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Endemic analysis of HIV/AIDS transmission in the presence of antiretroviral therapy

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This paper presents a dynamical model that studies the effect of anti-retroviral therapy on human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) transmission. Basic qualitative properties of the model are derived. The model is shown not to exhibit backward bifurcation and thus, disease eradication is possible when the basic reproduction number is less than unity. A critical level of anti-retroviral therapy administration that needs to be achieved for possible disease eradication was also derived.

Key words: HIV/AIDS, mathematical modeling, equlibrium points.

INTRODUCTION

Human Immunodeficiency Virus (HIV)/Acquired immunodeficiency syndrome (AIDS) epidemics are a major challenge to global health and much time, effort and resources have been devoted to a search for a cure to completely avert the situation, but still to no avail. The situation has transformed beyond the immediate effect of the virus into degenerating emotional challenges for the fact that HIV is incurable. The highly active antiretroviral therapy (HAART) has however proven to be effective in curtailing the spread of the HIV virus and AIDS related mortality (Perelson and Nelson, 1999; Palella Jr et al., 1998; Jones and Perelson, 2005). In 2005, about 3.1 million people died from AIDS and 4.9 million people became infected with HIV worldwide (Okosun et al., 2013). In 2010 it was estimated that about 34 million people were living with the HIV/AIDS virus worldwide with

about 2.7 million people newly infected. The number of people who died due to AIDS related sicknesses was 1.8 million (UNAIDS, UNAIDS World AIDS Day Report, 2011).

Sub-Saharan Africa is one of the worst hit continents with about 22.9 million people living with HIV/AIDS most of whom are within the active working population aged between 15 and 49 years.

Commercial sex is still an important factor in many of the HIV epidemics in Western, Central and Eastern Africa. It is estimated that sex workers (HIV infection among sex workers, their clients, or their other sex partners) alone accounted for almost one third (32%) of new HIV infections in Ghana, 14% in Kenya and 10% in Uganda (UNAIDS, 2010). The effects of the HIV/AIDS epidemic is the shock, then denial, guilt, anger,

and sadness before finally adjustment to the reality, a very common phenomenon with so many other diseases where, for example, there is a social stigma. Also, the repercussion of the infection is a reduction in productivity which subsequently aggravates the incidence of poverty.

Many preventive and treatment strategies such as use of condoms, sticking to one sex partner, antiretroviral therapy (ART) have been suggested. The ART provides a maximal and durable suppression of the viral load and helps to slow the disease progression, reduces HIV-related morbidity and mortality and improves the quality of the life of the infected person (Okosun et al., 2013).

A lot of mathematicians and scientists have conducted various studies to find a remedy to the HIV/AIDS pandemic. A very important tool that is usually employed in epidemiological studies of this nature is mathematical modelling. It can be used to study the epidemiological patterns for disease control to predict the short and long term transmission dynamics of HIV/AIDS. Anderson et al. (1986) presented a simple mathematical HIV transmission model to investigate the effects of various factors on the overall pattern of the AIDS epidemic. Makinde (2009) studied the transmission dynamics of infectious diseases with waning immunity using the non-perturbative approach while Agraj et al. (2007) also worked on the spread of AIDS epidemic with vertical transmission by considering a non-linear mathematical model. Several other mathematicians and scientists such as Busenburg et al. (1993), Karrakchou et al. (2006), Perelson and Nelson (1999) and Adams et al. (2004) have investigated into the HIV/AIDS transmission dynamics using mathematical modelling, a proven tool for epidemiological investigation. The study therefore seeks to analyze the dynamics of the long term effects of the treatment of HIV/AIDS on the spread of the disease.

FORMULATION OF THE MODEL

The spread of HIV/AIDs was studied with anti-retroviral treatment. The population was subdivided into four mutually exclusive compartments of susceptibles, S, infectives that are not on treatment, L_1, infectives on treatment, L_2 and full-blown AIDS population, A. The schematic diagram is as shown in Figure 1.

