Mathematical Biosciences and Engineering

http://www.aimspress.com/journal/mbe

MBE, 20(2): 3873–3917.
DOI: 10.3934/mbe.2023182
Received: 08 October 2022
Revised: 12 November 2022
Accepted: 25 November 2022
Published: 13 December 2022

Research article

Global dynamics of IAV/SARS-CoV-2 coinfection model with eclipse phase and antibody immunity

A. M. Elaiw*, Raghad S. Alsulami and A. D. Hobiny

Department of Mathematics, Faculty of Science, King Abdulaziz University, P. O. Box 80203, Jeddah 21589, Saudi Arabia

* **Correspondence:** Email: a_m_elaiw@yahoo.com, raghad.saud.alsulami@gmail.com, ahobany@kau.edu.sa.

Abstract: Coronavirus disease 2019 (COVID-19) and influenza are two respiratory infectious diseases of high importance widely studied around the world. COVID-19 is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), while influenza is caused by one of the influenza viruses, A, B, C, and D. Influenza A virus (IAV) can infect a wide range of species. Studies have reported several cases of respiratory virus coinfection in hospitalized patients. IAV mimics the SARS-CoV-2 with respect to the seasonal occurrence, transmission routes, clinical manifestations and related immune responses. The present paper aimed to develop and investigate a mathematical model to study the within-host dynamics of IAV/SARS-CoV-2 coinfection with the eclipse (or latent) phase. The eclipse phase is the period of time that elapses between the viral entry into the target cell and the release of virions produced by that newly infected cell. The role of the immune system in controlling and clearing the coinfection is modeled. The model simulates the interaction between nine compartments, uninfected epithelial cells, latent/active SARS-CoV-2-infected cells, latent/active IAV-infected cells, free SARS-CoV-2 particles, free IAV particles, SARS-CoV-2-specific antibodies and IAV-specific antibodies. The regrowth and death of the uninfected epithelial cells are considered. We study the basic qualitative properties of the model, calculate all equilibria, and prove the global stability of all equilibria. The global stability of equilibria is established using the Lyapunov method. The theoretical findings are demonstrated via numerical simulations. The importance of considering the antibody immunity in the coinfection dynamics model is discussed. It is found that without modeling the antibody immunity, the case of IAV and SARS-CoV-2 coexistence will not occur. Further, we discuss the effect of IAV infection on the dynamics of SARS-CoV-2 single infection and vice versa.

Keywords: COVID-19; SARS-CoV-2; influenza a virus; coinfection; global stability; Lyapunov function

1. Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and influenza A virus (IAV) are two respiratory RNA viruses with high pandemic potential. SARS-CoV-2 causes the coronavirus disease 2019 (COVID-19). According to the update provided by the World Health Organization (WHO) on 2 October 2022 [1], over 593 million confirmed cases and over 6.4 million deaths were reported globally. Influenza viruses infect about 20% of the world's population in annual epidemics, resulting in 3-5 million severe illnesses and 290,000–650,000 deaths each year [2].

Both SARS-CoV-2 and IAV infect the uninfected epithelial cells of the host respiratory tract [3, 4], and have analogous transmission ways. Moreover, they have common clinical manifestations including dyspnea, cough, fever, headache, rhinitis, myalgia and sore throat [5]. Viral shedding usually takes place 5 to 10 days in influenza, whereas it does 2 to 5 weeks in COVID-19 [5]. Acute respiratory distress is less common in influenza than in COVID-19 [5]. Deaths in influenza cases are less than 1%, while in cases of COVID-19 it ranges from 3 to 4% [5]. The precautionary measures implemented by governments to limit the transmission of SARS-CoV-2 can play a role in reducing the transmission of the IAV [6].

Eleven vaccines for COVID-19 were approved by WHO for emergency use. These include Novavax/Nuvaxovid, Bharat Biotech/Covaxin, CanSino/Convidecia, Pfizer/BioNTech/Comirnaty, Moderna/Spikevax, Serum Institute of India COVOVAX (Novavax formulation), Janssen (Johnson & Johnson)/Jcovden, Oxford/AstraZeneca/Vaxzevria, Serum Institute of India Covishield (Oxford/AstraZeneca formulation), Sinopharm (Beijing)/Covilo, and Sinovac/CoronaVac [7]. Currently, there are three types of influenza vaccines used worldwide: live attenuated influenza vaccine, inactivated influenza vaccine and recombinant hemagglutinin vaccine [8].

It was reported in [9] that, 94.2% of individuals with COVID-19 were also coinfected with several other microorganisms, such as fungi, bacteria and viruses. Important viral copathogens include the respiratory syncytial virus (RSV), human enterovirus (HEV), human rhinovirus (HRV), influenza A virus (IAV), influenza B virus (IBV), human metapneumovirus (HMPV), parainfluenza virus (PIV), human immunodeficiency virus (HIV), cytomegalovirus (CMV), dengue virus (DENV), Epstein Barr virus (EBV), hepatitis B virus (HBV) and other coronaviruses (COVs), among which the HRV, HEV and IAV are the most common copathogens [10]. Several coinfection cases of COVID-19 and influenza were reported in [5, 9, 11–13] (see also the review papers [14–18]). Lansbury et al. [14] presented a systematic review and meta-analysis that included 30 studies for evaluating coinfections among patients infected with COVID-19. It was reported that 7% of patients had a bacterial coinfection and 3% of patients had another respiratory virus, with RSV and IAV being among the most common coinfecting viruses. Dao et al. [15] conducted a systematic review and meta-analysis that included 54 publications and found that, 7% of COVID-19 patients are co-infected with influenza viruses. Most influenza co-infections were due to the IAV [15]. A respective study in Wuhan, China showed that the coinfection rate of IAV and SARS-CoV-2 was 49.8% during the outbreak period of COVID-19 [19]. Based on two separate studies presented in [11] and [12], COVID-19-influenza coinfection did not result in worse clinical outcomes [11]. In addition, this condition reduced the mortality rate among COVID-19-influenza coinfected patients. Coinfection with influenza virus in COVID-19 patients might render them less vulnerable to morbidities associated with COVID-19, and therefore, a better prognosis overall [12]. In [18], it is found that, although patients with IAV and

SARS-CoV-2 coinfection did not experience longer hospital stays compared with those SARS COV-2 single-infection, they usually presented with a more severe clinical conditions. In an animal study [20], it was found that the disease severity is increased in hamsters with SARS-CoV-2 and IAV coinfection compared with those with SARS-CoV-2 mono-infection.

Viral interference phenomenon can appear in case of infections with multiple competitive respiratory viruses [21–23]. One virus may be able to suppress the growth of another virus [21, 24]. In [22], it was reported that an H3N2 strain of IAV was inhibited by SARS-CoV-2 coinfection in the hamster model. Oishi et al. [23] used the golden Syrian hamster model, and found that, IAV interferes with SARS-CoV-2 replication in the lung, even more than one week after IAV clearance. Disease progression and outcome in SARS-CoV-2 infection are highly dependent on the host immune response, particularly in the elderly in whom immunosenescence may predispose to increased risk of coinfection [21].

1.1. Mathematical models of within-host IAV and SARS-CoV-2 infections

Over the years, mathematical models have demonstrated their ability to provide useful insight to gain a further understanding of the dynamics and mechanisms of the viruses within a host level. These models may assist in the development of viral therapies and vaccines as well as the selection of appropriate therapeutic and vaccine strategies. Moreover, these models are helpful in determining the sufficient number of factors to analyze the experimental results and explain the biological phenomena [3]. Stability analysis of the model's equilibria can help researchers to (i) expect the qualitative features of the model for a given set of values of the model's parameters, (ii) establish the conditions that ensure the persistence or deletion of this infection, and (iii) determine under what conditions the immune system is stimulated against the infection.

