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Threshold dynamics of an HIV-TB co-infection model with multiple time delays

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Abstract. In this article, a mathematical model to study the dynamics of HIV-TB co-infection with two time delays is proposed and analyzed. We compute the basic reproduction number for each disease (HIV and TB) which acts as a threshold parameters. The disease dies out when the basic reproduction number of both diseases are less than unity and persists when the basic reproduction number of atleast one of the disease is greater than unity. A numerical study on the model is also performed to investigate the influence of certain key parameters on the spread of the disease. Mathematical analysis of our model shows that switching co-infection (HIV and TB) to single infection (HIV) can be achieved by imposing treatment for both the disease simultaneously as TB eradication is made possible with effective treatment.

Keywords. Bifurcation, Co-infection, Delay differential equations, HIV-TB, Stability

1 Introduction

Mathematical modeling of biological systems is an interesting research topic that attracted the attention of many researchers. In particular, the study on population based mathematical models are much more interesting as the populations under study are divided into compartments. In this arena, the rate of transfer between compartments are expressed mathematically as derivatives with respect to time of the sizes of the compartments which results in systems of ordinary differential equations. In this row, let us discuss few properties of HIV and TB infection as we propose to study in this paper. HIV attacks a specific type of immune cell in the body known as CD4 helper cell or T cell and TB is an airborne transmitted disease. When someone has both HIV and TB each disease speeds up the progress of the other [1, 6, 25]. The World Health Organization has fore casted that tuberculosis (TB) and human immunodeficiency virus (HIV) infectious will be among the top 20 causes of death in 2030. In 2010, there were 8.8 million incident cases of TB and 1.1 million deaths from TB among HIV negative people and there was an additional 0.35 million deaths from HIV associated TB [28].

As our ultimate aim is to study the dynamical behavior of HIV-TB co-infection delay model, we can have a small briefing on the role of time delay. Mostly infectious diseases evolve by infection, and then there appear certain symptoms over a period of time (namely the incubation

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period). Therefore, if an epidemic model considers time delay, then it is more consistent with the actual situation. Delay-differential equations exhibit much more complicated dynamics than ordinary differential equations since a time delay could cause a stable equilibrium to become unstable and cause the populations to fluctuate [19, 21]. In this paper, we incorporate a discrete time delay to the model to describe the time necessary for susceptible to become HIV infected and susceptible to become TB infected. The resulting model forms a system of delay-differential equations.

In last few decades, mathematical models have been applied in the literature to the modeling of infectious disease. HIV and TB co-infection epidemiologies are the research topic of some of those models. Many researchers have focused on the dynamics of HIV-TB co-infection. In 2005 Naresh and Tripathi [23] has introduced a simple model of HIV-TB co-infection in a variable size population. This work was followed by Sunitha and Nareshkumar [26], who provided a threshold for the control of disease in a HIV-TB co-infection model. After this, in the year of 2014, Nita and Jyoti [24] have analyzed the HIV-TB co-infection model for all parameters responsible for the disease spread. This article was followed by Carla and Ana in the same year [2], who have introduced a simple co-infection model of HIV and HCV. Recently, in 2016, Bolarin and Omatola [3] have analyzed about HIV-TB co-infection model with six mutually exclusive compartments. After this, in 2017, Lusiana et al [20] studied a model of HIV-TB co-infection with ten compartments and analyzed about the reason for disease spread. Currently, in 2018, Grace and David [13] have carried out a case study of tigania west sub county, kenya for a HIV-TB co-infection model.

The rest of this paper is structured as follows. In Section 2, we present the positivity and boundedness of the delay system, followed by this, are the results on the existence of disease free, HIV free, TB free and endemic equilibrium points in the system (2.2). Then the local and global stability of four equilibria are analyzed which have been neglected in Carla and Ana [5] work. In addition bifurcation analysis is also carried out for our modified model. In Section 2, the local and global stability of system (2.2) has been discussed. In Section 3, we present some numerical simulations and discussion of our system (2.2). In Section 4, simulation of system (2.2) is compared with actual data. Lastly, in Section 5, we close with conclusion. Incorporation of delay and the above analysis added rich dynamics to our model when compared to Carla and Ana [5] model. Nextly we brief on the nonlinear delay system (2.2).

2 Model description

The motivation of present work is from the article of Abdullah et al. [5], which deals with integer and fractional order versions of HIV-TB co-infection model. We also modified the basic model proposed by Carla and Ana [5], by introducing recovered individual. Let $S(t)$ represents the susceptible individuals, $H(t)$ represents the HIV infected individuals, $A(t)$ represents the HIV infected individuals showing symptoms of AIDS, $T(t)$ represents the TB infected individuals, $D(t)$ represents the dually (HIV and TB) infected individuals, showing or not showing symptoms of AIDS and $R(t)$ represents the recovered individuals. The modified Carla and Ana [5] model

is governed by system of nonlinear differential equation as follows,

$$\begin{aligned}
\frac{dS(t)}{dt} =&\alpha - C_1\beta_1 H(t)S(t) - \beta_2 T(t)S(t) - \mu S(t),\\
\frac{dH(t)}{dt} =&C_1\beta_1 S(t)H(t) + \upsilon A(t) + t_1 D(t) + (1-\epsilon)\theta H(t)\\
&- \beta_3 T(t)H(t) - (\delta+\mu)H(t),\\
\frac{dA(t)}{dt} =&\delta H(t) - (\mu + d_1 + \upsilon)A(t),\\
\frac{dT(t)}{dt} =&\beta_2 S(t)T(t) - (\mu + d_2 + t_2)T(t),\\
\frac{dD(t)}{dt} =&\beta_3 T(t)H(t) - (\mu + d_3 + t_1)D(t),\\
\frac{dR(t)}{dt} =&t_2 T(t) - \mu R(t).
\end{aligned} \tag{2.1}$$

In epidemic models, there is a tacit assumption that the individuals being in contact with the others react on their stimuli immediately, for example, getting a disease makes them ill instantly, and such an assumption is practically indefensible. That is, in transmitted disease, the class of infectives need a time, during which they will be able to transmit the disease to susceptibles. Thus, the latent period of disease should be considered, and here it is the phenomena of time delay. In order to reflect the dynamical behaviors of the models depending on the past information, it is more reasonable to incorporate time delays into ODE system (2.1). In fact, inclusion of delays in epidemic models makes them more realistic by allowing the description of the effects of disease latency or immunity [12, 14, 22, 29]. Hence, the density dependent disease transmission model (2.1) is modified and extended by including two discrete delays τ_1 and τ_2, where τ_1 is the delay representing the time necessary for a susceptible to become HIV infected and τ_2 is the delay representing the time necessary for a susceptible to become TB infected. It is observed that the first five equations in system (2.1) do not depend on the sixth equation and so this equation can be omitted without loss of generality. This allows us to attack system (2.1) by studying the subsystem (2.2), which is governed by system of nonlinear delay differential equation as follows,

$$\begin{aligned}
\frac{dS(t)}{dt} =&\alpha - C_1\beta_1 H(t)S(t) - \beta_2 T(t)S(t) - \mu S(t),\\
\frac{dH(t)}{dt} =&\beta_1 C_1 S(t-\tau_1)H(t-\tau_1) + \upsilon A(t) + t_1 D(t)\\
&+ (1-\epsilon)\theta H(t) - \beta_3 T(t)H(t) - (\delta+\mu)H(t),\\
\frac{dA(t)}{dt} =&\delta H(t) - (\mu + d_1 + \upsilon)A(t),\\
\frac{dT(t)}{dt} =&\beta_2 S(t-\tau_2)T(t-\tau_2) - (\mu + d_2 + t_2)T(t),\\
\frac{dD(t)}{dt} =&\beta_3 T(t)H(t) - (\mu + d_3 + t_1)D(t).
\end{aligned} \tag{2.2}$$

In system (2.2), the total population $N(t)$ is divided into five compartments, such that $N(t) = S(t) + H(t) + A(t) + T(t) + D(t)$ because all five classes are mutually disjoint. A fraction of new born children are infected during birth and hence are directly recruited into the infectious classes, $H(t)$ at a rate $(1-\epsilon)\theta$ and other children die at birth $(0 \le \epsilon \le 1)$, where ϵ is the fraction of newborns infected with HIV who dies immediately after birth and θ is the rate of newborns

infected with HIV. The complete dynamics of system (2.1) is represented by the flow chart in Fig.(1), where as the description of parameters used in system (2.1) is in Table. 1.

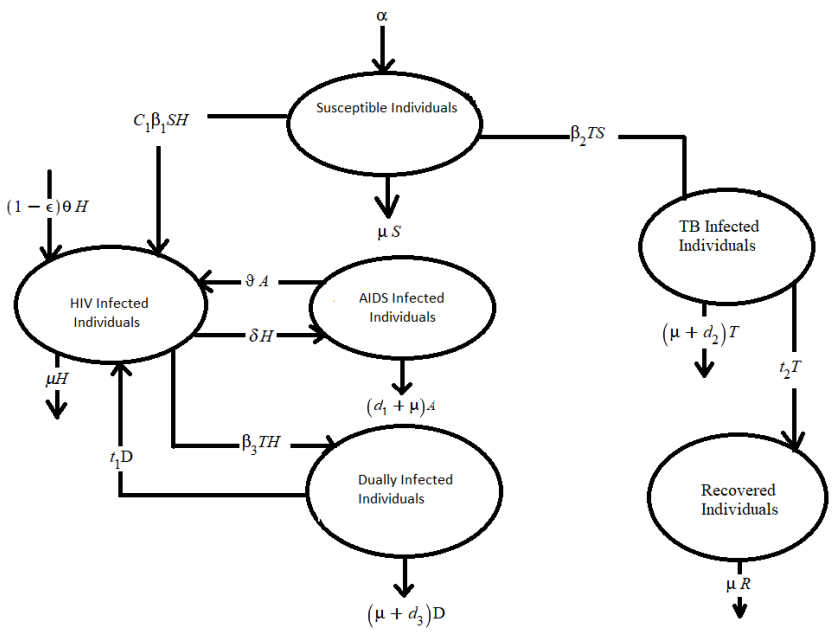


Figure 1: Flowchart diagram for model (2.1)

Table 1: Parameters description

Parameters	Description
α	The recruitment rate
υ	The rate at which individuals with AIDS are treated
μ	The natural death rate in all classes
δ	The rate at which infected HIV individuals $H(t)$, move to the AIDS class $A(t)$
β_1	The sexual contact rate
β_2	The tuberculosis transmission rate
β_3	The rate of progress to the class $D(t)$ by acquiring TB
C_1	The average number of sexual partners per person and per unit time
d_1	The death rate of individuals due to AIDS
d_2	The death rate due to failure of treatment
d_3	The death rate due to dual infection
t_1	The rate at which the dually infected individuals are treated for TB and move to $H(t)$ class
t_2	The rate at which TB infected individuals are treated for TB
ϵ	The fraction of newborns infected with HIV who dies immediately after birth
θ	The rate of newborns infected with HIV

Firstly, it is important to show that the positivity and the boundedness for the system (2.2) as they represent human populations. Positivity implies that the human population survives and the boundedness may be interpreted as a natural restriction to growth as a consequence of limited resources. Let us begin the analysis of the nonlinear system (2.2) by analyzing its positivity and

boundedness.

2.1 Positivity and Boundedness

We denote by C the Banach space of continuous function $\Psi : [-\tau, 0] \to \mathbb{R}^5$ with norm $\|\Psi\|=sup_{-\tau\leq\theta_1\leq 0}\ \{|\ \Psi_1(\theta_1)\ |, |\ \Psi_2(\theta_1)\ |, |\ \Psi_3(\theta_1)\ |, |\ \Psi_4(\theta_1)\ |, |\ \Psi_5(\theta_1)\ |\}$,
Where $\Psi = (\Psi_1, \Psi_2, \Psi_3, \Psi_4, \Psi_5)$ and $\tau = max\{\tau_1, \tau_2\}$.
Further, let
$C_+ = \{\Psi = (\Psi_1, \Psi_2, \Psi_3, \Psi_4, \Psi_5) \in C,\ \Psi_i \geq 0$ for all $\theta_1 \in [-\tau, 0], i = 1, 2, 3, 4, 5\}$.
The initial condition for the system (2.2) takes the form

$$\begin{aligned} S(\theta_1) = \Psi_1(\theta_1), H(\theta_1) = \Psi_2(\theta_1), A(\theta_1) = \Psi_3(\theta_1), \\ T(\theta_1) = \Psi_4(\theta_1), D(\theta_1) = \Psi_5(\theta_1), -\tau \leq \theta_1 \leq 0. \end{aligned} \tag{2.3}$$

Where $\Psi = (\Psi_1, \Psi_2, \Psi_3, \Psi_4, \Psi_5)$.
Now, the following result establishes the positivity and boundedness of solution for system (2.2) with initial conditions (2.3).