From the flow diagram, the model equations are as follows:

$$\frac{d}{dt} S(t) = Q - \frac{c\left(\beta_1 I_1 + \beta_2 I_2\right) S}{N} - \mu S$$

$$\frac{d}{dt} I_1(t) = \frac{c\left(\beta_1 I_1 + \beta_2 I_2\right) S}{N} - \left(\sigma_1 + \theta + \mu\right) I_1$$

$$\frac{d}{dt} I_2(t) = \theta I_1 - \left(\sigma_2 + \mu\right) I_2$$

$$\frac{d}{dt} A(t) = \sigma_1 I_1 + \sigma_2 I_2 - \left(\alpha + \mu\right) A$$

With initial conditions given as:

$$S(0) = S_0, I_1(0) = I_{10}, I_2(0) = I_{20}, A(0) = A_0$$

where the parameter in the model are described as follows: N(t) = total population size at time t, S(t) = size of the susceptible population at time t, I_1(t)= size of the infective population not under treatment at time t, I_2(t)= The size of the infective population under treatment at time t, A(t) = size of the full blown AIDS population at time t, Q_0 rate of recruitment of susceptibles into the population, u= natural death rate, α=rate of death due to the infection of the AIDS virus, c = the number of sexual partners of an infected person, β_1= rate of contact between the susceptible and those infectives not under treatment, β_1=rate of contact between the susceptible and those infectives under treatment, θ=rate at which the infectiv.es not under treatment are introduced to treatment, σ_1 and σ_2 are the rate of conversion from HIV to full blown AIDS of those not under treatment, and the under treatment, respectively.

Properties of the model

Feasible region

Summing all the model equations gives:

$$\frac{dN}{dt} = -\mu N + Q - A\alpha$$

Thus, we have:

$$N \le \frac{q}{\mu} \cdot \left(1 - e^{-\mu \cdot t}\right)$$

so that as:

$$t \to \infty \ N \to \frac{Q}{\mu}$$

The feasible region of the model given as:

$$\Omega = \left\{\left(S, I_1, I_2, A\right) \in \mathbb{R}^4 \middle| S + I_1 + I_2 + A \le \frac{Q}{\mu}\right\}$$

is positively invariant and hence, we can sufficiently perform the analysis of the model in Ω.

Basic reproduction number

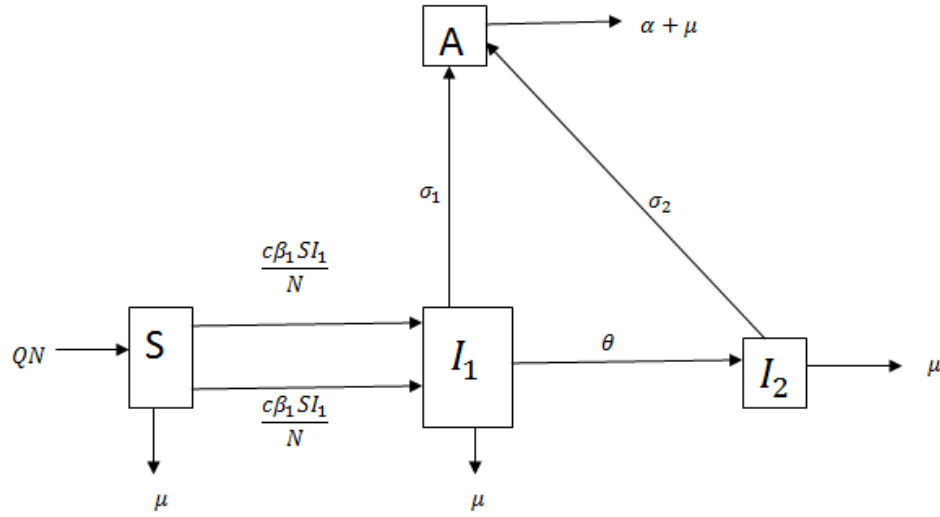It was taken note that the disease-free (DFE) of the

Figure 1. Schematic diagram of the model.

model is given by

$$DFE = \left(\frac{Q}{\mu}, 0, 0, 0 \right)$$

To determine the basic reproduction number of the model, we use the linearization technique, which seeks a condition under which all eigenvalues of the Jacobian model evaluated at the disease-free equilibrium will have negative real parts.

The Jacobian of the model is given by:

Where $\dfrac{c\left(\beta_1 I_1 + \beta_2 I_2 \right)}{N} = \lambda$ and $\dfrac{c\left(\beta_1 I_1 + \beta_2 I_2 \right)}{N^2} = \dfrac{\lambda}{N}$

