

Mathematical Model of HIV/AIDS with Two Different Stages of Infection Subpopulation and Its Stability Analysis

Ummu Habibah*, Trisilowati, Yona Lotusia Pradana, and Winadya Villadystian

Abstract—We propose mathematical model of HIV/AIDS with two different stages of infection subpopulation. The proposed model is more realistic since it establishes the compartment diagram based on data from the Indonesian Ministry of Health. The model consists of six compartments (susceptible, infected with and without treatment, AIDS, treatment, and recovered sub populations). We analyzed the model by proving the positivity and boundedness of the models solutions. Furthermore, we analyzed local and global stability of the solutions determined by the basic reproduction number as a threshold of disease transmission. The disease-free and endemic equilibrium points are locally asymptotically stable when $R_0 < 1$ and $R_0 > 1$ respectively. For global stability, we constructed the Lyapunov function. The results indicate that the disease-free equilibrium point is globally asymptotically stable when $R_0 < 1$ and that the endemic equilibrium point is globally asymptotically stable when $R_0 > 1$. We conducted numerical simulation to support the analytical results.

Index Terms—dynamical system; HIV/AIDS; different stages; stability analysis.

I. INTRODUCTION

AIDS (Acquired Immune Deficiency Syndrome) is a disease caused by human immunodeficiency virus (HIV) that has the ability to suppress T-cells in the body which functions to fight against infections. The cells are important part of the body-immune system. AIDS becomes a major problem in the world because people infected with HIV are prone to various diseases which might lead to death. Some countries have attempted to reduce the growth rate of AIDS disease by implementing infection control programs including the use of condoms and sterile syringes.

Mathematical models have significantly contributed to the understanding of the spread of HIV infection. In 2009, Cai et al. conducted a dynamic analysis of HIV / AIDS epidemic models with treatment [13]. The population was divided into four compartments namely susceptible (S), HIV infected (I), AIDS (A) and symptomatic (J) subpopulations. The symptomatic sub population was considered due to the fact that the infection period occurs for a long period, i.e more than 10 years before entering into the AIDS stage. In 2014, the study was developed by analyzing the dynamic of the HIV/AIDS model by adding the density of the dependency

factor for infection which is a function of the total population [12].

In 2016, Huo et al. formulated the HIV / AIDS epidemic model with the treatment stated in the SIATR model and by analyzing the dynamics of the epidemic model. Individuals in the T compartment received all types of treatment [5]. Unfortunately, the treatment did not completely eliminate HIV from the individuals body. When the treatment was successful, it suppressed the virus, even to an undetectable level. By suppressing the amount of virus in the body, people infected with HIV can live longer and have healthier lives. However, they can still transmit the virus and must take antiretroviral drugs continuously in order to maintain the quality of their health. The results of Huo et al's (2016) study showed an endemic situation.

In 2014, Huo and Chen conducted a dynamic analysis of the HIV / AIDS epidemic model with different stages of infection, namely positive individuals infected with HIV showing symptoms and without symptoms. After treatment, subpopulations with HIV symptoms will become HIV positive without symptoms. The analysis result was globally asymptotically stable for the equilibrium points [12]. Ulfa, et al. (2018) analyzed the dynamic model of HIV/AIDS with different stages of susceptible and infection [2] subpopulations. The susceptible subpopulation was divided into two, namely susceptible subpopulation that had knowledge about HIV/AIDS and susceptible individual that did not have knowledge about HIV/AIDS. The infected subpopulations were divided into two, the same as in Huo and Chen's (2014) model [4]. The results of the analysis were local asymptotically stable with certain conditions for equilibrium points. Mushayabasa and Bhunu (2011) [20], divided susceptible and infected populations into two, non-homosexual and homosexual susceptible subpopulations, and non-homosexual and homosexual HIV-infected subpopulations respectively.

In this research, we propose mathematical model of HIV/AIDS with two different stages of infection subpopulation. The proposed model is more realistic since it establishes the compartment diagram based on the real data of the Indonesian Ministry of Health (2019) [11]. It was estimated that there were 640.633 people with HIV in June 2018. From those, there were two kinds of infected individuals, subpopulation who made a report to the health station, about 47% (301.959) and individuals who did not make a report to the health station, around 53%. From these, we make an assumption that the individuals who make a report are called the HIV-positive individuals given treatment an ARV (I_1), and the individuals who do not make a report are called the HIV-positive not receiving an ARV (I_2) treatment. The

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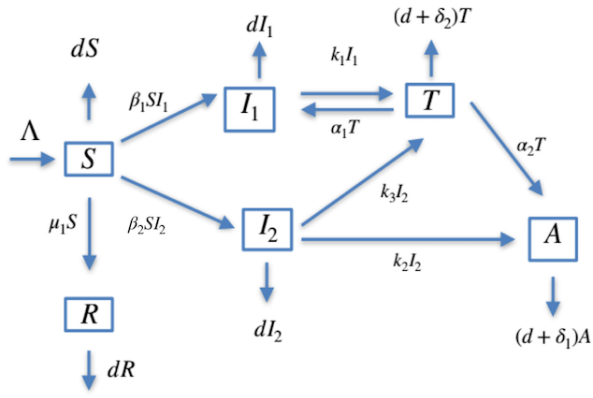


Fig. 1. The compartment diagram of an HIV/AIDS model with two different stages of infection subpopulation.

model obtained were analyzed dynamically. We prove the boundedness and positivity of the solutions of the system [3] [9]. Furthermore, we determined the disease-free and endemic equilibrium points as the solution of the model, and the basic reproduction number (R_0) [8]. Moreover, we analyzed the stability of equilibrium points locally and globally following [1][7][16][18][19][22][23]. The disease-free equilibrium point is locally asymptotically stable when $R_0 < 1$ and the endemic equilibrium point is locally asymptotically stable when $R_0 > 1$. For global stability, we constructed the Lyapunov function and the results show that the disease-free equilibrium is globally asymptotically stable when $R_0 < 1$ and the endemic equilibrium is globally asymptotically stable when $R_0 > 1$. Numerical simulations were performed using values of selected parameters to support the results of the analysis.

II. AN HIV/AIDS MODEL

An HIV/AIDS epidemic model had been modified from the model of Habibah and Sari (2018) [21] and new infected subpopulation was added according to real data from The Indonesian Ministry of Health (2019) [11] to establish the compartment diagram. The total population is divided into six compartments: $S(t)$, $I_1(t)$, $I_2(t)$, $A(t)$, $T(t)$, and $R(t)$. $S(t)$ represents the number of susceptible individuals; $I_1(t)$ represents the number of HIV-positive individuals consuming ARV so that this subpopulation can survive longer; and $I_2(t)$ represents the number of HIV-positive individuals not consuming ARV; $A(t)$ represents the number of individuals with full-blown AIDS not receiving treatment; $T(t)$ represents the number of individuals receiving ARV treatment; $R(t)$ represents the number of individuals who change their sexual habits and maintain the habits for the rest of their lives.

