ISSN 1 746-7233, England, UK
World Journal of Modelling and Simulation
Vol. 15 (2019) No. 3, pp. 228-240

Optimal Control Analysis of a Sex-structured HIV/AIDS Model

S.Athithan[1] *

Department of of Mathematics
SRM Institute of Science and Technology, Kattankulathur-603203, Kancheepuram District.

(*Received May 04 2017, Accepted June XX 2015*)

Abstract. This paper describes the optimal screening (with proper counseling) strategy to reduce the transmission of HIV/AIDS on a sex-structured model. Optimal control theory is applied to a non-linear mathematical model of HIV/AIDS which helps in obtaining time dependent case detection strategy while minimizing the cost of implementation of such strategy. The optimality of the system is deduced analytically and solved numerically. Optimal control results are compared with the simulation results of the model without control. It is observed that optimal control strategy gives better result in terms of minimizing the number of infectives. This paper/research work is significant because in developing countries like India, awareness among the disease for male and female differs according as they are living in city/town/village. Also the time factor plays vital role for the efforts to take against a disease. So that time dependent effect may exhibits the better understanding of the disease spread and control.

Keywords: HIV, AIDS, heterosexual, optimal control, simulation.

1 Introduction

The decimation of any infectious disease is not so easy since there are several factors hampering the success of HIV/AIDS control policies. $e.g.$ The factors like developing an effective vaccine, expensive and time-consuming diagnostic process, necessity of many months of treatment, etc. were the challenges in HIV/AIDS control. Also in a developing country like India, there are many unreported cases of HIV and AIDS. People in general have a tendency to avoid visiting medical practitioner until it becomes intolerable. This delay causes an increase in the infection prevalence of this disease.

The paper ([1]), concentrated on the study of an optimal control on vaccination program through a nonlinear mathematical SIR epidemic model. There are several other epidemic models where optimal control is used according to the situation and their model suitably, (see [2–9]).

In this paper a sex-structured mathematical model for HIV/AIDS with screening (with proper counseling) effect on both male and female as described in [10] has been considered to study the effectiveness of optimal control. In [10], the authors have considered constant rate of screening. But in reality, the screening of HIV/AIDS is highly depends upon the region, society, $etc.$ The population who are in slum areas may not have access of proper health center. In general they delay in approaching to the medical practitioner even when they are sick. There should be proper health network covering whole population under consideration irrespective of their class, religion, $etc.$ In our present work we have tried to project the optimal screening strategy so that the infection prevalence of HIV/AIDS can be minimized. Here the screening parameters were taken as the control parameters.

This paper is organized as follows: Section 2 describes the basic model, Section 3 describes the optimal control problem. Numerical simulation is performed in Section 4, and finally it ends with brief conclusion in Section 5.

* *E-mail address*: athithan1625@gmail.com

2 The model and results

We consider the model studied in [10] and apply optimal control theory to it. Here we consider the screening parameters γ_m and γ_f as the control parameters which are already defined as constant parameters in [10]. The adult age group is primarily involved in sexual transmission of HIV so our population under consideration is only the adult population. Here the total adult population at time t, denoted by $N(t)$ is divided into mutually exclusive compartments, namely class of HIV-susceptible males (S_m), HIV-susceptible females (S_f), HIV-infected males (I_m), HIV-infected females (I_f), AIDS-Class (A). Also it is assumed that the AIDS patients (infected individuals) are not participating in the transmission of virus as they become very sick by the time they develop AIDS. Hence we have not divided AIDS class into male and female subclasses. It is assumed that there are several screening centers where HIV screening is performed to identify whether an individual is infected with HIV or not? These screening centers are also providing proper counseling to infected individuals. So at a particular time there will be a fraction of the total infected individuals who have been screened and given proper counseling. Hence they will not be taking part in the sexual transmission of HIV. As HIV treatment is very expensive so we assume that only a fraction of the total screened HIV infectives will opt for treatment. And obviously those HIV infected individuals who are unscreened are unaware of having disease and will not go for treatment. The rates of progression of AIDS from HIV for treated and untreated HIV infectives, are different. In view of the above considerations the mathematical model is proposed as follows:

$$\begin{aligned}
\tfrac{dS_m}{dt} &= \Lambda_1 - dS_m - \lambda_m S_m, \\
\tfrac{dS_f}{dt} &= \Lambda_2 - dS_f - \lambda_f S_f, \\
\tfrac{dI_m}{dt} &= \lambda_m S_m - (d+d_1)I_m - k_1 I_m, \\
\tfrac{dI_f}{dt} &= \lambda_f S_f - (d+d_2)I_f - k_2 I_f, \\
\tfrac{dA}{dt} &= k_1 I_m + k_2 I_f - (d+d_3)A,
\end{aligned} \tag{1}$$

where,
$\lambda_m = \beta(1-\gamma_f)I_f = L_1 I_f, \quad \lambda_f = \beta(1-\gamma_m)I_m = L_2 I_m,$
$L_1 = \beta(1-\gamma_f)$ and $L_2 = \beta(1-\gamma_m),$
$k_1 = [\sigma_1\tau\gamma_m + \sigma_2(1-\tau)\gamma_m + \sigma_2(1-\gamma_m)],\ k_2 = [\sigma_1\tau\gamma_f + \sigma_2(1-\tau)\gamma_f + \sigma_2(1-\gamma_f)].$

The parameters used in the model Eq. (1) are described in Table. 1 and transfer diagram of the model is shown in Fig. 1a. Here Fig. 1b represents the tree diagram which shows the movement of individuals from HIV class (I) to AIDS class (A). The variable I in Fig. 1b represents I_m or I_f corresponding to male or female infectives respectively. Similarly γ in Fig. 1b denotes γ_m or γ_f depending upon male or female infectives respectively.

