Applied Mathematical Sciences, Vol. 8, 2014, no. 34, 1643 - 1657
HIKARI Ltd, www.m-hikari.com
http://dx.doi.org/10.12988/ams.2014.42116

A HIV/AIDS Model in a Homogeneous Population with Time Lags in the Transmission

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Abstract

We investigate a simple HIV/AIDS epidemic model in a heterosexual population by by modifying a Susceptible-Infective-Removed (SIR) model. The model considers sexual transmission of HIV where individuals are being recruited into sexually matured age group at a constant rate and incorporates time lags for one to become infective and the other to become fully blown. A complete qualitative analysis of the model, including the boundedness and positivity of the solutions, local stability of the equilibrium points is done. We applly the next generation matrix to determine the disease reproduction number R_0. The Model is shown to be completely determined by the reproduction number. The model is numerically analysed to asses the effects of the delay on the dynamics of HIV/AIDS and the demographic impact of the epidemic using the demographic and epidemiological parameters for Kenya.

Mathematics Subject Classification: 37L15

Keywords: Time Lag, Reproduction number, Next generation matrix

1 Introduction

Before getting into the mathematical model, it is important to understand the clinical stages of the HIV/AIDS progression. This will help us justify the case of developing a model with two time delays.

HIV undergoes a number of stages to culminate to AIDS. It follows three stages that we now state. After a primary infection, the HIV enters the body system. The immune system initiates a response to fight the virus (intruder). HIV is considered to have a high replication rate (see in [2]), hence making the viral load to grow faster than the immune system response. This period lasts for a number of weeks before the immune system recovers and starts to suppress the amount of virus present. Most of the clinical tests at this stage cannot detect the presence of the virus in the body system. Hence it requires some time delay, say $\tau_1 > 0$, for it to be detectable; that is, for an infected individual to become infective/infectious.

After the initial response by the immune system, a viral load "set point"is reached, with HIV replicating at a constant level. This period lasts a number of years without any outward-observable change on the patient's health. The numbers of $CD4^+$ T-cells are slowly depleted. The introduction of drug therapy means the viral load count can be reduced significantly. In other patients, continual administration of therapy decreases the viral load below detectable levels (as observed in [12]). Thus there is a time lag, $\tau_2 > 0$, that is required for an infective individual to progress from Infective to become fully blown with AIDS symptoms.

There is abundant literature on the the mathematical models of the transmission dynamics of HIV/AIDS in populations (see for instance in [1], [2], [8], [11], [12]). Most of these works use compartment models and a sytem of Ordinary Differential Equations to describe the epidemic dynamics. Another set of models that is close to what we wish to develope, uses a system of Delay Differential Equations to describe the dynamics of the compartment model. Although time delays have been incorporated in some of the models (such as in [4], [6], [8], [13]), very little attention has been given to the models that consider the following delays: time for an individual to become infective of the HIV (window period), and the time for one to become fully blown (AIDS). Hence, the formulation of the model in this paper is similar to that proposed by Luboobi *et al.* [8], but with the inclusion of a second time delay. We develop a model that sub-divides a population in a clinical set up into; Susceptible (uninfected) individuals, Infective individuals, and fully blown (AIDS) individuals. We then incorporate discrete time delays, say $\tau_1, \tau_2 > 0$, to represent the time it takes for an individual to become infectious, and to become fully blown (AIDS) respectively. This is incorporated into the model to describe the progression of the disease.

In §2 we present the HIV/AIDS model and state and proof basic properties that the model has to satisfy for it to be consistent with real biological conditions. In §3, sufficient conditions for local stability of long-term solutions are stated and proved. In §4 we present the numerical simulations of the HIV/AIDS model to asses the effects of the delay on the dynamics of HIV/AIDS and the demographic impact of the epidemic. Finally, in §5 we present the conclusion and recommendation for further research.

2 The Model

We consider a heterosexual population that can be divided into three compartments. Let sexually mature susceptibles at time $t > 0$ be denotes by $S(t)$. This is the number of the individuals that are not yet infected but may, if exposed to HIV. Let $I(t)$ denote the number of individuals at a time t who are already infected with HIV and are capable of transmitting the virus. The Variable $A(t)$ will represent the number of individuals who have developed full blown AIDS symptoms at a time t. At this stage, the HIV infected individual has progressed to AIDS.

Other parameters are defined as follows:

B:- Recruitment rate of susceptibles into a sexeually active population.

μ:- The AIDS-non related mortality rates per capita; that is, natural deaths.