Theorem 2.1. *Let $S(t)$, $H(t)$, $A(t)$, $T(t)$, $D(t)$ be the solution of the system (2.2) with initial conditions (2.3). Then $S(t), H(t), A(t), T(t)$ and $D(t)$ are all positive and bounded for $t > 0$ at which the solution exist.*

Proof. It is easy to see that $S(t)$ is positive. We proceed by contradiction, let t_3 be the first time such that $S(t_3) = 0$. By the first equation of system (2.2), then we have $\frac{dS(t)}{dt} = \alpha > 0$. That means $S(t) < 0$ for $t \in (t_3 - \bar{\epsilon}, t_3)$, where $\bar{\epsilon}$ is an arbitrarily small positive constant. This leads to a contradiction. It follows that $S(t)$ is always positive. Similarly we can see that $H(t), A(t), T(t)$ and $D(t)$ are positive $t > 0$. Now to prove the ultimate boundedness of solution, we define
$J(t) = S(t) + H(t + \tau_1) + A(t + \tau_1) + T(t + \tau_1) + D(t + \tau_1)$.
and $\nu_1 = \min\{\mu, d_1 + \mu, \mu + d_2 + t_2, d_3 + \mu\}$. By positivity of solution, it follows that

$$\begin{aligned} \frac{dJ(t)}{dt} =& \alpha - \mu S(t) - \mu H(t + \tau_1) - (\mu + d_1)A(t + \tau_1) \\ & - (\mu + d_2 + t_2)T(t + \tau_1) - (d_3 + \mu)D(t + \tau_1), \\ \frac{dJ(t)}{dt} \leq& \alpha - \nu_1 J(t). \end{aligned}$$

Therefore the following set is positively invariant set for the system (2.2) is

$$\Omega = \left\{(S(t), H(t), A(t), T(t), D(t)) | S(t) + H(t) + A(t) + T(t) + D(t) \leq \frac{\alpha}{\nu_1}\right\}. \tag{2.4}$$

It is easy to see that $S(t), H(t), A(t), T(t)$ and $D(t)$ are bounded in a invariant set Ω. This completes the proof. □

The above theorem shows the well-posedness of system (2.2) both mathematically and epidemiologically. R_0 can be defined as metric that helps to determine whether or not an infectious disease can spread through a population. A disease dies out if $R_0 < 1$ and spreads if $R_0 > 1$. The biological meaning of the basic reproduction number (R_0) is defined as the average number of secondary infections caused by a single infectious individual during the course of the infectious period.

2.2 The basic reproduction number and equilibrium points

The basic reproduction number for each of the two disease (HIV and TB) has been derived using the method of the next-generation matrix [5, 9, 15]. The basic reproduction number for HIV (R_{HIV}) is obtained by taking $T = D = 0$ in the system (2.2) is

$$R_{HIV} = \frac{\alpha C_1 \beta_1 (\upsilon + d_1 + \mu)}{\mu\{(\upsilon + d_1 + \mu)((\delta + \mu) - (1 - \epsilon)\theta) - \delta\upsilon\}}.$$

The basic reproduction number for TB (R_{TB}) is obtained by taking $H = A = D = 0$ in the system (2.2) is

$$R_{TB} = \frac{\beta_2 \alpha}{\mu(\mu + d_2 + t_2)}.$$

The associative basic reproduction number (R_0) is thus:

$$R_0 = max\{R_{HIV}, R_{TB}\}.$$

The nonlinear dynamical system (2.2) possesses four kinds of equilibrium points which are described below in Table. 2.

Table 2: Equilibrium points

Equilibrium Points	Notation	Values
Disease free	$E_0(S_0, 0, 0, 0, 0)$	$E_0\left(\frac{\alpha}{\mu}, 0, 0, 0, 0\right)$
HIV free	$E_1(S_1, 0, 0, T_1, 0)$	$E_1\left(\frac{\alpha}{\mu R_{TB}}, 0, 0, \frac{\mu(R_{TB} - 1)}{\beta_2}, 0\right)$
TB free	$E_2(S_2, H_2, A_2, 0, 0)$	$E_2\left(\frac{\alpha}{\mu R_{HIV}}, \frac{(R_{HIV} - 1)\mu}{C_1\beta_1}, \frac{\delta H_2}{\upsilon + d_1 + \mu}, 0, 0\right)$
Endemic	$E_3(S_3, H_3, A_3, T_3, D_3)$	$E_3\left(\frac{\alpha}{\mu R_{TB}}, H_3, \frac{\delta H_3}{\upsilon + d_1 + \mu}, \frac{\mu(R_{TB} - 1) - C_1\beta_1 H_3}{\beta_2}, \frac{\beta_3 T_3 H_3}{t_1 + d_3 + \mu}\right)$

HIV free equilibrium exists if $R_{TB} > 1$. TB free equilibrium exists if $R_{HIV} > 1$ where

$$H_3 = \frac{\left(\frac{R_{HIV}}{R_{TB}} - 1\right)\alpha C_1\beta_1\beta_2(\mu + d_3 + t_1) - \mu^2 R_{HIV}(\mu + d_3)\beta_3(R_{TB} - 1)}{\mu R_{HIV}\beta_1\beta_3(t_1 - C_1(\mu + d_3 + t_1))}.$$

The endemic equilibrium exists if

(i) $R_{HIV}, R_{TB} > 1$,

(ii) $\mu(R_{TB} - 1) > C_1\beta_1 H_3$,

(iii) $R_{HIV} > R_{TB}$,

(iv) $\left(\frac{R_{HIV}}{R_{TB}} - 1\right)\alpha C_1\beta_1\beta_2(\mu + d_3 + t_1) > \mu^2 R_{HIV}(\mu + d_3)\beta_3(R_{TB} - 1)$ and

(v) $t_1 > C_1(\mu + d_3 + t_1)$.

The stability analysis performed to determine whether a system is pushed slightly from a equilibrium point will return to that same equilibrium point with time. If this is true for small perturbations from equilibrium, then we say that this equilibrium is locally stable and if a system always returns to that equilibrium point, then we say that this equilibrium is globally stable. Nextly, we are going to analyze some of the basic properties of the nonlinear delay system, (i.e.,) the local and global behavior of the system (2.2) at each of its equilibrium points.

2.3 The local stability and Hopf bifurcation analysis

In this section, we shall provide the condition for the system to be locally asymptotically stable at its positive equilibrium points. In the history of infectious disease modeling the basic reproduction number R_0 play a vital role in the disease dynamics. In the present HIV-TB co-infection model the disease dynamics depend on the corresponding basic reproduction number R_{HIV} and R_{TB}.

Theorem 2.2. *The disease free equilibrium E_0 is locally asymptotically stable if $R_{TB} < 1$ and $R_{HIV} < 1$, provided that $\tau_1, \tau_2 \geq 0$.*

Theorem 2.3. *The HIV free equilibrium E_1 is locally asymptotically stable if $R_{HIV} < 1 < R_{TB}$, provided that $\tau_1, \tau_2 \geq 0$.*

Theorem 2.4. *The TB free equilibrium E_2 is locally asymptotically stable if $R_{HIV} > 1 > R_{TB}$, provided that $\tau_1, \tau_2 \geq 0$.*

Remark 1.

- The analytical result of the Theorem (2.2) reveals that the delay term τ_1 and τ_2 does not effect the stability of nonlinear system (2.2) at the disease free equilibrium point E_0.
- The analytical result of the Theorem (2.3) reveals that the delay term τ_1 and τ_2 does not effect the stability of the DDE system (2.2) at the HIV free equilibrium point E_1.
- The analytical result of the Theorem (2.4) reveals that the delay term τ_1 and τ_2 does not effect the stability of the system (2.2) at the TB free equilibrium point E_2.

The equilibrium point that gives deeper insights about the system under the study is the point E_3 which represents the overall dynamics of HIV, TB and co-infected population. Thus, in the following Theorem we study the local stability of the system (2.2) at the equilibrium point E_3.

Theorem 2.5. *If $\tau_1 > 0$ and $\tau_2 = 0$, then the model* (2.2) *is locally asymptotically stable at the endemic equilibrium E_3 when $R_{HIV} > 1$ and $R_{TB} > 1$.*

Proof. The Jacobian matrix of the system (2.2) at endemic equilibrium point E_3 in case of $\tau_1 > 0$ and $\tau_2 = 0$ as follows,

$$J(E_3) = \begin{bmatrix} -a_4 & h_4 & 0 & -i_4 & 0 \\ f_4 e^{-\lambda\tau_1} & -b_4 e^{-\lambda\tau_1} & \upsilon & -g_4 & t_1 \\ 0 & \delta & -j_4 & 0 & 0 \\ k_4 & 0 & 0 & q_4 & 0 \\ 0 & m_4 & 0 & n_4 & -p_4 \end{bmatrix},$$

where
$a_4 = C_1\beta_1 H_3 + \beta_2 T_3 + \mu$, $h_4 = C_1\beta_1 S_3$, $i_4 = \beta_3 S_3 - t_2$, $f_4 = C_1\beta_1 H_3$,
$b_4 = \beta_3 T_3 + (\delta + \mu) - (1-\epsilon)\theta - C_1\beta_1 S_3$, $g_4 = \beta_3 H_3$, $j_4 = v + d_1 + \mu$, $k_4 = \beta_2 T_3$,
$q_4 = \beta_2 S_3 - (\mu + d_2 + t_2)$, $m_4 = \beta_3 T_3$, $n_4 = \beta_3 H_3$, $p_4 = t_1 + d_3 + \mu$.
The characteristic polynomial of the jacobian matrix $J(E_3)$ in case of $\tau_1 > 0$ and $\tau_2 = 0$ is

$$\begin{aligned} H(\lambda, \tau_1) &= \lambda^5 + \hat{c}_1\lambda^4 + \hat{c}_2\lambda^3 + \hat{c}_3\lambda^2 + \hat{c}_4\lambda + \hat{c}_5 \\ &\quad + e^{-\lambda\tau_1}(\hat{z}_1\lambda^4 + \hat{z}_2\lambda^3 + \hat{z}_3\lambda^2 + \hat{z}_4\lambda + \hat{z}_5) = 0, \end{aligned} \tag{2.5}$$

where

$$\begin{aligned} \hat{c}_1 &= p_4 - q_4 + j_4 + a_4, \\ \hat{z}_1 &= b_4, \\ \hat{c}_2 &= a_4[j_4 + p_4 - q_4] + j_4[p_4 - q_4] + i_4k_4 - m_4t_1 - p_4q_4 - \delta v, \\ \hat{z}_2 &= b_4[a_4 + j_4 + p_4 - q_4] - f_4h_4, \\ \hat{c}_3 &= a_4j_4[p_4 - q_4] + m_4t_1[-a_4 - j_4 + q_4] + \delta v[-a_4 \\ &\quad - p_4 + q_4] - p_4q_4[a_4 + j_4] + k_4[g_4h_4 + i_4j_4 + k_4p_4], \\ \hat{z}_3 &= a_4b_4[j_4 + p_4 - q_4] + b_4j_4[p_4 - q_4] + b_4[i_4k_4 - p_4q_4] \\ &\quad - f_4h_4[j_4 + p_4 - q_4], \\ \hat{c}_4 &= h_4k_4[g_4j_4 - n_4t_1 + p_4g_4] + \delta v[-i_4k_4 + a_4q_4 - p_4a_4 + p_4q_4] \\ &\quad + m_4t_1[-a_4j_4 + a_4q_4 - i_4k_4 + j_4q_4] + p_4j_4[-a_4q_4 + k_4i_4], \\ \hat{z}_4 &= b_4j_4[i_4k_4 + p_4a_4 - a_4q_4 - p_4q_4] + f_4h_4[j_4q_4 - p_4j_4 + p_4q_4] \\ &\quad + p_4b_4[-a_4q_4 + k_4i_4], \\ \hat{c}_5 &= t_1j_4[-h_4k_4n_4 + a_4m_4q_4 - i_4k_4m_4] + p_4g_4h_4j_4k_4 + p_4\delta v[-i_4k_4 + a_4q_4], \\ \hat{z}_5 &= p_4b_4j_4[i_4k_4 - a_4q_4] + p_4f_4h_4j_4q_4. \end{aligned}$$

