Global Stability and Sensitivity Analysis of SIA Model for AIDS Disease

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Abstract. Over the years, cases of HIV and AIDS spread throughout Indonesia and continue to increase. This is becoming a serious concern so it requires a management or strategy to reduce its spread. In this article, a simple mathematical model will be built that represents HIV AIDS cases in general. The population assumed to be closed population and consisted of SIA (Susceptible, Infected, and AIDS case) population. Furthermore, this model will be analysed through basic reproduction number ($R_0$), global stability using Lyapunov function, and also sensitivity analysis from each parameters. The result of analysis and simulation shows that the rate contact between susceptible and infected is one of the most influential parameters in the spread of AIDS.

1. Introduction

HIV (Human Immunodeficiency Virus) is a ‘lentivirus’ that causes AIDS (Acquired Immunodeficiency Syndrome) that affects the immune system. Lentivirus literally means slow virus which take a long time to produce side effects on the patient's body [1]. In Indonesia, the AIDS cases firstly found in Bali in 1987 and then spread almost in all provinces and has experienced an increased number of sufferer each year [1], [2],[3]. At the end of 2015, the people that living with HIV were around 36.7 million people all over the world, 1.8 million people were infected, and 1 million people died [4], [5]. Indonesia is one of the fastest growing HIV epidemic in the world , and for several years it was concentrated among drug users, homosexual, and female sex workers [6].

HIV is one of the disease that transmitted directly from human to human. It can occurs through oral contact, sexual contact, use of syringes together, and exchange of some body fluids such as blood, breastmilk and others [5][7]. Nowadays, the government and many institutions are still trying hard to reduce the rate of spread of AIDS. The first thing in the prevention stage is to provide counseling to the community, especially in the high risk areas for contracting HIV/AIDS. Furthermore, for AIDS patients themselves, there is no cure but the medical path is to emphasizes the proliferation of the virus so it is not spread too quickly in the patient’s body [8].

Mathematical model have been used in research of epidemiology including HIV/AIDS cases to help improve understanding the factors that effect the transmission of HIV/AIDS [5]. There are many previous research such as model from Aldila, Aprilliani, and Malik [5] that discussed the HIV vertical transmission from mother to child through the breastmilk; model from Harnanti, Hidayati, and Miftahussurur [2] that discussed a retrospective study and treatment of antiretroviral to the patients with HIV/AIDS, model from Eduafo [9] that discussed basic SIA (Susceptible, Infected, AIDS cases) model, and model from Reddy [4] that discussed the elimination of mother-to-child transmission of HIV.

In this paper, the authors try to analyse the global stability and the sensitivity of the parameters from SIA model that the idea comes from Nurhalimah, Ilahi, and Wulan [1] paper. In the previous article, the authors discussed the local stability analysis and dynamical simulation of the model. In this paper the authors try to discussed the global stability analysis through Lyapunov function and sensitivity analysis of each parameters.
1.1 Model Formulation
The model in this paper is similar to the model in Nurhalima, Ilahi, and Wulan [1] paper. The human population divided into three subpopulation named susceptible population \( S \), infected population \( I \), and AIDS population \( A \). We will construct the mathematical model based on some assumptions such as the population is closed, the recruitment rate \( \alpha \) is only in the susceptible population, natural mortality rate is \( \mu \) for all populations, and there is the mortality caused by the AIDS denoted by \( \sigma \). Assumed that there is a new infection when the susceptible make any contact to the infected people or to the AIDS people with \( \beta_1 \) is the contact between susceptible and the infected, \( \beta_2 \) is the contact between susceptible and the AIDS people. The probability of success contact are denoted by \( \eta_1 \) and \( \eta_2 \) respectively while the transition from infected to the AIDS denoted by \( v \). The transmission diagram for the model is in Figure 1 below:

Based on the transmission diagram, the model of SIA for AIDS cases could be formulated by:

\[
\begin{align*}
\frac{dS}{dt} &= \alpha - \beta_1 \frac{SI}{N} - \beta_2 \frac{SA}{N} - \mu S \\
\frac{dI}{dt} &= \beta_1 \frac{SI}{N} + \beta_2 \frac{SA}{N} - (\mu + v) I \\
\frac{dA}{dt} &= v I - (\mu + \sigma) A
\end{align*}
\]

with all parameters assumed to be positive. The total population at time \( t \) is denoted by \( N(t) = S(t) + I(t) + A(t) \) with the upperbound is \( \lim_{t \to \infty} N(t) \leq \frac{\alpha}{\mu} \) in the domain of \( \mathbb{R}^3_+ \).

