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Full Length Research Article

HIV/AIDS-INVIVO MODEL WITH THE ROLES OF CTL IMMUNE CELLS AND ANTIRETROVIRAL THERAPHY

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ABSTRACT
In this work, we formulated a mathematical model to study the interaction between HIV/AIDS and Cluster of Differentiation 4 cells ($CD4^+T$), incorporating the roles of Cytotoxic T- lymphocytes (CTLs) cells and antiretroviral therapy. The proliferation of $CD4^+T$ cells was considered to follow the logistic growth pattern. The presence of HIV in the $CD4^+T$ cells stimulates the recruitment of $CD4^+T$ and CTL cells. The recruitment of uninfected $CD4^+T$ and CTL immune cells fall purely as an exponential function of time in the presence of HIV. The basic reproduction number (R_0) was obtained using the next generation matrix method. We adopted the Jacobian stability criterion and the Lyaponuv second method of stability to establish the local and global stabilities of the equilibrium states and show that HIV can be eliminated from $CD4^+T$ cells when $R_0 \leq 1$ but will continue to persist within $CD4^+T$ cells when $R_0 > 1$. Early medication therapy was observed to reduce viral load and increase the number of CTL cells, while $CD4^+T$ cells is kept above the AIDS bar. A high initial viral load was noticed to induce rapid decline in the number of $CD4^+T$ cells. To keep a healthy system, we recommended that the CTL and uninfected $CD4^+T$ cells population should be maintained by reducing viral load through early medication therapy and cloning of CTL cells within infected human, which fights and kills infected cells.

Keywords: Basic Reproduction Number (R_0), Virus-free Equilibrium (VFE), Endemic Equilibrium (EE), Locally Asymptotically Stable (LAS) and Globally Asymptotically Stable (GAS)

INTRODUCTION

One of the ever-known deadly diseases which has undoubtedly claimed millions of lives is Acquired Immune Deficiency Syndrome (AIDS). AIDS is the disease that results from the breakdown of the immune system, occasioned by the invasion of a virus called Human Immunodeficiency Virus (HIV). This disease kills and damages cells of the human body's immune system. It gradually destroys its ability to fight against other infections and diseases (Allali, Harroudi & Torres, 2018).

AIDS is one of the leading epidemics in the world. The first patient was diagnosed in 1981 (Bushnaq, *et al.,* 2018). As at 2016, about 36.7 million people were living with HIV/AIDS globally, out of which only 20.9 million people were accessing antiretroviral therapy. 1.8 million people became newly infected. In sum, about 78 million people have been infected with HIV since the discovery of the epidemic and about 35 million people have died from HIV/AIDS related diseases. Figure of newly infected persons stand at 2.1 million. In Nigeria, about 3.5 million persons are reported to be carrying the deadly virus. Number of death recorded due to HIV/AIDS is given as 180,000 persons, with a prevalent rate of 3.1% among adults, aged 15 and above (UNAIDS, 2016).

HIV/AIDS can be contracted through unprotected sex with an infected person, sharing of needle with an infected person, breast milk of an infected person and blood transfusion from an infected person (UNICEF, 2003).

It is important to study the pattern of HIV progression in the body. There are three stages of HIV/AIDS infection. They are the Primary Phase, Asymptomatic Phase and AIDS Phase. During the Primary Phase, an individual develop flu-like symptoms between 2 – 4 weeks after HIV infection (Miller *et al*., 2018). The symptoms could include fever, swollen glands, sore throat, rush, muscle and headache. This stage is sometimes referred to as Acute Retroviral Syndrome (ARS). During this stage, large amounts of virus are replicated in the cells of the body. The target cells are the Cluster of Differentiation 4 ($CD4^+T$) cells. As the activities of the virus increases, the $CD4^+T$ cells would eventually decline in numbers. The levels of HIV in the body blood stream are very high at this stage thereby there is a high risk of transmitting the virus to others. The Asymptomatic Phase of HIV infection is that period when HIV is living and replicating at a very low rate without manifesting symptoms. This stage is also referred to as chronic HIV infection phase. The final stage is the AIDS Phase. At this point, the HIV has badly damaged the immune system thereby making the infected individual vulnerable to opportunistic infections. This is signaled by the decline in the number of $CD4^+T$ cells. Once the $CD4^+T$ cells count falls below 200 cells/mm^3 of blood, an individual is considered to have progressed to AIDS stage (WHO, 2007; Mita, 2013).