τ_1:- The time taken for an individual to become infectious after being in contact with an infected individual.

τ_2:- The time taken for infected individuals to become fully blown after becoming infectious.

d:- The rate at which AIDS patients are dying due to AIDS causes.

υ:- The rate at which HIV infected individuals(infective) progress to AIDS.

C:- The rate at which one changes (acquires new) sexual partners.

β:- The transmission probability; that is, the probability of getting infected from a randomly chosen partner.

We assume that each individual that is susceptible randomly and uniformly draws a person from the population. If the individual chosen is infectious, the susceptible individual is assumed to get the virus. After a time lag, τ_1, the individual when tested will be considered infectious. Without drug intervention, an infected individual will then progress to fully blown after a time $\tau_2 > 0$. Each full blown individual remains full blown till death. We shall also make the following assumptions:

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

(ii) An individual once infected becomes and remains infective until death.

(iii) The population under study is homogeneous; that is, there is uniform mixing.

(iv) The force of infection depends on the number of infective in the population and the product $\beta\frac{C}{N}$, where, $N = S(t) + I(t) + A(t)$.

(v) The full blown AIDS individuals are no longer a threat in the spread of the epidemic as they are easily recognized in the population; that is, they do not participate in the transmission dynamics.

The susceptible population is assumed to be recruited into the compartment of Susceptibles by birth at the rate given by B, while the population can decrease due to natural deaths or infection as a result of interaction with infected individuals in compartment of infectives. Infected individuals may die due to natural death or progress to compartment of fully blown individuals. After progression to the compartment of fully blown, individuals are removed from this compartment due to natural deaths or disease induced deaths. The latter descriptions of the disease dynamics can be represented in the following diagram.

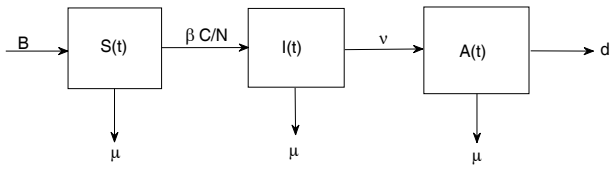

Figure 1: A schematic diagram of the disease progression.

The dynamics described has been represented mathematically by the equations

$$\begin{aligned}
\dot{S}(t) &= B - \mu S(t) - \frac{\beta C I(t) S(t)}{N(t)}, \\
\dot{I}(t) &= \frac{\beta C I(t) S(t)}{N(t)} - (\nu + \mu) I(t), \\
\dot{A}(t) &= \nu I(t) - (d + \mu) A(t). \qquad (1)
\end{aligned}$$

The system of equations in Equation(1) is overly simplistic. It assumes that cause and effect are instanteneous. This is not the case in a normal clinical set up. An individual after being in contact with an infected individual, takes some time lag, say τ_1, to be clinically infective. Likewise, an infected individual takes sometime say, τ_2, to become fully blown. These dynamics of the disease leads to the modification of Equation (1) to yield

$$\begin{aligned} \dot{S}(t) &= B - \mu S(t) - \frac{\beta C I(t) S(t)}{N(t)}, \\ \dot{I}(t) &= \frac{\beta C I(t-\tau_1) S(t-\tau_1)}{N(t-\tau_1)} - (\nu+\mu) I(t), \\ \dot{A}(t) &= \nu I(t-\tau_2) - (d+\mu) A(t). \end{aligned} \tag{2}$$

Let $\tau = \max\{\tau_1, \tau_2\}$, and $C := \mathcal{C}([-\tau, 0], \mathbb{R}^3_+)$, $\varphi(\theta) := (S(\theta), I(\theta), A(\theta))$ $\theta \in [-\tau, 0]$; $\varphi \in C$, with the norm of φ defined as $\| \varphi \| = sup_{-\tau \le \theta \le 0} \mid \varphi(\theta) \mid$ where $\mid \cdot \mid$ is a norm in $\mathbb{R}^3$. The initial condition for Equation (2) is

$$\varphi(\theta) = (S(\theta), I(\theta), A(\theta)), \tag{3}$$

where $S(\theta) \ge 0, I(\theta) \ge 0$, and $A(\theta) \ge 0 \; \forall \; \theta \in [-\tau, 0]$. Equation (2) subject to (3), has a unique solution, see for instance [7].

2.1 Basic properties

We need to show, for biological reasons, that the solution to Equation(1) subject to $\varphi(\theta)$ is positive and bounded.

