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MODELING THE EFFECT OF TOBACCO SMOKING ON THE IN-HOST DYNAMICS OF HIV/AIDS

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Abstract. In this paper, a simple model for the effect of tobacco smoking in the in-host dynamics of HIV is formulated with the aim of studying how tobacco smoking affects HIV in-host dynamics. The basic reproduction number here known as smoking induced reproduction number R_0 is computed, disease free and endemic equilibria are derived and conditions for their stability are established. Analytical results show that smoking affects both T-cells and Macrophages however, its effects are severe in macrophages than in T-cells. Stability for disease free and endemic equilibria is analyzed. High smoking rate renders disease free equilibrium to be locally and globally unstable. Low smoking rate leads to globally unstable endemic equilibrium. Numerical results reveal that tobacco smoking which confers insensitivity to T-cells and reducing phagocytosis in macrophages can promote in-host HIV dynamics.

Keywords: Tobacco smoking; HIV; In-host dynamics; Smoking induced reproduction number; T-cells.

2010 AMS Subject Classification: 97M10.

1. Introduction

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Tobacco smoking and the HIV/AIDS epidemic directly compromise the host immune system. Tobacco smoke contains compounds which are poisonous, carcinogenic and mutagenic in nature [39]. Persistent exposure to tobacco smoke weakens the immune system and leaves the body susceptible to various infections [27], [29], [37]. Tobacco smoke exerts a suppressive effect on the immune system[11], [14], [15] which impairs T-cells' and macrophages' functioning. Constant exposure makes T-cells insensitive and alters their responses to pathogens [27] and [37]. Insensitivity and altered responses for T-cells imply diminished ability of the T-cells and the immune system to respond to pathogens.

For macrophages, acute exposure to tobacco smoke reduces their phagocytic function [12], [17], [37], [38] and decreases their efficiency to clear the body out of the pathogens which is their core function in the human body [14]. Assessing the phagocytic function for macrophages on a chronic exposure to tobacco smoke, Thomas *et al*. [38] observed a diminished clearance ability and bactericidal activity for macrophages. However, the effect of tobacco smoke on T-cells and macrophages depends on the dose [25], [34] and duration of exposure to tobacco smoke, high smoking rates and constant exposure to tobacco smoke imply high rate of insensitivity in T-cells and high reduction rate of macrophages' phagocytic function.

T-cells and macrophages are also cellular targets for HIV/AIDS in vivo dynamics. Within the human host, HIV establishes itself by fusing with T-cells and macrophages, and thereby impairing their functioning in the immune system. T-cells and macrophages are incapacitated to the extent that they cannot perform their function to clear the harmful pathogens out of the body. Replication of infected T-cells and macrophages which release more virus offers inability to the immune system to clear out the virus within the body [9]. At this stage when the immune system fails to fight against the virus, the body becomes weak and vulnerable to opportunistic infections.

Impairment of T-cells and macrophages functioning by smoking and infection of the same cells, T-cells and macrophages by the HIV virus suggest that tobacco smoking and HIV attack a common target and may have a synergistic interaction. In our survey of literature, we did not find any study that has established a mathematical model to address the effect of tobacco smoking on the in-host dynamics of HIV. However, few theoretical studies on this topic have

been conducted, Valiathan *et al*. [39] investigated the activation effect of tobacco smoking to the immune system and impairment of T-cells function in HIV infected patients. The study concludes that both tobacco smoking and HIV infection independently influence T-cells immune activation and function, they both present the most horrible immune profile. The study further argued evaluation of cumulative effect of smoking on impairment of the immune system and accelerated disease progression.

Ande *et al*. [2] concentrated on the effect of mild to moderate smoking to viral load. The result shows that mild to moderate smoking increases the viral load in the plasma of HIV patient who are mild to moderate smokers compared to individuals who were non-smokers. Sanguansittianan *et al*. [36] also investigated how the number of CD4+ T-cells in HIV patients varies with smoking status. The results reveal that the average of the absolute CD4+ T-cells count among the HIV-infected smoking group was significantly lower in mild to moderate smokers than the HIV-infected non-smoking group.

Due to a growing number of people who are living with HIV and smoke, this research is interested in finding out how the immune system accommodates both tobacco smoking and HIV virus and how tobacco smoking affects HIV in host dynamics. We use a mathematical model to analyze the effect of tobacco smoking on the in-host dynamics of HIV.

2. Material and Methods

2.1. Model formulation and Analysis

The model for the effect of tobacco smoking in the in-host dynamics of HIV considers CD4+ T-cells which here will be referred to T-cells and macrophages. The model divides T-cells into three classes which are uninfected T-cells X, smoking impaired T-cells X_1 and HIV infected T-cells X_2. Macrophages as well are divided into three classes: healthy macrophages Y , smoking impaired macrophages Y_1 and HIV infected macrophages Y_2. The free virus population is represented by V respectively.

Uninfected T-cells are recruited at a rate $\frac{\Lambda}{k+V}$ which is a decreasing function of the free virus [7] and [30]. In the absence of virus, uninfected T-cells are recruited at a constant rate

$\pi = \frac{\Lambda}{k}$. The free virus V and HIV infected macrophages attack uninfected T-cells at rates β_1 and τ respectively. The uninfected T-cells also acquire impairment from smoking at a rate γ.

Smoking impaired T-cells X_1 are recruited when uninfected T-cells acquire smoking impairment at a rate γ. They are attacked by free virus V at a rate β_2 and further suffer smoking induced mortality at a rate α. The population of infected T-cells X_2 grows due to infection of uninfected and impaired T-cells by the virus at rates β_1 and β_2 respectively. However, it is reduced by HIV disease induced mortality at a rate μ_1. All T-cells compartments suffer natural mortality at a rate μ.

Healthy macrophages Y produced from the bone marrow are replenished at a constant rate λ [1] and [9]. Macrophages catch viral infection at a rate β_3 and are impaired by smoking at a rate ν. Impaired macrophages Y_1 as well are recruited by impairing the healthy macrophages due to smoking at a rate ν. This compartment suffers from HIV infection and smoking induced mortality at rates β_4 and α_1 correspondingly. HIV infected macrophages Y_2 are amplified by HIV viral infection from health and impaired macrophages at rates β_3 and β_4 respectively. However, the population of HIV infected macrophages suffer HIV induced mortality at a rate δ. All macrophages classes suffer natural mortality at a rate μ_y.

The free virus population is recruited by replication of infected T-cells and macrophages at rates $N_1\mu_1$ and $N_2\delta_1$, where N_1 refers to the number of the free virus released by a single HIV infected T-cell, N_2 is the number of free virus released by a single HIV infected macrophage. The population of free virus is reduced by the removal of the virus that takes place when the virus fuse with T-cells and macrophages to cause HIV infection at rates β_1, β_2, β_3 and β_4 respectively (this is under the assumption that, one free virus is responsible for each new infection [1]). It is further reduced by natural mortality at a rate μ_v. All variables and parameters are described in Tables 1 and 2 respectively. The interaction of variables is shown by Figure 1.

The model assumes that the relationship between the virus and uninfected T-cells, impaired T-cells, healthy macrophages and impaired macrophages is similar to that of prey and predator with virus functional response to T-cells and macrophages being $\beta_1 X$, $\beta_2 X_1$, $\beta_3 Y$ and $\beta_4 Y_1$ respectively [7], where T-cells and macrophages are preys and the free virus are the predators.

It is further assumed that tobacco smoke (nicotine) moves from one cell to another through cell to cell contact. Production of macrophages is assumed to remain constant throughout the infection [9]. However, since infection of T-cells and macrophages by free virus is infection for the rest of their lives, productively and non productively infected T-cells are grouped into the same compartment. HIV infected macrophages transfer viral infection to uninfected T-cells [18]. Tobacco smoking has no effect to free virus population.

