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MODELING TOBACCO SMOKING EFFECT ON THE HIV INFECTION OF CD4+ T-CELLS

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Abstract. Tobacco smoking impairs CD4+ T-cells which coordinate the immune system. In this paper we develop a mathematical model to study how tobacco smoking affects the HIV infection of CD4+ T-cells. We derive the model equilibrium states and investigate conditions for their stability. Analysis shows that, disease free equilibrium is locally stable when $R_{0T_1} < 1$ which implies low smoking rate and when $R_{0T_2} < 1$ which imply low HIV infection rate, it is globally stable when $R_{0T_1} < 1$. Endemic equilibrium is asymptotically stable when there is high smoking rate in which $R_{0T_1} > 1$ and high HIV infection in which $R_{0T_2} > 1$.

The model is numerically simulated, results indicate that increasing smoking rate decreases uninfected T-cells and increases the number of HIV infected T-cells and free virus. The reduction of uninfected T-cells and the increase of HIV infected T-cells and free virus compromises the immune system and expose a HIV smoker to opportunistic infections which marks a disease stage. To prolong and improve the quality of life for people living with HIV smoking cessation programs should be emphasized.

1. Introduction

The immune system is responsible for host defense against any external or internal argent. In performing its defensive role, the immune system responds to a variety of antigens using T-cells with receptors for specific antigens and recognize body's own antigens and activate harmful autoimmunity to the pathogens [10]. CD4+ T-cells in particular play a central role to protect the immune system through helping B cells to make antibodies, stirring macrophages' ability to build up improved microbicidal activity, recruiting neutrophils, eosinophils and basophils to the location where there is infection or inflammation [38].

Infection of T-cells by HIV virus and impaired antigen response due to tobacco smoking have a remarkable negative effect to the immune system [35] and [37]. T-cells which are unresponsive due to tobacco smoke and are infected with HIV cannot perform their defense role because they cannot respond to the stimulation [19], [28] and have HIV DNA copy transcribed into their DNA [26]. Compounds such as nicotine, tar, carbon dioxide and carbon

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monoxide from tobacco smoke induce anergy to T-cells and reduce their efficiency in responding to body antigens and in producing cytokines and chemokines which are important for coordinating the immune system. Apart from reducing their defense potentials, T-cells are also used by HIV to further its reproduction during replication. T-cells which are affected by tobacco smoke and HIV fail to perform their normal functions and make the host vulnerable to various infections [27].

Although tobacco smoking has a devastating effect to the immune system, its effect on the HIV infection of T-cells is less known and has not been given attention whereas smoking rate of people who are living with HIV is increasing [2], [25], [36]. Mehta et al. [19], Sopori [27] and Kalra et al. [11] studied the effect of tobacco smoking on the immune system. Reviewing the effect of tobacco smoking, Mehta et al. [19] concentrated on the immunosuppressive effects of tobacco smoke and mechanism through which tobacco smoking can compromise the immune system. On T-cells, which are the interest of this work, Mehta et al. [19] point out that smoking alters T-cells responses and reduce their defense potentials.

Sopori [27] as well addressed the effects of cigarette smoke on the immune system. The study asserts that chronic exposure to tobacco smoke affects a wide range of immunological functions including responses from innate and adaptive immune systems. According to the study, nicotine and tar being the components of tobacco smoke are main cause of T-cells' insensitivity, these two compounds nicotine and tar also account for the immunosuppressive and addictive effect of tobacco smoking. Kalra et al. [11] investigated the effect of cigarette smoke on the immune responses. The study put forward that chronic exposure to cigarette smoke affects T-cells responses, this can account for diminished T-cells proliferation and antibody responses within the host.

This study aims at using mathematical model to explore how tobacco smoking affects dynamics of HIV in T-cells and how T-cells accommodate tobacco smoking and HIV. The recruitment rate of T-cells in our model is similar to the recruitment rate of T-cells in the model developed by Das et al. [5], however, tobacco smoking, productively and unproductively T-cells differentiate the two models. Due to growing number of people who are living with HIV and smoke, this paper is interested to find out how tobacco smoking affects the HIV infection of CD4+ T-cells.

2. Materials and Methods

2.1. **Model development and Analysis.** The model for the effect of tobacco smoking in the dynamics of HIV in T-cells divides T-cells into three classes, uninfected T-cells X, smoking impaired T-cells X_1 and HIV infected T-cells X_2. The free virus population is represented by V. In this work, CD4+ T-cells which are the HIV target [35] are generally

referred to as T-cells.

Uninfected T-cells are recruited at a rate $\frac{\Lambda}{k+V}$ which is a decreasing function of the virus V [23] and [24], this is due to the ability of HIV virus to infect T-cells in the progenitor [5]. Uninfected T-cells acquire HIV and smoking impairment following a contact with free virus and smoking impaired T-cells at rates β_1 and γ respectively.

Smoking impaired T-cells X_1 grow when uninfected T-cells acquire smoking impairment at a rate γ, suffer HIV infection following a contact with free virus at a rate β_2 and further suffer smoking induced mortality at a rate α.

HIV infected T-cells X_2 replenish at rates β_1 and β_2 following a viral contact with uninfected T-cells and smoking impaired T-cells respectively. The class of HIV infected T-cells X_2 also suffers HIV induced mortality at a rate μ_1. The parameter μ represents T-cells natural mortality for all T-cells compartments.

Free virus V increase when HIV infected T-cells replicate at a rate $N\mu_1$ where N represents number of free virus released by a single T-cell. Free virus diminish when they fuse with smoking impaired and uninfected T-cells at rates $\beta_1 VX$ and $\beta_2 VX_1$ respectively. However, they suffer natural mortality at a rate μ_v.

The model assumes that free virus prey on T-cells with $\beta_1 VX$ and $\beta_2 VX_1$ as functional responses respectively [5], tobacco smoking is treated as a disease and it is transmitted from one cell to another through contact; upon HIV infection, T-cells are assumed to be productively infected hence can produce free virus [26] and [29]; free virus are not affected by smoking; the contact between T-cells and free virus is through mass action principle.
The state variables and parameters are defined in Tables 1, 2 respectively. The interaction between T-cells, smoking and free virus are shown by the Figure 1.

TABLE 1. Variables description

Variable	**Description**
X	Uninfected CD4+ T-cells
X_1	Smoking impaired CD4+ T-cells due to smoking
X_2	HIV infected CD4+ T-cells
V	Free virus

TABLE 2. Parameters' description

Parameter	Description
Λ	constant for CD4+ T-cells recruitment
k	half saturation constant for the virus
γ	rate of acquiring smoking impairment by CD4+ T-cells
μ	natural mortality rate for CD4+ T-cells
β_1	rate of HIV infection for uninfected CD4+ T-cells
β_2	rate of HIV infection for impaired CD4+ T-cells
μ_1	HIV induced death rate for CD4+ T-cells
μ_v	natural mortality rate for free virus
α	smoking induced death rate for impaired CD4+ T-cells

