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Mathematical Analysis of HIV/AIDS Anti-Retroviral Treatment Incorporating Adherence

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Authors' contributions

This work was carried out in collaboration between all authors. TKF designed the study, performed the mathematical analysis, wrote the protocol and first draft of the manuscript. Authors LOG and OAC managed the analyses of the study. All authors read and approved the final manuscript.

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ABSTRACT

Current treatment for HIV infection consists of Highly Active Antiretroviral (ART) therapy. However, lack of adherence to ART treatment has hampered the benefits of the ART treatment strategy and viral load suppression. Most of the treatment models studied so far do not explicitly include the relationship between adherence to ART regimens and viral load suppression. In this study, a mathematical model with ART adherence is developed. By an application of the next generation matrix approach, the reproduction number, R_0, is determined.Stability analysis of the model developed shows that the Disease Free Equilibrium (DFE) is locally asymptotically stable, if $R_0 < 1$, and an Endemic Equilibrium (EE) exists, which is unique and is locally asymptotically stable when $R_0 > 1$. Using Lyapunov functional approach, the endemic equilibrium is shown to be globally asymptotically stable, and hence persistence of the disease in the population.

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Sensitivity analysis of the model shows that the disease can be kept under check if the test and treat strategy is upscaled as well as adherence to treatment for the infected individuals is emphasized.

Keywords: Adherence; HIV/AIDS; stability analysis.

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1 Introduction

Human Immunodeficiency Virus(HIV) is the virus which causes Acquired Immune Deficiency Syndrome (AIDS). HIV infection depletes the central part of the immune system, leading to AIDS. The natural progression from HIV to AIDS, without drug therapy intervention [1], takes approximately 4-8 years [2] from the initial infection to the terminal stage. However, this duration can be much shorter depending on the presence of co-infections, individual age, how infection was transmitted, and access to palliative treatment and care [3].

Despite remarkable progress on HIV treatments, elimination of HIV/AIDS is still out of reach, and approximately two and half million people get infected every year [4]. Kenya for instance, has had the fastest-growing number of new HIV infections in sub-Saharan Africa in the last decade [5]. A new report by UNAIDS shows that between 2005 and 2015, the number of new HIV cases grew by an average of 7.1% per year in Kenya, one of the highest increases in the world [6]. More than half (53%) of the 1.6 million people living with HIV in Kenya are unaware of their HIV status [7]. This shows that the HIV/AIDS epidemic remains one of the biggest public health threats of our time [8].

Treatment of HIV/AIDS infection has improved dramatically in the past few decades but is still limited by the development of drug resistance and the inability of current therapies to completely eradicate the virus from an infected individual. Antiretroviral therapy (ART) has the potential to prevent HIV/AIDS transmission by reducing the concentration of HIV in blood and genital secretions [9]. Recent trials have proven that early ART improves both individual clinical outcomes, and decreases HIV transmission [10]. Drug resistance is an important issue, especially over the long timescales, because it effectively weakens the impact of existing first-line regimens and could cause greater reliance on second- and third-line treatment regimens, which are currently more expensive [11]. Monitoring patients receiving ART is an important part of HIV care: it determines whether treatment is successful, or if a different drug regimen or improved adherence is required [12]. Patients with treatment failure are more likely to experience progressive disease and are at greater risk of dying, while patients with non-suppressed virus are also at risk of developing resistance and transmitting HIV infections to others. Poor ART adherence increases the risk of viral drug-resistance, limits treatment efficacy, leading to disease progression, and reduces future therapeutic options [13] as well as increasing the risk of transmission due to unsuppressed viral replication [14].

2 Model Description and Formulation

A non-linear mathematical model is proposed to study the dynamics of HIV/AIDS with treatment. The population $N(t)$ is subdivided into the Susceptibles $S(t)$, Infectives $I(t)$, Treatment class $T(t)$, and AIDS class $A(t)$ with natural mortality rate μ in all the classes. The interaction between the classes is assumed as follows; the susceptibles become infected via sexual contacts with infectives. It's also assumed that the infective individuals proceed to AIDS class at a rate ν or move to the treatment class at a rate θ. If individuals under treatment become non-adherent to drug uptake,

they proceed to AIDS class at a rate $\gamma = 1 - \theta$. AIDS individuals are assumed to suffer disease induced mortality at a rate d.

