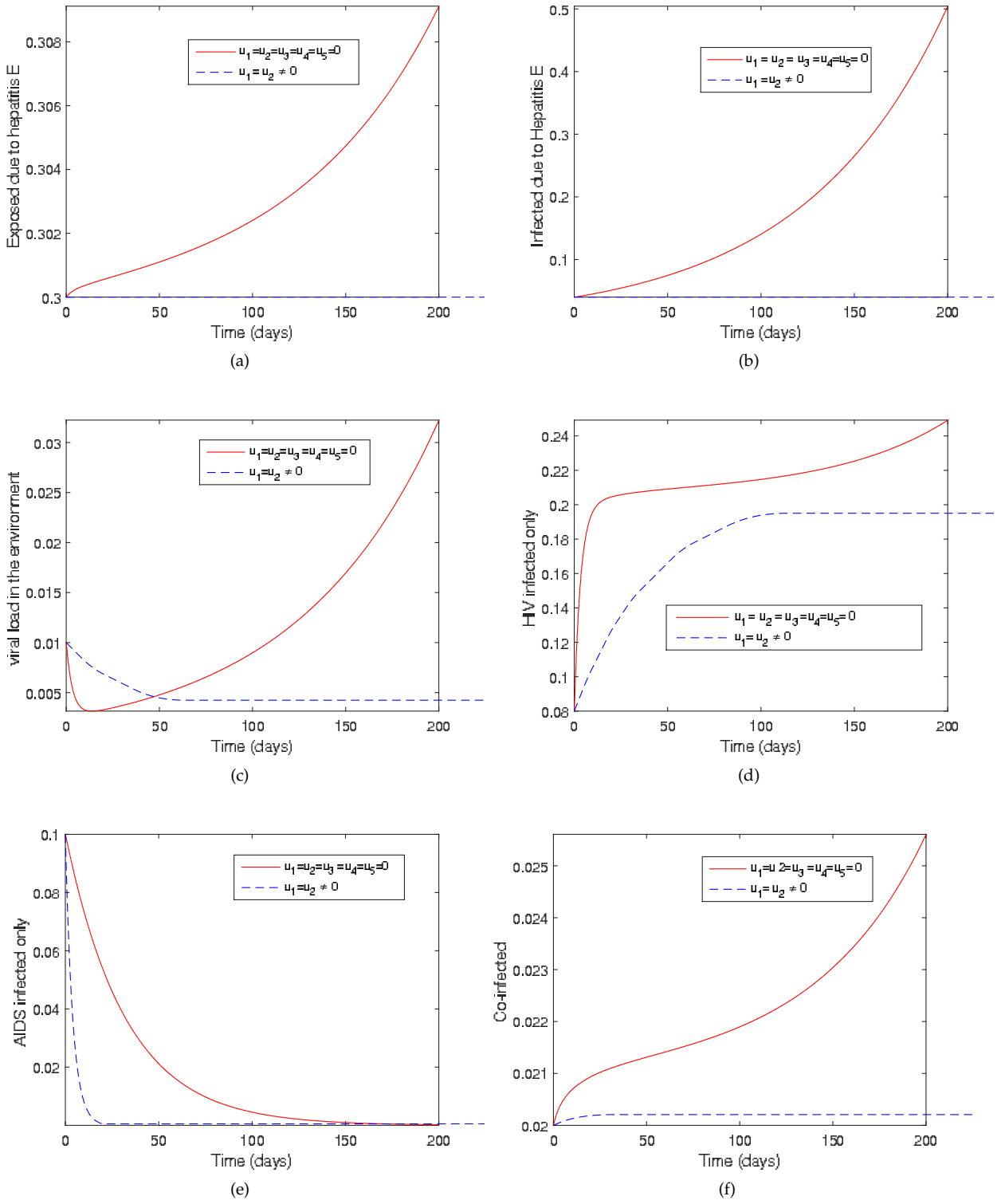

Figure 3: The plot shows the combination of the controls $u_1 = u_2 \neq 0$.