TABLE 1. Variables description

Variable	**Description**
X	Uninfected CD4+ T-cells
X_1	Smoking impaired CD4+ T-cells
X_2	HIV infected CD4+ T-cells
Y	Healthy macrophages
Y_1	Impaired macrophages due to smoking
Y_2	HIV infected macrophages
V	Free virus

TABLE 2. Parameters' description

Parameter	Description
Λ	constant for CD4+ T-cells recruitment
k	half saturation constant for the virus
λ	recruitment rate for macrophages
γ	smoking impairment rate for CD4+ T-cells
μ	natural mortality rate for CD4+ T-cells
β_1	HIV infection rate for uninfected CD4+ T-cells
β_2	HIV infection rate for impaired CD4+ T-cells
β_3	HIV infection rate for uninfected macrophages
β_4	HIV infection rate for impaired macrophages
ν	smoking impairment rate for macrophages
μ_1	HIV induced death rate for CD4+ T-cells
μ_y	natural mortality rate for macrophages
δ	HIV induced death rate for macrophages
μ_v	natural mortality rate for free virus
α_1	smoking induced death rate for impaired macrophages
α	smoking induced death rate for impaired CD4+ T-cells
τ	HIV transmission rate by infected macrophages to CD4+ T-cells

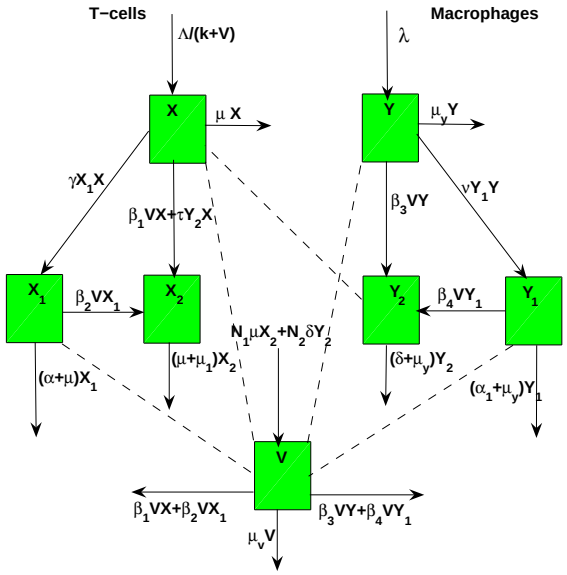

FIGURE 1. Interaction of T-cells, macrophages, smoking and free virus

Putting all formulations and assumptions together, we have the following system of differential equations:

$$\frac{dX}{dt} = \frac{\Lambda}{k+V} - \beta_1 VX - \tau Y_2 X - \gamma X_1 X - \mu X, \tag{1a}$$

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

$$\frac{dX_2}{dt} = \beta_1 VX + \tau Y_2 X + \beta_2 V X_1 - (\mu_1+\mu)X_2, \tag{1c}$$

$$\frac{dY}{dt} = \lambda - \beta_3 VY - \nu Y_1 Y - \mu_y Y, \tag{1d}$$

$$\frac{dY_1}{dt} = \nu Y_1 Y - \beta_4 V Y_1 - (\alpha_1+\mu_y)Y_1, \tag{1e}$$

$$\frac{dY_2}{dt} = \beta_3 VY + \beta_4 V Y_1 - (\delta+\mu_y)Y_2, \tag{1f}$$

$$\frac{dV}{dt} = N_1\mu_1 X_2 + N_2\delta_1 Y_2 - \beta_1 VX - \beta_2 V X_1 - \beta_3 VY - \beta_4 V Y_1 - \mu_v V. \tag{1g}$$

2.1.1. Invariant Region

Though T-cells, macrophages and virus are found in the blood of HIV infected individual to find the invariant region we consider each population separately as:

$$T = X + X_1 + X_2,\ M = Y + Y_1 + Y_2, \text{ and } V.$$

Considering T-cells and macrophages we have:

$$\frac{dT}{dt} \leq \pi - \mu T \text{ and } \frac{dM}{dt} \leq \lambda - \mu_y M$$

which leads to

$$T(t) \leq \frac{\pi}{\mu} + \left(T_0 - \frac{\pi}{\mu}\right) e^{-\mu t} \text{ and } M(t) \leq \frac{\lambda}{\mu_y} + \left(M_0 - \frac{\lambda}{\mu_y}\right) e^{-\mu_y t}, \tag{2}$$

$$\text{where } T_0 = X(0) + X_1(0) + X_2(0) \text{ and } M_0 = Y(0) + Y_1(0) + Y_2(0).$$

We consider two cases to analyze the solution (2):
When $T_0 > \frac{\pi}{\mu}$ and $M_0 > \frac{\lambda}{\mu_y}$ and when $T_0 < \frac{\pi}{\mu}$ and $M_0 < \frac{\lambda}{\mu_y}$.

$$\text{Case 1: When } T_0 > \frac{\pi}{\mu} \text{ and } M_0 > \frac{\lambda}{\mu_y}.$$

In this case, we obtain

$$T(t) \leq \frac{\pi}{\mu} \leq \frac{\pi}{\mu} + \left(T_0 - \frac{\pi}{\mu}\right) e^{-\mu t} \text{ and } M(t) \leq \frac{\lambda}{\mu_y} \leq \frac{\lambda}{\mu_y} + \left(M_0 - \frac{\lambda}{\mu_y}\right) e^{-\mu_y t} \tag{3}$$

$$\text{Case 2: When } T_0 < \frac{\pi}{\mu} \text{ and } M_0 < \frac{\lambda}{\mu_y}.$$

We obtain

$$T(t) \leq \frac{\pi}{\mu} + \left(T_0 - \frac{\pi}{\mu}\right) e^{-\mu t} \leq \frac{\pi}{\mu} \text{ and } M(t) \leq \frac{\lambda}{\mu_y} + \left(M_0 - \frac{\lambda}{\mu_y}\right) e^{-\mu_y t} \leq \frac{\lambda}{\mu_y} \tag{4}$$

For all two cases we have:

$$\limsup_{t\to\infty} T(t) \leq \frac{\pi}{\mu} \text{ and } \limsup_{t\to\infty} M(t) \leq \frac{\lambda}{\mu_y} \tag{5}$$

Since

$$\limsup_{t\to\infty} (X + X_1 + X_2) \leq \frac{\pi}{\mu} \text{ and } \limsup_{t\to\infty} (Y + Y_1 + Y_2) \leq \frac{\lambda}{\mu_y}, \tag{6}$$

$$\limsup_{t\to\infty} X_2 \leq \frac{\pi}{\mu} \text{ and } \limsup_{t\to\infty} Y_2 \leq \frac{\lambda}{\mu_y}. \tag{7}$$

Substitution of (7) in equation (1g) gives

$$\limsup_{t\to\infty} V \leq \Phi = \frac{N_1 \mu_1 \pi}{\mu \mu_v} + \frac{N_2 \delta_1 \lambda}{\mu \mu_v} \tag{8}$$

This shows that, all solutions of system (1) enter the region

$$\Omega = \{(X, X_1, X_2, Y, Y_1, Y_2, V) \in R_+^7 : 0 \leq T \leq \frac{\pi}{\mu},\ 0 \leq M \leq \frac{\lambda}{\mu_y},\ 0 \leq V \leq \Phi\}. \tag{9}$$

The region Ω is positive invariant with respect to the system (1). All the solutions on the boundaries of the region Ω enter the interior of this region and remain bounded. The results of existence, uniqueness and continuity for the system (1) hold in Ω. Since this region is positive invariant, the in-host mathematical model is biologically and epidemiologically meaningful. The flow generated by the dynamics of the system (1) can now be considered. This result can be summarized in the following theorem:

Theorem 2.1. All the solutions of the model system (1) enter the region

$$\Omega = \{(X, X_1, X_2, Y, Y_1, Y_2, V) \in R_+^7 : 0 \leq T \leq \frac{\pi}{\mu},\ 0 \leq M \leq \frac{\lambda}{\mu_y},\ 0 \leq V \leq \Phi\}$$

2.2. Disease Free Equilibrium and Reproduction number

The model system (1) has a disease free equilibrium point given by

$$E^0\left(X^0, X_1^0, X_2^0, Y^0, Y_1^0, Y_2^0, V^0\right) = \left(\frac{\pi}{\mu}, 0, 0, \frac{\lambda}{\mu_y}, 0, 0, 0\right). \tag{10}$$

At this steady state, T-cells are recruited at a constant rate π. T-cells and macrophages grow asymptotically. Using the parameter values $\mu = 0.02$ [18], $\mu_y = 0.02002$, $\pi = 20$ and $\lambda = 10$, the growth of T-cells and macrophages is shown by Figure 2. T-cells grow asymptotically to 1000 $cells/mm^3$ and macrophages to 500 $cells/mm^3$. In this case 1000 $cells/mm^3$ is the maximum number of T-cells [32] and 500 $cells/mm^3$ for macrophages.

2.2.1. Smoking induced reproduction number R_0

Definition 1.1. The basic reproduction number R_0 is defined as the average number of new infections generated by a single infectious individual when introduced in an entirely susceptible population [8] and [42]. In cellular level, it is defined as the average number of new infections generated by a single infectious cell when introduced into entirely susceptible population of cells. $R_0 < 1$ measures the likelihood of the disease being eradicated and persistence of the disease when $R_0 > 1$.

