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DYNAMICAL BEHAVIOR OF HIV-1 EPIDEMIC MODEL WITH TIME DEPENDENT DELAY

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Abstract. The delayed HIV-1 infection mathematical model with two delays is proposed. One of which represents the latent period between the time of contacting and entering of virions into the target cells while the second one stands for virus production period between the new virions to be produced within and released from the infected cells. The basic reproduction number R_0 is found for the proposed model and it is proved that the uninfected steady state is globally asymptotically stable if $R_0 < 1$ and unstable if $R_0 > 1$. And if $R_0 > 1$, then an infected steady state occurs which is proved to be locally as well as globally asymptotically stable. The formulae for R_0 shows that it is the decreasing function of both delays.

Keywords: Epidemic model; HIV-1 infection; Delay differential equations; Global stability analysis.

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1. Introduction

Human immunodeficiency virus (HIV) is a serious mortal lentivirus, which can cause acquired immunodeficiency syndrome (AIDS). The HIV infection is characterized by three different phases, namely, the primary infection, clinically asymptomatic stage (chronic infection), and acquired immunodeficiency syndrome (AIDS) or drug therapy. The scientists and researchers

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have been focusing on the study of controlling the infections. Recent research shows that recombinant virus can control the infections of HIV-1 [1, 2].

Revilla et al.[3], investigate the control of the infections by introducing recombinant virus. Jiang et al. [4] studied this model in detail to show various bifurcation patters. In [5], control strategies are discussed

Tian et al. [6] introduced a time lag into the model and focused on the dynamical behavior of the system with delay, in particular, on equilibrium solution and their bi-furcations. More importantly, they discussed the impact of delay on the dynamical behavior of delayed HIV-1 model.

In addition to the time lag which was proposed in [6], there is another delay that is, the virus production period for new virions to be produced within and released from the infected cells (see [7, 8, 9] for details). Therefore, in this paper, we extend the work of Tian et al. [6] to account for both delays, the latent period τ_1 and virus production period τ_2. Then, our model becomes

$$
\begin{aligned}
\dot{x}(t) &= \lambda - dx(t) - \beta x(t)v(t), \\
\dot{y}(t) &= \beta e^{-a_1\tau_1} x(t-\tau_1)v(t-\tau_1) - ay(t) - \alpha w(t)y(t), \\
\dot{z}(t) &= aw(t)y(t) - bz(t), \qquad (1) \\
\dot{v}(t) &= ke^{-a_2\tau_2} y(t-\tau_2) - pv(t), \\
\dot{w}(t) &= cz(t) - qw(t).
\end{aligned}
$$

Here $x(t)$ stands for uninfected target cells and $y(t)$ denotes the density of infected cells and $v(t)$ is the density of free virus at the time t . β is infection rate of infected cells and the healthy cells are assumed to be produced at a constant rate λ. a is the death rate of infected cells either due to the action of the virus or the immune system, and in the mean time, each produces HIV-1 virus particles at a rate k during their life which on average has length $1/a$. w is the density of recombinant virus and the density of the double infected cells is represented by z. We will study the dynamical behavior and bifurcation patterns of this model, and will show how the two delays influence stability.

The organization of this paper is as follows. In the next section, we discuss the positivity and

well-posedness of the solution. In section 3, by analyzing the corresponding characteristic equations, we study the local asymptotic stability of an infection-free equilibrium and global stability of the infection-free equilibrium. Section 4 is devoted to the local and global stabilities of chronic-infection equilibrium of system (1). Section 5 is considered for concluding this work.

2. Positivity and well- posedness of the solution

In this section we discuss the positivity and well-posedness of the solution.