The process of virus replication in the immune cells increases rapidly with time in infected individuals that are not placed on medication therapy. The introduction of medications therapy in treating HIV/AIDS infection would definitely suppress or slow down the rate of virus activities in the immune system. Current research shows that more than 16 antiretroviral drugs have been developed and approved by World Health Organization (WHO), United Nations Children Fund (UNICEF) and Joint United Nations Programmes for AIDS (UNAIDS), the most common being Protease Inhibitors and RT Inhibitors. The former functions by meddling with the process of virus replication so that virus would only replicate themselves but prevented from invading the host cell. The later on the other hand "deceives" the reverse transcriptase (enzyme which produce the viral particles) to create false DNA that will not replicate HIV. The most effective medication therapy is called Highly Active Antiretroviral Therapy (HAART). It combines two or more antiretroviral medications to fight HIV/AIDS. The main function of HAART is to decrease viral load in the immune system, so that the immune system can

recover some strength.

LITERATURE REVIEW

Biological processes are complex to study. However, modeling of biological processes such as epidemiology and virology has paved ways to scientist to undertake research using mathematical tools to study the components and parameters of such processes. In line with this, several authors have written on the progression and diffusion of HIV infection in human immune system.

Roy & Chatterjee (2010), built a mathematical model of HIV-1 infection to CD4⁺T cells and included a combination of inhibitor-drugs (lamivudine and zidovudine) as medication therapy. This is in variant with the model formulated by Srivastava *et al.* (2009), which incorporated only a single drug. They had observed from available clinical results that patients infected with type-1 HIV and treated with these inhibitor-drugs show a 10 to 25% growth in the healthy CD4⁺T cells count. In developing their model, they considered $x(t)$ and $y(t)$ to be uninfected and infected cells respectively at time t. Uninfected CD4⁺T cells are produced at a constant rate and are removed from the system through the natural death rate d. It was assumed that at the steady state, the free virus population is proportional to the virus-producing CD4⁺T cells which are already infected. The process of infection of infected CD4⁺T cells obeys the law of mass action. This necessarily implies that the number of new infection at steady state is proportional to $x(t)y(t)$. The production rate of new immunocompetent T cells produced by lymphatic system is taken to be β and it does not depend on the number of T cells. It was also assumed that T cells may be produced by the proliferation of existing T cells and its production is governed by the logistic growth law. That is, T cells cannot increase infinitely. Hence, the proliferation of T cells was represented in a logistic manner where p, the maximum proliferation rate is constant and it proliferates to a maximum given by T_m (the point at which T cell population cannot exceed). In line with these assumptions, the following equation model resulted:

$$\frac{dx}{dt} = \alpha + px\left(1 - \frac{x}{T_m}\right) - dx - \beta xy \qquad (1)$$

$$\frac{dy}{dt} = \beta xy - ay \qquad (2)$$

where a is the death rate of infected CD4⁺T cells.

The rate of replication of virus declines whenever a HIV-1 infected individual is treated with drugs. This effect was incorporated in their model by reducing the numerical value of the parameter β. Another variable z was included to address the long term immune of the model. z is taken to be the density of CTL responses against infected cells. In sum, Roy & Chartejee (2010), came up with a dynamic model presented as equations (3) – (5).

$$\frac{dx}{dt} = \alpha + px\left(1 - \frac{x}{T_m}\right) - dx - \beta xy \qquad (3)$$

$$\frac{dy}{dt} = \beta xy - ay - kyz \qquad (4)$$

$$\frac{dz}{dt} = sy - bx \qquad (5)$$

where k is the killing rate of virus producing cells by CTL, s is the rate of stimulation (recruitment) of CTL and b is the mortality rate of CTL. The result of their analysis and stimulation reveals the following:

(i) the proliferation rate is always greater than the death rate of uninfected cells, which implies that the disease free system cannot be obtained,

(ii) if the proliferation rate increases, then the uninfected cell increases fast but the infected and CTL population increases slowly,

(iii) if the force of infection β, increases, then the numerical value of infected cell and CTL population decreases.

They concluded that the system competes with the killing rate of infected T-cells as well as stimulation rate of CTL. While the modelers included the effect of CTL immune in the model, the equation did not consider viral particles as a population to study.

Parumasur & Willie (2008), carried out a research to analyse model parameters in HIV/AIDS equation models. Their model comprises four compartments, namely: virus population (v), uninfected target cells (x), infected cells (y) and immune system response cells (z). The model is shown below.

$$\frac{dv}{dt} = ay - bv \qquad (6)$$

$$\frac{dx}{dt} = c - d_1 x - \beta xy \qquad (7)$$

$$\frac{dy}{dt} = \beta xy - fy - \gamma yz \qquad (8)$$

$$\frac{dz}{dt} = g - hz \qquad (9)$$

where a is the rate of virus reproduction, b is the rate of death of viruses, c is the reproduction of uninfected cells, d is the death rate of uninfected cells, β is the multiplying constant of being infected, g is the reproduction rate of cells z, h is the death rate of cells z and γ is the multiplying constant to the elimination of infected cells. The model will be more robust if drug therapy was included.

The study of HIV/AIDS infection dynamics came with diverse challenges. No single models have been developed thus far, so exhaustive enough to address all the multifaceted dimensions of HIV/AIDS infections.