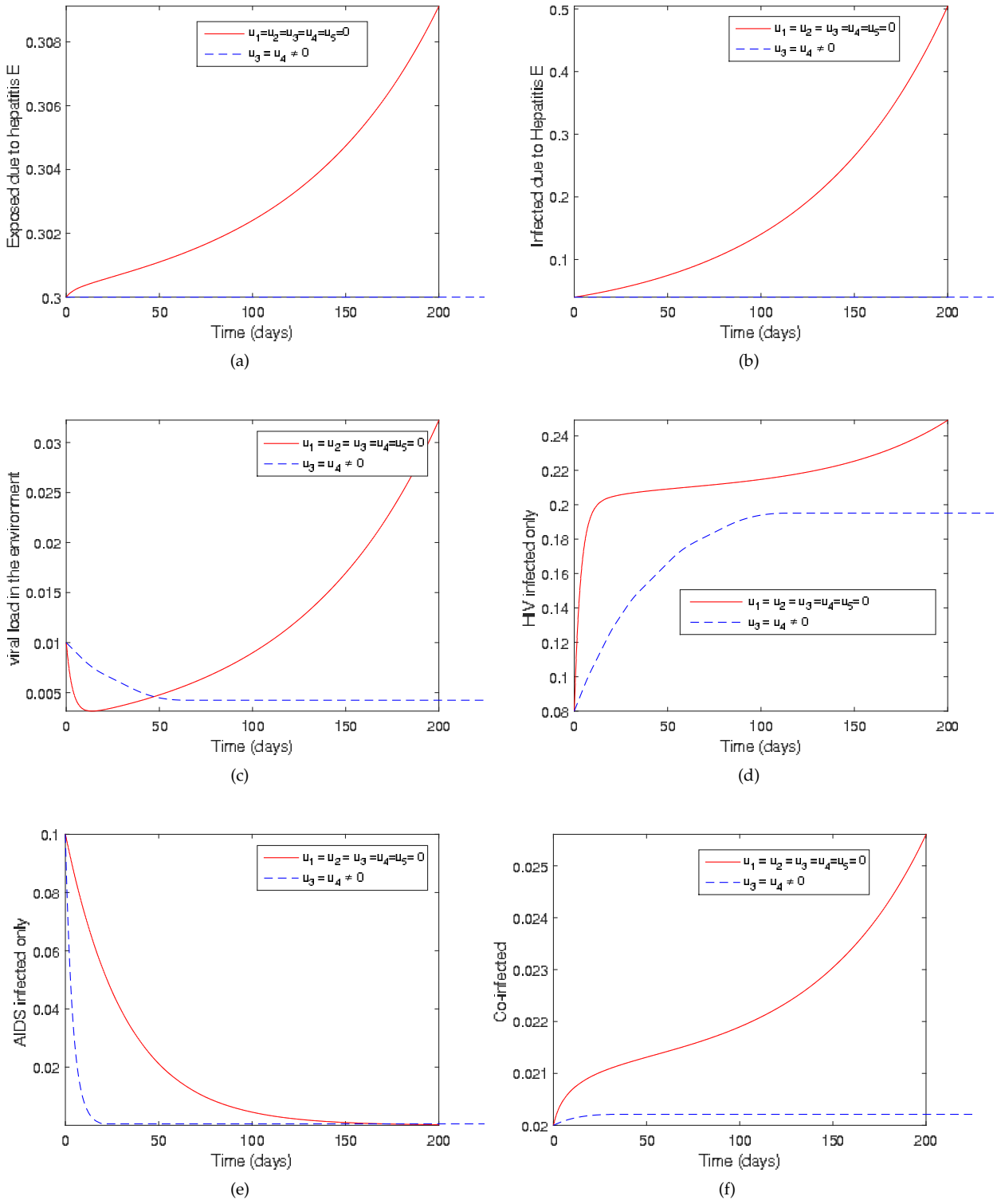

Figure 4: The plot shows the combination of the controls $u_3 = u_4 \neq 0$.