2.1.1 The invariant region

Since Equation (2) describes a human population, we need to show that the solution will be positive for all $t \ge 0$. Hence Equation (2) will be analyzed in a suitable feasible region Γ defined thus:

$$\Gamma := \{(S(t), I(t), A(t)) \in \mathbb{R}_+ \times C \times C : S(t) + I(t) + A(t) \le \frac{B}{\mu}\}. \tag{4}$$

In other words, with given non negative initial data, the solution of Equation (2) is bounded and remains positive for all $t \ge 0$ in the region Γ. We thus state Lemma 2.1.

Lemma 2.1. *The feasible region Γ with initial conditions $\varphi(\theta)$ is positively invariant with respect to Equation (2).*

Proof. Adding all the three equations in Equation (2) we have;

$$\begin{aligned}(S(t)+I\dot{(}t)+A(t)) &= B-\mu(S(t)+I(t)+A(t))-\beta C\Big(\frac{I(t)S(t)}{N(t)}-\frac{I(t-\tau_1)S(t-\tau_1)}{N(t-\tau_1)}\Big)\\ &\quad -\nu(I(t)-I(t-\tau_2))-dA(t),\\ &\leq B-\mu(S(t)+I(t)+A(t))-\beta C\Big(\frac{I(t)S(t)}{N(t)}-\frac{I(t-\tau_1)S(t-\tau_1)}{N(t-\tau_1)}\Big)\\ &\quad -\nu(I(t)-I(t-\tau_2)). \qquad (5)\end{aligned}$$

For any increasing population growth, we have;

$$\frac{I(t)S(t)}{N(t)}-\frac{I(t-\tau_1)S(t-\tau_1)}{N(t-\tau_1)}>0, \text{and}\quad I(t)-I(t-\tau_2)>0.$$

Thus, Equation (5), becomes;

$$(S(t)+I(t)+A(t))' \leq B-\mu(S(t)+I(t)+A(t)) \qquad (6)$$

and by the Variations-of-constants formula, we have;

$$\limsup_{t\longrightarrow\infty}(S(t)+I(t)+A(t))<\frac{B}{\mu}.$$

Therefore $(S(t),I(t),A(t))$ is ultimately bounded in $\mathbb{R}_+\times C\times C$. □

2.1.2 Positivity of solutions

We now show that all the state variables in Equation (2) will remain non negative so that the solutions of the model with positive initial conditions will remain positive for all $t>0$.

Lemma 2.2. *For Equation (2), with initial conditions in the region* Γ*, the solution* $(S(t),I(t),A(t))$ *is non-negative for all* $t\geq 0$.

Proof. We have to prove that $S(t)\geq 0$, $I(t)\geq 0$, and $A(t)\geq 0$. Considering the first equation of Equation (2), we have

$$\dot{S}(t)=B-\Big(\frac{\beta CI(t)}{N(t)}+\mu\Big)S(t)>-\Big(\frac{\beta CI(t)}{N(t)}+\mu\Big)S(t) \qquad (7)$$

resulting in

$$S(t)>S(0)\exp\Big[-\int_0^t\frac{\beta CI(\xi)}{N(\xi)}+\mu)d\xi\Big]\geq 0.$$

For the second equation of Equation(2), we have

$$\dot{I}(t)=\frac{\beta CI(t-\tau_1)S(t-\tau_1)}{N(t-\tau_1)}-(\nu+\mu)I(t)>-(\nu+\mu)I(t) \qquad (8)$$

which on integration we have

$$I(t) > I(0)\exp\Big[-\int_0^t(\nu+\mu)d\xi\Big] \geq 0.$$

Lastly, we have the third Equation of (2) as

$$\dot{A}(t) = \nu I(t-\tau_2) - (d+\mu)A(t) > -(d+\mu)A(t) \tag{9}$$

which on integration we have

$$A(t) > A(0)\exp\Big[-\int_0^t(d+\mu)d\xi\Big] \geq 0.$$

Hence all solutions of Equation (2) are non-ngative for all $t > 0$ and thus epidemiologically well posed in the region Γ. □