2.1 Basic reproduction number

The basic reproduction number is defined as the expected number of secondary infections generated in a completely susceptible population, by a typical infected individual during his/her entire period of infectiousness [11]. To compute the reproduction number for the model, we have used the method described in [12] and using the same notation as of [12], we get the following:

$$\mathcal{F} - \mathcal{V} = \begin{pmatrix} L_1 I_f S_m \\ L_2 I_m S_f \\ k_1 I_m + k_2 I_f \end{pmatrix} - \begin{pmatrix} (d+d_1+k_1)I_m \\ (d+d_2+k_2)I_f \\ (d+d_3)A \end{pmatrix}.$$

From this we get,

Table 1: Description of parameters

Parameter	Description
Λ_1	Rate of recruitment in the Susceptible males Class (S_m),
Λ_2	Rate of recruitment in the Susceptible females Class (S_f),
d	Natural death rate,
d_1	Death rate due to infection in the male class,
d_2	Death rate due to infection in the female class,
d_3	Death rate due to AIDS,
γ_m	Rate of screening with proper counseling (male class),
γ_f	Rate of screening with proper counseling (female class),
σ_1	AIDS progression rate in treated class,
σ_2	AIDS progression rate in untreated class,
τ	Fraction of aware infectives taking treatment,
β	Rate of transmission of HIV.

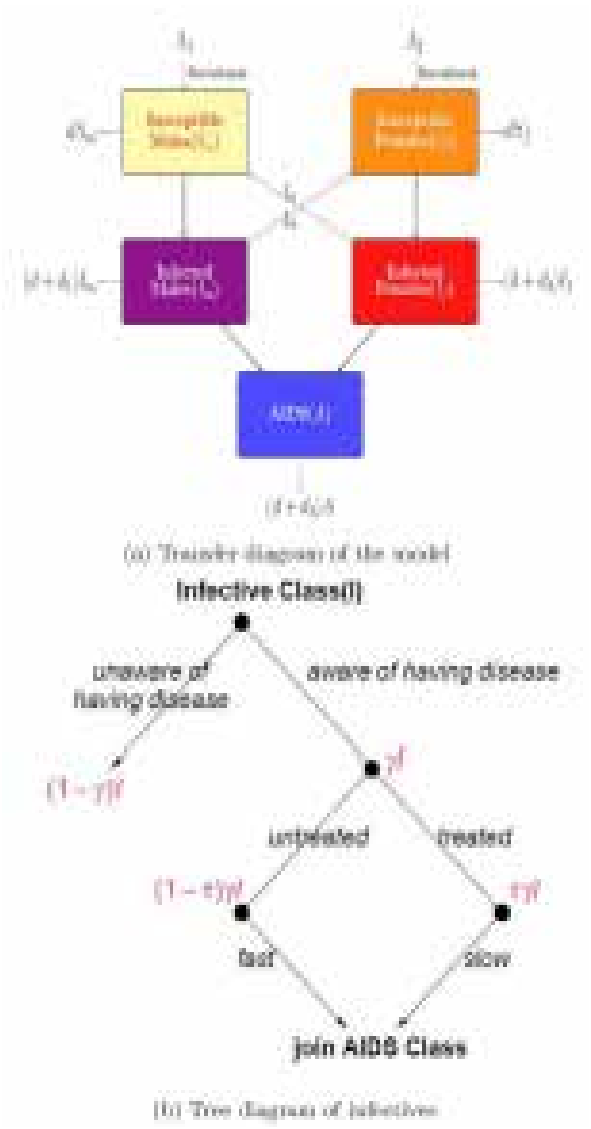

Fig. 1: Transfer diagram and Tree diagram for the model Eq. (1).

$$F = \begin{pmatrix} 0 & L_1 S_m^0 & 0 \\ L_2 S_f^0 & 0 & 0 \\ k_1 & k_2 & 0 \end{pmatrix}, V = \begin{pmatrix} (d + d_1 + k_1) & 0 & 0 \\ 0 & (d + d_2 + k_2) & 0 \\ 0 & 0 & (d + d_3) \end{pmatrix}.$$

We know that the basic reproduction number R_0 is the spectral radius of the matrix FV^{-1} and for our model it is as follows:

$$R_0 = \left[\frac{L_1 L_2 \Lambda_1 \Lambda_2}{(d+d_1+k_1)(d+d_1+k_2)d^2}\right]^{1/2}$$

From the expression of R_0, it is clear that with the increase of γ_f and γ_m, the value of R_0 decreases.

2.2 Existence of equilibria

The Model (2) has two non negative equilibria namely $E_0(S_m^0, S_f^0, 0, 0, 0)$, the disease free equilibrium(DFE) and $E_1(S_m^*, S_f^*, I_m^*, I_f^*, A^*)$, the endemic equilibrium(EE), where

$$S_m^0 = \frac{\Lambda_1}{d},\ \ S_f^0 = \frac{\Lambda_2}{d}\ , S_m^* = \left[\frac{\Lambda_1}{d+L_1 I_f^*}\right] = \left[\frac{(d+d_1+k_1)I_m^*}{L_1 I_f^*}\right],$$

$$S_f^* = \left[\frac{\Lambda_2}{d+L_2 I_m^*}\right] = \left[\frac{(d+d_2+k_2)I_f^*}{L_1 I_m^*}\right], I_f^* = \left[\frac{R_0^2-1}{P}\right],$$

$$I_m^* = \left[\frac{d(d+d_2+k_2)I_f^*}{L_2\Lambda_2 - L_2(d+d_2+k_2)I_f^*}\right] = \left[\frac{d(d+d_2+k_2)(R_0^2-1)}{P[L_2\Lambda_2-(d+d_2+k_2)(R_0^2-1)]}\right],$$

$$A^* = \left[\frac{k_1 I_m^* + k_2 I_f^*}{d+d_3}\right], \text{and } P = L_1 d^2(d+d_1+k_1)[L_2\Lambda_1 + d(d+d_1+k_1)].$$

