Global analysis of within-host SARS-CoV-2/HIV coinfection model with latency

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Abstract The coronavirus disease 2019 (COVID-19) is a respiratory disease caused by a virus called the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). In this paper, we analyze a within-host SARS-CoV-2/HIV coinfection model. The model is made up of eight ordinary differential equations. These equations describe the interactions between healthy epithelial cells, latently infected epithelial cells, productively infected epithelial cells, SARS-CoV-2 particles, healthy CD4+ T cells, latently infected CD4+ T cells, productively infected CD4+ T cells, and HIV particles. We confirm that the solutions of the developed model are bounded and nonnegative. We calculate the different steady states of the model and derive their existence conditions. We choose appropriate Lyapunov functions to show the global stability of all steady states. We execute some numerical simulations to assist the theoretical contributions. Based on our results, weak CD4+ T cell immunity in SARS-CoV-2/HIV coinfected patients causes an increase in the concentrations of productively infected epithelial cells and SARS-CoV-2 particles. This may lead to severe SARS-CoV-2 infection in HIV patients. This result agrees with many studies that discussed the high risk of severe infection and death in HIV patients when they get SARS-CoV-2 infection. On the other hand, increasing the death rate of infected epithelial cells during the latency period can reduce the severity of SARS-CoV-2 infection in HIV patients. More studies are needed to understand the dynamics of SARS-CoV-2/HIV coinfection and find better ways to treat this vulnerable group of patients.

1 Introduction

The coronavirus disease 2019 (COVID-19) is a new epidemic that emerged in China in late 2019. It is a respiratory disease ascribed to a virus called the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). According to COVID-19 weekly epidemiological update of October 13, 2021, by the World Health Organization (WHO) [1], the cumulative number of confirmed cases reported globally exceeded 237 million and the total number of deaths reached over 4.8 million [1]. The number of new weekly COVID-19 cases has showed a decline since late August 2021 in most countries of the world [1]. SARS-CoV-2/HIV coinfection has become a concern especially in HIV patients who are not receiving antiretroviral therapy (ART) or have low CD4+ T cell counts [2,3]. As there were approximately 37.7 million people living with HIV at the end of 2020 [4], understanding SARS-CoV-2/HIV coinfection should take a special attention.

SARS-CoV-2 is an RNA virus and it is a member of the Coronavirusidae family [5]. It binds to the angiotensin-converting enzyme 2 (ACE2) receptor of epithelial cells [5,6]. The principal target of SARS-CoV-2 is the alveolar epithelial type 2 cells of the lungs [7]. ACE2 is also expressed in many organs like the kidney, liver, and heart [8]. SARS-CoV-2 is mainly transmitted through respiratory droplets which carry virus particles [9]. Many COVID-19 therapies are being clinically tested to evaluate their effectiveness and safety [10]. The U.S. Food and Drug Administration (FDA) has approved the antiviral drug Veklury to treat COVID-19 in adults and some pediatric patients who need hospitalization [10]. There are seven vaccines approved for use by WHO: Pfizer/BioNTech, Moderna, Janssen(Johnson & Johnson), Oxford/AstraZeneca, Serum Institute of India, Sinpharm (Beijing), and Sinovac [11].

On the other hand, HIV is a member of RNA lentiviruses [9]. The principal receptor of HIV is CD4 receptor [6,9]. CD4 is expressed in different immune cells like CD4+ T cells, macrophages, and dendritic cells [6]. Nevertheless, CD4+ T cells are the primary target of HIV. CD4+ T cells help other immune cells like CD8+ T cells and B cells in fighting against viral infections [12]. Targeting CD4+ T cells by HIV causes a reduction in the number of these cells. Therefore, the body of HIV patient becomes susceptible to other viral infections [13]. HIV is transmitted through blood or sexual contact [6]. Antiretroviral therapy (ART) is used to treat HIV infection, which reduces the viral load and prevents the development to the acquired immunodeficiency syndrome (AIDS) [14]. Notably, no HIV vaccines have been approved yet [6].

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The first case of SARS-CoV-2/HIV coinfection was reported for a 61-year-old man from China [9]. Other coinfection cases were reported in Spain, Italy, and the USA [9]. The most typical symptoms of coinfection were fever, cough, and shortness of breath [9]. It has been found that HIV patients are more likely to experience severe COVID-19 when infected [3]. The risk of severe infection increases further in HIV patients who do not receive antiretroviral therapy or have low CD4+ T cell counts [3,15]. Furthermore, the severity risk increases in the presence of other comorbidities like hypertension, diabetes, respiratory disease, cardiovascular disease, and chronic kidney disease [3,16,17]. Based on WHO recommendations [18], many COVID-19 vaccines are safe for people living with HIV.

Mathematical modeling has been considered a significant tool for studying and investigating viral infections. HIV within-host models have received great attention and lead to the significant results. These models were formulated using ordinary differential equations (ODEs) [19–23], delay differential equations (DDEs) [24–27], partial differential equations (PDEs) [28–31], delay partial differential equations (DPDEs) [13,32–34], and fractional differential equations (FDEs) [35,36]. These models exhibit mainly the interactions between HIV, uninfected CD4+ T cells, different types of infected CD4+ T cells, and the immune system.

However, very few models have studied so far to investigate the dynamics of SARS-CoV-2 within the human body. For example, Li et al. [37] formulated a within-host ODE model to characterize the interactions between uninfected epithelial cells, infected epithelial cells, and SARS-CoV-2 particles. Du and Yuan [38] analyzed a similar model with taking into consideration the effect of antiviral drugs which prevent either infection or the production of SARS-CoV-2 particles. Al Agha et al. [7] used a within-host DDE to depict the effect of SARS-CoV-2 infection on cancer patients and the impact of infection on immune responses. Pinky and Dobrovolny [39] established a within-host model to study SARS-CoV-2 coinfection with other viruses like influenza A virus and human rhinovirus. Fadai et al. [40] proposed an ODE model with the assumption that uninfected epithelial cells follow logistic growth.

To the best of our knowledge, no within-host SARS-CoV-2/HIV models have been studied so far. However, it is worth mentioning that Bellomo et al. [41,42] studied the within-host dynamics of SARS-CoV-2 within a multiscale approach and the mathematical theory of active particles. The multiscale approach accounts for the interaction of different spatial scales where the dynamics at the high scale of individuals depends on the dynamics at the microscopic scale. Microscopic scale is determined by the competition between virus particles and the immune cells. Thus, the multiscale approach can be used to predict the time evolution of the number of healthy, infected, recovered, and dead individuals. Nevertheless, in this paper we concentrate on the interactions at the microscopic scale of coinfection between SARS-CoV-2 and HIV. Coinfection models are needed to help understand the dynamics of SARS-CoV-2 infection in HIV patients and the role of the immune system, to support medical research, and to find better ways to treat this vulnerable group of patients. In this paper, we establish a within-host model of SARS-CoV-2/HIV coinfection. For this model, we (i) demonstrate that all solutions are bounded and nonnegative, (ii) calculate all steady-state solutions and the corresponding positivity conditions of their components. (iii) show the global stability of the steady states, (iv) execute some numerical simulations to enhance the results of computations, (v) discuss the effect of low concentration of CD4+ T cells on coinfected patients, (vi) test the impact of latency on the number of SARS-CoV-2 particles and HIV particles, and (vii) suggest some possible future works.

The paper is organized as follows. Section 2 describes the model under consideration. Section 3 shows that all solutions are bounded and greater than or equal zero. In addition, it lists all steady states with the positivity conditions of their components. Section 4 proves the global stability of all steady states computed in Sect. 3. Section 5 displays some numerical simulations. Finally, Sect. 6 discusses the results with some suggestions for future works.

2 SARS-CoV-2/HIV coinfection model with latency

This section describes the model intended to be studied in this paper. The proposed model takes the form

\[
\begin{align*}
\dot{X} &= \rho - d_1 X - \eta VX, \\
\dot{N} &= \eta VX - (k + d_2)N, \\
\dot{Y} &= kN - d_3 Y - \mu Y S, \\
\dot{V} &= aY - d_4 V, \\
\dot{S} &= \xi + uYS - d_5 S - \theta HS, \\
\dot{T} &= (1 - b)\theta HS - (\alpha + d_6)T, \\
\dot{W} &= b_H HS + \alpha T - d_7 W, \\
\dot{H} &= \lambda W - d_8 H,
\end{align*}
\]

(1)

where \((X, N, Y, V, S, T, W, H) = (X(t), N(t), Y(t), V(t), S(t), T(t), W(t), H(t))\) denote the concentrations of uninfected epithelial cells, latently infected epithelial cells, actively infected epithelial cells, free SARS-CoV-2 particles, uninfected CD4+ T cells, latently infected CD4+ T cells, actively infected CD4+ T cells, and free HIV particles at time \(t\). Epithelial cells are produced from a source at a constant rate \(\rho\), die at rate \(d_1 X\), and get infected by SARS-CoV-2 at rate \(\eta VX\). Latently infected epithelial cells proliferate at rate \(\eta VX\), turn into active infected cells at rate \(kN\), and die at rate \(d_2 N\). Actively infected epithelial cells die at rate \(d_3 Y\) and are
Table 1  Values of parameters of model (1)

| Par. | Description                                         | Value     | References |
|------|-----------------------------------------------------|-----------|------------|
| ρ    | Recruitment rate of uninfected epithelial cells     | 0.02241   | [43]       |
| d₁   | Death rate constant of uninfected epithelial cells  | 10⁻³      | [43]       |
| n    | Infection rate constant of epithelial cells         | Varied    | –          |
| k    | Transmission rate constant of latently infected epithelial cells into active cells | 4.08      | [39]       |
| d₂   | Death rate constant of latently infected epithelial cells | 10⁻³      | [39]       |
| d₃   | Death rate constant of actively infected epithelial cells | 0.11      | [43]       |
| μ    | Indirect killing rate constant of CD4⁺ T cells      | Varied    | –          |
| a    | Production rate constant of SARS-CoV-2 by actively infected epithelial cells | 0.24      | [43]       |
| d₄   | Death rate constant of free SARS-CoV-2 particles    | Varied    | –          |
| ξ    | Recruitment rate of uninfected CD4⁺ T cells         | 10        | [21]       |
| u    | Stimulation rate constant of CD4⁺ T cells           | 0.1       | [44]       |
| d₅   | Death rate constant of uninfected CD4⁺ T cells      | 0.01      | [45]       |
| θ    | Infection rate constant of CD4⁺ T cells             | Varied    | –          |
| α    | Transmission rate constant of latently infected CD4⁺ T cells into active cells | 0.2       | [46]       |
| d₆   | Death rate constant of latently infected CD4⁺ T cells | 0.02      | [46]       |
| b    | A fraction of newly infected CD4⁺ T cells that become active | 0.7       | [46]       |
| d₇   | Death rate constant of actively infected CD4⁺ T cells | 0.5       | [47]       |
| λ    | Production rate constant of HIV by actively infected cells | 5         | [48]       |
| d₈   | Death rate constant of free HIV particles           | 2         | [48]       |