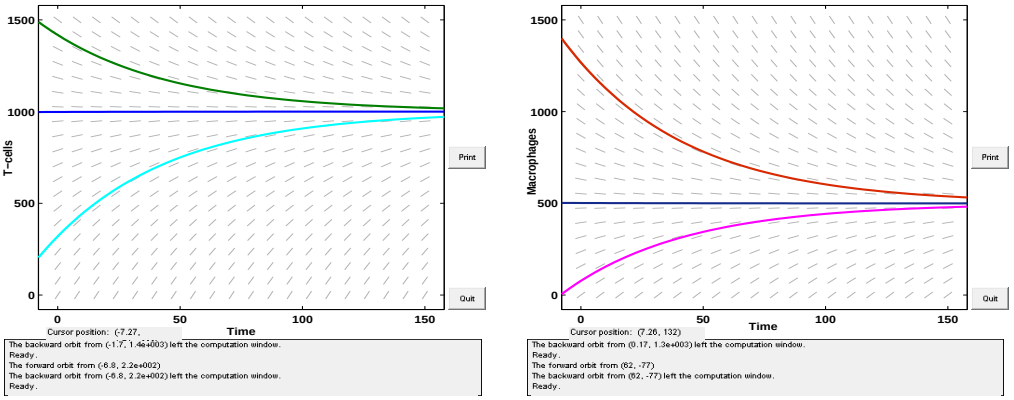

FIGURE 2. Growth of T-cells and macrophages in the absence of free virus and smoking.

To compute the basic reproduction number R_0 which in this work is referred to as smoking induced reproduction number, we apply van den Driessche and Watmough [42] approach. Adopting definitions of matrices for new infections F and transfer terms V in van den Driessche and Watmough [42], the basic reproduction number is now given by

$$R_0 = \rho\left(FV^{-1}\right). \tag{11}$$

The matrices F and V derived from the system (1) are:

$$\mathbf{F} = \begin{pmatrix} \frac{\gamma\pi}{\mu} & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \frac{\tau\pi}{\mu} & \frac{\beta_1\pi}{\mu} \\ 0 & 0 & \frac{\nu\lambda}{\mu_y} & 0 & 0 \\ 0 & 0 & 0 & 0 & \frac{\beta_3\lambda}{\mu_y} \\ 0 & N_1\mu_1 & 0 & N_2\delta & 0 \end{pmatrix} \tag{12}$$

and

$$\mathbf{V} = \begin{pmatrix} (\alpha+\mu) & 0 & 0 & 0 & 0 \\ 0 & (\mu_1+\mu) & 0 & 0 & 0 \\ 0 & 0 & (\mu_y+\alpha_1) & 0 & 0 \\ 0 & 0 & 0 & (\delta+\mu_y) & 0 \\ 0 & 0 & 0 & 0 & \mu_v \end{pmatrix} \tag{13}$$

The product of matrices F and V^{-1} is given by

$$\mathbf{FV^{-1}} = \begin{pmatrix} \frac{\gamma\pi}{\mu(\alpha+\mu)} & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \frac{\tau\pi}{\mu(\delta+\mu_y)} & \frac{\beta_1\pi}{\mu\mu_v} \\ 0 & 0 & \frac{\nu\lambda}{\mu_y(\mu_y+\alpha_1)} & 0 & 0 \\ 0 & 0 & 0 & 0 & \frac{\beta_3\lambda}{\mu\mu_v} \\ 0 & \frac{N_1\mu_1}{(\mu_1+\mu)} & 0 & \frac{N_2\delta}{\delta+\mu_y} & 0 \end{pmatrix} \tag{14}$$

From (14), the smoking induced reproduction number R_0 is given by

$$R_0 = \rho\left(FV^{-1}\right) = Max\left\{\frac{\gamma\pi}{\mu(\alpha+\mu)}, \frac{\nu\lambda}{\mu_y(\alpha_1+\mu_y)}\right\} \tag{15}$$

where we name them as

$$R_{01} = \frac{\gamma\pi}{\mu(\alpha+\mu)},\ R_{02} = \frac{\nu\lambda}{\mu_y(\alpha_1+\mu_y)}.$$

The partial reproduction number R_{01} defines the number of secondary infections which purely occur in T-cells and R_{02} the average number of secondary infections which purely occur in macrophages. Both partial reproduction numbers R_{01} and R_{02} depend on smoking impairment rates, the average period a cell (T-cell or macrophage) spends in smoking compartment, the life span of the cell T-cell or macrophage and their recruitment rate respectively. Using parameter values in Table 3 $R_{02} > R_{01}$, hence

$$R_0 = \frac{\nu\lambda}{\mu_y(\alpha_1+\mu_y)}. \tag{16}$$

The smoking induced reproduction number R_0 increases linearly with smoking impairment rate for macrophages and average time an individual macrophage spends in a macrophage smoking compartment. Increasing the rate of smoking and the average time an individual macrophage spends in a macrophage smoking compartment will increase new infections in macrophages as referred to smoking induced reproduction number in (16).

2.3. Stability analysis of disease free equilibrium

2.3.1. Local stability of a disease free equilibrium

Linearization method is used to investigate the local stability of a disease free equilibrium. In dynamical systems, linearization is used to assess the local stability of the given equilibrium point which is under consideration (en.wikipedia.org/wiki/Linearization, 30th April, 2015), [13].

To determine the local stability of the disease free equilibrium given in equation (10), we linearize the model system (1) at the disease free equilibrium point and obtain the following Jacobian matrix

$$\mathbf{J_{E^0}} = \begin{pmatrix} -\mu & -\frac{\gamma\pi}{\mu} & 0 & 0 & 0 & -\frac{\tau\pi}{\mu} & -\frac{\pi(\mu+\beta_1 k)}{\mu k} \\ 0 & \psi_1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & -w_4 & 0 & 0 & \frac{\tau\pi}{\mu} & \frac{\beta_1\pi}{\mu} \\ 0 & 0 & 0 & -\mu_y & -\frac{\nu\lambda}{\mu_y} & 0 & -\frac{\beta_3\lambda}{\mu_y} \\ 0 & 0 & 0 & 0 & \psi_2 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & -(\delta+\mu_y) & \frac{\beta_3\lambda}{\mu_y} \\ 0 & 0 & N_1\mu_1 & 0 & 0 & N_2\delta & -\frac{\Gamma}{\mu\mu_y} \end{pmatrix} \tag{17}$$

where

$$\psi_1 = (\alpha+\mu)(R_{01}-1),\ w_4 = \mu_1+\mu,\ \Gamma = \mu_y\beta_1\pi + \mu\beta_3\lambda + \mu\mu_y\mu_v,$$
$$\psi_2 = (\alpha_1+\mu_y)(R_0-1).$$

From the first, second, third, fifth and sixth columns, the Jacobian matrix has eigenvalues $-\mu$, ψ_1, $-w_4$, $-\mu_y$ and ψ_2 respectively. The Jacobian matrix (17) now reduces to a 2x2 matrix given by

$$\mathbf{J_{E_{01}}} = \begin{pmatrix} -(\delta+\mu_y) & \frac{\beta_3\lambda}{\mu_y} \\ N_2\delta & -\frac{\Gamma}{\mu\mu_y} \end{pmatrix} \tag{18}$$

which is analyzed by the use of trace and determinant. $detJ_{E_{01}}$ denotes determinant and $trJ_{E_{01}}$ trace, local stability holds if $detJ_{E_{01}} > 0$ and $trJ_{E_{01}} < 0$.

$$trJ_{E_{01}} = -(\delta+\mu_y) - \frac{\Gamma}{\mu\mu_y} < 0.$$

and

$$detJ_{E_{01}} = \left(\frac{\delta+\mu_y}{\mu_y}\right)\left(\frac{\Gamma}{\mu} - \frac{N_2\delta\beta_3\lambda}{(\delta+\mu_y)}\right). \tag{19}$$

$$detJ_{E_{01}} > 0 \text{ iff } \frac{\Gamma}{\mu} > \frac{N_2\delta\beta_3\lambda}{(\delta+\mu_y)} \tag{20}$$

The trace is negative. However, if equation (20) holds then the matrix (18) represents a system with a stable disease free equilibrium.

The eigenvalues of the model system (1) are negative except ψ_1 and ψ_2. The eigenvalues ψ_1 and ψ_2 will therefore be negative if and only if

$$R_{01} < 1 \text{ and } R_0 < 1. \tag{21}$$

Since $R_{01}$and R_0 are functions of smoking impairment rates γ and ν respectively, we see that

$$\frac{\partial R_{01}}{\partial \gamma} = \frac{\pi}{\mu(\alpha+\mu)} > 0, \ \frac{\partial R_0}{\partial \nu} = \frac{\lambda}{\mu_y(\alpha_1+\mu_y)} > 0, \tag{22}$$

which means that, high tobacco smoking impairment rate in both T-cells and macrophages will result into $R_{01} > 1$ and $R_0 > 1$ which implies locally unstable disease free equilibrium. Therefore high smoking rate will result into local instability of disease free equilibrium and this is summarized in the following theorem:

Theorem 2.2. The disease free equilibrium is locally asymptotically stable if $R_0 < 1$ and $R_{01} < 1$ and unstable if $R_0 > 1$ and $R_{01} > 1$.