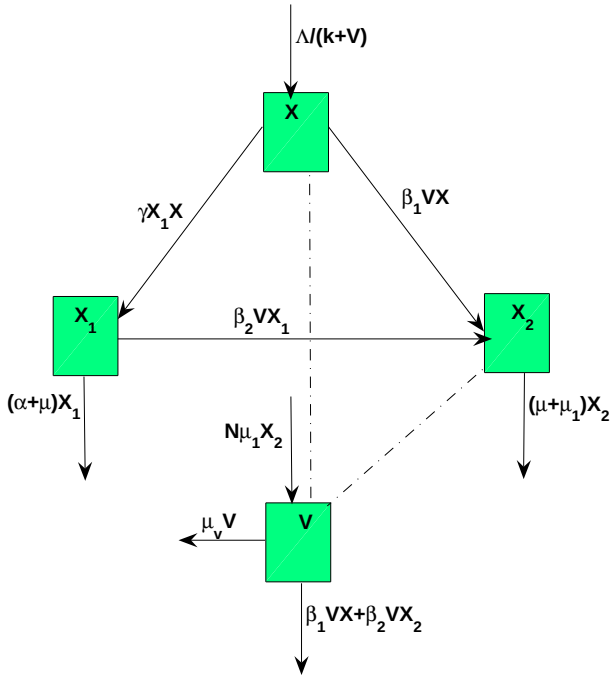

FIGURE 1. Interaction of T-cells with smoking and free virus

Combining formulations and assumptions, the system that describes tobacco smoking effect on the HIV infection of T-cells is given by

$$\frac{dX}{dt} = \frac{\Lambda}{k+V} - \beta_1 VX - \gamma X_1 X - \mu X, \tag{1a}$$

$$\frac{dX_1}{dt} = \gamma X_1 X - \beta_2 V X_1 - (\alpha+\mu)X_1, \tag{1b}$$

$$\frac{dX_2}{dt} = \beta_1 VX + \beta_2 V X_1 - (\mu+\mu_1)X_2, \tag{1c}$$

$$\frac{dV}{dt} = N\mu_1 X_2 - \beta_1 VX - \beta_2 V X_1 - \mu_v V. \tag{1d}$$

2.1.1. *Invariant Region.* To obtain the region where solutions of the model system (1) are feasible, we adopt the approach in [29] and the reference therein. The population for T-cells denoted by X_T and free virus V are considered where we have:

$$X_T = X + X_1 + X_2. \tag{2}$$

$$\frac{dX_T}{dt} \quad < \pi - \mu X_T, \text{ for } \pi = \frac{\Lambda}{k}$$

The solution is given by:

$$X_T \leq \frac{\pi}{\mu} + \left(X_T(0) - \frac{\pi}{\mu}\right) e^{-\mu t}$$
$$\text{for } X_T(0) = X(0) + X_1(0) + X_2(0).$$

Analysis of the solution X_T considers two cases; $X_T(0) > \frac{\pi}{\mu}$ and $X_T(0) < \frac{\pi}{\mu}$.

$$\begin{aligned} &\text{for } X_T(0) > \frac{\pi}{\mu};\ X_T \leq \frac{\pi}{\mu} \leq \frac{\pi}{\mu} + \left(X_T(0) - \frac{\pi}{\mu}\right) e^{-\mu t} \text{ and} \\ &\text{for } X_T(0) > \frac{\pi}{\mu};\ X_T \leq \frac{\pi}{\mu} + \left(X_T(0) - \frac{\pi}{\mu}\right) e^{-\mu t} \leq \frac{\pi}{\mu}. \end{aligned} \tag{3}$$

$$\begin{aligned} &\text{Since } \limsup_{t\longrightarrow\infty} \left(X_T(0) - \frac{\pi}{\mu}\right) e^{-\mu t} \longrightarrow 0, \\ &\limsup_{t\longrightarrow\infty} X_T \leq \frac{\pi}{\mu}. \end{aligned} \tag{4}$$

From the definition of X_T, it follows that:

$$\limsup_{t\longrightarrow\infty} X_2 \leq \frac{\pi}{\mu} \tag{5}$$

Substitution of equation(5) in (1d) leads to:

$$\limsup_{t\longrightarrow\infty} V \leq \frac{N\mu_1\pi}{\mu\mu_v}. \tag{6}$$

Therefore we conclude that, the model system (1) is positive invariant in the region

$$\Gamma = \{(X, X_1, X_2, V) \in R_+^4 : 0 \leq X + X_1 + X_2 \leq \frac{\pi}{\mu},\ 0 \leq V \leq \frac{N\mu_1\pi}{\mu\mu_v}\} \tag{7}$$

Solutions for the model system (1) which are starting on the boundary of the region Γ enter the interior of the region and remain bounded. Results for existence, uniqueness and continuity for the system (1) hold in the invariant region Γ. Since the model is well posed we can therefore consider the flow generated by the model system (1). The result is summarized in the following theorem:

Theorem 1. : *All the solutions of the model system (1) enter the region*

$$\Gamma = \{(X, X_1, X_2, V) \in R_+^4 : 0 \leq X + X_1 + X_2 \leq \frac{\pi}{\mu},\ 0 \leq V \leq \frac{N\mu_1\pi}{\mu\mu_v}\}$$

2.2. **Disease free equilibrium and Reproduction number.** We obtain disease free equilibrium when $X_1 = X_2 = V = 0$ and it is given by

$$E_0\left(X, X_1, X_2, V\right) = \left(\frac{\pi}{\mu}, 0, 0, 0\right). \tag{8}$$

In the absence of tobacco smoking and HIV, T-cells within human host assume their normal growth and function. The body at this state can fight against any pathogen that plans an invasion. At disease free equilibrium, the system of equations (1) reduces to

$$\frac{dX}{dt} = \pi - \mu X. \tag{9}$$

The graph of T-cells showing asymptotic growth behaviour in the infection free state using parameters $\pi = 20$ and $\mu = 0.02$ [24] is illustrated in Figure 2.

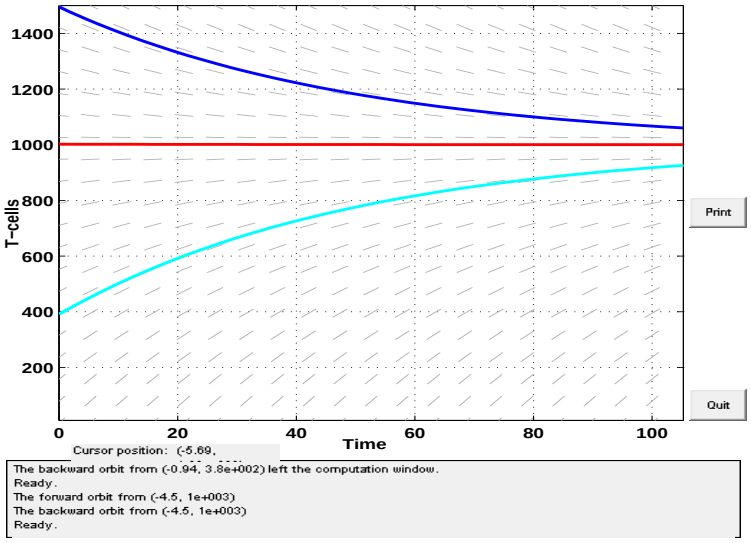

FIGURE 2. Behaviour of T-cells in the absence of smoking and free virus

2.2.1. *Basic Reproduction number.* To measure the effect of tobacco smoking in T-cells, the basic reproduction number which predicts the potentials of the disease [22] is computed . It determines how the two epidemics influence each other and which epidemic in particular accelerates the other. The basic reproduction number is defined as secondary infections caused by a single infected cell when introduced in the entirely susceptible population of cells [33]. To compute basic reproduction number R_{0T}, the next generation method as described by van den Driessche and Watmough [31] is adopted. Using this approach, new infections and transfer terms are denoted by $\mathcal{F}_i$ and $\mathcal{V}_i$ respectively. The basic reproduction number R_{0T} is given by:

$$R_{0T} = \rho\left(\mathcal{F}\mathcal{V}^{-1}\right), \tag{10}$$

that is the maximum eigenvalue of the matrix $\mathcal{F}\mathcal{V}^{-1}$, where

$$\mathcal{F} = \frac{\partial \mathcal{F}_i}{\partial X_j}(X_0) \text{ and } \mathcal{V} = \frac{\partial \mathcal{V}_i}{\partial X_j}(X_0)$$