indirectly eliminated by CD4⁺ T cells at rate μYS. SARS-CoV-2 particles are produced from infected cells at rate aV and die at rate d₄V. Uninfected CD4⁺ T cells are produced at a constant rate ξ, stimulated by infected epithelial cells at rate uYS, die at rate d₅S, and get infected by HIV at rate θHS. A fraction b ∈ [0, 1] of new infected CD4⁺ T cells will be active and the rest 1 − b will be latent. Latently infected CD4⁺ T cells are transmitted into active cells at rate αT and die at a natural death rate d₆T. Actively infected CD4⁺ T cells die at a natural death rate d₇W. HIV particles are produced by infected cells at rate λW and die at rate d₈H. The descriptions of the different parameters are summarized in Table 1.

3 Basic properties

This section verifies the nonnegativity and boundedness of solutions of model (1). Moreover, it calculates all possible steady states with the associated threshold conditions.

3.1 Nonnegativity and boundedness

We define a compact set

\[ \Theta = \left\{ (X, N, Y, V, S, T, W, H) \in \mathbb{R}^8_{\geq 0} : 0 \leq X(t), N(t), Y(t) \leq \Omega_1, 0 \leq V(t) \leq \Omega_2, 0 \leq S(t), T(t), W(t) \leq \Omega_3, 0 \leq H(t) \leq \Omega_4 \right\}, \]

where Ω_j > 0, j = 1, . . . , 4.

Proposition 1  The set Θ is positively invariant for model (1).
Then, we get
\[ \dot{X} \big|_{X=0} = \rho > 0, \]
\[ \dot{N} \big|_{N=0} = \eta V X \geq 0 \text{ for all } V, X \geq 0, \]
\[ \dot{Y} \big|_{Y=0} = kN \geq 0 \text{ for all } N \geq 0, \]
\[ \dot{V} \big|_{V=0} = aY \geq 0 \text{ for all } Y \geq 0, \]
\[ \dot{S} \big|_{S=0} = \xi > 0, \]
\[ \dot{T} \big|_{T=0} = (1-b)\theta HS \geq 0 \text{ for all } H, S \geq 0, \]
\[ \dot{W} \big|_{W=0} = b\theta HS + \alpha T \geq 0 \text{ for all } H, S, T \geq 0, \]
\[ \dot{H} \big|_{H=0} = \lambda W \geq 0 \text{ for all } W \geq 0. \]

Thus, we get \( (X(t), N(t), Y(t), V(t), S(t), T(t), W(t), H(t)) \in \mathbb{R}^8 \geq 0 \) for all \( t \geq 0 \) when \( (X(0), N(0), Y(0), V(0), S(0), T(0), W(0), H(0)) \in \mathbb{R}^8 \geq 0. \)

To prove the boundedness of all state variables, we define

\[ \Psi(t) = X + N + Y + \frac{d_3}{2a} V + \frac{\mu}{u} (S + T + W) + \frac{\mu d_7}{2u\lambda} H. \]

Then, we get

\[ \dot{\Psi}(t) = \rho + \frac{\mu}{u} \xi - d_1 X - d_2 N - \frac{d_3}{2} Y - \frac{d_3 d_4}{2a} V - \frac{\mu d_6}{u} S - \frac{\mu d_7}{u} T - \frac{\mu d_7}{2u\lambda} W - \frac{\mu d_7 d_8}{2u\lambda} H \]

\[ \leq \left( \rho + \frac{\mu}{u} \xi \right) - \phi \left[ X + N + Y + \frac{d_3}{2a} V + \frac{\mu}{u} (S + T + W) + \frac{\mu d_7}{2u\lambda} H \right] \]

\[ = \left( \rho + \frac{\mu}{u} \xi \right) - \phi \Psi(t), \]

where \( \phi = \min \left\{ d_1, d_2, \frac{d_3}{2}, d_4, d_5, d_6, \frac{d_7}{2}, d_8 \right\} \). It follows that

\[ \Psi(t) \leq e^{-\phi t} \left( \Psi(0) - \frac{\rho + \frac{\mu}{u} \xi}{\phi} \right) + \frac{\rho + \frac{\mu}{u} \xi}{\phi}. \]

Hence, \( 0 \leq \Psi(t) \leq \Omega_1 \) if \( \Psi(0) \leq \Omega_1 \) for \( t \geq 0 \), where \( \Omega_1 = \frac{\rho + \frac{\mu}{u} \xi}{\phi} \). As \( X, N, Y, V, S, T, W \) and \( H \) are nonnegative, we have \( 0 \leq X(t), N(t), Y(t) \leq \Omega_1, 0 \leq V(t) \leq \Omega_2, 0 \leq S(t), T(t), W(t) \leq \Omega_3, 0 \leq H(t) \leq \Omega_4 \) if \( X(0) + N(0) + Y(0) + \frac{d_3}{2a} V(0) + \frac{\mu}{u} (S(0) + T(0) + W(0)) + \frac{\mu d_7}{2u\lambda} H(0) \leq \Omega_1 \), where \( \Omega_2 = \frac{2a}{d_3}, \Omega_3 = \frac{1}{\mu} \Omega_1, \) and \( \Omega_4 = \frac{2u\lambda}{\mu d_7} \Omega_1 \). This shows that the set \( \Theta \) is positively invariant. \( \square \)

### 3.2 Steady states

In this subsection, we calculate all possible steady states of model (1) and conclude the threshold conditions that cover the existence of these steady states.

To compute the steady states of the model we solve the following system of algebraic equations:

\[
\begin{cases}
0 = \rho - d_1 X - \eta V X, \\
0 = \eta V X - (k + d_2) N, \\
0 = kN - d_3 Y - \mu Y S, \\
0 = aY - d_4 V, \\
0 = \xi + a Y S - d_5 S - \theta H S, \\
0 = (1-b)\theta HS - (\alpha + d_6) T, \\
0 = b\theta HS + \alpha T - d_7 W, \\
0 = \lambda W - d_8 H.
\end{cases}
\]

We find that model (1) has four steady states:

(i) The uninfected steady state \( \Delta_0(X_0, 0, 0, 0, S_0, 0, 0, 0) \), where \( X_0 = \frac{\rho}{d_1} \) and \( S_0 = \frac{\xi}{d_5} \).
(ii) The single SARS-CoV-2–infection steady state $\Delta_H(X_1, 0, 0, S_1, T_1, W_1, H_1)$, where

$$X_1 = \frac{\rho}{d_1} = X_0, \quad S_1 = \frac{d_2 d_8 (d_6 + \alpha)}{\theta \lambda (\alpha + d_6 b)} = \frac{S_0}{R_1},$$

$$T_1 = (1 - b) \left( \frac{\xi}{d_0 + \alpha} - \frac{d_6 d_7 d_8}{\theta \lambda (\alpha + d_6 b)} \right) = \frac{d_6 d_7 d_8 (1 - b)}{\theta \lambda (\alpha + d_6 b)} (R_1 - 1),$$

$$W_1 = - \frac{d_5 d_8}{\theta \lambda} + \frac{\xi (\alpha + d_6 b)}{d_7 (d_6 + \alpha)} = \frac{d_6 d_8}{\theta \lambda} (R_1 - 1),$$

where $R_1 = \frac{\xi \theta \lambda (\alpha + d_6 b)}{d_6 d_7 d_8 (d_6 + \alpha)}$. Here, $R_1$ is the basic reproduction number of HIV infection. It determines the establishment of HIV infection in the body. We see that $X_1$ and $S_1$ are always positive, while $T_1, W_1$ and $H_1$ are positive if $R_1 > 1$. Therefore, $\Delta_H$ exists when $R_1 > 1$.

(iii) The single SARS-CoV-2–infection steady state $\Delta_V(X_2, N_2, Y_2, V_2, S_2, 0, 0, 0)$, where

$$Y_2 = \frac{d_4 V_2}{a}, \quad S_2 = \frac{\xi}{d_5 - a Y_2}, \quad X_2 = \frac{(k + d_2) Y_2 d_3 + S_2 Y_2 \mu}{k \eta Y_2}, \quad N_2 = \frac{Y_2 d_3 + S_2 Y_2 \mu}{k},$$

and $V_2$ satisfies the following equation:

$$\frac{P_1 V_2^2 + P_2 V_2 + P_3}{a k \eta (a d_5 - a d_4 V)} = 0,$$

where

$$\begin{align*}
P_1 &= u d_2 \eta d_3 (k + d_2), \\
P_2 &= u d_1 d_2 d_3 (k + d_2) - a d_3 d_4 \eta d_3 (k + d_2) - a d_4 \eta \mu \xi (k + d_2) - a u d_4 \eta \mu k, \\
P_3 &= - a d_1 d_3 d_4 \xi (k + d_2) - a d_4 \mu \eta \xi (k + d_2) + a^2 d_3 d_5 \eta k.
\end{align*}$$