2.3.2. Global stability of disease free equilibrium

To investigate global stability of the disease free equilibrium we adopt the approach in Castillo-Chavez et al. [6]. Using this approach, the system (1) is now written in the following form

$$\begin{aligned} \frac{dX_N}{dt} &= B(X_N - X_{DFE}) + B_1X_t, \\ \frac{dX_t}{dt} &= B_2X_t, \end{aligned} \tag{23}$$

where X_N and X_t are non-transmitting and transmitting classes respectively. X_{DFE} is a disease free equilibrium, B, B_1 and B_2 are matrices to be computed from equation (23). For disease free equilibrium to be globally stable, the matrix B should have real negative eigenvalues and matrix

B_2 should be a Metzler matrix [28], mathematically denoted by $B_2(x_{ij}) \geq 0 \; \forall i \neq j$.

We define

$$X_N = (X,Y)^T,\ X_t = (X_1,X_2,Y_1,Y_2,V)^T,$$
$$X_{DFE} = \left(\frac{\pi}{\mu}, \frac{\lambda}{\mu_y}\right)^T \text{ and}$$
$$X_N - X_{DFE} = \left(X - \frac{\pi}{\mu}, Y - \frac{\lambda}{\mu_y}\right)^T$$

Using the form of equation (23), first and second parts can now be written as

$$\begin{pmatrix} \frac{\Lambda}{k+V} - \beta_1 VX - \tau XY_2 - \gamma X_1 X - \mu X \\ \lambda - \beta_3 VY - \nu Y_1 Y - \mu_y Y \end{pmatrix} = B \begin{pmatrix} X - \frac{\pi}{\mu} \\ Y - \frac{\lambda}{\mu_y} \end{pmatrix} + B_1 \begin{pmatrix} X_1 \\ X_2 \\ Y_1 \\ Y_2 \\ V \end{pmatrix} \tag{24}$$

and

$$\begin{pmatrix} \gamma X_1 X - \beta_2 VX_1 - (\alpha+\mu)X_1 \\ \beta_1 VX + \beta_2 VX_1 + \tau Y_2 X - (\mu_1+\mu)X_2 \\ \nu Y_1 Y - \beta_4 VY_1 - (\alpha_1+\mu_y)Y_1, \\ \beta_3 VY + \beta_4 VY_1 - (\delta+\mu_y)Y_2, \\ N_1\mu_1 X_2 + N_2\delta Y_2 - \beta_1 VX - \beta_2 VX_1 - \beta_3 VY \\ -\beta_4 VY_1 - \mu_v V \end{pmatrix} = B_2 \begin{pmatrix} X_1 \\ X_2 \\ Y_1 \\ Y_2 \\ V \end{pmatrix} \tag{25}$$

respectively. Using non-transmitting and transmitting classes from equation (23), we obtain matrices B, and B_2 are

$$\mathbf{B} = \begin{pmatrix} -\mu & 0 \\ 0 & -\mu_y \end{pmatrix} \tag{26}$$

and

$$\mathbf{B_2} = \begin{pmatrix} \psi_1 & 0 & 0 & 0 & 0 \\ 0 & -w_4 & 0 & \frac{\tau\pi}{\mu} & \frac{\beta_1\pi}{\mu} \\ 0 & 0 & \psi_2 & 0 & 0 \\ 0 & 0 & 0 & -(\delta+\mu_y) & \frac{\beta_3\lambda}{\mu_y} \\ 0 & N_1\mu_1 & 0 & N_2\delta & -\frac{\Gamma}{\mu\mu_y} \end{pmatrix} \tag{27}$$

All eigenvalues from matrix B are negative , the off diagonal elements in matrix B_2 are positive and the diagonal elements are negative except ψ_1 and ψ_2. The two eigenvalues will either be positive or negative depending on the rate of smoking. High smoking rate will make two eigenvalues positive which imply instability and low smoking rate will make two eigenvalues negative which signifies stable condition for disease free equilibrium, therefore ψ_1 and ψ_2 will be negative if and only if

$$R_0 < 1 \text{ and } R_{01} < 1. \tag{28}$$

We find that tobacco smoking in T-cells and macrophages hold the guarantee for global stability of disease free equilibrium. Low smoking impairment rates will result into global stability of disease free equilibrium, high smoking impairment rates will render the disease free equilibrium to be globally unstable. This leads to the following theorem

Theorem 2.3. The disease free equilibrium is globally asymptotically stable when $R_0 < 1$ and $R_{01} < 1$ and it is unstable if $R_0 > 1$ and $R_{01} > 1$.

2.4. Endemic Equilibrium

At endemic equilibrium, the model system (1) is now written as

$$\frac{\Lambda}{k+V} - \beta_1 VX - \tau Y_2 X - \gamma X_1 X - \mu X = 0, \tag{29a}$$

$$\gamma X_1 X - \beta_2 V X_1 - (\alpha+\mu)X_1 = 0, \tag{29b}$$

$$\beta_1 VX + \beta_2 VX_1 + \tau Y_2 X - (\mu_1 + \mu)X_2 = 0, \tag{29c}$$

$$\lambda - \beta_3 VY - \nu Y_1 Y - \mu_y Y = 0, \tag{29d}$$

$$\nu Y_1 Y - \beta_4 VY_1 - (\alpha_1 + \mu_y)Y_1 = 0, \tag{29e}$$

$$\beta_3 VY + \beta_4 VY_1 - (\delta + \mu_y)Y_2 = 0, \tag{29f}$$

$$N_1\mu_1 X_2 + N_2\delta_1 Y_2 - \beta_1 VX - \beta_2 VX_1 - \beta_3 VY - \beta_4 VY_1 - \mu_v V = 0. \tag{29g}$$

Beginning with equation (29e),

$$Y_1\,(\nu Y - \beta_4 V - w_1) = 0,\ w_1 = \alpha_1 + \mu_y,$$
$$Y_1^* = 0 \text{ or } Y^* = \frac{\beta_4 V^* + w_1}{\nu}.$$

$Y_1^* = 0$ corresponds to disease free equilibrium when $V^* = 0$ however, it does not correspond to disease free equilibrium when $V^* \neq 0$ and

$$Y^* = \frac{\beta_4 V^* + w_1}{\nu} \tag{30}$$

corresponds to endemic equilibrium. Substitution of (30) in (29d) yields

$$Y_1^* = \frac{\nu\lambda - (\beta_3 V^* + \mu_y)(\beta_4 V^* + w_1)}{\nu(\beta_4 V^* + w_1)}. \tag{31}$$

To obtain Y_2^*, we substitute Y_1^* and Y^* in equation (29f) where we have

$$Y_2^* = \frac{(w_1\beta_3 - \mu_y\beta_4)(\beta_4 V^* + w_1)V^* + \nu\lambda\beta_4 V^*}{w_2\nu(\beta_4 V^* + w_1)},\ w_2 = \delta + \mu_y. \tag{32}$$

To find X, equation (29b) is re-written as

$$\gamma X_1 X - \beta_2 VX_1 - w_3 X_1 = X_1(\gamma X - \beta_2 V - w_3) = 0,$$
$$X_1(\gamma X - \beta_2 V - w_3) = 0,\ X_1^* = 0,\ \text{or } X^* = \frac{\beta_2 V^* + w_3}{\gamma},\ w_3 = \alpha + \mu.$$

The equation

$$X^* = \frac{\beta_2 V^* + w_3}{\gamma} \tag{33}$$

represents endemic equilibrium point, $X_1^* = 0$ when $V^* \neq 0$ represents endemic equilibrium in the absence of tobacco smoking in T-cells. However, it can represent disease free equilibrium

when $V^* = 0$.