Based on the compartment diagram Figure 1, we establish an HIV/AIDS model with two different stages of infected subpopulation in the form of a system of non linear differential equations as follows.

$$\begin{aligned}\dot{S} &= \Lambda - \beta_1 S I_1 - \beta_2 S I_2 - a S, \\ \dot{I}_1 &= \beta_1 S I_1 + \alpha_1 T - b I_1, \\ \dot{I}_2 &= \beta_2 S I_2 - c I_2, \\ \dot{A} &= k_2 I_2 + \alpha_2 T - e A, \\ \dot{T} &= k_1 I_1 + k_3 I_2 - f T, \\ \dot{R} &= \mu_1 S - d R,\end{aligned}\quad (1)$$

with $a = \mu_1 + d$, $b = k_1 + d$, $c = k_2 + k_3 + d$, $e = \delta_1 + d$, and $f = \alpha_1 + \alpha_2 + \delta_2 + d$. where Λ is recruitment rate of the population, β_1 and β_2 are transmission coefficient of the infection stage I_1 and I_2 respectively, d is natural mortality rate, α_1 is the proportion of successful treatment, α_2 is the proportion of treatment failure, k_1 is progression rate from I_1 to T , k_2 is progression rate from I_2 to A , k_3 is progression rate from I_2 to T , δ_1 is the disease-related death rate of the AIDS, δ_2 is the disease-related death rate of being treated, and μ_1 is the rate of susceptible individuals who changed their habits. In Table I, we summarize the parameters and values used in the simulation.

TABLE I
PARAMETERS AND DESCRIPTIONS FOR SIMULATIONS ARE ADAPTED FROM HUO *et al.* (2016)

Parameter	Description	Value
Λ	Recruitment rate	0.55
β_1	Transmission coefficient of I_1	0.0023
β_2	Transmission coefficient of I_2	0.0033
α_1	The proportion of successful treatment	0.02
α_2	The proportion of treatment failure	0.05
k_1	Progression rate from I_1 to T	0.0498
k_2	Progression rate from I_2 to A	0.008
k_3	Progression rate from I_2 to T	0.05
μ_1	The rate of susceptible individuals who changed their habits	0.03

III. THE MODEL ANALYSIS

In this section, we analyze the boundedness and positivity of the solutions, determine the equilibrium points and the basic reproductions number, and analyze the stability of the solutions locally and globally.

A. Basic properties

Invariant region: The solution of system (1) with positive initial value will remain positive for all $t > 0$, necessarily to be proved.

Theorem 1. All feasible $S(t)$, $I_1(t)$, $I_2(t)$, $A(t)$, $T(t)$ and $R(t)$ of system (1) are bounded by the region $D = \{(S, I_1, I_2, A, T, R) \in \mathbb{R}^6 : S + I_1 + I_2 + A + T + R \leq \Lambda/d\}$.

Proof: From system equation (1)

$$\begin{aligned}\dot{N} &= \dot{S} + \dot{I}_1 + \dot{I}_2 + \dot{A} + \dot{T} + \dot{R}, \\ &= \Lambda - dN(t) - \delta_1 A - \delta_2 T,\end{aligned}\quad (2)$$

implies that

$$\dot{N} \leq \Lambda - dN(t),\quad (3)$$

and it follows that

$$N \leq \Lambda/d + N(0)e^{-dt}, \quad (4)$$

where $N(0)$ is the initial value of total sub population. Thus

$$\lim_{t \rightarrow \infty} \sup N(t) \leq \Lambda/d, \quad (5)$$

we end up $S + I_1 + I_2 + A + T + R \leq \Lambda/d$. For the analysis of the model (1), we get the region which is given by the set $D = \{(S, I_1, I_2, A, T, R) \in \mathbb{R}^6 : S + I_1 + I_2 + A + T + R \leq \Lambda/d\}$ which is a positivity invariant set for system(1). We need to consider the dynamics of system (1) on the set D nonnegative of solutions. ■

B. Positivity of solutions of the model

Theorem 2. *If $S(0) \geq 0, I_1(0) \geq 0, I_2(0) \geq 0, A(0) \geq 0, T(0) \geq 0,$ and $R(0) \geq 0,$ then the solution of system (1) $S(t), I_1(t), I_2(t), A(t), T(t)$ and $R(t)$ are positive for all $t > 0.$*

Proof: From the first equation of (1), we have

$$\begin{aligned} \dot{S} &= \Lambda - \beta_1 S I_1 - \beta_2 S I_2 - a S, \\ &= \Lambda - S[\beta_1 I_1 - \beta_2 I_2 - a], \\ &= \Lambda - Q_1(t) S, \end{aligned} \quad (6)$$

where $Q_1(t) = \beta_1 I_1 - \beta_2 I_2 - a$. We multiply equation (6) by $e^{\int_0^t Q_1(r) dr}$ to yield

$$\frac{dS}{dt} e^{\int_0^t Q_1(r) dr} = \{\Lambda - Q_1(t) S(t)\} e^{\int_0^t Q_1(r) dr}, \quad (7)$$

which implies

$$\frac{dS}{dt} e^{\int_0^t Q_1(r) dr} + Q_1(t) S(t) e^{\int_0^t Q_1(r) dr} = \Lambda e^{\int_0^t Q_1(r) dr}. \quad (8)$$

Furthermore, the left hand side of equation (8) can be written as derivative of $S(t)e^{\int_0^t Q_1(r) dr}$ with respect to t , to get

$$\frac{d}{dt} \{S(t)e^{\int_0^t Q_1(r) dr}\} = \Lambda e^{\int_0^t Q_1(r) dr}, \quad (9)$$

thus by taking integral with respect to q from 0 to t , we obtain

$$S(t)e^{\int_0^t Q_1(r) dr} - S(0) = \Lambda \left\{ \int_0^t e^{\int_0^q Q_1(r) dr} dq \right\}. \quad (10)$$

We multiply equation (10) by $e^{-\int_0^t Q_1(r) dr}$ to get

$$S(t) - S(0) e^{-\int_0^t Q_1(r) dr} = \Lambda e^{-\int_0^t Q_1(r) dr} \left\{ \int_0^t e^{\int_0^q Q_1(r) dr} dq \right\}. \quad (11)$$

Finally we get

$$\begin{aligned} S(t) &= S(0) e^{-\int_0^t Q_1(r) dr} \\ &+ \Lambda e^{-\int_0^t Q_1(r) dr} \left\{ \int_0^t e^{\int_0^q Q_1(r) dr} dq \right\} \geq 0, \end{aligned} \quad (12)$$

means the solution of system (1) for $S(t)$ is positive.