To develop the model, the following assumptions are made;

(i) The recruitment into the population of study (sexually mature adults) is mainly by birth, with all recruits assumed susceptible.

(ii) An individual who is asymptotically infected is placed under ART treatment.

(iii) The full blown AIDS individuals, whose symptoms are easily recognizable, are no longer a threat in the spread of the epidemic. Its assume that individuals at this stage are not sexually active.

Taking into account the above considerations, the following schematic flow diagram is developed.

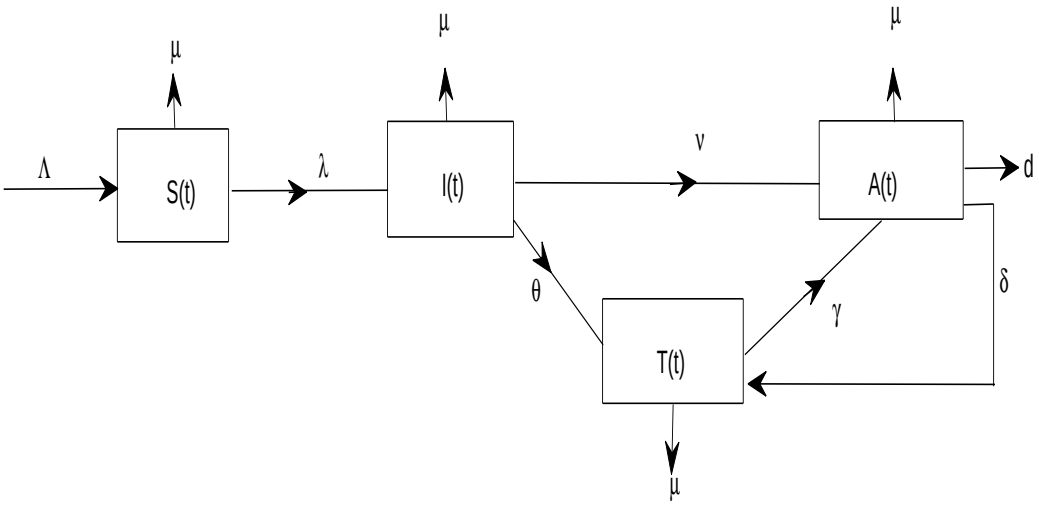

Fig. 1. A schematic diagram of the disease dynamics.

The model is thus governed by the following system of equations

$$\begin{aligned}
\dot{S}(t) &= \Lambda - \mu S(t) - \frac{\beta c I(t) S(t)}{N(t)}, \\
\dot{I}(t) &= \frac{\beta c I(t) S(t)}{N(t)} - (\nu + \theta + \mu) I(t), \\
\dot{T}(t) &= \delta A(t) + \theta I(t) - (\gamma + \mu) T(t), \\
\dot{A}(t) &= \gamma T(t) + \nu I(t) - (d + \mu + \delta) A(t),
\end{aligned} \tag{2.1}$$

where

$$N(t) = S(t) + I(t) + T(t) + A(t).$$

Table 1. A summary of the variables and Parameters used in the model

Parameter or Variable	Description
$S(t)$	Number of the individuals that are not infected
$I(t)$	Number of individuals who are already infected with HIV
$T(t)$	Number of individuals who are infected ART treatment
$A(t)$	Number of individuals who are full blown with AIDS
Λ	Recruitment rate of susceptibles
μ	The AIDS-non related mortality rates per capita (natural deaths).
ν	The rate at which HIV infected individuals progress to AIDS.
c	The rate at which one changes/acquires new sexual partners.
β	The probability of getting infected from a randomly chosen partner.
θ	Rate of recruitment to treatment of infected individuals.
$\lambda = \frac{\beta c I(t)}{N(t)}$	Force of infection.
δ	Rate at which AIDS patients get treatment.
γ	Rate at which individuals on treatment proceed to fully blown
d	Disease induced death rate

The summary of the parameters and variables used in the description of the model is as shown in Table 2 below.

For biological feasibility, Equation (2.1) is analyzed in a suitable region Γ defined as

$$\Gamma = \left\{ (S(t), I(t), T(t), A(t)) \in \mathbb{R}^4_+ : S(t) + I(t) + T(t) + A(t) \leq \frac{\Lambda}{\mu} \right\} \tag{2.2}$$

Since the model describes human population, the solutions of Equation (2.1), with initial conditions in region Γ will remain positive and bounded for all $t \geq 0$. Hence the model developed is mathematically and epidemiologically well posed in the region Γ.