Now we show that there exists a positive root for Eq. (3). We define a function $G(V)$ as

$$G(V) = \frac{P_1 V^2 + P_2 V + P_3}{a k \eta (a d_5 - a d_4 V)}.$$

We have

$$G(0) = \frac{- a d_1 d_3 d_4 \xi (k + d_2) - a d_3 d_4 \eta \mu \xi (k + d_2) + a^2 d_5 d_4 \eta k}{a^2 d_3 d_5 \eta k} = \frac{(k + d_2) (d_1 d_3 d_4 d_5 + d_1 d_4 d_5 \xi)}{a d_5 d_4 \eta k} (R_2 - 1),$$

where $R_2 = \frac{a d_5 d_4 \eta k}{d_1 d_4 (k + d_2) (d_5 d_3 + \mu \xi)}$. This implies that $G(0) > 0$ when $R_2 > 1$. Moreover, we find that

$$\lim_{V \to \frac{a d_5}{a d_4}} G(V) = - \infty.$$

It follows that there exists $0 < V_2 < \frac{a d_5}{a d_4}$ such that $G(V_2) = 0$. From Eq. (2) we get $Y_2 > 0$, $S_2 > 0$, $X_2 > 0$ and $N_2 > 0$. As a result, $\Delta_V$ exists when $R_2 > 1$. The parameter $R_2$ is the basic reproduction number of SARS-CoV-2 infection. It determines the establishment of SARS-CoV-2 infection in the body.
(iv) The SARS-CoV-2/HIV coinfection steady state \( \Delta_{VH}(X_3, N_3, Y_3, V_3, S_3, W_3, H_3) \), where

\[
X_3 = \frac{d_3(k + d_2)[d_3\theta\lambda(\alpha + d_6b) + \mu d_7d_8(d_6 + \alpha)]}{ak\eta\theta\lambda(\alpha + d_6b)},
\]
\[
N_3 = -\frac{d_1d_4[d_3\theta\lambda(\alpha + d_6b) + \mu d_7d_8(d_6 + \alpha)]}{ak\eta\theta\lambda(\alpha + d_6b)} + \frac{\rho}{k + d_2},
\]
\[
Y_3 = -\frac{d_1d_4}{a\eta} + \frac{\theta\lambda\rho k(\alpha + d_6b)}{(k + d_2)[d_3\theta\lambda(\alpha + d_6b) + \mu d_7d_8(d_6 + \alpha)]},
\]
\[
V_3 = -\frac{d_1}{\eta} + \frac{d_4(k + d_2)[d_3\theta\lambda(\alpha + d_6b) + \mu d_7d_8(d_6 + \alpha)]}{ak\theta\lambda\rho(\alpha + d_6b)},
\]
\[
S_3 = \frac{d_7d_8(d_6 + \alpha)}{\theta\lambda(\alpha + d_6b)},
\]
\[
T_3 = \frac{d_7d_8(1 - b)(d_1d_4u + ad_5\eta)}{a\eta\theta\lambda(\alpha + d_6b)} \times \left[ \frac{a\eta\theta\lambda(\alpha + d_6b)}{a\eta\theta\lambda(d_3 + d_1d_4u)} \left( \frac{\xi}{d_7d_8(d_6 + \alpha)} + \frac{upk}{(k + d_2)[d_3\theta\lambda(\alpha + d_6b) + \mu d_7d_8(d_6 + \alpha)]} - 1 \right) \right].
\]
\[
W_3 = \frac{d_8(a\eta\theta\lambda + d_1d_4u)}{a\eta\theta\lambda},
\]
\[
H_3 = \frac{a\eta\theta\lambda}{a\eta\theta\lambda} \times \left[ \frac{a\eta\theta\lambda(\alpha + d_6b)}{a\eta\theta\lambda(d_3 + d_1d_4u)} \left( \frac{\xi}{d_7d_8(d_6 + \alpha)} + \frac{upk}{(k + d_2)[d_3\theta\lambda(\alpha + d_6b) + \mu d_7d_8(d_6 + \alpha)]} - 1 \right) \right].
\]

It follows that \( T_3 > 0 \), \( W_3 > 0 \) and \( H_3 > 0 \) only when \( \frac{a\eta\theta\lambda(\alpha + d_6b)}{a\eta\theta\lambda(d_3 + d_1d_4u)} \left( \frac{\xi}{d_7d_8(d_6 + \alpha)} \right) + \frac{upk}{(k + d_2)[d_3\theta\lambda(\alpha + d_6b) + \mu d_7d_8(d_6 + \alpha)]} > 1 \). On the other hand, \( N_3 > 0 \), \( Y_3 > 0 \) and \( V_3 > 0 \) only when \( \frac{a\eta\theta\lambda(\alpha + d_6b)}{a\eta\theta\lambda(d_3 + d_1d_4u)} \left( \frac{\xi}{d_7d_8(d_6 + \alpha)} \right) > 1 \).

Thus, we can rewrite the components of \( \Delta_{VH} \) as

\[
X_3 = \frac{X_0}{R_4}, \quad N_3 = \frac{d_1d_4[d_3\theta\lambda(\alpha + d_6b) + \mu d_7d_8(d_6 + \alpha)]}{a\eta\theta\lambda(k(\alpha + d_6b))} \left( R_4 - 1 \right),
\]
\[
Y_3 = \frac{d_1d_4}{a\eta} \left( R_4 - 1 \right), \quad V_3 = \frac{d_1}{\eta} \left( R_4 - 1 \right),
\]
\[
S_3 = \frac{d_7d_8(d_6 + \alpha)}{\theta\lambda(\alpha + d_6b)}, \quad T_3 = \frac{d_7d_8(1 - b)(d_1d_4u + ad_5\eta)}{a\eta\theta\lambda(\alpha + d_6b)} \left( R_3 - 1 \right),
\]
\[
W_3 = \frac{d_8(a\eta\theta\lambda + d_1d_4u)}{a\eta\theta\lambda} \left( R_3 - 1 \right), \quad H_3 = \frac{a\eta\theta\lambda}{a\eta\theta\lambda} \left( R_3 - 1 \right),
\]

where

\[
R_3 = \frac{a\eta\theta\lambda(\alpha + d_6b)}{a\eta\theta\lambda(d_3 + d_1d_4u)} \left( \frac{\xi}{d_7d_8(d_6 + \alpha)} + \frac{upk}{(k + d_2)[d_3\theta\lambda(\alpha + d_6b) + \mu d_7d_8(d_6 + \alpha)]} \right),
\]
\[
R_4 = \frac{a\eta\theta\lambda(\alpha + d_6b)}{a\eta\theta\lambda(k(\alpha + d_6b))} \left( R_4 - 1 \right).
\]

Therefore, \( \Delta_{VH} \) exists when \( R_3 > 1 \) and \( R_4 > 1 \). At this point, \( R_3 \) and \( R_4 \) are threshold numbers that determine the occurrence of SARS-CoV-2/HIV coinfection.

All steady states of model (1) and their existence conditions are summarized in Table 2.
Theorem 1 presented in [49]. We define

$$\Theta_1$$

in this section, we prove the global asymptotic stability of all steady states by constructing Lyapunov functions following the method

$$\Delta_1$$

Steady state Definition Existence conditions

| Steady state | Definition | Existence conditions |
|--------------|------------|---------------------|
| $\Delta_0 = (X_0, 0, 0, 0, S_0, 0, 0, 0)$ | Uninfected steady state | None |
| $\Delta_H = (X_1, 0, 0, 0, S_1, T_1, W_1, H_1)$ | Single HIV-infection steady state | $R_1 > 1$ |
| $\Delta_V = (X_2, N_2, Y_2, V_2, S_2, 0, 0, 0)$ | Single SARS-CoV-2–infection steady state | $R_2 > 1$ |
| $\Delta_{IV} = (X_3, N_3, Y_3, V_3, S_3, T_3, W_3, H_3)$ | SARS-CoV-2/HIV coinfection steady state | $R_3 > 1$ and $R_4 > 1$ |

The four threshold parameters are given as follows:

$$R_1 = \frac{\xi \theta \lambda (\alpha + \delta_b)}{d \delta_d (\alpha + \delta_b)},
R_2 = \frac{\alpha \theta \lambda (\alpha + \delta_b)}{d \delta_d (\alpha + \delta_b)},
R_3 = \frac{\xi \theta \lambda (\alpha + \delta_b)}{(\alpha + \delta_d) \eta \theta \lambda (\alpha + \delta_b) + \mu \delta_d (\alpha + \delta_b)},
R_4 = \frac{\alpha \theta \lambda (\alpha + \delta_b)}{d \delta_d (\alpha + \delta_b)}.$$

4 Global stability of steady states

In this section, we prove the global asymptotic stability of all steady states by constructing Lyapunov functions following the method presented in [49]. We define $F(v) = v - 1 - \ln v$. We will use the arithmetic–geometric mean inequality

$$\frac{1}{n} \sum_{i=1}^{n} x_i \geq \left( \prod_{i=1}^{n} x_i \right)^{\frac{1}{n}}, \quad x_i \geq 0, \quad i = 1, 2, \ldots$$

which yields

$$\frac{S_j}{S} + \frac{S_j W_i H_j}{S_j W_i H_j} + \frac{W H_i}{W_i H_j} \geq 3, \quad j = 1, 3,$n
$$\frac{S_j}{S} + \frac{S_j W_i H_j}{S_j W_i H_j} + \frac{W H_i}{W_i H_j} + \frac{T W_j}{T_j W} \geq 4, \quad j = 1, 3,$$n
$$\frac{X_j}{X} + \frac{X_j N j}{X_j N j} + \frac{Y V_j}{Y_j V} + \frac{N Y_j}{N_j Y} \geq 4, \quad j = 2, 3.$$n

Theorem 1 If $R_1 \leq 1$ and $R_2 \leq 1$, then $\Delta_0$ is globally asymptotically stable (G.A.S).