Evaluating the Jacobian at the DFE gives:

$$J = \begin{vmatrix} \dfrac{\lambda S}{N} - \lambda - \mu & -\dfrac{c\beta_1 S}{N} + \dfrac{\lambda S}{N} & -\dfrac{c\beta_2 S}{N} + \dfrac{\lambda S}{N} & \dfrac{\lambda S}{N} \\ -\dfrac{\lambda S}{N} + \lambda & \dfrac{c\beta_1 S}{N} - \dfrac{\lambda S}{N} - \sigma_1 - \theta - \mu & \dfrac{c\beta_2 S}{N} - \dfrac{\lambda S}{N} & -\dfrac{\lambda S}{N} \\ 0 & \theta & -\sigma_2 - \mu & 0 \\ 0 & \sigma_1 & \sigma_2 & -\alpha - \mu \end{vmatrix}$$

$$J = \begin{bmatrix} \dfrac{\lambda S}{N} - \lambda - \mu & -\dfrac{c\beta_1 S}{N} + \dfrac{\lambda S}{N} & -\dfrac{c\beta_2 S}{N} + \dfrac{\lambda S}{N} & \dfrac{\lambda S}{N} \\ -\dfrac{\lambda S}{N} + \lambda & \dfrac{c\beta_1 S}{N} - \dfrac{\lambda S}{N} - \sigma_1 - \theta - \mu & \dfrac{c\beta_2 S}{N} - \dfrac{\lambda S}{N} & -\dfrac{\lambda S}{N} \\ 0 & \theta & -\sigma_2 - \mu & 0 \\ 0 & \sigma_1 & \sigma_2 & -\alpha - \mu \end{bmatrix}$$

The Jacobian evaluated at the DFE has four eigenvalues, two of which are-μ and -(α+μ) which are negative. The remaining two are eigenvalues of the sub-Jacobian given by:

$$J_1(DFE) = \begin{bmatrix} c\beta_1 - \sigma_1 - \theta - \mu & c\beta_2 \\ \theta & -\sigma_2 - \mu \end{bmatrix}$$

The eigenvalues of the sub-Jacobian are solutions of the characteristic equation given by:

$$\lambda^2 + \left(-c\beta_1 + \left(\sigma_1 + \theta + \mu\right) + \left(\sigma_2 + \mu\right)\right)\lambda + \left(-c\beta_1 + \left(\sigma_1 + \theta + \mu\right)\right)\left(\sigma_2 + \mu\right) - \theta c\beta_2 = 0$$

It is easy to show that the eigenvalues are both negative (or have negative real parts) if

$$c\left(\beta_1\left(\sigma_2 + \mu\right) + \beta_2\theta\right) < \left(\sigma_1 + \theta + \mu\right)\cdot\left(\sigma_2 + \mu\right).$$

If we define the basic reproduction number of the model as $R_0 = \dfrac{c\left(\beta_1\left(\sigma_2 + \mu\right) + \beta_2\theta\right)}{\left(\sigma_1 + \theta + \mu\right)\cdot\left(\sigma_2 + \mu\right)}$,

then the following lemma is implied.

Lemma 1: The DFE is locally asymptotically stable if $R_0 < 1$

Solving for θ in $R_0 \leq 1$ gives a critical value below which θ must not go if we seek to control the spread of the disease. This critical value is given by:

$$\theta_{critical} = \frac{\left(c\beta_1 - \left(\sigma_1 + \mu\right)\right)\left(\sigma_2 + \mu\right)}{\left(c\cdot\beta_2 - \left(\sigma_2 + \mu\right)\right)}.$$

ENDEMIC EQUILIBRIUM OF THE MODEL

The model can be shown to have an endemic equilibrium $E^* = \left(S^*, I_1^*, I_2^*, A^*\right)$ defined as

$$S^{*`} = \frac{Q}{\lambda + \mu}, \qquad I_1^{*`} = \frac{\lambda Q}{\left(\lambda + \mu\right)\left(\sigma_1 + \theta + \mu\right)}, \quad I_2^{*`} = \frac{\theta\lambda Q}{\left(\lambda + \mu\right)\left(\sigma_1 + \theta + \mu\right)\left(\sigma_2 + \mu\right)},$$

and

$$A^{*`} = \frac{\left(\sigma_1\cdot\left(\sigma_2 + \mu\right) + \sigma_2\theta\right)\lambda Q}{\left(\lambda + \mu\right)\left(\sigma_1 + \theta + \mu\right)\left(\alpha + \mu\right)\cdot\left(\sigma_2 + \mu\right)}$$

Substituting the endemic equilibrium into $\lambda = \dfrac{c\left(\beta_1 I_1 + \beta_2 I_2\right)}{N}$ gives the following quadratic equation:

$$\left[\mu\left(\left(\sigma_2 + \mu\right)\cdot\left(\sigma_1 + \theta + \mu\right) + \left(\mu + \sigma_2 + \theta\right)\alpha\right)\right]\lambda^2 - \mu\left(\alpha + \mu\right)\cdot\left(\sigma_1 + \theta + \mu\right)\cdot\left(\sigma_2 + \mu\right)\cdot\left(R_0 - 1\right)\lambda = 0$$