3 Optimal control problem

Infectious diseases are major health problem in our society. In this prospect it is very important to improve the control measures to decrease the infected population. Optimal control theory is very useful tool in controlling the number of infectives in the total population. In the preceding model with screening, we considered the fixed value of the screening parameters throughout the analysis. But in reality these parameters may be dependent of time. Therefore we used these parameters as time dependent parameters and we study the optimal control over the screening parameters. Through this study we develop a strategy using the objective function for minimizing the cost as well as the infectives. We shall use Pontryagin's Maximum Principle (see [13–15], *etc.*) to accomplish our task. The optimal control system with the objective functional is developed and to be optimized is given below:

$$\begin{aligned}
\tfrac{dS_m}{dt} &= \Lambda_1 - \mu S_m - \beta(1-\gamma_f(t))S_m I_f,\\
\tfrac{dS_f}{dt} &= \Lambda_2 - \mu S_f - \beta(1-\gamma_m(t))S_f I_m,\\
\tfrac{dI_m}{dt} &= \beta(1-\gamma_f(t))S_m I_f - (\mu+\mu_1+k_1(t))I_m,\\
\tfrac{dI_f}{dt} &= \beta(1-\gamma_m(t))S_f I_m - (\mu+\mu_2+k_2(t))I_f,\\
\tfrac{dA}{dt} &= k_1(t)I_m + k_2(t)I_f - (\mu+\mu_3)A,
\end{aligned} \tag{2}$$

where,

$k_1(t) = [\sigma_1\tau\gamma_m + \sigma_2(1-\tau)\gamma_m(t) + \sigma_2(1-\gamma_m(t))] = (\sigma_1-\sigma_2)\tau\gamma_m(t) + \sigma_2,$

$k_2(t) = [\sigma_1\tau\gamma_f + \sigma_2(1-\tau)\gamma_f(t) + \sigma_2(1-\gamma_f(t))] = (\sigma_1-\sigma_2)\tau\gamma_f(t) + \sigma_2.$

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

$$J = \int_0^T \left(C_1 I_m + C_2 I_f + C_3 A + \frac{1}{2}C_4\gamma_m^2 + \frac{1}{2}C_5\gamma_f^2\right)dt. \tag{3}$$

subject to the state system given by Eq. (2).

Our objective is to find a control γ_m^* and γ_f^* such that

$$J(\gamma_m^*, \gamma_f^*) = \min_{\gamma_m,\, \gamma_f \in \Omega} \quad J(\gamma_m,\ \gamma_f)$$

where $\Omega = \{\gamma_m,\ \gamma_f$: measurable and $0 \leq \gamma_m(t),\ \gamma_f(t) \leq 1$ for $t \in [0, t_1 = T]$ is the set for the controls.

Here, the value $\gamma_m(t) = 1,\ \gamma_f(t) = 1$ represents the maximal control of detection on HIV and AIDS class respectively. The quantities $C_1,\ C_2,\ C_3,\ C_4$ and C_5 represent, respectively, the weight constants. The term $C_4\gamma_m^2$ and $C_5\gamma_f^2$ describes the cost associated with detection control on HIV and AIDS class respectively.

The Lagrangian of this problem is given by

$$L(I_m, I_f, A, \gamma_m, \gamma_f) = C_1 I_m + C_2 I_f + C_3 A + \frac{1}{2} C_4 \gamma_m^2 + \frac{1}{2} C_5 \gamma_f^2 \tag{4}$$

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

$$\begin{aligned} H(S_m, S_f, I_m, I_f, A, \gamma_m, \gamma_f) &= L(I_m, I_f, A, \gamma_m, \gamma_f) + \lambda_1 \tfrac{dS_m}{dt} + \lambda_2 \tfrac{dS_f}{dt} \\ &\quad + \lambda_3 \tfrac{dI_m}{dt} + \lambda_4 \tfrac{dI_f}{dt} + \lambda_5 \tfrac{dA}{dt} \end{aligned}$$

where $\lambda_i,\ i = 1,\ 2,\ 3,\ 4,\ 5$ are the adjoint variables or the co-state variables and can be determined by solving the following system of differential equations:

$$\begin{aligned} \tfrac{d\lambda_1}{dt} = -\tfrac{\partial H}{\partial S_m} &= \lambda_1 \{\mu + \beta(1-\gamma_f) I_f\} - \lambda_3 \{\beta(1-\gamma_f) I_f\}, \\ \tfrac{d\lambda_2}{dt} = -\tfrac{\partial H}{\partial S_f} &= \lambda_2 \{\mu + \beta(1-\gamma_m) I_m\} - \lambda_4 \{\beta(1-\gamma_m) I_m\}, \\ \tfrac{d\lambda_3}{dt} = -\tfrac{\partial H}{\partial I_m} &= -C_1 + \lambda_2 \{\beta(1-\gamma_m) S_f\} \\ &\quad + \lambda_3 \{(\mu + \mu_1 + k_1)\} - \lambda_4 \{\beta(1-\gamma_m) S_f\} - \lambda_5 k_1, \\ \tfrac{d\lambda_4}{dt} = -\tfrac{\partial H}{\partial I_f} &= -C_2 + \lambda_1 \{\beta(1-\gamma_f) S_m\} - \lambda_3 \{\beta(1-\gamma_f) S_m\} \\ &\quad + \lambda_4 \{(\mu + \mu_2 + k_2)\} - \lambda_5 k_2, \\ \tfrac{d\lambda_5}{dt} = -\tfrac{\partial H}{\partial A} &= -C_3 + \lambda_5(\mu + \mu_3) \end{aligned} \tag{5}$$

Let $\widetilde{S}_m,\ \widetilde{S}_f,\ \widetilde{I}_m,\ \widetilde{I}_f$ and $\widetilde{A}$ be the optimum value of $S_m,\ S_f,\ I_m,\ I_f$ and A. Also let $\{\widetilde{\lambda}_1, \widetilde{\lambda}_2, \widetilde{\lambda}_3, \widetilde{\lambda}_4, \widetilde{\lambda}_5\}$ be the solutions of the system (Eq. 5).