Using the model system (1) and the approach in van den Driessche and Watmough [31], $\mathcal{F}_i$ and $\mathcal{V}_i$ are defined as follows;

$$\mathcal{F}_{\mathbf{i}} = \begin{pmatrix} \gamma X_1 X \\ \beta_1 V X + \beta_2 V X_1 \\ N\mu_1 X_2 \end{pmatrix} \tag{11}$$

and

$$\mathcal{V}_{\mathbf{i}} = \begin{pmatrix} (\alpha+\mu)X_1 \\ (\mu+\mu_1)X_2 \\ \mu_v V \end{pmatrix} \tag{12}$$

whose eigenvalues λ satisfy the equation

$$|\mathcal{F}\mathcal{V}^{-1} - \lambda I| = 0, \tag{13}$$

I is an identity matrix. The product of $\mathcal{F}\mathcal{V}^{-1}$ is given

$$\mathcal{F}\mathcal{V}^{-\mathbf{1}} = \begin{pmatrix} \frac{\gamma\pi}{\mu(\alpha+\mu)} & 0 & 0 \\ 0 & 0 & \frac{\beta_1\pi}{\mu\mu_v} \\ 0 & \frac{N\mu_1}{\mu+\mu_1} & 0 \end{pmatrix} \tag{14}$$

Thus the basic reproduction number R_{0T} is therefore given by

$$R_{0T} = Max\left\{R_{0T_1}, R_{0T_2}\right\}. \tag{15}$$

where

$$R_{0T_1} = \frac{\gamma\pi}{\mu(\alpha+\mu)} \text{ and } R_{0T_2} = \sqrt{\frac{N\mu_1\beta_1\pi}{\mu\mu_v(\mu+\mu_1)}}. \tag{16}$$

The partial reproduction numbers R_{0T_1} and R_{0T_2} are representing new infections due to smoking and HIV respectively. R_{0T_1} depends on smoking impairment rate, the average time smoking impaired T-cell spends before death, life expectancy for T-cells and recruitment of T-cells in the absence of free virus, R_{0T_2} depends on the number of free virus which are produced by T-cells' replication, HIV virus infection rate, life expectancy of T-cells and free virus and the recruitment of T-cells in the absence of free virus.
We plot both partial reproduction numbers R_{0T_1} and R_{0T_2} against recruitment rate using parameters in Table 3 to compare the two epidemics in case of producing new infections. As indicated in Figure 3, tobacco smoking produces many new infections compared to HIV infection.

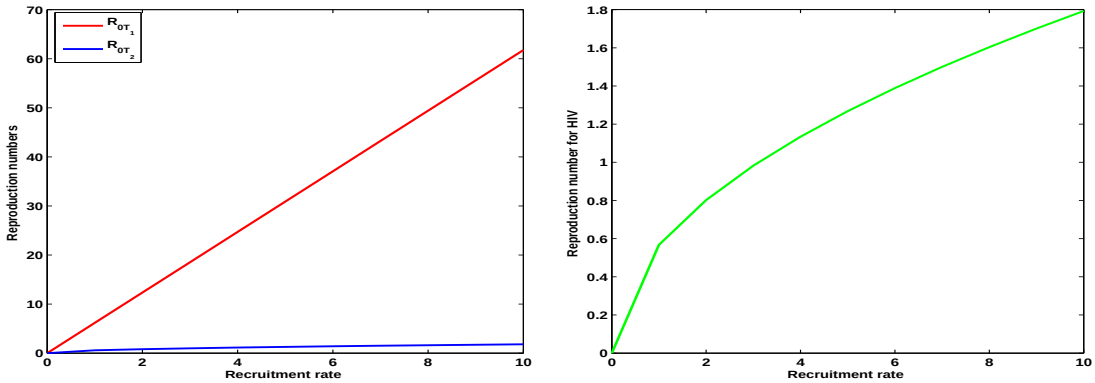

FIGURE 3. Comparison of smoking and HIV new infections

2.3. **Stability of Disease Free Equilibrium.**

2.3.1. *Local Stability of Disease Free Equilibrium.* The basic reproduction number R_{0T} obtained by decomposition technique can be used to determine local stability of disease free equilibrium [8]. Disease free equilibrium is locally stable if $R_{0T} < 1$ and locally unstable if $R_{0T} > 1$. From the definition of R_{0T} in (15), $R_{0T} < 1$ will mean either $R_{0T_1} < 1$ or $R_{0T_2} < 1$. $R_{0T_1} < 1$ if smoking rate is low and $R_{0T_1} > 1$ if smoking rate is high. In the same way $R_{0T_2} < 1$ if replication rate for T-cells is low and $R_{0T_2} > 1$ if replication rate is high. To analyze the local stability, we state and prove the following theorem:

Theorem 2. : *The disease free equilibrium for the model system (1) is locally asymptotically stable when* $R_{0T} < 1$ *and is locally asymptotically unstable when* $R_{0T} > 1$

Proof

To prove local stability of the model system (1), we linearize the system around a disease free equilibrium and obtain the following matrix:

$$\mathbf{J_{E_0}} = \begin{pmatrix} -\mu & -\frac{\gamma\pi}{\mu} & 0 & -\frac{\pi}{k} - \frac{\beta_1\pi}{\mu} \\ 0 & \frac{\gamma\pi}{\mu} - \alpha - \mu & 0 & 0 \\ 0 & 0 & -(\mu_1+\mu) & \frac{\beta_1\pi}{\mu} \\ 0 & 0 & N\mu_1 & -\frac{\beta_1\pi}{\mu} - \mu_v \end{pmatrix} \tag{17}$$

For disease free equilibrium to be locally asymptotically stable, eigenvalues of Jacobian matrix should be negative. From the first and second columns of the Jacobian matrix we obtain $-\mu$ and $\frac{\gamma\pi}{\mu} - \alpha - \mu$ which we re-write as;

$$(\alpha+\mu)\left(\frac{\gamma\pi}{\mu(\alpha+\mu)} - 1\right) = (\alpha+\mu)\left(R_{0T_1} - 1\right). \tag{18}$$

It is negative if and only if

$$R_{0T_1} < 1. \tag{19}$$

The Jacobian matrix (17) is now a 2×2 matrix;

$$\mathbf{J_{E_1}} = \begin{pmatrix} -(\mu_1+\mu) & \frac{\beta_1\pi}{\mu} \\ N\mu_1 & -\frac{\beta_1\pi}{\mu} - \mu_v \end{pmatrix} \tag{20}$$

To establish local stability of disease free equilibrium, trace and determinant are computed. Local stability holds if the trace is negative and determinant is positive. Trace of the matrix J_{E_1} is given by

$$trJ_{E_1} = -(\mu_1+\mu) - \frac{\beta_1\pi}{\mu} - \mu_v < 0. \tag{21}$$

The determinant of the matrix J_{E_1} is:

$$detJ_{E_1} = \frac{\beta_1\pi(\mu+\mu_1)}{\mu} + \mu_v(\mu+\mu_1) - \frac{N\mu_1\beta_1\pi}{\mu}, \tag{22}$$

which simplifies to

$$\begin{aligned} detJ_{E_1} &= \frac{\beta_1\pi}{\mu_v\mu} + 1 - R_{0T_2}^2, \\ &= \frac{\beta_1\pi}{\mu_v\mu} + (1+R_{0T_2})(1-R_{0T_2}). \end{aligned} \tag{23}$$

It follows that

$$detJ_{E_1} > 0, \text{ iff } R_{0T_2} < 1 \tag{24}$$

From equations (19) and (24), disease free equilibrium is locally asymptotically stable when $R_{0T_1} < 1$ and $R_{0T_2} < 1$. This completes the proof.