Similarly for the second up to sixth equations of system (1), we have

$$\begin{aligned} I_1(t) &= I_1(0) e^{\int_0^t Q_2(r) dr} \\ &+ e^{\int_0^t Q_2(r) dr} \left\{ \int_0^t \alpha_1 T(t) e^{-\int_0^q Q_2(r) dr} dq \right\} \geq 0, \end{aligned} \quad (13)$$

$$I_2(t) = I_2(0) e^{Bt} \geq 0, \quad (14)$$

$$A(t) = A(0) e^{-et} + e^{-et} \int_0^t e^{et} Q_3(r) dr \geq 0, \quad (15)$$

$$T(t) = T(0) e^{-ft} + e^{-ft} \int_0^t e^{ft} Q_4(r) dr \geq 0, \quad (16)$$

$$R(t) = R(0) e^{-dt} + e^{-dt} \int_0^t e^{dt} Q_5(r) dr \geq 0, \quad (17)$$

where $Q_2(t) = \beta_1 S(t) - b, B = \beta_2 S(t) - e, Q_3(t) = k_2 I_2(t) + \alpha_2 T(t), Q_4(t) = k_1 I_1(t) + k_3 I_2(t)$ and $Q_5(t) = \mu_1 S(t)$. Therefore we can say that $S(t) \geq 0, I_1(t) \geq 0, I_2(t) \geq 0, A(t) \geq 0, T(t) \geq 0,$ and $R(t) \geq 0$ for all $t \geq 0,$ and this completes the proof. ■

Furthermore, we will determine equilibrium points. An HIV/AIDS model is analyzed by determining equilibrium points as the constant solutions of the system (1).

C. The equilibrium points and the basic of reproduction number

The proposed HIV/AIDS model has two equilibrium points. One is the disease-free equilibrium point (X^0) and the other one is the endemic equilibrium point (X^*). The equilibrium points are defined by setting the right side of system (1) equal to zero.

$$\dot{S} = \dot{I}_1 = \dot{I}_2 = \dot{A} = \dot{T} = \dot{R} = 0.$$

The disease-free equilibrium point is $X^0 = (S^0, I_1^0, I_2^0, A^0, T^0, R^0) = (\frac{\Lambda}{a}, 0, 0, 0, 0, \frac{\mu_1 \Lambda}{da})$. This equilibrium point means when we have Λ/a as the number of the susceptible subpopulation with zero the positive-infected subpopulation with ARV consumption (I_1) and the positive-infected subpopulation without ARV consumption (I_2) yield the full-blown AIDS subpopulation (A) and treatment subpopulation (T) are equal zero. It means there is no infection transmission in the population.

Furthermore, an endemic equilibrium point X^* is found when $I_1 \neq 0$ and $I_2 \neq 0$ such that we get

$$X^* = (S^*, I_1^*, I_2^*, A^*, T^*, R^*),$$

where

$$\begin{aligned} S^* &= \frac{c}{\beta_2}, \\ I_1^* &= \frac{\alpha_1 k_3 (\Lambda \beta_2 - ac)}{\alpha_1 k_3 \beta_1 c + \beta_2 b f c - \beta_1 f c^2 - c \alpha_1 k_1 \beta_2}, \\ I_2^* &= \frac{(f \beta_2 b - f \beta_1 c - \alpha_1 k_1 \beta_2)}{\alpha_1 k_3 \beta_2} I_1^*, \\ A^* &= \frac{k_2 (\beta_2 b f - \beta_1 c f - \alpha_1 k_1 \beta_2) + k_3 \alpha_2 (\beta_2 b - \beta_1 c)}{\alpha_1 k_3 \beta_2 e} I_1^*, \\ T^* &= \frac{\beta_2 b - \beta_1 c}{\beta_2 \alpha_1} I_1^*, \\ R^* &= \frac{\mu_1 c}{\beta_2 d}. \end{aligned} \quad (18)$$

To determine the threshold of the infected of HIV is predicted die out or present in the model, the basic reproduction number is calculated. The basic reproduction number is calculated by applying the next generation method. In order to construct the next generation matrix (Heffernan, et. al, 2005) [8], we only involve the infected subpopulations such that from equation (1). We have

$$x'_i = F_i - V_i, i = 1, 2$$

where $F = (\beta_1 SI_1, \beta_2 SI_2)$ and $V = (bI_1, cI_2)$. Jacobi matrix F and V are obtained by partial derivative with respect to I_1 and I_2 at point X_0 .

$$F(X^0) = \begin{bmatrix} \frac{\beta_1 \Delta}{a} & 0 \\ 0 & \frac{\beta_2 \Delta}{a} \end{bmatrix},$$

and

$$V(X^0) = \begin{bmatrix} b & 0 \\ 0 & c \end{bmatrix}.$$

Thus, by inverting $V(X^0)$ and multiplied by $F(X^0)$, it is easy to yield the next generation matrix

$$K = F(X_0)V^{-1}(X_0), \\ = \begin{bmatrix} \frac{\beta_1 \Delta}{ab} & 0 \\ 0 & \frac{\beta_2 \Delta}{ac} \end{bmatrix}. \quad (19)$$

Thus, we get two pair eigen value

$$\lambda_1 = \frac{\beta_1 \Delta}{ac},$$

and

$$\lambda_2 = \frac{\beta_2 \Delta}{ac}.$$

The basic reproduction number is $R_0 = \max(\lambda_1, \lambda_2)$. Since the spread of HIV infection is determined by contact between susceptible and positive-HIV individuals not consuming ARV, then we choose the basic reproduction number

$$R_0 = \frac{\beta_2 \Delta}{ac},$$

in which β_2 is transmission rate between susceptible with $I_2(t)$ subpopulations. Finally, endemic equilibrium points can be written in the form of the basic reproduction number as follows

$$S^* = \frac{c}{\beta_2}, \\ I_1^* = \frac{\alpha_1 k_3 a c (\frac{\Delta \beta_2}{ac} - 1)}{\alpha_1 k_3 \beta_1 c + \beta_2 b f c - \beta_1 f c^2 - c \alpha_1 k_1 \beta_2}, \\ = \frac{\alpha_1 k_3 a c (R_0 - 1)}{\alpha_1 k_3 \beta_1 c + \beta_2 b f c - \beta_1 f c^2 - c \alpha_1 k_1 \beta_2}, \\ I_2^* = \frac{(f \beta_2 b - f \beta_1 c - \alpha_1 k_1 \beta_2)}{\alpha_1 k_3 \beta_2} I_1^*, \quad (20) \\ A^* = \frac{k_2 (\beta_2 b f - \beta_1 c f - \alpha_1 k_1 \beta_2) + k_3 \alpha_2 (\beta_2 b - \beta_1 c)}{\alpha_1 k_3 \beta_2 e} I_1^*, \\ T^* = \frac{\beta_2 b - \beta_1 c}{\beta_2 \alpha_1} I_1^*, \\ R^* = \frac{\mu_1 c}{\beta_2 d}.$$

Obviously, in the steady state solution, the infected sub population I_1 is exist if only if $R_0 > 1$.

IV. STABILITY ANALYSIS

In this part, we investigate stability analysis of the equilibrium points locally and globally.