From equation (29a), we express X_1 in terms of other variables as

$$X_1^* = \frac{\Lambda}{\gamma(k+V^*)X^*} - (\beta_1 V^* + \tau Y_2^* + \mu) \tag{34}$$

Substitution of X^* and Y_2^* in (34) leads to

$$X_1^* = \frac{\Lambda}{(\beta_2 V^* + w_3)(k+V^*)} + \frac{\tau(\mu_y\beta_4 - w_1\beta_3)(\beta_4 V^* + w_1)V^*}{\nu w_2(\beta_4 V^* + w_1)}$$

$$-\frac{w_2\nu(\beta_1 V^* + \mu)(\beta_4 V^* + w_1)}{\nu w_2(\beta_4 V^* + w_1)} - \frac{\tau\nu\lambda\beta_4 V^*}{\nu w_2(\beta_4 V^* + w_1)}.$$

From equation (29c), we solve for X_2^* in terms of the other variables as

$$X_2^* = \frac{\beta_1 V^* X^* + \beta_2 V^* X_1^*}{w_4} + \frac{\tau Y_2^* X^*}{w_4},\ w_4 = \mu + \mu_1. \tag{35}$$

Substitution of X^*, X_1^* and Y_2^* in (35) gives

$$X_2^* = \frac{\tau\beta_2(\mu_y\beta_4 - w_1\beta_3)(\beta_2 V^* + w_3)(\beta_4 V^* + w_1)(k+V^*)V^{*2}}{\nu w_2 w_4(\beta_2 V^* + w_3)(\beta_4 V^* + w_1)(k+V^*)}$$

$$+\frac{\Lambda\nu w_2\beta_2 V^*(\beta_4 V^* + w_1) + \tau(w_1\beta_3 - \mu_y\beta_4)(\beta_2 V^* + w_3)(\beta_4 V^* + w_1)V^*}{\nu\gamma w_2 w_4(\beta_4 V^* + w_1)}$$

$$+\frac{\tau\nu\lambda\beta_4 V^*(\beta_2 V^* + w_3) + \beta_1 V^*(\beta_2 V^* + w_3)}{\gamma w_4}$$

$$-\frac{w_2\beta_2\nu(\beta_1 V^* + \mu)(\beta_2 V^* + w_3)(\beta_4 V^* + w_1)(k+V^*)V^*}{\nu w_2 w_4(\beta_2 V^* + w_3)(\beta_4 V^* + w_1)(k+V^*)}$$

$$-\frac{\tau\nu\lambda\beta_2\beta_4(\beta_2 V^* + w_3)(k+V^*)V^{*2}}{\nu w_2 w_4(\beta_2 V^* + w_3)(\beta_4 V^* + w_1)(k+V^*)}.$$

To obtain V^*, substitute X^*, X_1^*, X_2^*, Y^*, Y_1^* and Y_2^* in equation (29g). This results to a fifth degree polynomial which represents both disease free and endemic equilibriums. It shows that there are at most four possible roots for V^* which implies there are at most four possible endemic equilibriums.

2.4.1. Global stability of endemic equilibrium

The Lyapunov Method and LaSalles Invariance Principle have been traditionally used to analyze stability of autonomous systems of differential equations. Korobeinikov [19] and [20] proposed explicit Lyapunov function which was used to analyze SEIR and SEIS epidemic models. Goh [10] constructed a logarithmic Lyapunov function to analyze Lotka-Volterra systems and later this function was applied by Korobeinikov [21] to analyze endemic equilibrium for SIR, SIRS and SIS epidemic models. Vargas-De-Leon [41] put forward the composite quadratic Lyaponuv function to analyze stability of endemic equilibrium for SIR, SIRS and SIS epidemic models and later constructed a composite-Volterra function to analyze endemic equilibrium for the model with relapse [42]. In this work we adopt explicit Lyapunov function

$$L = \sum z_i (y_i - y^* \ln y_i) \tag{36}$$

which was proposed by Korobeinikov [19]& [20] to analyze the endemic equilibrium of the model system (1). In the function (36), z_i are constants that are to be correctly selected, y_i is the population of cells in i^{th} compartment and y^* is endemic equilibrium point. Adopting McCluskey [26] approach and the reference therein, we use the model system (1) to define the Lyapunov function

$$L : \{(X, X_1, X_2, Y, Y_1, Y_2, V) \in \Omega : X, X_1, X_2, Y, Y_1, Y_2, V > 0\} \to \mathbf{R} \text{ by}$$

$$\begin{aligned} L(X, X_1, X_2, Y, Y_1, Y_2, V) &= z_1(X - X^* \ln X) + z_2(X_1 - X_1^* \ln X_1) \\ &+ z_3(X_2 - X_2^* \ln X_2) + z_4(Y - Y^* \ln Y) + z_5(Y_1 - Y_1^* \ln Y_1) \\ &+ z_6(Y_2 - Y_2^* \ln Y_2) + z_7(V - V^* \ln V). \end{aligned} \tag{37}$$

$z_i > 0$ for $i = 1, 2, ...7$ in Ω, the function L and its constants z_i are continuous and differentiable in Ω and $L(\Omega^*) = 0$ for $\Omega^* = (X^*, X_1^*, X_2^*, Y^*, Y_1^*, Y_2^*, V^*)$. Global stability for endemic equilibrium holds if $\frac{dL}{dt} \leq 0$. Thus

$$\begin{aligned} \frac{dL}{dt} &= z_1\left(1 - \frac{X^*}{X}\right)\frac{dX}{dt} + z_2\left(1 - \frac{X_1^*}{X_1}\right)\frac{dX_1}{dt} + z_3\left(1 - \frac{X_2^*}{X_2}\right)\frac{dX_2}{dt} + \\ &z_4\left(1 - \frac{Y^*}{Y}\right)\frac{dY}{dt} + z_5\left(1 - \frac{Y_1^*}{Y_1}\right)\frac{dY_1}{dt} + z_6\left(1 - \frac{Y_2^*}{Y_2}\right)\frac{dY_2}{dt} + z_7\left(1 - \frac{V^*}{V}\right)\frac{dV}{dt} \end{aligned} \tag{38}$$

which leads to the equation

$$
\begin{aligned}
&\frac{dL}{dt} = z_1\left(1-\frac{X^*}{X}\right)[\frac{\Lambda}{k+V}-\beta_1 VX-\tau Y_2 X-\gamma X_1 X-\mu X]\\
&+z_2\left(1-\frac{X_1^*}{X_1}\right)[\gamma X_1 X-\beta_2 V X_1-(\alpha+\mu)X_1]\\
&+z_3\left(1-\frac{X_2^*}{X_2}\right)[\beta_1 VX+\tau Y_2 X+\beta_2 V X_1-(\mu_1+\mu)X_2]\\
&+z_4\left(1-\frac{Y^*}{Y}\right)[\lambda-\beta_3 VY-\nu Y_1 Y-\mu_y Y]\\
&+z_5\left(1-\frac{Y_1^*}{Y_1}\right)[\nu Y_1 Y-\beta_4 V Y_1-(\alpha_1+\mu_y)Y_1]\\
&+z_6\left(1-\frac{Y_2^*}{Y_2}\right)[\beta_3 VY+\beta_4 V Y_1-(\delta+\mu_y)Y_2]\\
&+z_7\left(1-\frac{V^*}{V}\right)[N_1\mu_1 X_2+N_2\delta_1 Y_2-\beta_1 VX-\beta_2 V X_1\\
&-\beta_3 VY-\beta_4 V Y_1-\mu_v V]
\end{aligned}
\tag{39}
$$

At endemic equilibrium, we have

$$
\begin{aligned}
&\frac{dL}{dt} = z_1\left(1-\frac{X^*}{X}\right)[\beta_1 V^*X^*+\tau Y_2^* X^*+\gamma X_1^* X^*+\mu X^*-\beta_1 VX\\
&-\tau Y_2 X-\gamma X_1 X-\mu X]+z_2\left(1-\frac{X_1^*}{X_1}\right)[\beta_2 V^* X_1^*+(\alpha+\mu)X_1^*\\
&-\beta_2 V X_1-(\alpha+\mu)X_1]+z_3\left(1-\frac{X_2^*}{X_2}\right)[(\mu_1+\mu)X_2^*-\tau Y_2^* X^*+\tau Y_2 X\\
&-(\mu_1+\mu)X_2]+z_4\left(1-\frac{Y^*}{Y}\right)[\beta_3 V^*Y^*-\nu Y_1^* Y^*-\mu_y Y^*-\beta_3 VY\\
&-\nu Y_1 Y-\mu_y Y]+z_5\left(1-\frac{Y_1^*}{Y_1}\right)[\beta_4 V^* Y_1^*+(\alpha_1+\mu_y)Y_1^*\\
&-\beta_4 V Y_1-(\alpha_1+\mu_y)Y_1]+z_6\left(1-\frac{Y_2^*}{Y_2}\right)[-\beta_4 V^* Y_1^*+(\delta+\mu_y)Y_2^*\\
&+\beta_4 V Y_1-(\delta+\mu_y)Y_2]+z_7\left(1-\frac{V^*}{V}\right)[\beta_1 V^*X^*+\beta_2 V^* X_1^*+\beta_3 V^*Y^*\\
&+\beta_4 V^* Y_1^*+\mu_v V^*-\beta_1 VX-\beta_2 V X_1-\beta_3 VY-\beta_4 V Y_1-\mu_v V]
\end{aligned}
\tag{40}
$$