We proposed a set of equations that considers the following factors in a single deterministic model:

(i) combinatory effects of CTL immune cells and drug therapy on HIV infection,

(ii) both the CD4+ cells and the CTL immune cells have two sources; they proliferate and are produced from the bone marrow and from other immune-producing hormones respectively (Olaniyi, *et al.,* 2013),

(iii) no cell type in the human body continues to proliferate unboundedly. Hence the CD4+ cells was considered to follow a logistic growth pattern, and

(iv) the production of uninfected CD4+ cells and CTL immune cells fall purely as an exponential function of time in the presence of HIV.

(v) the activities of CTL immune cells in the system can reduce infectivity but cannot eliminate free viruses in the system,

(vi) the invasion of HIV in the system triggers the proliferation of CTL immune cells but causes a decline in the production of CD4+ cells and CTL immune cells (Allali, Harroudi & Torres, 2018) and

(vii) drug therapy blocks new infections and slow down the rate of virus recruitment but cannot eliminate HIV.

Uninfected CD4+T cells proliferates and are recruited according to a logistic growth term at the rates ρ_1 and s_1 respectively, with natural death rate μ_1. We noted that the proliferation and recruitment of CD4+T cells cannot continue to increase unboundedly, hence, the introduction of the logistic growth terms with CD4+T cells size $T_{\max}$ as the carrying capacity.

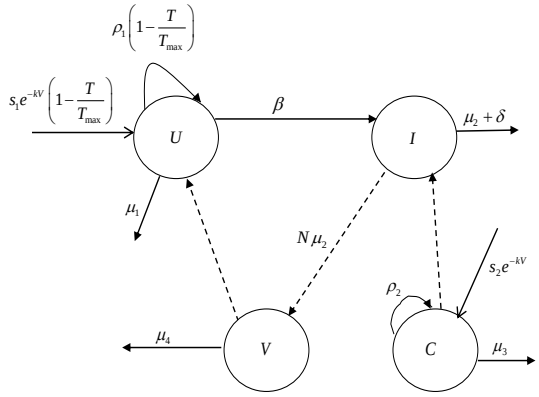

Fig. 1: Schematic Diagram of HIV in-vivo Model

The term e^{-kV} is a reduction factor that accounts for decrease in the number of healthy CD4+T cells and CTL immune cells that will be produced once an antigen is introduced into the system, where $k = 0,\ 1,\ 2,\ 3,\ 4,\ldots$, takes on the values of t . We assumed that the recruitment of uninfected CD4+T cells and CTL immune cells fall purely as an exponential function of time. This is in line with the work of Wodarz & Nowak (2002).

In the case that antiretroviral therapy are not administered, uninfected CD4+T cells become infected by free virus at the rate β . Infected CD4+T cells die naturally at the rate μ_2 as well as due to CTL immune cells at the rate δ .

Free viruses are produced whenever infected CD4+T cells burst. This is represented by the term $NI\mu_2$, where N is number of new viruses. Virus density decreases due to natural death at the rate μ_4 . We assume that a CTL immune cells proliferate and are recruited in response to an antigen at the rate ρ_2 and s_2 respectively. The CTL immune cells die naturally at the rate μ_3 .

The model is described by a system of ordinary differential equations given in (10) – (13).

$$\frac{dU}{dt} = \left(s_1e^{-kV} + \rho_1U\right)\left(1-\frac{T}{T_{\max}}\right) - \beta VU - \mu_1U \quad (10)$$

$$\frac{dI}{dt} = \beta VU - \delta CI - \mu_2I \quad (11)$$

$$\frac{dC}{dt} = s_2e^{-kV} + \rho_2CI - \mu_3C \quad (12)$$

$$\frac{dV}{dt} = \mu_2NI - \beta VU - \mu_4V \quad (13)$$

Since the model is dealing with populations, all the variables and parameters of the model are positive with the natural death rates positive, i.e. $\left(\mu_1, \mu_2, \mu_3, \mu_4 > 0\right)$, thus considering the region Ω where:

$$\Omega = \left\{(U,I,C,V) \in \mathbf{R}_+^4 : U \geq 0, I \geq 0, C \geq 0, V \geq 0\right\} \quad (14)$$

It can be established that all solutions of the system starting in Ω remain in Ω for all $t \geq 0$. In this region, the usual existence, uniqueness and continuation of results hold for the system.