Put $\lambda = i\hat{\omega}$ ($\hat{\omega} > 0$) be the root of (2.5), and separating the real and imaginary parts, we have

$$\begin{aligned} \hat{c}_1\hat{\omega}^4 - \hat{c}_3\hat{\omega}^2 + \hat{c}_5 &= cos(\hat{\omega}\tau_1)[-\hat{z}_1\hat{\omega}^4 + \hat{\omega}^2\hat{z}_3 - \hat{z}_5] + sin(\hat{\omega}\tau_1)[z_2\hat{\omega}^3 - \hat{\omega}\hat{z}_4] \\ \hat{\omega}^5 - \hat{c}_2\hat{\omega}^3 + \hat{c}_4\hat{\omega} &= cos(\hat{\omega}\tau_1)[\hat{z}_2\hat{\omega}^3 - \hat{\omega}\hat{z}_4] - sin(\hat{\omega}\tau_1)[-\hat{z}_1\hat{\omega}^4 + \hat{\omega}^2\hat{z}_3 - \hat{z}_5]. \end{aligned} \tag{2.6}$$

Squaring and adding the equations (2.6), we obtain

$$\begin{aligned} &\hat{\omega}^{10} + [\hat{c}_1^2 - 2\hat{c}_2 - \hat{z}_1^2]\hat{\omega}^8 + [\hat{c}_2^2 - 2\hat{c}_1\hat{c}_3 + 2\hat{z}_1\hat{z}_3 - \hat{z}_2^2]\hat{\omega}^6 + [2\hat{c}_1\hat{c}_5 + 2\hat{c}_4 + \hat{c}_3^2 \\ &-2\hat{c}_2\hat{c}_4 - \hat{z}_3^2 - 2\hat{z}_5\hat{z}_1 + 2\hat{z}_4\hat{z}_2]\hat{\omega}^4 + [\hat{c}_4^2 - 2c_3c_5 + 2\hat{z}_5\hat{z}_3 - \hat{z}_4^2]\hat{\omega}^2 + \hat{c}_5^2 - \hat{z}_5^2 = 0, \end{aligned} \tag{2.7}$$

put $\hat{\omega}^2 = \hat{y}$ into (2.7), we have

$$\hat{y}^5 + F_1\hat{y}^4 + F_2\hat{y}^3 + F_3\hat{y}^2 + F_4\hat{y} + F_5 = F(\hat{y}) = 0, \tag{2.8}$$

where

$$\begin{aligned} F_1 &= \hat{c}_1^2 - 2\hat{c}_2 - \hat{z}_1^2, \\ F_2 &= \hat{c}_2^2 - 2\hat{c}_1\hat{c}_3 + 2\hat{z}_1\hat{z}_3 - \hat{z}_2^2, \\ F_3 &= 2\hat{c}_1\hat{c}_5 + 2\hat{c}_4 + \hat{c}_3^2 - 2\hat{c}_2\hat{c}_4 - \hat{z}_3^2 - 2\hat{z}_5\hat{z}_1 + 2\hat{z}_4\hat{z}_2, \end{aligned}$$

$$F_4 = \hat{c}_4^2 - 2c_3c_5 + 2\hat{z}_5\hat{z}_3 - \hat{z}_4^2,$$
$$F_5 = \hat{c}_5^2 - \hat{z}_5^2.$$

It may be noted that Eq.(2.8) will have all the roots with negative real part iff the Routh-Hurwitz criterion is satisfied and hence (2.5) no purely imaginary root.
It is easy to show that $F_1 > 0, F_2 > 0, F_3 > 0, F_4 > 0$ and $F_5 > 0$, hence the Routh-Hurwitz criterion is satisfied if

$$\begin{aligned} &(i) && F_1F_2F_3 > F_3^2 + F_1^2F_4, \\ &(ii) && (F_1F_4 - F_5)(F_1F_2F_3 - F_3^2 - F_1^2F_4) > F_5(F_1F_2 - F_3)^2 + F_1F_5^2. \end{aligned} \tag{2.9}$$

Hence Eq.(2.8) will have all the roots with negative real parts provided (2.9) is satisfied. Now this shows that for any value of τ_1 the characteristic equation (2.5) will always have roots in negative half-plane only. Therefore if $R_{HIV} > 1$ and $R_{TB} > 1$, then the infected steady state E_3 of system (2.2) is locally asymptotically stable in the case of $\tau_1 > 0$ and $\tau_2 = 0$. Thus the Theorem (2.5) is true. □

Now we proceed to investigate the existence of Hopf bifurcation in the following Theorem.

Theorem 2.6. *If $\tau_1 = 0$ and $\tau_2 > 0$, then the model* (2.2) *is locally asymptotically stable at the endemic equilibrium E_3 when $\tau_2 < {\tau_2}^*$. Moreover, it undergoes Hopf bifurcation at E_3 when $\tau_2 = {\tau_2}^*$.*

Proof. The Jacobian matrix of the system (2.2) at the equilibrium point E_3 in case of $\tau_1 = 0$ and $\tau_2 > 0$ as follows,

$$J(M_5) = \begin{bmatrix} -a_5 & -b_5 & 0 & -r_5 & 0 \\ d_5 & -f_5 & \upsilon & -p_5 & t_1 \\ 0 & \delta & -k_5 & 0 & 0 \\ l_5e^{-\lambda\tau_2} & 0 & 0 & m_5e^{-\lambda\tau_2} - g_5 & 0 \\ 0 & n_5 & 0 & p_5 & -q_5 \end{bmatrix},$$

where
$a_5 = C_1\beta_1H_3 + \beta_2T_3 + \mu, b_5 = C_1\beta_1S_3, r_5 = \beta_2S_3 - t_2, d_5 = C_1\beta_1H_3,$
$f_5 = \beta_3T_3 + (\delta + \mu) - C_1\beta_1S_3 - (1 - \epsilon)\theta, p_5 = \beta_3H_3, k_5 = \upsilon + d_1 + \mu,$
$l_5 = \beta_2T_3, m_5 = \beta_2S_3, p_5 = \beta_3H_3, g_5 = \mu + d_2 + t_2, n_5 = \beta_3T_3, q_5 = t_1 + d_3 + \mu.$
The characteristic polynomial of the above matrix $J(M_5)$ can be written as

$$\begin{aligned} H(\lambda, \tau_2) = {} & \lambda^5 + c_1\lambda^4 + c_2\lambda^3 + c_3\lambda^2 + c_4\lambda + c_5 \\ & + e^{-\lambda\tau_2}(z_1\lambda^4 + z_2\lambda^3 + z_3\lambda^2 + z_4\lambda + z_5) = 0, \end{aligned} \tag{2.10}$$

where

$$\begin{aligned} c_1 &= q_5 + g_5 + k_5 + f_5 + a_5, \\ z_1 &= -m_5, \\ c_2 &= a_5[f_5 + g_5 + k_5 + q_5] + f_5[g_5 + k_5 + q_5] + k_5[g_5 + q_5] + b_5d_5 - n_5t_1 - \delta\upsilon, \\ z_2 &= -m_5[a_5 + f_5 + k_5 + q_5], \\ c_3 &= a_5f_5[g_5 + k_5 + q_5] + a_5g_5[k_5 + q_5] + k_5q_5[a_5 + f_5 + g_5] + b_5d_5[g_5 + k_5 + q_5] \\ &\quad + f_5g_5[k_5 + q_5] - \delta\upsilon[a_5 + g_5 + q_5] - n_5t_1[a_5 + g_5 + k_5], \\ z_3 &= -a_5m_5[f_5 + k_5 + g_5] + r_5l_5[f_5 + k_5 + q_5] - m_5q_5[f_5 + k_5] \end{aligned}$$

$$
\begin{aligned}
&- m_5[b_5d_5 + f_5k_5 - n_5t_1],\\
c_4 &= -\delta v[a_5q_5 + a_5g_5 + g_5q_5] + a_5f_5[g_5k_5 + q_5g_5 + q_5k_5] + b_5d_5[g_5k_5 + q_5g_5]\\
&- n_5t_1[g_5a_5 + k_5a_5 + g_5k_5] + q_5k_5[a_5g_5 + b_5d_5 + f_5g_5],\\
z_4 &= \delta v[-r_5l_5 + a_5m_5 + q_5m_5] + f_5l_5[r_5q_5 + r_5k_5] + n_5t_1[m_5a_5 - l_5r_5 + m_5k_5]\\
&- q_5m_5[a_5f_5 + a_5k_5 + b_5d_5 + f_5k_5] + q_5l_5[r_5k_5 - b_5p_5] - k_5m_5[a_5f_5 + b_5d_5]\\
&+ p_5l_5[b_5t_1 - b_5k_5],\\
c_5 &= g_5k_5[-n_5t_1a_5 + q_5a_5f_5 + q_5b_5d_5] - q_5a_5g_5\delta v,\\
z_5 &= q\delta v[a_5m_5 - r_5l_5] - q_5b_5k_5[l_5p_5 + d_5m_5] + l_5r_5k_5[q_5f_5 - n_5t_1]\\
&+ a_5k_5m_5[n_5t_1 - q_5f_5] + k_5p_5l_5b_5t_1.
\end{aligned}
$$

Suppose $i\omega$ is a root of (2.10), by separating the real and imaginary parts of $H(i\omega, \tau_2)$ we have,

$$
\begin{aligned}
c_1\omega^4 - c_3\omega^2 + c_5 &= cos(\omega\tau_2)[-z_1\omega^4 + \omega^2 z_3 - z_5] + sin(\omega\tau_2)[z_2\omega^3 - \omega z_4]\\
\omega^5 - c_2\omega^3 + c_4\omega &= cos(\omega\tau_2)[z_2\omega^3 - \omega z_4] - sin(\omega\tau_2)[-z_1\omega^4 + \omega^2 z_3 - z_5].
\end{aligned} \tag{2.11}
$$

Squaring and adding the two equations in (2.11), we obtain,

$$
\begin{aligned}
&\omega^{10} + [c_1^2 - 2c_2 - z_1^2]\omega^8 + [c_2^2 - 2c_1c_3 + 2z_1z_3 - z_2^2]\omega^6 + [2c_1c_5 + 2c_4 + c_3^2\\
&-2c_2c_4 - z_3^2 - 2z_5z_1 + 2z_4z_2]\omega^4 + [c_4^2 - 2c_3c_5 + 2z_5z_3 - z_4^2]\omega^2 + c_5^2 - z_5^2 = 0,
\end{aligned} \tag{2.12}
$$

Let $y = \omega^2$, the above Eq. (2.12) becomes,

$$
\begin{aligned}
&y^5 + [c_1^2 - 2c_2 - z_1^2]y^4 + [c_2^2 - 2c_1c_3 + 2z_1z_3 - z_2^2]y^3\\
&+[2c_1c_5 + 2c_4 + c_3^2 - 2c_2c_4 - z_3^2 - 2z_5z_1 + 2z_4z_2]y^2\\
&+[c_4^2 - 2c_3c_5 + 2z_5z_3 - z_4^2]y + c_5^2 - z_5^2 = F(y) = 0.
\end{aligned} \tag{2.13}
$$

Taking derivative with respect to y of Eq. (2.13), with $y = \omega^{*2}$ yields

$$
\begin{aligned}
F^{'}(\omega^{*2}) =&5(\omega^*)^8 + 4(\omega^*)^6[c_1^2 - 2c_2 - z_1^2] + 3(\omega^*)^4[c_2^2 - 2c_1c_3 + 2z_1z_3 - z_2^2]\\
&+ 2(\omega^*)^2[2c_1c_5 + 2c_4 + c_3^2 - 2c_2c_4 - z_3^2 - 2z_5z_1 + 2z_4z_2]\\
&+ [c_4^2 - 2c_3c_5 + 2z_5z_3 - z_4^2].
\end{aligned} \tag{2.14}
$$

It is easy to verify that $c_1^2 - 2c_2 - z_1^2 > 0, c_2^2 - 2c_1c_3 + 2z_1z_3 - z_2^2 > 0$
$2c_1c_5 + 2c_4 + c_3^2 - 2c_2c_4 - z_3^2 - 2z_5z_1 + 2z_4z_2 > 0$, $c_4^2 - 2c_3c_5 + 2z_5z_3 - z_4^2 > 0$ and hence $F^{'}((\omega^*)) > 0$.