1.1.1. Mathematical models of IAV single-infection

Mathematical models of within-host IAV single-infection were developed in several works (see the review papers [25–29]). Baccam et al. [30] presented the following IAV-single-infection with limited target cells and eclipse (or latent) phase:

$$\begin{cases} \dot{X} = -\overbrace{\beta_P X P}^{\text{IAV infectious transmission}}, \\ \dot{E} = \overbrace{\beta_P X P}^{\text{IAV infectious transmission}} - \overbrace{\delta_E E}^{\text{latent transition}}, \\ \dot{I} = \overbrace{\delta_E E}^{\text{latent transition}} - \overbrace{\gamma_I I}^{\text{natural death}}, \\ \dot{P} = \overbrace{\kappa_P I}^{\text{IAV production}} - \overbrace{\pi_P P}^{\text{natural death}}, \end{cases} \tag{1.1}$$

where $X = X(t)$, $E = E(t)$, $I = I(t)$ and $P = P(t)$ are the concentrations of uninfected epithelial cells, latent IAV-infected epithelial cells, active IAV-infected epithelial cells and free IAV particles, at time t, respectively. The model was fitted using real data from six patients infected with influenza [30].

Several works were devoted to developing IAV single-infection dynamics models by considering the following:

- Innate immune response: It represents the first line of defense that recognizes the antigens and activate the adaptive immune response. In [30], the effect of interferon (IFN) response was included in the IAV infection model. The dynamics of the IFN are given as:

$$\dot{F} = \varpi_F I(t-\tau) - \mu_F F,$$

where, F is the concentration of IFN, ϖ_F is the IFN production rate constant, μ_F is the IFN decay rate constant, and τ is the time lag that occurs between the initiation of an IAV infection and the appearance of IFN. IFN can reduce viral replication in an infected cell, the rate of viral production in the presence of IFN was modeled by replacing δ_E by $\frac{\delta_E}{1+\epsilon_E F}$. The rate that IAV-infected cells in the eclipse phase begin virus production (κ_P) may also be altered and was accounted for by replacing this parameter by $\frac{\kappa_P}{1+\epsilon_P F}$. The efficiency of these interferon effects is reflected by the parameters ϵ_E and ϵ_P [30, 31]. Saenz et al. [32] presented an influenza model with interferon response. It is reported that the model with interferon response provided better fitting with real data than that without interferon response.

- Adaptive immune response: Cytotoxic T Lymphocytes (CTLs) and antibodies are the two major components of the adaptive immune response. CTLs destroy the viral-infected cells, while the antibodies neutralize the viruses. An influenza dynamics model with different forms of the CTL response was developed in [33]. It was shown that slight changes in the virus dynamics was observed when different choices of CTL response were implemented. Both CTL and antibody immunities were included into the IAV model in [34].

- Both innate and adaptive immune responses [3, 35–38]. The model presented in [37] predicted that, the level and time of the viral peak are affected by the innate interferon response, while the clearance phase and duration of infection are determined by the CTL response. Handel et al. [38] showed that, both the innate and adaptive immune responses are required to give an appropriate explanation of the real data.

- Drug therapy: There are two approved anti-IAV drugs, adamantane antiviral drugs which block infection by reducing the rate of infection, and neuraminidase inhibitors which block the production of newly formed virions [31]. Beauchemin et al. [39] used model (1.1) to study the effect of the antiviral drug amantadine on IAV infection. Handel et al. [40] presented a mathematical model for within-host influenza infection under the effect of neuraminidase inhibitors drugs. Lee et al. [34] included the effect of a combination of neuraminidase inhibitors and anti-IAV therapies in the IAV model. The IAV model predicts that the drug therapies are more beneficial when they are administered early.

- Regrowth and death of the uninfected epithelial cells. In [34], the first equation of model (1.1) was modified by considering the target cell production and death as:

$$\dot{X} = \overbrace{\alpha X(0)}^{\text{epithelial cells production}} - \overbrace{\alpha X}^{\text{natural death}} - \overbrace{\beta_P X P}^{\text{IAV infectious transmission}}, \tag{1.2}$$

where $X(0)$ is the initial concentration of the uninfected epithelial cells.

Mathematical analysis of within-host IAV infection model was studied in a few papers [33, 41, 42].

1.1.2. Mathematical models of SARS-CoV-2 single-infection

Model (1.1) was utilized to characterize the dynamics of SARS-CoV-2 within a host in [43–45]. Li et al. [46], used Eq (1.2) for the uninfected epithelial cell dynamics in case of SARS-CoV-2 infection. The model with target-cell limited and model with regrowth and death of the uninfected epithelial cells presented, respectively, in [43, 46] were extended and modified by including (i) effect of immune response [44, 47–51], (ii) effect of different drug therapies [52, 53], and (iii) effect of time delay [54].

Stability analysis of within-host SARS-CoV-2 single-infection models was investigated in [49–51, 55].

Mathematical model of IAV/SARS-CoV-2 coinfection. Recently, mathematical models were developed to characterize within-host co-dynamics of COVID-19 with other diseases, such as: SARS-CoV-2-cancer [56], SARS-CoV-2/HIV coinfection [57], SARS-CoV-2/malaria coinfection [58]. Based on the target cell-limited model (1.1), and the Pinky and Dobrovolny [24] developed a model for the within-host dynamics of two respiratory viruses coinfection (SARS-CoV-2 and IAV).

$$\begin{cases} \dot{X} = -\overbrace{\beta_V XV}^{\text{SARS-CoV-2 infectious transmission}} - \overbrace{\beta_P XP}^{\text{IAV infectious transmission}}, \\ \dot{L} = \overbrace{\beta_V XV}^{\text{SARS-CoV-2 infectious transmission}} - \overbrace{\delta_L L}^{\text{latent transition}}, \\ \dot{E} = \overbrace{\beta_P XP}^{\text{IAV infectious transmission}} - \overbrace{\delta_E E}^{\text{latent transition}}, \\ \dot{Y} = \overbrace{\delta_L L}^{\text{latent transition}} - \overbrace{\gamma_Y Y}^{\text{natural death}}, \\ \dot{I} = \overbrace{\delta_E E}^{\text{SARS-CoV-2 production}} - \overbrace{\gamma_I I}^{\text{natural death}}, \\ \dot{V} = \overbrace{\kappa_V Y}^{\text{IAV production}} - \overbrace{\pi_V V}^{\text{natural death}}, \\ \dot{P} = \overbrace{\kappa_P I}^{\text{IAV production}} - \overbrace{\pi_P P}^{\text{natural death}}, \end{cases} \tag{1.3}$$

where $L = L(t)$, $Y = Y(t)$ and $V = V(t)$ are the concentrations of latent SARS-CoV-2-infected epithelial cells, active SARS-CoV-2-infected epithelial cells and free SARS-CoV-2 particles, at time t, respectively. Model (1.3) describes the competition between two respiratory viruses, SARS-CoV-2 and IAV. However, the effect of the immune response was not modeled. Further, the regrowth and death of the uninfected epithelial cells were not considered. Furthermore, mathematical analysis of the model was not studied.

The objective of the present work is to formulate a mathematical model for within-host IAV/SARS-CoV-2 coinfection with eclipse phase. The model is a generalization of the model (1.3) by taking into account (i) the regrowth and death of the uninfected epithelial cells, (ii) the death of the latent SARS-CoV-2-infected cells and latent IAV-infected cells, (iii) the effect of SARS-CoV-2-specific antibody and IAV-specific antibody. We study the basic qualitative properties of the model, calculate all equilibria, investigate the global stability of equilibria and demonstrate the theoretical results via numerical simulations. We discuss the importance of including the antibody immunity in the IAV/SARS-CoV-2 co-infection model.