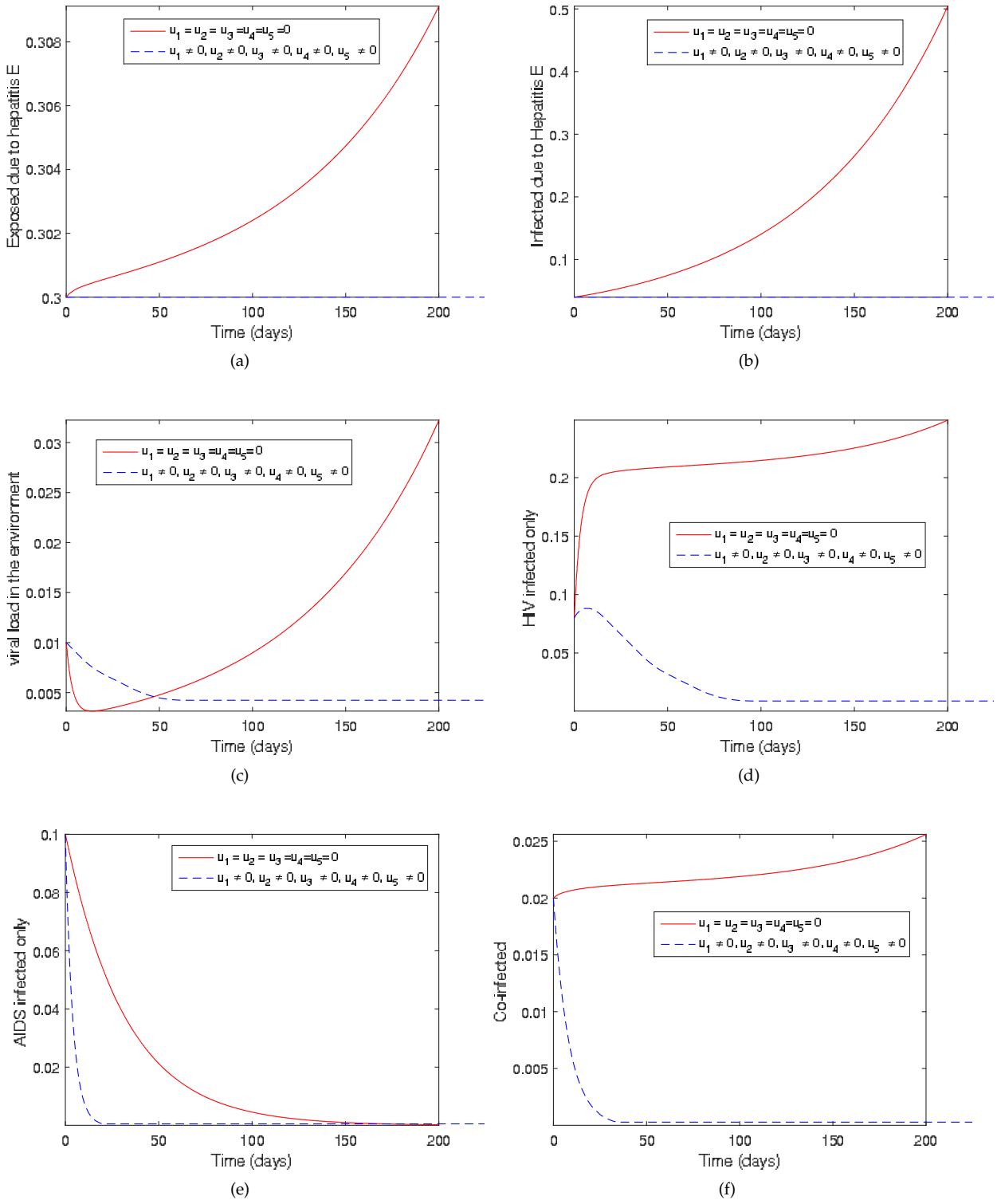

Figure 5: The plot shows the combination of the controls $u_i \neq 0$ for $i = 1, 2, ...5$.