2.1.3 The Basic Reproduction Number R_0

The Reproduction number R_0 is the average number of secondary infections due to a single infectious individual introduced in a fully susceptible population. The constant R_0 is determined by the method of next generation matrix see for instance [5]. From Equation(2) we let

$$\Phi(t) := [\frac{\beta C I(t) S(t)}{N(t)}], \quad \text{and} \quad \Psi(t) := [(\mu+\nu)I(t)], \tag{10}$$

where Φ and Ψ are the transmission and transition matrices respectively. Since $I(t)$ is the cause for new infections, we differentiate Φ and Ψ with respect to $I(t)$ and ignore higher order terms to obtain

$$F := \frac{d\Phi}{dI} = \frac{\beta C S(t)}{N(t)}, \quad \text{and} \quad V := \frac{d\Psi}{dI} = (\mu+\nu). \tag{11}$$

The reproduction number R_0 is then given by $R_0 = \rho(FV^{-1})$, as described in [5], is the spectral radius of the matrix (FV^{-1}). Hence,

$$R_0 = \rho(FV^{-1}) = \frac{\beta C S}{N(\nu+\mu)}. \tag{12}$$

3 Stability analysis

For long term solutions, we need to determine equilibriuum solutions of Equation(2). The following are equilibrium solutions

(i) If $S(t) = I(t) = A(t) = 0$, the population is wiped out.

(ii) When $I(t) = A(t) = 0$, and $S \neq 0$ then $S(t) = \frac{B}{\mu}$.

(iii) When all components of $(S(t), I(t), A(t)) =: (S^*, I^*, A^*)$ are nonzero, then we have on computing that

$$S^* = \frac{N^*(\mu+\nu)}{\beta C}, \quad I^* = \frac{B}{\mu+\nu} - \frac{N^*\mu}{\beta C}, \quad A^* = \frac{\nu}{(d+\mu)}\left(\frac{B}{\mu+\nu} - \frac{N^*\mu}{\beta C}\right), \quad N^* = S^* + I^* + A^*. \tag{13}$$

Equation (2) has two nontrivial steady states; the uninfected steady state $E_0 = (\frac{B}{\mu}, 0, 0)$ and the infected steady state $E_1 = (S^*, I^*, A^*)$ where S^*, I^*, A^* are as defined in Equation (13). At E_1, the infectives are persistent with a constant force $I^* > 0$ hence the risk of the development of AIDS in the population. To study their stability, we linearize the system about these points. Let's define

$$x(t) := S(t) - S^*, \quad y(t) := I(t) - I^*, \quad z(t) := A(t) - A^*, \tag{14}$$

and by Taylor series expansion of Equation(2) about (S^*, I^*, A^*) and upon ignoring higher order terms, we obtain

$$\begin{aligned} \dot{x}(t) &= -(\mu + \frac{\beta C I^*}{N^*})x(t) - \frac{\beta C S^*}{N^*}y(t), \\ \dot{y}(t) &= \frac{\beta C I^*}{N^*}x(t-\tau_1) - (\mu+\nu)y(t) + \frac{\beta C S^*}{N^*}y(t-\tau_1), \\ \dot{z}(t) &= \nu y(t-\tau_2) - (d+\mu)z(t). \end{aligned} \tag{15}$$

Equation (15) can be expressed in a matrix form as

$$\dot{Y}(t) = AY(t) + B_1 Y(t-\tau_1) + B_2 Y(t-\tau_2), \tag{16}$$

where

$$A := \begin{pmatrix} -(\mu + \frac{\beta C I^*}{N^*}) & -\frac{\beta C S^*}{N^*} & 0 \\ 0 & -(\mu+\upsilon) & 0 \\ 0 & 0 & -(d+\mu) \end{pmatrix}, \; B_1 := \begin{pmatrix} 0 & 0 & 0 \\ \frac{\beta C I^*}{N^*} & \frac{\beta C S^*}{N^*} & 0 \\ 0 & \nu & 0 \end{pmatrix}, \; B_2 := \begin{pmatrix} 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & \nu & 0 \end{pmatrix}$$

$$Y(t) := \begin{pmatrix} x(t) \\ y(t) \\ z(t) \end{pmatrix}, \text{and } Y(t-\tau_i) := \begin{pmatrix} x(t-\tau_i) \\ y(t-\tau_i) \\ z(t-\tau_i) \end{pmatrix}, \quad i = 1, 2.$$

Equation (16) is a linear system and its characteristic equation is given by

$$\begin{vmatrix} -\mu - \frac{\beta C I^*}{N^*} - \lambda & -\frac{\beta C S^*}{N^*} & 0 \\ \frac{\beta C I^*}{N^*} e^{-\tau_1 \lambda} & (\frac{\beta C S^*}{N^*})e^{-\tau_1\lambda} - (\mu+\nu) - \lambda & 0 \\ 0 & \nu e^{-\tau_2 \lambda} & -(d+\mu) - \lambda \end{vmatrix} = 0. \tag{17}$$

At E_0, Equation(17) has two eigenvalues that are negative and are given by

$$\lambda = -\mu, \lambda = -(d+\mu).$$

For the other eigenvalues, we consider

$$H(\lambda) + D(\lambda)e^{-\lambda\tau_1} = 0, \tag{18}$$

with

$$H(\lambda) = \lambda + \mu + v, \quad D(\lambda) = -(\frac{\beta C S^*}{N^*}).$$

For asymptotic stability we need $Re\lambda < 0$ for all $\tau_1 > 0$.