We now state and prove the following theorem by following [16] and [13].

Theorem 1. *There exists optimal controls $\gamma_m^*, \gamma_f^* \in \Omega$ such that*

$$J(\gamma_m^*, \gamma_f^*) = \min_{\gamma_m,\, \gamma_f \in \Omega} \quad J(\gamma_m, \gamma_f)$$

subject to the system (Eq. 2). None

Proof. We use [16] to prove this theorem. Here the control and the state variables are nonnegative values. The necessary convexity of the objective functional in γ_m and γ_f is satisfied for this minimizing problem. The control variable set $\gamma_m,\ \gamma_f \in \Omega$ is also convex and closed by definition. The optimal system is bounded which determines the compactness needed for the existence of the optimal control. In addition, the integrand in the Eq. (3), $C_1 I_1 + C_2 I_2 + \frac{1}{2} C_3 \gamma_m^2 + \frac{1}{2} C_4 \gamma_f^2$ is convex on the control set Ω and the state variables are bounded. This completes the proof of this theorem. None

Since there exists an optimal control for minimizing the functional subject to equations Eq. (2) and Eq. (5), we use Pontryagin's Maximum Principle to derive the necessary conditions to find the optimal solution as follows:
If (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.

$$\begin{aligned} \frac{dx}{dt} &= \frac{\partial H(t,x,u,\lambda)}{\partial \lambda}, \\ 0 &= \frac{\partial H(t,x,u,\lambda)}{\partial u}, \\ \frac{d\lambda}{dt} &= -\frac{\partial H(t,x,u,\lambda)}{\partial x}. \end{aligned} \tag{6}$$

With the help of Pontryagin's Maximum Principle [17] and the theorem (1) we now state and prove the following theorem.

Theorem 2. *The optimal controls γ_m^*, γ_f^* minimizes J over the region Ω given by*

$$\begin{aligned} \gamma_m^* &= max\{0, min(\widetilde{\gamma_m}, 1)\} \text{ and} \\ \gamma_f^* &= max\{0, min(\widetilde{\gamma_f}, 1)\} \end{aligned}$$

where

$$\begin{aligned} \widetilde{\gamma_m} &= \frac{1}{C_4}\left\{(\widetilde{\lambda}_4 - \widetilde{\lambda}_2)\beta\widetilde{S}_f\widetilde{I}_m + \widetilde{\lambda}_3(\sigma_1 - \sigma_2)\tau\widetilde{I}_m\right\}, \\ \widetilde{\gamma_f} &= \frac{1}{C_5}\left\{(\widetilde{\lambda}_3 - \widetilde{\lambda}_1)\beta\widetilde{S}_m\widetilde{I}_f + \widetilde{\lambda}_4(\sigma_1 - \sigma_2)\tau\widetilde{I}_f\right\}, \end{aligned}$$

None

Proof. Using the optimality conditions

$$\frac{\partial H}{\partial \gamma_m} = 0 \text{ and } \frac{\partial H}{\partial \gamma_f} = 0$$

we get

$$\begin{aligned} \widetilde{\gamma_m} &= \frac{1}{C_4}\left\{(\widetilde{\lambda}_4 - \widetilde{\lambda}_2)\beta\widetilde{S}_f\widetilde{I}_m + \widetilde{\lambda}_3(\sigma_1 - \sigma_2)\tau\widetilde{I}_m\right\}(=\widetilde{\gamma_m}), \\ \widetilde{\gamma_f} &= \frac{1}{C_5}\left\{(\widetilde{\lambda}_3 - \widetilde{\lambda}_1)\beta\widetilde{S}_m\widetilde{I}_f + \widetilde{\lambda}_4(\sigma_1 - \sigma_2)\tau\widetilde{I}_f\right\}(=\widetilde{\gamma_f}). \end{aligned}$$

This control is bounded with upper and lower bounds are respectively 0 and 1 i.e. $\gamma_m = 0$ if $\widetilde{\gamma_m} < 0$ and $\gamma_m = 1$ if $\widetilde{\gamma_m} > 1$ and $\gamma_f = 0$ if $\widetilde{\gamma_f} < 0$ and $\gamma_f = 1$ if $\widetilde{\gamma_f} > 1$, otherwise $\gamma_m = \widetilde{\gamma_m}$ and $\gamma_f = \widetilde{\gamma_f}$. Hence for this controls (γ_m^*) and (γ_f^*) we get the optimum value of the functional J given by Eq. (3). Hence the theorem.None

4 Numerical simulation for the optimal control problem

To demonstrate the effect of optimal control strategy, we accomplished the numerical simulation in this section. The control profile is applied for the period of 10 years. The optimality system in Section 3 is solved by iterative method with the help of Runge-Kutta fourth order procedure (see Jung et. al.[18], Lenhart and Workman[19], *etc*). At first we solve the state equations by the forward Runge-Kutta fourth order procedure for the time interval [0, 10] starting with an initial guess for the adjoint variables. Then we use the backward

Runge-Kutta fourth order procedure to solve the adjoint variables in the same time interval with the help of the solutions of the state variables and the transversality conditions.