Proof Construct a Lyapunov function $\varnothing_0(X, N, Y, V, S, T, W, H)$ as:

$$\varnothing_0 = X_0 F \left( \frac{X}{X_0} \right) + N + \frac{k + d_2}{k} Y + \eta X_0 \frac{V}{d_4} + \frac{\mu (k + d_2)}{uk} \frac{S_0 F \left( \frac{S}{S_0} \right)}{W} + \frac{\lambda \mu d_2 (k + d_2) (\alpha + \delta_b)}{\lambda \mu \alpha (d_2 + \delta_b)}.$$n

Clearly, $\varnothing_0(0, 0, 0, S_0, 0, 0, 0, 0) = 0$. By calculating $d \varnothing_0 / dt$, we get

$$\frac{d \varnothing_0}{dt} = \left( 1 - \frac{X_0}{X} \right) \dot{X} + \dot{N} + \frac{k + d_2}{k} \dot{Y} + \frac{\eta X_0}{d_4} \dot{V} + \frac{\mu (k + d_2)}{uk} \left( 1 - \frac{S_0}{S} \right) \dot{S} + \frac{\lambda \mu d_2 (k + d_2)}{\lambda \mu \alpha (d_2 + \delta_b)} \dot{H}.$$n

$$= \left( 1 - \frac{X_0}{X} \right) \left( \rho - d_1 X - \eta Y X + \eta Y X - (k + d_2) N \right) + \frac{k + d_2}{k} \left( k N - d_3 Y - \mu Y S + \eta X_0 \frac{V}{d_4} (\alpha Y - d_4 V) \right)$$n

$$+ \frac{\mu (k + d_2)}{uk} \left( 1 - \frac{S_0}{S} \right) \left( \xi \mu S - d_3 S - \theta H S + \frac{\mu \alpha (k + d_2)}{\lambda \mu \alpha (d_2 + \delta_b)} (1 - b) \theta H S - (\alpha + d_6) T \right)$$n

$$+ \frac{\mu (k + d_2)}{uk} \left( \frac{\lambda \mu d_2 (k + d_2)}{\lambda \mu \alpha (d_2 + \delta_b)} (b \theta H S + \alpha T - d_7 W) + \frac{\mu \alpha (k + d_2)}{\lambda \mu \alpha (d_2 + \delta_b)} \left( \lambda W - d_8 H \right) \right).$$
Using $\rho = d_1 X_0$ and $\xi = d_5 S_0$, we obtain

\[
\frac{d\rho_0}{dt} = -\frac{d_1 X_0}{X} (X - X_0)^2 - \eta V X + \eta V X_0 + \eta V X - (k + d_2) N + (k + d_2) N - \frac{k + d_2}{k} d_3 Y - \frac{k + d_2}{k} \mu Y S + \frac{\eta X_0}{d_4} a Y - \eta X_0 V - \frac{\mu d_5 (k + d_2)}{u k S} (S - S_0)^2 + \frac{k + d_2}{k} \mu Y S - \frac{k + d_2}{k} \mu Y S_0 - \frac{\mu (k + d_2)}{u k} \theta H S + \frac{\mu (k + d_2)}{u k (\alpha + d_6 b)} (S - S_0) H + \frac{\mu (k + d_2)}{u k (\alpha + d_6 b)} \frac{\theta S_0 H}{(1 - b) \theta H S - \frac{\mu \alpha (k + d_2)}{u k (\alpha + d_6 b)}} (\alpha + d_6) T + \frac{\mu (k + d_2) (d_6 + \alpha)}{u k (\alpha + d_6 b)} \theta H S + \frac{\mu (k + d_2) (d_6 + \alpha)}{u k (\alpha + d_6 b)} \alpha T - \frac{\mu (k + d_2) (d_6 + \alpha)}{u k (\alpha + d_6 b)} \theta H S + \frac{\mu (k + d_2) (d_6 + \alpha)}{u k (\alpha + d_6 b)} \theta H S + \frac{\mu (k + d_2) (d_6 + \alpha)}{u k (\alpha + d_6 b)} \theta H S + \frac{\mu (k + d_2) (d_6 + \alpha)}{u k (\alpha + d_6 b)} \theta H S + \frac{\mu (k + d_2) (d_6 + \alpha)}{u k (\alpha + d_6 b)} \theta H S + \frac{\mu (k + d_2) (d_6 + \alpha)}{u k (\alpha + d_6 b)} \theta H S + \frac{\mu (k + d_2) (d_6 + \alpha)}{u k (\alpha + d_6 b)} \theta H S + \frac{\mu (k + d_2) (d_6 + \alpha)}{u k (\alpha + d_6 b)} \theta H S + \frac{\mu (k + d_2) (d_6 + \alpha)}{u k (\alpha + d_6 b)} \theta H S
\]

As $R_1 \leq 1$ and $R_2 \leq 1$, we get $\frac{d\rho_0}{dt} \leq 0$ for all $X, N, Y, V, S, T, W, H > 0$ and $\frac{d\rho_0}{dt} = 0$ when $X = X_0, S = S_0$ and $Y = H = 0$.

Define $\Upsilon_0 = \{ (X, N, Y, V, S, T, W, H) : \frac{d\rho_0}{dt} = 0 \}$ and let $\Upsilon_0'$ be the largest invariant subset of $\Upsilon_0$. The solutions of model (1) converge to $\Upsilon_0$. The set $\Upsilon_0'$ includes elements with $X = X_0$, $S = S_0$ and $Y = H = 0$, and hence $\dot{Y} = \dot{H} = 0$. The third and last equations of model (1) yield

\[
0 = \dot{Y} = k N, \\
0 = \dot{H} = \lambda W.
\]

Thus, $N(t) = W(t) = 0$ for all $t$. The second and seventh equations give

\[
0 = \dot{N} = \eta V X_0, \\
0 = \dot{W} = a T.
\]

Thus, $V(t) = T(t) = 0$ for all $t$. Therefore, $\Upsilon_0' = \{ \Delta_0 \}$ and by applying Lyapunov–LaSalle asymptotic stability theorem [50–52] we get that $\Delta_0$ is G.A.S.

**Theorem 2** If $R_1 > 1$ and $R_4 \leq 1$, then $\Delta_H$ is globally asymptotically stable (G.A.S.).

**Proof** Define a Lyapunov function $\vartheta_1(X, N, Y, V, S, T, W, H)$ as

\[
\vartheta_1 = X_1 F \left( \frac{X}{X_1} \right) + N + \frac{k + d_2}{k} Y + \frac{\eta X_0}{d_4} V + \frac{\mu (k + d_2)}{u k} S_1 F \left( \frac{S}{S_1} \right) + \frac{\mu \alpha (k + d_2)}{u k (\alpha + d_6 b)} T_1 F \left( \frac{T}{T_1} \right) + \frac{\mu (k + d_2) (d_6 + \alpha)}{u k (\alpha + d_6 b)} W_1 F \left( \frac{W}{W_1} \right) + \frac{\mu d_5 (k + d_2) (d_6 + \alpha)}{\lambda u k (\alpha + d_6 b)} H_1 F \left( \frac{H}{H_1} \right).
\]

\[\square\] Springer
By differentiating $\vartheta_1$, we obtain

$$\frac{d\vartheta_1}{dr} = \left(1 - \frac{X_1}{X}\right) + \frac{k + d_2}{k} Y + \frac{\eta X_1}{d_4} \frac{\nu(k + d_2)}{u k} \left(1 - \frac{S_1}{S}\right) S + \frac{\mu \alpha (k + d_2)}{u k (\alpha + d_6 b)} \left(1 - \frac{T_1}{T}\right) \frac{\lambda}{H}$$

where $\vartheta_1 = \frac{d_2}{d_1} a Y_k - \frac{\eta X_1}{d_4} S + \frac{\nu(k + d_2)}{u k (\alpha + d_6 b)} \left(1 - \frac{T_1}{T}\right) \frac{\lambda}{H}$

Using steady-state conditions for $\Delta H$, we get

$$\begin{align*}
\rho &= d_1 X_1, \\
\xi &= d_2 S_1 + \theta H_1 S_1, \\
(1 - b) \theta H_1 S_1 &= (\alpha + d_6) T_1, \\
\lambda W_1 &= d_8 H_1.
\end{align*}$$

Then, we obtain

$$\frac{d\vartheta_1}{dr} = -\frac{d_1}{X} (X - X_1)^2 + \frac{\eta X_1}{d_4} a - \frac{k + d_2}{k} d_3 - \frac{k + d_2}{k} \frac{\nu S_1}{u k S} Y - \frac{\mu S_1}{u k (\alpha + d_6 b)} (S - S_1)^2$$

$$+ \frac{\mu (k + d_2)}{u k} \theta H_1 S_1 - \frac{\nu(k + d_2)}{u k} \theta H_1 S_1 + \frac{\mu (k + d_2)}{u k} \theta H S_1 - \frac{\mu \alpha (k + d_2)}{u k (\alpha + d_6 b)} (1 - b) \theta H S_1 \frac{T_1}{T}$$

$$+ \frac{\mu \alpha (k + d_2)}{u k (\alpha + d_6 b)} (1 - b) \theta H S_1 - \frac{\nu S_1}{u k (\alpha + d_6 b)} \theta H S_1 \frac{T W_1}{T_1 W}$$

$$+ \frac{\mu (k + d_2)}{u k (\alpha + d_6 b)} \theta H S_1 \frac{W H_1}{W_1 H} - \frac{\mu (k + d_2)}{u k (\alpha + d_6 b)} \theta H S_1 \frac{W H_1}{W_1 H}$$

$$+ \frac{\nu S_1}{u k (\alpha + d_6 b)} \theta H S_1 \frac{T W_1}{T_1 W}$$

$$+ \frac{\mu (k + d_2)}{u k (\alpha + d_6 b)} \theta H S_1 \frac{W H_1}{W_1 H}$$

$$+ \frac{\mu \alpha (k + d_2)}{u k (\alpha + d_6 b)} (1 - b) \theta H S_1$$

$$+ \frac{\mu \alpha (k + d_2)}{u k (\alpha + d_6 b)} (1 - b) \theta H S_1$$

$$+ \frac{\nu S_1}{u k (\alpha + d_6 b)} \theta H S_1 \frac{T W_1}{T_1 W}$$

$$+ \frac{\mu (k + d_2)}{u k (\alpha + d_6 b)} \theta H S_1 \frac{W H_1}{W_1 H}$$

$$+ \frac{\mu \alpha (k + d_2)}{u k (\alpha + d_6 b)} (1 - b) \theta H S_1$$

$$+ \frac{\nu S_1}{u k (\alpha + d_6 b)} \theta H S_1 \frac{T W_1}{T_1 W}$$

$$+ \frac{\mu (k + d_2)}{u k (\alpha + d_6 b)} \theta H S_1 \frac{W H_1}{W_1 H}$$