Rearranging the terms leads to

$$
\begin{aligned}
\frac{dL}{dt} &= z_1\left(1-\frac{X^*}{X}\right)[-\beta_1 VX\left(1-\frac{V^*X^*}{VX}\right)-\tau Y_2X\left(1-\frac{Y_2^*X^*}{Y_2X}\right)]\\
&+z_1\left(1-\frac{X^*}{X}\right)[-\gamma X_1X\left(1-\frac{X_1^*X^*}{X_1X}\right)-\mu\left(1-\frac{X^*}{X}\right)]\\
&+z_2\left(1-\frac{X_1^*}{X_1}\right)[-\beta_2 VX_1\left(1-\frac{V^*X_1^*}{VX_1}\right)-(\alpha+\mu)X_1\left(1-\frac{X_1^*}{X_1}\right)]\\
&+z_3\left(1-\frac{X_2^*}{X_2}\right)[-(\mu_1+\mu)X_2\left(1-\frac{X_2^*}{X_2}\right)]\\
&+z_4\left(1-\frac{Y^*}{Y}\right)[-\beta_3 VY(1-\frac{V^*Y^*}{VY})-\nu\left(1-\frac{Y_1^*Y^*}{Y_1Y}\right)-\mu_yY\left(1-\frac{Y^*}{Y}\right)]\\
&+z_5\left(1-\frac{Y_1^*}{Y_1}\right)[-\beta_4 VY_1\left(1-\frac{V^*Y_1^*}{VY_1}\right)-(\alpha_1+\mu_y)Y_1\left(1-\frac{Y_1^*}{Y_1}\right)]\\
&+z_6\left(1-\frac{Y_2^*}{Y_2}\right)[-\beta_4 VY_1\left(1-\frac{V^*Y_1^*}{VY_1}\right)-(\delta+\mu_y)Y_2\left(1-\frac{Y_2^*}{Y_2}\right)]\\
&+z_7\left(1-\frac{V^*}{V}\right)[-\beta_1 VX\left(1-\frac{V^*X^*}{VX}\right)-\beta_2 VX_1\left(1-\frac{V^*X_1^*}{VX_1}\right)\\
&-\beta_3 VY\left(1-\frac{V^*Y^*}{VY}\right)-\beta_4 VY_1\left(1-\frac{V^*Y_1^*}{VY_1}\right)-\mu_vV\left(1-\frac{V^*}{V}\right)]
\end{aligned}
\tag{41}
$$

Further simplification of terms yields the following equation

$$
\begin{aligned}
\frac{dL}{dt} &= -z_1\mu\frac{(X-X^*)^2}{X}-z_2(\alpha+\mu)\frac{(X_1-X_1^*)^2}{X_1}-z_3(\mu_1+\mu)\frac{(X_2-X_2^*)^2}{X_2}\\
&-z_4\mu_y\frac{(Y-Y^*)^2}{Y}-z_5(\alpha_1+\mu_y)\frac{(Y_1-Y_1^*)^2}{Y_1}-z_6(\delta+\mu_y)\frac{(Y_2-Y_2^*)^2}{Y_2}\\
&-z_7\mu_v\frac{(V-V^*)^2}{V}-z_1\beta_1\frac{(X-X^*)(VX-V^*X^*)}{X}\\
&-z_1\tau\frac{(X-X^*)(Y_2X-Y_2^*X^*)}{X}-z_1\gamma\frac{(X-X^*)(X_1X-X_1^*X^*)}{X}\\
&-z_2\beta_2\frac{(X_1-X_1^*)(VX_1-V^*X_1^*)}{X_1}-z_4\beta_3\frac{(Y-Y^*)(VY-V^*Y^*)}{Y}\\
&-z_4\nu\frac{(Y-Y^*)(Y_1Y-Y_1^*Y^*)}{Y}-z_5\beta_4\frac{(Y_1-Y_1^*)(VY_1-V^*Y_1^*)}{Y_1}\\
&-z_6\beta_4\frac{(Y_2-Y_2^*)(VY_1-V^*Y_1^*)}{Y_2}-z_7\beta_1\frac{(V-V^*)(VX-V^*X^*)}{V}\\
&-z_7\beta_2\frac{(V-V^*)(VX_1-V^*X_1^*)}{V}-z_7\beta_3\frac{(V-V^*)(VY-V^*Y^*)}{V}\\
&-z_7\beta_4\frac{(V-V^*)(VY_1-V^*Y_1^*)}{V}
\end{aligned}
\tag{42}
$$

Applying McCluskey [26] approach, the final form is given by

$$\begin{aligned}
\frac{dL}{dt} &= -z_1\mu\frac{(X-X^*)^2}{X} - z_2(\alpha+\mu)\frac{(X_1-X_1^*)^2}{X_1} - z_3(\mu_1+\mu)\frac{(X_2-X_2^*)^2}{X_2} \\
&-z_4\mu_y\frac{(Y-Y^*)^2}{Y} - z_5(\alpha_1+\mu_y)\frac{(Y_1-Y_1^*)^2}{Y_1} - z_6(\delta+\mu_y)\frac{(Y_2-Y_2^*)^2}{Y_2} \\
&-z_7\mu_v\frac{(V-V^*)^2}{V} + G(\Omega),
\end{aligned}$$

where

$$\begin{aligned}
G(\Omega) &= -z_1\beta_1\frac{(X-X^*)(VX-V^*X^*)}{X} - z_1\tau\frac{(X-X^*)(Y_2X-Y_2^*X^*)}{X} \\
&-z_1\gamma\frac{(X-X^*)(X_1X-X_1^*X^*)}{X} - z_2\beta_2\frac{(X_1-X_1^*)(VX_1-V^*X_1^*)}{X_1} \\
&-z_4\beta_3\frac{(Y-Y^*)(VY-V^*Y^*)}{Y} - z_4\nu\frac{(Y-Y^*)(Y_1Y-Y_1^*Y^*)}{Y} \\
&-z_5\beta_4\frac{(Y_1-Y_1^*)(VY_1-V^*Y_1^*)}{Y_1} - z_6\beta_4\frac{(Y_2-Y_2^*)(VY_1-V^*Y_1^*)}{Y_2} \\
&-z_7\beta_1\frac{(V-V^*)(VX-V^*X^*)}{V} - z_7\beta_2\frac{(V-V^*)(VX_1-V^*X_1^*)}{V} \\
&-z_7\beta_3\frac{(V-V^*)(VY-V^*Y^*)}{V} - z_7\beta_4\frac{(V-V^*)(VY_1-V^*Y_1^*)}{V}
\end{aligned} \tag{43}$$

The function $G(\Omega)$ is non-positive, thus $G \leq 0$ for all Ω. Therefore $\frac{dL}{dt} \leq 0$ in Ω and is zero when $\Omega = \Omega^*$. Since $\frac{dL}{dt} \leq 0$ in Ω and is zero when $\Omega = \Omega^*$, this implies that the largest compact set in Ω when $\frac{dL}{dt} = 0$ is the singleton $\{\Omega^*\}$ which is the endemic equilibrium. By LaSalle's invariant principle [23] and [24] then it implies that the endemic equilibrium Ω^* is globally asymptotically stable in the interior of Ω when $R_0 > 1$. R_0 depends on the rate at which the cells are impaired by tobacco smoking. $R_0 > 1$ occurs when smoking rate is high however, since endemic equilibrium is stable when $R_0 > 1$, it implies that high smoking rate makes endemic equilibrium to be globally asymptotically stable. We thus have established the following result

Theorem 2.4. The system (1) has a globally asymptotically stable endemic equilibrium Ω^* when $R_0 > 1$ and has a globally asymptotically unstable endemic equilibrium when $R_0 < 1$.

3. Numerical Simulations

The study modelled the effect of tobacco smoking on HIV in vivo dynamics. The analytical results show that though tobacco smoking affects T-cells and macrophages, its effect is severe

in macrophages compared to T-cells . Stability analysis for disease free and endemic equilibria shows to be affected by tobacco smoking. To compliment the analytical results, numerical simulations for the model system (1) is carried out to study the long term behaviour for tobacco smoking and HIV in the host.

In simulations, the effect of tobacco smoking on the immune system and on the dynamics of HIV *in vivo* is given due weight to reveal its long term impacts. Features of the general dynamics considering the long term behaviours for T-cells and macrophages are explored and studied. The rate of tobacco smoking impairment is then varied to observe the corresponding behaviours of T-cells and macrophages. This variation also helps to study and analyze the behaviour of HIV dynamics into HIV infected compartments.

Parameter values from the literature are used. The parameters whose units are per day are converted to the unit per year for the aim of revealing the long term behaviour of the two epidemics tobacco smoking and HIV. Basing on the behaviour of the two epidemics some parameters are estimated as the studies that have modelled the effect of tobacco smoking on the in-host dynamics of HIV are very limited. The parameters are as they are listed in Table 3.