By Descartes rule of signs, Eq. (2.13) has positive real root y^* and thus Eq. (2.12) has a pair of purely imaginary roots $\pm i\omega^*$. From the transcendental Eq. (2.11), we obtain $\tan(\omega\tau_2^*) = \frac{N_1}{N_2}$, where, $N_1 = (z_2\omega^3 - \omega z_4)(c_1\omega^4 - \omega^2 c_3 + c_5) - (-z_1\omega^4 + \omega^2 z_3 - z_5)(\omega^5 - \omega^3 c_2 + \omega c_4)$ and $N_2 = (z_2\omega^3 - \omega z_4)(\omega^5 - \omega^3 c_2 + \omega c_4) + (-z_1\omega^4 + \omega^2 z_3 - z_5)(c_1\omega^4 - \omega^2 c_3 + c_5)$. Then, the corresponding positive value of ω^*, τ_2^* is given by

$$
\tau_2^* = \frac{1}{\omega^*}\left[tan^{-1}\left(\frac{N_1}{N_2}\right) + k\pi\right], \text{where} \qquad k = 0, 1, 2.... \tag{2.15}
$$

Now, we determine $sign\{\frac{dRe(\lambda)}{d\tau_2}|_{\tau_2=\tau_2^*}\}$ where $sign$ is the signum function and $Re(\lambda)$ is the real part of λ. By using the following mathematical calculation, we can say that the endemic equilibrium of system (2.2) remains stable for $\tau_2 < \tau_2^*$ and Hopf bifurcation occurs when $\tau_2 = \tau_2^*$. Differentiating the Eq. (2.10) with respect to τ_2, we have,

$$
\{5\lambda^4 + 4c_1\lambda^3 + 3c_2\lambda^2 + 2c_3\lambda + c_4 - \tau_3\ e^{-\lambda\tau_2}(z_1\lambda^4 + z_2\lambda^3 + z_3\lambda^2 + z_4\lambda + z_5)
$$

$$+ e^{-\lambda\tau_2}(4\lambda^3 z_1 + 3\lambda^2 z_2 + 2\lambda z_3 + z_4)\}\frac{d\lambda}{d\tau_2} = \lambda e^{-\lambda\tau_2}(z_1\lambda^4 + z_2\lambda^3 + z_3\lambda^2 + z_4\lambda + z_5). \quad (2.16)$$

From Eq. (2.10) we get,

$$e^{-\lambda\tau_2} = \frac{-(\lambda^5 + c_1\lambda^4 + c_2\lambda^3 + c_3\lambda^2 + c_4\lambda + c_5)}{z_1\lambda^4 + z_2\lambda^3 + z_3\lambda^2 + z_4\lambda + z_5}. \quad (2.17)$$

Now Eq. (2.16) becomes

$$\begin{aligned}\left(\frac{d\lambda}{d\tau_2}\right)^{-1} &= \frac{-(5\lambda^4 + 4c_1\lambda^3 + 3c_2\lambda^2 + 2c_3\lambda + c_4)}{\lambda(\lambda^5 + c_1\lambda^4 + c_2\lambda^3 + c_3\lambda^2 + c_4\lambda + c_5)} \\ &+ \frac{4\lambda^3 z_1 + 3\lambda^2 z_2 + 2\lambda z_3 + z_4}{\lambda(z_1\lambda^4 + z_2\lambda^3 + z_3\lambda^2 + z_4\lambda + z_5)} - \frac{\tau_2}{\lambda}.\end{aligned} \quad (2.18)$$

For the imaginary root $\lambda = i\omega^*$, taking the real part of $(\frac{d\lambda}{d\tau_2})^{-1}$, at $\tau_2 = \tau_2^*$, we have,

$$Re\left[\left(\frac{d\lambda}{d\tau_2}\right)^{-1}\Bigg|\,\tau_2 = \tau_2^*\right] = \frac{\xi_1}{\xi_2} + \frac{\xi_3}{\xi_4}, \quad (2.19)$$

where

$$\begin{aligned}\xi_1 =& 5\omega^{*8} + \omega^{*6}(-3c_2 - 5c_2 + 4c_1^2) + \omega^{*4}(c_4 + 3c_2^2 + 5c_4 - 6c_3c_1) \\ &+ \omega^{*2}(-c_4c_2 - 3c_2c_4 + 2c_3^2 + 4c_1c_5) + (c_4^2 - 2c_3c_5), \\ \xi_2 =& \omega^{*10} + \omega^{*8}(c_1^2 - 2c_2) + \omega^{*6}(2c_4 + c_2^2 - 2c_1c_3) + \omega^{*4}(c_3^2 + 2c_1c_5 - 2c_4c_2) \\ &+ \omega^{*2}(c_4^2 - 2c_3c_5) + c_5^2, \\ \xi_3 =& \omega^{*6}(-4z_1^2) + \omega^{*4}(-3z_2^2 + 6z_1z_3) + \omega^{*2}(4z_4z_2 - 2z_3^2 - 4z_1z_5) + (2z_3z_5 - z_4^2), \\ \xi_4 =& \omega^{*8}z_1^2 + \omega^{*6}(z_2^2 - z_1z_3) + \omega^{*4}(z_3^2 - 2z_3z_4 + 2z_5z_1) + \omega^{*2}(z_4^2 - 2z_3z_5) + z_5^2.\end{aligned}$$

Using Eq. (2.14) the above equation is reduced to

$$Re\left[\left(\frac{d\lambda}{d\tau_2}\right)^{-1}\Bigg|\,\tau_2 = \tau_2^*\right] = \frac{F'((\omega^*)^2)}{\xi_4}. \quad (2.20)$$

Hence

$$sign\left\{\frac{dRe(\lambda)}{d\tau_2}|_{\tau_2=\tau_2^*}\right\} = sign\left\{Re\left[(\frac{d\lambda}{d\tau_2})^{-1}|_{\tau_2=\tau_2^*}\right]\right\} = sign\left\{F'(\omega^*)^2\right\}.$$

Since $\left\{F'(\omega^*)^2\right\} > 0$, $\frac{dRe(\lambda)}{d\tau_2}$ is positive at $\tau_2 = \tau_2^*$. Thus the solution curve of the characteristic Eq.(2.10) crosses the imaginary axis. This shows that a Hopf bifurcation occurs at $0 < \tau_2 = \tau_2^*$. By continuity, the endemic equilibrium is locally asymptotically stable when $\tau_2 < \tau_2^*$. □

Remark 2. The existence of endemic equilibrium assures the persistence of the disease among the population with the the condition that the basic reproduction number must be greater than unity. The Theorem (2.6) reveals that the system (2.2) undergo Hopf bifurcation at endemic equilibrium point when $0 < \tau_2 = \tau_2^*$. Hopf bifurcation is the characteristic phenomenon of a nonlinear system, where the system stability switches and a periodic solution arises, when it passes through the critical point.

Previous section only establish the local stability of the system (2.2). In the following section, by constructing a Lyapunov functional, we can actually obtain globally asymptotic stability of the system (2.2) under certain conditions.

2.4 Global behavior at equilibrium points

To establish global stability, we construct suitable Lyapunov functionals and use the theory of LaSalle's invariance principle. We define a function $g : \mathbb{R}^+ \longrightarrow \mathbb{R}^+ \cup \{0\}$ as $g(u) = u - 1 - \ln u$. Note that, $g(u) \geq 0$ for any $u > 0$ and attains a global minimum 0 at $u = 1$. The Lyapunov functionals used here are similar to those used in [4, 16, 27] essentially.

Theorem 2.7. *If $R_{HIV} < 1$ and $R_{TB} < 1$, the disease free equilibrium E_0 of the system (2.2) is globally asymptotically stable for any $\tau_1, \tau_2 \geq 0$.*

Proof. Let $(S(t), H(t), A(t), T(t), D(t))$ be any positive solution of the system (2.2) with the initial condition (2.3), define a Lyapunov functional $W_1(t)$ as follows,

$$\begin{aligned} W_1(t) = \eta_1 g\left(\frac{S(t)}{S_0}\right) + \eta_1 H(t) + \upsilon A(t) + \frac{\eta_1\beta_2\alpha}{\mu(\mu+d_2+t_2)}T(t) + \eta_1 D(t) \\ + C_1\beta_1\eta_1 \int_{t-\tau_1}^{t} S(\xi)H(\xi)d\xi + \frac{\eta_1{\beta_2}^2\alpha}{\mu(\mu+d_2+t_2)} \int_{t-\tau_2}^{t} S(\xi)T(\xi)d\xi, \end{aligned} \tag{2.21}$$

where $\eta_1 = \upsilon + d_1 + \mu$.
Differentiating $W_1(t)$ along the solution of system (2.2), we obtain

$$\begin{aligned} \frac{dW_1(t)}{dt} &= \eta_1\left(1 - \frac{S_0}{S(t)}\right)(\alpha - C_1\beta_1 H(t)S(t) - \beta_2 T(t)S(t) - \mu S(t)) \\ &+ \eta_1\Big(\beta_1 C_1 S(t-\tau_1)H(t-\tau_1) + \upsilon A(t) + t_1 D(t) + (1-\epsilon)\theta H(t) \\ &- \beta_3 T(t)H(t) - (\delta+\mu)H(t)\Big) + \upsilon\Big(\delta H(t) - (\mu + d_1 + \upsilon)A(t)\Big) \\ &+ \frac{\eta_1\beta_2\alpha}{\mu(\mu+d_2+t_2)}\Big(\beta_2 S(t-\tau_2)T(t-\tau_2) - (\mu+d_2+t_2)T(t)\Big) \\ &+ \eta_1\Big(\beta_3 T(t)\,H(t) - (\mu+d_3+t_1)\,D(t)\Big) + C_1\beta_1\eta_1 S(t)H(t) \\ &- C_1\beta_1\eta_1 S(t-\tau_1)H(t-\tau_1) + \frac{\eta_1\beta_2^2 S(t)T(t)\alpha}{\mu\,(\mu+d_2+t_2)} \\ &- \frac{\eta_1\beta_2^2 S\,(t-\tau_2)\,T\,(t-\tau_2)\,\alpha}{\mu\,(\mu+d_2+t_2)}. \end{aligned} \tag{2.22}$$

Using $\dfrac{\alpha}{\mu} = S_0$ in (2.22) we obtain,

$$\begin{aligned} \frac{dW_1(t)}{dt} &= \frac{-\eta_1\mu}{S(t)}(S(t)-S_0)^2 + \frac{\eta_1\alpha\beta_2^2 S(t)T(t)}{\mu(\mu+d_2+t_2)} - \eta_1\beta_2 S(t)T(t) \\ &+ H(t)\left(\frac{\eta_1\alpha C_1\beta_1}{\mu} - \frac{\alpha C_1\beta_1\eta_1}{R_{HIV}\mu}\right) - \eta_1(\mu+d_3)D(t). \end{aligned} \tag{2.23}$$

$$\begin{aligned} \frac{dW_1(t)}{dt} &= \frac{-\eta_1\mu}{S(t)}(S(t)-S_0)^2 + \eta_1\beta_2 S(t)T(t)(R_{TB}-1) \\ &+ \frac{\alpha C_1\beta_1\eta_1 H(t)}{R_{HIV}\mu}(R_{HIV}-1) - \eta_1(\mu+d_3)D(t). \end{aligned} \tag{2.24}$$

