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Optimal Control Analysis for HIV/AIDS Pediatrics Model

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Abstract:

A model to assess the impact of some control measures in the dynamics of HIV/AIDS Pediatrics is considered. The model is proposed and analyzed using differential equations. We have introduced appropriate optimal control measures and their impact on disease control and also investigated the necessary conditions for the control of disease. An optimal control theory is used to identify and evaluate the control policies. The controls account for the cost associated with preventive measure control for the mother and antiviral treatment control for infected pediatrics is considered. We use Pontryagin's Maximum Principle of optimal control theory. The optimality system is derived and then solved numerically using matlab.

Keywords: Optimal Control, Pontryagin's Maximum Principle, Prevention, Treatment, Vertical transmission.

1. INTRODUCTION

Infectious disease can be transmitted in many ways, some of which can be classified as either horizontal or vertical. In the case of HIV/AIDS, horizontal transmission can result from direct physical contact between an infected individual and a susceptible individual. Vertical transmission, on the other hand, can result from direct transfer of a disease from an infected mother to an unborn or newborn offspring. Vertical transmission of HIV/AIDS can occur during pregnancy, delivery or breastfeeding and is influenced by many factors, including maternal viral load and the type of delivery [1]. The vast majority of HIV-positive children worldwide acquire the infection through vertical transmission. HIV infection transmitted from an HIV-infected mother to her child during pregnancy, labour, delivery or breastfeeding is known as mother-

to-child transmission (MTCT). According to global health status report over, 3.2 million children were living with HIV in 2013. In the same year 240 000 were newly infected with HIV. Only 23% of children living with HIV receive treatment, compared to 37% of adults. The World Health Organization (WHO) estimated 3.2 million children were living with HIV at the end of 2013, mostly in sub-Saharan Africa. Majority of them acquire HIV from their HIV-infected mothers during pregnancy, birth or breastfeeding. By introducing effective interventions the risk of mother-to-child HIV transmission can be reduced. However, such interventions are still not widely accessible or available in most resource-limited countries where the burden of HIV is highest. The prevention of mother-to-child transmission (PMTCT) is a highly effective intervention and has huge potential to improve both maternal and child health.

HIV infection spreads rapidly in populations through unsafe sexual interaction with an accompanying risk of vertical transmission. Therefore, we have considered this aspect in the modeling of HIV/AIDS epidemic, where the infection may be transmitted vertically at a very high rate. Various mathematical models have been used extensively in research into the epidemiology of HIV/AIDS, which helps us to improve our understanding of the major contributing factors in reducing the infection. In recent years, a few studies of vertical transmission have been conducted to describe the effects of various epidemiological and demographical factors. In particular, Brauer [2] considered models for disease with vertical transmission with non-linear population dynamics. Busenberg and Cooke [3] discussed about the variety of diseases that transmit both horizontally and vertically, and gave a comprehensive survey of the formulation and the mathematical analysis of compartmental models that also incorporate vertical transmission. Li et al [4] proposed a model for an infectious disease that spreads in the host population through both horizontal and vertical transmission. Wang et. al [5] explains the dynamic characteristics of the HIV mother to child transmission (MTCT) epidemic in China, and based on their result they have suggested some remedies to eradicate mother to child transmission of HIV/AIDS epidemic. Gani et al [6] proposed a deterministic model dynamic characteristic analysis of HIV Mother to Child Transmission in India, which is analytically solvable and used to analyze how the parameters related to key factors that alters the trend of the epidemic. Based on their model we have constructed optimal control of HIV/AIDS Pediatrics model with preventive measure control for mother and treatment control for the infected pediatrics.

This study aims to characterize the pediatric HIV/AIDS epidemic using deterministic mathematical model to prevent Mother-to-Child-Transmission (MTCT). We have formulated an optimal control model for the transmission dynamics of HIV/AIDS pediatrics with vertical transmission in order to derive optimal control strategies with minimal implementation cost. The mathematical foundation of the control model and the derivation of the optimal control variables are derived using Pontryagin's Maximum Principle [7] and the proof for the existence of the optimal control is established using Fleming and Rishel [8].