A. Local stability analysis

In this section, we analyze the local stability of the free-disease equilibrium points by following the suggestion of the basic reproduction number R_0 .

Theorem 3. *The free-disease equilibrium point X^0 is locally asymptotically stable when $R_0 < 1$ and unstable otherwise.*

Proof: An HIV/AIDS model is in the form of non linear differential equations. To analyze the stability, we linearize system (1) to yield the Jacobian matrix

$$J = \begin{bmatrix} \psi_1 & -\beta_1 S & -\beta_2 S & 0 & 0 & 0 \\ \beta_1 I_1 & -\beta_1 S - b & 0 & 0 & \alpha_1 & 0 \\ -\beta_2 I_2 & 0 & -\beta_2 S - c & 0 & 0 & 0 \\ 0 & 0 & k_2 & -e & \alpha_2 & 0 \\ 0 & k_1 & k_3 & 0 & -f & 0 \\ \mu_1 & 0 & 0 & 0 & 0 & -d \end{bmatrix}. \quad (21)$$

where $\psi_1 = -\beta_1 I_1 - \beta_2 I_2 - a$. The Jacobian matrix of each equilibrium point is obtained by substituting the disease-free and endemic equilibrium points in the Jacobian matrix (21). The Jacobian matrix of the disease-free equilibrium points is

$$J(X^0) = \begin{bmatrix} -a & -\frac{\beta_1 \Delta}{a} & -\frac{\beta_2 \Delta}{a} & 0 & 0 & 0 \\ 0 & \frac{\beta_1 \Delta}{a} - b & 0 & 0 & \alpha_1 & 0 \\ 0 & 0 & \frac{\beta_2 \Delta}{a} - c & 0 & 0 & 0 \\ 0 & 0 & k_2 & -e & \alpha_2 & 0 \\ 0 & k_1 & k_3 & 0 & -f & 0 \\ \mu_1 & 0 & 0 & 0 & 0 & -d \end{bmatrix}. \quad (22)$$

We introduce $A_1 = -\beta_1 (\frac{\Delta}{a})$, $A_2 = -\beta_2 (\frac{\Delta}{a})$, $A_3 = \beta_1 (\frac{\Delta}{a}) - b$, and $A_4 = \beta_2 (\frac{\Delta}{a}) - c$. Eigen values of matrix (22) are obtained by solving the characteristic equation $|J(X^0) - \lambda I| = 0$ as follows

$$|J(X^0) - \lambda I| = \begin{vmatrix} -a & A_1 & A_2 & 0 & 0 & 0 \\ 0 & \Gamma_1 & 0 & 0 & \alpha_1 & 0 \\ 0 & 0 & \Gamma_2 & 0 & 0 & 0 \\ 0 & 0 & k_2 & \Gamma_3 & \alpha_2 & 0 \\ 0 & k_1 & k_3 & 0 & \Gamma_4 & 0 \\ \mu_1 & 0 & 0 & 0 & 0 & \Gamma_5 \end{vmatrix} = 0, \quad (23)$$

where $\Gamma_1 = A_3 - \lambda$, $\Gamma_2 = A_4 - \lambda$, $\Gamma_3 = -e - \lambda$, $\Gamma_4 = -f - \lambda$, $\Gamma_5 = -d - \lambda$, I is the identity matrix with the same dimension as $J(X^0)$, and λ is the eigenvalue. Thus equation (23) yields the eigen values $\lambda_1 = -d < 0$, $\lambda_2 = -e < 0$, $\lambda_3 = -a < 0$, $\lambda_4 = A_4 = (R_0 - 1)c < 0$ if only if $R_0 < 1$, $a, c, d, e > 0$, and $\lambda_{5,6}$ that satisfies the quadratic polynomial

$$\lambda^2 + B\lambda + C = 0, \quad (24)$$

with $B = f - A_3$, $C = -A_3 f - \alpha_1 k_1$. The discriminant of equation (24) is

$$D = B^2 - 4C, \\ = (f - A_3)^2 - 4(-A_3 f - \alpha_1 k_1), \\ = (f + A_3)^2 + 4\alpha_1 k_1 > 0, \quad (25)$$

and the value of $\lambda_5\lambda_6 = -A_3f - \alpha_1k_1 > 0$ and $\lambda_5 + \lambda_6 = -(f - A_3) < 0$. Since we get all negative values of the eigen values, the disease-free equilibrium point is asymptotically stable when $R_0 < 1$ and unstable when $R_0 > 1$. ■

Theorem 4. *The endemic equilibrium X^* is globally asymptotically stable when $R_0 > 1$ and unstable otherwise.*

Proof: The Jacobian matrix of endemic equilibrium point is

$$J(X^*) = \begin{bmatrix} -A_1 & -\beta_1S^* & -\beta_2S^* & 0 & 0 & 0 \\ \beta_1I_1^* & -A_2 & 0 & 0 & \alpha_1 & 0 \\ -\beta_2I_2^* & 0 & -A_3 & 0 & 0 & 0 \\ 0 & 0 & k_2 & -e & \alpha_2 & 0 \\ 0 & k_1 & k_3 & 0 & -f & 0 \\ \mu_1 & 0 & 0 & 0 & 0 & -d \end{bmatrix}, \quad (26)$$

with $A_1 = \beta_1I_1^* + \beta_2I_2^* + a$, $A_2 = \beta_1S^* + b$, and $A_3 = \beta_2S^* + c$. Using the same steps in the stability analysis of the disease-free equilibrium point, the eigen values of equation (26) are obtained by substituting the endemic equilibrium point (20) into $|J(X^*) - \lambda I| = 0$ such that we get

$$|J(X^*) - \lambda I| = \begin{vmatrix} \Psi_1 & -\beta_1S^* & -\beta_2S^* & 0 & 0 & 0 \\ \beta_1I_1^* & \Psi_2 & 0 & 0 & \alpha_1 & 0 \\ -\beta_2I_2^* & 0 & \Psi_3 & 0 & 0 & 0 \\ 0 & 0 & k_2 & \Psi_4 & \alpha_2 & 0 \\ 0 & k_1 & k_3 & 0 & \Psi_5 & 0 \\ \mu_1 & 0 & 0 & 0 & 0 & \Psi_6 \end{vmatrix}, \quad (27)$$

where $\Psi_1 = -A_1 - \lambda$, $\Psi_2 = -A_2 - \lambda$, $\Psi_3 = -A_3 - \lambda$, $\Psi_4 = -e - \lambda$, $\Psi_5 = -f - \lambda$, $\Psi_6 = -d - \lambda$. We obtain the eigen values $\lambda_1 = -d$, $\lambda_2 = -e$ whereas for the other eigen values are $\lambda_3, \lambda_4, \lambda_5$, and λ_6 . From equation (27), we determine the determinate of sub matrix