From Fig. 2, it is evident that the control takes the value nearly 0.75 in starting period and after some period of time (nearly at the point of time 7 years of optimal strategic time period) the profile values are reduced slowly and finally comes to nearly 2.5 level. It exhibits that the screening effect should continued till seven years at the same level and after that the screening may be reduced slowly and come down to the level 2.5. Fig. 3 also reveals the similar type of phenomena but this profile is to be maintained at 0.5 throughout the optimal control strategic period. It shows that the screening effect should be maintained according to the costs applied on screening HIV and AIDS patients over the whole period of control. Here the point is clear from the observation that the awareness of females are not to be slows down because of their awareness compared to that of males in countries like India. So the screening has to be continued in the same level till the end of optimal control strategic period. From these Fig. 2 and Fig. 3, we observed that the screening effect on HIV/AIDS to be maintained depends on the awareness of the male and female in the HIV/AIDS population. Fig. 4 showing how the control profile of γ_m getting changed by the effect/change in the cost values. It is clear that the cost effect plays a vital role on controlling the optimal control strategy/scheme. Also Fig. 5 shows, there is no effect happened even though different values of costs are applied because of the awareness fact told earlier. It is evident from the Fig. 6 - Fig. 10 that the optimal control strategy gives the better result than the fixed control effect on the classes I_m, I_f, A, S_m and S_f. In these figures, the comparison of optimal control scheme with different fixed control values of γ_m and γ_f is carried out. It also shows that these screening control makes the impact on infected population among the total population which makes the existence of susceptible population only and increases it by the rapid decrease of the HIV and AIDS peoples volume.

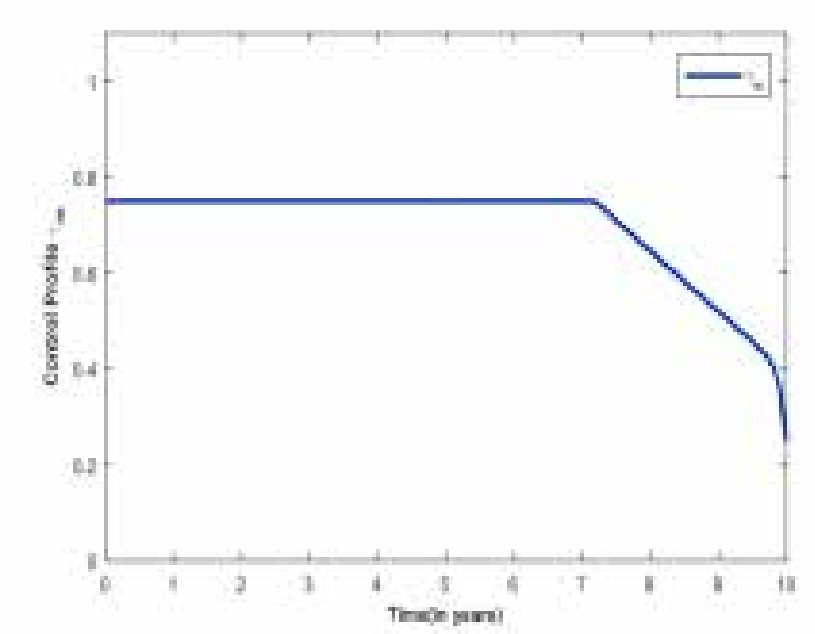

Fig. 2: Simulation of the model Eq. (2) showing the control profile γ_m of the intervention strategies

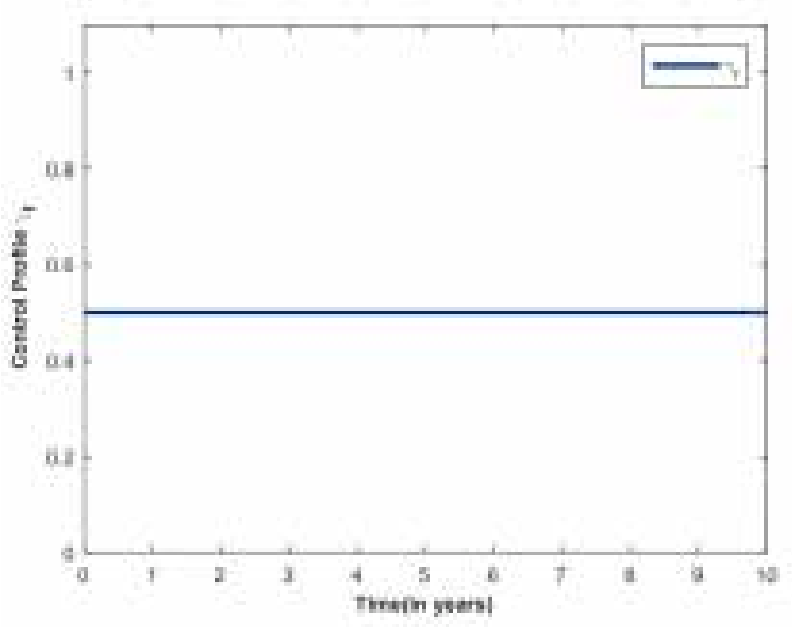

Fig. 3: Simulations of the model Eq. (2) showing the control profile γ_f of the intervention strategies