Our proposed model can be helpful to characterize the dynamics of coinfection with SARS-CoV-2 strains (Alpha, Beta, Gamma, Delta, Lambda and Omicron), or coinfection of SARS-CoV-2 (or IAV) and other respiratory viruses. Moreover, the model may help to predict new treatment regimens for viral coinfections.

2. Model formulation

In this section, we present an IAV/SARS-CoV-2 coinfection dynamics model with a latent phase. The dynamics of IAV/SARS-CoV-2 coinfection is presented in the diagram Figure 1. We denote $Z = Z(t)$ and $M = M(t)$ for the concentrations of SARS-CoV-2-specific antibodies and IAV-specific antibodies, at time t, respectively. The ODEs that describe the coinfection dynamics are:

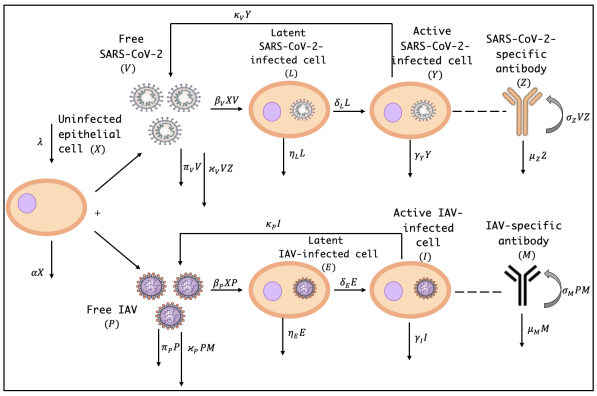


Figure 1. The schematic diagram of the IAV/SARS-CoV-2 coinfection dynamics within-host.

$$
\begin{cases}
\dot{X} = \overbrace{\lambda}^{\text{epithelial cells production}} - \overbrace{\alpha X}^{\text{natural death}} - \overbrace{\beta_V XV}^{\text{SARS-CoV-2 infectious transmission}} - \overbrace{\beta_P XP}^{\text{IAV infectious transmission}}, \\
\dot{L} = \overbrace{\beta_V XV}^{\text{SARS-CoV-2 infectious transmission}} - \overbrace{\eta_L L}^{\text{natural death}} - \overbrace{\delta_L L}^{\text{latent transition}}, \\
\dot{E} = \overbrace{\beta_P XV}^{\text{IAV infectious transmission}} - \overbrace{\eta_E E}^{\text{natural death}} - \overbrace{\delta_E E}^{\text{latent transition}}, \\
\dot{Y} = \overbrace{\delta_L L}^{\text{latent transition}} - \overbrace{\gamma_Y Y}^{\text{natural death}}, \\
\dot{I} = \overbrace{\delta_E E}^{\text{latent transition}} - \overbrace{\gamma_I I}^{\text{natural death}}, \\
\dot{V} = \overbrace{\kappa_V Y}^{\text{SARS-CoV-2 production}} - \overbrace{\pi_V V}^{\text{natural death}} - \overbrace{\varkappa_V VZ}^{\text{SARS-CoV-2 neutralization}}, \\
\dot{P} = \overbrace{\kappa_P I}^{\text{IAV production}} - \overbrace{\pi_P P}^{\text{natural death}} - \overbrace{\varkappa_P PM}^{\text{IAV neutralization}}, \\
\dot{Z} = \overbrace{\sigma_Z VZ}^{\text{SARS-CoV-2-specific antibody proliferation}} - \overbrace{\mu_Z Z}^{\text{natural death}}, \\
\dot{M} = \overbrace{\sigma_M PM}^{\text{IAV-specific antibody proliferation}} - \overbrace{\mu_M M}^{\text{natural death}}.
\end{cases}
\tag{2.1}
$$

where $(X, L, E, Y, I, V, P, Z, M) = (X(t), L(t), E(t), Y(t), I(t), V(t), P(t), Z(t), M(t))$.

In model (2.1) the regrowth death of the uninfected epithelial cells is considered. Further, the death of the latent SARS-CoV-2-infected and latent IAV-infected cells are included, Furthermore, the effect of SARS-CoV-2-specific and IAV-specific antibodies are modeled. First, we start our mathematical analysis of the system by examining the nonnegativity and boundedness of the system's solutions.

3. Basic qualitative properties

Here, we study the basic qualitative properties of system (2.1).

Lemma 1. *The solutions of system (2.1) are nonnegative and bounded.*

Proof. We have that

$$\begin{aligned}
&\dot{X}\mid_{X=0}= \lambda > 0, && \dot{L}\mid_{L=0}= \beta_V XV \geq 0 \text{ for all } X, V \geq 0,\\
&\dot{E}\mid_{E=0}= \beta_P XP \geq 0 \text{ for all } X, P \geq 0, && \dot{Y}\mid_{Y=0}= \delta_L L \text{ for all } L \geq 0,\\
&\dot{I}\mid_{I=0}= \delta_E E \text{ for all } E \geq 0, && \dot{V}\mid_{V=0}= \kappa_V Y \geq 0 \text{ for all } Y \geq 0,\\
&\dot{P}\mid_{P=0}= \kappa_P I \geq 0 \text{ for all } I \geq 0, && \dot{Z}\mid_{Z=0}= 0,\\
&\dot{M}\mid_{M=0}= 0.
\end{aligned}$$

This guarantees that, $(X(t), L(t), E(t), Y(t), I(t), V(t), P(t), Z(t), M(t)) \in \mathbb{R}^9_{\geq 0}$ for all $t \geq 0$ when $(X(0), L(0), E(0), Y(0), I(0), V(0), P(0), Z(0), M(0)) \in \mathbb{R}^9_{\geq 0}$. Let us define

$$\Psi = X + L + E + Y + I + \frac{\gamma_Y}{2\kappa_V}V + \frac{\gamma_I}{2\kappa_P}P + \frac{\gamma_Y \varkappa_V}{2\kappa_V \sigma_Z}Z + \frac{\gamma_I \varkappa_P}{2\kappa_P \sigma_M}M.$$

Then

$$\begin{aligned}
\dot{\Psi} &= \lambda - \alpha X - \eta_L L - \eta_E E - \frac{\gamma_Y}{2}Y - \frac{\gamma_I}{2}I - \frac{\gamma_Y \pi_V}{2\kappa_V}V - \frac{\gamma_I \pi_P}{2\kappa_P}P - \frac{\gamma_Y \varkappa_V \mu_Z}{2\kappa_V \sigma_Z}Z - \frac{\gamma_I \varkappa_P \mu_M}{2\kappa_P \sigma_M}M\\
&\leq \lambda - \phi\left[X + L + E + Y + I + \frac{\gamma_Y}{2\kappa_V}V + \frac{\gamma_I}{2\kappa_P}P + \frac{\gamma_Y \varkappa_V}{2\kappa_V \sigma_Z}Z + \frac{\gamma_I \varkappa_P}{2\kappa_P \sigma_M}M\right] = \lambda - \phi\Psi,
\end{aligned}$$

where $\phi = \min\{\alpha, \eta_L, \eta_E, \frac{\gamma_Y}{2}, \frac{\gamma_I}{2}, \pi_V, \pi_P, \mu_Z, \mu_M\}$. Hence, $0 \leq \Psi(t) \leq \Delta_1$ if $\Psi(0) \leq \Delta_1$ for $t \geq 0$, where $\Delta_1 = \frac{\lambda}{\phi}$. Since X, L, E, Y, I, V, P, Z and M are all nonnegative, then $0 \leq X(t), L(t), E(t), Y(t), I(t) \leq \Delta_1$, $0 \leq V(t) \leq \Delta_2$, $0 \leq P(t) \leq \Delta_3$, $0 \leq Z(t) \leq \Delta_4$, $0 \leq M(t) \leq \Delta_5$ if $X(0) + L(0) + E(0) + Y(0) + I(0) + \frac{\gamma_Y}{2\kappa_V}V(0) + \frac{\gamma_I}{2\kappa_P}P(0) + \frac{\gamma_Y \varkappa_V}{2\kappa_V \sigma_Z}Z(0) + \frac{\gamma_I \varkappa_P}{2\kappa_P \sigma_M}M(0) \leq \Delta_1$, where $\Delta_2 = \frac{2\kappa_V}{\gamma_Y}\Delta_1$, $\Delta_3 = \frac{2\kappa_P}{\gamma_I}\Delta_1$, $\Delta_4 = \frac{2\sigma_Z \kappa_V}{\varkappa_V \gamma_Y}\Delta_1$ and $\Delta_5 = \frac{2\sigma_M \kappa_P}{\varkappa_P \gamma_I}\Delta_1$. This proves the boundedness of the solutions. □