$$+ \frac{\mu \alpha (k + d_2)}{u k (\alpha + d_6 b)} (1 - b) \theta H S_1$$

$$+ \frac{\nu S_1}{u k (\alpha + d_6 b)} \theta H S_1 \frac{T W_1}{T_1 W}$$

$$+ \frac{\mu (k + d_2)}{u k (\alpha + d_6 b)} \theta H S_1 \frac{W H_1}{W_1 H}$$

$$+ \frac{\mu \alpha (k + d_2)}{u k (\alpha + d_6 b)} (1 - b) \theta H S_1$$

$$+ \frac{\nu S_1}{u k (\alpha + d_6 b)} \theta H S_1 \frac{T W_1}{T_1 W}$$

$$+ \frac{\mu (k + d_2)}{u k (\alpha + d_6 b)} \theta H S_1 \frac{W H_1}{W_1 H}$$

$$+ \frac{\mu \alpha (k + d_2)}{u k (\alpha + d_6 b)} (1 - b) \theta H S_1$$

$$+ \frac{\nu S_1}{u k (\alpha + d_6 b)} \theta H S_1 \frac{T W_1}{T_1 W}$$

$$+ \frac{\mu (k + d_2)}{u k (\alpha + d_6 b)} \theta H S_1 \frac{W H_1}{W_1 H}$$

$$+ \frac{\mu \alpha (k + d_2)}{u k (\alpha + d_6 b)} (1 - b) \theta H S_1$$

$$+ \frac{\nu S_1}{u k (\alpha + d_6 b)} \theta H S_1 \frac{T W_1}{T_1 W}$$

$$+ \frac{\mu (k + d_2)}{u k (\alpha + d_6 b)} \theta H S_1 \frac{W H_1}{W_1 H}$$

$$+ \frac{\mu \alpha (k + d_2)}{u k (\alpha + d_6 b)} (1 - b) \theta H S_1$$

$$+ \frac{\nu S_1}{u k (\alpha + d_6 b)} \theta H S_1 \frac{T W_1}{T_1 W}$$

$$+ \frac{\mu (k + d_2)}{u k (\alpha + d_6 b)} \theta H S_1 \frac{W H_1}{W_1 H}$$

$$+ \frac{\mu \alpha (k + d_2)}{u k (\alpha + d_6 b)} (1 - b) \theta H S_1$$

$$+ \frac{\nu S_1}{u k (\alpha + d_6 b)} \theta H S_1 \frac{T W_1}{T_1 W}$$

$$+ \frac{\mu (k + d_2)}{u k (\alpha + d_6 b)} \theta H S_1 \frac{W H_1}{W_1 H}$$

$$+ \frac{\mu \alpha (k + d_2)}{u k (\alpha + d_6 b)} (1 - b) \theta H S_1$$

$$+ \frac{\nu S_1}{u k (\alpha + d_6 b)} \theta H S_1 \frac{T W_1}{T_1 W}$$

$$+ \frac{\mu (k + d_2)}{u k (\alpha + d_6 b)} \theta H S_1 \frac{W H_1}{W_1 H}$$

$$+ \frac{\mu \alpha (k + d_2)}{u k (\alpha + d_6 b)} (1 - b) \theta H S_1$$

$$+ \frac{\nu S_1}{u k (\alpha + d_6 b)} \theta H S_1 \frac{T W_1}{T_1 W}$$

$$+ \frac{\mu (k + d_2)}{u k (\alpha + d_6 b)} \theta H S_1 \frac{W H_1}{W_1 H}$$

$$+ \frac{\mu \alpha (k + d_2)}{u k (\alpha + d_6 b)} (1 - b) \theta H S_1$$

$$+ \frac{\nu S_1}{u k (\alpha + d_6 b)} \theta H S_1 \frac{T W_1}{T_1 W}$$

$$+ \frac{\mu (k + d_2)}{u k (\alpha + d_6 b)} \theta H S_1 \frac{W H_1}{W_1 H}$$

$$+ \frac{\mu \alpha (k + d_2)}{u k (\alpha + d_6 b)} (1 - b) \theta H S_1$$

$$+ \frac{\nu S_1}{u k (\alpha + d_6 b)} \theta H S_1 \frac{T W_1}{T_1 W}$$

$$+ \frac{\mu (k + d_2)}{u k (\alpha + d_6 b)} \theta H S_1 \frac{W H_1}{W_1 H}$$

$$+ \frac{\mu \alpha (k + d_2)}{u k (\alpha + d_6 b)} (1 - b) \theta H S_1$$

$$+ \frac{\nu S_1}{u k (\alpha + d_6 b)} \theta H S_1 \frac{T W_1}{T_1 W}$$

$$+ \frac{\mu (k + d_2)}{u k (\alpha + d_6 b)} \theta H S_1 \frac{W H_1}{W_1 H}$$

$$+ \frac{\mu \alpha (k + d_2)}{u k (\alpha + d_6 b)} (1 - b) \theta H S_1$$
By differentiating $\vartheta$ subset of $\Upsilon$ which yields when $\Delta_1 < 0$. Proof Define a Lyapunov function

\[
123123123
\]

which yields $N(t) = 0$ for all $t$. The solutions of model (1) converge to $Y$ the largest invariant subset of $\Upsilon_1 = \{(X, N, Y, V, S, T, W, H) : \frac{dV}{dt} = 0\}$. The set $\Upsilon_1$ includes $Y = 0$, and then $\dot{Y} = 0$. The third equation of model (1) implies that

\[
0 = \dot{Y} = kN,
\]

which yields $N(t) = 0$ for all $t$. We get from the second equation that

\[
0 = \dot{N} = \eta VX_1,
\]

which yields $V(t) = 0$ for all $t$. Hence, $\Upsilon_1 = \{\Delta_H\}$ and $\Delta_H$ is G.A.S using Lyapunov–LaSalle asymptotic stability theorem. \(\square\)

**Theorem 3** If $R_2 > 1$ and $R_3 \leq 1$, then $\Delta$ is globally asymptotically stable (G.A.S).

**Proof** Define a Lyapunov function $\vartheta_2(X, N, Y, V, S, T, W, H)$ as:

\[
\vartheta_2 = X_2 F \left( \frac{X}{X_2} \right) + N_2 F \left( \frac{N}{N_2} \right) + \frac{k + d_2}{k} Y_2 F \left( \frac{Y}{Y_2} \right) + \frac{\eta X_2}{d_4} V_2 F \left( \frac{V}{V_2} \right) + \frac{\mu (k + d_2)}{uk} S_2 F \left( \frac{S}{S_2} \right) + \frac{\mu \alpha (k + d_2)}{uk (\alpha + d_b)} W + \frac{\mu \alpha (k + d_2) (d_b + \alpha)}{uk (\alpha + d_b)} H.
\]

By differentiating $\vartheta_2$, we get

\[
\frac{d\vartheta_2}{dt} = \left( 1 - \frac{X_2}{X} \right) \dot{X} + \left( 1 - \frac{N_2}{N} \right) \dot{N} + \frac{k + d_2}{k} \left( 1 - \frac{Y_2}{Y} \right) \dot{Y} + \frac{\eta X_2}{d_4} \left( 1 - \frac{V_2}{V} \right) \dot{V} + \frac{\mu (k + d_2)}{uk} \left( 1 - \frac{S_2}{S} \right) \dot{S} + \frac{\mu \alpha (k + d_2)}{uk (\alpha + d_b)} \dot{W} + \frac{\mu \alpha (k + d_2) (d_b + \alpha)}{uk (\alpha + d_b)} \dot{H}.
\]

By using the steady-state conditions for $\Delta$

\[
\begin{align*}
\varrho &= d_1 X_1 + \eta V_2 X_2, \\
\eta V_2 X_2 &= (k + d_2) N_2, \\
k N_2 &= d_3 Y_2 + \mu Y_2 S_2, \\
\alpha Y_2 &= d_4 V_2, \\
\xi &= d_5 S_2 - a Y_2 S_2.
\end{align*}
\]
we obtain

\[
\frac{d\vartheta}{dt} = -\frac{d_1}{X}(X - X_2)^2 + \eta_2 X_2 - \eta_2 X_2 - \frac{\eta N_2}{2} + \eta_2 X_2 + \left( \frac{\eta X_2}{d_4} - \frac{k + d_2}{k} - \frac{d_3}{k} - \frac{k + d_2}{\mu S_2} \right) Y
\]

\[
- \frac{\mu d S(k + d_2)}{2k} (S - S_2)^2 - \frac{\mu d S(k + d_2)}{k} \mu Y_2 S_2 + \frac{\mu d S(k + d_2)}{k} \mu Y_2 S_2 + \frac{\mu(k + d_2)}{uk} \left( \vartheta S_2 - \frac{d_2 d_3 (d_6 + \alpha)}{\lambda(\alpha + d_3 b)} \right) H
\]

\[
= -\frac{d_1}{X}(X - X_2)^2 - \frac{d_1}{X}(X - X_2)^2 - \frac{k + d_2}{k} \mu Y_2 S_2 + \frac{\eta d S(k + d_2)}{uk} \left( \vartheta S_2 - \frac{d_2 d_3 (d_6 + \alpha)}{\lambda(\alpha + d_3 b)} \right) H
\]

\[
+ \frac{\mu(k + d_2)}{uk} \left( \vartheta S_2 - \frac{d_2 d_3 (d_6 + \alpha)}{\lambda(\alpha + d_3 b)} \right) H
\]

\[
+ \frac{\mu(k + d_2)}{uk} \left( \vartheta S_2 - \frac{d_2 d_3 (d_6 + \alpha)}{\lambda(\alpha + d_3 b)} \right) H
\]

Hence, if \( R_3 \leq 1 \), then \( \Delta V_H \) does not exist since \( H_3 \leq 0 \leq W_3 \) and \( T_3 \leq 0 \). This implies that

\[
\dot{H}(t) = \lambda W - d_1 H \leq 0,
\]

\[
\dot{W}(t) = b_0 HS + \alpha T - d_1 W \leq 0,
\]

\[
\dot{T}(t) = (1 - b)\theta HS - (\alpha + d_3) T \leq 0.
\]