The general dynamics reveal that, smoking impairment in T-cells and macrophages raises to its peak compared to HIV infection which grows slowly. However from the peak of smoking impairment, impaired T-cells and macrophages decline to their minimum while HIV infection in both T-cells and macrophages raises correspondingly as portrayed in Figure 3. HIV infection in macrophages is seen to grow without bound due to the fact that HIV infected macrophages live longer than HIV infected T-cells [4].

To provide clear illustration how tobacco smoking and HIV infection in T-cells and macrophages vary with respect to time, we plot impaired and HIV infected T-cells and macrophages with respect to time as shown in Figure 4. Smoking impairment in T-cells grows and reaches its peak point where it declines from its maximum to the minimum however, as smoking impairment is declining there is a corresponding raise of HIV infection. This behaviour is also observed in macrophages as demonstrated in Figures 3 and 4. The growth of the virus population is seen

TABLE 3. Parameter Values

Parameter	Description	Value	Source	Units
Λ	constant for CD4+ T-cells recruitment	120	[7]	$year^{-1}$
k	half saturation constant for the virus	12	[7]	
β_1	HIV infection rate for uninfected CD4+ T-cells	0.000292	[1]	$\frac{ml}{virusyear}$
β_2	HIV infection rate for impaired CD4+ T-cells	0.0019	Estimated	$\frac{ml}{virusyear}$
β_3	HIV infection rate for uninfected macrophages	0.000365	[18]	$\frac{ml}{virusyear}$
β_4	HIV infection rate for impaired macrophages	0.0043	Estimated	$\frac{ml}{virusyear}$
γ	smoking impairment rate for CD4+ T-cells	0.0025	Estimated	$year^{-1}$
ν	smoking impairment rate for macrophages	0.004	Estimated	$year^{-1}$
μ	natural mortality rate for CD4+ T-cells	0.02	[44]	$year^{-1}$
μ_1	HIV induced death rate for CD4+ T-cells	0.0245	Estimated	$year^{-1}$
μ_y	natural mortality rate for macrophages	0.00351	Estimated	$year^{-1}$
δ	HIV induced death rate for macrophages	0.00052	Estimated	$year^{-1}$
μ_v	natural mortality rate for free virus	10	[34]	$year^{-1}$
α_1	smoking induced death rate for impaired macrophages	0.015	Estimated	$year^{-1}$
α	smoking induced death rate for impaired CD4+ T-cells	0.00024	Estimated	$year^{-1}$
τ	HIV transmission rate by macrophages to CD4+ T-cells	0.000365	[18]	$year^{-1}$
λ	recruitment rate for macrophages	31.98	[1]	$\frac{cells}{mlyear}$

in two stages, initially the virus grow and reach their local maximum which remains constant before the growth without bound is attained as depicted in Figure 3.

where X represents Uninfected T-cells, X_1 Smoking impaired T-cells, X_2 HIV infected T-cells, Y Health macrophages, Y_1 Smoking impaired macrophages, Y_2 HIV infected macrophages and V Free virus.

To observe the effect of tobacco smoking in T-cells and macrophages, smoking impaired T-cells and macrophages are plotted against HIV infected T-cells and macrophages respectively. The graph shows that, from the initial point HIV infected T-cells and macrophages increase

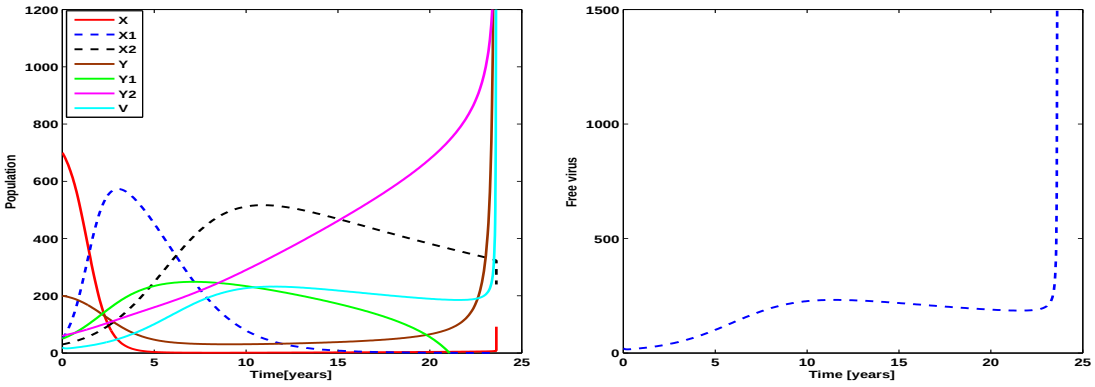

FIGURE 3. Variation of T-cells and macrophages in the presence of HIV and smoking.

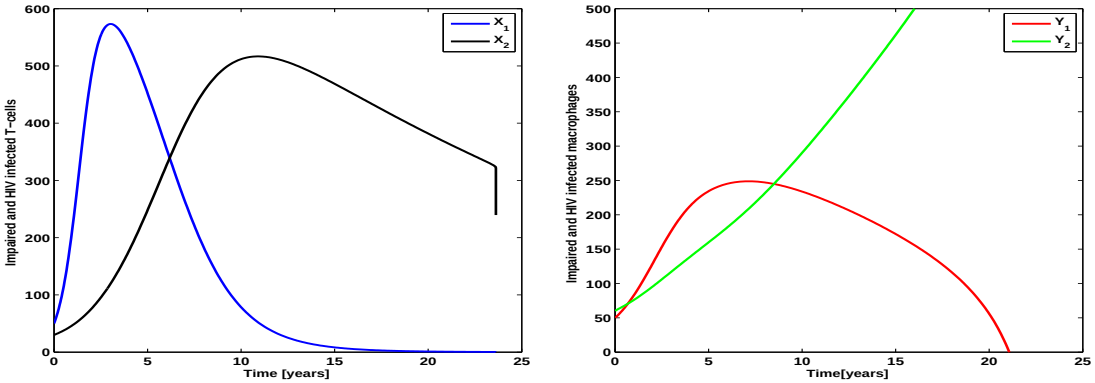

FIGURE 4. Variation of HIV infected and impaired T-cells and macrophages with respect to time.

slowly when smoking impaired T-cells and macrophages increase. However, it reaches a point when smoking impaired T-cells and macrophages cease to increase. At this point HIV infected T-cells and macrophages increase to their maximum while the smoking impaired T-cells and macrophages reach their lowest value as depicted in Figure 5.

To clarify how the immune system accommodates both tobacco smoking and HIV, the smoking impairment rate in both T-cells and Macrophages is varied. The dramatic decrease in T-cells and Macrophages when smoking impairment rate increases is observed as illustrated in Figure 6. Decreasing of T-cells and macrophages may weaken the immune system and leave the body vulnerable to HIV infection. In a smoking weakened immune system, HIV virus cannot encounter resistance from T-cells and macrophages because many are impaired by smoking. Figure 6 illustrates how smoking weakens the immune system by impairing T-cells and macrophages.

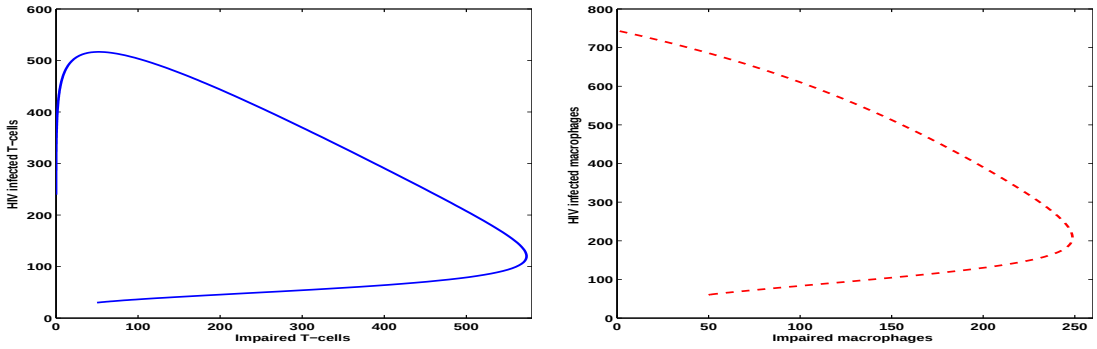

FIGURE 5. Variation of impaired T-cells and macrophages with HIV infected T-cells and macrophages

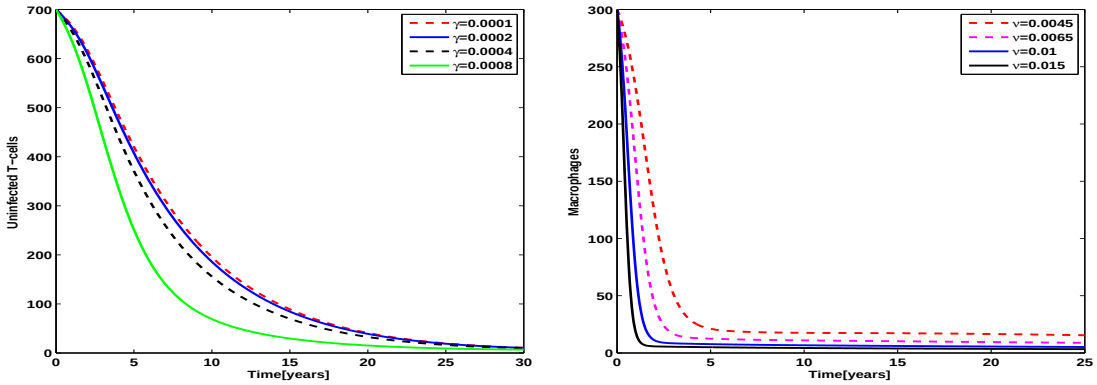

FIGURE 6. Variation of T-cells and macrophages with smoking impairment rate.