8. Conclusion

We presented a co-infection model on the dynamics of Hepatitis E and HIV/AIDS. The mathematical results for each model are investigated on the basis of basic reproduction number. The only Hepatitis E model is found to locally stable as well as globally. Further, we investigated the dynamics of the only HIV model. The only HIV model is locally asymptotically stable. Then, we showed that the co-infection model of Hepatitis E and HIV/AIDS model is locally asymptotically stable. We also showed the bifurcation analysis of the co-infection model. Further, we formulated the optimal control problems with five control variables. Different combinations of controls are considered for the possible elimination of the disease from the community. We presented a set of control combinations and optimized the objective functional and the results for each strategy are presented in detail. We observed that the Strategies 1 to 4 are useful for exposed due to Hepatitis E, infected due to Hepatitis E, for the viral load in the environment and the AIDS infected individuals but not suitable for the HIV infected only and the co-infected individuals. It must be noted that the Strategies 1 to 4 are obtained through the specific set of controls combinations for the possible eliminations of infection with less cost controls. From the first four strategies, it was observed that for some compartments of HIV and co-infected individuals we did not obtain the useful results, so, we utilized the Strategy 5, with activating all the controls. We observed reasonable results for each compartment and found it more useful than the previous ones. The numerical results suggest that the disease can be eliminated from the community if proper supply of clean water, reduction in the cases of pregnant women, early diagnose of HIV/AIDS patients and their treatment and the precautions are considered. The main routes from which HIV/AIDS spread vaginal fluids, blood, semen, and the breast milk, and it should be preventable by avoiding these. Also, using condoms and avoiding share of needles with others also decrease the chances of getting infection. The infected individuals due to HIV/AIDS should be treated by the HIV medicine that is Antiretroviral Therapy (ART). Therefore, it is recommended that the HIV and HEV infected patients should be properly treated and make them aware of possible prevention from these diseases. The educational and media campaign could be more useful for possible elimination of the disease burden in the community. The health authorities and the public health department should focus on such issue to get rid of these two dangerous diseases. Thus, the role of health authorities and other agencies can play the best role in the disease elimination of HEV and HIV. In future, we will work on the HEV and HIV co-dynamics with media coverage and educational campaign for possible elimination of the HEV and HIV co-infection.

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References

[1] H. R. Dalton, R. Bendall, S. Ijaz, M. Banks, Hepatitis E: an emerging infection in developed countries, *Lancet. Infect. Dis.* 8 (2008), 698-709.
[2] S. Ijaz, E. Arnold E, M. Banks M et al., Non-travel-associated Hepatitis E in England and Wales: demographic, clinical, and molecular epidemiological characteristics, *J.Infect. Dis.* 192 (2005), 1166-1172.
[3] S. Ijaz, A. J. Vyse, D. Morgan, R. G. Pebody, R. S. Tedder, D. Brown, Indigenous Hepatitis E virus infection in England: more common than it seems, *J. Clin. Virol.* 44 (2009), 272-276.
[4] J. M. Mansuy, J. M. Peron, F. Abravanel et al., Hepatitis E in the south west of France in individuals who have never visited an endemic area, *J. Med. Virol.* 74 (2004), 419-424.
[5] M. A. Widdowson, W. J. Jaspers, W. H. Poel et al, Cluster of cases of acute Hepatitis associated with Hepatitis E virus infection acquired in the Netherlands, *Clin. Infect. Dis.* 36 (2003), 29-33.
[6] N. Kamar, J. Selves J, Mansuy, et al., Hepatitis E virus and chronic Hepatitis in organ-transplant recipients, *N. Engl. J. Med.* 358 (2008), 811-817.