It follows that \( \vartheta S_2 - \frac{d_2 d_3 (d_6 + \alpha)}{\lambda(\alpha + d_3 b)} \leq 0 \) for all \( H > 0 \). Thus, \( \vartheta S_2 - \frac{d_2 d_3 (d_6 + \alpha)}{\lambda(\alpha + d_3 b)} \leq 0 \) and by using inequality (6), we get \( \frac{d\vartheta}{dt} \leq 0 \) for all \( X, N, Y, V, S, T, W, H > 0 \) with equality holding when \( X = X_2, S = S_2, N = N_2, Y = Y_2, V = V_2 \) and \( H = 0 \). The solutions of model (1) converge to \( \Upsilon_2' \), the largest invariant subset of \( \Upsilon_2 = \{(X, N, Y, V, S, T, W, H) : \frac{d\vartheta}{dt} = 0\} \). \( \Upsilon_2' \) contains elements with \( H = 0 \), and then \( \dot{H} = 0 \). Using the last equation of model (1), we obtain

\[
0 = \dot{H} = \lambda W,
\]

which gives \( W(t) = 0 \) for all \( t \). Using the seventh equation of model (1), we obtain

\[
0 = \dot{W} = \alpha T,
\]

which gives \( T(t) = 0 \) for all \( t \). Therefore, \( \Upsilon_2' = \{\Delta V\} \) and by applying Lyapunov–LaSalle asymptotic stability theorem we get that \( \Delta V \) is G.A.S. \( \square \)

**Theorem 4** If \( R_4 > 1 \) and \( 1 < R_3 \leq 1 + \frac{a_0^2 \lambda d_2 d_3 (d_6 + \alpha d_3 b)}{d_2 d_3 (d_6 + \alpha d_3 b)} \), then \( \Delta V_H \) is globally asymptotically stable (G.A.S).

**Proof** Define a Lyapunov function \( \vartheta_3(\textbf{X}, \textbf{N}, \textbf{Y}, \textbf{V}, \text{S}, \text{T}, \text{W}, \text{H}) \) as:

\[
\vartheta_3 = X_3 F \left( \frac{X}{X_3} \right) + N_3 F \left( \frac{N}{N_3} \right) + \frac{k + d_2}{k} Y_3 F \left( \frac{Y}{Y_3} \right) + \frac{\eta X_2}{d_4} V_3 F \left( \frac{V}{V_3} \right) + \frac{\mu(k + d_2)}{uk} S_3 F \left( \frac{S}{S_3} \right)
\]

\[
+ \frac{\mu \alpha(k + d_2)}{uk(\alpha + d_3 b)} T_3 F \left( \frac{T}{T_3} \right) + \frac{\mu(k + d_2)(d_6 + \alpha)}{uk(\alpha + d_3 b)} W_3 F \left( \frac{W}{W_3} \right) + \frac{\mu d_3 (k + d_2)(d_6 + \alpha)}{\lambda uk(\alpha + d_3 b)} H_3 F \left( \frac{H}{H_3} \right).
\]
Differentiating $\vartheta_3$ with respect to $t$ gives

$$\frac{d\vartheta_3}{dt} = \left(\frac{1 - X_3}{X}\right)\dot{X} + \left(1 - N_3 - N_3\right)\dot{N} + \frac{k + d_2}{k} \left(1 - Y_3\right)\dot{Y} + \frac{\eta X_3}{d_4} \left(1 - V_3\right)\dot{V} + \frac{\mu(k + d_2)}{uk} \left(1 - S_3\right)\dot{S}$$

$$+ \frac{\mu(a(k + d_2))}{uk(a + d_6)} \left(1 - T_3\right)\dot{T} + \frac{\mu(k + d_2)(d_6 + \alpha)}{uk(a + d_6)} \left(1 - W_3\right)\dot{W} + \frac{\mu d_7(k + d_2)(d_6 + \alpha)}{\lambda_uk(a + d_6)} \left(1 - H_3\right)\dot{H}$$

$$= \left(1 - \frac{X_3}{X}\right)\left(\rho - d_1 X - \eta V X\right) + \left(1 - \frac{N_3}{N}\right)\left[\eta V X - (k + d_2)N\right] + \frac{k + d_2}{k} \left(1 - \frac{Y_3}{Y}\right) \left(kN - d_3 Y - \mu Y S\right)$$

$$+ \frac{\eta X_3}{d_4} \left(1 - \frac{V_3}{V}\right) \left[(1 - \vartheta)HS - (\alpha + d_6)T\right] + \frac{\mu(k + d_2)(d_6 + \alpha)}{uk(a + d_6)} \left(1 - \frac{W_3}{W}\right) \left(b\vartheta HS + \alpha T - d_7 W\right)$$

$$+ \frac{\mu d_7(k + d_2)(d_6 + \alpha)}{\lambda_uk(a + d_6)} \left(1 - \frac{H_3}{H}\right) \left(\lambda W - d_8 H\right) + \frac{\mu(k + d_2)}{uk(a + d_6)} \left(1 - \frac{S_3}{S}\right) \left(\eta - d_s S\right) - \frac{k + d_2}{k} \mu Y S_3$$

By using the steady-state conditions of $\Delta V H$

$$\begin{align*}
\rho &= d_1 X_3 + \eta V_3 X_3, \\
\eta V_3 X_3 &= (k + d_2)N_3, \\
kN_3 &= d_1 Y_3 + \mu Y S_3, \\
aY_3 &= d_4 V_3, \\
x &= d_5 S_3 + \theta H_3 S_3 - uY_3 S_3, \\
(1 - \vartheta)HS &= (\alpha + d_6)T_3, \\
b\vartheta H_3 S_3 &= d_7 W_3 - \alpha T_3, \\
\lambda W_3 &= d_8 H_3,
\end{align*}$$

we get

$$\frac{d\vartheta_3}{dt} = -\frac{d_1}{X} (X - X_3)^2 + \eta V_3 X_3 - \eta V_3 X_3 - \eta V_3 X_3 \frac{X_3}{X} - \eta V_3 \frac{N_3}{N} + \eta V_3 X_3 + \left(\frac{\eta X_3}{d_4} \frac{V_3}{V} \frac{Y_3}{Y} - \frac{k + d_2}{k} \mu Y S_3 + \frac{k + d_2}{k} \mu Y S_3 - \eta V_3 X_3 \frac{Y_3 V_3}{V_3 Y_3} + \eta V_3 X_3 - \mu d_7(k + d_2)H S_3\right) \left(S - S_3\right)^2$$

$$+ \frac{\mu(k + d_2)}{uk(a + d_6)} \theta H_3 S_3 + \frac{\mu(k + d_2)}{uk(a + d_6)} \theta H_3 S_3 \left(1 - \frac{S_3}{S}\right) \left(1 - \frac{S_3}{S}\right) - \frac{\mu(k + d_2)}{uk(a + d_6)} \theta H_3 S_3 + \frac{\mu(k + d_2)}{uk(a + d_6)} \theta H_3 S_3 \left(1 - \frac{S_3}{S}\right) \left(1 - \frac{S_3}{S}\right)$$

$$- \frac{\mu(k + d_2)}{uk(a + d_6)} \theta H_3 S_3 \left(1 - \frac{S_3}{S}\right) \left(1 - \frac{S_3}{S}\right) - \frac{\mu(k + d_2)}{uk(a + d_6)} \theta H_3 S_3 + \frac{\mu(k + d_2)}{uk(a + d_6)} \theta H_3 S_3 \left(1 - \frac{S_3}{S}\right) \left(1 - \frac{S_3}{S}\right)$$

$$+ \frac{\mu(k + d_2)}{uk(a + d_6)} \theta H_3 S_3 \left(1 - \frac{S_3}{S}\right) \left(1 - \frac{S_3}{S}\right) - \frac{\mu(k + d_2)}{uk(a + d_6)} \theta H_3 S_3 + \frac{\mu(k + d_2)}{uk(a + d_6)} \theta H_3 S_3 \left(1 - \frac{S_3}{S}\right) \left(1 - \frac{S_3}{S}\right)$$

$$- \frac{\mu(k + d_2)}{uk(a + d_6)} \theta H_3 S_3 \left(1 - \frac{S_3}{S}\right) \left(1 - \frac{S_3}{S}\right) - \frac{\mu(k + d_2)}{uk(a + d_6)} \theta H_3 S_3 + \frac{\mu(k + d_2)}{uk(a + d_6)} \theta H_3 S_3 \left(1 - \frac{S_3}{S}\right) \left(1 - \frac{S_3}{S}\right)$$
The solutions of model (1) converge to \( \{X, Y, S, T, W, H \} \) : \( \frac{d\vartheta}{dt} = 0 \). Hence, \( \mathcal{Y}_3 = \{\Delta_{VH}\} \) and \( \Delta_{VH} \) is G.A.S using Lyapunov–LaSalle asymptotic stability theorem.

The global stability conditions of all steady states are summarized in Table 3.

