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STABILITY AND BIFURCATION ANALYSIS OF A CLASS OF DELAYED FRACTIONAL DIFFERENTIAL EQUATIONS DESCRIBING THE DYNAMICS OF HIV

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Abstract. In this paper, we propose a new delayed fractional-order model that describes the dynamics of human immunodeficiency virus (HIV). The proposed model incorporates three transmission modes, two types of infected cells, the adaptive immunity exerted by antibodies and CTL cells, two delays, one in viral production and the other in the activation time of antibodies, as well as four therapeutic parameters to represent different aspects of the therapy and the effect of memory described by Caputo fractional derivative. Additionally, we determine the equilibrium points and analyze their global stability with respect to specific threshold parameters. Moreover, we explore the existence of the Hopf bifurcation, demonstrating that the immune delay is the primary factor responsible for its occurrence.

Keywords: HIV infection; Caputo fractional derivative; delays; Hopf bifurcation; therapy.

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1. INTRODUCTION

Human immunodeficiency virus (HIV) is a virus that attacks the body's immune system. In spite of the progress of medicine around the world, the HIV infection remains a major global public health concern because, without treatment, it can progress to acquired immunodeficiency syndrome (AIDS). According to the World Health Organization (WHO) [1], HIV infection caused approximately 42.3 million deaths to date. As of the end of 2023, an estimated 39.9 million people were living with HIV, with about 65% of them residing in the WHO African region. In the same year, around 1.3 million people acquired HIV, and approximately 630 000 died from HIV-related causes. HIV is transmitted through the exchange of infected body fluids such as blood, semen, vaginal secretions, and breast milk. Additionally, it can be passed from mother to child during pregnancy, childbirth, or breastfeeding. However, casual contact, such as hugging or kissing, does not transmit HIV. Early stages of infection are often asymptomatic or present with mild flu-like symptoms, making early diagnosis difficult but critical.

Although there is no cure for HIV, it can be treated and prevented with antiretroviral therapy (ART). Untreated, it can progress to AIDS, often after many years. ART includes different classes of drugs, most notably reverse transcriptase inhibitors (RTIs) and protease inhibitors (PIs). RTIs prevent the conversion of viral RNA into DNA, which block the activity of reverse transcriptase and stop cell-to-cell transmission. PIs, on the other hand, block the protease enzyme that is crucial for the final maturation of new viral particles, which prevents infected cells from producing HIV virions. However, their introduction causes infected cells to produce non-infectious virions. However, HIV virions that were produced before the initiation of treatment remain infectious. Thus, there are two types of viral particles: those unaffected by protease inhibitors, which are still infectious, and those formed under the influence of the drugs, which are noninfectious.

The HIV weakens the immune system by targeting $CD4^{+}$T cells, which activates the body's adaptive immune response, playing a crucial role in fighting this infection. This response involves two primary forms of immunity: humoral immunity, which involves the production of antibodies by B cells that identify and bind specific viral antigens in order to neutralize the virus and prevent its entry into host cells and cellular immunity, which is mediated by cytotoxic T

lymphocytes (CTLs) that target and eliminate HIV-infected cells by recognizing viral peptides presented on the surface of these cells. This response plays an essential role in controlling viral replication, particularly in the early stages of infection. Both types of adaptive immunity, humoral and cellular, are characterized by specificity and immunological memory, allowing the immune system to respond more effectively when it encounters the virus again.

Recently, modeling the propagation and progression of HIV in the human population has attracted the attention of many researchers. Several studies have explored this infection dynamics using classical integer-order differential equations. Cai et al. [2] analyzed the effect of treatment delays on stability and showed the occurrence of Hopf bifurcations. Hattaf and Yousfi [3] investigated a mathematical model with delay to describe HIV infection of $CD4^+$T-cells during therapy. The model incorporates both therapy and delay, providing new insights into the dynamics of HIV infection under treatment. Later in 2018 [4], they proposed a mathematical model of HIV infection that incorporates both virus-to-cell and cell-to-cell transmission modes, while accounting for adaptive immunity. The study emphasized the importance of these modes in determining the stability of the disease dynamics. Ali et al. [5] modeled HIV/AIDS-TB co-infection with media awareness and studied the stability of multiple equilibria.

However, the above cited models are based on classical derivatives, which are local operators and cannot capture memory effects. This limitation has led researchers to turn to fractional differential equations (FDEs), which better reflect the memory and hereditary properties of biological processes. For example, Hajhouji et al. [6] developed a fractional HIV-1 model under Highly active antiretroviral therapy (HAART), incorporating humoral immunity and immunological memory, showing the relevance of fractional modeling in capturing long-term immune responses and treatment dynamics. Similarly, Phukan and Dutta [7], Rajivganthi and Rihan [8], developed a Caputo fractional-order model, where infection occurs through various modes, emphasizing the importance of fractional derivatives in capturing memory effects and providing a more accurate description of viral infections dynamics.

Motivated by the above biological and mathematical results, we propose a new mathematical model that describes the dynamics of HIV infection with therapy, delays and adaptive immunity. This paper is organized as follows. In Sect 2, the formulation of the developed model is

detailed. Continuing with Sect 3, we define the threshold parameters and determine the equilibrium points of our model. Sect 4 focuses on examining the global stability of the equilibria, while Sect 5 demonstrates that the second delay can induce periodic oscillations through Hopf bifurcations. Finally, the paper ends with a conclusion and some directions of future research.

2. Model Formulation and Its Special Cases

In medicine, it is known that the introduction of PIs in HIV infection leads to the emergence of two types of viruses: infectious and noninfectious viruses. Therefore, we propose the following model formulated by fractional delay differential equations (FDDEs):

$$
(1)\quad \begin{cases}
{}^{C}\mathscr{D}^{\alpha}S(t) = \lambda - dS(t) - \frac{(1-\varepsilon_1)\beta_1 S(t)V_I(t)}{1+\alpha_1 V_I(t)} - \frac{(1-\varepsilon_2)\beta_2 S(t)A(t)}{1+\alpha_2 A(t)} - \frac{(1-\varepsilon_3)\beta_3 S(t)L(t)}{1+\alpha_3 L(t)},\\
{}^{C}\mathscr{D}^{\alpha}L(t) = \eta\left(\frac{(1-\varepsilon_1)\beta_1 S(t)V_I(t)}{1+\alpha_1 V_I(t)} + \frac{(1-\varepsilon_2)\beta_2 S(t)A(t)}{1+\alpha_2 A(t)} + \frac{(1-\varepsilon_3)\beta_3 S(t)L(t)}{1+\alpha_3 L(t)}\right) - (e+r)L(t),\\
{}^{C}\mathscr{D}^{\alpha}A(t) = (1-\eta)\left(\frac{(1-\varepsilon_1)\beta_1 S(t)V_I(t)}{1+\alpha_1 V_I(t)} + \frac{(1-\varepsilon_2)\beta_2 S(t)A(t)}{1+\alpha_2 A(t)} + \frac{(1-\varepsilon_3)\beta_3 S(t)L(t)}{1+\alpha_3 L(t)}\right) + rL(t)\\
\qquad\qquad -aA(t) - p_1 A(t)C(t),\\
{}^{C}\mathscr{D}^{\alpha}V_I(t) = (1-\varepsilon_4)ke^{-m\tau_1}A(t-\tau_1) - \mu V_I(t) - pV_I(t)W(t),\\
{}^{C}\mathscr{D}^{\alpha}V_{NI}(t) = \varepsilon_4 ke^{-m\tau_1}A(t-\tau_1) - \mu V_{NI}(t),\\
{}^{C}\mathscr{D}^{\alpha}W(t) = gV_I(t-\tau_2)W(t-\tau_2) - hW(t),\\
{}^{C}\mathscr{D}^{\alpha}C(t) = \sigma A(t)C(t) - d_c C(t),
\end{cases}
$$

where $S(t), L(t), A(t), V_I(t), V_{NI}(t), W(t)$ and $C(t)$ represent respectively the concentrations of susceptible cells, non-productive infected cells, productive infected cells, infectious virus, non-infectious virus, antibodies and CTL cells. Susceptible host cells are produced at a constant rate λ, die at a rate dS, and become infected either by free infectious viruses or through direct contact with infected cells. The total infection rate is given by $\frac{(1-\varepsilon_1)\beta_1 S(t)V_I(t)}{1+\alpha_1 V_I(t)} + \frac{(1-\varepsilon_2)\beta_2 S(t)A(t)}{1+\alpha_2 A(t)} + \frac{(1-\varepsilon_3)\beta_3 S(t)L(t)}{1+\alpha_3 L(t)}$, where β_1, β_2, and β_3 represent the infection rates for virus-to-cell transmission, cell-to-cell transmission by productive infected cells, and cell-to-cell transmission by non-productive infected cells, respectively. The parameters ε_1, ε_2, and ε_3 denote the efficacy of RTIs in blocking infection through the corresponding modes of transmission. Once infected, a susceptible cell becomes either a non-productive infected cell with probability $\eta \in (0,1)$ or a productive infected cell with probability $1-\eta$. Non-productive infected cells die at rate eL and can transition into productive infected cells at rate rL. Productive infected cells die at rate

aA and are eliminated by CTLs at rate p_1AC. These productive cells are responsible for the generation of viral particles at rate k, which are either cleared at rate μ or neutralized by antibodies at rate pV_IW. Antibodies are activated in response to the infectious virus at rate gV_IW and decay at rate hW. CTL cells are stimulated by productive infected cells at rate σAC and die at rate d_cC. Furthermore, the parameter ε_4 denotes the efficacy of PIs that reduce the production of infectious virus, with τ_1 representing the intracellular delay required for newly produced viral particles to mature and become infectious. Additionally, τ_2 captures the time delay in the activation of antibodies following viral presence.

Obviously, none of the equations of system (1) depend on the variable V_{NI}. Then, model (1) can be rewritten by the following reduced system:

$$
(2)\quad \begin{cases}
{}^C\mathscr{D}^\alpha S(t) = \lambda - dS(t) - \frac{(1-\varepsilon_1)\beta_1 S(t)V_I(t)}{1+\alpha_1 V_I(t)} - \frac{(1-\varepsilon_2)\beta_2 S(t)A(t)}{1+\alpha_2 A(t)} - \frac{(1-\varepsilon_3)\beta_3 S(t)L(t)}{1+\alpha_3 L(t)},\\
{}^C\mathscr{D}^\alpha L(t) = \eta\left(\frac{(1-\varepsilon_1)\beta_1 S(t)V_I(t)}{1+\alpha_1 V_I(t)} + \frac{(1-\varepsilon_2)\beta_2 S(t)A(t)}{1+\alpha_2 A(t)} + \frac{(1-\varepsilon_3)\beta_3 S(t)L(t)}{1+\alpha_3 L(t)}\right) - (e+r)L(t),\\
{}^C\mathscr{D}^\alpha A(t) = (1-\eta)\left(\frac{(1-\varepsilon_1)\beta_1 S(t)V_I(t)}{1+\alpha_1 V_I(t)} + \frac{(1-\varepsilon_2)\beta_2 S(t)A(t)}{1+\alpha_2 A(t)} + \frac{(1-\varepsilon_3)\beta_3 S(t)L(t)}{1+\alpha_3 L(t)}\right) + rL(t)\\
\qquad\qquad -aA(t) - p_1 A(t)C(t),\\
{}^C\mathscr{D}^\alpha V_I(t) = (1-\varepsilon_4)ke^{-m\tau_1}A(t-\tau_1) - \mu V_I(t) - pV_I(t)W(t),\\
{}^C\mathscr{D}^\alpha W(t) = gV_I(t-\tau_2)W(t-\tau_2) - hW(t),\\
{}^C\mathscr{D}^\alpha C(t) = \sigma A(t)C(t) - d_cC(t).
\end{cases}
$$

In this study, we consider system (2) with the following initial conditions:

$$S(\theta) = \phi_1(\theta) \geq 0,\ L(\theta) = \phi_2(\theta) \geq 0,\ A(\theta) = \phi_3(\theta) \geq 0,\ V_I(\theta) = \phi_4(\theta) \geq 0,$$

$$W(\theta) = \phi_5(\theta) \geq 0,\ C(\theta) = \phi_6(\theta) \geq 0,\ \theta \in [-\tau, 0],\ \tau = \max\{\tau_1, \tau_2\}.$$

Here, ${}^C\mathscr{D}^\alpha$ is the Caputo fractional derivative of order α ($0 < \alpha \leq 1$) [9], defined for an arbitrary function f by

$${}^C\mathscr{D}^\alpha f(t) = \frac{1}{\Gamma(1-\alpha)}\int_0^t (t-s)^{-\alpha} f'(s)ds.$$

It is important to note that our proposed model includes numerous special cases available in the litterature. For example,

- When $\alpha = 1$, $\eta = 0$, $\beta_2 = \beta_3 = 0$, $\tau_1 = \tau_2 = 0$, $\varepsilon_2 = \varepsilon_3 = 0$, latently infected cells and adaptive immunity are neglected, we obtain the model described in [10].