3 Local Stability Analysis of the Disease Free Equilibrium

In this section we study the local stability of the Disease Free Equilibrium (DFE)E_0 for the model(2.1). DFE (E_0) is obtained when infection is absent in the population. Model (2.1) has a disease free equilibrium (DFE) given by

$$E_0 = (S_0, I_0, T_0, A_0) = \left(\frac{\Lambda}{\mu}, 0, 0, 0 \right) \tag{3.1}$$

Theorem 3.1. *If $R_0 = \frac{\beta C}{\nu+\theta+\mu} < 1$, then $E_0 = (\frac{\Lambda}{\mu}, 0, 0, 0)$ is the equilibrium in Γ and is locally asymptotically stable.*

Proof. The Jacobi matrix of model (2.1) at DFE $I(t) = T(t) = A(t) = 0$ and $N = S = \frac{\Lambda}{\mu}$ is given by

$$J(E_0) = \begin{pmatrix} -\mu & -\beta c & 0 & 0 \\ 0 & \beta c - (\mu + \nu + \theta) & 0 & 0 \\ 0 & \theta & -(\gamma + \mu) & \delta \\ 0 & \nu & \gamma & -(d + \mu + \delta) \end{pmatrix} \tag{3.2}$$

To investigate the stability of the DFE, we compute the eigenvalues of Equation (3.2)

$$|J(E_0)| = \begin{pmatrix} -\mu-\lambda & -\beta c & 0 & 0 \\ 0 & (\mu+\nu+\theta)(R_0-1)-\lambda & 0 & 0 \\ 0 & \theta & -(\gamma+\mu)-\lambda & \delta \\ 0 & \nu & \gamma & -(d+\mu+\delta)-\lambda \end{pmatrix} = 0 \quad (3.3)$$

Applying Hurwitz Criterion [15], the trace of $J(E_0)$ is negative if $R_0 < 1$ while its determinant is

$$det\big[J(E_0)\big] = (-\mu)(\mu+\nu+\theta)(R_0-1)\big[\gamma d + \gamma\mu + \mu\delta + \mu^2 + \mu\delta\big] \quad (3.4)$$

The determinant is positive if $R_0 < 1$. Hence, the eigenvalues of Equation (3.3) have negative real parts whenever $R_0 < 1$ and hence guarantees local asymptotic stability [16]. □

Given a small initial infective population each infected individual in the entire period of infectivity will produce less than one infected individual on average if $R_0 < 1$, hence the disease will not invade the population.

4 Global Stability Analysis of the Disease Free Equilibrium

In this section we analyze the global asymptotic stability of the disease free equilibrium. Using the theorem by Castillo Chavez *et. al* [17]. The system (2.1) is rewritten in the form

$$\begin{aligned} \frac{dX(t)}{dt} &= F(X(t), Z(t)) \\ \frac{dZ(t)}{dt} &= G(X(t), Z(t)), \quad G(X(t), 0) = 0 \end{aligned} \quad (4.1)$$

where $X(t) = S(t)$ and $Z(t) = (I(t), T(t), A(t))$, with $X(t) \in \mathbb{R}_+$ denoting the total number of uninfected compartments and $Z(t) \in \mathbb{R}^3_+$ denoting the infected compartments. The disease free equilibrium is then denoted by

$$U_0 = (X^*, 0) \quad \text{where} \quad X^* = \frac{\Lambda}{\mu}$$

The conditions H_1 and H_2 below must be met to guarantee Global Asymptotic Stability

H_1: $\frac{dX(t)}{dt} = F(X(t), 0)$, X^* is Globally Asymptotic Stable.

H_2: $G(X(t), Z(t)) = AZ(t) - \hat{G}(X(t), Z(t))$, $\hat{G}(X(t), Z(t)) \geq 0$

for $((X(t), Z(t)) \in \Gamma$ where $A = D_Z G(U_0, 0)$ is a metzler matrix (the off diagonal elements of A are non-negative) and Γ is the region where the model makes biological sense.