Our paper is organized as follows: In Section-2 the formulation of the optimal control model is discussed using non-linear differential equations which describes the

transmission dynamics of hiv/aids pediatrics. In Section 3 optimal control analysis has been discussed using Pontryagin's Maximum principle. In section 4 we discuss the results of numerical simulations and the final section gives conclusions of the paper.

2. MODEL FORMULATION

A non linear optimal control model is formulated to study the dynamics of HIV/AIDS pediatrics with preventive measure control for the mother and treatment control for infected pediatrics. The total population is divided into four compartments. Susceptible mother $M(t)$, Infected pediatrics $P(t)$, Pediatrics on treatment $T(t)$ an AIDS class as $A(t)$. The flowchart of compartmental model is shown in figure.1. In this model we have not considered the infection rate of susceptible mother through their contact with sexual partners, concentrated only on the infected pediatrics born to HIV/AIDS infected mother. π is the rate of recruitment of susceptible mother. μ is the natural death rate. The fraction of new born children are infected during birth are directly recruited in the infective class at rate $\rho(1-u_1(t))M(t)$. We do not consider the direct recruitment of infection rate of susceptible mother but vertical transmission only. Newly infected pediatrics progress to treatment class at the rate $u_2P(t)$ and to AIDS class at the rate $\theta_1P(t)$. We have incorporated direct recruitment of immigrants (infected pediatrics) into the treatment class at rate $m_1P(t)$.Individuals in the AIDS class die at a natural death rate δ.

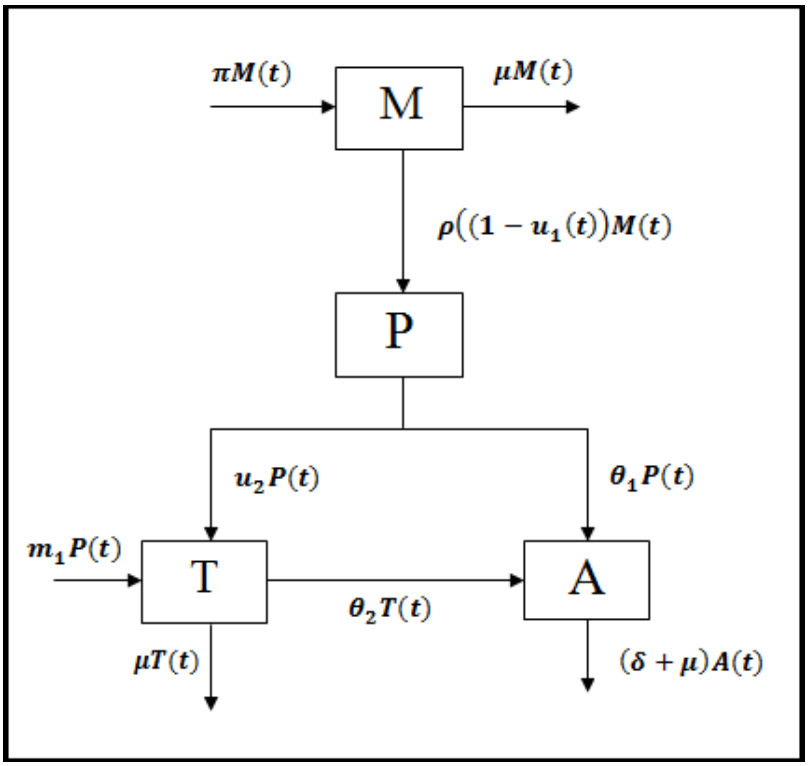

Figure.1: Flow diagram of optimal control HIV/AIDS Pediatrics model

The HIV/AIDS pediatrics model with controls is given by the following nonlinear system of differential equations.

$$\frac{dM(t)}{dt} = \pi M(t) - \mu M(t)$$
$$\frac{dP(t)}{dt} = \rho(1-u_1(t))M(t) - u_2(t)P(t) - \theta_1 P(t) - \mu P(t) \quad (1)$$
$$\frac{dT(t)}{dt} = u_2 P(t) + m_1 P(t) - (\theta_2 + \mu)T(t)$$
$$\frac{dA(t)}{dt} = \theta_1 P(t) + \theta_2 T(t) - (\delta + \mu)A(t)$$