- When $\alpha = 1$, $\beta_2 = \beta_3 = 0$, $\tau_1 = \tau_2 = 0$, $\varepsilon_1 = \varepsilon_2 = \varepsilon_3 = \varepsilon_4 = 0$ and adaptive immunity is ignored, we get the model in [11].
- When $\alpha = 1$, $\varepsilon_1 = \varepsilon_2 = \varepsilon_3 = \varepsilon_4 = 0$,$\tau_1 = \tau_2 = 0$ and adaptive immunity is neglected, we obtain the simplified version of the Hattaf and Dutta model [12].
- When $\alpha_1 = \alpha_2 = 1$, $\beta_3 = 0$, $\varepsilon_1 = \varepsilon_2 = \varepsilon_3 = \varepsilon_4 = 0$, $\tau_2 = 0$ and cellular immunity is excluded, we recover the Rajivganthi and Rihan model [8].
- When $\eta = 1$, $\varepsilon_1 = \varepsilon_2 = \varepsilon_3 = \varepsilon_4 = 0$, $\tau_1 = \tau_2 = 0$ and adaptive immunity is neglected, the system corresponds to the fractional model introduced in [7] for HIV dynamics is obtained.

3. Equilibria and Threshold Parameters

It is evident that our model (2) always possesses a unique equilibrium point $E_0 = (S_0, 0, 0, 0, 0, 0)$, where $S_0 = \frac{\lambda}{d}$. Then we define the basic reproduction number $\mathscr{R}_0$ of our system as follows

$$\mathscr{R}_0 = \frac{(\theta((1-\varepsilon_4)ke^{-m\tau_1}(1-\varepsilon_1)\beta_1 + \mu(1-\varepsilon_2)\beta_2) + a\mu\eta(1-\varepsilon_3)\beta_3)S_0}{\mu a(e+r)}, \tag{3}$$

where $\theta = r + (1-\eta)e$.

The other equilibrium points of the model (2) satisfy the following system

$$\begin{cases} \lambda - dS - \frac{(1-\varepsilon_1)\beta_1 SV_I}{1+\alpha_1 V_I} - \frac{(1-\varepsilon_2)\beta_2 SA}{1+\alpha_2 A} - \frac{(1-\varepsilon_3)\beta_3 SL}{1+\alpha_3 L} = 0, \\ \eta\left(\frac{(1-\varepsilon_1)\beta_1 SV_I}{1+\alpha_1 V_I} + \frac{(1-\varepsilon_2)\beta_2 SA}{1+\alpha_2 A} + \frac{(1-\varepsilon_3)\beta_3 SL}{1+\alpha_3 L}\right) - (e+r)L = 0, \\ (1-\eta)\left(\frac{(1-\varepsilon_1)\beta_1 SV_I}{1+\alpha_1 V_I} + \frac{(1-\varepsilon_2)\beta_2 SA}{1+\alpha_2 A} + \frac{(1-\varepsilon_3)\beta_3 SL}{1+\alpha_3 L}\right) + rL - aA - p_1 AC = 0, \\ (1-\varepsilon_4)ke^{-m\tau_1}A - \mu V_I - pV_I W = 0, \\ gV_I W - hW = 0, \\ \sigma AC - d_c C = 0. \end{cases} \tag{4}$$

By using the last two equations of the system (4), we obtain $W = 0$ or $V_I = \frac{h}{g}$ and $C = 0$ or $A = \frac{d_c}{\sigma}$. Then we discuss four cases.

- If $W = 0$ and $C = 0$, we get $L = \frac{\eta(\lambda - dS)}{e+r}$, $A = \frac{(r+(1-\eta)e)(\lambda - dS)}{a(e+r)}$, $V_I = \frac{(1-\varepsilon_4)k(r+(1-\eta)e)e^{-m\tau_1}(\lambda - dS)}{a\mu(e+r)}$ and

$$\frac{(1-\varepsilon_1)\beta_1 S(1-\varepsilon_4)k(r+(1-\eta)e)e^{-m\tau_1}}{(1+\alpha_1 f(S))}+\frac{(1-\varepsilon_2)\beta_2 S(r+(1-\eta)e)\mu}{(1+\alpha_2 g(S))}$$
$$+\frac{(1-\varepsilon_3)\beta_3 S\eta\mu a}{(1+\alpha_3 Q(s))}-a\mu(e+r)=0$$

with $f(S)=\frac{(1-\varepsilon_4)k(r+(1-\eta)e)e^{-m\tau_1}(\lambda-dS)}{\mu a(e+r)}, g(S)=\frac{(r+(1-\eta)e)(\lambda-dS)}{a(e+r)}$ and $Q(S)=\frac{\eta(\lambda-dS)}{e+r}$. Since $L\geq 0$, we have $S\leq\frac{\lambda}{d}$. This implies that there is no biological equilibrium when $S>\frac{\lambda}{d}$.

Let F be a function defined on the closed interval $[0,\frac{\lambda}{d}]$ as follows

$$F(S)=\frac{(1-\varepsilon_1)\beta_1 S(1-\varepsilon_4)k(r+(1-\eta)e)e^{-m\tau_1}}{(1+\alpha_1 f(S))}+\frac{(1-\varepsilon_2)\beta_2 S(r+(1-\eta)e)\mu}{(1+\alpha_2 g(S))}$$
$$+\frac{(1-\varepsilon_3)\beta_3\eta S\mu a}{(1+\alpha_3 Q(S))}-a\mu(e+r).$$

We have $F(0)=-a\mu(e+r)<0, F(\frac{\lambda}{d})=\mu a(e+r)(\mathscr{R}_0-1)$ and

$$F'(S)=\frac{(1-\varepsilon_1)\beta_1(1-\varepsilon_4)k(r+(1-\eta)e)e^{-m\tau_1}}{(1+\alpha_1 f(S))^2}$$
$$+\frac{\alpha_1(1-\varepsilon_1)\beta_1(1-\varepsilon_4)^2k^2e^{-2m\tau_1}(r+(1-\eta)e)^2\lambda}{\mu a(e+r)(1+\alpha_1 f(S))^2}$$
$$+\frac{(1-\varepsilon_2)\beta_2\mu(r+(1-\eta)e)a(e+r)+(1-\varepsilon_2)\beta_2\mu(r+(1-\eta)e)^2\alpha_2\lambda}{a(e+r)(1+\alpha_2 g(S))^2}$$
$$+\frac{(1-\varepsilon_3)\beta_3\mu a\eta(e+r)+(1-\varepsilon_3)\beta_3\alpha_3\eta^2\mu a\lambda}{(e+r)(1+\alpha_3 Q(S))^2}>0.$$

Then the equation $F(S)=0$ has a unique solution $S_1\in(0,\frac{\lambda}{d})$ if $\mathscr{R}_0>1$. Therefore, the model (2) has a unique equilibrium point without immune response $E_1(S_1,L_1,A_1,V_{I_1},0,0)$ when $R_0>1$.

- If $W\neq 0$ and $C=0$, then $V_I=\frac{h}{g}$. Based on the system (4), we get $L=\frac{\eta(\lambda-dS)}{e+r}, A=\frac{(r+(1-\eta)e)(\lambda-dS)}{a(e+r)}$, $W=\frac{g(1-\varepsilon_4)k(r+(1-\eta)e)e^{-m\tau_1}(\lambda-dS)-\mu ah(e+r)}{aph(e+r)}$ and

$$\frac{(1-\varepsilon_1)\beta_1 Sh(e+r)}{g+\alpha_1 h}+\frac{(1-\varepsilon_2)\beta_2 S(r+(1-\eta)e)(\lambda-dS)}{a(1+\alpha_2 u(S))}+\frac{(1-\varepsilon_3)\beta_3\eta S(\lambda-dS)}{1+\alpha_3 v(S)}$$
$$-(e+r)(\lambda-dS)=0,$$

where $u(S)=\frac{(r+(1-\eta)e)(\lambda-dS)}{a(e+r)}$ and $v(S)=\frac{\eta(\lambda-dS)}{e+r}$.

Since $W \geq 0$, we have $S \leq \frac{\lambda}{d} - \frac{\mu ah(e+r)}{dgk(r+(1-\eta)e)e^{-m\tau_1}}$. This implies that there is no equilibrium when $S > \frac{\lambda}{d} - \frac{\mu ah(e+r)}{dg(1-\varepsilon_4)k(r+(1-\eta)e)e^{-m\tau_1}}$ or $\frac{\lambda}{d} - \frac{\mu ah(e+r)}{dg(1-\varepsilon_4)k(r+(1-\eta)e)e^{-m\tau_1}} \leq 0$.
Let's consider $s^* = \frac{\lambda}{d} - \frac{\mu ah(e+r)}{dg(1-\varepsilon_4)k(r+(1-\eta)e)e^{-m\tau_1}}$ and G the function defined on the closed interval $[0, s^*]$ as follows

$$\begin{aligned} G(S) =& \frac{(1-\varepsilon_1)\beta_1 Sh(e+r)}{g+\alpha_1 h} + \frac{(1-\varepsilon_2)\beta_2 S(r+(1-\eta)e)(\lambda - dS)}{a(1+\alpha_2 u(S))} \\ &+ \frac{(1-\varepsilon_3)\beta_3 \eta S(\lambda - dS)}{1+\alpha_3 v(S)} - (e+r)(\lambda - dS). \end{aligned}$$

We have $G(0) = -\lambda(e+r) < 0$, and

$$\begin{aligned} G'(S) =& \frac{(1-\varepsilon_1)\beta_1 h(e+r)}{g+\alpha_1 h} + \frac{(1-\varepsilon_2)\beta_2 (r+(1-\eta)e)(\lambda - dS)}{a(1+\alpha_2 u(S))} \\ &- \frac{(1-\varepsilon_2)\beta_2 S(r+(1-\eta)e)(\lambda - dS)\alpha_2 u'(S)}{a(1+\alpha_2 u(S))^2} + \frac{(1-\varepsilon_3)\beta_3(\lambda - dS)}{1+\alpha_3 v(S)} \\ &- \frac{(1-\varepsilon_3)\beta_3 S(\lambda - dS)\alpha_3 v'(S)}{(1+\alpha_3 v(S))^2} + d\left(e+r - \frac{(1-\varepsilon_2)\beta_2 S(r+(1-\eta)e)}{a(1+\alpha_2 u(S))}\right. \\ &\left. - \frac{(1-\varepsilon_3)\beta_3 \eta S}{1+\alpha_3 v(S)}\right). \end{aligned}$$

Since $u'(S) = \frac{-d(r+(1-\eta)e)}{(e+r)a} < 0$, $v'(S) = \frac{-d\eta}{e+r} < 0$ and

$$e+r - \frac{(1-\varepsilon_2)\beta_2 S(r+(1-\eta)e)}{a(1+\alpha_2 u(S))} - \frac{(1-\varepsilon_3)\beta_3 \eta S}{1+\alpha_3 v(S)} = \frac{(1-\varepsilon_1)\beta_1 Sh(e+r)}{(g+\alpha_1 h)(\lambda - dS)} > 0,$$

then $G'(S) > 0$.

When the humoral immune response has not been established, we have $gV_{I_1} - h \leq 0$. Hence, we define another threshold parameter called the reproduction number for humoral immunity as follows

$$\mathscr{R}_1^W = \frac{gV_{I_1}}{h}, \tag{5}$$

where $\frac{1}{h}$ is the average life span of antibodies and V_1 is the quantity of viruses at the steady state E_1. So, the number $\mathscr{R}_1^W$ can biologically determine the average number of antibodies activated by virus.

Note that when $\mathscr{R}_1^W > 1$, we have $V_{I_1} > \frac{h}{g}$ and $S_1 < \frac{\lambda}{d} - \frac{\mu ah(e+r)}{dg(1-\varepsilon_4)ke^{-m\tau_1}(r+(1-\eta)e)}$ so that we will subsequently demonstrate that $G(s^*) > 0$. And thus the equation $G(S) = 0$

admits a unique solution $S_2 \in (0, \frac{\lambda}{d} - \frac{\mu a h(e+r)}{dg(1-\varepsilon_4)ke^{-m\tau_1}(r+(1-\eta)e)})$ if $\mathscr{R}_1^W > 1$. Therefore, the model (2) has a unique infection equilibrium with only humoral immunity $E_2(S_2, L_2, A_2, V_{I_2}, W_2, 0)$ when $\mathscr{R}_1^W > 1$.

- If $W = 0$ and $C \neq 0$, then $A = \frac{d_c}{\sigma}$. Based on the system (4), we get $L = \frac{\eta(\lambda - dS)}{e+r}, V_I = \frac{(1-\varepsilon_4)ke^{-m\tau_1}d_c}{\sigma\mu}$, $C = \frac{(r+(1-\eta)e)\sigma(\lambda - dS) - ad_c(e+r)}{d_c p_1(e+r)}$ and

$$\frac{(1-\varepsilon_1)\beta_1 S(1-\varepsilon_4)ke^{-m\tau_1}d_c(e+r)}{\mu\sigma + \alpha_1(1-\varepsilon_4)ke^{-m\tau_1}d_c} + \frac{(1-\varepsilon_2)\beta_2 S d_c(e+r)}{\sigma + \alpha_2 d_c} + \frac{(1-\varepsilon_3)\beta_3\eta S(\lambda - dS)}{1+\alpha_3 h(S)} - (e+r)(\lambda - dS) = 0,$$

where $h(S) = \frac{\eta(\lambda - dS)}{e+r}$.