Theorem 3.1. *For all $\tau_1 > 0$, the disease free equilibrium exists and is asymptotically stable if the reproduction rate $R_0 < 1$.*

To prove Theorem 3.1, we use Lemma 3.2 due to Boese [3].

Lemma 3.2. *For any $\tau_1 > 0$, the roots of (18) will lie to the left of the complex plane, if the following are satisfied:*

(i) All zeros of $H(\lambda)$ satisfy $Re\lambda \leq 0$,

(ii) $|H(0)| \geq |D(0)|$.

Proof. Condition (i) is satisfiesd as the roots of $H(\lambda)$ are $-(\mu+v)$ whilst at, E_0, $|H(0)| \geq |D(0)|$ would imply that $R_0 = \frac{\beta C}{(\mu+v)} < 1$. □

At endemic equilibrium, $E_1 = (S^*, I^*, A^*)$, Equation (17) becomes;

$$\begin{vmatrix} -(\mu + \frac{\beta C I^*}{N^*}) - \lambda & -\frac{\beta C S^*}{N} & 0 \\ \frac{\beta C I^*}{N^*} e^{-\tau_1\lambda} & \frac{\beta C S^*}{N^*} e^{-\lambda\tau_1} - (\mu+v) - \lambda & 0 \\ 0 & \nu e^{-\lambda\tau_1} & -(d+\mu) - \lambda \end{vmatrix} = 0. \tag{19}$$

Clearly $-(d+\mu)$ is an eigenvalue. For the other eigenvalues λ, we have

$$H(\lambda) + D(\lambda)e^{-\lambda\tau_1} = 0, \tag{20}$$

where

$$H(\lambda) := \lambda^2 + (2\mu + \nu + \frac{\beta C I^*}{N^*})\lambda + \mu^2 + \mu\nu + (\mu+\nu)\frac{\beta C I^*}{N^*}$$

and

$$D(\lambda) := -\frac{\beta C S^*}{N^*}\lambda - \frac{\beta C S^* \mu}{N^*}.$$

If the roots of Equation (20) have negative real parts, then the endemic equilibrium is asymptotically stable. This leads us to the following Theorem;

Theorem 3.3. *For all values of $\tau_1 > 0$ and $R_0 \geq \mu$, the disease equilibrium E_1,is positively bounded and asymptotically stable.*

To check whether the roots of Equation(20) are negative, we use Lemma 3.2 with $H(\lambda)$ and $D(\lambda)$ as defined in Equation(20).

Proof. The roots of $H(\lambda)$ are given by $-\mu - \nu$, and $-\mu - \frac{\beta C I^*}{N^*}$. To prove Condition (ii) we have $H(0) = \mu^2 + \mu\nu + (\mu + \nu)\frac{\beta C I^*}{N^*}$ and $D(0) = \frac{\beta C S^* \mu}{N^*}$ and we require that

$$\mid \mu^2 + \mu\nu + (\mu + \nu)\frac{\beta C I^*}{N^*} \mid \geq \mid \frac{\beta C S^* \mu}{N^*} \mid \tag{21}$$

Using I^* and S^* as defined in Equation (13), we get;

$$\left|\mu^2 + \mu\nu + (\mu + \nu)\frac{\beta C}{N^*}\left(\frac{B}{\mu + \nu} - \frac{N^* \mu}{\beta C}\right)\right| \geq \left|\frac{\beta C \mu}{N^*}\left(\frac{N^*(\mu + \nu)}{\beta C}\right)\right| \tag{22}$$

that reduces to; $R_0 \geq \mu$. □

By Lemma 2.1 and Lemma 2.2, all solutions are positive and bounded, and by Lemma 3.2, asymptotic stability for the disease equilibrium is guaranteed when $R_0 \geq \mu$ and is independent of the delay τ_1. Hence the proof.