4. Equilibria

Here, we calculate the system's equilibria and deduce the conditions of their existence. Any equilibrium point $\Xi = (X, L, E, Y, I, V, P, Z, M)$ satisfies:

$$0 = \lambda - \alpha X - \beta_V XV - \beta_P XP, \tag{4.1}$$

$$0 = \beta_V XV - (\eta_L + \delta_L)L, \tag{4.2}$$

$$0 = \beta_P XP - (\eta_E + \delta_E)E, \tag{4.3}$$

$$0 = \delta_L L - \gamma_Y Y, \tag{4.4}$$

$$0 = \delta_E E - \gamma_I I, \tag{4.5}$$
$$0 = \kappa_V Y - \pi_V V - \varkappa_V VZ, \tag{4.6}$$
$$0 = \kappa_P I - \pi_P P - \varkappa_P PM, \tag{4.7}$$
$$0 = \sigma_Z VZ - \mu_Z Z, \tag{4.8}$$
$$0 = \sigma_M PM - \mu_M M. \tag{4.9}$$

Solving Eqs (4.1)–(4.9), we get eight equilibria.

(i) Infection-free equilibrium, $\Xi_0 = (X_0, 0, 0, 0, 0, 0, 0, 0, 0)$, where $X_0 = \lambda/\alpha$.

(ii) SARS-CoV-2 single-infection equilibrium without antibody immunity $\Xi_1 = (X_1, L_1, 0, Y_1, 0, V_1, 0, 0, 0)$, where

$$X_1 = \frac{\gamma_Y \pi_V (\eta_L + \delta_L)}{\kappa_V \beta_V \delta_L}, \qquad L_1 = \frac{\alpha \gamma_Y \pi_V}{\kappa_V \beta_V \delta_L}\left[\frac{X_0 \kappa_V \beta_V \delta_L}{\gamma_Y \pi_V (\eta_L + \delta_L)} - 1\right],$$
$$Y_1 = \frac{\alpha \pi_V}{\kappa_V \beta_V}\left[\frac{X_0 \kappa_V \beta_V \delta_L}{\gamma_Y \pi_V (\eta_L + \delta_L)} - 1\right], \quad V_1 = \frac{\alpha}{\beta_V}\left[\frac{X_0 \kappa_V \beta_V \delta_L}{\gamma_Y \pi_V (\eta_L + \delta_L)} - 1\right].$$

Therefore, $L_1 > 0$, $Y_1 > 0$ and $V_1 > 0$ when $\frac{X_0 \kappa_V \beta_V \delta_L}{\gamma_Y \pi_V (\eta_L + \delta_L)} > 1$. We define the basic SARS-CoV-2 single-infection reproductive ratio as:

$$\mathfrak{R}_1 = \frac{X_0 \kappa_V \beta_V \delta_L}{\gamma_Y \pi_V (\eta_L + \delta_L)}.$$

The parameter $\mathfrak{R}_1$ determines whether or not a SARS-CoV-2 single-infection can be established. Thus, we can write

$$X_1 = \frac{X_0}{\mathfrak{R}_1}, \qquad L_1 = \frac{\alpha \gamma_Y \pi_V}{\kappa_V \beta_V \delta_L}(\mathfrak{R}_1 - 1),$$
$$Y_1 = \frac{\alpha \pi_V}{\kappa_V \beta_V}(\mathfrak{R}_1 - 1), \quad V_1 = \frac{\alpha}{\beta_V}(\mathfrak{R}_1 - 1).$$

It follows that, Ξ_1 exists if $\mathfrak{R}_1 > 1$.

(iii) IAV single-infection equilibrium without antibody immunity, $\Xi_2 = (X_2, 0, E_2, 0, I_2, 0, P_2, 0, 0)$, where

$$X_2 = \frac{\gamma_I \pi_P (\eta_E + \delta_E)}{\kappa_P \beta_P \delta_E}, \qquad E_2 = \frac{\alpha \gamma_I \pi_P}{\kappa_P \beta_P \delta_E}\left[\frac{X_0 \kappa_P \beta_P \delta_E}{\gamma_I \pi_P (\eta_E + \delta_E)} - 1\right],$$
$$I_2 = \frac{\alpha \pi_P}{\kappa_P \beta_P}\left[\frac{X_0 \kappa_P \beta_P \delta_E}{\gamma_I \pi_P (\eta_E + \delta_E)} - 1\right], \quad P_2 = \frac{\alpha}{\beta_P}\left[\frac{X_0 \kappa_P \beta_P \delta_E}{\gamma_I \pi_P (\eta_E + \delta_E)} - 1\right].$$

Therefore, $E_2 > 0$, $I_2 > 0$ and $P_2 > 0$ when $\frac{X_0 \kappa_P \beta_P \delta_E}{\gamma_I \pi_P (\eta_E + \delta_E)} > 1$. We define the basic IAV-infection reproductive ratio as:

$$\mathfrak{R}_2 = \frac{X_0 \kappa_P \beta_P \delta_E}{\gamma_I \pi_P (\eta_E + \delta_E)}.$$

The parameter $\mathfrak{R}_2$, determines whether or not the IAV single-infection can be established. In terms of $\mathfrak{R}_2$, we can write:

$$X_2 = \frac{X_0}{\mathfrak{R}_2}, \qquad E_2 = \frac{\alpha \gamma_I \pi_P}{\kappa_P \beta_P \delta_E}(\mathfrak{R}_2 - 1),$$

$$I_2 = \frac{\alpha\pi_P}{\kappa_P\beta_P}(\mathfrak{R}_2 - 1), \quad P_2 = \frac{\alpha}{\beta_P}(\mathfrak{R}_2 - 1).$$

Therefore, Ξ_2 exists if $\mathfrak{R}_2 > 1$

(iv) SARS-CoV-2 single-infection equilibrium with stimulated SARS-CoV-2-specific antibody immunity, $\Xi_3 = (X_3, L_3, 0, Y_3, 0, V_3, 0, Z_3, 0)$, where

$$X_3 = \frac{\lambda\sigma_Z}{\beta_V\mu_Z + \alpha\sigma_Z}, \quad L_3 = \frac{\lambda\beta_V\mu_Z}{(\eta_L + \delta_L)(\beta_V\mu_Z + \alpha\sigma_Z)}, \quad Y_3 = \frac{\lambda\beta_V\mu_Z\delta_L}{\gamma_Y(\eta_L + \delta_L)(\beta_V\mu_Z + \alpha\sigma_Z)},$$
$$V_3 = \frac{\mu_Z}{\sigma_Z}, \quad Z_3 = \frac{\pi_V}{\varkappa_V}\left[\frac{\lambda\beta_V\sigma_Z\kappa_V\delta_L}{\gamma_Y\pi_V(\eta_L + \delta_L)(\beta_V\mu_Z + \alpha\sigma_Z)} - 1\right].$$