Existence of Virus-free Equilibrium, E^0

The rate of change of the systems in (10) – (13) is equal to zero at the point of equilibrium. That is

$$\frac{dU}{dt} = \frac{dI}{dt} = \frac{dC}{dt} = \frac{dV}{dt} = 0 \quad (15)$$

At any arbitrary equilibrium point, let

$$\left(U,I,C,V\right) = \left(U^*, I^*, C^*, V^*\right) \quad (16)$$

Hence we have

$$\left(s_1e^{-kV} + \rho_1U\right)\left(1-\frac{T}{T_{\max}}\right) - \beta VU - \mu_1U = 0 \quad (17)$$

$$\beta VU - \delta CI - \mu_2I = 0 \quad (18)$$

$$s_2e^{-kV} + \rho_2CI - \mu_3C = 0 \quad (19)$$

$$\mu_2NI - \beta VU - \mu_4V = 0 \quad (20)$$

We solved equations (17) – (20) simultaneously to obtain our virus-free equilibrium as

$$E^0 = \begin{pmatrix} \frac{U_1 \pm U_2}{2\rho_1} \\ 0 \\ \frac{s_2}{\mu_3} \\ 0 \end{pmatrix} \quad (21)$$

where

$$U_1 = \rho_1 T_{\max} - s_1 - \mu_1 T_{\max} \quad (22)$$

and

$$U_2 = \sqrt{\left(\rho_1 T_{\max} - s_1 - \mu_1 T_{\max}\right)^2 + 4\rho_1 s_1 T_{\max}} \quad (23)$$

Basic Reproduction Number, R_0

Yuan (2010), elucidated a method for obtaining R_0. The method is known as the next generation matrix method. This technique was adopted to obtain the effective reproduction number of the model equations (10) – (13). We have,

$$F = \begin{pmatrix} 0 & \beta U^0 \\ \mu_2 N & 0 \end{pmatrix} \quad (24)$$

and

$$D = \begin{pmatrix} \delta C^0 + \mu_2 & 0 \\ 0 & \beta U^0 + \mu_4 \end{pmatrix} \quad (25)$$

So that,

$$FD^{-1} = \begin{pmatrix} 0 & \frac{\beta U^0}{\beta U^0 + \mu_4} \\ \frac{\mu_2 N}{\delta C^0 + \mu_2} & 0 \end{pmatrix} \quad (26)$$

Therefore,

$$R_0 = \sqrt{\frac{\mu_2 \beta N U^0}{\left(\delta C^0 + \mu_2\right)\left(\beta + \mu_4\right)}} \quad (27)$$

Local Stability of Virus-free Equilibrium

Theorem 1: The virus-free equilibrium of the model equations (10) – (13) is locally asymptotically stable if $R_0 < 1$.

Proof: The Jacobian stability technique was employed in determining the local stability of the system. The Jacobian matrix obtained by operating on equations (10) – (13), at virus-free equilibrium, E^0 is given as

$$J\left(E^0\right) = \begin{pmatrix} -J_1 & -J_2 & 0 & J_3 \\ 0 & -J_4 & 0 & \beta U^0 \\ 0 & \rho_2 C^0 & -\mu_3 & -k s_2 \\ 0 & \mu_2 N & 0 & -J_5 \end{pmatrix} \quad (28)$$

where

$$J_1 = \left(s_1 + 2\rho_1 U^0 - \rho_1 T_{\max} + \mu_1 T_{\max}\right) \quad (29)$$

$$J_2 = \left(s_1 + \rho_1 U^0\right) \quad (30)$$

$$J_3 = -\left(k s_1 \left[T_{\max} - U^0\right] + \beta T_{\max} U^0\right) \quad (31)$$

$$J_4 = \left(\delta C^0 + \mu_2\right) \quad (32)$$

$$J_5 = \left(\beta U^0 + \mu_4\right) \quad (33)$$

The characteristic equation of the Jacobian matrix in equation (28) is given by

$$\left|J\left(E^0\right) - \lambda I\right| = \begin{vmatrix} -J_1 - \lambda & -J_2 & 0 & J_3 \\ 0 & -J_4 - \lambda & 0 & \beta U^0 \\ 0 & \rho_2 C^0 & -\mu_3 - \lambda & -k s_2 \\ 0 & \mu_2 N & 0 & -J_5 - \lambda \end{vmatrix} \quad (34)$$

So that the eigenvalues are

$$\lambda_1 = -\left(s_1 + 2\rho_1 U^0 - \rho_1 T_{\max} + \mu_1 T_{\max}\right) < 0 \quad (35)$$

$$\lambda_2 = -\left(\delta C^0 + \mu_2\right) < 0 \quad (36)$$

$$\lambda_3 = -\mu_3 < 0 \quad (37)$$

$$\lambda_4 = -\frac{\left(\beta U^0 + \mu_4\right)\left(\delta C^0 + \mu_2\right) - \mu_2 \beta N U^0}{\delta C^0 + \mu_2} \quad (38)$$

For λ_4 to be negative,

$$-\frac{\left(\beta U^0 + \mu_4\right)\left(\delta C^0 + \mu_2\right) - \mu_2 \beta N U^0}{\delta C^0 + \mu_2} < 0 \quad (39)$$

Simplifying equation (39) gives

$$\sqrt{\frac{\mu_2 \beta N U^0}{\left(\delta C^0 + \mu_2\right)\left(\beta + \mu_4\right)}} < 1 \quad (40)$$

That is,

$$R_0 < 1 \quad (41)$$

It is logical therefore to say that $\lambda_4 < 0$ if $R_0 < 1$. It follows that the virus-free equilibrium, E^0, of the model equations (10) – (13) is locally asymptotically stable if $R_0 < 1$. By implication, HI virus can be removed from the CD4$^+$T cells if $R_0 < 1$.