2.3.2. *Global stability for Disease Free Equilibrium.* Local stability of disease free equilibrium gives the overview for the behaviour of the disease around the disease free equilibrium point. To provide comprehensive understanding for the behaviour of the disease beyond disease free equilibrium point, global stability analysis for disease free equilibrium point is carried out and we adopt the method in Castillo-Chavez et al. [3]. Using this method, the system (1) is re-written as

$$\begin{aligned} \frac{dX_n}{dt} &= C(X_n - X_{dfe}) + C_1 X_i, \\ \frac{dX_i}{dt} &= C_2 X_i, \end{aligned} \tag{25}$$

where X_n represents non-transmitting classes, X_i represents transmitting classes and X_{dfe} a disease free equilibrium point respectively. C, C_1 and C_2 are matrices to be obtained from the system (25). Global stability is guaranteed if eigenvalues of matrix C are negative and C_2 is a Metzler matrix [20] defined mathematically as $C_2(x_{ij}) \geq 0 \ \forall i \neq j$. Adopting the form in equation (25), the system (1) is written as;

$$\left(\frac{\Lambda}{k+V} - \beta_1 VX - \gamma X_1 X - \mu X\right) = C\left(X - \frac{\pi}{\mu}\right) + C_1 \begin{pmatrix} X_1 \\ X_2 \\ V \end{pmatrix} \tag{26}$$

and

$$\begin{pmatrix} \gamma X_1 X - \beta_2 V X_1 - (\alpha+\mu)X_1 \\ \beta_1 VX + \beta_2 VX_1 - (\mu_1+\mu)X_2 \\ N\mu_1 X_2 - \beta_1 VX - \beta_2 VX_1 - \mu_v V \end{pmatrix} = C_2 \begin{pmatrix} X_1 \\ X_2 \\ V \end{pmatrix} \tag{27}$$

Matrix C is 1×1 matrix and it is $C = -\mu$ with eigenvalue $-\mu$. Matrix C_1 is a 1×3 matrix given by

$$\mathbf{C_1} = \begin{pmatrix} \frac{\gamma\pi}{\mu} & 0 & -\frac{\pi}{k} - \frac{\beta_1\pi}{\mu} \end{pmatrix}$$

Matrix C_2 is also given by

$$\mathbf{C_2} = \begin{pmatrix} \frac{\gamma\pi}{\mu} - (\alpha+\mu) & 0 & 0 \\ 0 & -(\mu_1+\mu) & \frac{\beta_1\pi}{\mu} \\ 0 & d & -\frac{\beta_1\pi}{\mu} - \mu_v \end{pmatrix} \tag{28}$$

where $d = N\mu_1$. The matrix (28) has non-negative off diagonal elements and all diagonal elements are negative except $\frac{\gamma\pi}{\mu} - (\alpha + \mu)$ which is further written as

$$\begin{aligned} &\frac{\gamma\pi}{\mu} - (\alpha+\mu) = (\alpha+\mu)\left(R_{0T_1} - 1\right), \\ &(\alpha+\mu)\left(R_{0T_1} - 1\right) < 0, \text{ iff } R_{0T_1} < 1. \end{aligned} \tag{29}$$

$R_{0T_1} < 1$ implies low smoking rate and $R_{0T_1} > 1$ high smoking rate. From this findings it is seen that low smoking rate guarantees global stability of disease free equilibrium and high smoking rate renders global instability of disease free equilibrium. These findings are summarized in the following theorem:

Theorem 3. : *The disease free equilibrium is globally asymptotically stable if* $R_{0T_1} < 1$ *and it is globally unstable if* $R_{0T_1} > 1$.

2.4. **Endemic Equilibrium.** To determine how the two epidemics interact within the host, we compute the endemic equilibrium and derive the condition for its stability. To compute endemic equilibrium, system (1) is written in the following form:

$$\frac{\Lambda}{k+V} - \beta_1 VX - \gamma X_1 X - \mu X = 0, \tag{30a}$$

$$\gamma X_1 X - \beta_2 V X_1 - (\alpha+\mu)X_1 = 0, \tag{30b}$$

$$\beta_1 VX + \beta_2 V X_1 - (\mu+\mu_1)X_2 = 0, \tag{30c}$$

$$N_1\mu_1 X_2 - \beta_1 VX - \beta_2 V X_1 - \mu_v V = 0. \tag{30d}$$

Beginning with equation (30b), we have

$$\begin{aligned} &\gamma X_1 X - \beta_2 V X_1 - (\alpha+\mu)X_1 = X_1[\gamma X - \beta_2 V - (\alpha+\mu)] = 0, \\ &X_1^* = 0,\ X^* = \frac{\beta_2 V^* + u_1}{\gamma},\ u_1 = \alpha+\mu. \end{aligned} \tag{31}$$

$X_1^* = 0$ represents disease free equilibrium when $V_1^* = 0$. To obtain X_1^* we substitute X^* in (30a) where the equation now becomes

$$\begin{aligned} &\frac{\Lambda}{k+V} - \beta_1 V\left(\frac{\beta_2 V^* + u_1}{\gamma}\right) - X_1\left(\beta_2 V^* + u_1\right) - \mu\left(\frac{\beta_2 V^* + u_1}{\gamma}\right) = 0, \\ &X_1^* = \frac{\Lambda}{(k+V^*)(\beta_2 V^* + u_1)} - \frac{\beta_2 V^* + \mu}{\gamma}, \end{aligned}$$

In a simplified form, we have

$$X_1^* = \frac{\Lambda\gamma - (k+V^*)(\beta_2 V^* + u_1)(\beta_1 V^* + \mu)}{\gamma(k+V^*)(\beta_2 V^* + u_1)}. \tag{32}$$

From equation (30c), we can obtain X_2^* as follows;

$$X_2^* = \frac{\beta_1 V^* X^* + \beta_2 V^* X_1^*}{u_2},\ u_2 = \mu + \mu_1. \tag{33}$$

Substitution of X^* and X_1^* into equation (33) results into the expression for X_2^*

$$X_2^* = \frac{(k+V^*)(\beta_2 V^* + u_1) + (u_1\beta_1 - \mu\beta_2)V^* + \Lambda\gamma\beta_2 V^*}{u_2\gamma(k+V^*)(\beta_2 V^* + u_1)} \tag{34}$$

All variables, X^*, X_1^* and X_2^* are in terms of V^*. To find V^*, X^*, X_1^* and X_2^* are substituted in equation (30d) where we obtain

$$\begin{aligned} &\frac{d(k+V^*)(\beta_2 V^* + u_1)(u_1\beta_1 - \mu\beta_2)V^* + \Lambda\gamma\beta_2 V^*}{u_2\gamma(k+V^*)(\beta_2 V^* + u_1)} - \frac{\beta_1 V^*(\beta_2 V^* + u_1)}{\gamma} \\ &+\frac{\beta_2 V^*(k+V^*)(\beta_1 V^* + \mu)(\beta_2 V^* + u_1) - \Lambda\gamma\beta_2 V^*}{\gamma(k+V^*)(\beta_2 V^* + u_1)} - \mu_v V^* = 0. \end{aligned} \tag{35}$$

Expansion and rearrangements of terms in equation (35) yields a third degree polynomial in variable V^*;

$$aV^{*3} + bV^{*2} + cV^* = 0, \tag{36}$$

written as

$$\begin{aligned} &V^*[aV^{*2} + bV^* + c] = 0, \\ &a = \beta_2[(d-u_2)(u_1\beta_1 - \mu\beta_2) - \gamma\mu_v u_2], \\ &b = (k\beta_2 + u_1)[(u_1\beta_1 - \mu\beta_2)(d-u_2) - \gamma\mu_v u_2], \\ &c = (d-u_2)[\gamma\Lambda\beta_2 + u_1 k(u_1\beta_1 - \mu\beta_2)] - \gamma\mu_v u_1 u_2 k. \end{aligned} \tag{37}$$

$V^* = 0$ represents disease free equilibrium when $X_1^* = 0$. The equation

$$aV^{*2} + bV^* + c = 0, \tag{38}$$

represents endemic equilibrium. Using general quadratic formula in equation (38),

$$\begin{aligned} &V^* = \frac{-b + \sqrt{b^2 - 4ac}}{2a}. \\ &V^* > 0 \text{ iff } \frac{-b + \sqrt{b^2 - 4ac}}{2a} > 0, \text{ and} \\ &\frac{-b + \sqrt{b^2 - 4ac}}{2a} > 0 \text{ iff } ac < 0. \\ &ac < 0 \text{ iff } a < 0 \text{ or } c < 0. \end{aligned}$$

$$\begin{aligned} &a < 0 \text{ iff } \frac{\gamma\mu_v u_2}{(d-u_2)(u_1\beta_1 - \mu\beta_2)} > 1 \text{ or} \\ &c < 0 \text{ iff } \gamma\left[\frac{\mu_v u_2}{(u_1\beta_1 - \mu\beta_2)(d-u_2)} - \frac{\Lambda\beta_2}{u_1 k(u_1\beta_1 - \mu\beta_2)}\right] > 1 \end{aligned} \tag{39}$$