It follows from Eq.(2.24) that $\frac{dW_1(t)}{dt} \leq 0$ with equality holding $S(t) = S_0, H(t) = A(t) = T(t) = D(t) = 0$. According to the Theorem (2.2), E_0 is locally asymptotically stable. By the LaSalle invariance principle, the disease free equilibrium E_0 of the model (2.2) is globally asymptotically stable. □

Theorem 2.8. *If $R_{HIV} < 1 < R_{TB}$, the HIV free equilibrium E_1 of the system* (2.2) *is globally asymptotically stable for any $\tau_1, \tau_2 \geq 0$.*

Proof. Let us consider a Lyapunov functional $W_2(t)$ as follows.

$$\begin{aligned} W_2(t) = {} & \eta_2 g\left(\frac{S(t)}{S_1}\right) + \eta_2 H(t) + \frac{\eta_2 \upsilon}{\upsilon + d_1 + \mu} A(t) + \eta_2 g\left(\frac{T(t)}{T_1}\right) \\ & + \eta_2 D(t) + \eta_2 C_1 \beta_1 \int_{t-\tau_1}^{t} S(\xi) H(\xi) d\xi \\ & + \eta_2 \beta_2 S_1 T_1 \int_{t-\tau_2}^{t} \left(\frac{S(\xi)T(\xi)}{S_1 T_1} - 1 - \ln \frac{S(\xi)T(\xi)}{S_1 T_1}\right) d\xi, \end{aligned} \tag{2.25}$$

where $\eta_2 = \dfrac{(\upsilon + d_1 + \mu)\beta_2 \alpha}{\mu(\mu + d_2 + t_2)}$.
Differentiating $W_2(t)$ along the solution of system (2.2), we obtain

$$\begin{aligned} \frac{dW_2(t)}{dt} = {} & \eta_2 \left(1 - \frac{S_1}{S(t)}\right)\left(\alpha - C_1\beta_1 H(t)S(t) - \beta_2 T(t)S(t) - \mu S(t)\right) \\ & + \eta_2 \Big(\beta_1 C_1 (t-\tau_1) H(t-\tau_1) + \upsilon A(t) + t_1 D(t) + (1-\epsilon)\theta H(t) \\ & - \beta_3 T(t) H(t) - (\delta + \mu) H(t)\Big) \\ & + \frac{\upsilon \eta_2}{\upsilon + d_1 + \mu}\Big(\delta H(t) - (\mu + d_1 + \upsilon) A(t)\Big) \\ & + \eta_2 \left(1 - \frac{T_1}{T(t)}\right)\Big(\beta_2 S(t-\tau_2) T(t-\tau_2) - (\mu + d_2 + t_2) T(t)\Big) \\ & + \eta_2 \Big(\beta_3 T(t) H(t) - (\mu + d_3 + t_1) D(t)\Big) \\ & + \eta_2 C_1 \beta_1 S(t) H(t) - \eta_2 C_1 \beta_1 S(t-\tau_1) H(t-\tau_1) \\ & + \eta_2 \beta_2 S_1 T_1 \left(\frac{S(t)T(t)}{S_1 T_1} - \frac{S(t-\tau_2)T(t-\tau_2)}{S_1 T_1} + \ln\left(\frac{S(t-\tau_2)T(t-\tau_2)}{S(t)T(t)}\right)\right). \end{aligned} \tag{2.26}$$

Let,

$$\begin{aligned} \alpha - \beta_2 T_1 S_1 - \mu S_1 = 0, \\ \beta_2 S_1 T_1 - (\mu + d_2 + t_2) T_1 = 0. \end{aligned} \tag{2.27}$$

Using Eq.(2.27) in Eq.(2.26), we get

$$\begin{aligned}\frac{dW_2(t)}{dt} &= \eta_2\left(1-\frac{S_1}{S(t)}\right)\Big(\beta_2 T_1 S_1 + \mu S_1 - C_1\beta_1 H(t)S(t)\\ &\quad - \beta_2 T(t)S(t) - \mu S(t)\Big) + \eta_2\beta_1 C_1 S(t-\tau_1)H(t-\tau_1) + \eta_2 \upsilon A(t)\\ &\quad + \eta_2 t_1 D(t) - \eta_2\beta_3 T(t)H(t) + H(t)\eta_2((1-\epsilon)\theta - (\delta+\mu)) + \frac{\upsilon\eta_2\delta H(t)}{\upsilon + d_1 + \mu}\\ &\quad - \upsilon\eta_2 A(t) + \eta_2\left(1+\frac{T_1}{T(t)}\right)\Big(\beta_2 S(t-\tau_2)T(t-\tau_2) - \beta_2 S_1 T(t)\Big)\\ &\quad + \eta_2\beta_3 T(t)H(t) - \eta_2(\mu + d_3 + t_1)D(t) + \eta_2 C_1\beta_1 S(t)H(t)\\ &\quad - \eta_2 C_1\beta_1 S(t-\tau_1)H(t-\tau_1) + \eta_2\beta_2 S(t)T(t) - \eta_2\beta_2 S(t-\tau_2)T(t-\tau_2)\\ &\quad + \eta_2\beta_2 S_1 T_1 \ln\left(\frac{S(t-\tau_2)T(t-\tau_2)}{S(t)T(t)}\right).\end{aligned} \tag{2.28}$$

$$\begin{aligned}\frac{dW_2(t)}{dt} &= -\frac{\mu}{S(t)}\eta_2(S-S_1)^2\\ &\quad + \frac{\eta_2\alpha C_1\beta_1 H(t)}{\mu R_{HIV}}\left(\frac{R_{HIV}}{R_{TB}} - 1\right) - \eta_2(\mu + d_2)D(t)\\ &\quad - \eta_2\beta_2 S_1 T_1\left(\frac{S_1}{S(t)} - 1 - 1n\left(\frac{S_1}{S(t)}\right)\right)\\ &\quad - \eta_2\beta_2 S_1 T_1\left(\frac{S(t-\tau_2)T(t-\tau_2)}{T(t)S_1} - 1 - \ln\left(\frac{S(t-\tau_2)T(t-\tau_2)}{T(t)S_1}\right)\right).\end{aligned} \tag{2.29}$$

Since the function $g(u) = u - 1 - \ln u$ is always positive except for $u = 1$ where $g(1) = 0$. It follows from Eq.(2.29) that $\frac{dW_2(t)}{dt} \leq 0$ with equality holding $S(t) = S_1, T(t) = T_1, H(t) = A(t) = D(t) = 0$. According to the Theorem (2.3), E_1 is locally asymptotically stable. By the LaSalle invariance principle, the HIV free equilibrium E_1 of the model (2.2) is globally attracting. □

Theorem 2.9. *If $R_{HIV} > 1 > R_{TB}$, the TB free equilibrium E_2 of the system* (2.2) *is globally asymptotically stable for any $\tau_1, \tau_2 \geq 0$.*

Proof. Define a Lyapunov functional $W_3(t)$ as follows,

$$\begin{aligned}W_3(t) &= S(t) + H(t) + \eta_3 A(t) + T(t) + D(t)\\ &\quad + C_1\beta_1\int_{t-\tau_1}^{t} S(\xi)H(\xi)d\xi + \beta_2\int_{t-\tau_2}^{t} S(\xi)T(\xi)d\xi\end{aligned} \tag{2.30}$$

where $\eta_3 = \dfrac{\upsilon}{\upsilon + d_1 + \mu}$.

We calculate the derivative of $W_3(t)$ along the solution of the system (2.2), we obtain

$$\begin{aligned}\frac{dW_3(t)}{d(t)} &= \alpha - C_1\beta_1 H(t)S(t) - \beta_2 T(t)S(t) - \mu S(t) + \Big(C_1\beta_1 S(t-\tau_1)H(t-\tau_1)\\ &+ \upsilon A(t) + t_1 D(t) + (1-\epsilon)\theta H(t) - \beta_3 T(t)H(t) - (\delta+\mu)H(t)\Big)\\ &+ \eta_3\Big(\delta H(t) - (\mu + d_1\upsilon)A(t)\Big) + \Big(\beta_2 S(t-\tau_2)T(t-\tau_2)\\ &- (\mu + d_2 + t_2)T(t)\Big) + \Big(\beta_3 T(t)H(t) - (\mu + d_3 t_1)D(t)\Big) + C_1\beta_1 S(t)H(t)\\ &- C_1\beta_1 S(t-\tau_1)H(t-\tau_1) + \beta_2 S(t)T(t) - \beta_2 S(t-\tau_2)T(t-\tau_2).\end{aligned} \tag{2.31}$$

Note that

$$\begin{aligned}\alpha - C_1\beta_1 H_2 S_2 - \mu S_2 &= 0,\\ C_1\beta_1 S_2 H_2 + \upsilon A_2 + (1-\epsilon)\theta H_2 - (\delta+\mu)H_2 &= 0,\\ \delta H_2 - (\upsilon + d_1 + \mu)A_2 &= 0.\end{aligned} \tag{2.32}$$

Substituting (2.32) into (2.31), we obtain

$$\begin{aligned}\frac{dW_3(t)}{dt} &= C_1\beta_1 H_2 S_2 + \mu S_2 - C_1\beta_1 H(t)S(t) - \beta_2 T(t)S(t) - \mu S(t)\\ &+ C_1\beta_1 S(t-\tau_1)H(t-\tau_1) + \upsilon A(t) + t_1 D(t) + (1-\epsilon)\theta H(t)\\ &- \beta_3 T(t)H(t) - \Big(C_1\beta_1 S_2 + \frac{\upsilon A_2}{H_2} + (1-\epsilon)\theta\Big)H(t)\\ &+ \frac{\eta_3(\upsilon + d_1 + \mu)A_2 H(t)}{H_2} - \upsilon A(t) + \beta_2 S(t-\tau_2)T(t-\tau_2)\\ &- (\mu + d_2 + t_2)T(t) + \beta_3 T(t)H(t) - (\mu + d_3 + t_1)D(t) + C_1\beta_1 S(t)H(t)\\ &- C_1\beta_1 S(t-\tau_1)H(t-\tau_1) + \beta_2 S(t)T(t) - \beta_2 S(t-\tau_2)T(t-\tau_2).\end{aligned} \tag{2.33}$$

$$\begin{aligned}\frac{dW_3(t)}{dt} &\le -C_1\beta_1 S_2 H(t) + \frac{T(t)\alpha\beta_2}{\mu R_{TB}}\left(\frac{R_{TB}}{R_{HIV}} - 1\right)\\ &- (\mu + d_3)D(t) - \frac{\beta_2\alpha T(t)}{\mu R_{HIV}}.\end{aligned} \tag{2.34}$$

It follows from Eq.(2.34) that $\frac{dW_3(t)}{dt} \le 0$ with equality holding $S(t) = S_2, H(t) = H_2, A(t) = A_2, T(t) = D(t) = 0$. According to the Theorem (2.4), E_2 is locally asymptotically stable. By the LaSalle invariance principle, the TB free equilibrium E_2 of the model (2.2) is globally asymptotically stable. This completes the proof. □

Theorem 2.10. *Let $R_{HIV} > 1$ and $R_{TB} > 1$, if endemic equilibrium E_3 of the system (2.2) exist, then it is is globally asymptotically stable for any $\tau_1, \tau_2 \ge 0$, when $\tau_2 < \tau_2^*$, provided that*

$$\frac{\beta_3 H_3\alpha}{\mu} + \upsilon A_3 + \frac{\alpha(d_3+\mu)D_3}{\mu H_3} + \frac{\alpha(d_1+\mu)A_3}{\mu H_3} < (d_3+\mu)D_3.$$

Proof. Let us consider a Lyapunov functional $W_4(t)$ as follows,

$$\begin{aligned} W_4(t) &= g\left(\frac{S(t)}{S_3}\right) + g\left(\frac{H(t)}{H_3}\right) + A(t) + g\left(\frac{T(t)}{T_3}\right) + D(t) \\ &+ C_1\beta_1 S_3 H_3 \int_{t-\tau_1}^{t} \left(\frac{S(\xi)H(\xi)}{S_3H_3} - 1 - \ln\frac{S(\xi)H(\xi)}{S_3H_3}\right)d\xi \\ &+ \beta_2 S_3 T_3 \int_{t-\tau_2}^{t} \left(\frac{S(\xi)T(\xi)}{S_3T_3} - 1 - \ln\frac{S(\xi)T(\xi)}{S_3T_3}\right)d\xi. \end{aligned} \tag{2.35}$$