### 5 Numerical simulations

This section presents some numerical simulations to assist the results obtained in the previous parts. In addition, it shows the impact of low number of CD4\(^+\) T cells on SARS-CoV-2/HIV coinfection. Furthermore, it illustrates the effect of death rates during the latency periods on viral loads. To achieve these goals, we consider three sets of initial conditions as follows:

- \( \Delta_0 = (X_0, 0, 0, S_0, 0, 0, 0) \)
- \( \Delta_H = (X_1, 0, 0, S_1, T_1, W_1, H_1) \)
- \( \Delta_V = (X_2, N_2, Y_2, V_2, S_2, T_2, W_2, H_2) \)
- \( \Delta_{VH} = (X_3, N_3, Y_3, V_3, S_3, T_3, W_3, H_3) \)

### Table 3: Global stability conditions of the steady states of model (1)

| Steady state       | Global stability conditions |
|--------------------|-----------------------------|
| \( \Delta_0 \)     | \( R_1 \leq 1 \) and \( R_2 \leq 1 \) |
| \( \Delta_H \)     | \( R_1 > 1 \) and \( R_4 \leq 1 \) |
| \( \Delta_V \)     | \( R_2 > 1 \) and \( R_3 \leq 1 \) |
| \( \Delta_{VH} \)  | \( R_3 > 1 \) and \( 1 < R_3 \leq 1 + \frac{a\eta\theta\lambda^k (\alpha + d_b)}{d_d \delta^d (\delta + \alpha) (a \delta d_5 + d_1 \delta d_4)} \) |

Since \( 1 < R_3 \leq 1 + \frac{a\eta\theta\lambda^k (\alpha + d_b)}{d_d \delta^d (\delta + \alpha) (a \delta d_5 + d_1 \delta d_4)} \) and using inequalities (4), (5) and (6) we get \( \frac{d\vartheta}{dt} \leq 0 \) for all \( X, Y, S, T, W, H > 0 \). Moreover, \( \frac{d\vartheta}{dt} = 0 \) when \( X = X_3, S = S_3, N = N_3, Y = Y_3, V = V_3, T = T_3, W = W_3 \) and \( H = H_3 \). The solutions of model (1) converge to \( \mathcal{Y}_3 \) the largest invariant subset of \( \mathcal{Y}_3 \) = \( \{X, Y, S, T, W, H \} \) : \( \frac{d\vartheta}{dt} = 0 \).

Hence, \( \mathcal{Y}_3 = \{\Delta_{VH}\} \) and \( \Delta_{VH} \) is G.A.S using Lyapunov–LaSalle asymptotic stability theorem.

The global stability conditions of all steady states are summarized in Table 3.
Fig. 1 The numerical simulations of model (1) for $\eta = 0.9$, $\mu = 1$, $d_4 = 5.36$, and $\theta = 0.0001$ with three different sets of initial conditions. The uninfected steady state $\Delta_0 = (22.24, 0, 0, 0, 0, 1000, 0, 0, 0)$ is GAS.

(a) Uninfected epithelial cells

(b) Latently infected epithelial cells

(c) Actively infected epithelial cells

(d) SARS-CoV-2

(e) Uninfected $CD^4^+$ T cells

(f) Latently infected $CD^4^+$ T cells

(g) Actively infected $CD^4^+$ T cells

(h) HIV
Fig. 2  The numerical simulations of model (1) for $\eta = 0.55$, $\mu = 1$, $d_4 = 5.36$, and $\theta = 0.0016$ with three different sets of initial conditions. The single HIV–infection steady state $\Delta_H = (22.41, 0, 0, 0, 128.505, 11.88, 16.95, 42.39)$ is G.A.S.
Fig. 3  The numerical simulations of model (1) for $\eta = 2.9$, $\mu = 0.02$, $d_4 = 0.03$, and $\theta = 0.0001$ with three different sets of initial conditions. The single SARS-CoV-2–infection steady state $\Delta V = (0.876, 0.0053, 0.0011, 0.0085, 1010.71, 0, 0, 0)$ is G.A.S.
Fig. 4 The numerical simulations of model (1) for $\eta = 2.9$, $\mu = 0.02$, $\delta = 0.1$, and $\theta = 0.0016$ with three different sets of initial conditions. The SARS-CoV-2/HIV coinfection steady state $\Delta V_H = (0.385, 0.0054, 0.0082, 0.02, 128.505, 12.028, 17.16, 42.89)$ is G.A.S.
Table 4  Local stability of the steady state $\Delta_{VH}$

| Case | The steady states | Re($\mathcal{L}_j$), $j = 1, \ldots, 8$ | Stability |
|------|-------------------|------------------------------------------|-----------|
| (iv) | $\Delta_0 = (22.41, 0, 0, 0, 1000, 0, 0, 0)$ | $(-19.907, -4.94688, -3.70454, 1.29544, 0.562873, -0.310899, -0.01, -0.001)$ | Unstable |
|      | $\Delta_H = (22.41, 0, 0, 0, 128.505, 11.88, 16.95, 42.39)$ | $(-4.46776, -4.46776, -2.37868, 2.07443, -0.340978, -0.0390795, -0.0390795, -0.001)$ | Unstable |
|      | $\Delta_V = (2.918, 0.005, 0.0096, 0.0023, 1009.69, 0, 0, 0)$ | $(-20.2784, -4.20655, -3.71538, 1.30623, -0.310848, -0.00380659, -0.00380659, -0.00987671)$ | Unstable |
|      | $\Delta_{VH} = (0.385, 0.0054, 0.0082, 0.02, 128.505, 12.03, 17.16, 42.89)$ | $(-3.81897, -3.04464, -2.3788, -0.340867, -0.0395697, -0.0395697, -0.0273365, -0.0273365)$ | Stable |
Fig. 5 The effect of decreasing \( \mu \) on the concentrations of SARS-CoV-2 particles \( V(t) \). The parameters considered are \( \eta = 2.9, d_1 = 0.1, \) and \( \theta = 0.0016 \) with initial conditions 
\[
(X(0), N(0), Y(0), V(0), S(0), T(0), W(0), H(0)) = (5, 0.0001, 0.0002, 0.0003, 100, 5, 10, 15)
\]
(iii) We select \( \eta = 2.9, \mu = 0.02, d_4 = 0.03, \) and \( \theta = 0.0001. \) This gives \( R_2 = 25.8471 > 1 \) and \( R_3 = 0.4916 < 1. \) In this case, the solutions globally converge to the steady state \( \Delta = (0.876, 0.0053, 0.0011, 0.0085, 1010.71, 0, 0, 0). \) This result agrees with Theorem 3 and is displayed in Fig. 3. This case represents a person with SARS-CoV-2 infection, but he does not have HIV disease.
(iv) We consider \( \eta = 2.9, \mu = 0.02, d_4 = 0.1, \) and \( \theta = 0.0016. \) This implies that \( R_3 = 7.8541 > 1, \) \( R_3 < 1 + \frac{d_7 d_8 (d_6 + \alpha) (\alpha \theta \lambda \xi (\alpha + d_6 b))}{d^2 d_5 (d_6 + \alpha)} = 8.7707, \) and \( R_4 = 58.1828 > 1. \) In harmony with Theorem 4, the steady state \( \Delta_{V_H} = (0.385, 0.0054, 0.0082, 0.02, 128.505, 12.028, 17.16, 42.89) \) is G.A.S (see Fig. 4). In this situation, SARS-CoV-2/HIV co-infection occurs, where an HIV patient gets infected with COVID-19. CD4\(^+\) T cells are stimulated to eliminate SARS-CoV-2 infection from the body. Nevertheless, if the patient has low CD4\(^+\) T cell counts, the clearance of SARS-CoV-2 may not be achieved. This can lead to severe infection and death.

For further verification of the asymptotic stability of \( \Delta_{V_H} \), we calculate the Jacobian matrix of model (1) at the steady state \( \Delta = (X, N, Y, V, S, T, W, H) \) as

\[
J(\Delta) = \\
\begin{bmatrix}
-d_1 - \eta V & 0 & 0 & -\eta X & 0 & 0 & 0 & 0 \\
\eta V & -k - d_2 & 0 & -\eta X & 0 & 0 & 0 & 0 \\
0 & k & -d_3 - \mu S & 0 & -\mu Y & 0 & 0 & 0 \\
0 & 0 & a & -d_4 & 0 & 0 & 0 & 0 \\
0 & 0 & a S & 0 & -d_5 - \theta H & 0 & 0 & -\theta S \\
0 & 0 & 0 & 0 & (1 - b) \theta H & -d_6 - \alpha & 0 & (1 - b) \theta S \\
0 & 0 & 0 & 0 & b \theta H & a & -d_7 & b \theta S \\
0 & 0 & 0 & 0 & 0 & \lambda & -d_8 & -d_8 \\
\end{bmatrix}
\]

Next, we calculate the eigenvalues \( \mathcal{L}_j \) \((j = 1, 2, \ldots, 8)\) of the Jacobian matrix at all possible steady states. For asymptotic stability of \( \Delta_{V_H} \), we need to prove that

\[
\text{Re}(\mathcal{L}_j) < 0, \quad \text{for all } j = 1, 2, \ldots, 8,
\]

and all other steady states have eigenvalues with positive real parts. The computations are organized in Table 4.

5.1 The effect of the CD4\(^+\) T cells killing rate

To check the impact of changing the value of \( \mu \) on the stability of model (1), we take the same values used in case (iv) \((\eta = 2.9, d_4 = 0.1, \) and \( \theta = 0.0016)\) with increasing the value of \( \mu \) from 0.02 to 1.5. It follows that \( R_1 = 7.7818 > 1 \) and \( R_4 = 0.8085 < 1. \) Thus, the steady state \( \Delta_{H} = (22.41, 0, 0, 0.128.505, 11.88, 16.95, 42.39) \) is G.A.S. Mathematically, increasing the value of \( \mu \) switches the value of \( R_4 \) from \( R_4 = 58.183 > 1 \) to \( R_4 = 0.8085 < 1. \) This means that there is a bifurcation at \( R_4 = 1. \) Accordingly, the steady state \( \Delta_{V_H} \) becomes unstable and \( \Delta_{H} \) becomes G.A.S.

In addition, to characterize the effect of increasing or decreasing the value of \( \mu \) on the number of actively infected epithelial cells and SARS-CoV-2 particles, we examine case (iv) with different values of \( \mu \) (Fig. 5). We find out that decreasing the value of \( \mu \) increases the concentration of actively infected epithelial cells and, accordingly, the concentration of SARS-CoV-2 particles is increased. On the other hand, increasing the value of \( \mu \) decreases SARS-CoV-2 viral load.
Biologically, these results imply that high killing rate $\mu$ of CD4$^+$ T cells is needed to remove SARS-CoV-2 from the body of HIV patient. Conversely, low killing rates can cause severe SARS-CoV-2 infection for HIV patient.

5.2 The effect of latency

To see the effect of the eclipse phase on the production of SARS-CoV-2 particles, we take the same values considered in case (iv) with increasing the value of $d_2$. We observe from Fig. 6a that increasing the death rate of latently infected epithelial cells decreases the concentration of SARS-CoV-2 particles in coinfected patients. Similarly, increasing the death rate ($d_b$) of latently infected CD4$^+$ T cells decreases the density of HIV particles (See Fig. 6b). Thus, the death rates during the latency periods can have a strong impact on the viral loads.