[7] A. Tamura, Y. K. Shimizu, T. Tanaka et al., Persistent infection of Hepatitis E virus transmitted by blood transfusion in a patient with T-cell lymphoma, *Hepatol. Res.* 37 (2007), 113-120.

[8] H. R. Dalton, R. P. Bendall, F. E. Keane, R. S. Tedder, S. Ijaz, Persistent carriage of Hepatitis E virus in patients with HIV infection, *N. Engl. J. Med.* 361 (2009), 1025-1027.
[9] P. Colson, M. Kaba, J. Moreau, P. Brouqui, Hepatitis E in an HIV-infected patient, *J. Clin. Virol.* 45 (2009), 269-271.
[10] F. Nancy, Crum-Cianflone et al., Hepatitis E Virus Infection in HIV-infected Persons, *Emer. Infec. Dis.* 18(3) (2012, 502-506.
[11] G. Scotto, et al., Hepatitis E virus co-infection in HIV-infected patients in Foggia and Naples in southern Italy, *Infec. Dis.* 47(10), 711-717. DOI: 10.3109/23744235.2015.1049658
[12] H. R. Dalton, et al., Autochthonous Hepatitis E in Developed Countries and HEV/HIV Co-infection, *Semin. Liver. Dis.* 33 (2013), 50-61.
[13] H. Joulaei, et al., Hepatitis E virus seroprevalence in HIV positive individuals in Shiraz, Southern Iran, *Iran. J. Microbiol.* 7(2) (2015), 103108.
[14] Gbenga J. A , Nizar M, Witbooi P.J, Okosun K.O. A model for control of HIV/AIDS with parental care, *Int. Jour. of Biomatg.* 6 (2013), (2013) 1350006 (15 pages).
[15] UN, UNAIDS, World Health Organization, 2011 AIDS epidemic update avail- able, http://news.yahoo.com/s/afp/20110603/hl afp/healthaidsanniversary-unaids 20110603181329 (November 2011).
[16] R. M. S. Costa, P. Pavone, Invasive plants and natural habitats: The role of alien species in the urban vegetation, *Acta. Hortic.* 1215 (2018), 57-60.
[17] R.M.S. Costa, P. Pavone, Diachronic biodiversity analysis of a metropolitan area in the Mediterranean region, *Acta. Hortic.* 1215 (2018), 49-52.
[18] M. Behjaty, Z. Monfared, Modeling and dynamic behavior of a discontinuous tourism-based social-ecological dynamical system, *Filomat*, (2019) 33(18), 5991- 6004.
[19] Luo, D., The study of global stability of a diffusive michaelis-menten and tanner predator-prey model, *Filomat*, 33(17), 5651-5659.
[20] K. O. Okosun ,O.D. Makinde, A co-infection model of malaria and cholera diseases with optimal control, *Math. Biosci.* 258 (2014), 19-32.
[21] K. O. Okosun, M. A. Khan, E. Bonyah, et al. On the dynamics of HIV-AIDS and cryptosporidiosis, *Eur. Phys. J. Plus.* 132 (2017) 363. https://doi.org/10.1140/epjp/i2017-11625-3.
[22] H. Joshi, S. Lenhart, K. Albright, K. Gipson, Modelling the effect of information campaigns on the HIV epidemic in Uganda, *Math. Biosci. Eng.* 5 (2008), 33
[23] F. Nyabadza, A Mathematical model for combating HIV/AIDS in Southern Africa, *J. Biol. Sys.* 14 (2006), 357-372.
[24] D. L. Higgins , C. Galavotti, K. R. Reilly, Evidence for the effects of HIV antibody counselling and testing on risk behaviors, *J. Amer. Med. Assoc.* 266 (1991), 2419-2429.
[25] S. Mushayabasa, C. P. Bhunu, Modeling Schistosomiasis and HIV/AIDS co- dynamics, *Comp. Mathematical Methods. Medic.*, 2011 (2011), 1-15. doi:10:1155/2011/846174.
