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Impact of Case Detection and Treatment on the Spread of HIV/AIDS: a Mathematical Study

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ABSTRACT

Here a simple mathematical model for HIV/AIDS with standard incidence is formulated and analyzed. It is assumed that only a fraction of total HIV and AIDS infected are detected. So only this fraction of infectives are subjected to proper counseling and are not taking part in the hetero-sexual transmission of HIV/AIDS. The model is first analyzed by considering the case detection parameters as constants. The basic reproduction number R_0 of the model is computed and its relation with the existence and stability of different equilibria of the model is investigated. It is found that the disease-free equilibrium of the model is locally and globally asymptotically stable for $R_0 < 1$. When $R_0 > 1$, the endemic equilibrium exists and is locally and globally asymptotically stable under some restriction on parameters. Next the optimal control problem is formulated by considering case detection parameters as time dependent. This problem is analyzed using Pontryagin's maximum principle. Numerical simulation is performed to show the impact of optimal control and it is found that optimal control strategy gives a better result.

Keywords: HIV/AIDS, mathematical model, stability, optimal control.

1. Introduction

Although, more than 35 years have passed since the first HIV case was identified in USA, still there is no cure for this disease. As per the Global Health Observatory (GHO) data, an estimated 0.8% of the adult population of world aged between 15 to 49 years are living with HIV. However the burden of this epidemic varies considerably between countries and regions. The sub-saharan Africa is badly affected followed by Americas, South-East Asia, Europe, Eastern Mediterranean, Pacific countries WHO (2015).

It is an established fact that mathematical modeling helps in control and prediction of an infectious disease. Although, there exist many mathematical models which describes the transmission dynamics of HIV/AIDS, but because the dynamics of HIV varies from one region to another depending upon infection prevalence, social and cultural environments, etc., the existing models do have limitations in applicability of their results and selection of model parameters. At present, different types of incidence functions are being used to model different scenarios and the importance of different types of incidence functions for HIV models is discussed in Cai et al. (2014), Sharomi et al. (2007). Here in Sharomi et al. (2007), the vaccine-induced backward bifurcation is demonstrated and in Cai et al. (2014) the resulting incidence term incorporates both the bilinear and the standard incidence.

In the Athithan and Ghosh (2015), we have presented the simple mass action model for HIV which is applicable for the region where HIV prevalence is very high. Now, here in this paper, we are going to present an HIV model with standard incidence which is suitable for the region where infection prevalence of HIV/AIDS is moderate to low. The HIV/AIDS models with standard incidence have been formulated and analyzed by some researchers (See Cremin et al. (2013), Lima et al. (2008), Naresh et al. (2006), Nyabadza and Mukandavire (2011), Sharomi et al. (2008)) but not much emphasis has been given to case detection and screening and HIV models which incorporate screening of infectives followed a different modelling approach.

In this paper, first a simple mathematical model for HIV with standard incidence is formulated and analyzed by considering a constant rate of case detection. Later, an optimal control problem is formulated and analyzed by considering the case detection parameter as the control parameter.

This paper is organized as follows: Section 2 describes the basic model and its formulation, Section 3 exhibits the existence of equilibria and stability analysis with subsections as Basic Reproduction Number R_0, Existence of Equilibria and Jacobian, Local Stability of Disease Free Equilibrium (DFE), Local Stability of Endemic Equilibrium (EE) and Global Stability of DFE. In Section 3.5, we present numerical computations to support our analytical findings. Section 4 deals with the optimal control problem which contains the optimal control model with subsections as Hamiltonian and Adjoint Equations, and Optimal Control Theorems. Section 5 explores the numerical simulation for the optimal control model and finally the results of our model are discussed in detail in Section 6.

2. Model Formulation

The disease HIV/AIDS caused mainly by sexual transmission, so our population under consideration is only the adult population. We first divide the whole adult population into three disjoint compartments: $S(t), I_1(t)$ and $I_2(t)$ with $N(t) = S(t) + I_1(t) + I_2(t)$ as total population. Here $S(t), I_1(t)$ and $I_2(t)$ denote the susceptible individuals, the HIV infectious individuals and the AIDS infected individuals, respectively, at time t. The total population is assumed to be variable and homogeneously mixed *i.e.,* all are equally likely to acquire infection by the infectious individuals in case they come into contact. The fraction of total HIV and AIDS infectives who are detected are given by η and ν respectively. Further it is assumed that the rate of transmission of HIV due to detected group of infected individuals will be less compared to rate of transmission due to undetected group of infected individuals. Let τ be the rate of treatment in HIV class. By these assumptions the individuals who are either undetected or untreated will progress to AIDS class fast compared to those HIV infectives who are opting for treatment.

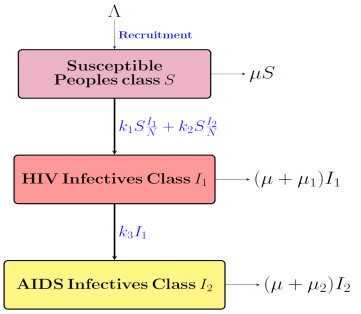

Figure 1: Transfer diagram of the model (1)

The transfer diagram of our proposed model is presented in Fig. 1. Based on above assumptions, we formulate our mathematical model as follows:

$$\begin{aligned} \frac{dS}{dt} &= \Lambda - \mu S - \left(k_1 \frac{I_1}{N} + k_2 \frac{I_2}{N}\right) S, \\ \frac{dI_1}{dt} &= \left(k_1 \frac{I_1}{N} + k_2 \frac{I_2}{N}\right) S - (\mu + \mu_1) I_1 - k_3 I_1, \\ \frac{dI_2}{dt} &= k_3 I_1 - (\mu + \mu_2) I_2, \end{aligned} \tag{1}$$

where $k_1 = \alpha_1[\eta + \psi_1(1-\eta)]$, $k_2 = \alpha_2[\nu + \psi_2(1-\nu)]$ and $k_3 = \sigma_1\tau\eta + \sigma_2[(1-\tau)\eta + (1-\eta)]$

The parameters used in the model (1) are described in Table 1.