Theorem 2.1. *The solutions of the system (1) remain non-negative and bounded, given that the initial conditions are non-negative.*

Proof. Letting $X = C([-\max(\tau_1,\tau_2),0];R^5)$, be the Banach space of continuous mapping from $[-\max(\tau_1,\tau_2),0]$ to R^5 equipped with the sup-norm. For the system (1), consider the initial conditions for $\big(x(\phi),y(\phi),z(\phi),v(\phi),w(\phi)\big) \in X$ satisfying

$$x(\phi)\geq 0, y(\phi)\geq 0, z(\phi)\geq 0, v(\phi)\geq 0, w(\phi)\geq 0, \phi\in[-\max(\tau_1,\tau_2),0]. \tag{2}$$

Now, there exists a unique solution $x(t),y(t),z(t),v(t)$ and $w(t)$ for the given initial conditions in (2), by using the fundamental theory of functional differential equations (see, e.g. [10]).
The solution $x(t),y(t),z(t),v(t)$ and $w(t)$, can be found by using constant of variation formulae:

$$\begin{aligned}
x(t) &= x(0)e^{-\int_0^t (d+\beta v(\zeta))d\zeta} + \lambda\int_0^t e^{-\int_\eta^t (d+\beta v(\zeta))d\zeta}d\eta,\\
y(t) &= y(0)e^{-\int_0^t (a+\alpha w(\zeta))d\zeta} + \int_0^t \big(\beta e^{-a\tau_1}x(t-\tau_1)v(t-\tau_1)\big)e^{-\int_\eta^t (a+\alpha w(\zeta))d\zeta}d\eta,\\
z(t) &= z(0)e^{-bt} + \int_0^t \alpha w(t)y(t)e^{-b(t-\eta)}d\eta,\\
v(t) &= v(0)e^{-pt} + \int_0^t ke^{-a\tau_2}y(t-\tau_2)e^{-p(t-\eta)}d\eta,\\
w(t) &= w(0)e^{-kt} + \int_0^t cz(\eta)e^{-k(t-\eta)}d\eta,
\end{aligned}$$

which clearly indicates that all the solutions are positive.

Next, for boundedness of the solution $x(t), y(t), z(t), v(t)$ and $w(t)$, we consider

$$D(t) = cke^{-a_1\tau_1}x(t-\tau_1) + cky(t) + ckz(t) + \frac{ac}{2}e^{a_2\tau_2}v(t+\tau_2) + \frac{bk}{2}w(t).$$

Calculating the derivative f the above equation and using system (1), we have

$$\begin{aligned}
\frac{dD(t)}{dt} &= cke^{-a_1\tau_1}\Big(\lambda - dx(t-\tau_1) - \beta x(t-\tau_1)v(t-\tau_1)\Big) + ck\Big(\beta e^{-a_1\tau_1}x(t-\tau_1)v(t-\tau_1) \\
&\quad -ay(t) - \alpha w(t)y(t)\Big) + ck\Big(aw(t)y(t) - bz(t)\Big) \\
&\quad +\frac{ac}{2}e^{a_2\tau_2}\Big(ke^{-a_2\tau_2}y(t) - pv(t+\tau_2)\Big) + \frac{bk}{2}\Big(cz(t) - qw(t)\Big), \\
&= ck\lambda e^{-a\tau_1} - \Big(dcke^{-a_1\tau_1}x(t-\tau_1) + \frac{a}{2}cky(t) + \frac{b}{2}kcz(t) + q\frac{bk}{2}w(t) + p\frac{ac}{2}e^{a_2\tau_2}v(t+\tau_2)\Big) \\
&\leq ck\lambda e^{-a_1\tau_1} - \varepsilon D(t).
\end{aligned}$$

Here $\varepsilon = \min\{d, \frac{a}{2}, \frac{b}{2}, q, p\}$. Thus $D(t)$ is bounded. We find equilibria of the system (1), which has three equilibria. The disease-free equilibrium $E_0(x_0, y_0, z_0, v_0, w_0)$, single-infection equilibrium $E_1(x_1, y_1, z_1, v_1, w_1)$ and double-infection equilibrium $E_2(x_2, y_2, z_2, v_2, w_2)$, which are:

$$\begin{aligned}
E_0 &= \big(\frac{\lambda}{d}, 0, 0, 0, 0\big). \\
E_1 &= \left(\frac{ape^{-a_1\tau_1-a_2\tau_2}}{\beta k}, \frac{k\beta\lambda e^{-a_1\tau_1-a_2\tau_2} - adp}{a\beta k e^{-a_2\tau_2}}, 0, \frac{k\beta\lambda e^{-a_1\tau_1-a_2\tau_2} - adp}{ap\beta}, 0\right). \\
E_2 &= \left(\frac{\alpha\lambda cp}{\alpha cdp + \beta kqbe^{-a_2\tau_2}}, \frac{qb}{\alpha c}\frac{q(k\beta\lambda ae^{-a_1\tau_1-a_2\tau_2} - adp)}{ap\beta}, \frac{kqbe^{-a_2\tau_2}}{\alpha cp}\right. \\
&\qquad \left., \frac{\alpha c\beta k\lambda e^{-a_1\tau_1-a_2\tau_2} - \alpha cadp - abqk\beta e^{-a_2\tau_2}}{\alpha cdp + bkq\beta e^{-a_2\tau_2}}\right).
\end{aligned}$$

We define the basic reproduction number as follows:

$$R_0 = e^{-a_1\tau_1-a_2\tau_2}\frac{\lambda\beta k}{apd}.$$

If $R_0 < 1$, then the only biologically meaningful equilibrium is E_0. If $R_0 > 1$, then the single infection equilibrium E_1 occurs. The double-infection equilibrium E_2 will exist if and only if

$R_2 > 1$, where

$$R_2 = \frac{\alpha cdp}{\beta e^{-a_2\tau_2} bkq}(R_0 - 1).$$

Hence, $R_2 > 1$ if and only if $R_0 > R_1$, where $R_1 = 1 + \frac{\beta e^{-a_2\tau_2} bkq}{\alpha cdp}$.

To find the local stability of the equilibria, we find the characteristic equation corresponding to linearized system of (1) at any equilibrium point $\overline{E}(\overline{x}, \overline{y}, \overline{z}, \overline{v}, \overline{w})$, which is $det[\eta I - J(\overline{E})] =$

$$det \begin{pmatrix} \eta + (d + \beta\overline{v}) & 0 & 0 & \beta\overline{x} & 0 \\ -\beta e^{-\tau_1(\eta+a_1)}\overline{v} & \eta + a & 0 & \beta e^{-\tau_1(\eta+a_1)}\overline{x} + \alpha\overline{w} & \alpha\overline{w} \\ 0 & -\alpha\overline{w} & \eta + b & 0 & -\alpha\overline{y} \\ 0 & -ke^{-\tau_2(\eta+a_2)} & 0 & \eta + p & 0 \\ 0 & 0 & c & 0 & \eta + q \end{pmatrix} = 0.$$

3. Stability of the disease-free equilibrium E_0

In this section we show the dynamical behavior of the system (1) at E_0.

Theorem 3.1. *When $R_0 < 1$ the disease-free equilibrium E_0 is locally asymptotically stable, while for $R_0 > 1$, E_0 becomes unstable and the single-infection equilibrium E_1 occurs.*

Proof. The characteristic equation of the Jacobian matrix corresponding to the linearized system of (1) at $E_0(x_0, y_0, z_0, v_0, w_0)$ is

$$det[\eta I - J(E_0)] = (b + \eta)(d + \eta)(q + \eta)\left[(a + \eta)(p + \eta) - \frac{\lambda}{d}\beta k e^{-\tau_1(\eta+a_1)} e^{-\tau_2(\eta+a_2)}\right] = 0.$$

Three roots of the above equation are $\eta_1 = -b$ and $\eta_2 = -d$ and $\eta_3 = -q$, which are negative. And the remaining two roots are given by the following equation

$$(a + \eta)(p + \eta) = \frac{\lambda}{d}\beta k e^{-\tau_1(\eta+a_1)} e^{-\tau_2(\eta+a_2)}. \tag{3}$$

If η has non-negative real part, then modulus of the left hand side of (3) satisfies

$$|(a + \eta)(p + \eta)| \geq ap.$$

While modulus of the right hand side of (3) satisfies

$$\frac{\lambda}{d}\beta k |e^{-\tau_1(\eta+a_1)} e^{-\tau_2(\eta+a_2)}| = |apR_0| < ap.$$