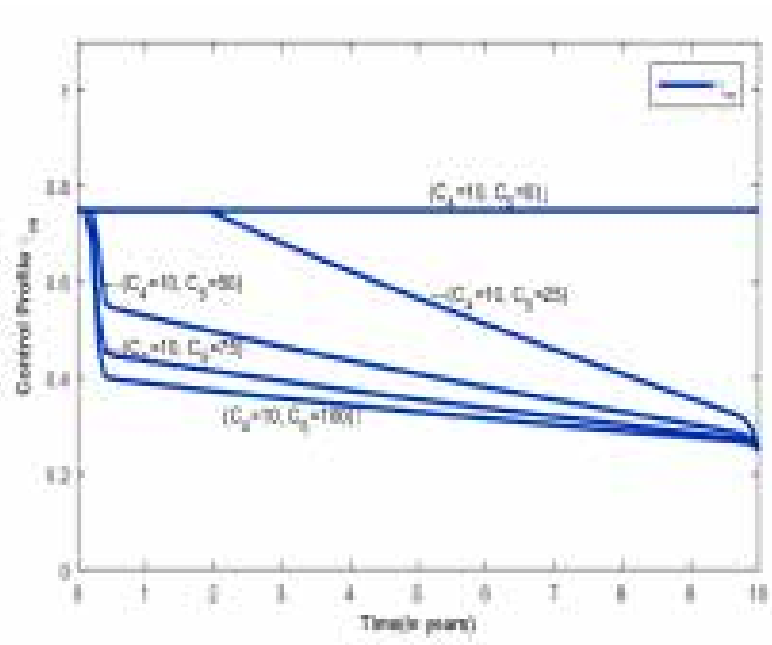

Fig. 4: Simulations of the model Eq. (2) showing the effect of costs $C_4,\ C_5$ on control profile γ_m

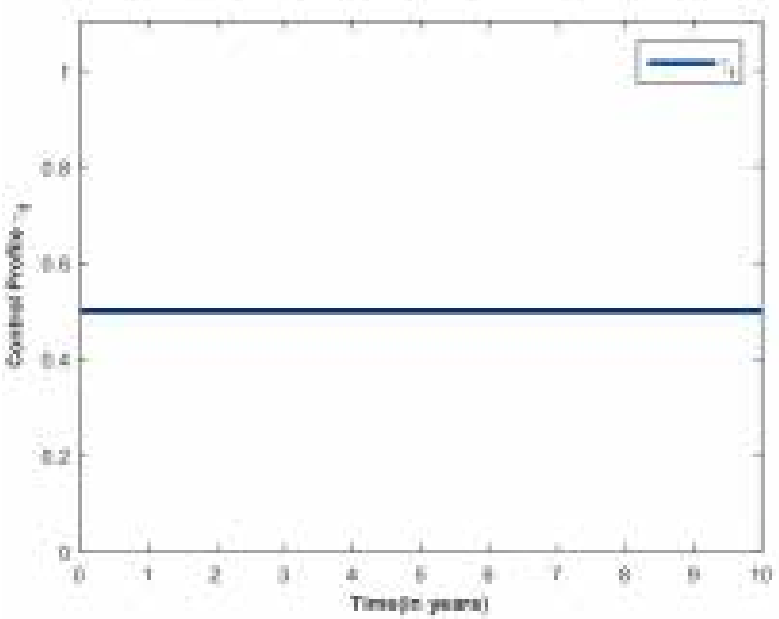

Fig. 5: Simulations of the model Eq. (2) showing the effect of costs $C_4,\ C_5$ on control profile γ_m

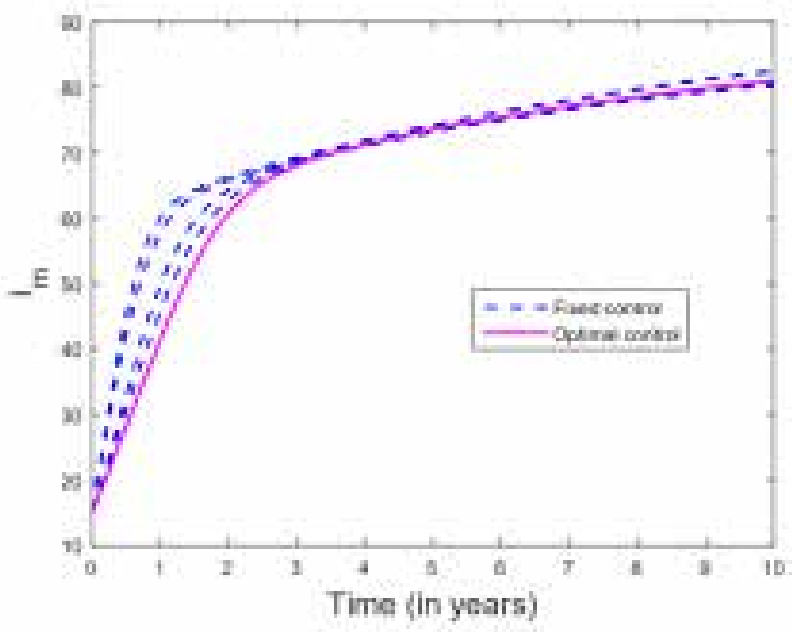

Fig. 6: Comparison of optimal control effect on on I_m with different fixed control values of γ_m and γ_f of the model Eq. (2)

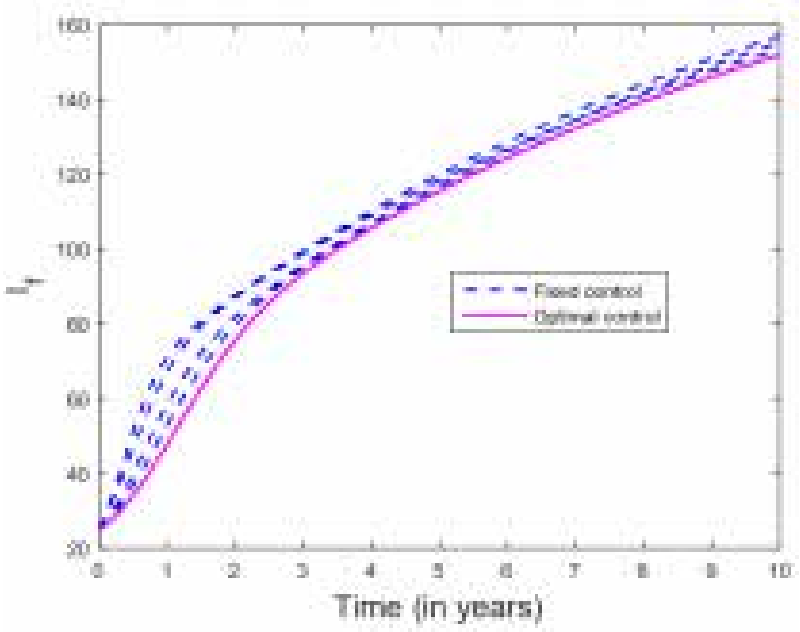

Fig. 7: Comparison of optimal control effect on I_f with different fixed control values of γ_m and γ_f of the model Eq. (2)