Since $C \geq 0$, we have $S \leq \frac{\lambda}{d} - \frac{ad_c(e+r)}{d(r+(1-\eta)e)\sigma}$. This implies that there is no equilibrium when $S > \frac{\lambda}{d} - \frac{ad_c(e+r)}{d(r+(1-\eta)e)\sigma}$ or $\frac{\lambda}{d} - \frac{ad_c(e+r)}{d(r+(1-\eta)e)\sigma} \leq 0$. Let's consider $s_1 = \frac{\lambda}{d} - \frac{ad_c(e+r)}{d(r+(1-\eta)e)\sigma}$ and H the function defined on the closed interval $[0, s_1]$ as follows

$$H(S) = \frac{(1-\varepsilon_1)\beta_1 S(1-\varepsilon_4)ke^{-m\tau_1}d_c(e+r)}{\mu\sigma + \alpha_1(1-\varepsilon_4)ke^{-m\tau_1}d_c} + \frac{(1-\varepsilon_2)\beta_2 S d_c(e+r)}{\sigma + \alpha_2 d_c} + \frac{(1-\varepsilon_3)\beta_3\eta S(\lambda - dS)}{1+\alpha_3 h(S)} - (e+r)(\lambda - dS).$$

We have $H(0) = -\lambda(e+r) < 0$, and

$$H'(S) = \frac{(1-\varepsilon_1)\beta_1(1-\varepsilon_4)ke^{-m\tau_1}d_c(e+r)}{\mu\sigma + \alpha_1(1-\varepsilon_4)ke^{-m\tau_1}d_c} + \frac{(1-\varepsilon_2)\beta_2 d_c(e+r)}{\sigma + \alpha_2 d_c} + \frac{(1-\varepsilon_3)\beta_3\eta(\lambda - dS)}{1+\alpha_3 h(S)} - \frac{(1-\varepsilon_3)\beta_3\eta S(\lambda - dS)\alpha_3 h'(S)}{(1+\alpha_3 h(S))^2} + d(e+r - \frac{(1-\varepsilon_3)\beta_3\eta S}{1+\alpha_3 h(S)}).$$

Since $h'(S) = \frac{-d\eta}{e+r} < 0$ and

$$e+r - \frac{(1-\varepsilon_3)\beta_3\eta S}{1+\alpha_3 h(S)} = \frac{(1-\varepsilon_1)\beta_1 S(1-\varepsilon_4)ke^{-m\tau_1}d_c(e+r)}{(\mu\sigma + \alpha_1(1-\varepsilon_4)ke^{-m\tau_1}d_c)(\lambda - dS)} + \frac{(1-\varepsilon_2)\beta_2 S d_c(e+r)}{(\sigma + \alpha_2 d_c)(\lambda - dS)} > 0,$$

then $H'(S) > 0$. When the cellular immune response has not been established, we have $\sigma A_1 - d_c \leq 0$. Hence, we define another threshold parameter called the reproduction number for cellular immunity as follows

$$\mathscr{R}_1^C = \frac{\sigma A_1}{d_c}, \tag{6}$$

which represents the average numbre of the activated CTL cells by the productive infected cells during the period of infection when the humoral immunity have not been started.

When $\mathscr{R}_1^C > 0$, we have $A_1 > \frac{d_c}{\sigma}$ and $S_1 < \frac{\lambda}{d} - \frac{ad_c(e+r)}{d(r+(1-\eta)e)\sigma}$ so that we obtain $H(s_1) > 0$. Hence, when $\mathscr{R}_1^C > 1$, there exists a unique infection equilibrium with only cellular immunity $E_3(S_3, L_3, A_3, V_{I_3}, 0, C_3)$.

- If $W \neq 0$ and $C \neq 0$, then $V_I = \frac{h}{g}$ and $A = \frac{d_c}{\sigma}$. From the system (4), we obtain $L = \frac{\eta(\lambda - dS)}{e+r}$, $W = \frac{g(1-\varepsilon_4)k(r+(1-\eta)e)e^{-m\tau_1}(\lambda - dS) - \mu ah(e+r)}{aph(e+r)}$, $C = \frac{(r+(1-\eta)e)\sigma(\lambda - dS) - ad_c(e+r)}{d_c p_1(e+r)}$ and

$$\frac{(1-\varepsilon_1)\beta_1 Sh(e+r)}{g+\alpha_1 h} + \frac{(1-\varepsilon_2)\beta_2 Sd_c(e+r)}{\sigma+\alpha_2 d_c} + \frac{(1-\varepsilon_3)\beta_3\eta S(\lambda - dS)}{1+\alpha_3 R(S)} - (e+r)(\lambda - dS) = 0,$$

where $R(S) = \frac{\eta(\lambda - dS)}{e+r}$.

Since $C \geq 0$, we have $S \leq \frac{\lambda}{d} - \frac{ad_c(e+r)}{\sigma(r+(1-\eta)e)d}$. This implies that there is no equilibrium when $S > \frac{\lambda}{d} - \frac{ad_c(e+r)}{\sigma(r+(1-\eta)e)d}$ or $\frac{\lambda}{d} - \frac{ad_c(e+r)}{\sigma(r+(1-\eta)e)d} \leq 0$. Let's consider $s_2 = \frac{\lambda}{d} - \frac{ad_c(e+r)}{\sigma(r+(1-\eta)e)d}$ and M the function defined on the closed interval $[0, s_2]$ as follows

$$M(S) = \frac{(1-\varepsilon_1)\beta_1 Sh(e+r)}{g+\alpha_1 h} + \frac{(1-\varepsilon_2)\beta_2 Sd_c(e+r)}{\sigma+\alpha_2 d_c} + \frac{(1-\varepsilon_3)\beta_3\eta S(\lambda - dS)}{1+\alpha_3 R(S)} - (e+r)(\lambda - dS).$$

We have $M(0) = -\lambda(e+r)$, and

$$\begin{aligned} M'(S) = &\frac{(1-\varepsilon_1)\beta_1 h(e+r)}{g+\alpha_1 h} + \frac{(1-\varepsilon_2)\beta_2 d_c(e+r)}{\sigma+\alpha_2 d_c} + \frac{(1-\varepsilon_3)\beta_3\eta(\lambda - dS)}{1+\alpha_3 R(S)} \\ &- \frac{(1-\varepsilon_3)\beta_3\eta S(\lambda - dS)\alpha_3 R'(S)}{(1+\alpha_3 h(S))^2} + d(e+r - \frac{(1-\varepsilon_3)\beta_3\eta S}{1+\alpha_3 h(S)}) > 0. \end{aligned}$$

Now, in addition to $\mathscr{R}_1^C$, we define the reproduction number for cellular immunity in competition by

$$\mathscr{R}_2^C = \frac{\sigma A_2}{d_c}, \tag{7}$$

which represents the average number of the activates CTL cells by productive infected cells during the period of infection in the presence of humoral immunity. If $\mathscr{R}_2^C > 1$, then $S_2 > \frac{\lambda}{d} - \frac{ad_c(e+r)}{\sigma(r+(1-\eta)e)d}$ so that we get $M(s_2) > 0$. Hence, the equation $M(S) = 0$ has a unique solution $S_4 \in (0, \frac{\lambda}{d} - \frac{ad_c(e+r)}{\sigma(r+(1-\eta)e)d})$. By the system (4), we obtain $W =$

$\frac{g(1-\varepsilon_4)ke^{-m\tau_1}d_c-\mu h\sigma}{ph\sigma}$. As $W \geq 0$, In addition to $\mathscr{R}_1^W$, we define the reproduction number for humoral immunity in competition as

$$\mathscr{R}_2^W = \frac{gV_{I_3}}{h}, \tag{8}$$

wich represents the the average number of the activates antibodies by virus during the period of infection when the cellular immunity is established. Then we conclude that when $\mathscr{R}_2^W > 1$ and $\mathscr{R}_2^C > 1$ there exists a unique infection equilibrium with both humoral and cellular immunity $E_4 = (S_4, L_4, A_4, V_{I_4}, W_4, C_4)$.

Theorem 1. *Let $\mathscr{R}_0$, $\mathscr{R}_1^W$, $\mathscr{R}_1^C$, $\mathscr{R}_2^C$ and $\mathscr{R}_2^W$ defined respectively in* (3)*,* (5)*,* (6)*,* (7) *and* (8)*.*

(1) If $\mathscr{R}_0 \leq 1$, then model (2) *has a unique infection-free equilibrium $E_0 = (S_0, 0, 0, 0, 0, 0)$, where $S_0 = \frac{\lambda}{d}$.*

(2) If $\mathscr{R}_0 > 1$, then model (2) *has a unique immune-free infection equilibrium $E_1 = (S_1, L_1, A_1, V_{I_1}, 0, 0)$ besides E_0, where $S_1 \in (0, \frac{\lambda}{d}), L_1 = \frac{\eta(\lambda - dS_1)}{e+r}, A_1 = \frac{(r+(1-\eta)e)(\lambda - dS_1)}{a(e+r)}$ and*
$V_{I_1} = \frac{(1-\varepsilon_4)k(r+(1-\eta)e)e^{-m\tau_1}(\lambda - dS_1)}{\mu a(e+r)}$.

(3) If $\mathscr{R}_1^W > 1$, then model (2) *has a unique infection equilibrium with only humoral immunity $E_2 = (S_2, L_2, A_2, V_{I_2}, W_2, 0)$ besides E_0 and E_1, where $S_2 \in (0, \frac{\lambda}{d} - \frac{\mu ah(e+r)}{dg(1-\varepsilon_4)k(r+(1-\eta)e)e^{-m\tau_1}})$,*
$V_{I_2} = \frac{h}{g}, L_2 = \frac{\eta(\lambda - dS_2)}{e+r}, A_2 = \frac{(r+(1-\eta)e)(\lambda - dS_2)}{a(e+r)}$ and $W_2 = \frac{g(1-\varepsilon_4)k(r+(1-\eta)e)e^{-m\tau_1}(\lambda - dS_2) - \mu ah(e+r)}{aph(e+r)}$.

(4) If $\mathscr{R}_1^C > 1$, then model (2) *has a unique infection equilibrium with only cellular immunity $E_3 = (S_3, L_3, A_3, V_{I_3}, 0, C_3)$ besides E_0, E_1 and E_2 where $S_3 \in (0, \frac{\lambda}{d} - \frac{ad_c(e+r)}{d(r+(1-\eta)e)\sigma})$, $L_3 = \frac{\eta(\lambda - dS_3)}{e+r}$, $V_{I_3} = \frac{(1-\varepsilon_4)ke^{-m\tau_1}d_c}{\sigma\mu}$ and $C_3 = \frac{(r+(1-\eta)e)\sigma(\lambda - dS_3) - ad_c(e+r)}{d_c p_1(e+r)}$.*

(5) If $\mathscr{R}_2^W > 1$ and $\mathscr{R}_2^C > 1$, then model (2) *has a unique infection equilibrium with both humoral and cellular immunity $E_4 = (S_4, L_4, A_4, V_{I_4}, W_4, C_4)$ besides E_0, E_1, E_2 and E_3 where $S_4 \in (0, \frac{\lambda}{d} - \frac{ad_c(e+r)}{\sigma(r+(1-\eta)e)d})$, $L_4 = \frac{\eta(\lambda - dS_4)}{e+r}$, $A_4 = \frac{d_c}{\sigma}$, $V_{I_4} = \frac{h}{g}$, $W_4 = \frac{g(1-\varepsilon_4)ke^{-m\tau_1}d_c - \mu h\sigma}{ph\sigma}$ and $C_4 = \frac{\sigma(r+(1-\eta)e)(\lambda - dS_4) - ad_c(e+r)}{p_1 d_c(e+r)}$.*

4. GLOBAL STABILITY

Theorem 2. *If $\mathscr{R}_0 \leq 1$, then the infection-free equilibrium E_0 is globally asymptotically stable for any delays $\tau_1, \tau_2 \geq 0$.*

Proof. Let $u = (S, L, A, V_I, W, C)$ be a solution of (2) and let's construct a Lyapunov function in E_0 as follows

$$\mathscr{H}_0(u) = \frac{\eta}{2S_0}(S - S_0)^2 + L.$$

Further, $\mathscr{H}_0(u) = 0$ if and only if $S(t) = S_0, L(t) = A(t) = V_I(t) = W(t) = C(t) = 0$.