This leads to contradiction. Thus when $R_0 < 1$, all the eigenvalues have negative real parts, and hence the infection free state E_0 is locally asymptotically stable provided that $\tau_1 \geq 0$ and $\tau_2 \geq 0$. When $R_0 > 1$, then consider

$$\begin{aligned} g(\eta) &= (a+\eta)(p+\eta) - \frac{\lambda}{d}\beta k e^{-\tau_1(\eta+a_1)} e^{-\tau_2(\eta+a_2)}, \\ &= \eta^2 + (a+p)\eta + ap(1 - e^{-\eta(\tau_1+\tau_2)} R_0). \end{aligned}$$

Now $g(0) = ap(1-R_0) < 0$ and $\lim_{\eta\to\infty} g(\eta) = +\infty$. By the continuity of $g(\eta)$, there exists at least one positive root of $g(\eta) = 0$. Thus, the infection-free equilibrium is unstable if $R_0 > 1$. This completes the proof.

Theorem 3.2. *When $R_0 < 1$, the disease-free equilibrium E_0 is globally asymptotically stable.*

Proof. Let us consider the following Lyapunov functional

$$V_0(t) = V_{01}(t) + V_{02}(t), \tag{4}$$

where

$$V_{01}(t) = e^{-a_1\tau_1}(x(t) - \frac{\lambda}{d})^2 + \frac{\lambda}{d}y(t) + \frac{\lambda}{d}z(t) + e^{a_2\tau_2}\frac{a\lambda}{kd}v(t) + \frac{b\lambda}{cd}w(t), \tag{5}$$

and

$$V_{02}(t) = e^{-a_1\tau_1}\frac{\lambda\beta}{d}\int_{t-\tau_1}^{t} x(\zeta)v(\zeta)d(\zeta) + \frac{a\lambda}{d}\int_{t-\tau_2}^{t} y(\zeta)d\zeta, \tag{6}$$

Taking derivative of equation (5) and using system (1), we have

$$\begin{aligned} \dot{V_{01}}(t) &= e^{-a_1\tau_1}(x(t) - \frac{\lambda}{d})\big(\lambda - dx(t) - \beta x(t)v(t)\big) \\ &\quad + \frac{\lambda}{d}\big(\beta e^{-a_1\tau_1}x(t-\tau_1)v(t-\tau_1) - ay(t) - \alpha w(t)y(t)\big) \\ &\quad + \frac{\lambda}{d}\big(\alpha w(t)y(t) - bz(t)\big) + e^{a_2\tau_2}\frac{a\lambda}{kd}\big(ke^{-a_2\tau_2}y(t-\tau_2) - pv(t)\big) + \frac{b\lambda}{cd}\big(cz(t) - qw(t)\big). \end{aligned}$$

The above equation, after some simplification, becomes

$$\begin{aligned} \dot{V_{01}}(t) &= -e^{-a_1\tau_1}(x(t)-\frac{\lambda}{d})^2(d+\beta v(t))+\frac{\lambda}{d}\beta e^{-a_1\tau_1}x(t-\tau_1)v(t-\tau_1)-\frac{\lambda}{d}ay(t) \\ &\quad +\frac{a\lambda}{d}y(t-\tau_2)-e^{a_2\tau_2}\frac{a\lambda}{kd}pv(t)-\frac{b\lambda}{cd}qw(t). \end{aligned} \tag{7}$$

The derivative of equation (6) yields

$$\begin{aligned} \dot{V_{02}}(t) &= e^{-a_1\tau_1}\frac{\lambda\beta}{d}x(t)v(t)-e^{-a_1\tau_1}\frac{\lambda\beta}{d}x(t-\tau_1)v(t-\tau_1) \\ &\quad +\frac{a\lambda}{d}y(t)-\frac{a\lambda}{d}y(t-\tau_2). \end{aligned} \tag{8}$$