$$|J(X^*) - \lambda I| = \begin{vmatrix} -A_1 - \lambda & -\beta_1S^* & -\beta_2S^* & 0 \\ \beta_1I_1^* & -A_2 - \lambda & 0 & \alpha_1 \\ -\beta_2I_2^* & 0 & -A_3 - \lambda & 0 \\ 0 & k_1 & k_3 & -f - \lambda \end{vmatrix},$$

such that we have the fourth-order polynomial

$$\lambda^4 + a_1\lambda^3 + a_2\lambda^2 + a_3\lambda + a_4 = 0, \quad (28)$$

with

$$\begin{aligned} a_1 &= A_1 - A_2 - A_3 + f, \\ a_2 &= I_1^*S^*\beta_1^2 + I_2^*S^*\beta_2^2 - A_1A_2 - A_1A_3 + A_1f + A_2A_3 - A_2f + A_3f - \alpha_1k_1, \\ a_3 &= -A_2I_2^*S^*\beta_2^2 - A_3I_1^*S^*\beta_1^2 + I_1^*S^*\beta_1^2f + I_2^*S^*\beta_2^2f + A_1A_2A_3 - A_1A_2f - A_1A_3 - A_1\alpha_1k_1 - A_2A_3f + A_3\alpha_1k_1, \\ a_4 &= -A_2I_2^*S^*\beta_2^2f - A_3I_1^*S^*\beta_1^2f + I_2^*S^*\beta_1\beta_2\alpha_1k_3 - I_2^*S^*\beta_2^2\alpha_1k_1 + A_1A_2A_3f + A_1A_3\alpha_1k_1. \end{aligned}$$

It is rather difficult to determine the roots of fourth order polynomial (28). Using the Routh-Hurwitz criteria [9], the real parts of eigen values ($\text{Re}(\lambda_i)$, $i = 1, 2, 3, 4$) of polynomial (28) are negative if they satisfy the following conditions

- 1) $D_1 = |a_1| = a_1 > 0$,
- 2) $D_2 = a_1a_2 - a_3 > 0$,
- 3) $D_3 = a_1a_2a_3 - a_1^2a_4 - a_3^2 > 0$,
- 4) $D_4 = a_1a_2a_3a_4 - a_1^2a_4^2 - a_3^2a_4 > 0$.

According to the Routh-Hurwitz stability criteria, all real parts of eigen values are negative. Hence the endemic equilibrium point is locally asymptotically stable when $R_0 > 1$

and unstable when $R_0 < 1$. We will show these conditions numerically in the next section. ■

B. Global stability analysis of equilibrium points

To show that the solutions of the system (1) are globally asymptotically stable, we use the Lyapunov function theory. First, we present the global stability of free-disease X^0 equilibrium point when $R_0 < 1$ by proofing following theorems.

Theorem 5. *The free-disease equilibrium point X^0 is globally asymptotically stable if $R_0 < 1$ and unstable otherwise.*

Proof: Let the Lyapunov function

$$L_5 = pI_2(t), \quad (29)$$

where p is a positive constant.

The derivative of $L_5(S(t), I_1(t), I_2(t), A(t), T(t), R(t))$ with respect to t gives

$$\begin{aligned} \frac{dL_5}{dt} &= p \frac{dI_2(t)}{dt}, \\ &= p(\beta_2S(t)I_2(t) - cI_2(t)), \\ &= pc\left(\frac{\beta_2\Lambda}{ac} - 1\right) = pc(R_0 - 1), \end{aligned} \quad (30)$$

where $p = 1/c$. Thus we have $dL_5/dt = 0$ when $R_0 \leq 1$. Furthermore $dL_5/dt = 0$ if only if $I_2(t) = 0$, hence by LaSalle's invariance principle [14], X^0 is globally asymptotically stable. ■

Furthermore, we will prove global stability of the endemic equilibrium point.

Theorem 6. *The endemic equilibrium X^* is globally asymptotically stable if $R_0 > 1$ and unstable otherwise.*

Proof: Let define the Lyapunov function motivated in [6][17]

$$\begin{aligned} Y(S, I_1, I_2, A, T, R) &= (S - S^* - S^* \ln \frac{S}{S^*}) \\ &\quad + A(I_1 - I_1^* - I_1^* \ln \frac{I_1}{I_1^*}) \\ &\quad + B(I_2 - I_2^* - I_2^* \ln \frac{I_2}{I_2^*}), \end{aligned} \quad (31)$$

with A and B which are positive constant such that $Y(S, I_1, I_2, A, T, R) < 0$ in $\Omega = (S, I_1, I_2, A, T, R) | S, I_1, I_2, A, T, R > 0$. In order to know whether the Lyapunov function is weak or strong, we should investigate the condition by following the definition of weak and strong Lyapunov functions explained in [10],

- 1) $Y(X^*) = 0$. It is clear that X^* are constant solutions of system, consequently $Y'(X^*) = 0$.
- 2) $Y(X^*) > 0$, $\forall X \neq X^*$ in W with W is some neighborhood of X^* . It is clear that $Y(X^*) > 0$, $\forall X \neq X^*$ in W .
- 3) $Y'(X^*) \leq 0$, $\forall X$ in W (weak Lyapunov function) or $Y'(X^*) < 0$, $\forall X \neq X^*$ in W (strong Lyapunov function).

According to the chain rule, the derivative of \dot{Y} with respect to t is

$$\dot{Y}' = (1 - \frac{S^*}{S})S' + A(1 - \frac{I_1^*}{I_1})I_1' + B(1 - \frac{I_2^*}{I_2})I_2'. \quad (32)$$

Substitute equation (1) into (32), we obtain

$$\begin{aligned} \dot{Y}' &= (1 - \frac{S^*}{S})[\Lambda - \beta_1 S I_1 - \beta_2 S I_2 - a S] \\ &+ A(1 - \frac{I_1^*}{I_1})[\beta_1 S I_1 + \alpha_1 T - b I_1] \\ &+ B(1 - \frac{I_2^*}{I_2})[\beta_2 S I_2 - c I_2], \end{aligned} \quad (33)$$

$$\begin{aligned} \dot{Y}' &= (1 - \frac{S^*}{S})[\beta_1(S^* I_1^* - S I_1) + \beta_2(S^* I_2^* - S I_2) \\ &+ a(S^* - A)] + A(1 - \frac{I_1^*}{I_1})[-\beta_1(S^* I_1^* - S I_1) \\ &- \alpha_1(T^* - T) + b(I_1^* - I_1)] \\ &+ B(1 - \frac{I_2^*}{I_2})[-\beta_2(S^* I_1^* - S I_1) + c(I_2^* - I_2)]. \end{aligned} \quad (34)$$