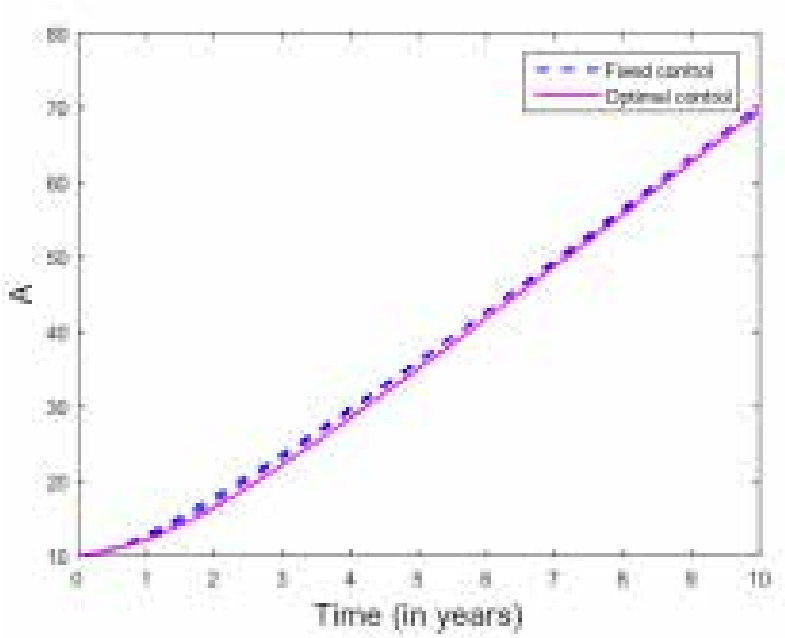

Fig. 8: Comparison of optimal control effect on A with different fixed control values of γ_m and γ_f of the model Eq. (2)

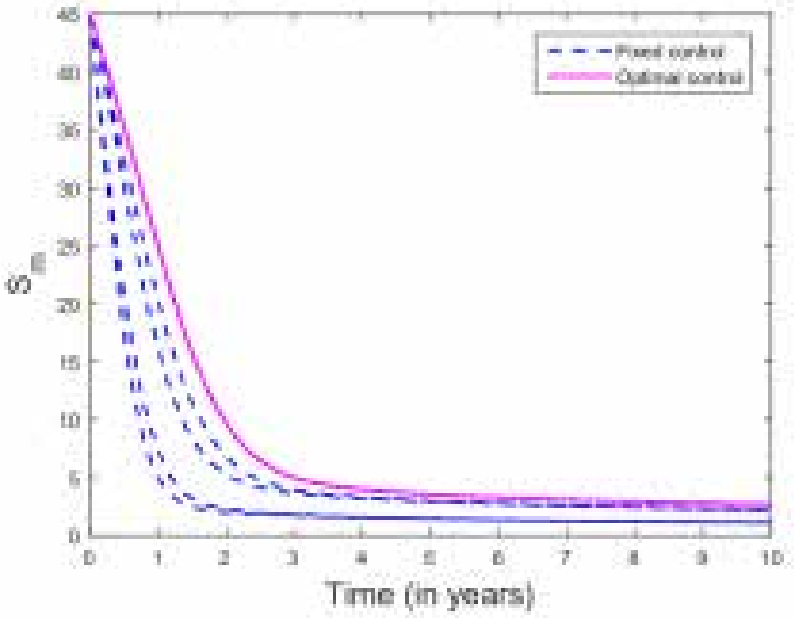

Fig. 9: Comparison of optimal control effect on S_m with different fixed control values of γ_m and γ_f of the model Eq. (2)

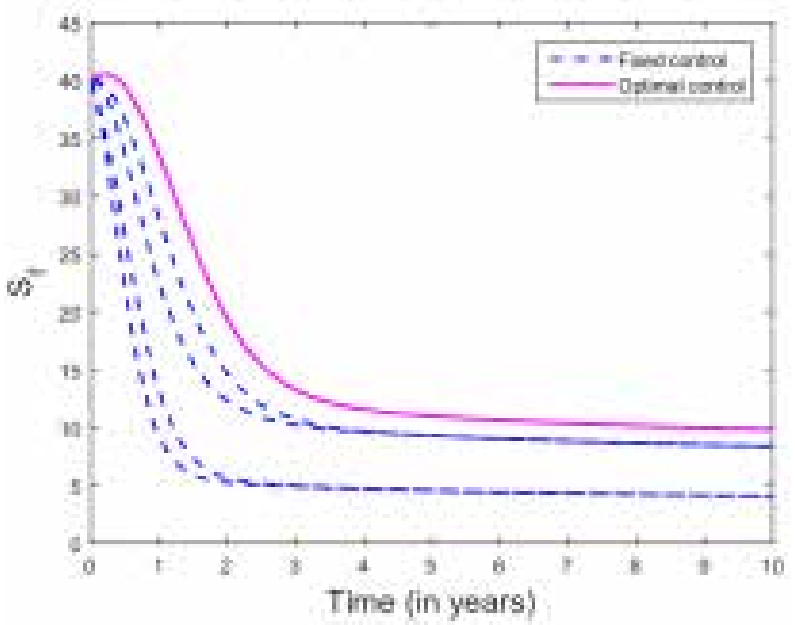

Fig. 10: Comparison of optimal control effect on S_f with different fixed control values of γ_m and γ_f of the model Eq. (2)