4 Numerical Simulations

We use Matlab software to illustrate the numerical simulations describing the theoretical results for model (2). We describe the variables and parameters values to enable us make numerical simulations. Parameter values are hypothetical.

Table: Data for the HIV/AIDS model

Variables and Parameters	Initial or default values	Source
$S(t)$ susceptible individuals	4000	Estimate
$I(t)$ infected individuals	800	Estimate
$A(t)$ fully blown individuals	97	Estimate
B Recruitment rate	29 per year	Estimate
β Probability of getting the disease	0.011-0.95	[9],[8]
C the number of sexual partners per year	3 per year	[9]
μ mortality rate	0.01562	[10]
d HIV/AIDS related death rate	0.333 per year	[9]
ν Rate of progression to AIDS	0.125 per year	[9]

If $R_0 > 1$, the HIV/AIDS free equilibrium becomes unstable while the endemic equilibrium E_1 becomes stable. Additionally, if $R_0 > 1$, the endemic equilibrium is asymptotically stable. In Figure 2, solutions converge to E_1.

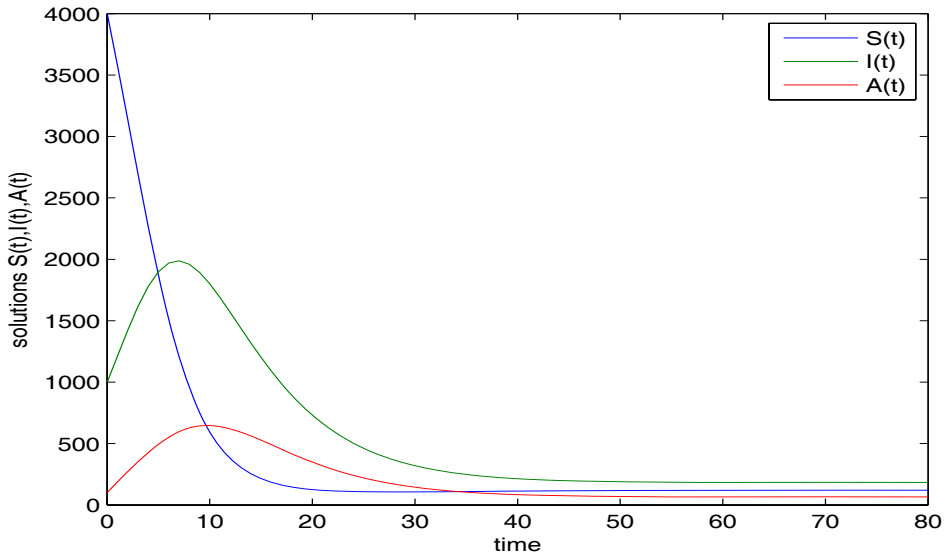

Figure 2: Numerical solution of Equation(2) when $R_0 > 1$.

From Figure 2, the infection persists in the population, that is, the number of infectives in the population will increase until it attains an equilibrium E_1.

When the delay parameter $\tau_1 > 0$ is large, the infectious individuals in the population will take a longer time to be eliminated (removed) in the population, hence increasing the force of infection leading to more infectives in the population. This leads to an increase of infective population as numerically shown in Figure 3.

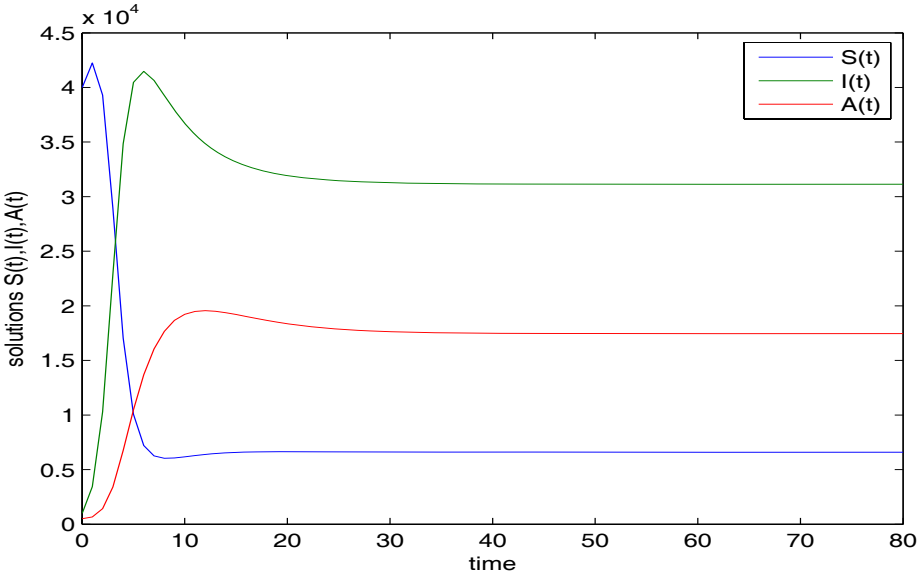

Figure 3: Numerical solution of Equation(2) when $\tau_1 > 0$ is large.