Table 1: Description of parameters

Parameter	Description
Λ	Recruitment rate
μ	Natural death rate
η	Fraction of total HIV infectives, who are detected
ν	Fraction of total individuals with AIDS, who are detected
α_1	Rate of transmission(in HIV class)
α_2	Rate of transmission(in AIDS class)
$\psi_1,\ \psi_2$	Modification parameters
τ	Rate of treatment
σ_1	Rate of progression to AIDS(detected & treated)
σ_2	Rate of progression to AIDS(undetected & untreated)
μ_1	Death rate due to HIV infection
μ_2	Death rate due to AIDS

As $N(t) = S(t) + I_1(t) + I_2(t)$, for the analysis purpose we consider the following system:

$$\begin{aligned} \frac{dN}{dt} &= \Lambda - \mu N - \mu_1 I_1 - \mu_2 I_2, \\ \frac{dI_1}{dt} &= \left(k_1 \frac{I_1}{N} + k_2 \frac{I_2}{N}\right) S - (\mu + \mu_1) I_1 - k_3 I_1, \\ \frac{dI_2}{dt} &= k_3 I_1 - (\mu + \mu_2) I_2, \end{aligned} \tag{2}$$

Here $S \geq 0, I_1 \geq 0, I_2 \geq 0$. Model systems (1) and (2) are involving human population, hence all the variables and parameters of the proposed model are

positive. The region of attraction of the model is given by

$$\Omega = \left\{ (S, I_1, I_2) \in R_+^3 : S + I_1 + I_2 = N \leq \frac{\Lambda}{\mu} \right\}.$$

We now show the positive invariance of Ω. We have $N(t) = S(t) + I_1(t) + I_2(t)$. The rate of change of the total population under consideration is given by adding all the equations in the (1) and is given by:

$$\frac{dN}{dt} = \Lambda - \mu N - \mu_1 I_1 - \mu_2 I_2$$

Clearly whenever $N > \frac{\Lambda}{\mu}$, $\frac{dN}{dt} < 0$. Note that $\frac{dN}{dt}$ is bounded by $\Lambda - \mu N$. By using standard comparison theorem Lakshmikantham et al. (1989) it can be shown that $0 \leq N(t) \leq \frac{\Lambda}{\mu}(1 - e^{-\mu t}) + N(0)e^{-\mu t}$. In particular, $N(t) \leq \frac{\Lambda}{\mu}$ if $N(0) \leq \frac{\Lambda}{\mu}$. Hence, the region $\Omega = \left\{ (S, I_1, I_2) \in R_+^3 : N \leq \frac{\Lambda}{\mu} \right\}$ is positively invariant for the system (2).

Now we prove that all the variables of the model (1) are non-negative. This confirms that the solution of the system with positive initial conditions remains positive for all $t > 0$. The fact is described in the following lemma.

Lemma 2.1. *If $S(0) \geq 0,\ I_1(0) \geq 0,\ I_2(0) \geq 0$, the solutions $S(t), I_1(t)$ and $I_2(t)$ of the system (1) are positive for all $t > 0$.*

Proof. Assume that $N(t) \neq 0\ \forall\ t > 0$. We prove this lemma by using a contradiction.
We assume that there exists a first time t_1 such that:

$$S(t_1) = 0,\ \frac{dS}{dt}(t_1) < 0,\ I_1(t) \geq 0,\ I_2(t) \geq 0,\ 0 \leq t \leq t_1 \tag{3}$$

there exists a first time t_2 such that:

$$I_1(t_2) = 0,\ \frac{dI_1}{dt}(t_2) < 0,\ S(t) \geq 0,\ I_2(t) \geq 0,\ 0 \leq t \leq t_2 \tag{4}$$

there exists a first time t_3 such that:

$$I_2(t_3) = 0,\ \frac{dI_2}{dt}(t_3) < 0,\ S(t) \geq 0,\ I_1(t) \geq 0,\ 0 \leq t \leq t_3 \tag{5}$$

From (3) $\frac{dS}{dt}(t_1) = \Lambda > 0$, which is a contradiction to our assumption $\frac{dS}{dt}(t_1) < 0$ and meaning that $\frac{dS}{dt}(t) \geq 0,\ t \geq 0$.
From (4) $\frac{dI_1}{dt}(t_2) = k_2 \frac{I_2(t_2)S(t_2)}{N(t_2)} = k_2 \frac{I_2(t_2)S(t_2)}{S(t_2)+I_2(t_2)} > 0$ and not negative, which is again a contradiction to our assumption $\frac{dI_1}{dt}(t_2) < 0$ and meaning that $\frac{dI_1}{dt}(t) \geq 0,\ t \geq 0$.
From (5) $\frac{dI_2}{dt}(t_3) = k_3 I_1(t_3) > 0$ which is again a contradiction to our assumption $\frac{dI_2}{dt}(t_3) < 0$ and meaning that $\frac{dI_2}{dt}(t) \geq 0,\ t \geq 0$.

Hence we conclude that $I_2(t) \geq 0$ for $t \geq 0$. Thus the solutions $S(t), I_1(t), I_2(t)$ of the system (1) remain positive for all $t > 0$. □

3. Equilibria and Stability Analysis

3.1 Basic Reproduction Number R_0

The basic reproduction number is defined as the average number of secondary cases generated by an infected individual in his/her whole infectious period in a fully susceptible population. We follow the method described in Driessche and Watmough (2002) and compute the basic reproduction number (R_0). Using the same notation as in Driessche and Watmough (2002) the matrices $\mathcal{F}$ and $\mathcal{V}$ are given by

$$\mathcal{F} = \begin{pmatrix} \left(k_1 \frac{I_1}{N} + k_2 \frac{I_2}{N}\right)(N - I_1 - I_2) \\ 0 \end{pmatrix}, \qquad \mathcal{V} = \begin{pmatrix} (\mu + \mu_1 + k_3) I_1 \\ -k_3 I_1 + (\mu + \mu_2) I_2 \end{pmatrix}.$$

Now, the matrices F and V evaluated at disease-free equilibrium point are given by

$$F = \begin{pmatrix} k_1 & k_2 \\ 0 & 0 \end{pmatrix}, \qquad V = \begin{pmatrix} \mu + \mu_1 + k_3 & 0 \\ -k_3 & \mu + \mu_2 \end{pmatrix}.$$

The Next Generation matrix FV^{-1} is given by

$$FV^{-1} = \begin{pmatrix} \left[\frac{k_1}{(\mu+\mu_1+k_3)} + \frac{k_2 k_3}{(\mu+\mu_2)(\mu+\mu_1+k_3)}\right] & \frac{k_2}{(\mu+\mu_2)} \\ 0 & 0 \end{pmatrix}.$$

So, the reproduction number R_0 which is the spectral radius of the matrix FV^{-1} is given by

$$R_0 = \frac{k_1}{(\mu + \mu_1 + k_3)} + \frac{k_2 k_3}{(\mu + \mu_2)(\mu + \mu_1 + k_3)}$$

The reproduction number R_0 gives the average number of infected humans generated by one typical infected human in a fully susceptible population.