Global Stability of Virus-free Equilibrium, E^0

Theorem 2: The VFE of the system (10) – (13) is globally asymptotically stable in Ω if $R_0 \le 1$.

Proof: The Lyaponuv's second method for stability theorem was adopted to establish the global stability of the system (Lyaponuv, 1892).

Consider the Lyapunov function in equation (42):

$$L = \mu_2 N I + \left(\delta C + \mu_2\right) V \quad (42)$$

Differentiating (42) gives

$$L^{'} = \mu_2 NI^{'} + (\delta C + \mu_2)V^{'} \quad (43)$$

Substituting the values of $I^{'}$ and $V^{'}$ into (43) yield

$$\begin{aligned} L^{'} &= \mu_2 N(\beta VU - \delta CI - \mu_2 I) \\ &\quad + (\delta C + \mu_2)(NI - \beta VU - \mu_4 V) \end{aligned} \quad (44)$$

Simplifying and resolving equation (44) further gives

$$L^{'} = (\delta C + \mu_2)(\beta U + \mu_4)V\left[\frac{\mu_2 \beta NU}{(\delta C + \mu_2)(\beta U + \mu_4)} - 1\right] \quad (45)$$

At any arbitrary point at equilibrium state, $U \le U^0$ and $C \le C^0$. Equation (45) therefore becomes

$$L^{'} \le (\delta C + \mu_2)(\beta U + \mu_4)V\left[\frac{\mu_2 N \beta U^0}{(\delta C^0 + \mu_2)(\beta U^0 + \mu_4)} - 1\right] \quad (46)$$

Thus,

$$L^{'} \le (\delta C + \mu_2)(\beta U + \mu_4)V\left[R_0^2 - 1\right] \quad (47)$$

From (42), it is obvious that for $I = V = 0$, $L = 0$ and for $I = V \neq 0$, $L > 0$. Furthermore, from (47), it can be shown that $L^{'} \le 0$ if $R_0 \le 1$ and $V \neq 0$. $L^{'} = 0$ is true when $R_0 = 1$. If $R_0 > 1$, then $L^{'} > 0$ except when $V = 0$. Hence, by Lyapunov's second method for stability theorem, the virus-free equilibrium state is proved to be globally asymptotically stable.

RESULTS AND DISCUSSION

The infection rate β, is reduced by $(1 - \varepsilon_b \psi)$ when antiretroviral drugs are administered. $0 < \varepsilon_b < 1$ is taking to be the potency of the drugs in blocking the ability of HIV from actively infecting the healthy CD4$^+$T cells. Due to the application of antiretroviral therapy, the recruitment of free viruses is reduced by $(1 - \varepsilon_p \psi)$, where $0 < \varepsilon_p < 1$ is the potency of the drugs in slowing down the rate at which free viruses are recruited. ψ is the level of adherence to the usage of drugs. The potency of the drug when medication plans are followed is estimated at 95% (UNAIDS, 2015).

Variables and Parameters Value

Variables and parameters of HIV/AIDS models are usually estimated based on HIV/AIDS available data. The values used in this research work are presented in Table 1.

Table 1: Variables and parameters value

Symbols	Values	Source
$U(0)$	1000 mm^{-3}	Culshaw & Ruan (2000)
$I(0)$	0	Culshaw & Ruan (2000)
$V(0)$	Varies	Assumed
$C(0)$	200000 mm^{-3}	Assumed
$T_{\max}$	1500 mm^{-3}	Roy & Chartterjee (2010)
N	Varies	Assumed
ε_b, ε_b	0.95	UNAIDS (2015)
ψ	Varies	Assumed
s_1	10 mm^{-3} day^{-1}	Roy & Chartterjee (2010)
s_2	0.2 mm^{-3} day^{-1}	Roy & Chartterjee (2010)
ρ_1	0.03 day^{-1}	Culshaw & Ruan (2000)
ρ_2	0.03 day^{-1}	Culshaw & Ruan (2000)
μ_1	0.02 day^{-1}	Culshaw & Ruan (2000)
μ_2	0.24 day^{-1}	Culshaw & Ruan (2000)
μ_3	0.02 day^{-1}	Culshaw & Ruan (2000)
μ_4	0.2 day^{-1}	Culshaw & Ruan (2000)
β	0.000024 mm^3 day^{-1}	Culshaw & Ruan (2000)
δ	0.001 day^{-1}	Roy & Chartterjee (2010)
k	Varies	Assumed