With initial conditions

$M(0) = M_0,\ P(0) = P_0,\ T(0) = T_0,\ A(0) = A_0$ *and*

$N(t) = M(t) + P(t) + T(t) + A(t)$

3. OPTIMAL CONTROL ANALYSIS

In the above model we have considered two control measures that is preventive measure control for mother and treatment control for infected pediatrics. $u_1(t)$ is the proportion of the susceptible mother that are given preventive measures per unit time. $u_2(t)$ is the antiviral treatment control per unit time. Here the control functions $u_1(t)$ and $u_2(t)$ are bounded by Lebesgue integral function. We investigate the prevention policies to minimize the total number of individuals keeping total cost of the policies low during the spread. The time-dependent optimal control policies can be obtained by minimizing the following objective functional:

$$J(u_1,u_2) = \int_0^{t_f} (A_1 M(t) + A_2 P(t) + A_3 T(t) + \frac{W_1}{2}u_1^2(t) + \frac{W_2}{2}u_2^2(t))dt \quad (2)$$

Subject to the state equations (1) for a given set of initial conditions, where t_f is the final time and the co-efficient A_1, A_2, A_3, W_1, W_2 are balancing cost factors. A quadratic function is implemented for measuring the control cost.

The problem becomes that of finding a pair of functions (u_1^*, u_2^*)

$$J(u_1^*,u_2^*) = \min_U J(u_1,u_2), \quad (3)$$

Where, for $i = 1,2$ *and* LB_i *and* UB_i are fixed constants in $[0,1]$,

$$U = \{(u_1(t),u_2(t)) \in L^1(0,t_f) \parallel 0 \le u_i(t) \le 1, t \in [0,t_f]\}, \quad (4)$$

The pair of function (u_1^*, u_2^*) are the optimal controls. The existence of optimal controls u_1 and u_2 for this model is guaranteed by standard results in Optimal Control Theory by Fleming and Rishel[8]. Necessary conditions that the controls must satisfy are derived via Pontryagin's Maximum Principle. The optimal control problem given by expressions (1)-(4) is equivalent to that of minimizing the Hamiltonian H:

$$\begin{aligned} H = {} & A_1 M(t) + A_2 P(t) + A_3 T(t) + \frac{W_1}{2} u_1^2(t) + \frac{W_2}{2} u_2^2(t) + \lambda_1(t)[\pi M(t) - \mu M(t)] \\ & + \quad \lambda_2(t)[\rho(1 - u_1(t)M(t) - u_2(t)P(t) - \theta_1 P(t) - \mu P(t)] \\ & + \quad \lambda_3(t)[u_2 P(t) + m_1 P(t) \\ & - (\theta_2 + \mu)T(t)] \end{aligned} \tag{5}$$

A standard application of Pontryagin's Maximum Principle [Pontryagin's.L(1962)], We obtain

Theorem 3.1: Let M^*, P^*, T^* *and* A^* be optimal state with associated optimal control variables $(u_1^*(t), u_2^*(t))$ respectively for the optimal control problem. Then there exist adjoint variables $\lambda_i(t)(i = 1,2,3,4)$ satisfying

$$\begin{aligned} \dot{\lambda}_1(t) &= -A_1 - \lambda_1(t)[\pi - \mu] - \lambda_2[\rho(1 - u_1(t))] \\ \dot{\lambda}_2(t) &= -A_2 + \lambda_2(t)[u_2(t) + \theta_1 + \mu] - \lambda_3(t)[u_2(t) + \mu] \\ \dot{\lambda}_3(t) &= -A_3 + \lambda_3(t)[\theta_2 + \mu] \end{aligned} \tag{6}$$

With transversality conditions,

$$\lambda_1(t_f) = \lambda_2(t_f) = \lambda_3(t_f) = 0 \tag{7}$$

Furthermore the control functions $u_1^*(t), u_2^*(t)$ *are given by,*

$$\begin{aligned} u_1^*(t) &= \min\left\{\max\left\{0, \frac{\lambda_2(t)M(t)}{W_1}\right\}, 1\right\} \\ u_2^*(t) &= \min\left\{\max\left\{0, \frac{(\lambda_2 - \lambda_3)P(t)}{W_2}\right\}, 1\right\} \end{aligned} \tag{8}$$