If the delay parameter τ_1 is not large, the infected individuals will die out faster i.e, infected individuals are eliminated from the population faster as the rate at which they progress to fully blown is small. The simulation for this case is as shown in Figure 4.

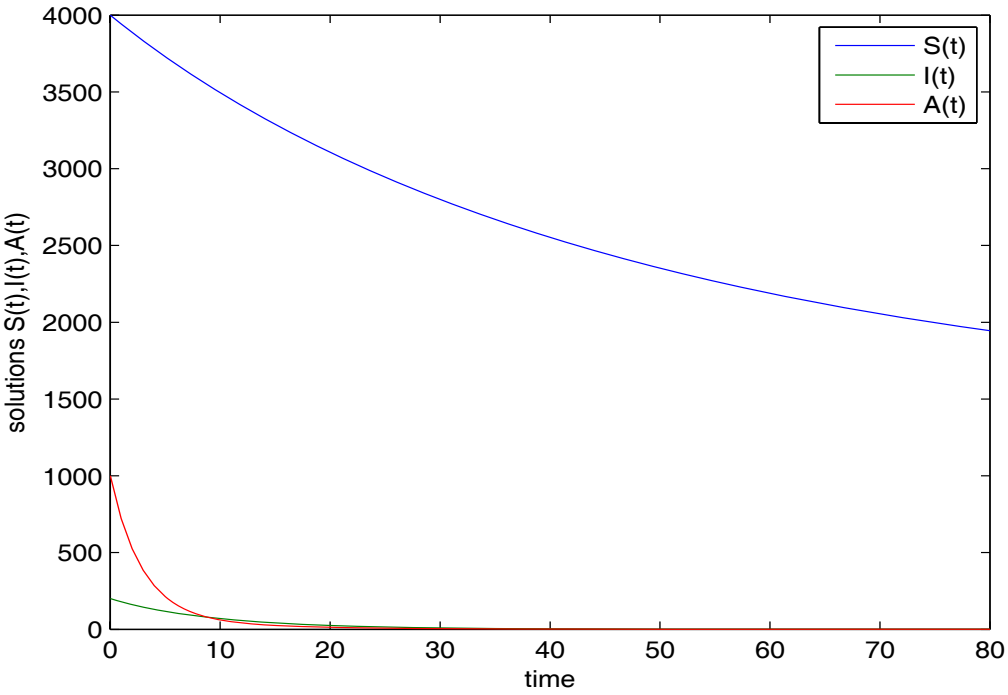

Figure 4: Numerical solution of Equation(2) when $\tau_1 > 0$ is small.

Globally, if the spread of the infection is not addressed, the susceptibles population will decrease in comparison to the infected population. This can be illustrated by the following numerical simulation