Theorem 4.1. *The fixed point $U_0 = (X^*, 0)$ is Globally Asymptotic Stable equilibrium of Equation (2.1) provided $R_0 < 1$ and the assumptions H_1 and H_2 are satisfied.*

Proof. We have

$$\begin{aligned} \frac{dX(t)}{dt} = F(X(t), Z(t)) &= \Lambda - \mu S(t) - \frac{\beta c I(t) S(t)}{N(t)} \\ F(X(t), 0) &= \Lambda - \mu S(t) \\ \frac{dZ(t)}{dt} &= G(X(t), Z(t)) = \begin{pmatrix} \frac{\beta c I(t) S(t)}{N(t)} - (\nu+\theta+\mu) I(t) \\ \delta A(t) + \theta I(t) - (\gamma+\mu) T(t) \\ \gamma T(t) + \nu I(t) - (d+\mu+\delta) A(t) \end{pmatrix} \end{aligned}$$

and $G(X(t), 0) = 0$

Therefore

$$\begin{aligned}\frac{dX(t)}{dt} = F(X(t),0) &= \Lambda - \mu S(t)\\ A = D_Z G(X_0,0) &= \begin{pmatrix}\beta c - (\nu+\theta+\mu) & 0 & 0\\ \theta & -(\gamma+\mu) & \delta\\ \nu & \gamma & -(d+\mu+\delta)\end{pmatrix}\end{aligned}$$

$$\text{and}\quad \hat{G}(X(t),Z(t)) = \begin{pmatrix}\hat{G}_1(X(t),Z(t))\\ \hat{G}_2(X(t),Z(t))\\ \hat{G}_3(X(t),Z(t))\end{pmatrix} = \begin{pmatrix}\beta c\left(1-\frac{1}{N}\right)I(t)\\ 0\\ 0\end{pmatrix}$$

It follows that $\hat{G}_1(X(t),Z(t)) \geq 0,\ \hat{G}_2)(X(t),Z(t)) = \hat{G}_3(X(t),Z(t)) = 0$ thus $\hat{G}(X(t),Z(t)) \geq 0$. Conditions H_1 and H_2 are satisfied and thus U_0 is Globally Asymptotically Stable for $R_0 < 1$. □

Epidemiologically, any perturbation of the model by the introduction of infectives shows that the model solutions will converge to the DFE whenever $R_0 < 1$. Global asymptotic stability shows that regardless of any starting solution, the solutions of the model will converge to DFE whenever $R_0 < 1$.

5 Local Stability Analysis of the Endemic Equilibrium

At the endemic equilibrium, there is persistence of infection, thus at least one of the infected classes is greater than zero. The positive endemic equilibrium of model (2.1) is denoted by

$$E^* = (S^*, I^*, T^*, A^*) \tag{5.1}$$

Using $R_0 = \frac{\beta c}{\nu+\theta+\mu}$ and the limiting value of $N = \frac{\Lambda}{\mu}$, the endemic states are

$$\begin{aligned}S^* &= \frac{\Lambda}{\mu\beta c}\Big(\nu+\theta+\mu\Big),\\ I^* &= \frac{\Lambda}{\beta c}\Big(R_0-1\Big),\\ T^* &= \frac{\delta}{\gamma+\mu}\left\{\left(\frac{\gamma\theta+\nu(\gamma+\mu)}{(\gamma+\mu)(d+\mu+\delta)-\gamma\delta}\right)\frac{\Lambda}{\beta c}\Big(R_0-1\Big)\right\} + \frac{\theta}{\gamma+\mu}\frac{\Lambda}{\beta c}\Big(R_0-1\Big),\\ A^* &= \left(\frac{\gamma\theta+\nu(\gamma+\mu)}{(\gamma+\mu)(d+\mu+\delta)-\gamma\delta}\right)\frac{\Lambda}{\beta c}\Big(R_0-1\Big).\end{aligned} \tag{5.2}$$

Additionally, a positive endemic state equilibrium exists provided $R_0 > 1$.

Theorem 5.1. *If $R_0 > 1$, then $E^* = (S^*, I^*, T^*, A^*)$, the endemic equilibrium, is locally asymptotically stable.*

Proof. The Jacobi matrix of Equation (2.1) at endemic equilibrium E^*, is

$$J = \begin{pmatrix}-R_0\mu & -(\nu+\theta+\mu) & 0 & 0\\ -\mu(R_0-1) & 0 & 0 & 0\\ 0 & \theta & -(\gamma+\mu) & \delta\\ 0 & \nu & \gamma & -(d+\mu+\delta)\end{pmatrix} \tag{5.3}$$