We consider the following variables substitutions by letting,

$$\frac{S}{S^*} = x_1, \quad \frac{I_1}{I_1^*} = x_2, \quad \frac{I_2}{I_2^*} = x_3, \quad (35)$$

the equation (34) after doing simple algebra, it becomes

$$\begin{aligned} \dot{Y}' &= [(1 - A)\beta_1 S^* I_1^* + (1 - B)\beta_2 S^* I_2^* \\ &+ 2a S^* - A\alpha_1 T^* + 2Ab I_1^* + 2Bc I_2^*] \\ &- \frac{1}{x_1}(\beta_1 S^* I_1^* + \beta_2 S^* I_2^* + a S^*) \\ &- \frac{1}{x_3}(B\beta_2 S^* I_2^* + Bc I_2^*) - \frac{x_5}{x_2}(A\alpha_1 T^*) \\ &+ x_1 x_2 (A - 1)\beta_1 S^* I_1^* + x_1 x_3 (B - 1)\beta_2 (S^* I_2^* - S I_2) \\ &+ x_1 (A\beta_1 S^* I_1^* - B\beta_2 (S^* I_2^* - a S)) \\ &+ x_2 (\beta_1 S^* I_1^* - Ab I_1^*) + \frac{1}{x_2} (A\beta_1 S^* I_1^* + A\alpha_1 T^* + Ab I_1^*) \\ &+ x_3 (\beta_2 (S^* I_2^* - Bc I_2^*)). \end{aligned} \quad (36)$$

The only variables that appears in equation (36) with positive coefficients are $x_1 x_2, x_1 x_3, x_1, x_2, x_3, 1/x_2$. If the total of these coefficients are positive then there is a possibility that \dot{Y}' could be positive. By making the terms with the coefficients $x_1 x_2, x_1 x_3, x_1, x_2, x_3, 1/x_2$ are equal to zero, we get

$$\begin{aligned} (A - 1)\beta_1 S^* I_1^* &= 0, \\ (B - 1)\beta_2 (S^* I_2^* - S I_2) &= 0, \\ (A\beta_1 S^* I_1^* - B\beta_2 (S^* I_2^* - a S)) &= 0, \\ (\beta_1 S^* I_1^* - Ab I_1^*) &= 0, \\ (A\beta_1 S^* I_1^* + A\alpha_1 T^* + Ab I_1^*) &= 0, \\ (\beta_2 (S^* I_2^* - Bc I_2^*)) &= 0, \end{aligned} \quad (37)$$

we have several choices of P_1 and P_2 . By choosing

$$A = \frac{\beta_1 S^*}{b}, \quad B = \frac{\beta_2 S^*}{c} \quad (38)$$

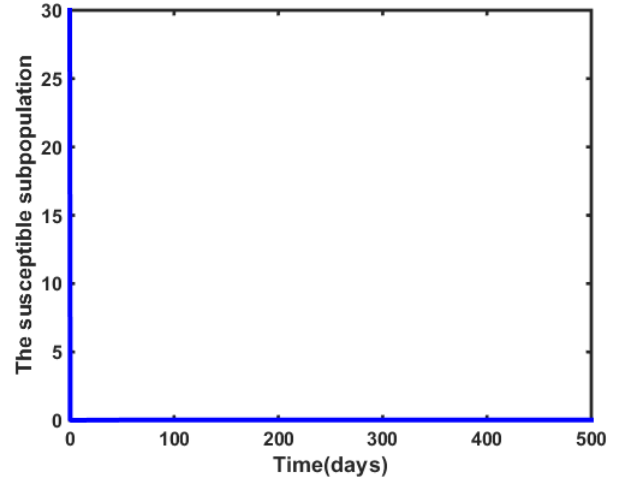


Fig. 2. Numerical simulation of the disease-free equilibrium point for the susceptible subpopulation

and substituting A and B into equation (36), we end up

$$\begin{aligned} \dot{Y}' &= \beta_1 S^* I_1^* (3 - \frac{1}{x_1}) + \beta_2 S^* I_2^* (3 - \frac{1}{x_1} - \frac{1}{x_3}) \\ &+ a S^* (2 - \frac{1}{x_1}) - \frac{\beta_1 S^* \alpha_1 T^*}{b} (1 + \frac{x_5}{x_2}) \\ &- \frac{\beta_2^2 S^{*2} I_2^*}{c} (1 + \frac{1}{x_3}) - \frac{\beta_2^2 S^{*2} I_1^*}{b}. \end{aligned} \quad (39)$$

By applying the Theorem in Peter [15], it is said that the arithmetical mean is greater than or equal to the geometrical mean, then we have $3 - \frac{1}{x_1} \leq 0$, $3 - \frac{1}{x_1} - \frac{1}{x_3} \leq 0$, $2 - \frac{1}{x_1} \leq 0$, $1 + \frac{x_5}{x_2} \geq 0$, and $1 + \frac{1}{x_3} \geq 0$. Hence $\dot{Y}' \leq 0$, for $x_1, x_2, x_3, x_5 > 0$ and satisfies the definition of Lyapunov function. Therefore, the endemic equilibrium point X^* is globally asymptotically stable by LaSalle's invariance principle [14] when $R_0 > 1$, and unstable otherwise. ■

V. NUMERICAL SIMULATION

Numerical simulation is conducted in order to understand the behavior of the proposed HIV/AIDS model and to confirm the stability analysis of the equilibrium points (disease-free and endemic equilibrium points) in the previous section. We will show that the disease-free equilibrium point is asymptotically stable when $R_0 < 1$ and the endemic equilibrium point is asymptotically stable when $R_0 > 1$.

We choose the parameter values in order to satisfies reproduction number $R_0 < 1$ for stability condition for the disease-free equilibrium point. According to Table I, and by choosing the parameters $\beta_1 = 0.0023$ and $\beta_2 = 0.0033$, we get the basic reproduction number $R_0 = 0.00284 < 1$. Let set initial values for each subpopulation, $N_0 = (30, 25, 35, 16, 20, 50)$, the solutions of the system (1) converge to the disease-free equilibrium point $X^0 = (S^0, I_1^0, I_2^0, T^0, A^0, R^0)$, that is $X^0 = (11.0887, 0, 0, 0, 0, 16.9719)$.

When the basic reproduction number, the dynamics of HIV/AIDS models is shown in Figure 2 to 7 for each subpopulation. The figures show that the infected and full-blown AIDS individual will vanish in the future. The numerical results support analytical results.