The quadratic equation above has two roots; namely $\lambda=0$, which corresponds to the DFE and the second root is given by:

$$\lambda = \frac{\mu\left(\left(\sigma_2 + \mu\right)\cdot\left(\sigma_1 + \theta + \mu\right) + \left(\mu + \sigma_2 + \theta\right)\alpha\right)}{\mu\left(\alpha + \mu\right)\cdot\left(\sigma_1 + \theta + \mu\right)\cdot\left(\sigma_2 + \mu\right)\cdot\left(R_0 - 1\right)}$$,which corresponds to the endemic equilibrium

The following result is easily established.

Lemma 2: When the model has a globally asymptotically stable DFE.

Proof
When the non-zero root of the endemic equilibrium polynomial equation is negative, leading to a negative endemic equilibrium, which epidemiologically does not exist? Hence, for, only the DFE exists which is asymptotically stable. Therefore, the DFE is globally asymptotically stable when concluding the proof.

BIFURCATION ANALYSIS

The condition that R_0 be less than unity for disease eradication is sometimes not sufficient even though it is always necessary. When forward bifurcation occurs, then the condition is necessary and sufficient, but when backwards bifurcation occurs, the condition is no longer sufficient for disease eradication. Here, we perform bifurcation analysis of the model by using Theorem 4.2 of Casillo-Chavez and Song (2004), which states if 0 is an equilibrium point of the dynamical system:

$$\frac{dx}{dt} = f(x) \;,$$

then the local dynamics of the system are completely determined by the bifurcation coefficients given by:

$$a = \sum_{ijk=1}^{4} v_k w_i w_j \frac{\partial^2}{\partial x_i \, \partial x_j} f_k\left(DFE, c^*\right)$$

and

$$b = \sum_{ijk=1}^{4} v_k w_i \frac{\partial^2}{\partial x_i \, \partial c^*} f_k\left(DFE, c^*\right)$$

where f_k (x) is the kth component of f(x) and c^* is a bifurcation parameter.

The Jacobian of the model evaluated at the disease-free equilibrium can be shown to have right and left eigenvectors (associated with a simple Eigenvalue) given respectively by:

$$w = \left[-\frac{\left(\sigma_1 + \theta + \mu\right)\left(\sigma_2 + \mu\right)}{\mu}, \quad \frac{\sigma_2 + \mu}{\theta}, \quad 1 \;, \quad \frac{\sigma_1\left(\sigma_2 + \mu\right) + \sigma_2\theta}{\theta\left(\alpha + \mu\right)} \right]^T$$

and

$$v = \left[0, \ \frac{(\sigma_2 + \mu)\,\theta}{(\sigma_2 + \mu)^2 + c\,\beta_2\,\theta}, \ \frac{c\,\beta_2\,\theta}{(\sigma_2 + \mu)^2 + c\,\beta_2\,\theta}, \ 0 \right]$$, so that the bifurcation coefficients are given

by:

$$a = -2 \cdot \frac{(\sigma_2 + \mu)\, c\,\mu \left(\beta_1\,(\sigma_2 + \mu) + \beta_2\,\theta\right)\left((\sigma_2 + \mu)\,(\mu + \alpha + \sigma_1 + \theta) + \alpha\,\theta\right)}{\left((\sigma_2 + \mu)^2 + \theta\,c\,\beta_2\right)\theta\,(\alpha + \mu)\,Q}$$

and

$$b = \frac{(\sigma_2 + \mu)\left(\beta_1\,(\sigma_2 + \mu) + \beta_2\,\theta\right)}{(\sigma_2 + \mu)^2 + \theta\,c\,\beta_2}$$.

Lemma 3: The model exhibits forward bifurcation for R_0 in the neighborhood of unity.

Conclusion

In this paper, a nonlinear epidemic model has been proposed and qualitatively analysed to study the effect of anti-retro-viral therapy on the dynamics of HIV/AIDs transmission. Basic properties of the model are derived and discussed. It is shown that when the basic reproduction number is less than unity, the disease eradication is possible and when the basic reproduction number is greater than unity then the disease persists. A minimum level of anti-retro-viral therapy administration needed for successful combating of the disease is derived.

Conflict of interests

The authors have not declared any conflict of interests.

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