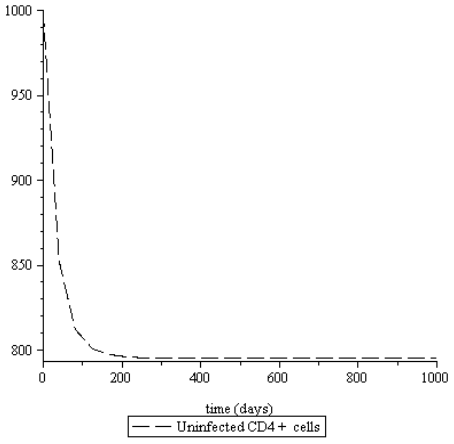

Fig. 2: Plot of uninfected CD4$^+$T cells versus time at virus-free equilibrium state, corresponding to $V(0) = 0$ and $N = 0$.

Fig. 2 shows the behavior of the uninfected CD4$^+$T cells at virus-free equilibrium. This is the state at which the entire CD4$^+$T cells population is free from HIV. Decline in the number of uninfected cells is due to natural death. The lower limit is greater than 700cell/mm^3 CD4$^+$T cells count for all values of $t > 0$, which is far above the AIDS upper bound.

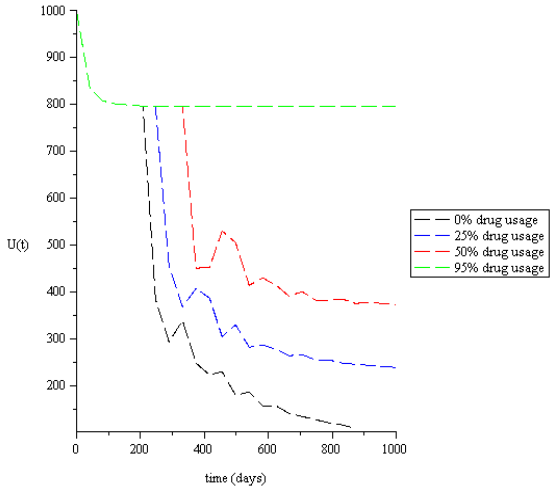

Fig. 3: Plot of uninfected CD4⁺T cells versus time at different level of patients' adherance to antiretroviral therapy (drug usage), keeping the initial volume of virus at minimal level of $V(0)=10$ and $N=500$.

We observed a fast downward movement of healthy CD4⁺T cells when the level of drug usage was 0%. The population of uninfected CD4⁺T cells thus fall below 200cell/mm^3 within the first two years of viral infection, a situation that fast track the progression of HIV to AIDS stage. At 25% and 50% levels of drug usage, the CD4⁺T cells maintained a value just above 200mm^{-3}, but clearly, the trend shows a downward movement. As viral load increases, the count will definitely go below 200cell/mm^3. The best fit was obtained when drug usage was 95%. Though, there was a liitle drop from the number of healthy CD⁺T cells from 1000cell/mm^3 to 800cell/mm^3, we observe no further decline. This implies that at 95% level of usage of antiretroviral therapy, patients who are HIV-positive can keep their CD4⁺T cells count above 200cell/mm^3, thereby not resulting into AIDS. Life expentancy for infected persons in this category is estimated at between 20 – 50 years (Klatt, 2014).

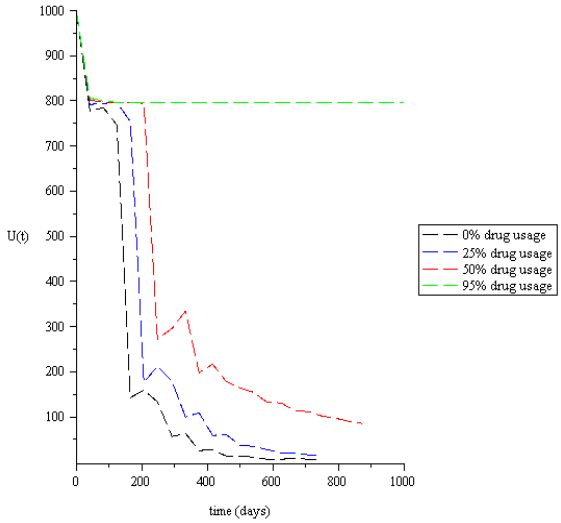

Fig. 4: Plot os the behaviour of uninfected CD4⁺T cells with respect to time, at different level of patient's adherance to drug usage with $V(0)=100$ and $N=2000$.

In this case, the initial volume of viral particle introduced into the system was inreased from 10 to 100, thereby causing more viruses to be produced by the process of lysing of infected CD4⁺T cells. Thus, with a larger volume of viral particles in the system, the decrease in the number of heathy CD4⁺T cells was more rapid than the scene in Fig. 3. At 0%, 25% and 50% level of adherence to drug usage, within the periods less than 2 years, the infection has progressed to AIDS stage except at 95% where the infection is still in check and above AIDS line indicator.