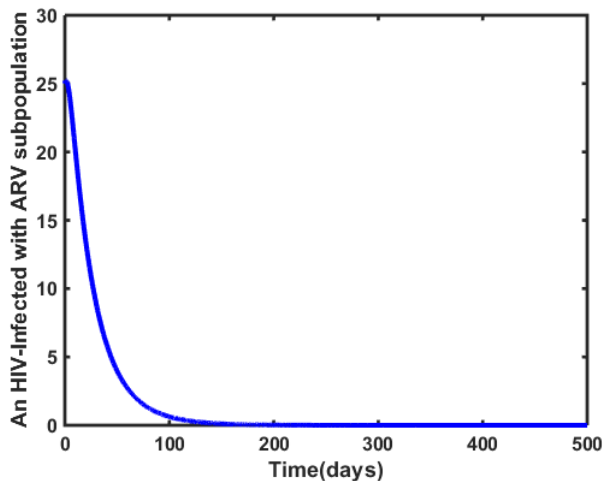


Fig. 3. Numerical simulation of the disease-free equilibrium point for the HIV-positive individuals consuming ARV

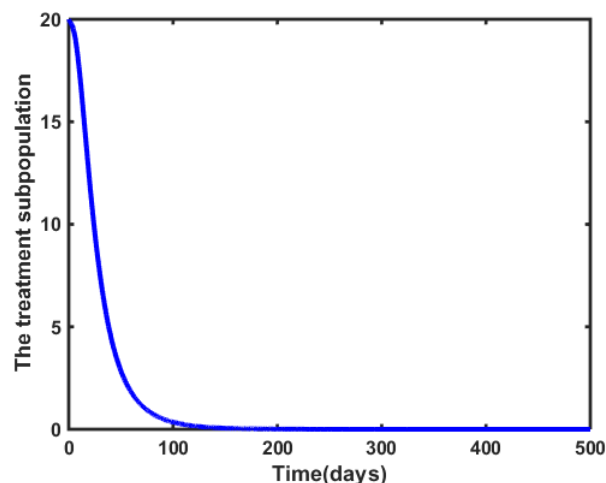


Fig. 6. Numerical simulation of the disease-free equilibrium point for the treatment subpopulation

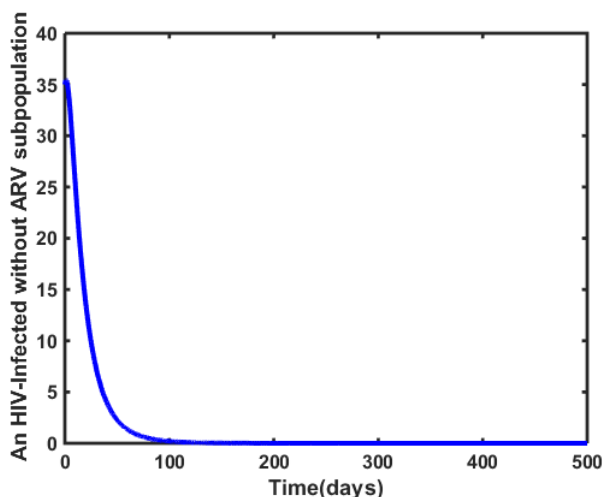


Fig. 4. Numerical simulation of the disease-free equilibrium point for the HIV-positive individuals not consuming ARV

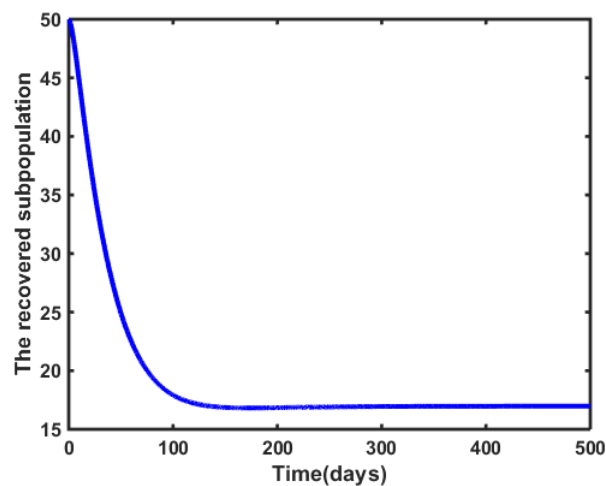


Fig. 7. Numerical simulation of the disease-free equilibrium point for the recovered subpopulation

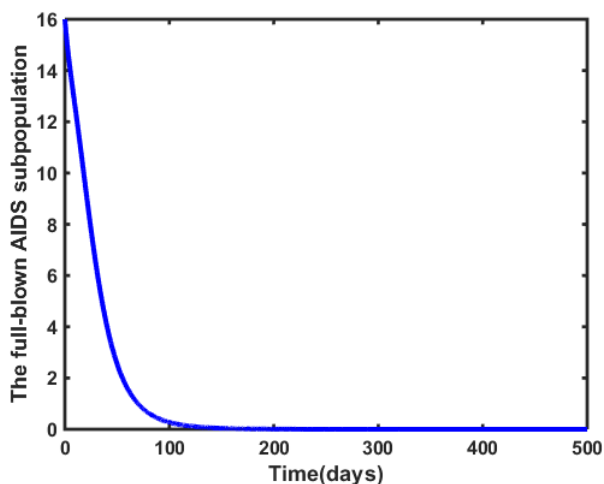


Fig. 5. Numerical simulation of the disease-free equilibrium point for the full-blown AIDS subpopulation

Next, we simulate the stability of model solutions for the endemic equilibrium point numerically. We choose the parameter values in order to satisfy the basic reproduction number $R_0 > 1$ as shown in Table I, and the parameters $\beta_1 = 2.3$ and $\beta_2 = 3.3$, the basic reproduction number is $R_0 = 2.8396 > 1$. Let set initial values for each subpopulation, $N_1 = (30, 25, 35, 16, 20, 50)$, and using the condition of the Routh-Hurwitz criteria $D_1 > 0, D_2 > 0, D_3 > 0$ and $D_4 > 0$, the solutions of the system (1) converge to the endemic equilibrium point $X^* = (S^*, I_1^*, I_2^*, T^*, A^*, R^*)$, that is $X^* = (0.0235, 3.4042, 4.6953, 1.5103, 2.5867, 0.0388)$.

In the other hand, when the basic reproduction number $R_0 > 1$, the behavior of HIV/AIDS model can be shown in Figure 8 to 13 for each subpopulation. This is different with previous simulation (the disease-free equilibrium point). The figures show that for long-time simulation, the subpopulation of infected and full-blown AIDS exist. This shows that endemic occurred in the proposed model. The numerical solution is coincided with the analytical solution. In the next research, it necessary to apply control optimal theory in order to minimize the infected and full-blown AIDS individuals by adding control strategies in the proposed model.