From equation (39), $a < 0$ if there is high smoking impairment rate γ and low HIV infection rate β_2 for smoking impaired T-cells and $c < 0$ if there is high smoking impairment rate γ and high HIV infection rate β_2 for smoking impaired T-cells. Therefore either $a < 0$ or $c < 0$ but not both. Endemic equilibrium is defined by the set Γ^* such that

$$\Gamma^* = \{(X^*, X_1^*, X_2^*, V^*) \geq 0\}, \tag{40}$$

where the values of X^*, X_1^* and X_2^* in terms of V^* are given in equations (31), (32) and (34). This result is summarized in the following theorem:

Theorem 4. : *High smoking impairment rate provides the necessary condition for endemic equilibrium* $\Gamma^* = \{X^*, X_1^*, X_2^*, V^*\}$ *of model system (1) to exist.*

2.4.1. *Global stability of endemic equilibrium.* Stability analysis explores the behaviour of the epidemic near the equilibrium points. Solutions which start near the equilibrium point and remain near for all times are stable solutions and represent a stable behaviour of the epidemic. Solutions which start near the equilibrium point and converge to the equilibrium point are asymptotically stable and they represent asymptotically stable behaviour of the epidemic. The solution which show neither of the two behaviours represent unstable behaviour of the epidemic.

The Lyapunov method and LaSalle's invariance principle have been widely used to investigate the stability of epidemics. Using Lyapunov method and LaSalle's invariance principle different functions are constructed depending on the types of the models formulated.

Logarithmic Lyapunov function [7] was developed to analyze stability of Lotka-Volterra systems. Korobeinikov [15] used it to analyze stability for SIS, SIR and $SIRS$ models. Vargas-De-Leon [32] used composite quadratic Lyapunov function to prove global stability for SIS, SIR and $SIRS$ models and Korobeinikov [13] and [14] used explicit Lyapunov function to analyze SEIR and SEIS epidemic models.
To analyze the endemic equilibrium for the model system (1), we adopt explicit Lyapunov function

$$H(y_i) = \sum_{i=1}^{n} w_i(y_i - y_i^* \ln y_i) \tag{41}$$

where w_i are constants that are to be carefully selected, y_i represents number of cells in class i and y_i^* represents equilibrium state in class i. According to the approach in McCluskey [18], using the model system (1) we now define the explicit Lyapunov function

$$H : \{(X, X_1, X_2, V) \in \Gamma : X, X_1, X_2, V > 0\} \to R \text{ by;}$$

$$\begin{aligned} H(X, X_1, X_2, V) &= w_1(X - X^* \ln X) + w_2(X_1 - X_1^* \ln X_1) \\ &\quad + w_3(X_2 - X_2^* \ln X_2) + w_4(V - V^* \ln V). \end{aligned} \tag{42}$$

We assume that for $i = 1, ..., 4$ $w_i > 0$, function H and all w_i are continuous and differentiable in Γ. The value of the function H in Γ^* is zero.
Differentiating the explicit Lyapunov function H with respect to time leads to the following

equation

$$\begin{aligned}\frac{dH}{dt} &= w_1\left(1-\frac{X^*}{X}\right)\frac{dX}{dt}+w_2\left(1-\frac{X_1^*}{X_1}\right)\frac{dX_1}{dt}+w_3\left(1-\frac{X_2^*}{X_2}\right)\frac{dX_2}{dt}\\ &+w_4\left(1-\frac{V^*}{V}\right)\frac{dV}{dt},\end{aligned} \tag{43}$$

which further gives;

$$\begin{aligned}\frac{dH}{dt} &= w_1\left(1-\frac{X^*}{X}\right)[\frac{\Lambda}{k+V}-\beta_1 VX-\gamma X_1X-\mu X]\\ &+w_2\left(1-\frac{X_1^*}{X_1}\right)[\gamma X_1X-\beta_2VX_1-(\alpha+\mu)X_1]\\ &+w_3\left(1-\frac{X_2^*}{X_2}\right)[\beta_1VX+\beta_2VX_1-(\mu+\mu_1)X_2]\\ &+w_4\left(1-\frac{V^*}{V}\right)[N\mu_1X_2-\beta_1VX-\beta_2VX_1-\mu_vV],\end{aligned} \tag{44}$$

At endemic equilibrium, equation (44) becomes;

$$\begin{aligned}\frac{dH}{dt} &= w_1\left(1-\frac{X^*}{X}\right)[\beta_1V^*X^*+\gamma X_1^*X^*+\mu X^*-\beta_1VX-\gamma X_1X-\mu X]\\ &+w_2\left(1-\frac{X_1^*}{X_1}\right)[\beta_2V^*X_1^*-(\alpha+\mu)X_1^*-\beta_2VX_1-(\alpha+\mu)X_1]\\ &+w_3\left(1-\frac{X_2^*}{X_2}\right)[(\mu+\mu_1)X_2^*-(\mu+\mu_1)X_2]\\ &+w_4\left(1-\frac{V^*}{V}\right)[\beta_1V^*X^*+\beta_2V^*X_1^*+\mu_vV^*-\beta_1V^*X^*-\beta_2V^*X_1^*\\ &-\mu_vV^*].\end{aligned} \tag{45}$$

Rearrangement of terms and further simplification gives

$$\begin{aligned}\frac{dH}{dt} &= -w_1\mu\frac{(X-X^*)^2}{X}-w_2(\alpha+\mu)\frac{(X_1-X_1^*)^2}{X_1}\\ &-w_3(\mu+\mu_1)\frac{(X_2-X_2^*)^2}{X_2}-w_4\mu_v\frac{(V-V^*)^2}{V}\\ &-w_1\beta_1\frac{(X-X^*)\,(VX-V^*X^*)}{X}-w_1\gamma\frac{(X-X^*)\,(X_1X-X_1^*X^*)}{X}\\ &-w_2\beta_2\frac{(X_1-X_1^*)\,(VX_1-V^*X_1^*)}{X_1}-w_4\beta_1\frac{(V-V^*)\,(VX-V^*X^*)}{V}\\ &-w_4\beta_2\frac{(V-V^*)\,(VX_1-V^*X_1^*)}{V},\end{aligned} \tag{46}$$

which is written as

$$\begin{aligned}\frac{dH}{dt} &= -w_1\mu\frac{(X-X^*)^2}{X}-w_2(\alpha+\mu)\frac{(X_1-X_1^*)^2}{X_1}\\ &-w_3(\mu+\mu_1)\frac{(X_2-X_2^*)^2}{X_2}-w_4\mu_v\frac{(V-V^*)^2}{V}+F(\Gamma).\end{aligned} \tag{47}$$

where

$$\Gamma=\{(X,X_1,X_2,V)>0\}$$

and

$$\begin{aligned} F(\Gamma) &= -w_1\beta_1\frac{(X-X^*)(VX-V^*X^*)}{X} - w_1\gamma\frac{(X-X^*)(X_1X-X_1^*X^*)}{X} \\ &\quad -w_2\beta_2\frac{(X_1-X_1^*)(VX_1-V^*X_1^*)}{X_1} - w_4\beta_1\frac{(V-V^*)(VX-V^*X^*)}{V} \\ &\quad -w_4\beta_2\frac{(V-V^*)(VX_1-V^*X_1^*)}{V}. \end{aligned}$$