3.2 Existence of Equilibria and Jacobian

The equilibria for our model are determined by setting right hand side of the model (2) to zero. The system (2) has the following equilibria namely Disease Free Equilibrium (DFE) $E_1\left(N^0, I_1^0, I_2^0\right) = \left(\frac{\Lambda}{\mu}, 0, 0\right)$ and Endemic Equilibrium (EE) $E_2\left(N^*, I_1^*, I_2^*\right)$, where

$$N^* = \frac{\Lambda - \mu_1 I_1^* - \mu_2 I_2^*}{\mu}, \qquad I_2^* = \left(\frac{k_3}{\mu + \mu_2}\right) I_1^* = k_4 I_1^*$$

and I_1^* is given by

$$\begin{aligned} I_1^* &= \frac{\Lambda\left[(k_1 + k_2k_4) - (\mu + \mu_1 + k_3)\right]}{(k_1 + k_2k_4)\left[\mu + \mu_1(\mu + \mu_2)k_4\right] - (\mu_1 + \mu_2k_4)(\mu + \mu_1 + k_3)} \\ &= \frac{\Lambda(R_0 - 1)}{(k_1 + k_2k_4) - (\mu_1 + \mu_2k_4)} > 0, \end{aligned}$$

as $R_0 > 1 \implies (k_1 + k_2k_4) > (\mu + \mu_1 + k_3)$
i.e. $(k_1 + k_2k_4) > \mu + \mu_1 + k_4(\mu + \mu_2) = \mu + (\mu_1 + \mu_2k_4) + \mu k_4$
$\implies (k_1 + k_2k_4) > (\mu_1 + \mu_2k_4)$.

The Jacobian matrix for the system (2) is given by $M = \begin{pmatrix} -\mu & -\mu_1 & -\mu_2 \\ a_{21} & a_{22} & a_{23} \\ 0 & a_{32} & a_{33} \end{pmatrix}$ where

$$a_{21} = k_1\frac{I_1^2}{N^2} + (k_1 + k_2)\frac{I_1I_2}{N^2} + k_2\frac{I_2^2}{N^2},$$

$$\begin{aligned} a_{22} &= k_1 - k_1\left[\frac{2NI_1 - I_1^2}{N^2}\right] - k_2\left[\frac{-I_2^2}{N^2}\right] + (k_1 + k_2)I_2\left[\frac{N - I_1}{N^2}\right] \\ &\quad -(\mu + \mu_1 + k_3), \end{aligned}$$

$$a_{23} = k_2 - -k_1\left[\frac{-I_1^2}{N^2}\right] - k_2\left[\frac{2NI_2 - I_2^2}{N^2}\right] + (k_1 + k_2)I_1\left[\frac{N - I_2}{N^2}\right],$$

$$a_{32} = k_3, \quad a_{33} = -(\mu + \mu_2).$$

3.3 Local Stability of DFE

Theorem 3.1. *The Disease Free Equilibrium E_1 is locally asymptotically stable provided $R_0 < 1$.*

Proof. The Jacobian matrix for the system (2) at DFE $E_1$is given by

$$M^0 = \begin{pmatrix} -\mu & -\mu_1 & -\mu_2 \\ 0 & k_1 - (\mu + \mu_1 + k_3) & k_2 \\ 0 & k_3 & -(\mu + \mu_2) \end{pmatrix}$$

Clearly $-\mu$ is one of the eigenvalue of M^0. The other two eigenvalues are computed from the matrix

$$\begin{pmatrix} k_1 - (\mu + \mu_1 + k_3) & k_2 \\ k_3 & -(\mu + \mu_2) \end{pmatrix}.$$

The characteristic polynomial of this matrix is given by

$$\lambda^2 + h_1\lambda + h_2 = 0,$$

where $h_1 = -[k_1 - (\mu + \mu_1 + k_3) - (\mu + \mu_2)]$ and $h_2 = -(k_1 - (\mu + \mu_1 + k_3))(\mu + \mu_2) - k_2k_3$.
By Routh-Hurwitz criteria the DFE E_1 is locally asymptotically stable when $h_1,\ h_2 > 0$. Now

$$\begin{aligned} h_1 &= (\mu + \mu_1 + k_3)\left[-\frac{k_1}{(\mu + \mu_1 + k_3)} + 1\right] + (\mu + \mu_2) \\ &= (\mu + \mu_1 + k_3)\left[(-R_0 + 1) + \frac{k_2k_3}{(\mu + \mu_2)(\mu + \mu_1 + k_3)}\right] + (\mu + \mu_2) > 0 \end{aligned}$$

when $R_0 < 1$.
Further,

$$\begin{aligned} h_2 &= -(k_1 - (\mu + \mu_1 + k_3))(\mu + \mu_2) - k_2k_3 \\ &= (\mu + \mu_1 + k_3))(\mu + \mu_2)\left[-\frac{k_1}{(\mu + \mu_1 + k_3)} - \frac{k_2k_3}{(\mu + \mu_2)(\mu + \mu_1 + k_3)} + 1\right] \\ &= (\mu + \mu_1 + k_3))(\mu + \mu_2)[1 - R_0] > 0 \end{aligned}$$

only when $R_0 < 1$.

Hence the Disease Free Equilibrium E_1 is locally asymptotically stable provided $R_0 < 1$. □

3.4 Local Stability of EE

Theorem 3.2. *The Endemic Equilibrium E_2 is locally asymptotically stable when $2\mu + \mu_2 > b_{22}$, $[\mu k_3 b_{23} + \mu_1(\mu + \mu_2)b_{21}] > [k_3\mu_2 b_{21} + \mu(\mu + \mu_2)b_{22}]$ and $\{2\mu + \mu_2 - b_{22}\} \times \{[\mu_1 b_{21} + \mu(\mu + \mu_2)] - (2\mu + \mu_2)b_{22} - k_3 b_{23}\} > \{\mu k_3 b_{23} + \mu_1(\mu + \mu_2)b_{21} - k_3\mu_2 b_{21} - \mu(\mu + \mu_2)b_{22}\}$.*