1.2 Basic Reproduction Number \( (R_0) \)
Basic reproduction number defined as the expected number of secondary cases caused by one primary case in a completely susceptible population during one infection period and denoted by \( R_0 \) [4], [5]. In this paper, the \( R_0 \) is determine through next generation matrix so that the basic reproduction number for this case is given by:

\[
R_0 = \frac{\beta_1 \eta_1 (\mu + \sigma) + \beta_2 \eta_2 v}{(\mu + v)(\mu + \sigma)}
\]

In the next section, the \( R_0 \) plays the important role to determine local stability and the analysis of the parameter sensitivity.

1.3 The Equilibrium Points and Local Stability Analysis
The equilibrium points of the system obtained by the reduction of system (1). This reduction is intend to simplify the model with only one interaction between susceptible and infected. The AIDS cases and infected population is assumed to be one population. Assumed that the infected population \( I \) represents
the infected and also the AIDS population and $\delta$ is the mortality caused by infection. So the reduction system is given by:

$$\frac{dS}{dt} = \alpha - \beta \eta \frac{SI}{N} - \mu S$$

$$\frac{dI}{dt} = \beta \eta \frac{SI}{N} - (\mu + \delta)I$$

The reduction system (2) has two equilibrium points that consist of disease free equilibrium and endemic equilibrium. The first equilibrium denoted by $E_1(S, I)$ and the second equilibrium denoted by $E_2(S^*, I^*)$ where

$$E_1(S, I) = \left( \frac{\alpha}{\mu}, 0 \right)$$

$$E_2(S^*, I^*) = \left( \frac{\alpha(\mu + \delta)}{\beta \eta \mu}, \frac{\alpha \beta \eta - \alpha (\mu + \delta)}{\beta \eta (\mu + \delta)} \right)$$

with $N \leq \frac{\alpha}{\mu}$ and the exist condition is $\beta \eta > (\mu + \delta)$.

Local stability will be analyzed by the linearization using Jacobian matrix where the eigenvalues of this matrix should be negative in order to make both equilibrium points locally asimptotically stable (LAS). The eigenvalues of disease-free equilibrium are

$$\lambda_{11} = -\mu$$

$$\lambda_{12} = \beta \eta - (\mu + \delta)$$

with stable condition is $\beta \eta < (\mu + \delta)$, while the eigenvalues of endemic equilibrium are

$$\lambda_{21} = \lambda_{22} = -A + B$$

where

$$A = -\frac{\beta \eta \mu}{2(\mu + \delta)}$$

$$B = (\beta^2 \eta^2 \mu^2 - 4\beta \eta \mu (\mu + \delta)^2 + 4\mu (\mu + \delta)^3)^{1/2}.$$  

with stable condition are $A > B$ and $\beta^2 \eta^2 \mu^2 > 4\beta \eta \mu (\mu + \delta)^2 + 4\mu (\mu + \delta)^3$.

1.4 Global Stability Analysis

Global stability will be analyzed by Lyapunov function on the second equilibrium which is endemic equilibrium [10], [11].

**Theorem [12]: Global Stability on Endemic Equilibrium**

Let

$$V(S, I) = \left( (S - S^*) - S^* \ln \frac{S}{S^*} \right) + \left( (I - I^*) - I^* \ln \frac{I}{I^*} \right)$$

is the Lyapunov function for endemic equilibrium in system (2) if satisfied the following condition:

i. $V(S, I) > 0 \ \forall \ S, I \in \mathbb{R}^2 \ \{ S = S^*, I = I^* \}$

ii. $V(S, I) = 0 \ \text{if and only if} \ \{ S = S^*, I = I^* \}$

iii. $\dot{V}(S, I) \leq 0 \ \text{and if} \ \dot{V}(S, I) < 0 \ \text{the system is globally asymptotically stable}.$

**Proof:**

i. If $S > S^*, I > I^*$ then there is $\varepsilon > 0$ such that $S = S^* + \varepsilon$ and

$$V(S) = \left( (S - S^*) - S^* \ln \frac{S}{S^*} \right)$$

$$V(S^* + \varepsilon) = \left( (S^* + \varepsilon - S^*) - S^* \ln \left( \frac{S^* + \varepsilon}{S^*} \right) \right)$$

$$V(S^* + \varepsilon) = \left( \varepsilon - S^* \ln \left( 1 - \frac{\varepsilon}{S^*} \right) \right)$$

both sides divided by $S^*$ so that obtain
\[ V(S^* + \varepsilon) = \left( \frac{\varepsilon}{S^*} - \ln \left( 1 - \frac{\varepsilon}{S^*} \right) \right) \]