Proof: To determine the ad joint equations and the transversality conditions, we use the Hamiltonian H in equation (4). The form of the adjoint equations and transversality conditions are standard results from Pontryagin's Maximum Principle. We differentiate the Hamiltonian with respect to each state (respectively as stated above), then the adjoint system can be written as:

$$\dot{\lambda}_1(t) = -\frac{\partial H}{\partial M}, \quad \dot{\lambda}_2(t) = -\frac{\partial H}{\partial P}, \quad \dot{\lambda}_3(t) = -\frac{\partial H}{\partial V}$$

With transversality conditions,

$$\lambda_1(t_f) = \lambda_2(t_f) = \lambda_3(t_f) = 0$$

To get the characterization of the optimal control we have to solve the equations,

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

for $u_1^*(t), u_2^*(t)$ *subject to the constraints, the characterization (8) can be derived and we have*

$$\frac{\partial H}{\partial u_1(t)} = W_1 u_1(t) - \lambda_2(t)\rho M(t) = 0$$

$$\frac{\partial H}{\partial u_2} = W_2 u_2 - \lambda_2(t)P(t) + \lambda_3(t)P(t) = 0$$

Then by standard variation arguments with the control bounds, we obtain the properties (8)

4. SIMULATION RESULTS AND DISCUSSIONS.

This section discusses the numerical simulations of the optimality system and the corresponding results of varying the optimal controls u_1 and u_2 using the real parameter values. Numerical solutions to the optimality system composing the state equation (1) and adjoint equation (6) are carried out in MATLAB 7.12.0 (2011a). We have plotted individuals by considering parameter values with initial conditions as $S(0) = 988,\ P(0) = 1,\ T(0) = 1,$. The weight constant of the objective functional are W_1= 10, W_2= 10, A_1= 10, A_2=10, A_3=10. The algorithm is the forward-backward scheme; starting with an initial guess for the optimal controls. The state variables are then solved forward in time using a Runge-Kutta method of the fourth order. Then, those state variables and initial guess for the controls are used to solve the adjoint Equation backward in time with given final conditions (7), again employing a fourth order Runge-Kutta method. The controls are updated and used to solve the state and then the adjoint system. This iterative process terminates when current state, adjoint, and control values converge sufficiently [9, 10]. The results from our simulations are displayed in the below figures.

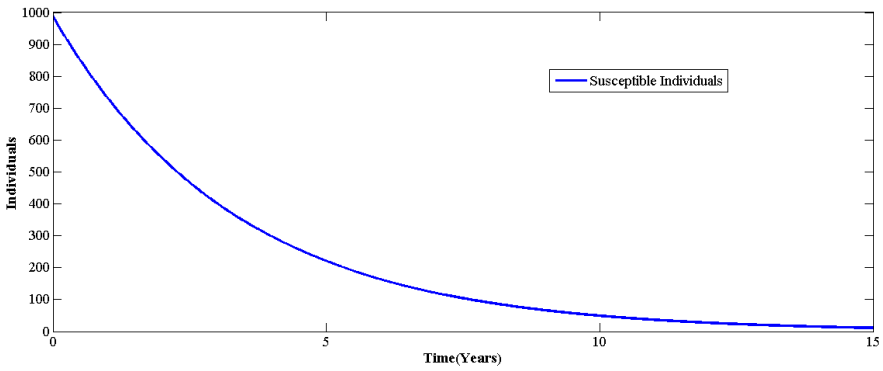

Figure.2: Simulations of the HIV/AIDS pediatrics model for the Susceptible individuals