Interchanging row two to be row one in (5.3) and maintaining the rest, Equation (5.3) becomes

$$J = \begin{pmatrix} -\mu(R_0-1) & 0 & 0 & 0 \\ -R_0\mu & -(\nu+\theta+\mu) & 0 & 0 \\ 0 & \theta & -(\gamma+\mu) & \delta \\ 0 & \nu & \gamma & -(d+\mu+\delta) \end{pmatrix} \tag{5.4}$$

For local asymptotic stability of Equation (5.4) at E^*, the eigenvalues of matrix (5.4) are obtained, that is

$$P(\lambda) = -\begin{vmatrix} \mu(R_0-1)-\lambda & 0 & 0 & 0 \\ -R_0\mu & -(\nu+\theta+\mu)-\lambda & 0 & 0 \\ 0 & \theta & -(\gamma+\mu)-\lambda & \delta \\ 0 & \nu & \gamma & -(d+\mu+\delta)-\lambda \end{vmatrix} = 0 \tag{5.5}$$

$$P(\lambda) = \big[-\mu(R_0-1)-\lambda\big]\big(-(\nu+\theta+\mu)-\lambda\big)\begin{vmatrix} -(\gamma+\mu)-\lambda & \delta \\ \gamma & -(d+\mu+\delta)-\lambda \end{vmatrix} = 0 \tag{5.6}$$

The eigenvalues of Equation (5.6) are;

$$\lambda = -\mu(R_0-1) \quad \text{and} \quad \lambda = -(\nu+\theta+\mu)$$

which are negative whenever $R_0 - 1 > 0$. Using the Routh Hurwitz criterion, the eigenvalues obtained by the matrix

$$\begin{vmatrix} -(\gamma+\mu)-\lambda & \delta \\ \gamma & -(d+\mu+\delta)-\lambda \end{vmatrix} = 0$$

are negative since the trace=$(\gamma + 2\mu + d + \delta) < 0$ and determinant=$\gamma(d+\mu) + \mu(d+\mu+\delta) > 0$. Hence, the endemic equilibrium E^* is locally asymptotically stable whenever $R_0 > 1$. □

Hence if $R_0 > 1$, model (2.1) at Endemic state is locally asymptotically stable. Therefore if $R_0 > 1$ and given a small infective population, each infected individual in the entire period of infectivity will produce more than one infected individual on average, which shows that the disease will persist in the population.

6 Global Stability Analysis of the Endemic Equilibrium

In this section, we investigate the global stability of the endemic equilibrium E^* under the condition $R_0 > 1$. We apply a Lyapunov function [18] that takes advantage of the properties of the function

$$h(x) = x - 1 - \ln(x), \tag{6.1}$$

which is positive in $(0, \infty)$ except at $x = 1$ where it vanishes.

Theorem 6.1. *The endemic equilibrium E^* of the model* (2.1) *is globally asymptotically stable in* Γ *whenever* $R_0 > 1$.

Proof. Consider the following Lyapunov function;

$$V = S - S^* \ln(S) + I - I^* \ln(I) + T - T^* \ln(T) + A - A^* \ln(A) \tag{6.2}$$

Differentiating V with respect to time gives

$$\dot{V} = \left(1 - \frac{S^*}{S}\right)\dot{S} + \left(1 - \frac{I^*}{I}\right)\dot{I} + \left(1 - \frac{T^*}{T}\right)\dot{T} + \left(1 - \frac{A^*}{A}\right)\dot{A} \tag{6.3}$$

Replacing $\dot{S}, \dot{I}, \dot{T}, \dot{A}$ from Equation (2.1) in (6.3), we obtain

$$\begin{aligned} \dot{V} &= \left(1 - \frac{S^*}{S}\right)\left[\Lambda - \mu S - \frac{\beta cIS}{N}\right] + \left(1 - \frac{I^*}{I}\right)\left[\frac{\beta cIS}{N} - (\nu + \theta + \mu)I\right] \\ &+ \left(1 - \frac{T^*}{T}\right)\left[\delta A + \theta I - (\gamma + \mu)T\right] + \left(1 - \frac{A^*}{A}\right)\left[\gamma T + \nu I - (d + \mu + \delta)A\right] \end{aligned} \tag{6.4}$$