The long term bahaviour of T-cells and macrophages in the presence of tobacco smoking is explored by varying smoking impairment rate for T-cells and macrophages. Varying smoking impairment rate for T-cells, we observe that as smoking impairment increases, HIV infected T-cells increase correspondingly with respect to smoking impaired T-cells. The corresponding increase of HIV infected macrophages with respect to T-cells' smoking impairment rate is also observed as demonstrated in Figure 7. Contrastingly as HIV infection increases in T-cells, smoking impaired T-cells decline to zero while HIV infected and smoking impaired macrophages reach their maximum.

By varying smoking impairment rate in T-cells, we find that HIV infected T-cells and macrophages will increase as per increase of smoking impairment rate in T-cells. According to Figure 8 the increase of T-cells is observed in the first twenty years and this increase becomes unstable there after. The unstable increase of HIV infected T-cells is due to the fact that many HIV infected

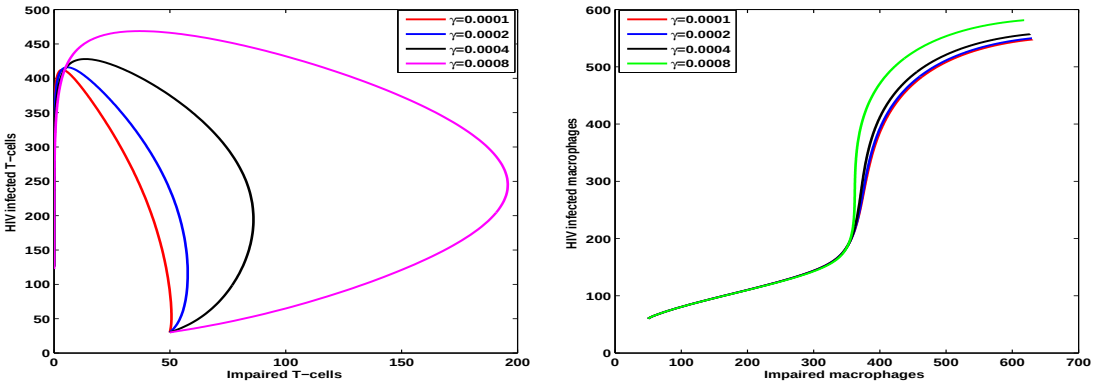

FIGURE 7. Variation of smoking impaired T-cells and macrophages with HIV infected T-cells and macrophages.

T-cells will result to a high replication rate to produce free virus. The correspondingly increase in HIV infected macrophages is also observed when smoking impairment rate for T-cells increases. This increase is observed in entire time as demonstrated in Figure 8.

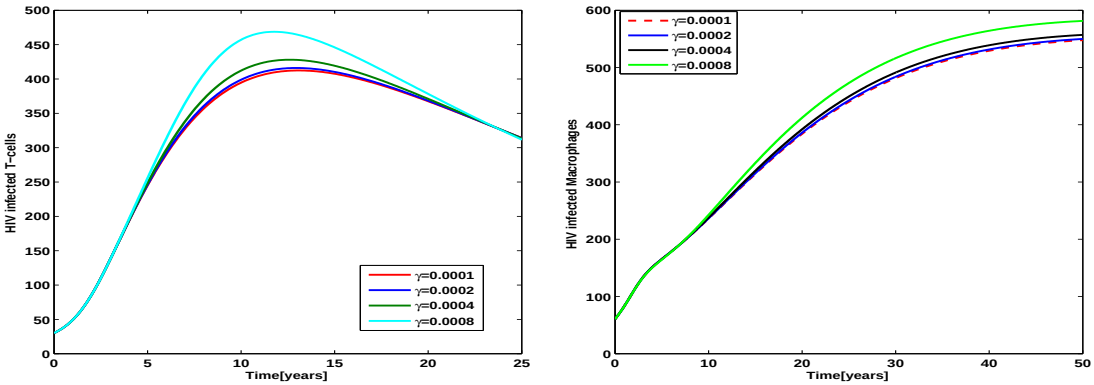

FIGURE 8. Variation of HIV infected T-cells and HIV infected macrophages with respect to smoking impairment rate in T-cells.

Variation of smoking impairment rate in macrophages has effect in HIV infected T-cells. Increase of smoking impairment rate results into a corresponding increase of HIV infected T-cells. In macrophages increasing smoking impairment rate results into decreasing HIV infected macrophages. Since tobacco smoking accelerate apoptosis of macrophages [3], the decrease of HIV infected macrophages may be accelerated by apoptosis. This is demonstrated in Figure 9.

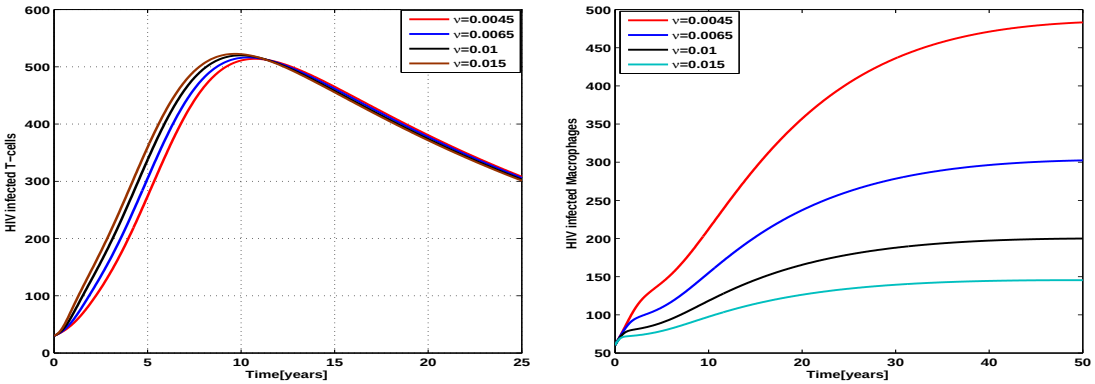

FIGURE 9. Variation of HIV infected T-cells and HIV infected macrophages with smoking impairment rate in macrophages.

4. Discussion and Concluding remarks

In this work, a simple model is proposed with the aim of studying how tobacco smoking may affect HIV in-host dynamics. The model includes T-cells which is a target for HIV virus [44] and macrophages which act as cellular reservoir for the HIV virus [4].

The basic reproduction number R_0 which determines the potentials of the disease is computed in equation (16). It shows that although tobacco smoking affects both T-cells and macrophages, its impacts are severe in macrophages compared to T-cells. The effects of tobacco smoking to T-cells and macrophages which are the first cellular target for HIV virus might cripple the immune system and hence accelerate HIV progression to the disease stage when both tobacco smoking and HIV attack the host concurrently.

To compare tobacco smoking and HIV within the host we refer the basic reproduction number R_0 in equation (16) and partial reproductive number R_{01}. The basic reproduction number R_0 and partial reproduction number R_{01} consist of new infections which are purely from tobacco smoking and are not represented as the combination of the new infections from tobacco smoking and HIV. Since the new infections are purely from tobacco smoking it implies that the two epidemics do not show a direct influence to each other.

Equilibrium states, disease free and endemic equilibria are derived and conditions for their stability established. Stability analysis shows that local and global stability of disease free equilibrium is affected by tobacco smoking. Low smoking rates will render disease free equilibrium point locally and globally stable while high smoking rates will cause local and global instability. For endemic equilibrium, there are multiple endemic equilibria and high smoking rate will confer global stability of endemic equilibrium.

In numerical analysis we find that, tobacco smoking may promote HIV infection in T-cells and macrophages because T-cells which are affected by tobacco smoking become insensitive and their response to HIV is altered [27] and [37]. Macrophages as well whose phagocytic function are reduced by smoking [38] can be attacked by HIV virus easily.

Conflict of Interests

The authors declare that there is no conflict of interests.

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