Differentiating the Eq. (2.35), with respect to time yields

$$\begin{aligned} \frac{dW_4(t)}{dt} &= \left(1 - \frac{S_3}{S(t)}\right)(\alpha - C_1\beta_1 H(t)S(t) - \beta_2 T(t)S(t) - \mu S(t)) \\ &+ \left(1 - \frac{H_3}{H(t)}\right)\Big(C_1\beta_1 S(t-\tau_1)H(t-\tau_1) + \upsilon A(t) + t_1 D(t) \\ &+ (1-\epsilon)\theta H(t) - \beta_3 T(t)H(t) - (\delta+\mu)H(t)\Big) \\ &+ \delta H(t) - (\upsilon + d_1 + \mu)A(t) \\ &+ \left(1 - \frac{T_3}{T(t)}\right)\Big(\beta_2 S(t-\tau_2)T(t-\tau_2) - (\mu + d_2 + t_2)T(t)\Big) \\ &+ \beta_3 T(t)H(t) - (t_1 + d_3 + \mu)D(t) \\ &+ C_1\beta_1 S_3 H_3\left(\frac{S(t)H(t)}{S_3H_3} - \frac{S(t-\tau_1)H(t-\tau_1)}{S_3H_3} + \ln\frac{S(t-\tau_1)H(t-\tau_1)}{S(t)H(t)}\right) \\ &+ \beta_2 S_3 T_3\left(\frac{ST}{S_3T_3} - \frac{S(t-\tau_2)T(t-\tau_2)}{S_3T_3} + \ln\frac{S(t-\tau_2)T(t-\tau_2)}{S(t)T(t)}\right). \end{aligned} \tag{2.36}$$

Note that

$$\begin{aligned} &\alpha - C_1\beta_1 H_3 S_3 - \beta_2 T_3 S_3 - \mu S_3 = 0, \\ &C_1\beta_1 H_3 S_3 + \upsilon A_3 + t_1 D_3 + (1-\epsilon)\theta H_3 - \beta_3 T_3 H_3 - (\delta+\mu)H_3 = 0, \\ &\beta_2 S_3 T_3 - (\mu + d_2 + t_2)T_3 = 0. \end{aligned} \tag{2.37}$$

By using (2.37) in (2.36) , we get

$$\begin{aligned} \frac{dW_4(t)}{dt} &= -\frac{\mu}{S(t)}(S(t) - S_3)^2 - C_1\beta_1 S_3 H_3\left(\frac{S(t-\tau_1)H(t-\tau_1)}{S_3H(t)} + \frac{S_3}{S(t)} - 2\right. \\ &\left. - \ln\left(\frac{S(t-\tau_1)H(t-\tau_1)}{S(t)H(t)}\right)\right) - \beta_2 S_3 T_3\left(\frac{S(t-\tau_2)T(t-\tau_2)}{S_3T(t)}\right. \\ &\left. + \frac{S_3}{S(t)} - 2 - \ln\left(\frac{S(t-\tau_2)T(t-\tau_2)}{S(t)T(t)}\right)\right) + \upsilon A(t) + t_1 D(t) - \frac{\upsilon A(t)H_3}{H(t)} \\ &- \frac{t_1 D_3 H_3}{H(t)} + \beta_3 H_3 T(t) + \upsilon A_3 + t_1 D_3 - \beta_3 T_3 H_3 - \upsilon\frac{A_3}{H_3}H(t) - t_1\frac{D_3}{H_3}H(t) \\ &+ \beta_3 T_3 H(t) + \delta H(t) - (\upsilon + d_1 + \mu)A(t) - (t_1 + d_3 + \mu)D(t). \end{aligned} \tag{2.38}$$

Note that

$$\begin{aligned} \delta H_3 - (\upsilon + d_1 + \mu)A_3 = 0, \\ \beta_3 T_3 H_3 - (t_1 + d_3 + \mu)D_3 = 0. \end{aligned} \tag{2.39}$$

By using (2.39) in (2.38) , we get

$$\begin{aligned}\frac{dW_4(t)}{dt} &= \frac{-\mu(S(t)-S_3)^2}{S(t)} - C_1\beta_1 S_3 H_3\left(\frac{S_3}{S(t)} - 1 - \ln\left(\frac{S_3}{S(t)}\right)\right)\\ &- C_1\beta_1 S_3 H_3\left(\frac{S(t-\tau_1)H(t-\tau_1)}{S_3 H(t)} - 1 - \ln\left(\frac{S(t-\tau_1)H(t-\tau_1)}{S_3 H(t)}\right)\right)\\ &- \beta_2 T_3 S_3\left(\frac{S_3}{S(t)} - 1 - \ln\left(\frac{S_3}{S(t)}\right)\right)\\ &- \beta_2 S_3 T_3\left(\frac{S(t-\tau_2)T(t-\tau_2)}{T(t)S_3} - 1 - \ln\left(\frac{S(t-\tau_2)T(t-\tau_2)}{T(t)S_3}\right)\right)\\ &- \frac{H_3}{H(t)}\Big(\upsilon A(t) + t_1 D(t)\Big) + \beta_3 H_3 T(t) + \upsilon A_3 - (d_3+\mu)D_3 - \frac{\upsilon A_3 H(t)}{H_3}\\ &- \frac{t_1 D_3 H(t)}{H_3} + \beta_3 T_3 H(t) + \frac{(\upsilon + d_1 + \mu)A_3 H(t)}{H_3} - (d_1+\mu)A(t).\end{aligned} \tag{2.40}$$

$$\begin{aligned}\frac{dW_4(t)}{dt} &\le \frac{-\mu(S(t)-S_3)^2}{S(t)} - C_1\beta_1 S_3 H_3\left(\frac{S_3}{S(t)} - 1 - \ln\left(\frac{S_3}{S(t)}\right)\right)\\ &- C_1\beta_1 S_3 H_3\left(\frac{S(t-\tau_1)H(t-\tau_1)}{S_3 H(t)} - 1 - \ln\left(\frac{S(t-\tau_1)H(t-\tau_1)}{S_3 H(t)}\right)\right)\\ &- \beta_2 T_3 S_3\left(\frac{S_3}{S(t)} - 1 - \ln\left(\frac{S_3}{S(t)}\right)\right)\\ &- \beta_2 S_3 T_3\left(\frac{S(t-\tau_2)T(t-\tau_2)}{T(t)S_3} - 1 - \ln\left(\frac{S(t-\tau_2)T(t-\tau_2)}{T(t)S_3}\right)\right)\\ &- \frac{H_3}{H(t)}(\upsilon A(t) + t_1 D(t)) - (d_1+\mu)A(t) + \Bigg(\frac{\beta_3 H_3 \alpha}{\mu} + \upsilon A_3\\ &+ \frac{\alpha(d_3+\mu)D_3}{\mu H_3} + \frac{\alpha(d_1+\mu)A_3}{\mu H_3} - (d_3+\mu)D_3\Bigg).\end{aligned} \tag{2.41}$$

Since the function $g(u) = u - 1 - \ln u$ is always positive except for $u = 1$ where $g(1) = 0$. It follows from Eq. (2.41) that $\frac{dW_4(t)}{dt} \le 0$ with equality holding $S(t) = S_3, H(t) = H_3, A(t) = A_3, T(t) = T_3, D(t) = D_3$. According to the Theorem (2.6), E_3 is locally asymptotically stable when $\tau_2 < \tau_2^*$. By the LaSalle invariance principle, the endemic equilibrium E_3 of the model (2.2) is globally asymptotically stable, in the case of $\tau_2 < \tau_2^*$. □

Remark 3. The main objective of the above Theorems (2.7)-(2.10) is to analyze the global stability of the equilibrium points of the nonlinear delay system (2.2). That is to find conditions for local and global stability of the equilibria and work out the relations among these stability conditions. Here, the basic reproduction number acts as the threshold parameter. The above Theorems (2.7)-(2.10) reveal that the nonlinear delay system (2.2) always return to its corresponding equilibrium points with time, meaning there by, the solution trajectories of the system will be attracted towards the equilibrium point with time and establishing the global stability of the system at equilibrium points. The condition for the existence of local and global stability of four equilibria have been tabulated in Table. 3. In the following section 3, we estimate the length of the delay as we aim to preserve the stability of the system.

Table 3: Condition for existence and stability of equilibrium points

Equilibrium Point	Condition for Existence	Stability
Disease free	Always exist	g.a.s when $R_{HIV} < 1$ and $R_{TB} < 1$
HIV free	Exists when $R_{HIV} < 1 < R_{TB}$	g.a.s when $R_{HIV} < 1 < R_{TB}$
TB free	Exists when $R_{HIV} > 1 > R_{TB}$	g.a.s when $R_{HIV} > 1 > R_{TB}$
Endemic	Exists when $R_{HIV} > 1$ and $R_{TB} > 1$	g.a.s when $R_{HIV} > 1$ and $R_{TB} > 1$

Table 4: Values for model parameters

Parameters	Case 1	Case 2	Case3	Case 4	Units [Assumed]
α	24000	24000	24000	24000	day^{-1}
υ	0.23	0.06	0.1	0.04	day^{-1}
μ	0.98	2	0.05	3.96	day^{-1}
δ	0.6	0.6	0.3	8.8	day^{-1}
β_1	0.0000001	0.00002	0.0000001	0.00008	day^{-1}
β_2	0.00000015	0.00025	0.000000001	0.00136	day^{-1}
β_3	0.000001	0.001	0.0000001	0.0008	day^{-1}
C_1	1	1	1	8	day^{-1}
d_1	0.893	0.03	0.3125	7.65	day^{-1}
d_2	0.035	0.035	0.0625	2.1	day^{-1}
d_3	0.21	0.21	0.375	0.00004	day^{-1}
t_1	0.11	0.11	0.11	0.0000004	day^{-1}
t_2	0.2	0.34	0.2	0.8	day^{-1}
ϵ	0.2	0.2	0.2	0.2	day^{-1}
θ	0.3	0.3	0.3	0.3	day^{-1}

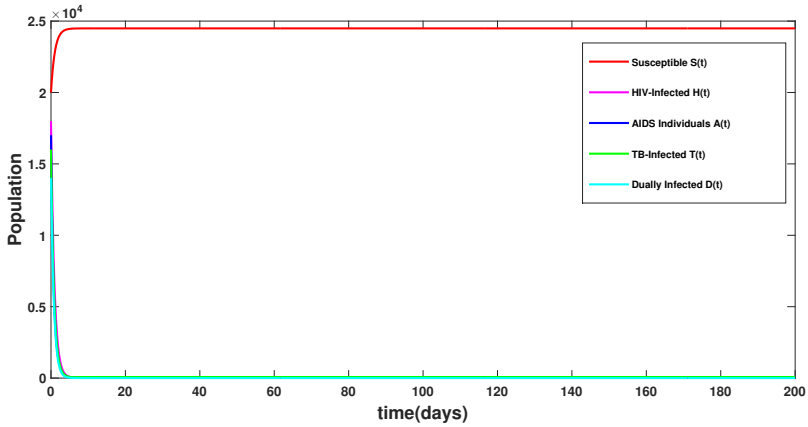
3 Numerical Simulation and Discussion

To illustrate the main theoretical results of HIV-TB co-infection model, the numerical calculations have been carried out using *MATLAB(R2015)*. We have selected parameter set given in Table. 4, to investigate the effect of the sexual contact rate β_1, the tuberculosis transmission rate β_2, the treatment rate υ, t_2 and effect of parameter β_3.
First, we simulate the four equilibrium points of the system (2.2) as follows:
Case 1: Using the parameters as listed in the 2^{nd} column of Table. 4, by simple computing, we can obtain that $R_{HIV} = 0.0019 < 1$ and $R_{TB} = 0.0030 < 1$. (Note Fig.(2)).
Case 2: Using the parameters as listed in the 3^{rd} column of Table. 4, by simple computing, we can obtain that $R_{HIV} = 0.1024 < 1$ and $R_{TB} = 1.2623 > 1$. (Note Fig.(3)).
Case 3: Using the parameters as listed in the 4^{th} column of Table. 4, by simple computing, we can obtain that $R_{HIV} = 1.0635 > 1$ and $R_{TB} = 0.0015 < 1$. (Note Fig.(4)).
Case 4: Using the parameters as listed in the 5^{th} column of Table. 4, by simple computing, we can obtain that $R_{HIV} = 1.2393 > 1$ and $R_{TB} = 1.2015 > 1$. (Note Fig.(5)).