At the boundary $N \leq \frac{\Lambda}{\mu}$, thus we let $N = \frac{\Lambda}{\mu}$ and Equation (6.4) can be written as

$$\begin{aligned} \dot{V} &= \left(1 - \frac{S^*}{S}\right)\left[\Lambda - \mu S - \frac{\beta\mu cIS}{\Lambda}\right] + \left(1 - \frac{I^*}{I}\right)\left[\frac{\beta\mu cIS}{\Lambda} - (\nu + \theta + \mu)I\right] \\ &+ \left(1 - \frac{T^*}{T}\right)\left[\delta A + \theta I - (\gamma + \mu)T\right] + \left(1 - \frac{A^*}{A}\right)\left[\gamma T + \nu I - (d + \mu + \delta)A\right] \end{aligned} \tag{6.5}$$

At steady state the following equations results from model (2.1),

$$\begin{aligned} \Lambda = \mu S^* + \frac{\beta\mu cI^*S^*}{\Lambda}, \quad \gamma T^* + \nu I^* = (d + \mu + \delta)A^*, \\ \frac{\mu\beta cS^*}{\Lambda} = (\nu + \theta + \mu), \quad \delta A^* + \theta I^* = (\gamma + \mu)T^* \end{aligned} \tag{6.6}$$

Substituting(6.6) in Equation (6.5) and upon simplification, Equation (6.5) becomes

$$\begin{aligned} \dot{V} &= \left(1 - \frac{S^*}{S}\right)\left[\mu S^* + \frac{\beta\mu cI^*S^*}{\Lambda} - \mu S - \frac{\beta\mu cIS}{\Lambda}\right] + \left(1 - \frac{I^*}{I}\right)\left[\frac{\beta\mu cIS}{\Lambda} - (\nu + \theta + \mu)I\right] \\ &+ \left(1 - \frac{T^*}{T}\right)\left[\delta A + \theta I - (\gamma + \mu)T\right] + \left(1 - \frac{A^*}{A}\right)\left[\gamma T + \nu I - (d + \mu + \delta)A\right] \\ &= \left(1 - \frac{S^*}{S}\right)\frac{\beta\mu cI^*S^*}{\Lambda} + \mu S^*\left(2 - \frac{S}{S^*} - \frac{S^*}{S}\right) - \frac{\beta\mu cIS}{\Lambda} + \frac{\beta\mu cIS^*}{\Lambda} \\ &+ \left(1 - \frac{I^*}{I}\right)\left[\frac{\beta\mu cIS}{\Lambda} - (\nu + \theta + \mu)I\right] + \left(1 - \frac{T^*}{T}\right)\left[\delta A + \theta I - (\gamma + \mu)T\right] \\ &+ \left(1 - \frac{A^*}{A}\right)\left[\gamma T + \nu I - (d + \mu + \delta)A\right] \\ &= \left(\frac{\beta\mu cI^*S^*}{\Lambda} + \mu S^*\right)\left(2 - \frac{S}{S^*} - \frac{S^*}{S}\right) + \gamma T^*\left(1 - \frac{A}{A^*}\frac{T}{T^*}\right) + \nu I^*\left(1 - \frac{A^*}{A}\frac{I}{I^*}\right) \\ &+ \delta A^*\left(1 - \frac{T^*}{T}\frac{A}{A^*}\right) + \theta I^*\left(1 - \frac{T^*}{T}\frac{I}{I^*}\right) \end{aligned} \tag{6.7}$$

At $S = S^*, I = I^*, T = T^*, A = A^*$ and from the property that the geometric mean is less than or equal to the arithmetic mean, the inequality $\dot{V} \leq 0$ holds iff (S, I, T, A) takes the equilibrium values (S^*, I^*, T^*, A^*). Therefore, by Lassalles's invariance principle [19], the endemic equilibrium E^* is Globally Asymptotically stable. □

Global asymptotic stability shows that regardless of any starting solution, the solutions of the model will converge to E^* whenever $R_0 > 1$. Epidemiologically, any perturbation of the model by the introduction of infectives shows that the model solutions will converge to the E^* whenever $R_0 > 1$.