According to McCluskey [18] and Korobeinikov [14] $F(\Gamma)$ is non-positive in Γ and therefore $F(\Gamma) \leq 0$ for all Γ. The derivative $\frac{dH}{dt} \leq 0$ in Γ, equality holds when $\Gamma = \Gamma^*$. Since $\frac{dH}{dt} \leq 0$ for all Γ and $\frac{dH}{dt} = 0$ when $\Gamma = \Gamma^*$, it means that the largest invariant set in Γ when $\frac{dH}{dt} = 0$ is a singleton $\{\Gamma^*\}$ which is the endemic equilibrium. Hence by LaSalle's invariance principle [16] and [17] it means that the endemic equilibrium point Γ^* is asymptotically stable in Γ when $R_{0T} > 1$. This result is summarized in the Theorem 5:

Theorem 5. : *Endemic equilibrium of the model system (1) is globally asymptotically stable when $R_{0T} > 1$ and it is globally asymptotically unstable otherwise.*

3. Numerical simulations

To accomplish the findings of this study, numerical simulations are carried out to analyze the long term behaviour of the two epidemics. Analytical results show that tobacco smoking has devastating effect to HIV infection of T-cells. High smoking rate provides a condition for endemic equilibrium to exist. Stability analysis of disease free equilibrium shows that tobacco smoking provides necessary condition for local and global stability of disease free equilibrium.

To study further the effect of tobacco smoking on the HIV infection of T-cells, the general dynamics is examined to reveal the features for the epidemics in T-cells. Then the specific features which give the overall behaviour for the two epidemics are highlighted.

The life expectancy of a HIV infected patient according to Nakagawa et al.[21], is 9-10 years from primary infection. We will use this time span in our simulations. However, to critically study provide a clear picture of the two epidemics, we will increase the time span to 20-30 years. The parameter values from the literature are used. According to Kirshner and Webb (1997), the normal recruitment of CD4+ T-cells is $10/mm^3$ per day as also seen in [29] and [34]. However, due to HIV infection this rate falls from $10/mm^3$ per day to $3/mm^3$ per day [12]. In this work the recruitment of $3/mm^3$ per day which is for a person living with HIV [12] is used. Basing on the bahaviour of tobacco smoking and HIV epidemic, estimated parameter values will also be used due to limited studies which have addressed tobacco smoking and HIV. The parameters are listed in the Table 3.

TABLE 3. Parameter Values

Parameter	Description	Value	Source
Λ	constant for CD4+ T-cells recruitment	1095 $year^{-1}$	[12]
k	Half saturation constant	12	[5]
β_1	HIV infection rate for T-cells	0.000292 $\frac{ml}{virus\ year}$	[1]
γ	Smoking impairment rate for T-cells	0.0025 $year^{-1}$	[9]
μ	natural mortality rate for T-cells	0.02 $year^{-1}$	[35]
β_2	HIV infection rate for impaired T-cells	0.0019 $\frac{ml}{virus\ year}$	[9]
μ_1	HIV induced mortality	0.0245 $year^{-1}$	[9]
μ_v	natural mortality rate for virus	10 $year^{-1}$	[24]
α	Smoking induced mortality	0.00024 $year^{-1}$	[9]

The general dynamics of HIV in T-cells in the presence of tobacco smoking is plotted in Figure 4. It reveals that smoking impairment grows faster within the first five years. HIV infection raises when smoking impairment is on the decline. At this point, the uninfected T-cells decline dramatically and reach their lowest value as portrayed by Figure 4.

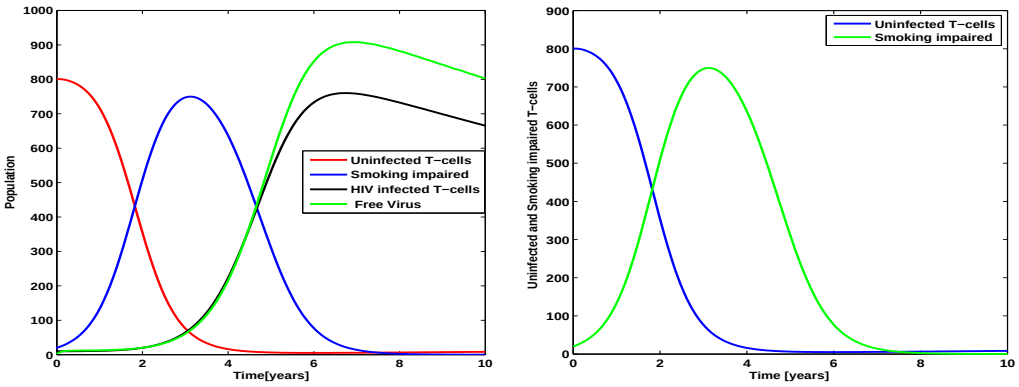

FIGURE 4. Variation of T-cells in the presence of smoking and HIV

The growth of HIV infection which results into increase of HIV infected T-cells while smoking impaired T-cells are declining shows that smoking impaired T-cells are infected by HIV at a high rate. The graph of smoking impaired T-cells against HIV infected T-cells shows a corresponding increase of HIV infected T-cells with respect to smoking impaired T-cells. Initially smoking impaired T-cells increase but it reaches a point where it ceases. At this point HIV infected T-cells grow to their maximum and decline thereafter to attain the value that does not change as illustrated in Figure 5. However, when time span tripled HIV infected T-cells decline to their lowest value due to replication and natural mortality.

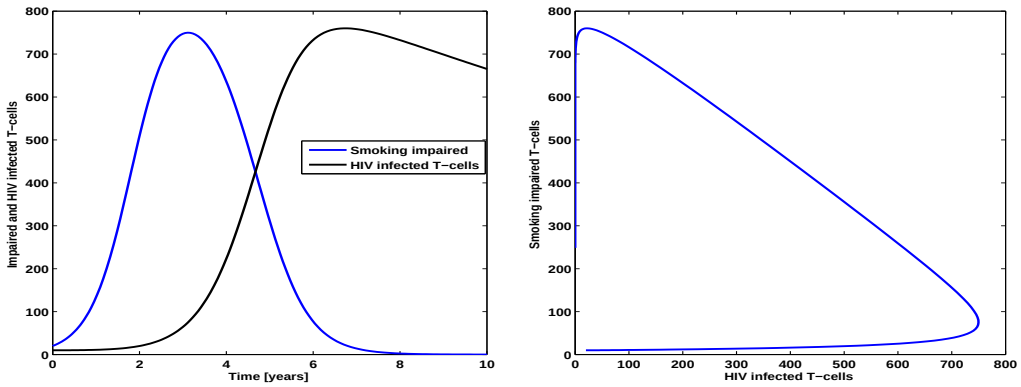

FIGURE 5. Variation of Smoking impaired and HIV infected T-cells with respect time and Variation of smoking impaired T-cells with HIV infected T-cells

Smoking impairment rate is then varied to see its effect on the dynamics of HIV in T-cells. Our aim in this case is to observe how does this variation affects uninfected T-cells, smoking impaired T-cells and HIV infected T-cells. We also look at the relationship between impaired T-cells and HIV infected T-cells and the corresponding effect on free virus.

The uninfected T-cells decrease as smoking impairment rate increases, free virus also increase per smoking impairment increase as demonstrated in Figure 6. Decreasing of the uninfected T-cells and increasing of free virus can worsen T-cells' profile and pave a way for various infections which can accelerate HIV infection to the disease stage AIDS and ultimately death of the human host.