Using the property of fractional derivatives referenced in [13], we obtain

$$\begin{aligned}
{}^{C}D^{\alpha}\mathscr{H}_0 &= \frac{\eta}{2S_0}{}^{C}D^{\alpha}(S - S_0)^2 + {}^{C}D^{\alpha}L, \\
&\leq \frac{\eta}{S_0}(S - S_0)\,{}^{C}D^{\alpha}S(t) + {}^{C}D^{\alpha}L(t), \\
&\leq \frac{\eta}{S_0}(S - S_0)\left(\lambda - dS - \frac{(1-\varepsilon_1)\beta_1 S V_I}{1+\alpha_1 V_I} - \frac{(1-\varepsilon_2)\beta_2 S A}{1+\alpha_2 A} - \frac{(1-\varepsilon_3)\beta_3 S L}{1+\alpha_3 L}\right) \\
&\quad + \eta\left(\frac{(1-\varepsilon_1)\beta_1 S V_I}{1+\alpha_1 V_I} + \frac{(1-\varepsilon_2)\beta_2 S A}{1+\alpha_2 A} + \frac{(1-\varepsilon_3)\beta_3 S L}{1+\alpha_3 L}\right) - (e+r)L.
\end{aligned}$$

Utilizing the infection-free equilibrium condition of the model $S_0 = \frac{\lambda}{d}$, we get

$$\begin{aligned}
{}^{C}D^{\alpha}\mathscr{H}_0 &\leq -\frac{d\eta}{S_0}(S - S_0)^2 - \frac{\eta}{S_0}\left(\frac{(1-\varepsilon_1)\beta_1 V_I}{1+\alpha_1 V_I} + \frac{(1-\varepsilon_2)\beta_2 A}{1+\alpha_2 A} + \frac{(1-\varepsilon_3)\beta_3 L}{1+\alpha_3 L}\right)(S - S_0)^2 \\
&\quad + \eta\left(\frac{(1-\varepsilon_1)\beta_1 V_I}{1+\alpha_1 V_I} + \frac{(1-\varepsilon_2)\beta_2 A}{1+\alpha_2 A} + \frac{(1-\varepsilon_3)\beta_3 L}{1+\alpha_3 L}\right) S_0 - (e+r)L, \\
&\leq -\frac{\eta}{S_0}\left(d + \frac{(1-\varepsilon_1)\beta_1 V_I}{1+\alpha_1 V_I} + \frac{(1-\varepsilon_2)\beta_2 A}{1+\alpha_2 A} + \frac{(1-\varepsilon_3)\beta_3 L}{1+\alpha_3 L}\right)(S - S_0)^2 \\
&\quad + \eta\left(\frac{(1-\varepsilon_1)\beta_1 k e^{-m\tau_1}(r + (1-\eta)e)L}{\mu a \eta} + \frac{(1-\varepsilon_2)\beta_2 (r + (1-\eta)e)L}{a\eta} + (1-\varepsilon_3)\beta_3 L\right) S_0 \\
&\quad - (e+r)L, \\
&\leq -\frac{\eta}{S_0}\left(d + \frac{(1-\varepsilon_1)\beta_1 V_I}{1+\alpha_1 V_I} + \frac{(1-\varepsilon_2)\beta_2 A}{1+\alpha_2 A} + \frac{(1-\varepsilon_3)\beta_3 L}{1+\alpha_3 L}\right)(S - S_0)^2 + (e+r)(\mathscr{R}_0 - 1)L.
\end{aligned}$$

Based on the assumptions $\mathscr{R}_0 \leq 1$, we obtain ${}^{C}D^{\alpha}\mathscr{H}_0(t) < 0$, with equality if and only if $S = S_0, L = 0, A = 0, V_I = 0, W = 0$ and $C = 0$. Consequently, the largest invariant set of $\{(S, L, A, V_I, W, C) \in \mathbb{R}^6_+ : {}^{C}D^{\alpha}\mathscr{H}_0(t) = 0\}$ is the singleton $\{E_0\}$. Therefore, by the LaSalle's invariance principle [14], the equilibrium point E_0 is globally asymptotically stable. □

Assume that $\mathscr{R}_0 > 1$. We now state the following theorems under this condition.

Theorem 3. *If $\mathscr{R}_1^W \leq 1$ and $\mathscr{R}_1^C \leq 1$ then the immune-free infection equilibrium E_1 is globally asymptotically stable for $\eta = 1$ and any delays $\tau_1, \tau_2 \geq 0$.*

Proof. Let $u = (S, L, A, V_I, W, C)$, to prove E_1 is globally asymptotically stable, construct the following Lyapunov functional

$$\begin{aligned}
\mathscr{H}_1(u) =& S_1\Phi\left(\frac{S}{S_1}\right) + L_1\Phi\left(\frac{L}{L_1}\right) + \frac{1}{rL_1}\left(\frac{(1-\varepsilon_1)\beta_1 S_1 V_{I_1}}{1+\alpha_1 V_{I_1}} + \frac{(1-\varepsilon_2)\beta_2 S_1 A_1}{1+\alpha_2 A_1}\right) A_1\Phi\left(\frac{A}{A_1}\right) \\
&+ \frac{(1-\varepsilon_1)\beta_1 S_1 V_{I_1} e^{m\tau_1}}{(1-\varepsilon_4)kA_1(1+\alpha_1 V_{I_1})} V_{I_1}\Phi\left(\frac{V}{V_{I_1}}\right) + \frac{p(1-\varepsilon_1)\beta_1 S_1 V_{I_1} e^{m\tau_1}}{g(1-\varepsilon_4)kA_1(1+\alpha_1 V_{I_1})} W \\
&+ \frac{p_1}{\sigma r L_1}\left(\frac{(1-\varepsilon_1)\beta_1 S_1 V_{I_1}}{1+\alpha_1 V_{I_1}} + \frac{(1-\varepsilon_2)\beta_2 S_1 A_1}{1+\alpha_2 A_1}\right) C \\
&+ \frac{(1-\varepsilon_1)\beta_1 S_1 V_{I_1}}{1+\alpha_1 V_{I_1}} {}^C D_{\tau_1}^{-\alpha}\left(\frac{A(t-\sigma)}{A_1} - 1 - ln\frac{A(t-\sigma)}{A_1}\right) \\
&+ \frac{p(1-\varepsilon_1)\beta_1 S_1 V_{I_1} e^{m\tau_1}}{(1-\varepsilon_4)kA_1(1+\alpha_1 V_{I_1})} {}^C D_{\tau_2}^{-\alpha} V_I(t-\sigma) W(t-\sigma),
\end{aligned}$$

where ${}^C D_{\tau}^{-\alpha}$ represents the fractional integral, $\sigma \in [0, \tau]$ and $\Phi(x) = x - 1 - ln(x)$, for $x > 0$. It is clear that $\Phi(x) \geq 0$ for all $x > 0$, and $\Phi(x) = 0$ if and only if $x = 1$. Thus, $\mathscr{H}_1(S, L, A, V_I, W, C) > 0$ for all $S, L, A, V_I, W, C > 0$ and $\mathscr{H}_1(S_1, L_1, A_1, V_{I_1}, W_1, C_1) = 0$.

By applying the property of fractional derivatives presented in [15], we get

$$\begin{aligned}
{}^C D^{\alpha}\mathscr{H}_1 \leq& \left(1 - \frac{S_1}{S}\right) {}^C D^{\alpha} S(t) + \left(1 - \frac{L_1}{L}\right) {}^C D^{\alpha} L(t) \\
&+ \frac{1}{rL_1}\left(\frac{(1-\varepsilon_1)\beta_1 S_1 V_{I_1}}{1+\alpha_1 V_{I_1}} + \frac{(1-\varepsilon_2)\beta_2 S_1 A_1}{1+\alpha_2 A_1}\right)\left(1 - \frac{A_1}{A}\right) {}^C D^{\alpha} A(t) \\
&+ \frac{(1-\varepsilon_1)\beta_1 S_1 V_{I_1} e^{m\tau_1}}{(1-\varepsilon_4)kA_1(1+\alpha_1 V_{I_1})}\left(1 - \frac{V_{I_1}}{V_I}\right) {}^C D^{\alpha} V_I(t) + \frac{p(1-\varepsilon_1)\beta_1 S_1 V_{I_1} e^{m\tau_1}}{g(1-\varepsilon_4)kA_1(1+\alpha_1 V_{I_1})} {}^C D^{\alpha} W(t) \\
&+ \frac{p_1}{\sigma r L_1}\left(\frac{(1-\varepsilon_1)\beta_1 S_1 V_{I_1}}{1+\alpha_1 V_{I_1}} + \frac{(1-\varepsilon_2)\beta_2 S_1 A_1}{1+\alpha_2 A_1}\right) {}^C D^{\alpha} C(t) \\
&+ \frac{(1-\varepsilon_1)\beta_1 S_1 V_{I_1}}{1+\alpha_1 V_{I_1}}\left(\frac{A(t)}{A_1} - ln\frac{A(t)}{A_1} - \frac{A(t-\tau_1)}{A_1} + ln\frac{A(t-\tau_1)}{A_1}\right) \\
&+ \frac{p(1-\varepsilon_1)\beta_1 S_1 V_{I_1} e^{m\tau_1}}{(1-\varepsilon_4)kA_1(1+\alpha_1 V_{I_1})}(V_I(t)W(t) - V_I(t-\tau_2)W(t-\tau_2)).
\end{aligned}$$

Now, by using equilibrium conditions, we have

$$\lambda = dS_1 + \frac{(1-\varepsilon_1)\beta_1 S_1 V_{I_1}}{1+\alpha_1 V_{I_1}} + \frac{(1-\varepsilon_2)\beta_2 S_1 A_1}{1+\alpha_2 A_1} + \frac{(1-\varepsilon_3)\beta_3 S_1 L_1}{1+\alpha_3 L_1},$$

$$\frac{(1-\varepsilon_1)\beta_1 S_1 V_{I_1}}{1+\alpha_1 V_{I_1}}+\frac{(1-\varepsilon_2)\beta_2 S_1 A_1}{1+\alpha_2 A_1}+\frac{(1-\varepsilon_3)\beta_3 S_1 L_1}{1+\alpha_3 L_1}=(e+r)L_1,$$

$$rL_1=aA_1,\mu V_{I_1}=(1-\varepsilon_4)ke^{-m\tau_1}A_1,$$

then we obtain

$$\begin{aligned}
&{}^{C}D^{\alpha}\mathscr{H}_1\\
\leq&\frac{(1-\varepsilon_1)\beta_1 S_1 V_{I_1}}{1+\alpha_1 V_{I_1}}\left(-1-\frac{V_I}{V_{I_1}}+\frac{(1+\alpha_1 V_{I_1})V_I}{(1+\alpha_1 V_I)V_{I_1}}+\frac{1+\alpha_1 V_I}{1+\alpha_1 V_{I_1}}\right)\\
&+\frac{(1-\varepsilon_2)\beta_2 S_1 A_1}{1+\alpha_2 A_1}\left(-1-\frac{A}{A_1}+\frac{(1+\alpha_2 A_1)A}{(1+\alpha_2 A)A_1}+\frac{1+\alpha_2 A}{1+\alpha_2 A_1}\right)\\
&+\frac{(1-\varepsilon_3)\beta_3 S_1 L_1}{1+\alpha_3 L_1}\left(-1-\frac{L}{L_1}+\frac{(1+\alpha_3 L_1)L}{(1+\alpha_3 L)L_1}+\frac{1+\alpha_3 L}{1+\alpha_3 L_1}\right)\\
&-\frac{(1-\varepsilon_1)\beta_1 S_1 V_{I_1}}{1+\alpha_1 V_{I_1}}\left[\Phi\left(\frac{S_1}{S}\right)+\Phi\left(\frac{LA_1}{L_1A}\right)+\Phi\left(\frac{A(t-\tau)V_{I_1}}{A_1V_I}\right)\right.\\
&\left.+\Phi\left(\frac{SV_IL_1(1+\alpha_1V_{I_1})}{S_1V_{I_1}L(1+\alpha_1V_I)}\right)+\Phi\left(\frac{1+\alpha_1V_I}{1+\alpha_1V_{I_1}}\right)\right]-\frac{(1-\varepsilon_2)\beta_2 S_1 A_1}{1+\alpha_2 A_1}\left[\Phi\left(\frac{S_1}{S}\right)+\Phi\left(\frac{LA_1}{L_1A}\right)\right.\\
&\left.+\Phi\left(\frac{SAL_1(1+\alpha_2A_1)}{S_1A_1L(1+\alpha_2A)}\right)+\Phi\left(\frac{1+\alpha_2A}{1+\alpha_2A_1}\right)\right]-\frac{(1-\varepsilon_3)\beta_3 S_1 L_1}{1+\alpha_3 L_1}\left[\Phi\left(\frac{S_1}{S}\right)\right.\\
&\left.+\Phi\left(\frac{S(1+\alpha_3L_1)}{S_1(1+\alpha_3L)}\right)+\Phi\left(\frac{1+\alpha_3L}{1+\alpha_3L_1}\right)\right]+\frac{ph(1-\varepsilon_1)\beta_1 S_1 V_{I_1}e^{m\tau_1}}{g(1-\varepsilon_4)kA_1(1+\alpha_1V_{I_1})}\left(\frac{gV_{I_1}}{h}-1\right)W\\
&+\frac{p_1d_c}{rL_1\sigma}\left(\frac{(1-\varepsilon_1)\beta_1 S_1 V_{I_1}}{1+\alpha_1 V_{I_1}}+\frac{(1-\varepsilon_2)\beta_2 S_1 A_1}{1+\alpha_2 A_1}\right)\left(\frac{\sigma A_1}{d_c}-1\right)C,\\
\leq&-d(S-S_1)^2-\frac{(1-\varepsilon_1)\beta_1 S_1 V_{I_1}\alpha_1(V_I-V_{I_1})^2}{(1+\alpha_1V_I)(1+\alpha_1V_{I_1})^2V_{I_1}}-\frac{(1-\varepsilon_2)\beta_2 S_1 A_1\alpha_2(A-A_1)^2}{(1+\alpha_2A)(1+\alpha_2A_1)^2A_1}\\
&-\frac{(1-\varepsilon_3)\beta_3 S_1 L_1\alpha_3(L-L_1)^2}{(1+\alpha_3L)(1+\alpha_3L_1)^2L_1}-\frac{(1-\varepsilon_1)\beta_1 S_1 V_{I_1}}{1+\alpha_1 V_{I_1}}\left[\Phi\left(\frac{S_1}{S}\right)+\Phi\left(\frac{LA_1}{L_1A}\right)\right.\\
&\left.+\Phi\left(\frac{A(t-\tau_1)V_{I_1}}{A_1V_I}\right)+\Phi\left(\frac{SV_IL_1(1+\alpha_1V_{I_1})}{S_1V_{I_1}L(1+\alpha_1V_I)}\right)+\Phi\left(\frac{1+\alpha_1V_I}{1+\alpha_1V_{I_1}}\right)\right]\\
&-\frac{(1-\varepsilon_2)\beta_2 S_1 A_1}{1+\alpha_2 A_1}\left[\Phi\left(\frac{S_1}{S}\right)+\Phi\left(\frac{LA_1}{L_1A}\right)+\Phi\left(\frac{SAL_1(1+\alpha_2A_1)}{S_1A_1L(1+\alpha_2A)}\right)+\Phi\left(\frac{1+\alpha_2A}{1+\alpha_2A_1}\right)\right]\\
&-\frac{(1-\varepsilon_3)\beta_3 S_1 L_1}{1+\alpha_3 L_1}\left[\Phi\left(\frac{S_1}{S}\right)+\Phi\left(\frac{S(1+\alpha_3L_1)}{S_1(1+\alpha_3L)}\right)+\Phi\left(\frac{1+\alpha_3L}{1+\alpha_3L_1}\right)\right]\\
&+\frac{ph(1-\varepsilon_1)\beta_1 S_1 V_1 e^{m\tau_1}}{g(1-\varepsilon_4)kA_1(1+\alpha_1V_{I_1})}(\mathscr{R}_1^W-1)W\\
&+\frac{p_1d_c}{rL_1\sigma}\left(\frac{(1-\varepsilon_1)\beta_1 S_1 V_{I_1}}{1+\alpha_1 V_{I_1}}+\frac{(1-\varepsilon_2)\beta_2 S_1 A_1}{1+\alpha_2 A_1}\right)(\mathscr{R}_1^C-1)C.
\end{aligned}$$