7 Sensitivity Analysis

In this section, sensitivity analysis of R_0 with respect to the model parameters is carried out in order to determine the drivers for transmission and prevalence of the disease. This helps in identifying the parameters to be targeted in designing intervention strategies [20]. To perform sensitivity analysis, the normalized forward sensitivity index also known as elasticity[21] is used. The normalized forward sensitivity index of the reproduction number R_0 with respect to a parameter value P is given by

$$\Gamma_P^{R_0} = \frac{\partial R_0}{\partial P} \times \frac{P}{R_0} \tag{7.1}$$

For $R_0 = \frac{\beta C}{\nu+\theta+\mu}$, we have

$$\begin{aligned}
\Gamma_\beta^{R_0} &= \frac{\partial R_0}{\partial \beta} \times \frac{\beta}{R_0} = 1 \\
\Gamma_c^{R_0} &= \frac{\partial R_0}{\partial c} \times \frac{c}{R_0} = 1 \\
\Gamma_\nu^{R_0} &= \frac{\partial R_0}{\partial \nu} \times \frac{\nu}{R_0} = -\frac{\nu}{\nu+\theta+\mu} \\
\Gamma_\theta^{R_0} &= \frac{\partial R_0}{\partial \theta} \times \frac{\theta}{R_0} = -\frac{\theta}{\nu+\theta+\mu} \\
\Gamma_\mu^{R_0} &= \frac{\partial R_0}{\partial \mu} \times \frac{\mu}{R_0} = -\frac{\mu}{\nu+\theta+\mu}
\end{aligned}$$

Using the baseline parameter values, we evaluate the sensitivity indices and summarize it in Table 7

Table 2. Sensitivity indices of the reproduction number for model parameters

Parameter	Value	Sensitivity
c	**3 per year**	**+1**
β	**[0.011-0.95]**	**+1**
θ	**0.00333 per year**	**-0.1059**
ν	**0.01562 per year**	**-0.3975**
μ	**0.0125 per year**	**-0.4967**

The parameters are ordered from the most sensitive to the least. For C and β the higher the average number of sexual contacts and transmission probability, the higher the increase of transmission. The sensitivity indices of R_0 with respect to the rate at which HIV infected individuals progress to AIDS (ν) is -0.3975 implying that decreasing (or increasing) ν by 10% increases (or decreases) R_0 by 3.975%. Increasing (or decreasing) the natural mortality (μ) by 10% decreases (or increases) the R_0 by 49.67%. Similarly, increasing (or decreasing) the rate of recruitment to treatment of infected individuals (θ) by 10% decreases (or increases) the R_0 by 10.59%. This shows that to reduce HIV/AIDS prevalence cases, strategies should be geared towards raising awareness on the need of the reduction of the number of sexual partners c to reduce the transmission probability β, and increase of adherence θ to drug uptake.

8 Numerical Simulation

In this section, MATLAB software is used to illustrate the numerical simulations describing the theoretical results for Equation (2.1).

Table 3. Parameter Estimates for the Model

Description	Parameters	Values	Source
Recruitment rate	Λ	2258 per year	Estimate
Probability of getting the disease	β	[0.011-0.95]	[13],[11]
The number of sexual partners per year	c	3	[3]
Mortality rate	μ	0.01562 per year	[5]
Recruitment to treatment	θ	0.333 per year	[3]
Rate of treatment of Aids patients	δ	0.01562 per year	[5]
Drug resistance	γ	0.004 per year	[3]
Disease induced death rate	d	0.0013 per year	[16]
Rate of progression to AIDS	ν	0.125 per year	[9]

Lack of adherence to antiretroviral therapy is one of the main causes for drug resistance worldwide and one of the main concerns when providing ARTs to developing countries. Poor adherence attenuates optimum clinical benefits and therefore reduces the overall effectiveness of health systems. Simulation of the model with lack of adherence is as shown in Figure 8.