Let \( p = \frac{\varepsilon}{S^*} \) then \( p > 0 \) such that \( \frac{V(S^* + \varepsilon)}{S^*} = p - \ln(1 - p) > 0 \). With the same way, proof for \( V(I) > 0 \) and \( V(S, I) > 0 \) for \( S < S^*, I < I^* \).

ii. On the equilibrium \((S^*, I^*)\) where \( S^* > 0, I^* > 0 \) with the condition \( S = S^*, I = I^* \) then we can apply

\[ V(S, I) = (S - S^*) - S^* \ln \frac{S}{S^*} + (I - I^*) - I^* \ln \frac{I}{I^*} \]

\[ V(S^*, I^*) = (S^* - S^*) - S^* \ln \frac{S^*}{S^*} + (I^* - I^*) - I^* \ln \frac{I^*}{I^*} \]

\[ V(S^*, I^*) = (0) - S^* \ln(1) + (0) - I^* \ln(1) \]

\[ V(S, I) = 0. \]

iii. Assumed that \( V(S, I) \) is differentiable function, then

\[ \dot{V}(S, I) = \frac{\partial V}{\partial S} \cdot \frac{dS}{dt} + \frac{\partial V}{\partial I} \cdot \frac{dI}{dt} \]

\[ \dot{V}(S, I) = \left( 1 - \frac{S^*}{S} \right) \cdot \left( a - \beta \eta \frac{SI}{N} - \mu S \right) + \left( 1 - \frac{I^*}{I} \right) \cdot \left( \beta \eta \frac{SI}{N} - (\mu + \delta) I \right) \]

On the endemic equilibrium we can apply that \( \frac{dS}{dt} = \frac{dI}{dt} = 0 \). With some algebra operations, we obtained that \( \dot{V} = X^T A X - (S - S^*) (\mu S - \mu S^*) - (I - I^*) ((\mu I - \mu I^*) + (\delta I - \delta I^*)) \) with \( X = \begin{bmatrix} S - S^* \\ I - I^* \end{bmatrix} \) and \( X^T = [S - S^* I - I^*] \) so that the eigenvalues of matrix \( A \) are negatives \( (\lambda_{A1} < 0, \lambda_{A2} < 0) \).

1.5 Sensitivity Analysis

In this section, we are going to analyse the sensitivity of the parameter that related to basic reproduction number \( R_0 \) using the following definition:

**Definition 1** [13]. Normalized sensitivity index of variables \( W \) differentiated in the parameters \( p \), defined as

\[ C^W_p = \frac{\partial W}{\partial p} \times \frac{p}{W} \]

where \( W \) is a variable that will be analyzed through the parameter \( p \).

From the system (1), we are trying to see the sensitivity analysis of parameter to the basic reproduction number \( R_0 \) related to parameter \( \beta_1 \) so that

\[ C^R_{\beta_1} = \frac{\partial R_0}{\partial \beta_1} \times \frac{\beta_1}{R_0} \]

\[ = \frac{\eta_1 (\mu + \sigma)}{(\mu + \nu) (\mu + \sigma)} \times \beta_1 (\mu + \nu) (\mu + \sigma) \]

\[ = \frac{\beta_1 \eta_1 (\mu + \sigma) + \beta_2 \eta_2 \nu}{\beta_2 \eta_2 \nu} \]

\[ = \frac{1}{\beta_1 \eta_1 (\mu + \sigma) + \beta_2 \eta_2 \nu} \]

With the same way, we could calculate the sensitivity index for others parameters in \( R_0 \) such that \( \eta_1, \eta_2, \beta_2, \nu, \sigma \).
2. Result and Discussion

In this part, the data that fit to stable condition will be presented to run dynamical and sensitivity simulation to make some prediction and show how well the analysis that we have been done. Assumed that susceptible and infected contact rates were $\beta_1 = 0.7$, the chance of success of HIV virus transmission from infected to susceptible was $\eta_1 = 0.7798$, susceptible and AIDS cases contact rates were $\beta_2 = 0.8$, the chance of successful transmission of HIV virus from AIDS cases to susceptible was $\eta_2 = 0.7798$, the rate of HIV infection to become AIDS sufferers is $\nu = 0.654 = 0.7$, the rate of death caused by AIDS is $\sigma = 0.163$, and the natural mortality rate is $\mu = 0.1047$. This value produces a value of $R_0 = 4.249762047$. Change in parameter value against $R_0$ showed in the following table:

