Optimal Control of HIV/AIDS Epidemic Model with Two Latent Stages, Vertical Transmission and Treatment

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Abstract. In this research, we discussed about optimal control of HIV/AIDS epidemic model with two latent stages, vertical transmission and treatment. In this model, the population is divided into five sub-populations, namely susceptible subpopulation, slow latent subpopulation, fast latent subpopulation, symptomatic subpopulation and AIDS subpopulation. The latent stage is divided into slow latent and fast latent stage depend on the condition of immune system which is different for each individual. Treatment (ART/antiretroviral) is given to infected individu in symptomatic stage. The rate of treatment from symptomatic stage to slow latent stage and to fast latent stage are set as $u_1(t)$ and $u_2(t)$ control variable, respectively. Here, the objective of optimal control is to minimize the number of infected as well as the cost of controls. The optimal control is obtained by applying Pontryagin’s Principle. In the end, we show some numerical simulations by using Forward-Backward Sweep Method. Numerical simulation result show that the combination of $u_1$ and $u_2$ control is the most effective control to reduce the number of infected/symptomatic subpopulation with minimum cost of controls.

Keywords: HIV/AIDS; two latent stages; vertical transmission; treatment; optimal control, Pontryagin’s Principle.

1. Introduction
Acquired Immune Deficiency Syndrome (AIDS) is the disease in human immune system that caused by human immune deficiency virus (HIV). HIV spread through both horizontal and vertical transmission. Horizontal transmission occurs through direct or indirect contact with infected individu, such as sexual intercourse, blood transfusion, using the HIV-contamined injection equipment and direct contact with HIV-infected blood or fluid. Vertical transmission is the process of spreading HIV/AIDS from a mother who has positive HIV to her baby, that can be happened during pregnancy, childbirth, or breastfeeding [1],[2].

AIDS has developed into a global epidemic in the world since first identified as a disease in 1981. There is no effective medicine to cure HIV/AIDS. One of the prevention strategy is avoid the contact with the virus. The spreading of HIV/AIDS can be represented in mathematical model. By analyzing the appropriate mathematical model, the better understanding of the major factors that caused the pandemic of HIV / AIDS can be obtained and be useful information to know the best prevention strategy. Many researches have been developed this model. May and Anderson [3] introduce the HIV /AIDS model for the first time at 1986. Li et al. [1] discussed about global dynamics of an SEIR epidemic model with vertical transmission. At 2013, Huo and Feng [4] constructed and analyzed an HIV/AIDS epidemic model with different latent stages (slow latent and fast latent) and treatment. Mahato et al., [2] proposed...
a mathematical model SEIA with vertical transmission of AIDS epidemic. Shofianah et al [5] developed model in Huo and Feng [4] by adding vertical transmission.

The optimal control of HIV/AIDS epidemic model also have been developed. Generally, the aim of optimal control on these cases is to minimize the infected subpopulation as well as the cost of control. In 2014, Sule and Abdullah discussed the treatment and education as control strategy. Numerical simulation show that treatment and education for infected individu has positive impact for the control of HIV/AIDS spreading. Silva and Torres (2017) studied the optimal control of HIV/AIDS epidemic model through PrEP. Based on numerical simulation, PrEP significantly reduce the spreading of HIV. Marsudi (2019) studied optimal control of HIV model with changing behavior through an education campaign, screening and treatment.

Here, we construct HIV/AIDS model with control and solve this optimal control problem. We construct HIV/AIDS model with control from model in [5], that is the HIV/AIDS epidemic model with two latent stages, vertical transmission and treatment. This model has some assumptions: some of the susceptible individuals have other chronic diseases, the vertical transmission is happened in case infected mother (in fast latent stage), the infant from infected mother always infected and enter the symptomatic stage, the number of infected baby is less than the number of individu who died because AIDS disease.

After that, we solve optimal control problem by applying Minimum Pontryagin Principle.

2. Mathematical Model

HIV/AIDS epidemic model with two latent stages, vertical transmission and treatment as in [5] consists of five subpopulations, namely susceptible (S), slow latent (I₁), fast latent (I₂), symptomatic (J) and AIDS (A). The model can be written as follows

\[
\begin{align*}
\frac{dS}{dt} &= \Lambda - \gamma I_2 - (\beta_1 I_2 S + \beta_2 JS) - \mu S, \\
\frac{dI_1}{dt} &= p\beta_1 I_2 S + q\beta_2 JS + \xi_1 J - (\varepsilon + \mu)I_1, \\
\frac{dI_2}{dt} &= (1-p)\beta_1 I_2 S + (1-q)\beta_2 JS + \varepsilon I_1 + \xi_2 J - (p_1 + \mu)I_2, \\
\frac{dJ}{dt} &= (p_1 + \gamma)I_2 - (\xi_1 + \xi_2 + p_2 + \mu)J, \\
\frac{dA}{dt} &= p_2 J - (\mu + \alpha)A.
\end{align*}
\]

The parameters that used in the models are described in Table 1.