Based on the assumptions $\mathscr{R}_1^W \leq 1$ and $\mathscr{R}_1^C \leq 1$, we obtain ${}^C D^\alpha \mathscr{H}_1(t) < 0$, with equality if and only if $S = S_1, L = L_1, A = A_1, V_I = V_{I_1}$, $W_1 = 0$ and $C_1 = 0$. Consequently, the largest invariant set of $\{(S,L,A,V_I,W,C) \in \mathbb{R}_+^6 : {}^C D^\alpha \mathscr{H}_1(t) = 0\}$ is the singleton $\{E_1\}$. Therefore, the equilibrium point E_1 is globally asymptotically stable. □

Theorem 4. *If $\mathscr{R}_2^C \leq 1 < \mathscr{R}_1^W$, then the infection equilibrium with only humoral immunity E_2 is globally asymptotically stable for $\eta = 1$ and $\tau_2 = 0$.*

Proof. Consider the following Lyapunov functional

$$\begin{aligned}
\mathscr{H}_2(S,L,A,V_I,W,C) =& S_2\Phi\left(\frac{S}{S_2}\right) + L_2\Phi\left(\frac{L}{L_2}\right) + \frac{1}{rL_2}\left(\frac{(1-\varepsilon_1)\beta_1 S_2 V_{I_2}}{1+\alpha_1 V_{I_2}} + \frac{(1-\varepsilon_2)\beta_2 S_2 A_2}{1+\alpha_2 A_2}\right) \\
& A_2\Phi\left(\frac{A}{A_2}\right) + \frac{(1-\varepsilon_1)\beta_1 S_2 V_{I_2} e^{m\tau_1}}{(1-\varepsilon_4)kA_2(1+\alpha_1 V_{I_2})} V_{I_2}\Phi\left(\frac{V_I}{V_{I_2}}\right) \\
& + \frac{p(1-\varepsilon_1)\beta_1 S_2 V_{I_2} e^{m\tau_1}}{g(1-\varepsilon_4)kA_2(1+\alpha_1 V_{I_2})} W_2\Phi\left(\frac{W}{W_2}\right) \\
& + \frac{p_1}{\sigma r L_2}\left(\frac{(1-\varepsilon_1)\beta_1 S_2 V_{I_2}}{1+\alpha_1 V_{I_2}} + \frac{(1-\varepsilon_2)\beta_2 S_2 A_2}{1+\alpha_2 A_2}\right) C \\
& + \frac{(1-\varepsilon_1)\beta_1 S_2 V_{I_2}}{1+\alpha_1 V_{I_2}} {}^C D_{\tau_1}^{-\alpha}\left(\frac{A(t-\sigma)}{A_2} - 1 - ln\frac{A(t-\sigma)}{A_2}\right).
\end{aligned}$$

By computing the fractional derivative of $\mathscr{H}_2$ along the solutions of model (2), we have

$$\begin{aligned}
{}^C D^\alpha \mathscr{H}_2 \leq & \left(1 - \frac{S_2}{S}\right) {}^C D^\alpha S(t) + \left(1 - \frac{L_2}{L}\right) {}^C D^\alpha L(t) \\
& + \frac{1}{rL_2}\left(\frac{(1-\varepsilon_1)\beta_1 S_2 V_{I_2}}{1+\alpha_1 V_{I_2}} + \frac{(1-\varepsilon_2)\beta_2 S_2 A_2}{1+\alpha_2 A_2}\right)\left(1 - \frac{A_2}{A}\right) {}^C D^\alpha A(t) \\
& + \frac{(1-\varepsilon_1)\beta_1 S_2 V_{I_2} e^{m\tau_1}}{(1-\varepsilon_4)kA_2(1+\alpha_1 V_{I_2})}\left(1 - \frac{V_{I_2}}{V_I}\right) {}^C D^\alpha V_I(t) \\
& + \frac{p(1-\varepsilon_1)\beta_1 S_2 V_{I_2} e^{m\tau_1}}{g(1-\varepsilon_4)kA_2(1+\alpha_1 V_{I_2})}\left(1 - \frac{W_2}{W}\right) {}^C D^\alpha W(t) \\
& + \frac{p_1}{\sigma r L_2}\left(\frac{(1-\varepsilon_1)\beta_1 S_2 V_{I_2}}{1+\alpha_1 V_{I_2}} + \frac{(1-\varepsilon_2)\beta_2 S_2 A_2}{1+\alpha_2 A_2}\right) {}^C D^\alpha C(t) \\
& + \frac{(1-\varepsilon_1)\beta_1 S_2 V_{I_2}}{1+\alpha_1 V_{I_2}}\left(\frac{A(t)}{A_2} - ln\frac{A(t)}{A_2} - \frac{A(t-\tau_1)}{A_2} + ln\frac{A(t-\tau_1)}{A_2}\right).
\end{aligned}$$

Using the following equilibrium condition at E_2, we get

$$\lambda = dS_2 + \frac{(1-\varepsilon_1)\beta_1 S_2 V_{I_2}}{1+\alpha_1 V_{I_2}} + \frac{(1-\varepsilon_2)\beta_2 S_2 A_2}{1+\alpha_2 A_2} + \frac{(1-\varepsilon_3)\beta_3 S_2 L_2}{1+\alpha_3 L_2},$$

$$\frac{(1-\varepsilon_1)\beta_1 S_2 V_{I_2}}{1+\alpha_1 V_{I_2}} + \frac{(1-\varepsilon_2)\beta_2 S_2 A_2}{1+\alpha_2 A_2} + \frac{(1-\varepsilon_3)\beta_3 S_2 L_2}{1+\alpha_3 L_2} = (e+r)L_2,$$
$$rL_2 = aA_2, \mu V_{I_2} = (1-\varepsilon_4)ke^{-m\tau_1}A_2 - pV_{I_2}W_2.$$

Then

$$\begin{aligned}
{}^{C}D^{\alpha}\mathscr{H}_2 \leq & -d(S-S_2)^2 - \frac{(1-\varepsilon_1)\beta_1 S_2 V_{I_2}\alpha_1(V-V_{I_2})^2}{(1+\alpha_1 V_I)(1+\alpha_1 V_{I_2})^2 V_{I_2}} - \frac{(1-\varepsilon_2)\beta_2 S_2 A_2 \alpha_2 (A-A_2)^2}{(1+\alpha_2 A)(1+\alpha_2 A_2)^2 A_2} \\
& - \frac{(1-\varepsilon_3)\beta_3 S_2 L_2 \alpha_3 (L-L_2)^2}{(1+\alpha_3 L)(1+\alpha_3 L_2)^2 L_2} - \frac{(1-\varepsilon_1)\beta_1 S_2 V_{I_2}}{1+\alpha_1 V_{I_2}}\left[\Phi\left(\frac{S_2}{S}\right) + \Phi\left(\frac{LA_2}{L_2 A}\right)\right. \\
& \left. + \Phi\left(\frac{A(t-\tau_1)V_{I_2}}{A_2 V_I}\right) + \Phi\left(\frac{SVL_{I_2}(1+\alpha_1 V_{I_2})}{S_2 V_{I_2} L(1+\alpha_1 V_I)}\right) + \Phi\left(\frac{1+\alpha_1 V_I}{1+\alpha_1 V_{I_2}}\right)\right] \\
& - \frac{(1-\varepsilon_3)\beta_2 S_2 A_2}{1+\alpha_2 A_2}\left[\Phi\left(\frac{S_2}{S}\right) + \Phi\left(\frac{LA_2}{L_2 A}\right) + \Phi\left(\frac{SAL_2(1+\alpha_2 A_2)}{S_2 A_2 L(1+\alpha_2 A)}\right) + \Phi\left(\frac{1+\alpha_2 A}{1+\alpha_2 A_2}\right)\right] \\
& - \frac{(1-\varepsilon_3)\beta_3 S_2 L_2}{1+\alpha_3 L_2}\left[\Phi\left(\frac{S_2}{S}\right) + \Phi\left(\frac{S(1+\alpha_3 L_2)}{S_2(1+\alpha_3 L)}\right) + \Phi\left(\frac{1+\alpha_3 L}{1+\alpha_3 L_2}\right)\right] \\
& + \frac{p_1 d_c}{\sigma r L_2}\left(\frac{(1-\varepsilon_1)\beta_1 S_2 V_{I_2}}{1+\alpha_1 V_{I_2}} + \frac{(1-\varepsilon_2)\beta_2 S_2 A_2}{1+\alpha_2 A_2}\right)(\mathscr{R}_2^C - 1)C(t).
\end{aligned}$$

When $\mathscr{R}_2^C \leq 1$, then ${}^{C}D^{\alpha}\mathscr{H}_2(S,L,A,V_I,W,C) < 0$, with equality if and only if $S = S_2, L = L_2, A = A_2, V = V_{I_2}, W = W_2$ and $C_2 = 0$. Therefore, the equilibrium point E_2 is globally asymptotically stable. □

Theorem 5. *If $\mathscr{R}_2^W \leq 1 < \mathscr{R}_1^C$, then the infection equilibrium with only cellular immunity E_3 is globally asymptotically stable for $\eta = 1$ and any delays $\tau_1, \tau_2 \geq 0$.*

Proof. To prove E_3 is globally asymptotically stable, construct the following Lyapunov functional

$$\begin{aligned}
\mathscr{H}_3(u) = & S_3\Phi\left(\frac{S}{S_3}\right) + L_3\Phi\left(\frac{L}{L_3}\right) + \frac{1}{rL_3}\left(\frac{(1-\varepsilon_1)\beta_1 S_3 V_{I_3}}{1+\alpha_1 V_{I_3}} + \frac{(1-\varepsilon_2)\beta_2 S_3 A_3}{1+\alpha_2 A_3}\right) \\
& A_3\Phi\left(\frac{A}{A_3}\right) + \frac{(1-\varepsilon_1)\beta_1 S_3 V_{I_3} e^{m\tau_1}}{(1-\varepsilon_4)kA_3(1+\alpha_1 V_{I_3})} V_{I_3}\Phi\left(\frac{V_I}{V_{I_3}}\right) + \frac{p(1-\varepsilon_1)\beta_1 S_3 V_{I_3} e^{m\tau_1}}{g(1-\varepsilon_4)kA_3(1+\alpha_1 V_{I_3})} W \\
& + \frac{p_1}{\sigma r L_3}\left(\frac{(1-\varepsilon_1)\beta_1 S_3 V_{I_3}}{1+\alpha_1 V_{I_3}} + \frac{(1-\varepsilon_2)\beta_2 S_3 A_3}{1+\alpha_2 A_3}\right) C_3\phi\left(\frac{C}{C_3}\right) \\
& + \frac{(1-\varepsilon_1)\beta_1 S_3 V_{I_3}}{1+\alpha_1 V_{I_3}} {}^{C}D_{\tau_1}^{-\alpha}\left(\frac{A(t-\sigma)}{A_3} - 1 - ln\frac{A(t-\sigma)}{A_3}\right) \\
& + \frac{p(1-\varepsilon_1)\beta_1 S_3 V_{I_3} e^{m\tau_1}}{(1-\varepsilon_4)kA_3(1+\alpha_1 V_{I_3})} {}^{C}D_{\tau_2}^{-\alpha} V_I(t-\sigma)W(t-\sigma),
\end{aligned}$$

where $u=(S,L,A,V_I,W,C)$. It's clear that $\mathscr{H}_3(S,L,A,V_I,W,C)>0$ for all $S,L,A,V_I,W,C>0$ and $\mathscr{H}_3(S_3,L_3,A_3,V_{I_3},W_3,C_3)=0$.