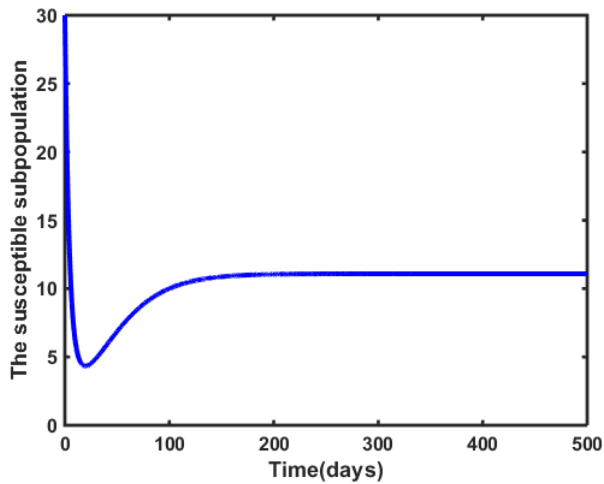


Fig. 8. Numerical simulation of the endemic equilibrium point for the susceptible subpopulation

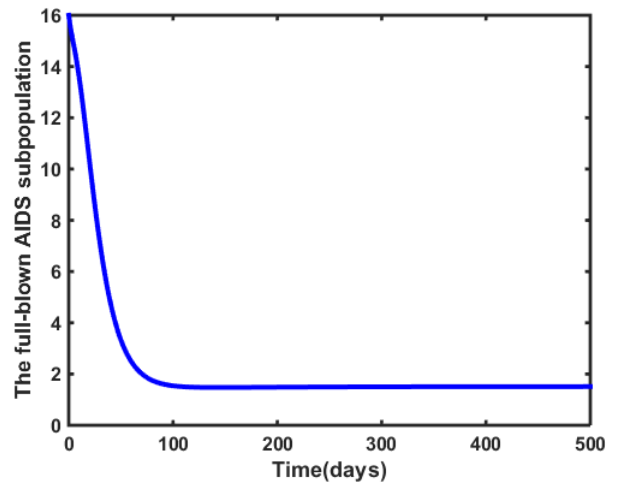


Fig. 11. Numerical simulation of the endemic equilibrium point for the full-blown AIDS subpopulation

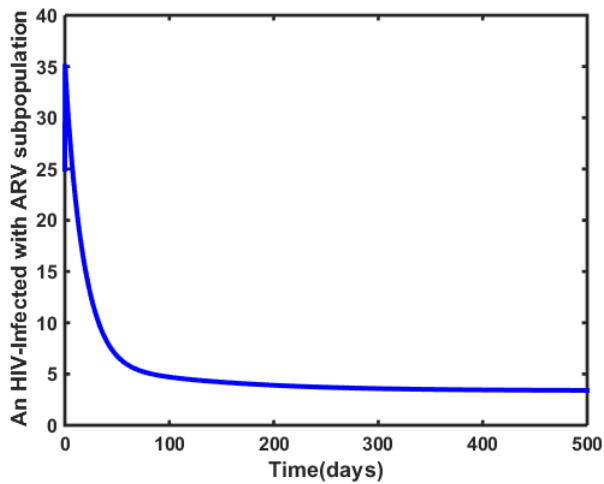


Fig. 9. Numerical simulation of the endemic equilibrium point for the HIV-positive individuals consuming ARV

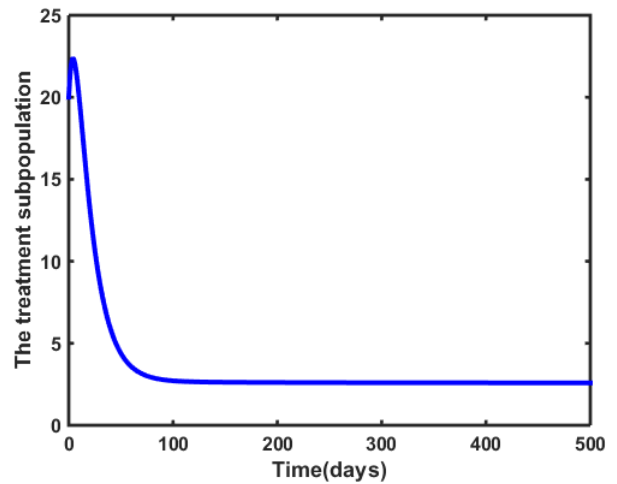


Fig. 12. Numerical simulation of the endemic equilibrium point for the treatment subpopulation

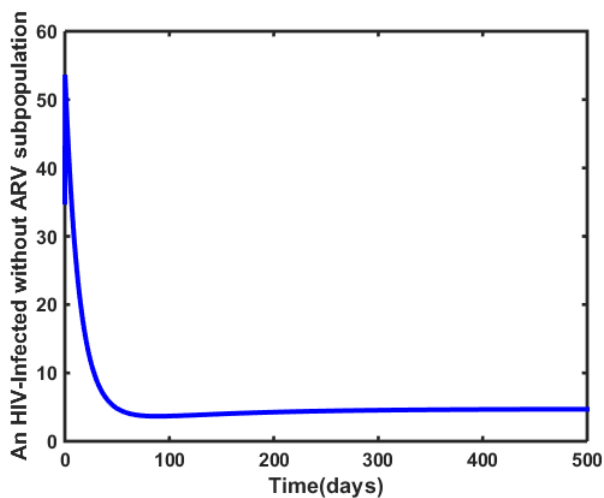


Fig. 10. Numerical simulation of the endemic equilibrium point for the HIV-positive individuals not consuming ARV

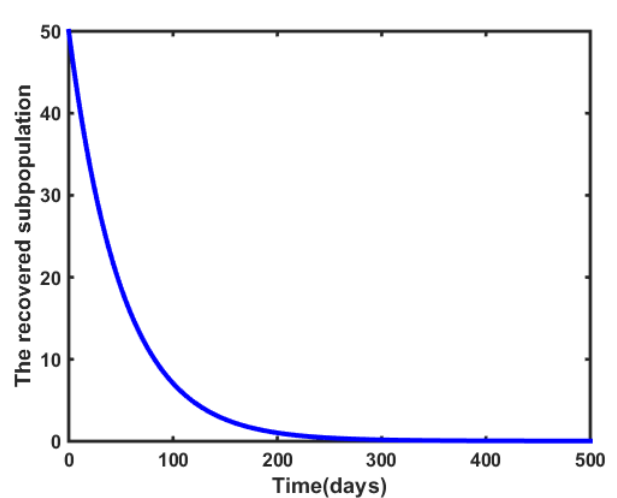


Fig. 13. Numerical simulation of the endemic equilibrium point for the recovered subpopulation

VI. CONCLUSION

The mathematical model of HIV/AIDS with two different stages of infection subpopulation has been established. The proposed model is more realistic since it establishes the compartments diagram based on real data from the Indonesian Ministry of Health. The model consists of six compartments (susceptible, infected with and without treatment, AIDS, treatment, and recovered sub populations). The infected subpopulations are an HIV-positive consuming ARV I_1 so that this subpopulation can survive longer, and HIV-positive not consuming ARV I_2 .

We have proved the positivity and boundedness of the model solutions. The stability analysis of HIV/AIDS model is determined according to the basic reproduction number. The disease-free equilibrium is locally asymptotically stable when $R_0 < 1$ and unstable when $R_0 > 1$. The endemic equilibrium is locally asymptotically stable when $R_0 > 1$ and unstable otherwise. Thus, for global stability, we construct the Lyapunov function. The disease-free equilibrium point is globally asymptotically stable when $R_0 < 1$ and unstable otherwise. The endemic equilibrium is globally asymptotically stable when $R_0 > 1$ and unstable otherwise. Numerical simulations are performed using values of selected parameters to support the analysis results.

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