We note that Ξ_3 exists when $\frac{\lambda\beta_V\sigma_Z\kappa_V\delta_L}{\gamma_Y\pi_V(\eta_L+\delta_L)(\beta_V\mu_Z+\alpha\sigma_Z)} > 1$. Let us define the SARS-CoV-2-specific antibody activation ratio in case of SARS-CoV-2 single-infection as:

$$\mathfrak{R}_3 = \frac{\lambda\beta_V\sigma_Z\kappa_V\delta_L}{\gamma_Y\pi_V(\eta_L + \delta_L)(\beta_V\mu_Z + \alpha\sigma_Z)}.$$

Thus, $Z_3 = \frac{\pi_V}{\varkappa_V}(\mathfrak{R}_3 - 1)$. The parameter $\mathfrak{R}_3$ determines whether or not the SARS-CoV-2-specific antibody immunity is activated in the absence of IAV infection.

(v) IAV single-infection equilibrium with stimulated of IAV-specific antibody immunity, $\Xi_4 = (X_4, 0, E_4, 0, I_4, 0, P_4, 0, M_4)$, where

$$X_4 = \frac{\lambda\sigma_M}{\beta_P\mu_M + \alpha\sigma_M}, \quad E_4 = \frac{\lambda\beta_P\mu_M}{(\eta_E + \delta_E)(\beta_P\mu_M + \alpha\sigma_M)}, \quad I_4 = \frac{\lambda\beta_P\mu_M\delta_E}{\gamma_I(\eta_E + \delta_E)(\beta_P\mu_M + \alpha\sigma_M)},$$
$$P_4 = \frac{\mu_M}{\sigma_M}, \quad M_4 = \frac{\pi_P}{\varkappa_P}\left[\frac{\lambda\beta_P\sigma_M\kappa_P\delta_E}{\gamma_I\pi_P(\eta_E + \delta_E)(\beta_P\mu_M + \alpha\sigma_M)} - 1\right].$$

We note that Ξ_4 exists when $\frac{\lambda\beta_P\sigma_M\kappa_P\delta_E}{\gamma_I\pi_P(\eta_E+\delta_E)(\beta_P\mu_M+\alpha\sigma_M)} > 1$. We define the IAV-specific antibody immunity activation ratio for IAV single-infection as:

$$\mathfrak{R}_4 = \frac{\lambda\beta_P\sigma_M\kappa_P\delta_E}{\gamma_I\pi_P(\eta_E + \delta_E)(\beta_P\mu_M + \alpha\sigma_M)}.$$

Thus, $M_4 = \frac{\pi_P}{\varkappa_P}(\mathfrak{R}_4 - 1)$. The parameter $\mathfrak{R}_4$ determines whether or not the IAV-specific antibody immunity is activated in the absence of SARS-CoV-2 infection.

(vi) IAV/SARS-CoV-2 coinfection equilibrium with only stimulated SARS-CoV-2-specific antibody immunity, $\Xi_5 = (X_5, L_5, E_5, Y_5, I_5, V_5, P_5, Z_5, 0)$, where

$$X_5 = \frac{\gamma_I\pi_P(\eta_E + \delta_E)}{\kappa_P\beta_P\delta_E}, \quad L_5 = \frac{\beta_V\mu_Z\gamma_I\pi_P(\eta_E + \delta_E)}{\kappa_P\beta_P\delta_E\sigma_Z(\eta_L + \delta_L)},$$
$$E_5 = \frac{\gamma_I\pi_P(\beta_V\mu_Z + \alpha\sigma_Z)}{\kappa_P\beta_P\delta_E\sigma_Z}\left[\frac{\lambda\beta_P\kappa_P\delta_E\sigma_Z}{\gamma_I\pi_P(\eta_E + \delta_E)(\beta_V\mu_Z + \alpha\sigma_Z)} - 1\right], \quad Y_5 = \frac{\beta_V\mu_Z\gamma_I\pi_P\delta_L(\eta_E + \delta_E)}{\kappa_P\beta_P\delta_E\sigma_Z\gamma_Y(\eta_L + \delta_L)},$$
$$I_5 = \frac{\pi_P(\beta_V\mu_Z + \alpha\sigma_Z)}{\kappa_P\beta_P\sigma_Z}\left[\frac{\lambda\beta_P\kappa_P\delta_E\sigma_Z}{\gamma_I\pi_P(\eta_E + \delta_E)(\beta_V\mu_Z + \alpha\sigma_Z)} - 1\right], \quad V_5 = \frac{\mu_Z}{\sigma_Z},$$
$$P_5 = \frac{\beta_V\mu_Z + \alpha\sigma_Z}{\beta_P\sigma_Z}\left[\frac{\lambda\beta_P\kappa_P\delta_E\sigma_Z}{\gamma_I\pi_P(\eta_E + \delta_E)(\beta_V\mu_Z + \alpha\sigma_Z)} - 1\right],$$

$$Z_5 = \frac{\pi_V}{\varkappa_V}\left[\frac{\kappa_V\beta_V\gamma_I\delta_L\pi_P\left(\eta_E+\delta_E\right)}{\kappa_P\beta_P\gamma_Y\delta_E\pi_V\left(\eta_L+\delta_L\right)}-1\right] = \frac{\pi_V}{\varkappa_V}\left(\mathfrak{R}_1/\mathfrak{R}_2-1\right).$$

We note that Ξ_5 exists when,

$$\frac{\mathfrak{R}_1}{\mathfrak{R}_2} > 1 \text{ and } \frac{\lambda\beta_P\kappa_P\delta_E\sigma_Z}{\gamma_I\pi_P\left(\eta_E+\delta_E\right)\left(\beta_V\mu_Z+\alpha\sigma_Z\right)} > 1.$$

Now, we define the SARS-CoV-2 infection reproductive ratio in the presence of IAV infection as:

$$\mathfrak{R}_5 = \frac{\lambda\beta_P\kappa_P\delta_E\sigma_Z}{\gamma_I\pi_P\left(\eta_E+\delta_E\right)\left(\beta_V\mu_Z+\alpha\sigma_Z\right)}.$$

The parameter $\mathfrak{R}_5$ determines whether or not SARS-CoV-2-infected patients could be coinfected with IAV. Hence,

$$E_5 = \frac{\gamma_I\pi_P(\beta_V\mu_Z+\alpha\sigma_Z)}{\kappa_P\beta_P\delta_E\sigma_Z}\left(\mathfrak{R}_5-1\right), \quad I_5 = \frac{\pi_P(\beta_V\mu_Z+\alpha\sigma_Z)}{\beta_P\sigma_Z\kappa_P}\left(\mathfrak{R}_5-1\right),$$
$$P_5 = \frac{\beta_V\mu_Z+\alpha\sigma_Z}{\beta_P\sigma_Z}\left(\mathfrak{R}_5-1\right).$$

and then Ξ_5 exists if $\frac{\mathfrak{R}_1}{\mathfrak{R}_2} > 1$ and $\mathfrak{R}_5 > 1$.