6 Discussion

In this paper, we developed a within-host SARS-CoV-2/HIV coinfection model that investigates the interactions between eight components: uninfected epithelial cells, latently infected epithelial cells, productively infected epithelial cells, SARS-CoV-2 particles, uninfected CD4$^+$ T cells, latently infected CD4$^+$ T cells, productively infected CD4$^+$ T cells, and HIV particles. The model has four steady states as the following:

(a) The uninfected steady state $\Delta_0$ always exists. It is G.A.S when $R_1 \leq 1$ and $R_2 \leq 1$. This represents the healthy state when the person does not suffer from neither SARS-CoV-2 infection nor HIV infection.

(b) The HIV infection steady state $\Delta_H$ is defined if $R_1 > 1$, and it is G.A.S if $R_4 \leq 1$. This represents the case of a patient carrying only HIV infection.

(c) The SARS-CoV-2–infection steady state $\Delta_V$ is defined if $R_2 > 1$, and it is G.A.S if $R_3 \leq 1$. This represents the case of a patient carrying only SARS-CoV-2 infection.

(d) The SARS-CoV-2/HIV coinfection steady state $\Delta_{VH}$ is defined and G.A.S if $R_4 > 1$ and $1 < R_3 \leq 1 + \frac{\alpha \eta \theta \lambda \delta (\alpha + d_0 b)}{d_2 d_b (d_b + \alpha) (\alpha d_3 + d_1 d_4 \mu)}$. This case simulates the occurrence of SARS-CoV-2 infection in HIV patients.

The numerical results are totally compatible with the theoretical results. We found that decreasing the killing rate ($\mu$) of CD4$^+$ T cells increases the concentrations of both productively infected epithelial cells and SARS-CoV-2 particles. This implies that low CD4$^+$ T cell counts can increase the severity of SARS-CoV-2 infection in HIV patients. This result comes in agreement with many results that discussed that HIV patients with low CD4$^+$ T cell counts or who do not receive ART are at higher risk of death when they get infected by SARS-CoV-2. In addition, we observed that increasing the death rate ($d_2$) of infected epithelial cells during the latency period decreases SARS-CoV-2 viral load in the body. Increasing $d_2$ means that more cells will die in the eclipse phase before converting into productively infected cells. This can have a positive effect on reducing the severity of SARS-CoV-2 infection in HIV patients. Comparing with previous studies, the model considered in this work is the first model that takes into consideration the coinfection of HIV with SARS-CoV-2. The results obtained in this paper can be examined and used to (i) understand SARS-CoV-2/HIV coinfection, (ii) estimate the values of the parameters that are needed to clear SARS-CoV-infection from the body of HIV patient, (iii) test the effect of increasing the killing rate ($\mu$) on SARS-CoV-2 viral load, and (iv) examine the effect of death rates during the latency periods on the concentrations of viral particles. The main limitation of this work is that we did not use real data due to its unavailability. Therefore, these results can be examined when more data become available.
The model studied in this paper can be improved by considering the effect of time delays that are associated with many biological processes. Furthermore, adding the effect of treatments may lead to the important results that can help to find treatments for this group of patients. In addition, the coinfection dynamics of SARS-CoV-2 and HIV can be studied within a multiscale approach which can provide a deeper understanding and help develop vaccines and antiviral therapies. Finally, the results can be developed with using real data to find an accurate estimation of the parameters of model (1).

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Conflict of interest The authors declare that they have no conflict of interest.

References

1. Coronavirus disease (COVID-19), weekly epidemiological update (13 October 2021), World Health Organization (WHO) (2021). Available online: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20211013_weekly_epi_update_61.pdf?sfvrsn=5092f979_3&download=true
2. Coronavirus disease (COVID-19): HIV and antiretrovirals, World Health Organization (WHO) (2020). Available online: https://www.who.int/news-room/q-a-detail/coronavirus-disease-covid-19-hiv-and-antiretrovirals
3. P. Sontongo, E.S. Heilbrunn, A.E. Sontongo, S. Advani et al., Epidemiology and outcomes of COVID-19 in HIV-infected individuals: a systematic review and meta-analysis. Sci. Rep. 11(1), 1–12 (2021)
4. HIV/AIDS: Fact sheets, World Health Organization (WHO) (2021). Available online: https://www.who.int/news-room/fact-sheets/detail/hiv-aids
5. Z. Bakouy, J.E. Hawley, T.K. Choueiri, S. Peters et al., COVID-19 and cancer: current challenges and perspectives. Cancer Cell 38, 629–646 (2020)
6. S. Gatechompol, A. Avihingsanon, O. Putcharoeng, K. Ruxrungtham, D.R. Kuritzkes, A.I.D.S. Res. Palliat. Care 13, 361–375 (2021)
7. The U.S. Food and Drug Administration, Know your treatment options for COVID-19 (2021). Available online: https://www.fda.gov/consumers/consumer-updates/know-your-treatment-options-covid-19
8. Coronavirus disease (COVID-19), Vaccine tracker, World Health Organization (WHO) (2021). Available online: https://covid19.trackvaccines.org/agency/who/
9. A. Al Agha, S. Alshehaiween, A. Elaiw, M. Alshaikh, Global analysis of delayed SARS-CoV-2/cancer model with immune response. Mathematics 9(11), 1–27 (2021)
10. L. Derosa, C. Melenotte, F. Griscelli, B. Gachot et al., The immuno-oncological challenge of COVID-19. Nat. Cancer 1(10), 946–964 (2020)
11. N. Evans, E. Martinez, N. Petrosillo, J. Nichols, SARS-CoV-2 and human immunodeficiency virus: pathogen pincer attack. HIV/AIDS Res. Palliat. Care 13, 361–375 (2021)
12. The U.S. Food and Drug Administration, Know your treatment options for COVID-19 (2021). Available online: https://www.fda.gov/consumers/consumer-updates/know-your-treatment-options-covid-19
13. Coronavirus disease (COVID-19), Vaccine tracker, World Health Organization (WHO) (2021). Available online: https://covid19.trackvaccines.org/agency/who/
33. C. Kang, H. Miao, X. Chen, J. Xu, D. Huang, Global stability of a diffusive and delayed virus dynamics model with Crowley-Martin incidence function and CTL immune response. Adv. Differ. Equ. 2017(324), 1–16 (2017)
34. H. Miao, Z. Teng, X. Abdurahman, Z. Li, Global stability of a diffusive and delayed virus infection model with general incidence function and adaptive immune response. Comput. Appl. Math. 37(3), 3780–3805 (2018)
35. M. Bachraoui, K. Hattaf, N. Yousfi, Global stability of a fractional order HIV infection model with cure of infected cells in eclipse stage. Revue Africaine de la Recherche en Informatique et Mathématiques Appliquées (2019). https://doi.org/10.46298/arima.4359
36. A.R.M. Carvalho, C.M.A. Pinto, D. Baleanu, HIV/HCV coinfection model: a fractional-order perspective for the effect of the HIV viral load. Adv. Differ. Equ. 2018(2), 1–22 (2018)
37. C. Li, J. Xu, J. Liu, Y. Zhou, The within-host viral kinetics of SARS-CoV-2. Math. Biosci. Eng. 17(4), 2853–2861 (2020)
38. S.Q. Du, W. Yuan, Mathematical modeling of interaction between innate and adaptive immune responses in COVID-19 and implications for viral pathogenesis. J. Med. Virol. 92(9), 1615–1628 (2020)
39. L. Pinky, H.M. Dobrovolny, SARS-CoV-2 coinfections: Could influenza and the common cold be beneficial? J. Med. Virol. 92, 1–8 (2020)
40. N.T. Fadai, R. Sachak-Patwa, H.M. Byrne, P.K. Maini, M. Bafadhel, D.V. Nicolau, Infection, inflammation and intervention: mechanistic modelling of epithelial cells in COVID-19. J. R. Soc. Interface (2021). https://doi.org/10.1098/rsif.2020.0950
41. N. Bellomo, D. Burini, G. Dosi, L. Gibelli et al., A multiscale model of virus pandemic: heterogeneous interactive entities in a globally connected world. Math. Models Methods Appl. Sci. 30(8), 1591–1651 (2020)
42. N. Bellomo, D. Buring, M.A.J. Chaplain, A.D. Hobiny et al., What is life? A perspective of the mathematical kinetic theory of active particles. Math. Models Methods Appl. Sci. 31(9), 1821–1866 (2021)
43. B.J. Nath, K. Dehingia, V.N. Mishra, Y. Chu, H.K. Sarmah, Mathematical analysis of a within-host model of SARS-CoV-2. Adv. Differ. Equ. 2021(1), 1–11 (2021)
44. M. Prakash, R. Rakkiyappan, A. Manivannan, J. Cao, Dynamical analysis of antigen-driven T-cell infection model with multiple delays. Appl. Math. Comput. 354, 266–281 (2019)
45. D.S. Callaway, A.S. Perelson, HIV-1 infection and low steady state viral loads. Bull. Math. Biol. 64, 29–64 (2002)
46. A.M. Elaiw, N.H. AlShamrani, A.D. Hobiny, Mathematical modeling of HIV/HTLV co-infection with CTL-mediated immunity. AIMS Math. 6(2), 1634–1676 (2021)
47. A.S. Perelson, P.W. Nelson, Mathematical analysis of HIV-1 dynamics in vivo. SIAM Rev. 41(1), 3–44 (1999)
48. D. Adak, N. Bairagi, Analysis and computation of multi-pathways and multi-delays HIV-1 infection model. Appl. Math. Model. 54, 517–536 (2018)
49. A. Korobeinikov, Global properties of basic virus dynamics models. Bull. Math. Biol. 66, 879–883 (2004)
50. E.A. Barbashin, Introduction to the Theory of Stability (Wolters-Noordhoff, 1970)
51. J.P. La Salle, The Stability of Dynamical Systems (Society for Industrial and Applied Mathematics, 1976)
52. A.M. Lyapunov, The general problem of the stability of motion. Int. J. Control 55(3), 531–534 (1992)