Proof. The Jacobian matrix for the system (2) at EE E_2 is given by

$$M^* = \begin{pmatrix} N & -\mu & -\mu_1 & -\mu_2 \\ I_1^* & b_{21} & b_{22} & b_{23} \\ I_2^* & 0 & b_{32} & b_{33} \end{pmatrix}$$

where

$$b_{21} = k_1 \frac{I_1^{*^2}}{N^{*^2}} + (k_1 + k_2)\frac{I_1^* I_2^*}{N^{*^2}} + k_2 \frac{I_2^{*^2}}{N^{*^2}},$$

$$b_{22} = k_1 - k_1\left[\frac{2N^* I_1^* - I_1^{*^2}}{N^{*^2}}\right] - k_2\left[\frac{-I_2^{*^2}}{N^{*^2}}\right] + (k_1 + k_2)I_2^*\left[\frac{N^* - I_1^*}{N^{*^2}}\right] - (\mu + \mu_1 + k_3),$$

$$b_{23} = k_2 - -k_1\left[\frac{-I_1^{*^2}}{N^{*^2}}\right] - k_2\left[\frac{2N^* I_2^* - I_2^{*^2}}{N^{*^2}}\right] + (k_1 + k_2)I_1^*\left[\frac{N^* - I_2^*}{N^{*^2}}\right],$$

$$b_{32} = k_3, \quad b_{33} = -(\mu + \mu_2).$$

The eigenvalues of this Jacobian matrix are given by the roots of the following cubic equation in λ: $\lambda^3 + g_1\lambda^2 + g_2\lambda + g_3 = 0$ which is the characteristic equation of the Jacobian matrix M^*, where

$$g_1 = -[-\mu + b_{22} + b_{33}] = 2\mu + \mu_2 - b_{22} > 0 \text{ if } b_{22} < 0,$$

$$g_2 = \begin{vmatrix} -\mu_1 & -\mu_1 \\ b_{21} & b_{22} \end{vmatrix} + \begin{vmatrix} b_{22} & b_{23} \\ k_3 & -(\mu + \mu_2) \end{vmatrix} + \begin{vmatrix} -\mu & -\mu_1 \\ 0 & -(\mu + \mu_2) \end{vmatrix}$$
$$= [\mu_1 b_{21} + \mu(\mu + \mu_2)] - (2\mu + \mu_2)b_{22} - k_3 b_{23}$$

$$g_3 = -\left\{k_3 \begin{vmatrix} -\mu_1 & -\mu_1 \\ b_{21} & b_{23} \end{vmatrix} - (\mu + \mu_2)\begin{vmatrix} -\mu & -\mu_1 \\ b_{21} & b_{22} \end{vmatrix}\right\}$$
$$= \mu k_3 b_{23} + \mu_1(\mu + \mu_2)b_{21} - k_3\mu_2 b_{21} - \mu(\mu + \mu_2)b_{22}.$$

By Routh-Hurwitz criteria the EE E_2 is locally asymptotically stable when $g_1,\ g_3 > 0$ and $g_1 g_2 > g_3$.
i.e. The EE E_2 is locally asymptotically stable when $2\mu + \mu_2 > b_{22}$, $[\mu k_3 b_{23} + \mu_1(\mu + \mu_2)b_{21}] > [k_3\mu_2 b_{21} + \mu(\mu + \mu_2)b_{22}]$ and $\{2\mu + \mu_2 - b_{22}\} \times \{[\mu_1 b_{21} + \mu(\mu + \mu_2)] - (2\mu + \mu_2)b_{22} - k_3 b_{23}\} > \{\mu k_3 b_{23} + \mu_1(\mu + \mu_2)b_{21} - k_3\mu_2 b_{21} - \mu(\mu + \mu_2)b_{22}\}$. □

3.5 Global Stability of DFE

Theorem 3.3. *The disease-free equilibrium E_1 of the model* (2) *is globally asymptotically stable if $\mathcal{R}_0 < 1$.*

Proof. We can prove the global stability of the DFE using the comparison theorem(see Ref. Lakshmikantham et al. (1989), p. 31). Re-writing the equations for the infected compartments in (2), we have

$$\begin{pmatrix} \frac{dI_1}{dt} \\ \\ \frac{dI_2}{dt} \end{pmatrix} = (F - V) \begin{pmatrix} I_1 \\ I_2 \end{pmatrix} - \begin{pmatrix} \frac{(I_1+I_2)}{N}(k_1 I_1 + k_2 I_2) \\ \\ 0 \end{pmatrix}$$

where F and V are as defined in Section 3.1. Since $\dfrac{I_1 + I_2}{N}(k_1(I_1 + k_2 I_2) \geq 0$ for all $t > 0$, it follows that

$$\begin{pmatrix} \frac{dI_1}{dt} \\ \\ \frac{dI_2}{dt} \end{pmatrix} \leq (F - V) \begin{pmatrix} I_1 \\ I_2 \end{pmatrix}.$$

Since the eigenvalues of the matrix $F - V$ all have negative real parts (this comes from the local stability results in Lemma 1 in Driessche and Watmough (2002)), then system (2) is stable whenever $\mathcal{R}_0 < 1$. So, $(I_1, I_2) \to (0,\ 0)$ as $t \to \infty$. By the comparison theorem, it follows that $(I_1, I_2) \to (0, 0)$ and $S \to \frac{A}{d}$ and as $t \to \infty$. Then $(S, I_1, I_2) \to E_1$ as $t \to \infty$. *i.e.* E_1 is globally asymptotically stable for $\mathcal{R}_0 < 1$ when $\beta = 0$. □

In this section we visualized our analytic result through numerical simulation. The system (2) is simulated for various set of parameters. To see the dynamic behavior of the model for disease-free equilibria the system is integrated numerically by fourth order Runge-Kutta method. We consider the parameter set given in Table 2. Here all the parameters are per day.

Table 2: Values of parameters

Parameter	Description	value	Ref.
Λ	Recruitment rate	200	Assumed
μ	Natural death rate	0.02	Okosun et al. (2013)
η	Fractn. of total HIV infectives who are detected	0.5	Assumed
ν	Fractn. of total AIDS infectives who are detected	0.1	Assumed
α_1	Rate of transmission(in HIV class)	0.2	Okosun et al. (2013)
α_2	Rate of transmission(in AIDS class)	0.25	Assumed
$\psi_1,\ \psi_2$	Modification parameters	1.9, 1.9	Assumed
τ	Rate of treatment	0.4	Okosun et al. (2013)
σ_1	Rate of progrsn. to AIDS(detected & treated)	0.1	Okosun et al. (2013)
σ_2	Rate of progrsn. to AIDS(undetected & untreated)	0.15	Assumed
μ_1	Death rate due to HIV infection	0.3	Assumed
μ_2	Death rate due to AIDS	0.5	Assumed

For the parameter set given in the table, the system (2) has only the disease-free equilibrium E_1 and it is locally asymptotically stable (see Fig. 2). Again for the parameter set given in the table except for $\mu_1 = 0.2$, the system (2) has two equilibria the disease-free equilibrium and the endemic equilibrium. Here the disease-free equilibrium E_1 is unstable and the endemic equilibrium E_2 is locally asymptotically stable (see Fig. 3).