(vii) IAV/SARS-CoV-2 coinfection equilibrium with only stimulated IAV-specific antibody immunity, $\Xi_6 = (X_6, L_6, E_6, Y_6, I_6, V_6, P_6, 0, M_6)$, where

$$X_6 = \frac{\gamma_Y\pi_V(\eta_L+\delta_L)}{\kappa_V\beta_V\delta_L}, \qquad L_6 = \frac{\gamma_Y\pi_V(\beta_P\mu_M+\alpha\sigma_M)}{\kappa_V\beta_V\delta_L\sigma_M}\left[\frac{\lambda\beta_V\kappa_V\delta_L\sigma_M}{\gamma_Y\pi_V(\eta_L+\delta_L)(\beta_P\mu_M+\alpha\sigma_M)}-1\right],$$
$$E_6 = \frac{\gamma_Y\beta_P\mu_M\pi_V\left(\eta_L+\delta_L\right)}{\kappa_V\beta_V\delta_L\sigma_M\left(\eta_E+\delta_E\right)}, \qquad Y_6 = \frac{\pi_V\left(\beta_P\mu_M+\alpha\sigma_M\right)}{\kappa_V\beta_V\sigma_M}\left[\frac{\lambda\beta_V\kappa_V\delta_L\sigma_M}{\gamma_Y\pi_V(\eta_L+\delta_L)(\beta_P\mu_M+\alpha\sigma_M)}-1\right],$$
$$I_6 = \frac{\beta_P\delta_E\mu_M\pi_V\gamma_Y\left(\eta_L+\delta_L\right)}{\kappa_V\beta_V\delta_L\sigma_M\gamma_I\left(\eta_E+\delta_E\right)}, \quad V_6 = \frac{\beta_P\mu_M+\alpha\sigma_M}{\beta_V\sigma_M}\left[\frac{\lambda\beta_V\kappa_V\delta_L\sigma_M}{\gamma_Y\pi_V(\eta_L+\delta_L)(\beta_P\mu_M+\alpha\sigma_M)}-1\right],$$
$$P_6 = \frac{\mu_M}{\sigma_M}, \quad M_6 = \frac{\pi_P}{\varkappa_P}\left[\frac{\kappa_P\beta_P\gamma_Y\delta_E\pi_V\left(\eta_L+\delta_L\right)}{\kappa_V\beta_V\gamma_I\delta_L\pi_P\left(\eta_E+\delta_E\right)}-1\right] = \frac{\pi_P}{\varkappa_P}\left(\mathfrak{R}_2/\mathfrak{R}_1-1\right).$$

We note that Ξ_6 exists when

$$\frac{\mathfrak{R}_2}{\mathfrak{R}_1} > 1 \text{ and } \frac{\lambda\beta_V\kappa_V\delta_L\sigma_M}{\gamma_Y\pi_V(\eta_L+\delta_L)(\beta_P\mu_M+\alpha\sigma_M)} > 1.$$

We define the SARS-CoV-2 infection reproductive ratio in the presence of IAV infection as:

$$\mathfrak{R}_6 = \frac{\lambda\beta_V\kappa_V\delta_L\sigma_M}{\gamma_Y\pi_V(\eta_L+\delta_L)(\beta_P\mu_M+\alpha\sigma_M)}.$$

Thus,

$$L_6 = \frac{\gamma_Y\pi_V(\beta_P\mu_M+\alpha\sigma_M)}{\kappa_V\beta_V\delta_L\sigma_M}\left(\mathfrak{R}_6-1\right), \quad Y_6 = \frac{\pi_V(\beta_P\mu_M+\alpha\sigma_M)}{\beta_V\sigma_M\kappa_V}\left(\mathfrak{R}_6-1\right),$$
$$V_6 = \frac{\beta_P\mu_M+\alpha\sigma_M}{\beta_V\sigma_M}\left(\mathfrak{R}_6-1\right).$$

The parameter $\mathfrak{R}_6$ determines whether or not SARS-CoV-2-infected patients could be coinfected with IAV.

(viii) IAV/SARS-CoV-2 coinfection equilibrium with stimulated both SARS-CoV-2-specific and IAV-specific antibody immunities, $\Xi_7 = (X_7, L_7, E_7, Y_7, I_7, V_7, P_7, Z_7, M_7)$, where

$$
\begin{aligned}
X_7 &= \frac{\lambda\sigma_Z\sigma_M}{\beta_P\mu_M\sigma_Z + \beta_V\mu_Z\sigma_M + \alpha\sigma_Z\sigma_M}, \quad L_7 = \frac{\beta_V\lambda\mu_Z\sigma_M}{(\eta_L+\delta_L)(\beta_P\mu_M\sigma_Z + \beta_V\mu_Z\sigma_M + \alpha\sigma_Z\sigma_M)},\\
E_7 &= \frac{\beta_P\lambda\mu_M\sigma_Z}{(\eta_E+\delta_E)(\beta_P\mu_M\sigma_Z + \beta_V\mu_Z\sigma_M + \alpha\sigma_Z\sigma_M)}, \quad Y_7 = \frac{\beta_V\delta_L\lambda\mu_Z\sigma_M}{\gamma_Y(\eta_L+\delta_L)(\beta_P\mu_M\sigma_Z + \beta_V\mu_Z\sigma_M + \alpha\sigma_Z\sigma_M)},\\
I_7 &= \frac{\beta_P\delta_E\lambda\mu_M\sigma_Z}{\gamma_I(\eta_E+\delta_E)(\beta_P\mu_M\sigma_Z + \beta_V\mu_Z\sigma_M + \alpha\sigma_Z\sigma_M)}, \quad V_7 = \frac{\mu_Z}{\sigma_Z}, \quad P_7 = \frac{\mu_M}{\sigma_M},\\
Z_7 &= \frac{\pi_V}{\varkappa_V}\left[\frac{\lambda\beta_V\kappa_V\delta_L\sigma_M\sigma_Z}{\gamma_Y\pi_V(\eta_L+\delta_L)(\beta_P\mu_M\sigma_Z + \beta_V\mu_Z\sigma_M + \alpha\sigma_Z\sigma_M)} - 1\right],\\
M_7 &= \frac{\pi_P}{\varkappa_P}\left[\frac{\lambda\beta_P\kappa_P\delta_E\sigma_M\sigma_Z}{\gamma_I\pi_P(\eta_E+\delta_E)(\beta_P\mu_M\sigma_Z + \beta_V\mu_Z\sigma_M + \alpha\sigma_Z\sigma_M)} - 1\right].
\end{aligned}
$$

It is obvious that Ξ_7 exists when

$$
\begin{aligned}
&\frac{\lambda\beta_V\kappa_V\delta_L\sigma_M\sigma_Z}{\gamma_Y\pi_V(\eta_L+\delta_L)(\beta_P\mu_M\sigma_Z + \beta_V\mu_Z\sigma_M + \alpha\sigma_Z\sigma_M)} > 1,\\
&\frac{\lambda\beta_P\kappa_P\delta_E\sigma_M\sigma_Z}{\gamma_I\pi_P(\eta_E+\delta_E)(\beta_P\mu_M\sigma_Z + \beta_V\mu_Z\sigma_M + \alpha\sigma_Z\sigma_M)} > 1.
\end{aligned}
$$

Now, we define

$$
\begin{aligned}
\mathfrak{R}_7 &= \frac{\lambda\beta_V\kappa_V\delta_L\sigma_M\sigma_Z}{\gamma_Y\pi_V(\eta_L+\delta_L)(\beta_P\mu_M\sigma_Z + \beta_V\mu_Z\sigma_M + \alpha\sigma_Z\sigma_M)},\\
\mathfrak{R}_8 &= \frac{\lambda\beta_P\kappa_P\delta_E\sigma_M\sigma_Z}{\gamma_I\pi_P(\eta_E+\delta_E)(\beta_P\mu_M\sigma_Z + \beta_V\mu_Z\sigma_M + \alpha\sigma_Z\sigma_M)}.
\end{aligned}
$$

Here, $\mathfrak{R}_7$ is the SARS-CoV-2-specific antibody activation ratio in case of IAV/SARS-CoV-2 coinfection, $\mathfrak{R}_8$ is the IAV-specific antibody activation ratio in case of IAV/SARS-CoV-2 coinfection. Hence, $Z_7 = \frac{\pi_V}{\varkappa_V}(\mathfrak{R}_7 - 1)$ and $M_7 = \frac{\pi_P}{\varkappa_P}(\mathfrak{R}_8 - 1)$. If $\mathfrak{R}_7 > 1$ and $\mathfrak{R}_8 > 1$, then Ξ_7 exists.