Based on dynamical analysis in [5], model (1) has two equilibrium point, that is disease-free equilibrium and endemic equilibrium point. If \(R_0 < 1\), the disease-free equilibrium point will be globally asymptotically stable, while if \(R_0 > 1\), the endemic equilibrium point globally asymptotically stable. Therefore, when \(R_0 > 1\), the outbreak of HIV/AIDS occured. We need to apply control in this condition. We add two time-dependent controls in the model (1), that is treatment \(u_1(t)\) and \(u_2(t)\) by changing constant treatment rate \(\xi_1\) and \(\xi_2\), respectively. The \(u_1(t)\) control treatment is the treatment for individu in slow latent stage \(I_1\), while the \(u_2(t)\) control treatment is the treatment for individu in fast latent stage.
I$_2$. Now we have the model (1) with controls,

\[
\frac{dS}{dt} = \Lambda - \gamma I_2 - (\beta_1 I_2 S + \beta_2 JS) - \mu S,
\]

\[
\frac{dI_1}{dt} = p\beta_1 I_2 S + q\beta_2 JS + u_1 J - (\varepsilon + \mu) I_1,
\]

\[
\frac{dI_2}{dt} = (1 - p) \beta_1 I_2 S + (1 - q) \beta_2 JS + \varepsilon I_1 + u_2 J - (p_1 + \mu) I_2,
\]

\[
\frac{dJ}{dt} = (p_1 + \gamma) I_2 - (u_1 + u_2 + p_2 + \mu) J,
\]

\[
\frac{dA}{dt} = p_2 J - (\mu + \alpha) A.
\]

with $S(0) = S_0, I_1(0) = I_{10}, I_2(0) = I_{20}, J(0) = J_0, A(0) = A_0$ as initial conditions.

3. Optimal Control

The aim for optimal control problem of model (2) is to minimize this cost function as objective function that given by

\[
F[u_1, u_2] = \int_0^T \left( \frac{w}{2} J^2 + \frac{w_1}{2} u_1^2 + \frac{w_2}{2} u_2^2 \right) dt
\]

with equation system (2) as the constraint. Here $w, w_1, w_2$ are weight related to symptomatic subpopulation, control $u_1$ and control $u_2$, respectively. $T$ is final time of control. The optimal control is determined such that

\[
F[u_1^*, u_2^*] = \min\{F[u_1, u_2]|u_1, u_2 \in U\}
\]

where $U = \{0 \leq u_1, u_2 \leq 1\}$. Then we construct Hamiltonian function,

\[
H = \frac{w}{2} J + \frac{w_1}{2} u_1^2 + \frac{w_2}{2} u_2^2 + \lambda_S (\Lambda - \gamma I_2 - (\beta_1 I_2 S + \beta_2 JS) - \mu S)
+ \lambda_{I_1} (p\beta_1 I_2 S + q\beta_2 JS + u_1 J - (\varepsilon + \mu) I_1)
+ \lambda_{I_2} ((1 - p) \beta_1 I_2 S + (1 - q) \beta_2 JS + \varepsilon I_1 + u_2 J - (p_1 + \mu) I_2)
+ \lambda_J ((p_1 + \gamma) I_2 - (u_1 + u_2 + p_2 + \mu) J) + \lambda_A (p_2 J - (\mu + \alpha) A)
\]

where $\lambda_S, \lambda_{I_1}, \lambda_{I_2}, \lambda_J, \lambda_A$ are costate variables.