| Parameter ($p$) | Value  | $p - 10\%$ | $p - 5\%$ | $p + 5\%$ | $p + 10\%$ |
|----------------|--------|-------------|------------|------------|-------------|
| $\beta_1$      | 0.1921 | 4.1681      | 4.2089     | 4.2906     | 4.3314      |
| $\beta_2$      | 0.8079 | 3.9064      | 4.0781     | 4.4214     | 4.5931      |
| $\eta_1$       | 0.1921 | 4.1681      | 4.2089     | 4.2906     | 4.3314      |
| $\eta_2$       | 0.8079 | 3.9064      | 4.0781     | 4.4214     | 4.5931      |
| $\nu$          | -0.1701| 4.3299      | 4.2878     | 4.2153     | 4.1839      |
| $\sigma$       | -0.7411| 4.5965      | 4.4148     | 4.0992     | 3.9612      |

Table 1 shows that $\beta_1, \beta_2, \eta_1, \eta_2$ are parameters that have a positive relation to changes in the value of $R_0$. That is, if the value of the parameter rises, then the value of $R_0$ is also rises. But, if the value of the parameters drop, the value of $R_0$ also drops. Whereas $\nu$ and $\sigma$ are parameters that have a negative relation to changes in the value $R_0$. That is, if the values of these parameters rise, then the value of $R_0$ will decrease. But if the values of these parameters drop, then the value of $R_0$ will rise. Furthermore, these changes will be present in the sensitivity simulation below:

Figure 2. The sensitivity simulation $\beta_1$ and $\eta_1$ against $R_0$
From Figure 2 if the value of $\beta_1$ gets bigger, then the value of $R_0$ will also be greater. Conversely, if the value of $\beta_1$ gets smaller, then the value of $R_0$ will also be smaller. Then, if the value of $\eta_1$ gets bigger, then the value of $R_0$ will also be greater. Conversely, if the value of $\eta_1$ gets smaller, then the value of $R_0$ will also be smaller. This can be interpreted that if susceptible people make contact intensively with infected people then there is a possibility that the susceptible will be infected HIV, which means the disease will be endemic. Conversely, if there is less contact between susceptible people and infected people then the susceptible will not contract the HIV virus by infected, which means it will be disease free.

Figure 3 if the value of $\beta_2$ gets bigger, then the value of $R_0$ will also be greater. Conversely, if the value of $\beta_2$ gets smaller, then the value of $R_0$ will also be smaller. Then, if the value of $\eta_2$ gets bigger, then the value of $R_0$ will also increase. Conversely, if the value of $\eta_2$ gets smaller, then the value of $R_0$ will also be smaller. This can be interpreted if healthy/susceptible people come into contact with people with AIDS, there is a possibility that susceptible will contract the HIV virus by AIDS cases, which means that it will be disease endemic. Conversely, if there is less contact between healthy people (susceptible) and people with AIDS, then there is a possibility that susceptible will not contract the HIV virus by AIDS cases, which means that it will be disease free.

Figure 4 if the value of $\mu$ gets bigger, then the value of $R_0$ will be smaller. Conversely, if the value of $\mu$ gets smaller, then the value of $R_0$ will be even greater. Then, if the $\sigma$ value gets bigger, then the value of $R_0$ will be smaller. Conversely, if the $\sigma$ value gets smaller, then the value of $R_0$ will be even greater. As shown in the figure 4, the increase or decrease the value of $\sigma$ does not significantly influence to the model because those values in the coincide curve. This can be interpreted that the infected with the HIV virus become AIDS sufferers and has a possibility to die because of AIDS, and if the AIDS people has no contact with susceptible, then the population will be remain free of disease.

3. Conclusion
According to the sensitivity analysis, the most influence parameter for the transmission of HIV virus is the amount of contact and the probability of success contact. If there is a small chance of successful transmission of the HIV virus from infected to susceptible, it will be disease free condition. Conversely, the greater the chance of successful transmission of the HIV virus from infected and/or AIDS Cases to Susceptible, the disease will be endemic. The Lyapunov function for this model is defined by
\[ V(S,I) = \left( (S - S^*) - S^* \ln \frac{S}{S^*} \right) + \left( (I - I^*) - I^* \ln \frac{I}{I^*} \right). \] The global stability analysis through this function conducted that the equilibrium points will be global asymptotically stable if \((\lambda_{A1} < 0, \lambda_{A2} < 0)\).

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