[26] S. Mushayabasa, C.P. Bhunu, N. A. Mhlanga, Modeling the Transmission Dynamics of Typhoid in Malaria Endemic Settings, *Applic. Appl. Math.: An Inter. Jour.* 9(1) (2014), 121-140.
[27] C. P. Bhunu, S. Mushayabasa, H. Kojouharov and J. M. Tchuenche, Mathematical analysis of an HIV/AIDS model: Impact of educational programs and abstinence in sub-Saharan Africa, *J. Math. Model. Algor.* 10(1) (2011) 3155.
[28] J. R. Andrews, N. S. Shah, D. Weissman, et al., Predictors of multidrug- and extensively drug-resistant tuberculosis in a high HIV prevalence community, *PLoS ONE*, 5 (12) (2010) e15735.
[29] D. Kirschner, Dynamics of co-infection with M. tuberculosis and HIV-1, *Theor. Pop. Biol.* 55 (1999), 94-109.
[30] S. Ramkissoon, H. G. Mwambi, A. P. Matthews, Modelling HIV and MTB co-infection including combined treatment strategies, *PLoS. ONE.* 7 (11) (2012), e49492.
[31] W. L. Roeger, Z. Feng, Z., C. Castillo-Chavez, Modeling TB and HIV co- infections, *Math. Biosci. Eng.* 6, (2009) 815-837.
[32] O. Sharomi, C. Podder, A. B. Gumel, Mathematical analysis of the transmis- sion dynamics of HIV/TB co-infection in the presence of treatment, *Math. Biosci. Eng.* 5 (2008), 145-174.
[33] S. Shenoi, S. Heysell, A. Moll, G. Friedland, Multidrug-resistant and exten- sively drug-resistant tuberculosis: consequences for the global HIV community, *Curr. Opin.Infect. Dis.* 22(1) (2009), 11-17. http://dx.doi.org/10.1097/QCO.0b013e3283210020.
[34] E. O. Alzahrani, and M. A. Khan. Modeling the dynamics of Hepatitis E with optimal control, *Chaos, Sol. & Frac.* 116 (2018): 287-301.
[35] Z. Mukandavire, A. B. Gumel, W. G. Jean, M. Tchuenche, Mathematical analysis of a model for HIV malaria co-infection, *Math. Bio-sciand Eng.* 6, (2009) 333-362.
[36] C. Bowman, A. B. Gumel, P. van den Driessche, J. Wu and H. Zhu, A mathematical model for assessing control strategies against West Nile virus, *Bull. Math. Biol.*, 67 (2005), 1107-1133.
[37] P. V. D. Driessche and J. Watmough, Reproduction number and sub-threshold endemic equilibria for compartmental models of disease transmission, *Math. Bios.*, 180 (2002), 2948.
[38] M. A. Khan, S. Islam, G. Zaman, Media coverage campaign in Hepatitis B transmission model, *Appl. Math. Comp.* 331 (2018), 378-393.
[39] MA Khan, R Khan, Y Khan, S Islam, A mathematical analysis of Pine Wilt disease with variable population size and optimal control strategies, *Chao. Sol. & Frac.* 108 (2019), 205-217.
[40] M. A. Khan, S. Islam, J. C. Valverde, S. A. Khan, Control strategies of Hepatitis B with three control variables,*Journal of Biological Systems*, 26 (2018), 1-21.
[41] M. A. Khan, Y. Khan, S. Islam, Complex dynamics of an SEIR epidemic model with saturated incidence rate and treatment, 'emphPhysica A: Statistical Mechanics and its Applications 493, (2018), 210-227.
[42] W. H. Fleming, R. W. Rishel, Deterministic and stochastic optimal control, *Springer Verlag*, New York (1975).
[43] B. Sumpter, J. Y. T. Mugisha, L. S. Luboobi, The Dynamics, Causes and Possible Prevention of Hepatitis E Outbreaks, *PLoS ONE*, 7(7) (2012): e41135. https://doi.org/10.1371/journal.pone.0041135,