Based on Pontryagin’s Principle, the optimal solution of Hamiltonian function can be obtained if it satisfy these conditions

3.1. State Equations

By differentiating the Hamiltonian function with respect to each costate variable, we get the state equations:

\[
\frac{dS}{dt} = \frac{\partial H}{\partial \lambda_S} = \Lambda - \gamma I_2 - (\beta_1 I_2 S + \beta_2 JS) - \mu S,
\]

\[
\frac{dI_1}{dt} = \frac{\partial H}{\partial \lambda_{I_1}} = p\beta_1 I_2 S + q\beta_2 JS + u_1 J - (\varepsilon + \mu) I_1,
\]

\[
\frac{dI_2}{dt} = \frac{\partial H}{\partial \lambda_{I_2}} = (1 - p) \beta_1 I_2 S + (1 - q) \beta_2 JS + \varepsilon I_1 + u_2 J - (p_1 + \mu) I_2,
\]

\[
\frac{dJ}{dt} = \frac{\partial H}{\partial \lambda_J} = (p_1 + \gamma) I_2 - (u_1 + u_2 + p_2 + \mu) J,
\]

\[
\frac{dA}{dt} = \frac{\partial H}{\partial \lambda_A} = p_2 J - (\mu + \alpha) A.
\]
with $S(0) = S_0, I_1(0) = I_{10}, I_2(0) = I_{20}, J(0) = J_0, A(0) = A_0$ as initial conditions.

3.2. Costate Equations
Costate equation is negative value of the Hamiltonian function differentiated with respect to costate variable:

$$\frac{d\lambda_S}{dt} = -\frac{\partial H}{\partial S} = (\beta_1 I_2 + \beta_2 J + \mu) \lambda_S - (p \beta_1 I_2 + q \beta_2 J) \lambda_{I_1} - ((1 - p) \beta_1 I_2 + (1 - q) \beta_2 J) \lambda_{I_2},$$

$$\frac{d\lambda_{I_1}}{dt} = -\frac{\partial H}{\partial I_1} = (\epsilon + \mu) \lambda_{I_1} - \epsilon \lambda_{I_2},$$

$$\frac{d\lambda_{I_2}}{dt} = -\frac{\partial H}{\partial I_2} = (\beta_1 S + \gamma) \lambda_S - p \beta_1 S \lambda_{I_1} - ((1 - p) \beta_1 S - p_1 - \mu + \gamma) \lambda_{I_2} - p_1 \lambda_J,$$

$$\frac{d\lambda_J}{dt} = -\frac{\partial H}{\partial J} = -\frac{w}{2} + \beta_2 S \lambda_S - (q \beta_2 S = u_1) \lambda_{I_1} - ((1 - q) \beta_2 S + u_2) \lambda_{I_2}$$

$$- (-u_1 - u_2 - p - \mu) \lambda_J - p_2 \lambda_A,$$

$$\frac{d\lambda_A}{dt} = -\frac{\partial H}{\partial A} = (\mu + \alpha) \lambda_A,$$

with $\lambda_S(T) = \lambda_{I_1}(T) = \lambda_{I_2}(T) = \lambda_J(T) = \lambda_A(T) = 0$ as transversal conditions.

3.3. Stationary Conditions
By differentiating the Hamiltonian function with respect to each variable control, we get the stationary conditions:

$$\frac{\partial H}{\partial u_1} = 0$$

$$w_1 u_1(t) + \lambda_{I_1} J(t) - J(t) \lambda_J = 0$$

$$u_1^*(t) = \frac{(\lambda_J - \lambda_{I_1}) J^*(t)}{w_1} \quad (4)$$

$$\frac{\partial H}{\partial u_2} = 0$$

$$w_2 u_2(t) + \lambda_{I_2} J(t) - J(t) \lambda_J = 0$$

$$u_2^*(t) = \frac{(\lambda_J - \lambda_{I_2}) J^*(t)}{w_2} \quad (5)$$

Since $u_1(t)$ and $u_2(t)$ are defined in $0 \leq u_1(t), u_2(t) \leq 1$, then based on (4) and (5), we get

$$u_1^* = \begin{cases} 0, & \text{if } \frac{(\lambda_J - \lambda_{I_1}) J^*(t)}{w_1} \leq 0 \\ \frac{(\lambda_J - \lambda_{I_1}) J^*(t)}{w_1}, & \text{if } 0 < \frac{(\lambda_J - \lambda_{I_1}) J^*(t)}{w_1} < 1 \\ 1, & \text{if } \frac{(\lambda_J - \lambda_{I_1}) J^*(t)}{w_1} \geq 1 \end{cases}$$

$$u_2^* = \begin{cases} 0, & \text{if } \frac{(\lambda_J - \lambda_{I_2}) J^*(t)}{w_2} \leq 0 \\ \frac{(\lambda_J - \lambda_{I_2}) J^*(t)}{w_2}, & \text{if } 0 < \frac{(\lambda_J - \lambda_{I_2}) J^*(t)}{w_2} < 1 \\ 1, & \text{if } \frac{(\lambda_J - \lambda_{I_2}) J^*(t)}{w_2} \geq 1 \end{cases}$$
and optimal control $u_1(t)$ and $u_2(t)$ can be simplified as

$$u_1^* = \min \left\{ \max \left( 0, \frac{(\lambda J - \lambda I_1) J^*(t)}{w_1} \right), 1 \right\}$$

$$u_2^* = \min \left\{ \max \left( 0, \frac{(\lambda J - \lambda I_2) J^*(t)}{w_2} \right), 1 \right\}$$