By applying the property of fractional derivatives presented in [15], we get

$$\begin{aligned}
{}^{C}D^{\alpha}\mathscr{H}_3 \leq{}& \left(1-\frac{S_3}{S}\right){}^{C}D^{\alpha}S(t)+\left(1-\frac{L_3}{L}\right){}^{C}D^{\alpha}L(t)\\
&+\frac{1}{rL_3}\left(\frac{(1-\varepsilon_1)\beta_1S_3V_{I_3}}{1+\alpha_1V_{I_3}}+\frac{(1-\varepsilon_2)\beta_2S_3A_3}{1+\alpha_2A_3}\right)\left(1-\frac{A_3}{A}\right){}^{C}D^{\alpha}A(t)\\
&+\frac{(1-\varepsilon_1)\beta_1S_3V_{I_3}e^{m\tau_1}}{(1-\varepsilon_4)kA_3(1+\alpha_1V_{I_3})}\left(1-\frac{V_{I_3}}{V_I}\right){}^{C}D^{\alpha}V_I(t)+\frac{p(1-\varepsilon_1)\beta_1S_3V_{I_3}e^{m\tau_1}}{g(1-\varepsilon_4)kA_3(1+\alpha_1V_{I_3})}{}^{C}D^{\alpha}W(t)\\
&+\frac{p_1}{\sigma rL_3}\left(\frac{(1-\varepsilon_1)\beta_1S_3V_{I_3}}{1+\alpha_1V_{I_3}}+\frac{(1-\varepsilon_2)\beta_2S_3A_3}{1+\alpha_2A_3}\right)\left(1-\frac{C_3}{C}\right){}^{C}D^{\alpha}C(t)\\
&+\frac{(1-\varepsilon_1)\beta_1S_3V_{I_3}}{1+\alpha_1V_{I_3}}\left(\frac{A(t)}{A_3}-ln\frac{A(t)}{A_3}-\frac{A(t-\tau_1)}{A_3}+ln\frac{A(t-\tau_1)}{A_1}\right)\\
&+\frac{p(1-\varepsilon_1)\beta_1S_3V_{I_3}e^{m\tau_1}}{(1-\varepsilon_4)kA_3(1+\alpha_1V_{I_3})}(V_I(t)W(t)-V_I(t-\tau_2)W(t-\tau_2)).
\end{aligned}$$

Now, by using equilibrium conditions, we have

$$\lambda=dS_3+\frac{(1-\varepsilon_1)\beta_1S_3V_{I_3}}{1+\alpha_1V_{I_3}}+\frac{(1-\varepsilon_2)\beta_2S_3A_3}{1+\alpha_2A_3}+\frac{(1-\varepsilon_3)\beta_3S_3L_3}{1+\alpha_3L_3},$$

$$\frac{(1-\varepsilon_1)\beta_1S_3V_{I_3}}{1+\alpha_1V_{I_3}}+\frac{(1-\varepsilon_2)\beta_2S_3A_3}{1+\alpha_2A_3}+\frac{(1-\varepsilon_3)\beta_3S_3L_3}{1+\alpha_3L_3}=(e+r)L_3,$$

$$rL_3=aA_3+p_1A_3C_3,\mu V_{I_3}=(1-\varepsilon_4)ke^{-m\tau_1}A_3,$$

then we obtain

$$\begin{aligned}
{}^{C}D^{\alpha}\mathscr{H}_3 \leq{}& -d(S-S_3)^2-\frac{(1-\varepsilon_1)\beta_1S_3V_{I_3}\alpha_1(V_I-V_{I_3})^2}{(1+\alpha_1V_I)(1+\alpha_1V_{I_3})^2V_{I_3}}-\frac{(1-\varepsilon_2)\beta_2S_3A_3\alpha_2(A-A_3)^2}{(1+\alpha_2A)(1+\alpha_2A_3)^2A_3}\\
&-\frac{(1-\varepsilon_3)\beta_3S_3L_3\alpha_3(L-L_3)^2}{(1+\alpha_3L)(1+\alpha_3L_3)^2L_3}-\frac{(1-\varepsilon_1)\beta_1S_3V_{I_3}}{1+\alpha_1V_{I_3}}\left[\Phi\left(\frac{S_3}{S}\right)+\Phi\left(\frac{LA_3}{L_3A}\right)\right.\\
&\left.+\Phi\left(\frac{A(t-\tau_1)V_{I_3}}{A_3V_I}\right)+\Phi\left(\frac{SV_IL_3(1+\alpha_1V_{I_3})}{S_3V_{I_3}L(1+\alpha_1V_I)}\right)+\Phi\left(\frac{1+\alpha_1V_I}{1+\alpha_1V_{I_3}}\right)\right]\\
&-\frac{(1-\varepsilon_2)\beta_2S_3A_3}{1+\alpha_2A_3}\left[\Phi\left(\frac{S_3}{S}\right)+\Phi\left(\frac{LA_3}{L_3A}\right)+\Phi\left(\frac{SAL_3(1+\alpha_2A_3)}{S_3A_3L(1+\alpha_2A)}\right)+\Phi\left(\frac{1+\alpha_2A}{1+\alpha_2A_3}\right)\right]\\
&-\frac{(1-\varepsilon_3)\beta_3S_3L_3}{1+\alpha_3L_3}\left[\Phi\left(\frac{S_3}{S}\right)+\Phi\left(\frac{S(1+\alpha_3L_3)}{S_3(1+\alpha_3L)}\right)+\Phi\left(\frac{1+\alpha_3L}{1+\alpha_3L_3}\right)\right]\\
&+\frac{ph(1-\varepsilon_1)\beta_1S_3V_{I_3}e^{m\tau_1}}{g(1-\varepsilon_4)kA_3(1+\alpha_1V_{I_3})}(\mathscr{R}_2^W-1)W.
\end{aligned}$$

Based on the assumptions $\mathscr{R}_2^W \leq 1$, we obtain ${}^C D^\alpha \mathscr{H}_3(t) < 0$, with equality if and only if $S = S_3, L = L_3, A = A_3, V_I = V_{I_3}, W = W_3 = 0$ and $C = C_3$. Consequently, the largest invariant set of $\{(S,L,A,V_I,W,C) \in \mathbb{R}_+^6 : {}^C D^\alpha \mathscr{H}_3(t) = 0\}$ is the singleton $\{E_3\}$. Therefore, the equilibrium point E_3 is globally asymptotically stable. □

Theorem 6. *If $\mathscr{R}_2^W > 1$ and $\mathscr{R}_2^C > 1$, then the infection equilibrium with both humoral and cellular immunity E_4 is globally asymptotically stable for $\eta = 1$ and $\tau_2 = 0$.*

Proof. Consider the following Lyapunov functional

$$\begin{aligned}\mathscr{H}_4(S,L,A,V_I,W,C) =& S_4\Phi\left(\frac{S}{S_4}\right) + L_4\Phi\left(\frac{L}{L_4}\right) + \frac{1}{rL_4}\left(\frac{(1-\varepsilon_1)\beta_1 S_4 V_{I_4}}{1+\alpha_1 V_{I_4}} + \frac{(1-\varepsilon_2)\beta_2 S_4 A_4}{1+\alpha_2 A_4}\right)\\ & A_4\Phi\left(\frac{A}{A_4}\right) + \frac{(1-\varepsilon_1)\beta_1 S_4 V_{I_4} e^{m\tau_1}}{(1-\varepsilon_4)kA_4(1+\alpha_1 V_{I_4})} V_{I_4}\Phi\left(\frac{V_I}{V_{I_4}}\right)\\ & + \frac{p(1-\varepsilon_1)\beta_1 S_4 V_{I_4} e^{m\tau_1}}{g(1-\varepsilon_4)kA_4(1+\alpha_1 V_{I_4})} W_4\Phi\left(\frac{W}{W_4}\right)\\ & + \frac{p_1}{\sigma rL_4}\left(\frac{(1-\varepsilon_1)\beta_1 S_4 V_{I_4}}{1+\alpha_1 V_{I_4}} + \frac{(1-\varepsilon_2)\beta_2 S_4 A_4}{1+\alpha_2 A_4}\right) C_4\Phi\left(\frac{C}{C_4}\right)\\ & + \frac{(1-\varepsilon_1)\beta_1 S_4 V_{I_4}}{1+\alpha_1 V_{I_4}} {}^C D_{\tau_1}^{-\alpha}\left(\frac{A(t-\sigma)}{A_4} - 1 - ln\frac{A(t-\sigma)}{A_4}\right).\end{aligned}$$

By computing the fractional derivative of $\mathscr{H}_4$ along the solutions of model (2), we have

$$\begin{aligned}{}^C D^\alpha \mathscr{H}_4 \leq & \left(1-\frac{S_4}{S}\right){}^C D^\alpha S(t) + \left(1-\frac{L_4}{L}\right){}^C D^\alpha L(t)\\ & + \frac{1}{rL_4}\left(\frac{(1-\varepsilon_1)\beta_1 S_4 V_{I_4}}{1+\alpha_1 V_{I_4}} + \frac{(1-\varepsilon_2)\beta_2 S_4 A_4}{1+\alpha_2 A_4}\right)\left(1-\frac{A_4}{A}\right){}^C D^\alpha A(t)\\ & + \frac{(1-\varepsilon_1)\beta_1 S_4 V_{I_4} e^{m\tau_1}}{(1-\varepsilon_4)kA_4(1+\alpha_1 V_{I_4})}\left(1-\frac{V_{I_4}}{V_I}\right){}^C D^\alpha V_I(t)\\ & + \frac{p(1-\varepsilon_1)\beta_1 S_4 V_{I_4} e^{m\tau_1}}{g(1-\varepsilon_4)kA_4(1+\alpha_1 V_{I_4})}\left(1-\frac{W_4}{W}\right){}^C D^\alpha W(t)\\ & + \frac{p_1}{\sigma rL_4}\left(\frac{\beta_1 S_4 V_{I_4}}{1+\alpha_1 V_{I_4}} + \frac{(1-\varepsilon_2)\beta_2 S_4 A_4}{1+\alpha_2 A_4}\right)\left(1-\frac{C_4}{C}\right){}^C D^\alpha C(t)\\ & + \frac{(1-\varepsilon_1)\beta_1 S_4 V_{I_4}}{1+\alpha_1 V_{I_4}}\left(\frac{A(t)}{A_4} - ln\frac{A(t)}{A_4} - \frac{A(t-\tau_1)}{A_4} + ln\frac{A(t-\tau_1)}{A_4}\right).\end{aligned}$$

Using the following equilibrium condition at E_4, we get

$$\lambda = dS_4 + \frac{(1-\varepsilon_1)\beta_1 S_4 V_{I_4}}{1+\alpha_1 V_{I_4}} + \frac{(1-\varepsilon_2)\beta_2 S_4 A_4}{1+\alpha_2 A_4} + \frac{(1-\varepsilon_3)\beta_3 S_4 L_4}{1+\alpha_3 L_4},$$

$$\frac{(1-\varepsilon_1)\beta_1 S_4 V_{I_4}}{1+\alpha_1 V_{I_4}} + \frac{(1-\varepsilon_2)\beta_2 S_4 A_4}{1+\alpha_2 A_4} + \frac{(1-\varepsilon_3)\beta_3 S_4 L_4}{1+\alpha_3 L_4} = (e+r)L_4,$$

$$rL_4 = aA_4 + p_1 A_4 C_4, \mu V_4 = (1-\varepsilon_4)ke^{-m\tau_1}A_4 - pV_{I_4}W_4.$$