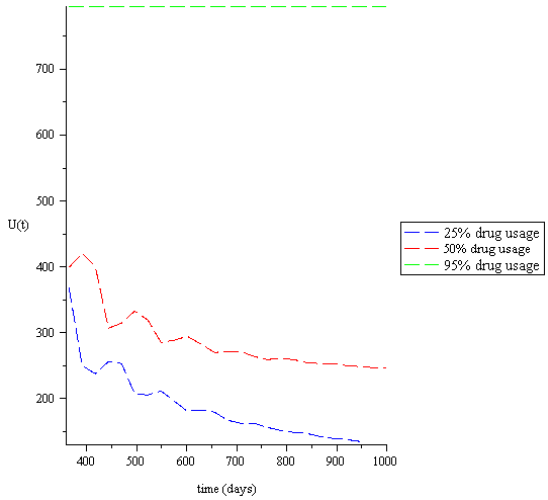

Fig. 5: Plot of the behaviour of uninfected CD4⁺T cells after a delay of 1 year before treatments begin. $V(0)=10$, $N=500$, at different level of adeherence to drug usage by patient.

From Fig. 5, it can be observed that due to delay in starting treatments, the number of healthy CD4⁺T cells have declined below 450cell/mm^3 and just above 250cell/mm^3 from the onset of treatments. Except treaments is sustained at 95% from this point, AIDS will result in less than 1 year (at 25% drug usage). At 50% drug usage, the patient may still be able to keep a CD4⁺T cells count just above the bar for another 2 years, owing to the low initial number of viral particles in the system, and the minimal number of virus produced by lysing of infected CD4⁺T cells.

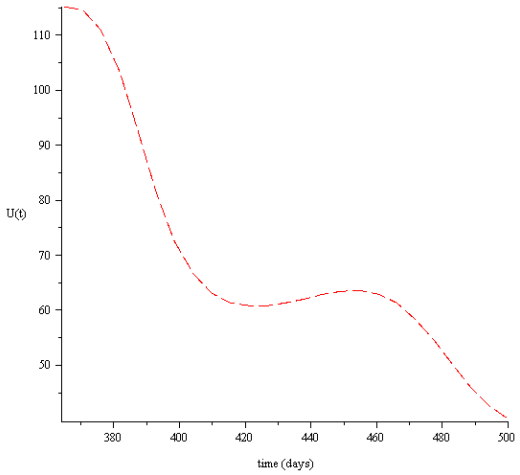

Fig. 6: Plot os the behaviour of uninfected CD4⁺T cells after a delay of 1 year after infection. $V(0)=200$, $N=5000$.

Fig. 6 is a case where the initial volume of viral particles introduced into the system is large. Invariably, the amount of viruses that will be produced when infected CD4⁺T cells burst will be higher than what we have in Fig. 5. The high viral particles in the system resulted into the decrease of healthy CD4⁺T cells below 200cell/mm^3. Hence, before HIV was diagnosed in this case, AIDS have resulted. This is typical of infected individuals who do not receive any form of treatment. Death usually occur within a year after the individual progresses from HIV to AIDS (Klatt, 2014).

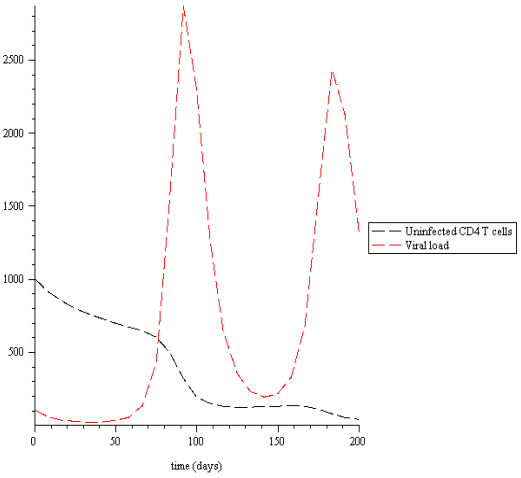

Fig. 7: Plot of viral load and uninfected CD4⁺T cells population versus time in the absence of antiretroviral therapy. $V(0)=100$, $N=5000$.

In Fig.7, the activities of HIV is at the peak in the system, hence the decrease in the number of healthy CD4⁺T cells. It is observed that treatment is absence in this sytem. Progression from HIV stage to AIDS stage will be faster.