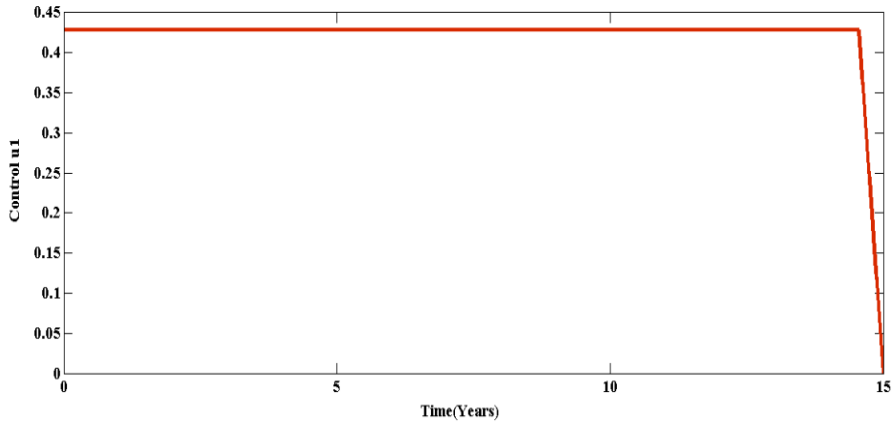

Figure.3: Time dependent optimal control strategy computed for control u_1

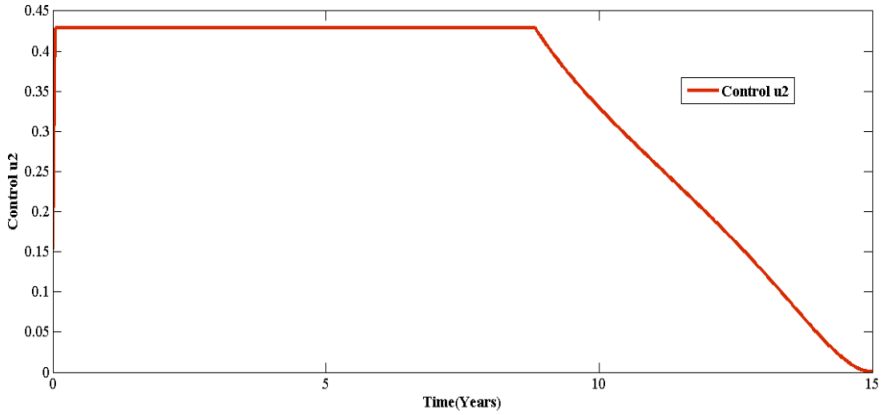

Figure.4 Time dependent optimal control strategy computed for control u_2

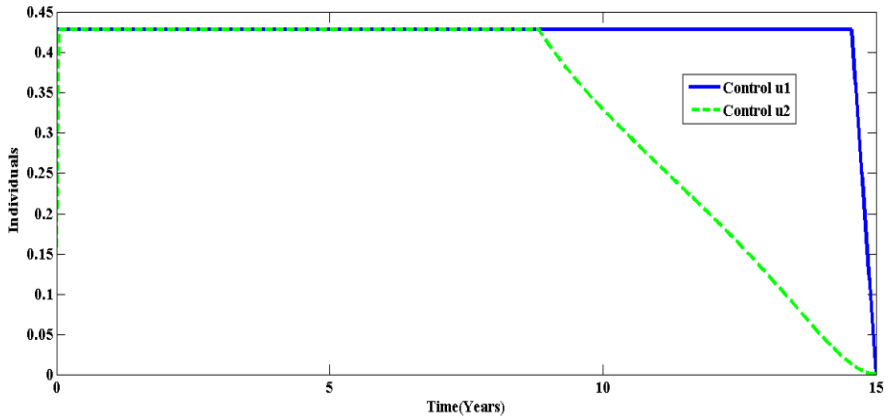

Figure.5 Time dependent optimal control strategies computed for both u_1 & u_2

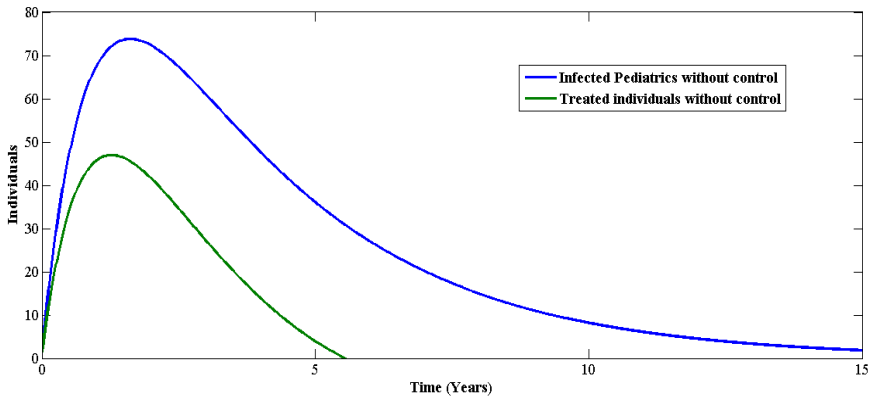

Figure.6: Simulations of the HIV/AIDS pediatrics model for the Infected pediatrics and treated individuals without controls.