3.1 Effect of treatment

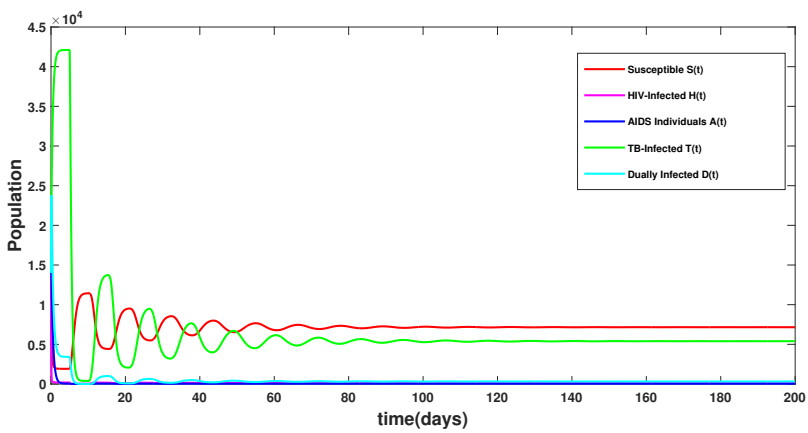
The ultimate aim of our research is to investigate the effect of treatment on AIDS infected and TB infected populations. To achieve our objective, we vary the parameters υ and t_2 which represent the rate at which the AIDS individuals and TB individuals are treated.

- Fig.(9) represents the TB infected of HIV free state (TB endemic state) where $R_{HIV} < 1$



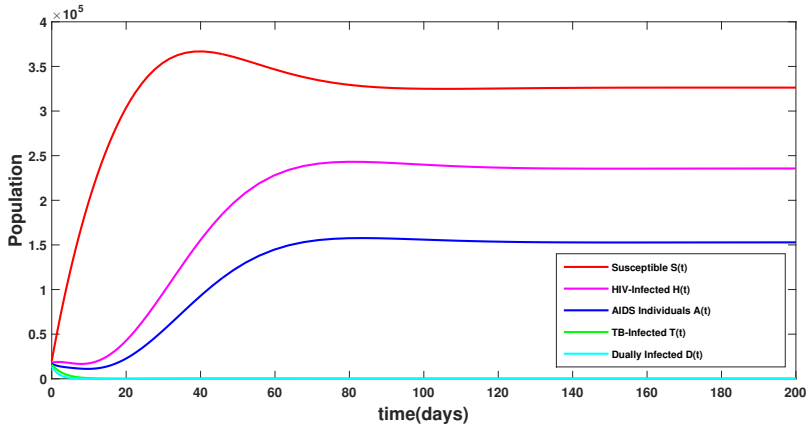
$R_{HIV} < 1$ and $R_{TB} < 1$

Figure 2: The above figure denotes graph trajectories of $S(t), H(t), A(t), T(t)$ and $D(t)$ versus time t of system (2.2) choosing the initial conditions as $S(0) = 20000, H(0) = 18000, A(0) = 17000, T(0) = 16000$ and $D(0) = 14000$, for $\tau_1 = 4$ and $\tau_2 = 5$. Where $R_{HIV} = 0.0019 < 1$ and $R_{TB} = 0.0030 < 1$.(For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article, DOI:10.5556/j.tkjm.53.2022.3295)



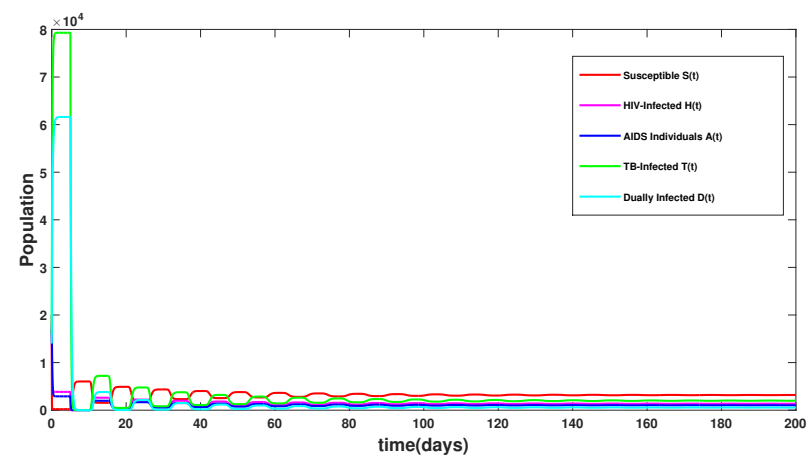
$R_{HIV} < 1 < R_{TB}$

Figure 3: The above figure denotes graph trajectories of $S(t), H(t), A(t), T(t)$ and $D(t)$ versus time t of system (2.2) choosing the initial conditions as $S(0) = 20000, H(0) = 18000, A(0) = 17000, T(0) = 16000$ and $D(0) = 14000$, for $\tau_1 = 4$ and $\tau_2 = 5$. Where $R_{HIV} = 0.1024 < 1$ and $R_{TB} = 1.2623 > 1$.(For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article, DOI:10.5556/j.tkjm.53.2022.3295)



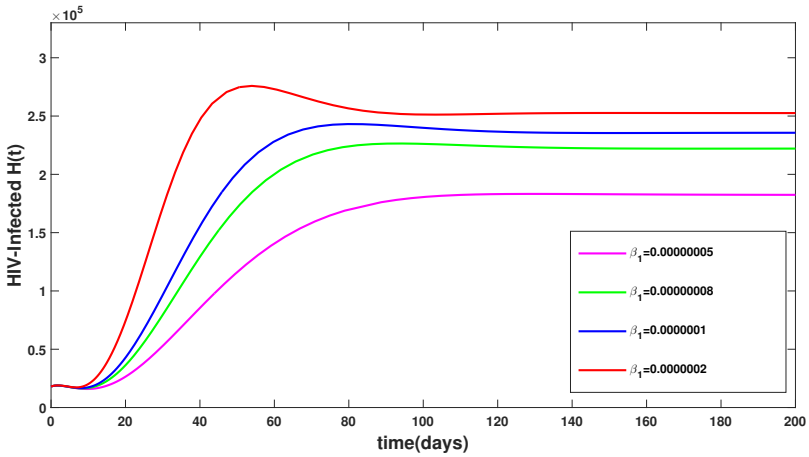
$R_{HIV} > 1 > R_{TB}$

Figure 4: The above figure denotes graph trajectories of $S(t), H(t), A(t), T(t)$ and $D(t)$ versus time t of system (2.2) choosing the initial conditions as $S(0) = 20000, H(0) = 18000, A(0) = 17000, T(0) = 16000$ and $D(0) = 14000$, for $\tau_1 = 4$ and $\tau_2 = 5$. Where $R_{HIV} = 1.0635 > 1$ and $R_{TB} = 0.0015 < 1$.(For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article, DOI:10.5556/j.tkjm.53.2022.3295)



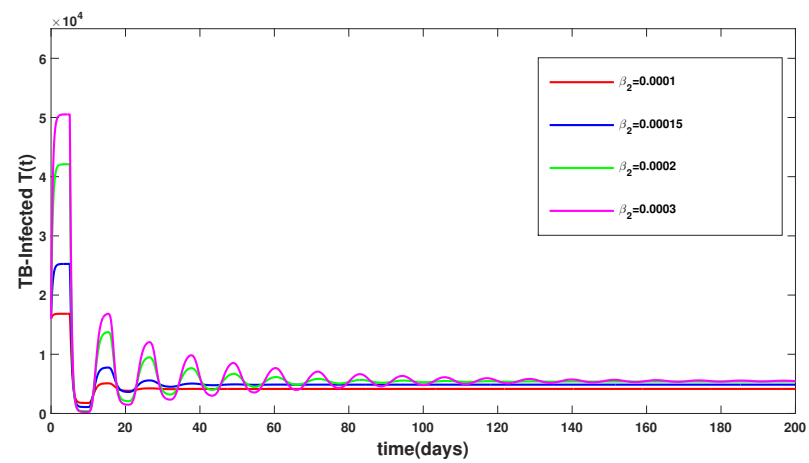
$R_{HIV} > 1$ and $R_{TB} > 1$

Figure 5: The above figure denotes graph trajectories of $S(t), H(t), A(t), T(t)$ and $D(t)$ versus time t of system (2.2) choosing the initial conditions as $S(0) = 20000, H(0) = 18000, A(0) = 17000, T(0) = 16000$ and $D(0) = 14000$, for $\tau_1 = 4$ and $\tau_2 = 5$. Where $R_{HIV} = 1.2393 > 1$ and $R_{TB} = 1.2015 > 1$.(For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article, DOI:10.5556/j.tkjm.53.2022.3295)



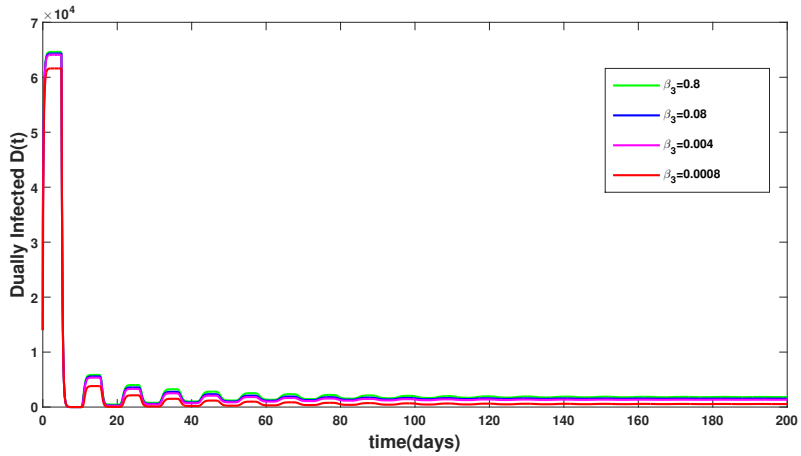
$$R_{HIV} > 1 > R_{TB}$$

Figure 6: The above figure has been plotted with same initial conditions and parameters used for Fig.(4), which denotes the variation of parameter β_1 among HIV infected population.(For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article, DOI:10.5556/j.tkjm.53.2022.3295)



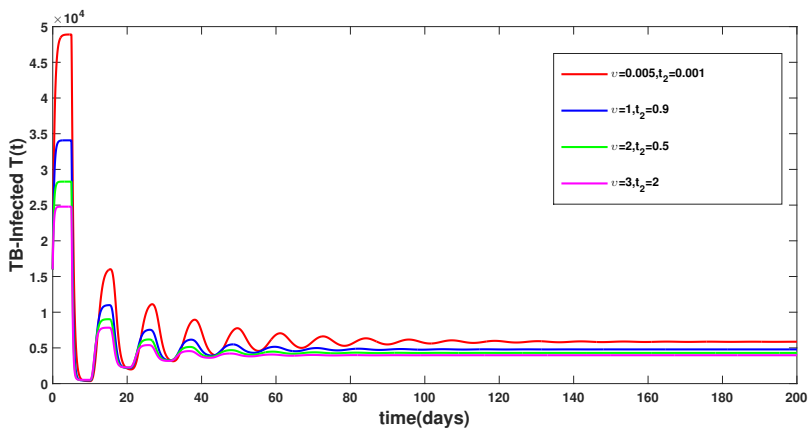
$$R_{HIV} < 1 < R_{TB}$$

Figure 7: The above figure has been plotted with same initial conditions and parameters used for Fig.(3), which denotes the variation of parameter β_2 among TB infected population.(For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article, DOI:10.5556/j.tkjm.53.2022.3295)



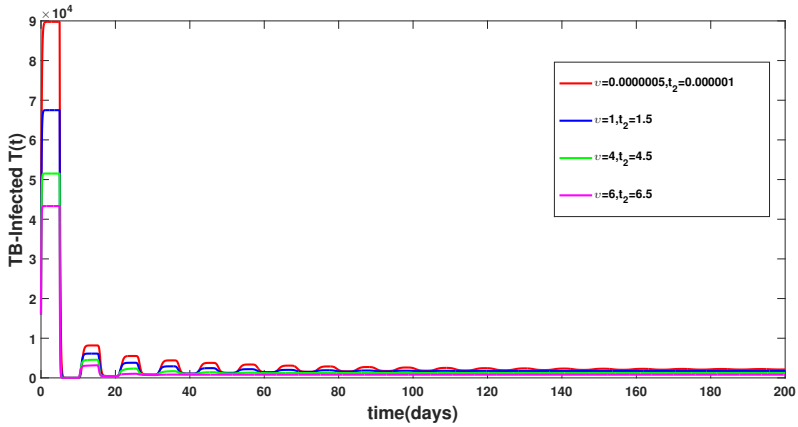
$R_{HIV} > 1$ and $R_{TB} > 1$

Figure 8: The above figure has been plotted with same initial conditions and parameters used for Fig.(5), which denotes the variation of parameter β_3 among dually infected population.(For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article, DOI:10.5556/j.tkjm.53.2022.3295)



$R_{HIV} < 1 < R_{TB}$

Figure 9: The above figure has been plotted with same initial conditions and parameters used for Fig.(3), which denotes the impact of treatment among TB infected population.(For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article, DOI:10.5556/j.tkjm.53.2022.3295)



$R_{HIV} > 1$ and $R_{TB} > 1$

Figure 10: The above figure has been plotted with same initial conditions and parameters used for Fig.(5), which denotes the impact of treatment among TB infected population.(For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article, DOI:10.5556/j.tkjm.53.2022.3295)

and $R_{TB} > 1$. It can be noted that the TB infected population decreases when the the treatment rate υ and t_2 is increases.