In summary, we have eight threshold parameters which determine the existence of the model's equilibria

$$
\begin{aligned}
\mathfrak{R}_1 &= \frac{X_0\kappa_V\beta_V\delta_L}{\gamma_Y\pi_V(\eta_L+\delta_L)}, \quad \mathfrak{R}_2 = \frac{X_0\kappa_P\beta_P\delta_E}{\gamma_I\pi_P(\eta_E+\delta_E)}, \quad \mathfrak{R}_3 = \frac{\lambda\beta_V\sigma_Z\kappa_V\delta_L}{\gamma_Y\pi_V(\eta_L+\delta_L)(\beta_V\mu_Z + \alpha\sigma_Z)},\\
\mathfrak{R}_4 &= \frac{\lambda\beta_P\sigma_M\kappa_P\delta_E}{\gamma_I\pi_P(\eta_E+\delta_E)(\beta_P\mu_M + \alpha\sigma_M)}, \quad \mathfrak{R}_5 = \frac{\lambda\beta_P\kappa_P\delta_E\sigma_Z}{\gamma_I\pi_P(\eta_E+\delta_E)(\beta_V\mu_Z + \alpha\sigma_Z)},\\
\mathfrak{R}_6 &= \frac{\lambda\beta_V\kappa_V\delta_L\sigma_M}{\gamma_Y\pi_V(\eta_L+\delta_L)(\beta_P\mu_M + \alpha\sigma_M)}, \quad \mathfrak{R}_7 = \frac{\lambda\beta_V\kappa_V\delta_L\sigma_M\sigma_Z}{\gamma_Y\pi_V(\eta_L+\delta_L)(\beta_P\mu_M\sigma_Z + \beta_V\mu_Z\sigma_M + \alpha\sigma_Z\sigma_M)},\\
\mathfrak{R}_8 &= \frac{\lambda\beta_P\kappa_P\delta_E\sigma_M\sigma_Z}{\gamma_I\pi_P(\eta_E+\delta_E)(\beta_P\mu_M\sigma_Z + \beta_V\mu_Z\sigma_M + \alpha\sigma_Z\sigma_M)}.
\end{aligned} \tag{4.10}
$$

5. Global stability

This section is devoted to studying the global asymptotic stability of all equilibria. We configure Lyapunov functions following the way outlined in [59]. The following arithmetic-mean-geometric-mean inequality will be utilized:

$$\frac{u_1+u_2+...+u_n}{n} \geq \sqrt[n]{(u_1)(u_2)...(u_n)},\ u_i \geq 0, \quad i=1,2,...,n. \tag{5.1}$$

Let a function $\Lambda_j(X,L,E,Y,I,V,P,Z,M)$ and $\tilde{\Omega}_j$ be the largest invariant subset of

$$\Omega_j = \left\{(X,L,E,Y,I,V,P,Z,M) : \frac{d\Lambda_j}{dt}=0\right\}, \quad j=0,1,...,7.$$

Define a function

$$F(\upsilon) = \upsilon - 1 - \ln\upsilon, \quad \upsilon > 0.$$

Theorem 1. *If $\Re_1 \leq 1$ and $\Re_2 \leq 1$, then Ξ_0 is globally asymptotically stable (G.A.S).*

Proof. Define

$$\Lambda_0 = X_0 F\left(\frac{X}{X_0}\right) + L + E + \frac{\eta_L+\delta_L}{\delta_L}Y + \frac{\eta_E+\delta_E}{\delta_E}I + \frac{\beta_V X_0}{\pi_V}V + \frac{\beta_P X_0}{\pi_P}P + \beta_V X_0 \frac{\varkappa_V}{\sigma_Z \pi_V}Z + \beta_P X_0 \frac{\varkappa_P}{\sigma_M \pi_P}M.$$

We note that, $\Lambda_0 > 0$ for all $X,L,E,Y,I,V,P,Z,M > 0$ and $\Lambda_0(X_0,0,0,0,0,0,0,0,0) = 0$. We calculate $\frac{d\Lambda_0}{dt}$ along the solutions of model (2.1) as:

$$\begin{aligned}
\frac{d\Lambda_0}{dt} &= \left(1-\frac{X_0}{X}\right)[\lambda - \alpha X - \beta_V XV - \beta_P XP] + \beta_V XV - (\eta_L+\delta_L)L + \beta_P XP - (\eta_E+\delta_E)E \\
&+ \frac{\eta_L+\delta_L}{\delta_L}[\delta_L L - \gamma_Y Y] + \frac{\eta_E+\delta_E}{\delta_E}[\delta_E E - \gamma_I I] + \frac{\beta_V X_0}{\pi_V}[\kappa_V Y - \pi_V V - \varkappa_V VZ] \\
&+ \frac{\beta_P X_0}{\pi_P}[\kappa_P I - \pi_P P - \varkappa_P PM] + \beta_V X_0 \frac{\varkappa_V}{\sigma_Z \pi_V}[\sigma_Z VZ - \mu_Z Z] + \beta_P X_0 \frac{\varkappa_P}{\sigma_M \pi_P}[\sigma_M PM - \mu_M M] \\
&= \left(1-\frac{X_0}{X}\right)(\lambda - \alpha X) - \frac{\gamma_Y(\eta_L+\delta_L)}{\delta_L}Y - \frac{\gamma_I(\eta_E+\delta_E)}{\delta_E}I + \frac{\kappa_V \beta_V X_0}{\pi_V}Y \\
&+ \frac{\kappa_P \beta_P X_0}{\pi_P}I - \frac{\beta_V X_0 \varkappa_V \mu_Z}{\pi_V \sigma_Z}Z - \frac{\beta_P X_0 \varkappa_P \mu_M}{\pi_P \sigma_M}M.
\end{aligned}$$

Using the equilibrium condition, $\lambda = \alpha X_0$ we get

$$\begin{aligned}
\frac{d\Lambda_0}{dt} &= -\alpha\frac{(X-X_0)^2}{X} + \frac{\gamma_Y(\eta_L+\delta_L)}{\delta_L}\left(\frac{\kappa_V \beta_V \delta_L X_0}{\gamma_Y \pi_V(\eta_L+\delta_L)} - 1\right)Y + \frac{\gamma_I(\eta_E+\delta_E)}{\delta_E}\left(\frac{\kappa_P \beta_P \delta_E X_0}{\gamma_I \pi_P(\eta_E+\delta_E)} - 1\right)I \\
&- \beta_V X_0 \frac{\varkappa_V \mu_Z}{\pi_V \sigma_Z}Z - \beta_P X_0 \frac{\varkappa_P \mu_M}{\pi_P \sigma_M}M \\
&= -\alpha\frac{(X-X_0)^2}{X} + \frac{\gamma_Y(\eta_L+\delta_L)}{\delta_L}(\Re_1 - 1)Y + \frac{\gamma_I(\eta_E+\delta_E)}{\delta_E}(\Re_2 - 1)I
\end{aligned}$$

$$-\beta_V X_0 \frac{\varkappa_V \mu_Z}{\pi_V \sigma_Z} Z - \beta_P X_0 \frac{\varkappa_P \mu_M}{\pi_P \sigma_M} M.$$