Now taking derivative of equation (4) and using (7) and (8), we get

$$\begin{aligned} \dot{V_0}(t) &= -e^{-a_1\tau_1}(x(t)-\frac{\lambda}{d})^2(d+\beta v(t))-e^{a_2\tau_2}\frac{ap\lambda}{kd}(1-\frac{\lambda\beta k}{apd}e^{-\tau_1 a_1}e^{-\tau_2 a_2})-\frac{\lambda bq}{cd}w(t). \\ &= -e^{-a_1\tau_1}(x(t)-\frac{\lambda}{d})^2(d+\beta v(t))-e^{a_2\tau_2}\frac{ap\lambda}{kd}(1-R_0)-\frac{\lambda bq}{cd}w(t). \end{aligned} \tag{9}$$

Thus, equation (9) implies that $\dot{V}_0(t) \leq 0$, when $R_0 < 1$. But the equality holds if $x_0 = \frac{\lambda}{d}$, $y(t) = 0$, $z(t) = 0$, $v(t) = 0$, $w(t) = 0$. Then by LaSalli invariance principle (see [11]), we conclude that E_0 is globally asymptotically stable. This completes the proof.

4. Stability of single infection equilibrium E_1

Theorem 4.1. *The single infection-free equilibrium E_1 is locally asymptotically stable provided that $1 < R_0 < R_1$. And when $R_0 > R_1$, then, E_1 becomes unstable and recombinant virus may persist.*

Proof. The characteristic equation of the Jacobian matrix of the corresponding to the linearized system of model (1) at E_1, is given by

$$\begin{aligned} det[\eta I - J(E_1)] &= \big((b+\eta)(q+\eta)-\alpha y_1 c\big)\Big[\big(d+\beta v_1+\eta\big)k\beta x_1 e^{-\tau_1(\eta+a_1)}e^{-\tau_2(\eta+a_2)} \\ &\quad -\beta^2 x_1 k v_1 e^{-(\tau_1+\tau_2)(a+\eta)}-(d+\beta v_1+\eta)(a+\eta)(p+\eta)\Big]=0. \end{aligned}$$

We can write the above equation in form $F_1(\eta)F_2(\eta) = 0$, where

$$\begin{aligned} F_1(\eta) &= (b+\eta)(q+\eta) - \alpha y_1 c, \\ F_2(\eta) &= (d+\beta v_1+\eta)k\beta x_1 e^{-\tau_1(\eta+a_1)}e^{-\tau_2(\eta+a_2)} - \beta^2 x_1 k v_1 e^{-\tau_1(\eta+a_1)}e^{-\tau_2(\eta+a_2)} \\ &\quad -(d+\beta v_1+\eta)(a+\eta)(p+\eta). \end{aligned}$$

Now $F_1(\eta)$ can be written as

$$F_1(\eta) = \eta^2 + (b+q)\eta + bq(1-R_2),$$

which shows that $F_1(\eta) = 0$ has two negative roots if and only if $R_2 < 1$ (i,e $R_0 < R_1$), but has one positive and one negative root if $R_2 > 1$ (i,e $R_0 > R_1$). In the later case, the single infection free equilibrium E_1 will be unstable. Also, $F_2(\eta) = 0$ can be written as

$$\eta^3 + m_0\eta^2 + m_1\eta + m_2 - (m_3\eta + m_4)e^{-\eta(\tau_1+\tau_2)} = 0, \tag{10}$$

where

$$\begin{aligned} m_0 &= a+p+d+\beta v_1, \\ m_1 &= ap + (a+p)(d+\beta v_1), \\ m_2 &= ap(d+\beta v_1), \\ m_3 &= ap, \\ m_4 &= apd. \end{aligned}$$

The dynamical behavior of the proposed model is dependent on the delay terms τ_1 and τ_2. When $\tau_1 = \tau_2 = 0$, then (10) can be written as

$$\eta^3 + n_0\eta^2 + n_1\eta + n_2 = 0. \tag{11}$$

Now applying the Rouths Hurtwits criterion [12, 13], we see that all the roots of (11) have negative real parts, because

$$\begin{aligned} n_0 &= a+p+d+\beta v_1 = a+p+dR_0 > 0, \\ n_1 &= (a+p)(d+\beta v_1) = (a+p)dR_0 > 0, \\ n_2 &= apd > 0, \end{aligned}$$

and

$$n_0 n_1 - n_2 = \left(a^2+b^2+ap+(a+p)R_0\right)dR_0 > 0.$$

Therefore, any root of (10) has negative real part when $\tau_1 = \tau_2 = 0$.