This fact is more clear from the Fig. 4, where phase portrait in $S - I_1 - I_2$ are shown for different set of initial conditions. Figs. 5-8 explore the relation between R_0 with other parameters. In Fig. 5 we see the relation between R_0, η and ν. From this figure it is clear that increase in detection parameters causes decrease in R_0. In Fig. 6 we see the relation between R_0, ψ_1 and ψ_2. So if these modification parameters are increasing then there is an increase in the value of basic reproduction number causing elimination of disease almost impossible.

In Fig. 7 we see the relation between R_0, σ_1 and σ_2. Here too increase in σ_1 and σ_2 causes increase in basic reproduction number. Fig. 8 is reflecting the relation between R_0 , α_1 and α_2. As expected increase in rates of transmission α_1 and α_2 causes increase in R_0. So our aim should be to manipulate these parameters using different control strategies such that the value of the basic reproduction number R_0 can be made less than one. This will lead to DFE to be globally stable causing the complete elimination of the disease from the population.

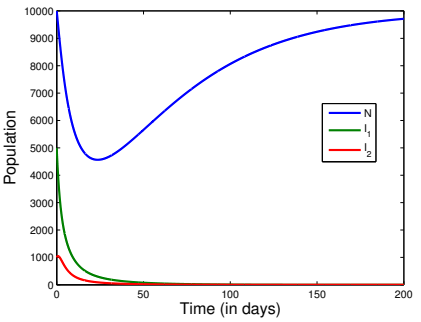

Figure 2: Variation of N, I_1, I_2 with time showing the stability of disease-free equilibrium (when $R_0 = 0.8956 < 1$) for the parameter values are given in Table 2

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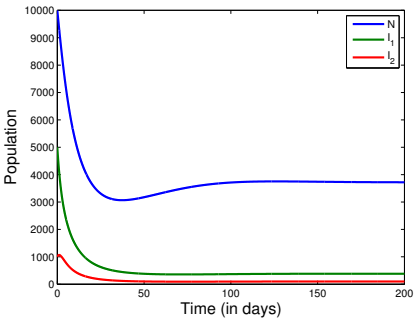

Figure 3: Variation of N, I_1, I_2 with time showing the stability of endemic equilibrium (when $R_0 = 1.1478 > 1$) for the parameter values are given in Table 2 except $\mu_1 = 0.2$

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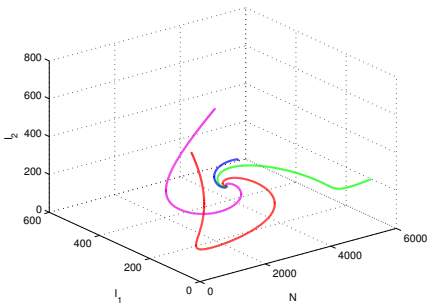

Figure 4: $N - I_1 - I_2$ phase plot showing the stability of the EE for $R_0 > 1$

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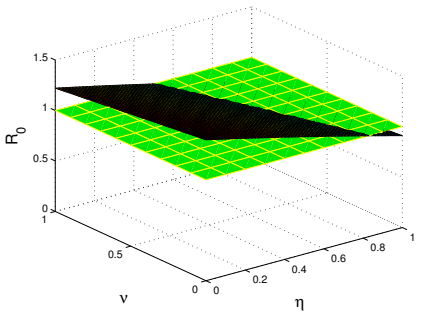

Figure 5: Variation of R_0 with ν and η showing the impact of η and ν on R_0

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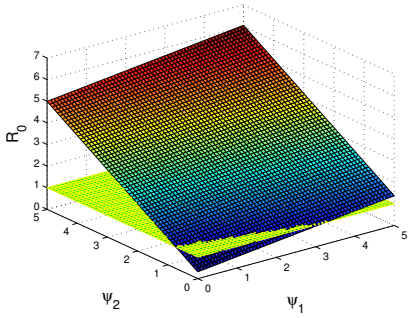

Figure 6: Variation of R_0 with ψ_1 and ψ_2 showing the impact of ψ_1 and ψ_2 on R_0

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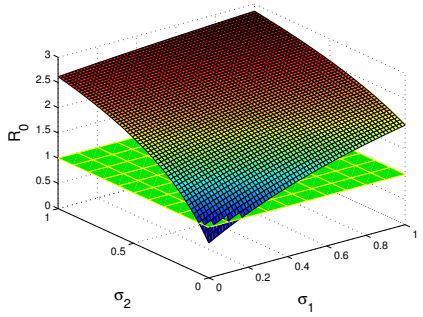

Figure 7: Variation of R_0 with σ_1 and σ_2 showing the impact of σ_1 and σ_2 on R_0

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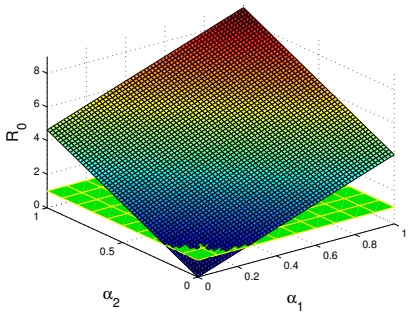

Figure 8: Variation of R_0 with α_1 and α_2 showing the impact of α_1 and α_2 on R_0