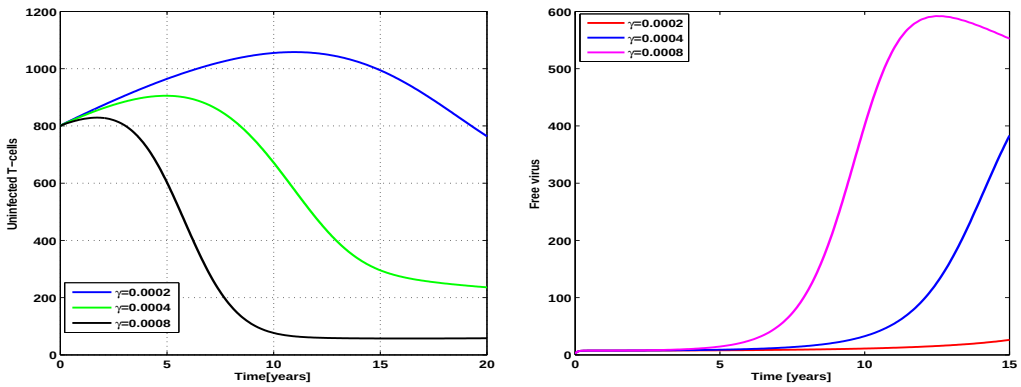

FIGURE 6. Variation of uninfected T-cells and free virus with smoking impairment rate.

The smoking impaired compartment is also studied when smoking impairment rate varies. This variation results into a corresponding increase of smoking impaired T-cells, this is observed within 10 years. Tripling time span results into increase of impaired T-cells but as smoking impaired T-cells increase they take less time to decline to their minimum. This is because the more the T-cells are impaired by smoking the faster they acquire HIV infection and this is the reason why they diminish for a short time as depicted in Figure 7. The result of high HIV infection rate to smoking impaired T-cells is reflected in HIV infected

T-cells because as smoking impairment rate increases there is a corresponding increase in HIV infected T-cells as demonstrated by Figures 8 and 9.

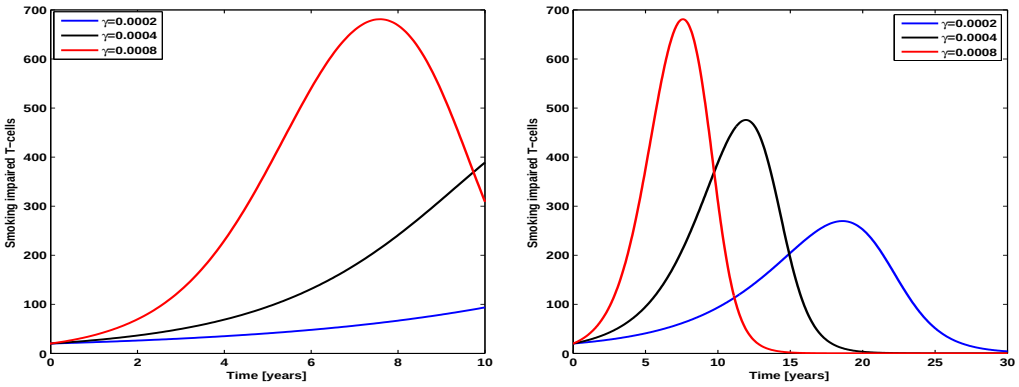

FIGURE 7. Variation of impaired T-cells with respect to smoking impairment rate.

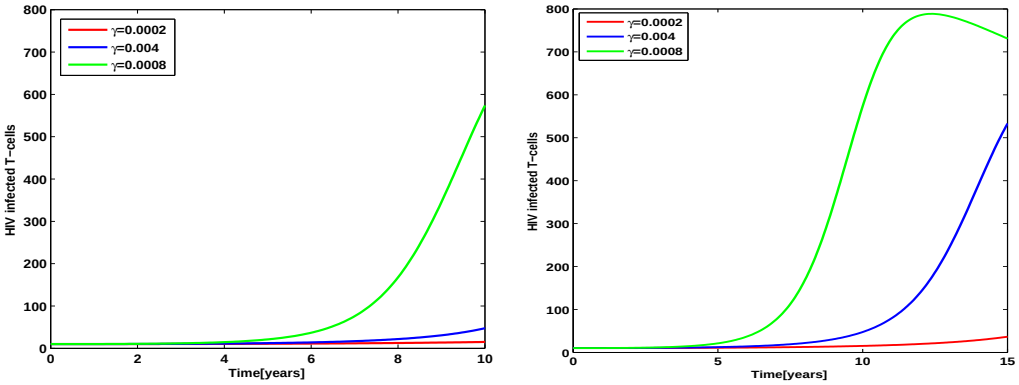

FIGURE 8. Variation of HIV infected T-cells with respect to time.

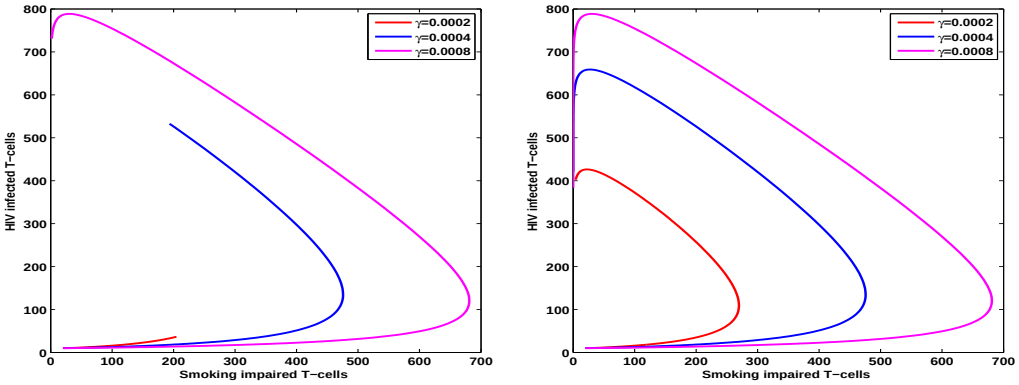

FIGURE 9. Variation of HIV infected T-cells with respect to smoking impaired T-cells.

4. Discussion and Concluding remarks

A simple model for tobacco smoking effect on the HIV infection of T-cells is formulated, equilibrium states and their condition for stability are derived and basic reproduction number

is computed. At disease free equilibrium, T-cells grow asymptotically. The basic reproduction number which is given as the maximum of partial reproductive numbers R_{0T_1} and R_{0T_2} shows that among the two epidemics tobacco smoking produces many new infections in T-cells compared to HIV infection as demonstrated by the Figure 3.

Analytical result shows that, equilibrium states (disease free and endemic equilibriums) exist and smoking affects the existence of endemic equilibrium. Stability analysis of the equilibrium states shows that; when $R_{0T_1} < 1$ and $R_{0T_2} < 1$ disease free equilibrium is locally asymptotically stable and it is globally stable when there is low smoking rate for which $R_{0T_1} < 1$. When $R_{0T_1} > 1$ which implies there is high smoking impairment rate and $R_{0T_2} > 1$ which implies there is high HIV infection rate, the endemic equilibrium is globally stable.

The model is numerically simulated to study the effect of tobacco smoking. We observe that as tobacco smoking impairment rate increases, uninfected T-cells reduces dramatically, HIV infected T-cells and free virus increase significantly. Decreasing of uninfected T-cells is due to smoking impairment and HIV infection. HIV infection of uninfected T-cells and smoking impaired T-cells results into many HIV infected T-cells which replicate to release free virus. As many T-cells are impaired by tobacco smoking, HIV infected T-cells increase correspondingly. This is due to the fact that smoking induced anergy affects the normal functioning of T-cells by making them unresponsive and easily attacked by HIV. This is reflected by increase of HIV infected T-cells when smoking impairment rate increases as depicted by the Figure 8.

Reduction of uninfected T-cells and increase of HIV infected T-cells and free virus present a compromised immune system for which a host is exposed to opportunistic infections [6] such as tuberculosis, oral candidiasis [4] and cancer. Tobacco smoking can therefore promote HIV infections in T-cells and deteriorate the T-cells' profile as proposed by Valiathan et al.[30]. For individuals living with HIV to live longer and improve the quality of life, the study calls for smoking cessation programs to emphasize the importance of abstinence from tobacco smoking and other risk behaviours.