Now, we consider the distribution of roots when $\tau_1 \neq 0$ and $\tau_2 \neq 0$. Let suppose that $i\delta(\delta > 0)$ be the pure imaginary roots of (10), then we get

$$-\delta^3 i - m_0\delta^2 + m_1\delta i + m_2 - (m_3\delta i + m_4)e^{-i\delta(\tau_1+\tau_2)} = 0. \tag{12}$$

Taking modula of he above equation, we get

$$M(\delta^2) = \delta^6 + (m_2^2 - 2m_1)\delta^4 + (m_1^2 - 2m_0m_2 - m_3^2)\delta^2 + (m_0^2 - m_4^2) = 0, \tag{13}$$

where

$$\begin{aligned} m_0^2 - 2m_1 &= a^2+p^2+(dR_0)^2 > 0, \\ m_1^2 - 2m_0m_2 - m_3^2 &= (a^2+p^2)(dR_0)^2 > 0, \\ m_2^2 - m_4^2 &= a^2p^2d^2(R_0-1)(R_0+1) > 0. \end{aligned}$$

Thus all the coefficient $M(\delta^2)$ are positive. Then the function $M(\delta^2)$ is monotonically increasing for $0 \leq \delta^2 \leq \infty$ with $M(0) > 0$. This implies that equation (13) has no positive roots if $R_0 > 1$. Hence, all the roots of (10) have negative real part for $\tau_1 \geq 0$ and $\tau_2 \geq 0$ if $R_0 > 1$. This completes the proof.

Theorem 4.2. *If $1 < R_0 < R_1$, then the single infection free equilibrium E_1 is globally asymptotically stable, implying that the recombinant cannot survive but the pathogen virus can.*

Proof. Let us construct the Lyapunove functional

$$W_1(t) = W_{11}(t) + \beta x_1 v_1 e^{-a_1\tau_1} W_{12}(t) + aW_{13}(t) \tag{14}$$

where

$$\begin{aligned}
W_{11}(t) &= e^{-a_1\tau_1}(x(t) - x_1 \ln x(t)) + (y(t) - y_1 \ln y(t) + z + e^{a_2\tau_2}\frac{a}{k}(v(t) - v_1 \ln v(t)) + \frac{b}{c}w(t).\\
W_{12}(t) &= \int_{t-\tau_1}^{t} (\frac{x(\xi)v(\xi)}{x_1 v_1} - \ln(\frac{x(\xi)v(\xi)}{x_1 v_1}))d\xi.\\
W_{13}(t) &= \int_{t-\tau 2}^{t} y(\xi)d\xi.
\end{aligned}$$

Taking derivative of (14), we obtain

$$\dot{W}_1(t) = \dot{W}_{11}(t) + \beta x_1 v_1 e^{-a_1\tau_1}\dot{W}_{12}(t) + a\dot{W}_{13}(t), \tag{15}$$

We find $\dot{W_{11}}(t)$,$\dot{W_{12}}(t)$ and $\dot{W_{13}}(t)$, as follows

$$\begin{aligned}
\dot{W_{11}}(t) &= e^{-a_1\tau_1}(1 - \frac{x_1}{x})\dot{x}(t) + (1 - \frac{y_1}{y})\dot{y}(t) + \dot{z}(t) + e^{a_2\tau_2}\frac{a}{k}(1 - \frac{v_1}{v})\dot{v}(t) + \frac{b}{c}\dot{w}(t)\\
&= e^{-a_1\tau_1}(1 - \frac{x_1}{x})\Big(\lambda - dx(t) - \beta x(t)v(t)\Big) + (1 - \frac{y_1}{y})\Big(\beta e^{-a_1\tau_1}x(t-\tau_1)v(t-\tau_1) - ay(t)\\
&\quad -\alpha w(t)y(t)\Big) + \Big(aw(t)y(t) - bz(t)\Big) + \frac{a}{k}(1 - \frac{v_1}{v})\Big(ke^{-a_2\tau_2}y(t-\tau_2) - pv(t)\Big)\\
&\quad +\frac{b}{c}\Big(cz(t) - qw(t)\Big)
\end{aligned} \tag{16}$$