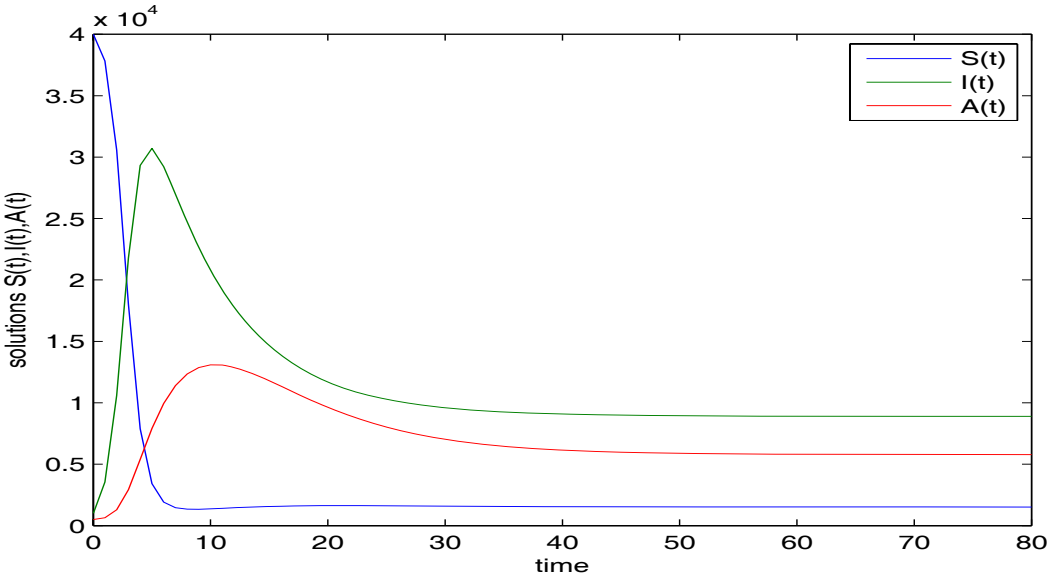

Figure 5: Numerical solution of Equation(2) if the force of infection is not reduced.

5 Conclusion

In the case where there is no delay, no infection occurs if $R_0 < 1$. So the ideal control strategy is the reduction of R_0 to a value below 1 in order to prevent new infections. However, when $R_0 > 1$ the infection becomes endemic. In the presence of delay and without any intervention programs, the longer the delay term, especially τ_1, the higher the prevalence rate of the disease provided $R_0 \geq \mu$.

We have considered an epidemic in a single location, ignoring travel between locations of individuals who may be infective. Modern transportation permits the rapid transfer of infectious diseases over great distances, and an aspect of epidemic control that has become important is the screening of travelers who may be infective. Epidemic models which include some movement into and out of populations can be considered. Our model also does not take into account behavioral changes in a population when an epidemic breaks out. For instance, when an epidemic occurs some individuals of the population will undoubtedly avoid people rumored to be infected. In other cases, individuals change their behaviors or adopt preventive measures to reduce the probability that a contact will transmit infection. This may occur because of personal

decisions or because of government instructions. Inclusion of these effects in an epidemic model is an important problem to be explored.

References

[1] Abbas A.K., Lichman A.H.,Pober J.S, (1994). *In: Cellular and Molecular Immunology 2nd (Ed)* Philadelphia, W.B Sounders, pp. 419-442 and 425-426.

[2] Bangham, C.R.,(2000). *The immune response for HTLV-1.*Curr Opin. IMmunol.,**12**,397-402.

[3] Boese, F. G. (1989).*Stability conditions for the general linear difference-differential equation with constant coefficients and one constant delay.* Journal of mathematical analysis and applications **140**, 136-176.

[4] Culshaw R.V., Ruan S.,(2000). *A Delay Differential Equation Model of HIV infection of $CD4^+$ T-Cells*. Math. Biosci. **165**, 27-39.

[5] Diekmann, O., Heesterbeek, J., Metz J.A,(1990). *On the definition and the computation of the basic reproduction ratio in models for infectious diseases in heterogenious populations*. Journal of Mathematical Biology. **167**, 67-78.

[6] Gao, S., Teng, D., Xie, W.,(2009). *The effects of pulse vaccination on SEIR model with two time delay*. Applied Math. Computation. **78**, 7-12.

[7] Jack, H., Hale, K.,(1977). *Theory of Functional Differential Equations* .2nd ed., Springer Verlag, New York.

[8] Luboobi, L.S.,Mugisha, Y.T.,(2000). *Mathematical Models for The dynamics of the HIV/AIDS epidemic.*Biometry for Development,**11**, 76-83.

[9] Mukandavire, Z., Chiyaka, C., (2010). *Asymptotic properties of an HIV/AIDS model with a time delay*. Journal of Mathematical Analysis and Applications. **3**, 43-67.

[10] Rodgers L., Chien S., (2012).*HIV/AIDS Epidemic in Kenya*. Journal of Experimental and Clinical Medicine. **4**, 231-234.

[11] Simwa, R.O., and Pokhariyal G.P.,(2003) *A dynamical model for stage specific HIV incidence with application to Sub-Saharan Africa*. Applied Mathematics and Computation. **146**, 93-104.

[12] Xu R.,(2012). *Global stability of a delayed epidemic model with latent period and vaccination strategy.*Journal of Applied Mathematical Modeling, **24**, 405-435.

[13] Zindoga, M., Christina, C., Winston G.,(2009). *Mathematical Analysis of a sex structured HIV/AIDS model with a discrete time delay.*Journal of nonlinear Analysis, **180**, 29-48.

Received: February 11, 2014