Then

$$\begin{aligned}
{}^C D^\alpha \mathscr{H}_4 \leq & -d(S-S_4)^2 - \frac{(1-\varepsilon_1)\beta_1 S_4 V_{I_4}\alpha_1 (V_I - V_{I_4})^2}{(1+\alpha_1 V_I)(1+\alpha_1 V_{I_4})^2 V_{I_4}} - \frac{(1-\varepsilon_2)\beta_2 S_4 A_4 \alpha_2 (A-A_4)^2}{(1+\alpha_2 A)(1+\alpha_2 A_4)^2 A_4} \\
& - \frac{(1-\varepsilon_3)\beta_3 S_4 L_4 \alpha_3 (L-L_4)^2}{(1+\alpha_3 L)(1+\alpha_3 L_4)^2 L_4} - \frac{(1-\varepsilon_1)\beta_1 S_4 V_{I_4}}{1+\alpha_1 V_{I_4}} \left[\Phi\left(\frac{S_4}{S}\right) + \Phi\left(\frac{LA_4}{L_4 A}\right) \right. \\
& \left. + \Phi\left(\frac{A(t-\tau_1)V_{I_4}}{A_4 V_I}\right) + \Phi\left(\frac{SV_I L_2(1+\alpha_1 V_{I_4})}{S_4 V_{I_4} L(1+\alpha_1 V_I)}\right) + \Phi\left(\frac{1+\alpha_1 V_I}{1+\alpha_1 V_{I_4}}\right) \right] \\
& - \frac{(1-\varepsilon_2)\beta_2 S_4 A_4}{1+\alpha_2 A_4} \left[\Phi\left(\frac{S_4}{S}\right) + \Phi\left(\frac{LA_4}{L_4 A}\right) + \Phi\left(\frac{SAL_2(1+\alpha_2 A_4)}{S_4 A_4 L(1+\alpha_2 A)}\right) + \Phi\left(\frac{1+\alpha_2 A}{1+\alpha_2 A_4}\right) \right] \\
& - \frac{(1-\varepsilon_3)\beta_3 S_4 L_4}{1+\alpha_3 L_4} \left[\Phi\left(\frac{S_4}{S}\right) + \Phi\left(\frac{S(1+\alpha_3 L_4)}{S_4(1+\alpha_3 L)}\right) + \Phi\left(\frac{1+\alpha_3 L}{1+\alpha_3 L_4}\right) \right].
\end{aligned}$$

Hence, ${}^C D^\alpha \mathscr{H}_4(S,L,A,V_I,W,C) < 0$, with equality if and only if $S = S_4, L = L_4, A = A_4, V_I = V_{I_4}$, $W = W_4$ and $C = C_4$. Therefore, the equilibrium point E_4 is globally asymptotically stable.

□

5. BIFURCATION ANALYSIS AT E_2 AND E_4

For $\tau_2 > 0$ and $\tau_1 = 0$, model (2) becomes

$$(9)\quad \begin{cases}
{}^C\mathscr{D}^\alpha S(t) = \lambda - dS(t) - \frac{(1-\varepsilon_1)\beta_1 S(t)V_I(t)}{1+\alpha_1 V_I(t)} - \frac{(1-\varepsilon_2)\beta_2 S(t)A(t)}{1+\alpha_2 A(t)} - \frac{(1-\varepsilon_3)\beta_3 S(t)L(t)}{1+\alpha_3 L(t)}, \\
{}^C\mathscr{D}^\alpha L(t) = \eta\left(\frac{(1-\varepsilon_1)\beta_1 S(t)V_I(t)}{1+\alpha_1 V_I(t)} + \frac{(1-\varepsilon_2)\beta_2 S(t)A(t)}{1+\alpha_2 A(t)} + \frac{(1-\varepsilon_3)\beta_3 S(t)L(t)}{1+\alpha_3 L(t)}\right) - (e+r)L(t), \\
{}^C\mathscr{D}^\alpha A(t) = (1-\eta)\left(\frac{(1-\varepsilon_1)\beta_1 S(t)V_I(t)}{1+\alpha_1 V_I(t)} + \frac{(1-\varepsilon_2)\beta_2 S(t)A(t)}{1+\alpha_2 A(t)} + \frac{(1-\varepsilon_3)\beta_3 S(t)L(t)}{1+\alpha_3 L(t)}\right) + rL(t) \\
\qquad\qquad -aA(t) - p_1 A(t)C(t), \\
{}^C\mathscr{D}^\alpha V_I(t) = k(1-\varepsilon_4)A(t) - \mu V_I(t) - pV_I(t)W(t), \\
{}^C\mathscr{D}^\alpha W(t) = gV_I(t-\tau_2)W(t-\tau_2) - hW(t), \\
{}^C\mathscr{D}^\alpha C(t) = \sigma A(t)C(t) - d_c C(t).
\end{cases}$$

In this section, we explore the existence of the Hopf bifurcation at the equilibrium points E_2 and E_4. For this, we first linearize the system (9) and the linearized system of (9) at an arbitrary

equilibrium $E^*(S^*,L^*,A^*,V_I^*,W^*,C^*)$ is described below.

$$
\begin{cases}
{}^C\mathscr{D}^\alpha S(t) = (-d - \frac{(1-\varepsilon_1)\beta_1 V_I^*}{1+\alpha_1 V_I^*} - \frac{(1-\varepsilon_2)\beta_2 A^*}{1+\alpha_2 A^*} - \frac{(1-\varepsilon_3)\beta_3 L^*}{1+\alpha_3 L^*})S(t) - \frac{(1-\varepsilon_3)\beta_3 S^*}{(1+\alpha_3 L^*)^2}L(t) \\
\qquad\qquad - \frac{(1-\varepsilon_2)\beta_2 S^*}{(1+\alpha_2 A^*)^2}A(t) - \frac{(1-\varepsilon_1)\beta_1 S^*}{(1+\alpha_1 V_I^*)^2}V_I(t), \\
{}^C\mathscr{D}^\alpha L(t) = \eta\left(\frac{(1-\varepsilon_1)\beta_1 V_I^*}{1+\alpha_1 V_I^*} + \frac{(1-\varepsilon_2)\beta_2 A^*}{1+\alpha_2 A^*} + \frac{(1-\varepsilon_3)\beta_3 L^*}{1+\alpha_3 L^*}\right)S(t) \\
\qquad\qquad + (\eta\frac{(1-\varepsilon_3)\beta_3 S^*}{(1+\alpha_3 L^*)^2} - (e+r))L(t) \\
\qquad\qquad + \eta\frac{(1-\varepsilon_2)\beta_2 S^*}{(1+\alpha_2 A^*)^2}A(t) + \eta\frac{(1-\varepsilon_1)\beta_1 S^*}{(1+\alpha_1 V_I^*)^2}V_I(t), \\
{}^C\mathscr{D}^\alpha A(t) = (1-\eta)\left(\frac{(1-\varepsilon_1)\beta_1 V_I^*}{1+\alpha_1 V_I^*} + \frac{(1-\varepsilon_2)\beta_2 A^*}{1+\alpha_2 A^*} + \frac{(1-\varepsilon_3)\beta_3 L^*}{1+\alpha_3 L^*}\right)S(t) \\
\qquad\qquad + ((1-\eta)\frac{(1-\varepsilon_3)\beta_3 S^*}{(1+\alpha_3 L^*)^2} + r))L(t) + ((1-\eta)\frac{(1-\varepsilon_2)\beta_2 S^*}{(1+\alpha_2 A^*)^2} - a - p_1 C^*)A(t) \\
\qquad\qquad + (1-\eta)\frac{(1-\varepsilon_1)\beta_1 S^*}{(1+\alpha_1 V_I^*)^2}V_I(t) - p_1 A^* C(t), \\
{}^C\mathscr{D}^\alpha V_I(t) = k(1-\varepsilon_4)A(t) - (\mu + pW^*)V_I(t) - pV_I^* W(t), \\
{}^C\mathscr{D}^\alpha W(t) = gW^* V_I(t-\tau_2) + gV_I^* W(t-\tau_2) - hW(t), \\
{}^C\mathscr{D}^\alpha C(t) = \sigma C^* A(t) + (\sigma A^* - d_c)C(t).
\end{cases} \tag{10}
$$

By applying the Laplace transform to both sides of the system (10), we obtain

$$
\begin{cases}
s^\alpha \mathscr{S}(s) - s^{\alpha-1}\phi_1(0) = (-d - \frac{(1-\varepsilon_1)\beta_1 V_I^*}{1+\alpha_1 V_I^*} - \frac{(1-\varepsilon_2)\beta_2 A^*}{1+\alpha_2 A^*} - \frac{(1-\varepsilon_3)\beta_3 L^*}{1+\alpha_3 L^*})\mathscr{S}(s) \\
\qquad\qquad - \frac{(1-\varepsilon_3)\beta_3 S^*}{(1+\alpha_3 L^*)^2}\mathscr{L}(s) - \frac{(1-\varepsilon_2)\beta_2 S^*}{(1+\alpha_2 A^*)^2}\mathscr{A}(s) - \frac{(1-\varepsilon_1)\beta_1 S^*}{(1+\alpha_1 V_I^*)^2}\mathscr{V}_{\mathscr{I}}(s), \\
s^\alpha \mathscr{L}(s) - s^{\alpha-1}\phi_2(0) = \eta\left(\frac{(1-\varepsilon_1)\beta_1 V_I^*}{1+\alpha_1 V_I^*} + \frac{(1-\varepsilon_2)\beta_2 A^*}{1+\alpha_2 A^*} + \frac{(1-\varepsilon_3)\beta_3 L^*}{1+\alpha_3 L^*}\right)\mathscr{S}(s) \\
\qquad\qquad + (\eta\frac{(1-\varepsilon_3)\beta_3 S^*}{(1+\alpha_3 L^*)^2} - (e+r))\mathscr{L}(s) + \eta\frac{(1-\varepsilon_2)\beta_2 S^*}{(1+\alpha_2 A^*)^2}\mathscr{A}(s) \\
\qquad\qquad + \eta\frac{(1-\varepsilon_1)\beta_1 S^*}{(1+\alpha_1 V_I^*)^2}\mathscr{V}_{\mathscr{I}}(s), \\
s^\alpha \mathscr{A}(s) - s^{\alpha-1}\phi_3(0) = (1-\eta)\left(\frac{(1-\varepsilon_1)\beta_1 V_I^*}{1+\alpha_1 V_I^*} + \frac{(1-\varepsilon_2)\beta_2 A^*}{1+\alpha_2 A^*} + \frac{(1-\varepsilon_3)\beta_3 L^*}{1+\alpha_3 L^*}\right)\mathscr{S}(s) \\
\qquad\qquad + ((1-\eta)\frac{(1-\varepsilon_3)\beta_3 S^*}{(1+\alpha_3 L^*)^2} + r))\mathscr{L}(s) \\
\qquad\qquad + ((1-\eta)\frac{(1-\varepsilon_2)\beta_2 S^*}{(1+\alpha_2 A^*)^2} - a - p_1 C^*)\mathscr{A}(s) \\
\qquad\qquad + (1-\eta)\frac{(1-\varepsilon_1)\beta_1 S^*}{(1+\alpha_1 V_I^*)^2}\mathscr{V}_{\mathscr{I}}(s) - p_1 A^*\mathscr{C}(s), \\
s^\alpha \mathscr{V}_{\mathscr{I}}(s) - s^{\alpha-1}\phi_4(0) = k(1-\varepsilon_4)\mathscr{A}(s) - (\mu + pW^*)\mathscr{V}_{\mathscr{I}}(s) - pV_I^*\mathscr{W}(s), \\
s^\alpha \mathscr{W}(s) - s^{\alpha-1}\phi_5(0) = gW^* e^{-s\tau_2}\mathscr{V}_{\mathscr{I}}(s) + (gV_I^* e^{-s\tau_2} - h)\mathscr{W}(s) \\
\qquad\qquad + e^{-s\tau_2}\int_{-\tau_2}^0 e^{-su}(\phi_4(u) + \phi_5(u))du, \\
s^\alpha \mathscr{C}(s) - s^{\alpha-1}\phi_6(0) = \sigma C^*\mathbf{A}(s) + (\sigma A^* - d_c)\mathscr{C}(s),
\end{cases} \tag{11}
$$

where $\mathscr{L}(S(t))(s) = \mathscr{S}(s), \mathscr{L}(L(t))(s) = \mathscr{L}(s), \mathscr{L}(A(t))(s) = \mathscr{A}(s), \mathscr{L}(V_I(t))(s) = \mathscr{V}_{\mathscr{I}}(s)$, $\mathscr{L}(W(t))(s) = \mathscr{W}(s)$ and $\mathscr{L}(C(t))(s) = \mathscr{C}(s)$.