Substituting the single infection equilibrium $E(x_1, y_1, z_1, v_1, w_1)$ in the system (1) yields the following three identities

$$\lambda = dx_1 - \beta x_1 v_1,$$

$$\beta e^{-a_1\tau_1} x_1 v_1 = ay_1,$$

$$ke^{-a\tau_2} y_1 = pv_1.$$

Using the above identities in (16) and simplifying, we get

$$\begin{aligned}\dot{W_{11}}(t) &= -e^{-a_1\tau_1}\big(2-\frac{x_1}{x}-\frac{x}{x_1}\big)+3\beta e^{-a_1\tau_1}x_1v_1-\beta e^{-a_1\tau_1}x_1v_1\frac{v_1y(t-\tau_2)}{vy_1}\\ &\quad -\frac{y_1}{y}\beta e^{-a_1\tau_1}x(t-\tau_1)v(t-\tau_1)-\beta e^{-a_1\tau_1}x(t)v(t)+\beta e^{-a_1\tau_1}x(t-\tau_1)v(t-\tau_1)\\ &\quad -ay(t)+ay(t-\tau_2)+\big(\alpha y_1-\frac{bq}{c}\big)w(t). \qquad (17)\end{aligned}$$

Calculating $\dot{W_{12}}(t)$ and $\dot{W_{13}}(t)$, we obtian

$$\dot{W_{12}}(t) = \frac{x(t)v(t)}{x_1v_1}-\ln(\frac{x(t)v(t)}{x_1v_1})-\frac{x(t-\tau_1)v(t-\tau_1)}{x_1v_1}+\ln(\frac{x(t-\tau_1)v(t-\tau_1)}{x_1v_1}). \qquad (18)$$

$$\dot{W_{13}}(t) = y(t)-y(t-\tau_2). \qquad (19)$$

Using (17), (18) and (19) in equation (15)and simplifying, we get

$$\dot{W_1}(t) = e^{-a_1\tau_1}(2-\frac{x_1}{x}-\frac{x}{x_1})+\beta x_1v_1e^{-a\tau_1}\Omega-\frac{\alpha dp}{\beta ke^{-a_2\tau_2}}(R_1-R_0). \qquad (20)$$

Now, the following inequalities hold (see [14])

$$(2-\frac{x_1}{x}-\frac{x}{x_1})\le 0$$

$$\Omega=\left(3-\frac{x_1}{x}-\frac{v_1y(t-\tau_2)}{vy_1}-\frac{y_1x(t-\tau_1)v(t-\tau_1)}{x_1v_1}y+\ln(\frac{x(t-\tau_1)v(t-\tau_1)}{x_1v_1})\right)\le 0,$$

Therefore, (20) implies that $\dot{W_1}(t)\le 0$, when $R_0\le R_1$. And the equality holds when $x=x_1$ and $y=y_1$, $v=v_1$, $z=z_1$ and $w=0$. Also, by LaSalles invariance principle [11], we conclude that E_1 is globally asymptotically stable. This completes the proof.

3. Conclusion and discussion

In this work, we have discussed the dynamics of an HIV-1 infection model with two fixed delays accounting for the time between the contacting and entering of viral into a target cell and time between the production and emission of viral particle from the infected cells. It was shown

that if the basic reproduction ratio R_0 is less than unity, then the infection-free equilibrium is locally asymptotically stable. If the basic reproduction ratio R_0 is greater than unity, the chronic-infection equilibrium exists which is locally asymptotically stable. The global stability of the infection-free equilibrium follows if $R_0 < 1$. Similarly, for chronic-infection equilibrium of proposed system is globally stable for $1 < R_0 < R_1$. Our results show the basic reproductive number can be decreased by increasing delay in latent period and virus production. Therefore, any drug that can prolong these delays, will be helpful in decreasing this infectious.

Conflict of Interests

The authors declare that there is no conflict of interests.

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