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4. Optimal Control Problem

In the preceding model with detection, we considered the fixed value of the detection parameter throughout the analysis. But in reality these parameters may be dependent on time. Therefore we used the detection parameters related to HIV and AIDS classes as time dependent parameters and we study the optimal control over the detection parameters. Through this study we develop a strategy through the objective function for minimizing the cost as well as the number of infectives. We use Pontryagin's Maximum Principle (see Bartl et al. (2010), Kar et al. (2012), Kar and Ghosh (2012), Zaman et al. (2008), *etc.*) to accomplish our aim. The optimal control system with the objective functional is given below:

$$\begin{aligned} \frac{dS}{dt} &= \Lambda - \mu S + \left(k_1(t)\frac{I_1}{N} + k_2(t)\frac{I_2}{N}\right) S, \\ \frac{dI_1}{dt} &= \left(k_1(t)\frac{I_1}{N} + k_2(t)\frac{I_2}{N}\right) S - (\mu + \mu_1 + k_3(t))I_1, \\ \frac{dI_2}{dt} &= k_3(t)I_1 - (\mu + \mu_2)I_2, \end{aligned} \tag{6}$$

where

$$\begin{aligned} N &= S + I_1 + I_2, \\ k_1(t) &= \alpha_1[\eta(t) + \psi_1(1 - \eta(t))] = \alpha_1[(1 - \psi_1)\eta(t) + \psi_1], \\ k_2(t) &= \alpha_2[\nu(t) + \psi_2(1 - \nu(t))] = \alpha_2[(1 - \psi_2)\nu(t) + \psi_2], \\ k_3(t) &= \{\sigma_1\tau\eta(t) + \sigma_2[(1 - \tau)\eta(t) + (1 - \eta(t))]\} = \sigma_1\tau\eta(t) + \sigma_2[1 - \tau\eta(t)] \\ &= \tau\eta(t)[\sigma_1 - \sigma_2] + \sigma_2. \end{aligned}$$

We formulate an optimal control problem with the objective (cost) functional given by

$$J = \int_0^T \left(C_1 I_1 + C_2 I_2 + \frac{1}{2}C_3\eta^2 + \frac{1}{2}C_4\nu^2\right)dt. \tag{7}$$

subject to the state system given by (6). Our objective is to find a control η^* and ν^* such that $J(\eta^*, \nu^*) = \min_{\eta,\ \nu\ \in\ \Omega} J(\eta,\ \nu)$, where $\Omega = \{\eta,\ \nu$: measurable and $0 \leq \eta(t),\ \nu(t) \leq 1$ for $t \in [0, t_1]\}$ is the set for the controls.

Here, the value $\eta(t) = 1,\ \nu(t) = 1$ represents the maximal control of detection on HIV and AIDS class respectively. The quantities $C_1,\ C_2,\ C_3$ and C_4 represent, respectively, the weight constants. The terms $C_3\eta^2$ and $C_4\nu^2$ describe the cost associated with detection control on HIV and AIDS class respectively.

4.1 Hamiltonian and Adjoint Equations

The Lagrangian of this problem is given by

$$L(S, I_1, I_2, \eta, \nu) = C_1 I_1 + C_2 I_2 + \frac{1}{2} C_3 \eta^2 + \frac{1}{2} C_4 \nu^2 \tag{8}$$

Next we form the Hamiltonian H for our problem as follows:

$$H(S, I_1, I_2, \eta, \nu) \quad = \quad L(S, I_1, I_2, \eta, \nu) + \lambda_1 \tfrac{dS}{dt} + \lambda_2 \tfrac{dI_1}{dt} + \lambda_3 \tfrac{dI_2}{dt} \tag{9}$$

where λ_i, $i = 1,\ 2,\ 3$ are the adjoint variables or the co-state variables and can be determined by solving the following system of differential equations:

$$\begin{aligned}
\tfrac{d\lambda_1}{dt} = -\tfrac{\partial H}{\partial S} &= \lambda_1 \left\{ \mu + (k_1 I_1 + k_2 I_2) \left[\tfrac{(S+I_1+I_2)\cdot 1 - S\cdot 1}{(S+I_1+I_2)^2} \right] \right\} \\
&\quad -\lambda_2 (k_1 I_1 + k_2 I_2) \left[\tfrac{I_1+I_2}{(S+I_1+I_2)^2} \right], \\
\tfrac{d\lambda_2}{dt} = -\tfrac{\partial H}{\partial I_1} &= -C_1 - \lambda_1 \left\{ -k_1 S \left[\tfrac{S+I_2}{(S+I_1+I_2)^2} \right] + k_2 \left[\tfrac{I_2 S}{(S+I_1+I_2)^2} \right] \right\} \\
&\quad -\lambda_2 \left\{ k_1 S \left[\tfrac{S+I_2}{(S+I_1+I_2)^2} \right] - k_2 \left[\tfrac{I_2 S}{(S+I_1+I_2)^2} \right] - (\mu + \mu_1 + k_3) \right\} \\
&\quad -\lambda_3 k_3, \\
\tfrac{d\lambda_3}{dt} = -\tfrac{\partial H}{\partial I_2} &= -C_2 - \lambda_1 \left\{ k_1 \left[\tfrac{I_1 S}{(S+I_1+I_2)^2} \right] - k_2 S \left[\tfrac{S+I_2}{(S+I_1+I_2)^2} \right] \right\} \\
&\quad -\lambda_2 \left\{ -k_1 \left[\tfrac{I_1 S}{(S+I_1+I_2)^2} \right] + k_2 S \left[\tfrac{S+I_2}{(S+I_1+I_2)^2} \right] \right\} + \lambda_3 (\mu + \mu_2),
\end{aligned} \tag{10}$$

Let $\widetilde{S}$, $\widetilde{I_1}$, $\widetilde{I_2}$ and $\widetilde{N}$ be the optimum value of S, I_1, I_2 and N. Also let $\{\widetilde{\lambda_1}, \widetilde{\lambda_2}, \widetilde{\lambda_3}\}$ be the solutions of the system (10).

4.2 Optimal Control Theorems

We now state and prove the following theorem by following Lukes (1982)and Zaman et al. (2008).

Theorem 4.1. *There exists optimal controls $\eta^*, \nu^* \in \Omega$ such that*

$$J(\eta^*, \nu^*) = \min_{\eta,\ \nu \in \Omega} J(\eta, \nu)$$

subject to the system (6).

Proof. This theorem is proved using Lukes (1982). It is easy to see that all the control and the state variables are nonnegative. Also the necessary convexity

of our objective functional in η and ν is satisfied for this minimizing problem. The control variable set $\eta,\ \nu\ \in\ \Omega$ is also closed and convex by definition. The boundedness of the optimal system determines the compactness required for the existence of the optimal control. In addition, the integrand in the functional (7), $C_1I_1 + C_2I_2 + \frac{1}{2}C_3\eta^2 + \frac{1}{2}C_4\nu^2$ is convex on the control set Ω and also the state variables are bounded. This proves the theorem. □

As there exists an optimal control for minimizing the functional subject to equations (6) and (10), the Pontryagin's Maximum Principle is used to obtain the necessary conditions to get the optimal solution as follows:
Let (x, u) is an optimal solution of an optimal control problem. Then there exists a non trivial vector function $\lambda = (\lambda_1, \lambda_2, ..., \lambda_n)$ satisfying the following equalities.

$$\begin{aligned} \frac{dx}{dt} &= \frac{\partial H(t,x,u,\lambda)}{\partial \lambda}, \\ 0 &= \frac{\partial H(t,x,u,\lambda)}{\partial u}, \\ \frac{d\lambda}{dt} &= -\frac{\partial H(t,x,u,\lambda)}{\partial x}. \end{aligned} \tag{11}$$

By using the Pontryagin's Maximum Principle Pontryagin et al. (1962) and the theorem (4.1) we are going to state and prove the below theorem.