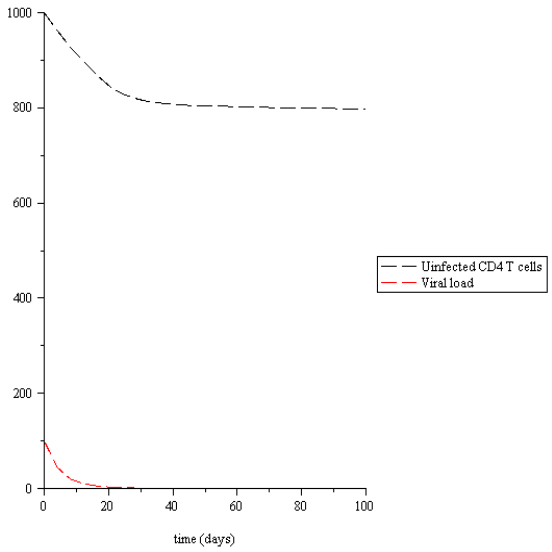

Fig. 8: Plot of viral load and uninfected CD4⁺T cells population versus time in the presence of antiretroviral therapy. $V(0)=10$, $N=100$ and $\psi=0.95$.

It is observed from Fig. 8 that viral load is kept at the base once drug usage level is 95% and begins early. This demonstrates the role of early treatment in suppressing the activities of the virus. The abundance of CD4⁺T cells in the system will make HIV to be undetectable when clinical tests are carried out (Perelson & Ribeiro, 2013).

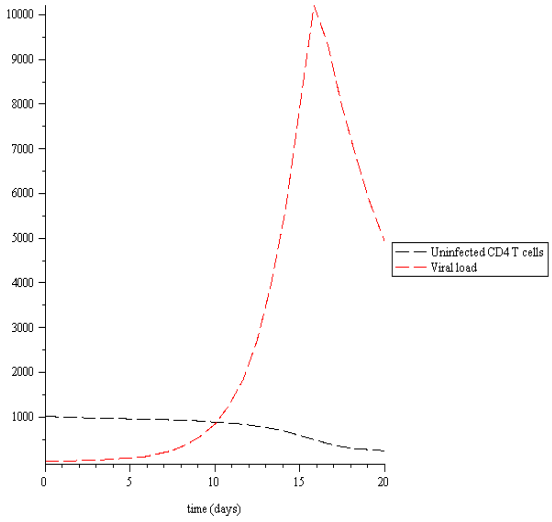

Fig. 9: Plot of uninfected CD4⁺T cells and viral load versus time at the point when the CTL immune cells term was deactivated in the model equation (i.e. when $C(0)=0$). $V(0)=100$, $N=2000$.

Fig. 9 displays the role of CTL immune cells in regulating viral load. The idea here was that of deactivating the CTL immune cells term in the model equation, a situation which is not feasible

in the immune system. However this picture provides some mathematical insight into the role of CTL immune cells. Obviously, as $C(0) \to 0$, $V(t) > 10,000$ and $U(t) < 200$ at $t \cong 15$ days. This is logical. The implication of this assertion is that, for the system to remain healthy, the population of CTL immune cells must be kept at a value greater than zero and the population of uninfected CD4+T cells must be kept above 200cell/mm^3.

Conclusion

In this work, we proposed and analysed a model of HIV/AIDS in-vivo with the roles of CTL immune cells and antiretroviral therapy. The model comprises four compartments, namely: uninfected CD4+T cells (U), infected CD4+ T cells (I), density of free virus (V), and CTLs (C). Results from the projections indicate that the introduction of antiretroviral therapy at the early stage of infection leads to a decrease in viral growth and increase in the population of healthy CD4+T cells. This agrees with conventional results (Wodarz & Nowak, 2002). Sustenance of such drugs should be more than one year (Perelson *et al.,* 1993). Deactivating the role of CTL immune cells in the model equation resulted in a drastic increase in viral load and a fast progression from HIV stage to AIDS stage. On the other hand, increasing the population of CTL immune cells keeps the viral load in check. This suggests that, with the multiplication of healthy CTL immune cells in the system, viral growth will be minimal. This scenario was also observed by Roy & Chatterjee (2010).

The absence of antiretroviral therapy or lack of adherence to medication plans will lead to a rise in virus replication within the host. Thus, there will be exponential fall in the number of CD4+T cells and CTL immune cells. This is another scenario where there will be a fast progression from HIV stage to AIDS stage. With the introduction of small initial population of free virus in the system, the probability of increase of virus is kept at a minimal level. On the contrary, a larger initial population size of virus increases the chance of free virus infecting more healthy CD4+T cells. Hence, any measure that will keep the initial viral population to the barest minimum will be a good one.

The study revealed that a large volume of CTL immune cells will slow down viral load, and kill infected CD4+T cells, hence, more effort should be geared towards producing CTL immune cells booster. The medical scientist should also intensify effort in discovering methods of cloning CTL immune cells in infected humans. This will aid in increasing the number of the CTL immune cells. Free and regular HIV/AIDS screening exercise, coupled with HIV/AIDS awareness, should be encouraged and sponsored by the Nigerian Government, to enable early detection of this viral infection.

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