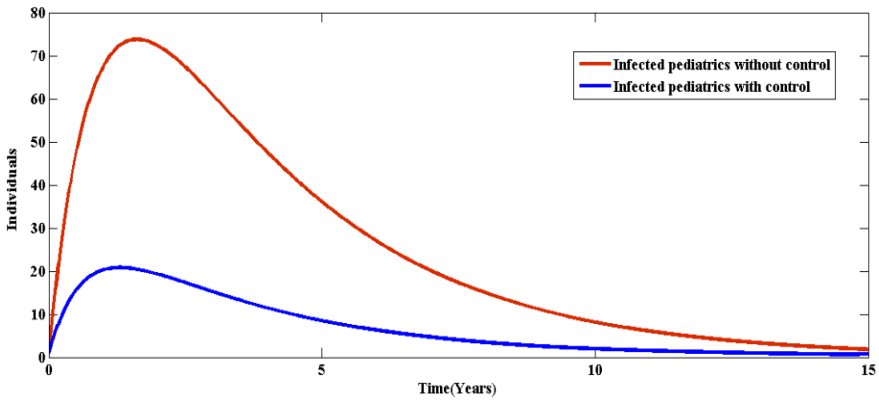

Figure.7: Simulations of the HIV/AIDS pediatrics model for the Infected pediatrics individuals with and without control.

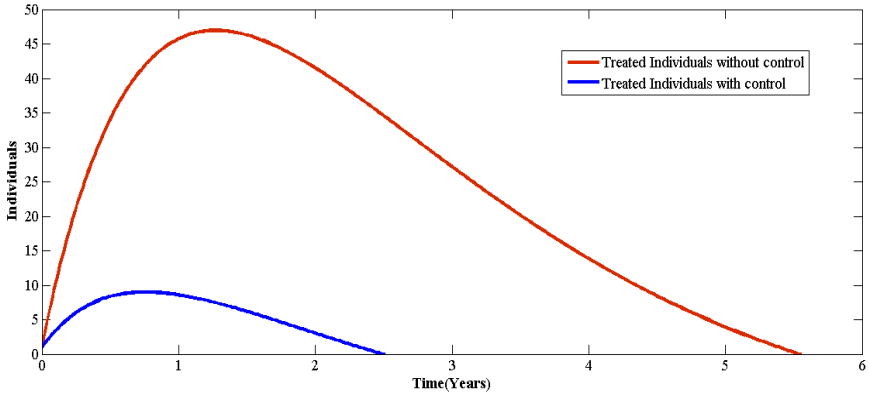

Figure.8: Simulations of the HIV/AIDS pediatrics model for the Infected pediatrics individuals with and without treatment control.

We have plotted individuals with and without control by considering real parameter values.When the controls are optimimized there is a significant decrease in number of individuals as shown in the above figures. The control plot u_1 is at the upper bound till the final time and control u_2 gradually dropped from upper bound to lower bound after 8 years.Figure 2 shows the decrease in the susceptible individualswith preventive measure control. Figure 3 & 4 represents the plot for controls u_1 and u_2. The figure 5 represents the plot for both the controls. Figure 6 represents the infected pediatrics and treated individuals without control. Figure 7 represents the plot for pediatrics with control and without control. Figure 8 represents the plot for the treated individuals with and without control.

5. CONCLUSION

An optimal control problem of the transmission dynamics of the pediatrics HIV/AIDS disease has been presented. We used Pontryagin's maximum principle to characterize the controls and derive the optimality system. Numerical simulations of the resulting optimality system showed that, successful use of preventive measure control and treatment control policies has a significant impact in reducing the number of susceptible and infected individuals.

Conflict of Interests:

There is no conflict of interests regarding the publication of this paper.

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