5 Conclusion

It is widely accepted that treatment is an effective way to control the transmission of any infectious disease. Delay in treatment can lead to many new infections. So it is necessary to identify/screening the infectives in their early stage and to provide proper counseling and treatment to those infectives. Here we have extended the work done in [10] by making the the parameters γ_m and γ_f as time dependent, where authors of [10] have considered a sex-structured model for HIV/AIDS with constant rate of screening (with proper counseling) parameters γ_m and γ_f. Using optimal control theory, time dependent rate of screening is obtained and it has been verified that optimal control theory is more effective than the constant rate of screening. Numerical simulation is carried out to support our analytical findings. The control profiles of the screening parameters are computed. From the numerical simulation, it has been verified that the optimal control strategy gives better result through the comparison of infected population in both male an female, AIDS population and susceptible male and female populations.

From Fig. 2 and Fig. 3 we observed that the screening effect should be maintained according to the screening costs applied on HIV and AIDS patients on control strategy/scheme period. From these observations, we see that the awareness of females are not to be slows down because of their actual/regular awareness compared to that of males in countries like India. So the screening in female population has to be continued in the same level till the end of optimal control strategic period. Overall, we observed that the screening effect on HIV/AIDS to be maintained depends on the awareness level of the male and female in any particular region on the HIV/AIDS population.

So from this particular research work, we got the notable effect on male and female to be screened among whole population in any region on account of the HIV/AIDS population.

References

[1] Kar, T.K., Batabyal, A., (2011) Stability analysis and optimal control of an SIR epidemic model with vaccination *Biosystems* **104** (1), (2011), 127–135.

[2] Chakraborty, K., Das, S., Kar, T.K., (2012) Optimal control of effort of a stage structured prey–predator fishery model with harvesting *Nonlinear Analysis: Real World Applications* **12** (2011), 3452–3467.

[3] Okosun, K.O., Makinde, O.D., Takaidza, I., (2013) Impact of optimal control on the treatment of HIV/AIDS and screening of unaware infectives *Applied Mathematical Modelling* **37** (2013), 3802–3820.

[4] Ghosh, M., Lashari, A.A., Li, X.Z., (2013) Biological control of malaria: A mathematical model *Applied Mathematics and Computation* **219** (2013), 7923–7939.

[5] Karrakchou, J., Rachik, M., Gourari, S., (2006) Optimal control and infectiology: Application to an HIV/AIDS model *Applied Mathematics and Computation* **177** (2006), 807–818.

[6] Bowong, S., Alaoui, A.M.A., (2013) Optimal intervention strategies for tuberculosis *Commun Nonlinear Sci Numer Simulat* **18** (2013), 1441–1453.

[7] Lashari,A.A., Hattaf, K., Zaman,G., and Li,X.Z., (2013) Backward bifurcation and optimal control of a vector borne disease *Applied Mathematics and Information Sciences* **7**(1) (2013), 301–309.

[8] Hattaf, K., Rachik, M., Saadi, S., Tabit, Y. and Yousfi, N., (2009a) Optimal Control of Tuberculosis with Exogenous Reinfection *Applied Mathematical Sciences* **3**(5) (2009), 231–240.

[9] S.Athithan, Ghosh, M., (2013) Mathematical modelling of TB with the effects of case detection and treatment *International Journal of Dynamics and Control* **1** (3) (2013), 223–230.

[10] S.Athithan, Mini Ghosh, (2014) Analysis of a sex-structured HIV/AIDS model with the effect of screening of infectives *International Journal of Biomathematics*, **7** (5), 2014, 1450054 (15 pages), DOI: 10.1142/S1793524514500545.

[11] O. Diekmann, J.A.P.Heestbeek and J.A.J Metz,(1990) On the definition and computation of the basic reproduction ratio R_0 in models for infectious diseases in heterogeneous populations, *J. Math. Bio.* **28** 365–382.

[12] P. Van den Driessche, James Watmough, (2002) Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission *Mathematical Biosciences* **180**, 29–48.

[13] Zaman, G., Kang, Y.H., Jung, I.H., (2008) Stability analysis and optimal vaccination of an SIR epidemic model, *Biosystems* **93** (2008), 240–249.

[14] Bartl, M., Li, P., Schuster, S., (2010) Modelling the optimal timing in metabolic pathway activation- Use of Pontryagin's Maximum Principle and role of the Golden section *Biosystems* **101** (1), (2010), 67–77.

[15] Kar, T.K., Ghorai, A., Jana, S., (2012) Dynamics of pest and its predator model with disease in the pest and optimal use of pesticide *J. Theor. Biol.* **310** (2012), 187–198.
[16] Lukes, D.L., (1982) Differential equations: classical to controlled *Mathematics in SCIENCE and Engineering, Academic Press* **162** (1982).
[17] Pontryagin, L.S., Boltyanskii, V.G., Gamkrelidze, R.V., Mishchenko, E.F., The Mathematical Theory of Optimal Processes *Wiley* New York **162** (1962).
[18] Jung, E., Lenhart, S., Feng, Z., (2002) Optimal control of treatments in a two-strain tuberculosis model *Discrete Contin. Dyn. Syst. Ser. B* **2** (4) (2002) 473–482.
[19] Lenhart, S., Workman, J.T., Optimal Control Applied to Biological Model. Mathematical and Computational Biology Series *Chapman & Hall/CRC* 2007.