- Fig.(10) represents the TB infected population of endemic state where $R_{HIV} > 1$ and $R_{TB} > 1$. It can be noted that the TB infected population is inversely proportional to the treatment rate υ and t_2. It biologically denotes that after the treatment infected population get cure from disease and return to the recovered compartment. This shows that the treatment is a good control measure for both AIDS and TB. If the treatment is emphasized, (i,e.,) when we increase the rate of t_2, TB infected population will be shifted to the recovery compartment.

3.2 Effect of sexual contact rate β_1

In our investigation process, next we concentrate on the effect of sexual contact rate among HIV infected population , we carry out some numerical simulations to show the contribution of sexual transmission rate β_1 during the whole infection. Then we increase the β_1 to observe the change in the HIV infected compartment. Fig.(6) ($\beta_1 = 0.00000005, \beta_1 = 0.00000008, \beta_1 = 0.0000001, \beta_1 = 0.0000002$) shows that the HIV infected population reach the peak level more quickly as β_1 increases. Therefore, sexual contact rate β_1 plays a vital role in whole infection. It can be seen that C_1 and β_1 always appear together and their product $C_1\beta_1$ determines the rate of R_{HIV}. It can be observed that, HIV population is directly proportional to R_{HIV}, where as R_{HIV} is directly proportional to β_1. We also find that, another way of controlling HIV other than treatment is by controlling the rate of $C_1\beta_1$.

3.3 Effect of TB transmission rate β_2

At the same time, TB transmission rate β_2 also has a great influence on the TB population dynamics. In the system (2.2), we set the TB transmission rate β_2 as ($\beta_2 = 0.0001, \beta_2 = 0.00015, \beta_2 = 0.0002, \beta_2 = 0.0003$) (see Fig.(7)) for monitoring the impact of parameter β_2. It can be viewed from Fig.(7), the TB population increases as β_2 increases. This happens because TB spreads when $R_{TB} > 1$ and dies out when $R_{TB} < 1$. Then, also the spread of TB disease is directly proportional to R_{TB}, where as R_{TB} is directly proportional to β_2. Other than implementing treatment for disease control, we can also control the TB spread by controlling the rate of β_2 as we did for HIV infection in the previous subsection.

3.4 Effect of parameter β_3

In this subsection, we study the effect of the parameter β_3 in the system (2.2). The rate of progress to the dually infected compartment, after acquiring TB is denoted by β_3. It can also be denoted as the rate at which the single infection become co-infection. We can observe from Fig.(8). that the co-infected population is proportional to β_3. So it is possible to make co-infection to single infection, by maintaining β_3 at a very low level.

- Here, Fig.(2). depicts the graphical representation of the system (2.2) when $R_{HIV} < 1$ and $R_{TB} < 1$. It can be observed that the disease dies out after some time and only the susceptible population attains a constant value hereby indicating that when $R_{HIV} < 1$ and $R_{TB} < 1$, the disease cannot persist for longer duration of time, biologically.

- Fig.(3). depicts the graphical representation of the system (2.2) when $R_{HIV} < 1 < R_{TB}$. It can be observed that HIV, AIDS and co-infected population decreases rapidly with time and finally vanishes while the susceptible and TB infected population approaches a constant value. This biologically means that the TB population exist as $R_{TB} > 1$, while the HIV population vanishes as $R_{HIV} < 1$.

- Fig.(4). depicts the graphical representation of the system (2.2) when $R_{HIV} > 1 > R_{TB}$. It can be observed that the TB and co-infected population decreases and finally vanishes with time while the HIV and AIDS infected population attains a constant value. This biologically means that the HIV and AIDS population exist as $R_{HIV} > 1$ while the TB population vanishes as $R_{TB} < 1$.

- Fig.(5). depicts the graphical representation of the system (2.2) when $R_{HIV} > 1$ and $R_{TB} > 1$. It can be observed that the HIV, AIDS, TB and co-infected population approaches a constant value . This biologically means that the infected population exist as $R_{HIV} > 1$ and $R_{TB} > 1$.

4 Parameter estimation

The baseline parameter values are obtained through curve fitting are presented under the caption of Fig.(11). The full list of parameter ranges used in the simulation is given in the 5^{th} column of Table. 4.

4.1 Data

The data were obtained from Pan American health Organization (PAHO, 2020). The data used represent new TB/HIV infection in America. Data are collected routinely on a yearly basis and was retrieved for the period beginning January 2005 to December 2018. The pictorial representation of the raw data is given in Fig.(11).

4.2 Curve fitting

In this section, we fit system (2.2) to data to determine the trend of HIV in male and female populations. Curve fitting is a process that allows us to quantitatively estimate the trend of the outcomes. The curve fitting process fits equations of approximating curves to the raw field data. However, for a given set of data, the fitting curves of a given type are generally not unique. Thus, a curve with a minimal deviation from all data points is desired. This best fitting curve can be obtained by the method of least squares. In this method, the parameters not known are approximated through minimization of the sum of the squared deviations between the data and the model. It minimizes the sum of squared distances between the observed values and the model values. This can be mathematically expressed as

$$RSS = \sum_{i=1}^{n} \theta_i^2 = \sum_{i=1}^{n} (Y_i - \hat{Y})^2$$

where $\theta_i = (Y_i - \hat{Y})$ and n refers to the data points and RSS refers to the sum of square error estimate which is assumed to follow a normal distribution. The following parameters were fixed at the following values: $\upsilon = 0.04, \mu = 3.96, \delta = 8.8, \beta_1 = 0.00008, \beta_2 = 0.00136, \beta_3 = 0.0008, C_1 = 8, d_1 = 7.65, d_2 = 2.1, d_3 = 0.00004, t_1 = 0.0000004, t_2 = 0.8, \epsilon = 0.2, \theta = 0.3$. The parameter ranges/values in parameter values in 5^{th} column of Table. 4 are used in the curve fitting and the resulting point values estimated are presented under the caption of Fig.(11). It is important to observe that the cases of dual(TB/HIV) infection peaked in the year 2014. The results show that there was a rise in dual(TB/HIV) infection between 2011 and 2014. We observe in Fig.(11) that the model fits well with the data.

5 Conclusion

In the recent times, the studies on co-infection models have gained more attention among the research communities. Particularly HIV-TB co-infection had become major global health challenge. Compared to the people with single infection, people with co-infection are reported to have poorer health and enhanced pathogen abundance. Co-infecting pathogen interact synergistically with each other so that the presence of one enhance the virulence of the other henceforth increasing the risk of co-infection [7, 8, 10]. In this article, a nonlinear mathematical model with discrete time delay is proposed and analyzed to study the transmission of HIV and curable TB pathogen. The novelty of the proposed delay model (2.2) consists in combining analysis on the two infections (HIV and TB) together into a single model. To our best knowledge, this has not been done before in the literature in such complex model. The study reveal the fact that the impact of delay made our model more accurate than the model introduced by Carla and Ana [5]. When the delay term τ_2 is fixed as bifurcation parameter, we found that the system (2.2) undergoes the Hopf bifurcation as delay value τ_2 crosses the critical value. Hence the subsystem of (2.1) shows complex dynamics when delay is taken into account. In the present work, the

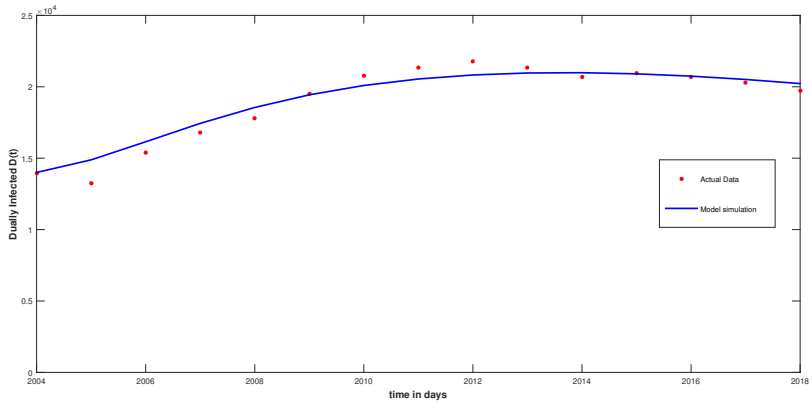


Figure 11: Model system (2.2) fitted to data for the dually infected cases. The baseline parameter values obtained from the curve fitting are: $\upsilon = 0.0535, \mu = 5.22, \delta = 7.469, \beta_1 = 0.00011, \beta_2 = 0.00058, \beta_3 = 0.00028, C_1 = 3, d_1 = 7.278, d_2 = 2.77, d_3 = 0.000039, t_1 = 0.000000387, t_2 = 0.942, \epsilon = 0.225, \theta = 0.001$.

stability analysis (local and global) has been performed for DDE system at their equilibrium points which have been neglected in the work of Carla and Ana [5].

We have also presented a numerical simulation for DDE model which depicts its dynamical behavior. We provide a accurate analytical study by examining the effects of introducing delay on stability of solutions something that was neglected in the analysis of previous non-delay model [5]. From our analytical study, we gained more useful results in the course of disease dynamics of the HIV-TB co-infection model which have discussed in a great detail in the previous section. Also the discussion section comprises useful results not only at the rate of basic reproduction number but also at the effects of some important parameters β_1, β_2, β_3, t_2 and υ. (Note Fig.(6) - Fig.(10)).

The number of co-infected population increases rapidly when the HIV infected individuals are co-infected by other disease that is TB. Thus by providing simultaneous treatment to both(HIV and TB) the disease, the spread of TB can be slowed down and the TB will be eradicated form the population with effective treatment. At this stage we have only HIV/AIDS infected individuals in population. The progression from HIV to AIDS can be slowed down by effective treatment. Thus, from our analysis we observed that the HIV infection can be suppressed at an early stage by drug therapy or other control mechanism thereby the life span of HIV individuals can be increased. It can be viewed graphically from (Fig.(9) and Fig.(10)) the infected population gradually decreases with increase in the treatment rate. The conclusion of the study is that to face the challenge of controlling the spread of co-infection by providing simultaneous treatment for both the disease. All TB patients should be tested for HIV/AIDS and all HIV/AIDS patients should be tested for TB. The co-infected patients should undergo treatment, so that the disease (TB) that can be controlled by treatment can be eradicated with perfect treatment and the disease (HIV) that cannot be eradicated can be treated to increase the life span of the infected individuals. From the results of the model, we infer possible measures that could be implemented in order to reduce the number of co-infected individuals.

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