We can rewrite (11) as follows

$$\Delta(s)\cdot\begin{pmatrix}\mathscr{S}(s)\\ \mathscr{L}(s)\\ \mathscr{A}(s)\\ \mathscr{V}_{\mathscr{I}}(s)\\ \mathscr{W}(s)\\ \mathscr{C}(s)\end{pmatrix}=\begin{pmatrix}g_1(s)\\ g_2(s)\\ g_3(s)\\ g_4(s)\\ g_5(s)\\ g_6(s)\end{pmatrix}, \tag{12}$$

where $\Delta(s)$ is the characteristic matrix and

$$\begin{cases} g_1(s)=s^{\alpha-1}\phi_1(0),\\ g_2(s)=s^{\alpha-1}\phi_2(0),\\ g_3(s)=s^{\alpha-1}\phi_3(0),\\ g_4(s)=s^{\alpha-1}\phi_4(0),\\ g_5(s)=s^{\alpha-1}\phi_5(0)+e^{-s\tau_2}\int_{-\tau_2}^{0}e^{-su}(\phi_4(u)+\phi_5(u))du,\\ g_6(s)=s^{\alpha-1}\phi_6(0). \end{cases}$$

We denote $H_1=\frac{(1-\varepsilon_1)\beta_1V_{I_2}}{1+\alpha_1V_{I_2}}+\frac{(1-\varepsilon_2)\beta_2A_2}{1+\alpha_2A_2}+\frac{(1-\varepsilon_3)\beta_3L_2}{1+\alpha_3L_2}$, $H_2=\frac{(1-\varepsilon_3)\beta_3S_2}{(1+\alpha_3L_2)^2}$, $H_3=\frac{(1-\varepsilon_2)\beta_2S_2}{(1+\alpha_2A_2)^2}$ and $H_4=\frac{(1-\varepsilon_1)\beta_1S_2}{(1+\alpha_1V_{I_2})^2}$. Then, the characteristic equation in Model (9) at $E_2=(S_2,A_2,L_2,V_{I_2},W_2,0)$ is given by

$$\begin{vmatrix} s^\alpha+d+H_1 & H_2 & H_3 & H_4 & 0 & 0\\ -\eta H_1 & s^\alpha-\eta H_2+e+r & -\eta H_3 & -\eta H_4 & 0 & 0\\ (\eta-1)H_1 & (\eta-1)H_2-r & s^\alpha+(\eta-1)H_3+a & (\eta-1)H_4 & 0 & p_1A_2\\ 0 & 0 & -k(1-\varepsilon_4) & s^\alpha+\mu+pW_2 & pV_{I_2} & 0\\ 0 & 0 & 0 & -gW_2e^{-s\tau_2} & s^\alpha-gV_{I_2}e^{-s\tau_2}+h & 0\\ 0 & 0 & 0 & 0 & 0 & s^\alpha-\sigma A_2+d_c \end{vmatrix}=0.$$

Calculating the corresponding determinant gives

$$(s^\alpha)^5+b_4(s^\alpha)^4+b_3(s^\alpha)^3+b_2(s^\alpha)^2+b_1s^\alpha+b_0+e^{-s\tau_2}(c_4(s^\alpha)^4+c_3(s^\alpha)^3+c_2(s^\alpha)^2+c_1s^\alpha+c_0)=0, \tag{13}$$

where

$$
\begin{aligned}
b_4 =& a+d+e+h+\mu+r+H_1-\eta H_2+(\eta-1)H_3+pW_2,\\
b_3 =& h(a+d+e+\mu+r+H_1+pW_2)+(d+H_1)(e+r)+(H_1+r+d+e)(a+\mu+pW_2)\\
&+a(\mu+pW_2)-H_3r+(\eta-1)H_3(d+e+h+\mu+pW_2)-\eta H_2(+a+d+h+\mu+pW_2),\\
b_2 =& h[(d+H_1)(e+r)+a(\mu+pW_2)+(d+H_1+e+r)(a+\mu+pW_2)]\\
&+a(\mu+pW_2)(d+H_1+e+r)+(d+H_1)(e+r)(a+\mu+pW_2)\\
&-H_3[r(d+\mu+h+pW_2)+(1-\eta)(de+dh+h\mu+e\mu+eh+d\mu)+(1-\eta)pW_2(d+e+h)]\\
&+H_4k[(\eta-1)(1-\varepsilon_4)(h+e+d)-(1-\varepsilon_4)r]\\
&-\eta H_2[d(a+h+\mu+pW_2)+h(a+\mu+pW_2)+a(\mu+pW_2)],\\
b_1 =& h[(d+H_1)(e+r)(a+\mu+pW_2)+a(\mu+pW_2)(d+H_1+e+r)]+(d+H_1)(e+r)a(\mu+pW_2)\\
&-(1-\varepsilon_4)kH_4(r(d+h)+(1-\eta)(dh+eh+de))-\eta H_2[(d+h)(\mu+pW_2)a+(a+\mu)dh+dh]\\
&-H_3[r((d+h)(\mu+pW_2)+dh)+(1-\eta)(deh+de\mu+dh\mu+eh\mu)+(1-\eta)pW_2(de+dh+eh)],\\
b_0 =& (d+H_1)(e+r)a(\mu+pW_2)h-kdhH_4(1-\varepsilon_4)(r+(1-\eta)e)-h(\mu+pW_2)(H_3d(r+(1-\eta)e)\\
&+\eta H_2ad),\\
c_4 =& -gV_{I_2}=-h,\\
c_3 =& -h(H_1+H_3+a+d+e+\mu+r),\\
c_2 =& h[H_3(r+(1-\eta)(d+e+\mu))-(d+H_1)(e+r)-a\mu-(a+\mu)(d+H_1+e+r)+\eta H_2(a+d+\mu)\\
&+H_4((1-\varepsilon_4)k-\eta k)],\\
c_1 =& h[kH_4(r(1-\varepsilon_4)+(1-\eta)(1-\varepsilon_4)(e+d))+H_3((r+(1-\eta)e)(d+\mu)+(1-\eta)d\mu))\\
&-a\mu(d+H_1+e+r)-(d+H_1)(e+r)(a+\mu)+\eta H_2(ad+\mu a+d\mu)],\\
c_0 =& h[kH_4((1-\varepsilon_4)dr+(1-(1-\eta)\varepsilon_4)de-d\eta k)+H_3(r+(1-\eta)e)d\mu-a\mu((d+H_1)(e+r)-\eta H_2d].
\end{aligned}
$$

We aim to prove that equation (13) has no purely imaginary roots for $\tau_2>0$. Suppose, by contradiction, that equation (13) has a purely imaginary root. Substituting $s(\tau_2)=iv(\tau_2)$ with $v>0$ into equation (13), we obtain

$$U_1+iV_1+(U_2+iV_2)(\cos v\tau_2-i\sin v\tau_2)=0, \tag{14}$$

where

$$U_1 = v^{5\alpha}\cos\frac{5\alpha\pi}{2} + b_4 v^{4\alpha}\cos 2\alpha\pi + b_3 v^{3\alpha}\cos\frac{3\alpha\pi}{2} + b_2 v^{2\alpha}\cos\alpha\pi + b_1 v^{\alpha}\cos\frac{\alpha\pi}{2} + b_0,$$

$$V_1 = v^{5\alpha}\sin\frac{5\alpha\pi}{2} + b_4 v^{4\alpha}\sin 2\alpha\pi + b_3 v^{3\alpha}\sin\frac{3\alpha\pi}{2} + b_2 v^{2\alpha}\sin\alpha\pi + b_1 v^{\alpha}\sin\frac{\alpha\pi}{2},$$

$$U_2 = c_4 v^{4\alpha}\cos 2\alpha\pi + c_3 v^{3\alpha}\cos\frac{3\alpha\pi}{2} + c_2 v^{2\alpha}\cos\alpha\pi + c_1 v^{\alpha}\cos\frac{\alpha\pi}{2} + c_0,$$

$$V_2 = c_4 v^{4\alpha}\sin 2\alpha\pi + c_3 v^{3\alpha}\sin\frac{3\alpha\pi}{2} + c_2 v^{2\alpha}\sin\alpha\pi + c_1 v^{\alpha}\sin\frac{\alpha\pi}{2}.$$

Separating the real and imaginary parts of equation (14), we obtain

$$\begin{aligned} V_2\sin v\tau_2 + U_2\cos v\tau_2 &= -U_1, \\ -U_2\sin v\tau_2 + V_2\cos v\tau_2 &= -V_1. \end{aligned} \tag{15}$$

From (15), we get

$$\cos v\tau_2 = -\frac{U_1U_2 + V_1V_2}{U_2^2 + V_2^2} \equiv G_1(v),$$

$$\sin v\tau_2 = \frac{V_1U_2 - U_1V_2}{U_2^2 + V_2^2} \equiv G_2(v).$$

Clearly, we have $G_1^2(v) + G_2^2(v) = 1$.

Thus,

$$\tau_2^j = \frac{1}{v}\left[\arccos\left(-\frac{U_1U_2 + V_1V_2}{U_2^2 + V_2^2}\right) + 2j\pi\right], \quad j = 0,1,2,\ldots$$

The values of v are obtained from the expressions of U_1, U_2, V_1, and V_2. This equation $G_1^2(v) + G_2^2(v) = 1$ has at least one positive root v_0. Define

$$\tau^* = \min\left\{\tau_2^j\right\}, \quad j = 0,1,2,\ldots$$

We take the derivative of equation (13) with respect to τ_2 to check the transversality condition at $\tau_2 = \tau^*$. We obtain

$$\frac{ds}{d\tau_2}D_1'(s) + \frac{ds}{d\tau_2}D_2'(s)e^{-s\tau_2} - D_2(s)(s + \tau_2\frac{ds}{d\tau_2})e^{-s\tau_2} = 0.$$

Then,

$$\frac{ds}{d\tau_2} = \frac{sD_2(s)e^{-s\tau_2}}{D_1'(s) + D_2'(s)e^{-s\tau_2} - \tau_2 D_2(s)e^{-s\tau_2}},$$

where $D_1(s) = U_1 + iV_1$ and $D_2(s) = U_2 + iV_2$, so

$$\frac{ds}{d\tau_2} = \frac{\mathscr{N}_{11} + i\mathscr{N}_{12}}{\mathscr{N}_{21} + i\mathscr{N}_{22}},$$

where

$$\mathscr{N}_{11} = vU_2 \sin v\tau_2 - vV_2 \cos v\tau_2,$$

$$\mathscr{N}_{12} = vV_2 \sin v\tau_2 + vU_2 \cos v\tau_2,$$

$$\mathscr{N}_{21} = (U_2' - \tau_2 U_2)\cos v\tau_2 + U_1' + (V_2' - \tau_2 V_2)\sin v\tau_2,$$

$$\mathscr{N}_{22} = (V_2' - \tau_2 V_2)\cos v\tau_2 + V_1' - (U_2' - \tau_2 U_2)\sin v\tau_2.$$

Hence,

$$\mathrm{Re}\left(\frac{ds}{d\tau}\right)\Big|_{\tau_2=\tau^*, v=v_0} = \frac{\mathscr{N}_{11}\mathscr{N}_{21} + \mathscr{N}_{12}\mathscr{N}_{22}}{\mathscr{N}_{21}^2 + \mathscr{N}_{22}^2}\Big|_{\tau_2=\tau^*, v=v_0}.$$

Therefore, the transversality condition holds when $(\mathscr{A}_1)$: $\frac{\mathscr{N}_{11}\mathscr{N}_{21}+\mathscr{N}_{12}\mathscr{N}_{22}}{\mathscr{N}_{21}^2+\mathscr{N}_{22}^2} \neq 0$, and then, we obtain the following theorem

Theorem 7. *If $(\mathscr{A}_1)$ holds, then E_2 is locally asymptotically stable for $0 < \tau_2 < \tau^*$, and the model may undergo a Hopf bifurcation at $\tau_2 = \tau^*$.*

By the same reasoning, we can demonstrate the existence of a Hopf bifurcation at the infection equilibrium with both humoral and cellular immunity E_4.

6. Conclusion

In this paper, we have proposed a novel general model using FDDEs with the Caputo fractional derivative, which describes the dynamics of HIV infection. Our model considered the three modes of transmission that are virus-to-cell, cell-to-cell by productive infected cells and cell-to-cell by non-productive infected cells, the two types of infected cells, the adaptive immunity exerted by antibodies and CTL cells, the delays in viral production and in the activation time of antibodies, and two types of viruses that are obtained through the introduction of the four therapeutic parameters. In the analysis of the model, we have identified five threshold parameters related to viral infection: the basic reproduction number $\mathscr{R}_0$, the reproduction number for humoral immunity $\mathscr{R}_1^W$,the reproduction number for cellular immunity $\mathscr{R}_1^C$, the reproduction number for cellular immunity in competition $\mathscr{R}_2^C$ and the reproduction number for humoral immunity in competition $\mathscr{R}_2^W$. Subsequently, we have proved that our model has also five equilibrium points based on specific conditions related to these threshold parameters. In addition, we established the global stability of these equilibirum points and explored the existence of the

Hopf bifurcation, which arises when the second delay exceeds a certain critical value, for both infection equilibrium points with only humoral immunity E_2 and with both humoral and cellular immunity E_4.

The memory in the present model was described by the Caputo fractional derivative with singular kernel and one order parameter. It will be interesting to model the memory effect on the dynamics of HIV infection by using the Hattaf fractal and fractional derivatives [16, 17, 18]. This issue will be addressed in our future research.

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CONFLICT OF INTERESTS

The authors declare that there is no conflict of interests.

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