Theorem 4.2. *The optimal controls η^*, ν^* minimizes J over the region Ω given by*

$$\begin{aligned} \eta^* &= max\{0, min(\widetilde{\eta}, 1)\} \quad and \\ \nu^* &= max\{0, min(\widetilde{\nu}, 1)\} \end{aligned}$$

where

$$\begin{aligned} \widetilde{\eta} &= \frac{1}{C_3}\left\{(\widetilde{\lambda}_1 - \widetilde{\lambda}_2)(1-\psi_1)\alpha_1\frac{\widetilde{I}_1\widetilde{S}}{\widetilde{N}} + (\widetilde{\lambda}_2 - \widetilde{\lambda}_3)(\sigma_1 - \sigma_2)\tau\widetilde{I}_1\right\}, \\ \widetilde{\nu} &= \frac{1}{C_4}\left\{(\widetilde{\lambda}_1 - \widetilde{\lambda}_2)(1-\psi_2)\alpha_2\frac{\widetilde{I}_2\widetilde{S}}{\widetilde{N}}\right\}. \end{aligned}$$

Proof. Using the optimality conditions

$$\frac{\partial H}{\partial \eta} = 0 \ \text{ and } \ \frac{\partial H}{\partial \nu} = 0$$

we get

$$\eta = \frac{1}{C_3}\left\{(\widetilde{\lambda}_1 - \widetilde{\lambda}_2)(1-\psi_1)\alpha_1\frac{\widetilde{I}_1\widetilde{S}}{\widetilde{N}} + (\widetilde{\lambda}_2 - \widetilde{\lambda}_3)(\sigma_1-\sigma_2)\tau\widetilde{I}_1\right\}(=\widetilde{\eta}),$$

$$\nu = \frac{1}{C_4}\left\{(\widetilde{\lambda}_1 - \widetilde{\lambda}_2)(1-\psi_2)\alpha_2\frac{\widetilde{I}_2\widetilde{S}}{\widetilde{N}}\right\}(=\widetilde{\nu}).$$

These controls are bounded with upper and lower bounds as 0 and 1 respectively. *i.e.* $\eta = 0$ if $\widetilde{\eta} < 0$ and $\eta = 1$ if $\widetilde{\eta} > 1$ and $\nu = 0$ if $\widetilde{\nu} < 0$ and $\nu = 1$ if $\widetilde{\nu} > 1$, otherwise $\eta = \widetilde{\eta}$ and $\nu = \widetilde{\nu}$. Hence for this controls (η^*) and (ν^*) we get the optimum value of the functional J given by equation (7). Hence the theorem. □

5. Numerical Simulation of the Optimal Control Model

To exhibit the effect of optimal control, we performed the numerical simulation in this section. The control profile is applied for the period of 100 days. As discussed in Athithan and Ghosh (2015), here too we assume that the weight associated with detection in HIV class (C_3) is greater than or equal to the weight associated with detection in AIDS class (C_4). The optimality system in Section 4 is solved by iterative method (see Jung et al. (2002), Lenhart and Workman (2007), *etc.*). At first we solve the state equations by the forward Euler method for the time interval [0, 1000] starting with an initial guess for the adjoint variables. Then we solve the adjoint variables in the same time interval by using the obtained solutions of the state variables and the transversality conditions backward in time. The following set of parameters is considered to simulate the optimal control model:

$$\Lambda = 200, \mu = 0.02, \alpha_1 = 0.25, \alpha_2 = 0.32, \tau = 0.8, \sigma_1 = 0.1,$$

$$\sigma_2 = 0.15, \mu_1 = 0.2, \mu_2 = 0.5, \psi_1 = 1.4, \psi_2 = 1.9.$$

The weight constants C_1 and C_2 are taken as 1 and C_3 and C_4 are varied. From Figs. 9 and 10, it is easy to observe that the controls take their highest value 1 in starting period and after some period of time (nearly at the end of optimal strategic time period) the control parameter values are toned down slowly and finally comes to the 0 level. Fig. 9 shows that the HIV detection rate should be maintained according to the cost applied on detecting HIV and AIDS patients over the period of control. Figs. 11-13 are showing the effects

of the costs C_3 and C_4 on effective control profiles of η and ν. Figs. 14-16 are showing the plots of adjoint variables. It is evident from the figures 17-19 that the optimal control strategy gives the better result than the fixed control effort. It is observed that in the case of optimal control, number of susceptible individuals starts increasing and the number of HIV and AIDS infectives start decreasing.

These facts are evidently showing that the optimal control program is to be conducted to detect the maximum number of infectives and to decrease the infection prevalence of HIV and AIDS infected population.

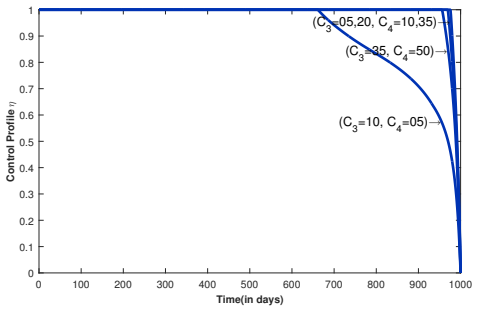

Figure 9: The control profile of η of the intervention strategies for different values of C_3 and C_4.

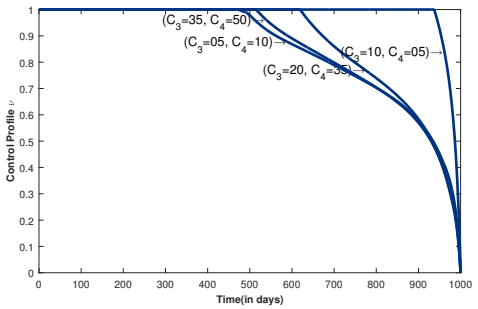

Figure 10: The control profile of ν of the intervention strategies for different values of C_3 and C_4.