Conflict of interests

The authors declare that there is no conflict of interests.

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References

[1] Adams, B.M., Banks, H.T., Da vidian, M., Hee-Dae Kwon , Tran, H.T., Wynne, S.N., and Rosenberg, E.S. HIV dynamics: Modeling, data analysis, and optimal treatment protocols. *Journal of Computational and Applied Mathematics* 184 (2004) 10-49.

[2] Burkhalter, J. E., Springer, C. M., Chhabra, R., Ostroff, J. S., and Rapkin, B. D., Tobacco use and readiness to quit smoking in low-income HIV-infected persons. *Nicotine & Tobacco Research*, 7 (2005), 511-522.

[3] Castillo-Chavez, C., Feng, Z. and Huang, W. (2002). *Mathematical Approaches for Emerging and Reemerging Infectious Diseases, An Introduction*. Springer Verlag.

[4] Chattopadhyay, A., and Patton, L. L. Smoking as a risk factor for oral candidiasis in HIV-infected adults. *Journal of Oral Pathology & Medicine*, 42 (2013), 302-308.

[5] Das, P., Mukherjee, D., Sen, A., Mukandavire, Z., and Chiyaka, C. Analysis of an In-host Model for HIV Dynamics with Saturation Effect and Discrete Time Delay. *Nonlinear Dynamics and Systems Theory*, 11 (2)(2011) 125-136.

[6] Duffin, R. P., and Tullis. R. H. Mathematical Models of the Complete Course of HIV Infection and AIDS. *Journal of Theoretical Medicine*, 4 (4) (2002), 215-221.

[7] Goh, B.-S. (1980). *Management and analysis of biological*. Elsevier Science, Amsterdam.

[8] Hove-Musekwa, S.D. and Nyabadza, F. The dynamics of an HIV/AIDS model with screened disease carriers.*Computational and Mathematical Methods in Medicine*, 10 (2009), 287-305.

[9] Irunde, J.I., Luboobi, L.S. and Nkansah-Gyekye, Y., Modeling the effect of tobacco smoking on the in-host dynamics of HIV/AIDS. *Journal of Mathematical and Computational Science*, 6(3) (2016), 406-436.

[10] Jiang, H., and Chess, L., Regulation of immune responses by T cells. *New England Journal of Medicine*, 354 (2006), 1166-1176.

[11] Kalra, R. and Singh, S. P., Savage, S. M., Finch, G. L. and Sopori, M. L. Effects of cigarette smoke on immune response: chronic exposure to cigarette smoke impairs antigen-mediated signaling in T cells and depletes IP3-sensitive Ca2+ stores. *Journal of Pharmacology and Experimental Therapeutics*, 293 (2000), No. 1, 166-171.

[12] Kirschner, D. E., and Webb, G. F. A mathematical model of combined drug therapy of HIV infection. *Computational and Mathematical Methods in Medicine*, 1 (1997), 25-34.

[13] Korobeinikov, A. Lyapunov functions and global properties for SEIR and SEIS epidemic models. *Mathematical Medicine & Biology: A Journal of the IMA*, 21 (2004), No.2.

[14] Korobeinikov, A. Global properties of infectious disease models with nonlinear incidence.*Bulletin of Mathematical Biology* 69 (2007), 1871- 1886.

[15] Korobeinikov, A. and Wake, G. C. Lyapunov functions and global stability for SIR, SIRS, and SIS epidemiological models.*Applied Mathematics Letters* 15 (2002), 955-961.

[16] LaSalle, J. P. *The stability of dynamical systems*, Philadelphia. SIAM, (1976).

[17] LaSalle, J. P. and Lefschetz, S. *The stability by Lyapunov-s direct method*, New York. Academic, (1961).

[18] McCluskey, C. C., Lyapunov functions for tuberculosis models with fast and slow progression.*Mathematical Biosciences and Engineering*, 3(4) (2006), 603-614.

[19] Mehta, H., Nazzal, K., and Sadikot, R. T. Cigarette smoking and innate immunity. *Journal of Inflamm. res.* 57 (2008), 497-503.

[20] Mlay, G. M., Luboobi, L. S., Kuznetsov, D., and Shahada, F. The role of re-infection in modelling the dynamics of one strain tuberculosis involving vaccination and treatment. *Asian Journal of Mathematics and application* 2014 (2014), 2307-7743.

[21] Nakagawa, F., May, M., and Phillips, A. . Life expectancy living with HIV: recent estimates and future implications. *Current opinion in infectious diseases*, 26 (2013), 17-25.

[22] Nishiura, H., Correcting the actual reproduction number: a simple method to estimate R0 from early epidemic growth data. *International journal of environmental research and public health*, 7 (2010), 291-302.

[23] Perelson, A. S., and Nelson, P.W. Mathematical Analysis of HIV-I Dynamics in Vivo. *Society for Industry and Applied Mathematics*, 41 (1999), No.1, 3-44.

[24] Perelson, A.S., and Kirschner, D.E., and De Boer, R., Dynamics of HIV infection of CD4+ T cells.*Mathematical biosciences*, 114 (1993), 81-125.

[25] Robinson, W., Moody-Thomas, S., Gruber, D., Patient perspectives on tobacco cessation services for persons living with HIV/AIDS. *AIDS care*, 24 (2012), 71-76.

[26] Rong, L., Gilchrist, M. A., Feng, Z., and Perelson, A.S., Modeling within-host HIV-1 dynamics and the evolution of drug resistance: trade-offs between viral enzyme function and drug susceptibility. *Journal of Theoretical biology*, 247 (2007), 804-818.

[27] Sopori, M., Effects of cigarette smoke on the immune system. *Nature Reviews Immunology*, 2 (2002), No 5, 372-377.

[28] Sopori, M.L., and Kozak, W., Immunomodulatory effects of cigarette smoke. *Journal of neuroimmunology*, 83 (1998), 148-156.

[29] Srivastava, P.K., Banerjee, M., and Chandra, P., Modeling the drug therapy for HIV infection.*Journal of Biological Systems*. 17 (2009), 213-223.

[30] Valiathan, R., Miguez, M. J., Patel, B., Arheart, K. L., and Asthana, D. Tobacco Smoking Increases Immune Activation and Impairs T-Cell Function in HIV Infected Patients on Antiretrovirals: A Cross-Sectional Pilot Study. *PLOS ONE*, 9(2014), Issue 5.

[31] van den Driesche, P. and Watmough, J. Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission. *Mathematical Biosciences*, 180 (2002): 29-48.

[32] Vargas-De-Leon, C. Constructions of lyapunov functions for classic SIS, SIR and SIRS epidemic models with variable population size. *Revista Electr-onica Foro Red. Mat.* 26 (2009), 1-12.

[33] Wang, L. and Li, M.Y. Mathematical analysis of the global dynamics of a model for HIV infection of CD4+ T cells. *Mathematical Biosciences*, .200 (2006), 44-57.

[34] Wang, Y., and Zhou, Y. Mathematical modeling and dynamics of HIV progression and treatment. *Chinese Journal of Engineering Mathematics*, 27 (2010), 534-548.

[35] Wang, X., and Song, X. Global stability and periodic solution of a model for HIV infection of CD4+ T cells.*Applied Mathematics and Computation*, 89 (2007), N0.2, 1331-1340.

[36] Webb, M. S., Vanable, P. A., Carey, M. P., and Blair, D. C., Cigarette smoking among HIV+ men and women: examining health, substance use, and psychosocial correlates across the smoking spectrum. *Journal of behavioral medicine*, 30 (2007), 371-383.

[37] Zavitz, C. J., Gaschler, G. J., Robbins, C. S., Botelho, F. M., Cox, P. G., and Stampfli, M. R., Impact of cigarette smoke on T and B cell responsiveness. *Cellular immunology*, 253 (2008), 38-44.

[38] Zhu, J., and Paul, W.E., CD4 T cells: fates, functions, and faults. *Blood*, 112 (2008), 1557-1569.

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