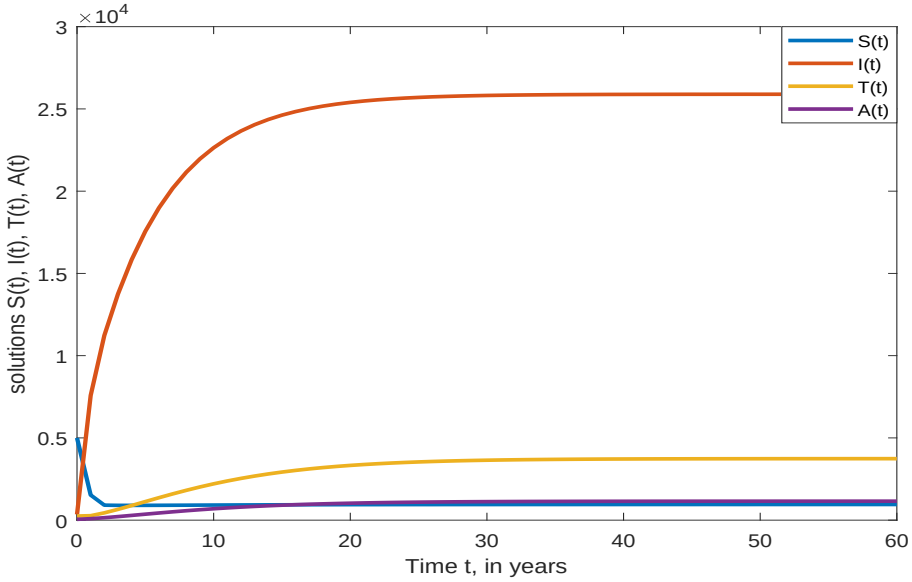

Fig. 2. Case of lack of adherence to ART treatment

Low levels of adherence results in reduction of clinical advantages of treatment and making the virus more difficult to eliminate from host populations.

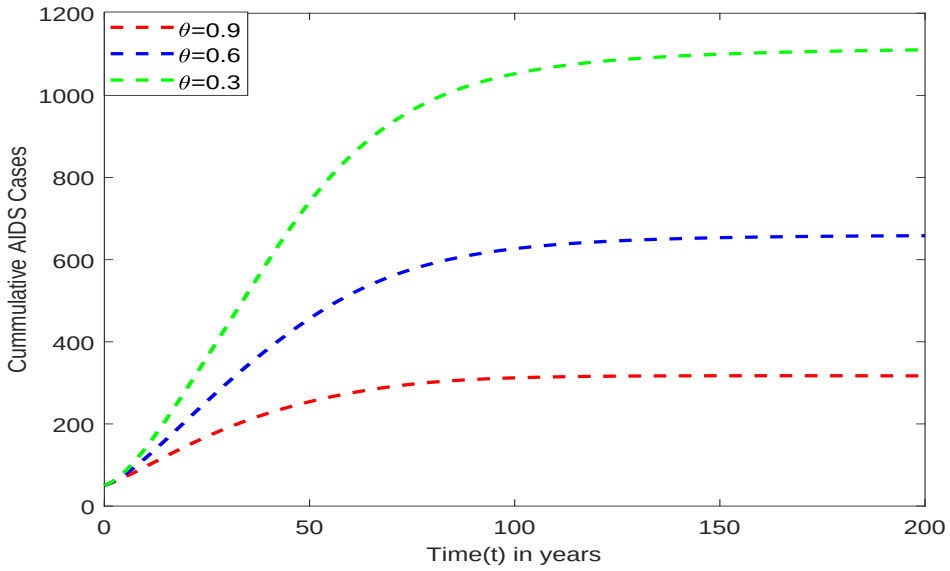

Fig. 3. Influence of adherence on the cumulative AIDS cases

From Figure 8, arise in levels of non-adherence ($\gamma = 1 - \theta$) to drug uptake results in increase of the number of individuals at AIDS stage. From research findings done by Muhammad [3], increase of the AIDS individuals is as a result of the development of new strains of virus that are difficult to eradicate. This confirms that low adherence levels results in high number of AIDS cases (Figure 8).

9 Discussion and Conclusion

Studies by Herbeck *et al.* [4], showed that patients on long term ART with undetectable levels of HIV still harbor replication virus. For this reason, with current medications, ART is a lifelong program. Because of the prolonged use of ART, lapses in the uptake may occur leading to non-adherence. Variables such as income, education and marital status have all been shown to affect adherence to ART, to differing degrees [3]. Analysis shows that disease free equilibrium E_0 is locally and globally asymptotically stable when $R_0 < 1$ while the endemic equilibrium is locally asymptotically stable when $R_0 > 1$. By construction of Lyapunov function and by use of Lassalle's invariance principle, the endemic equilibrium is shown to be globally asymptotically stable. From the simulations, maximal benefit of ART treatment is attained through the advocacy of test and treat strategy and follow-up to ensure adherence. This concurs with studies done by Okosun *et al.* [10], where they considered that good medication adherence is one of essential factors in attainment of optimal HIV care. Based on the results obtained, it is plausible that some of the parameters (such as the treatment and transmission rates) may vary with time. This additions will present an interesting problem that can be further examined.

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Competing Interests

Authors have declared that no competing interests exist.

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