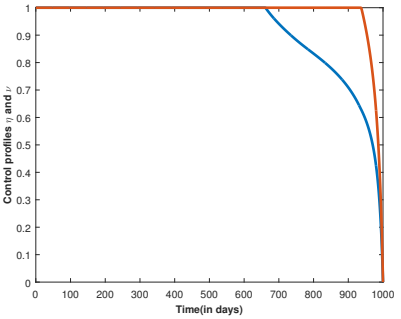

Figure 11: The control profiles of η and ν of the intervention strategies for the values $C_3 = 10$ and $C_4 = 5$.

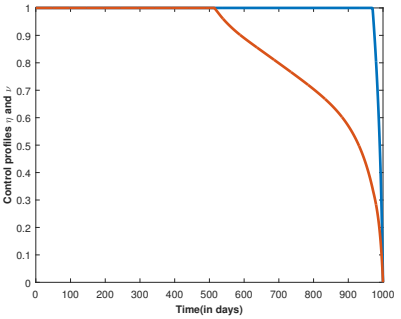

Figure 12: The control profiles of η and ν of the intervention strategies for the values $C_3 = 20$ and $C_4 = 35$.

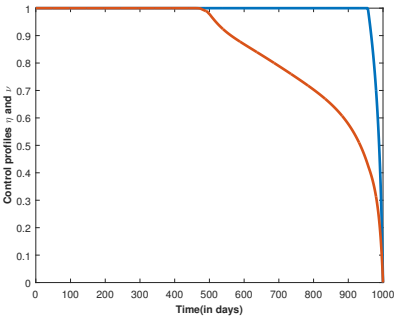

Figure 13: The control profiles of η and ν of the intervention strategies for the values $C_3 = 35$ and $C_4 = 50$.

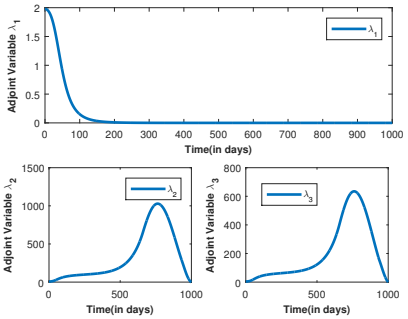

Figure 14: Simulation results showing the effect of control measures on adjoint variables (shadow price) for $C_3 = 10$ and $C_4 = 5$.

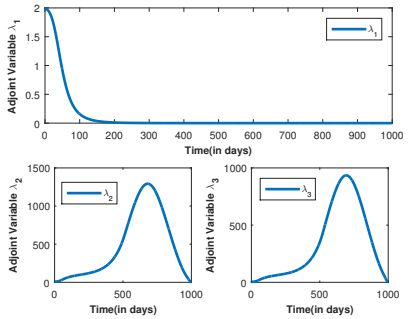

Figure 15: Simulation results showing the effect of control measures on adjoint variables (shadow price) for $C_3 = 20$ and $C_4 = 35$.

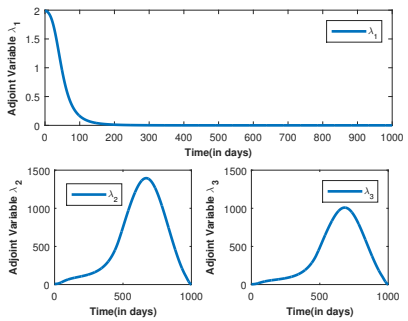

Figure 16: Simulation results showing the effect of control measures on adjoint variables (shadow price) for $C_3 = 35$ and $C_4 = 50$.

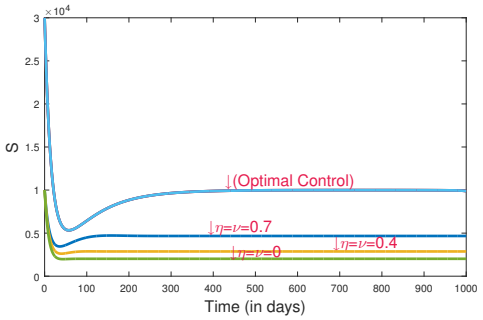

Figure 17: Variation of S with time for different levels of fixed controls and optimal control.

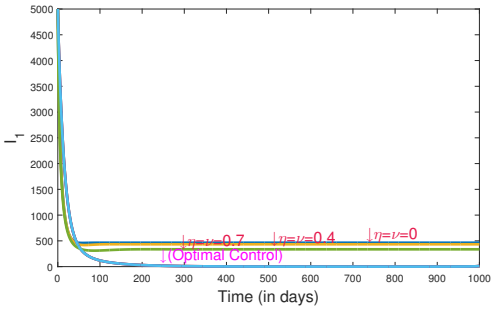

Figure 18: Variation of I_1 with time for different levels of fixed controls and optimal control.

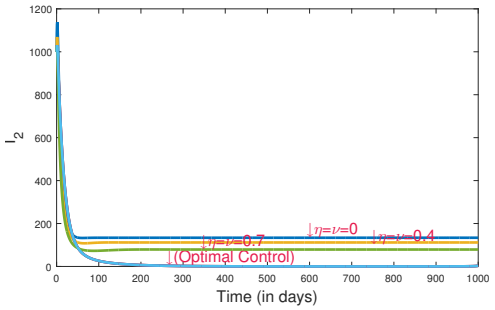

Figure 19: Variation of I_2 with time for different levels of fixed controls and optimal control.

6. Conclusion

Here an HIV/AIDS model with standard incidence is proposed and analyzed to exhibit the effects of case detection and treatment. The expression for the basic reproduction number R_0 is obtained and its relationship with other parameters are explored graphically. Equilibria of the model are found and their local and global stabilities are discussed in detail. It is observed that two nonnegative equilibria are possible for the system (1): the disease-free (E_1) which always exists and the endemic equilibrium (E_2) which exists only for $R_0 > 1$. It has been proved that the disease-free equilibrium is globally stable when $R_0 < 1$. The endemic equilibrium is locally asymptotically stable under some restriction on parameters.

Further, the proposed basic model is converted to an optimal control problem to know the dynamics of the disease when the control parameters become time dependent. The control profile for the detection parameters are obtained and the effect of optimal control on infectives are demonstrated using numerical simulation. The results of our simulation confirm that the optimal control strategies is better than fixed control as it helps in decreasing the number of infectives significantly in a specified interval of time.

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