4. Numerical Simulations

In order to solve the optimal control problem above, we use Forward-Backward Sweep method. We use forward-difference of fourth order Runge Kutta to solve the state equations, while backward-difference of fourth order of Runge Kutta to solve costate equations. In all numerical simulations we use parameter as in Table 1, $S(0) = 561.8, I_1(0) = 51.1, I_2(0) = 14.3, J(0) = 11.2, A(0) = 5$ as initial conditions and $w = 20, w_1 = 20, w_2 = 2$ as weights related to symptomatic subpopulation, control $u_1$ and control $u_2$, respectively.

| Parameter | Description | value |
|-----------|-------------|-------|
| $\Lambda$ | Recruitment rate of the population | 0.545 |
| $\beta_1$ | Transmission coefficient of $I_2$ | 0.0001 |
| $\beta_2$ | Transmission coefficient of $J$ | 0.006 |
| $p$ | Fraction of $S$ being infected by $I_2$ and entering $I_1$ | 0.9 |
| $q$ | Fraction of $S$ being infected by $J$ and entering $I_1$ | 0.9 |
| $\varepsilon$ | Progression rate $I_1$ to $I_2$ | 0.002 |
| $p_1$ | Progression rate $I_2$ to $J$ | 0.01 |
| $p_2$ | Progression rate $J$ to $A$ | 0.03 |
| $\xi_1$ | Treatment rate from $J$ to $I_1$ | $u_1(t)$ |
| $\xi_2$ | Treatment rate from $J$ to $I_2$ | $u_2(t)$ |
| $\gamma$ | Vertical transmission rate | 0.005 |
| $\mu$ | Naturally death rate | 0.01 |
| $\alpha$ | The disease-related death rate | 0.01 |

We simulate 3 strategies that possible to be applied:

(i) Strategy A: implementation control $u_1(t)$

Figure 1: Numerical simulation result of strategy A
(ii) Strategy B: implementation control $u_2(t)$

![Figure 2: Numerical simulation result of strategy B](image1)

(a) The number of subpopulation $J$

(b) The optimal control profile of $u_2(t)$

(iii) Strategy C: implementation of combination control $u_1(t)$ and $u_2(t)$

![Figure 3: Numerical simulation result of strategy C](image2)

(a) The number of subpopulation $J$

(b) The optimal control profile of $u_1(t)$ and $u_2(t)$

Figure 1, 2 and 3 show the numerical simulations result for implementation of strategy A, B, C, respectively. Based on Figure 1a, 2a and 3a, we can see that all strategies reduce the number of infected subpopulation significantly. There is no significant differences in all strategies based on the number of infected subpopulation result but regarding the cost, strategy C has the minimum cost. The optimal control profiles for each strategy is depicted in Figure 1b, 2b and 3b. The number of infected subpopulation $J$ in condition without and with control and its implementation cost for strategy A, B and C can be shown in Table 2.

| Strategy | $J$ without control | $J$ with control | Cost       |
|----------|---------------------|-----------------|------------|
| A        | 15.1836             | 0.6114          | 887.8016   |
| B        | 15.1836             | 0.6746          | 778.7879   |
| C        | 15.1835             | 0.3823          | 609.6369   |

Based on the simulation result, we can conclude that by using $w = 20, w_1 = 20, w_2 = 2$ as the weights, the combination of control $u_1(t)$ and $u_2(t)$ is effective to reduce the number of infected/symptomatic subpopulation with minimum cost of controls. For the next research, it can be useful if we also analyze the cost effectiveness for each strategy by using some methods such as Incremental Cost Effectiveness Ratio (ICER).
5. Conclusion
In this paper, we construct HIV/AIDS epidemic model with control by set the rate of treatments in HIV/AIDS model as control variables. By using Pontryagin Minimum Principle, we obtained the optimal control of HIV/AIDS model that have been constructed. Numerical simulations show that by using \( w = 20, w_1 = 20, w_2 = 2 \) as the weights, the combination of control \( u_1(t) \) and \( u_2(t) \) is effective to reduce the number of infected subpopulation with minimum cost of controls.

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