Since $\mathfrak{R}_1 \leq 1$ and $\mathfrak{R}_2 \leq 1$, then $\frac{d\Lambda_0}{dt} \leq 0$ for all $X, Y, I, Z, M > 0$. In addition $\frac{d\Lambda_0}{dt} = 0$, when $X = X_0$ and $Y = I = Z = M = 0$. The solutions of system (2.1) tend to $\tilde{\Omega}_0$ [60] which includes elements with $Y = I = 0$. Thus, $\dot{Y} = \dot{I} = 0$ and from the fourth and fifth equations of system (2.1) we have:

$$0 = \dot{Y} = \delta_L L \Longrightarrow L(t) = 0, \text{ for all } t,$$
$$0 = \dot{I} = \delta_E E \Longrightarrow E(t) = 0, \text{ for all } t.$$

In addition, from the second and third equations of system (2.1) we have:

$$0 = \dot{L} = \beta_V X_0 V \Longrightarrow V(t) = 0, \text{ for all } t,$$
$$0 = \dot{E} = \beta_P X_0 P \Longrightarrow P(t) = 0, \text{ for all } t.$$

Therefore, $\tilde{\Omega}_0 = \{\Xi_0\}$ and applying Lyapunov-LaSalle Asymptotic Stability Theorem (L-LAST) [61, 63], we obtain that Ξ_0 is G.A.S. □

Theorem 2. *Suppose that* $\mathfrak{R}_1 > 1$, $\mathfrak{R}_2/\mathfrak{R}_1 \leq 1$ *and* $\mathfrak{R}_3 \leq 1$, *then* Ξ_1 *is G.A.S.*

Proof. Let us formulate a Lyapunov function Λ_1 as:

$$\Lambda_1 = X_1 F\left(\frac{X}{X_1}\right) + L_1 F\left(\frac{L}{L_1}\right) + E + \frac{\eta_L + \delta_L}{\delta_L} Y_1 F\left(\frac{Y}{Y_1}\right) + \frac{\eta_E + \delta_E}{\delta_E} I + \frac{\beta_V X_1}{\pi_V} V_1 F\left(\frac{V}{V_1}\right)$$
$$+ \frac{\beta_P X_1}{\pi_P} P + \frac{\beta_V X_1 \varkappa_V}{\sigma_Z \pi_V} Z + \frac{\beta_P X_1 \varkappa_P}{\sigma_M \pi_P} M.$$

We calculate $\frac{d\Lambda_1}{dt}$ as:

$$\frac{d\Lambda_1}{dt} = \left(1 - \frac{X_1}{X}\right)[\lambda - \alpha X - \beta_V X V - \beta_P X P] + \left(1 - \frac{L_1}{L}\right)[\beta_V X V - (\eta_L + \delta_L) L]$$
$$+ \beta_P X P - (\eta_E + \delta_E) E + \frac{\eta_L + \delta_L}{\delta_L}\left(1 - \frac{Y_1}{Y}\right)[\delta_L L - \gamma_Y Y] + \frac{\eta_E + \delta_E}{\delta_E}[\delta_E E - \gamma_I I]$$
$$+ \frac{\beta_V X_1}{\pi_V}\left(1 - \frac{V_1}{V}\right)[\kappa_V Y - \pi_V V - \varkappa_V V Z] + \frac{\beta_P X_1}{\pi_P}[\kappa_P I - \pi_P P - \varkappa_P P M]$$
$$+ \beta_V X_1 \frac{\varkappa_V}{\sigma_Z \pi_V}[\sigma_Z V Z - \mu_Z Z] + \beta_P X_1 \frac{\varkappa_P}{\sigma_M \pi_P}[\sigma_M P M - \mu_M M]. \tag{5.2}$$

Simplifying Eq (5.2), we get

$$\frac{d\Lambda_1}{dt} = \left(1 - \frac{X_1}{X}\right)(\lambda - \alpha X) - \beta_V X V \frac{L_1}{L} + (\eta_L + \delta_L) L_1 - \frac{\gamma_Y (\eta_L + \delta_L)}{\delta_L} Y - (\eta_L + \delta_L) L \frac{Y_1}{Y}$$
$$+ \frac{\gamma_Y (\eta_L + \delta_L)}{\delta_L} Y_1 - \frac{\gamma_I (\eta_E + \delta_E)}{\delta_E} I + \beta_V X_1 \frac{\kappa_V}{\pi_V} Y - \beta_V X_1 \frac{\kappa_V}{\pi_V} Y \frac{V_1}{V} + \beta_V X_1 V_1$$
$$+ \beta_V X_1 \frac{\varkappa_V}{\pi_V} V_1 Z + \beta_P X_1 \frac{\kappa_P}{\pi_P} I - \beta_V X_1 \frac{\varkappa_V \mu_Z}{\sigma_Z \pi_V} Z - \beta_P X_1 \frac{\varkappa_P \mu_M}{\sigma_M \pi_P} M.$$

Using the equilibrium conditions for Ξ_1:

$$\lambda = \alpha X_1 + \beta_V X_1 V_1, \quad \beta_V X_1 V_1 = (\eta_L + \delta_L) L_1,$$

$$L_1 = \frac{\gamma_Y}{\delta_L} Y_1, \quad V_1 = \frac{\kappa_V}{\pi_V} Y_1,$$

we obtain

$$\begin{aligned}\frac{d\Lambda_1}{dt} &= \left(1 - \frac{X_1}{X}\right)(\alpha X_1 - \alpha X) + 4\beta_V X_1 V_1 - \beta_V X_1 V_1 \frac{X_1}{X} - \beta_V X_1 V_1 \frac{L_1 X V}{L X_1 V_1} - \beta_V X_1 V_1 \frac{Y_1 L}{Y L_1} \\ &\quad - \beta_V X_1 V_1 \frac{V_1 Y}{V Y_1} + \frac{\gamma_I (\eta_E + \delta_E)}{\delta_E} \left(\frac{\beta_P X_1 \kappa_P \delta_E}{\gamma_I \pi_P (\eta_E + \delta_E)} - 1\right) I + \frac{\beta_V X_1 \varkappa_V \mu_Z}{\sigma_Z \pi_V} \left(\frac{\sigma_Z}{\mu_Z} V_1 - 1\right) Z \\ &\quad - \beta_P X_1 \frac{\varkappa_P \mu_M}{\sigma_M \pi_P} M. \end{aligned} \tag{5.3}$$

Then collecting terms of (5.3), we get

$$\begin{aligned}\frac{d\Lambda_1}{dt} &= -\frac{\alpha(X - X_1)^2}{X} + \beta_V X_1 V_1 \left[4 - \frac{X_1}{X} - \frac{L_1 X V}{L X_1 V_1} - \frac{Y_1 L}{Y L_1} - \frac{V_1 Y}{V Y_1}\right] \\ &\quad + \frac{\gamma_I (\eta_E + \delta_E)}{\delta_E} \left(\frac{\mathfrak{R}_2}{\mathfrak{R}_1} - 1\right) I + \frac{\varkappa_V X_1 (\alpha \sigma_Z + \beta_V \mu_Z)}{\sigma_Z \pi_V} (\mathfrak{R}_3 - 1) Z - \beta_P X_1 \frac{\varkappa_P \mu_M}{\sigma_M \pi_P} M.\end{aligned}$$

Using inequality (5.1), we get

$$4 - \frac{X_1}{X} - \frac{L_1 X V}{L X_1 V_1} - \frac{Y_1 L}{Y L_1} - \frac{V_1 Y}{V Y_1} \leq 0.$$

Since $\mathfrak{R}_2/\mathfrak{R}_1 \leq 1$ and $\mathfrak{R}_3 \leq 1$, then $\frac{d\Lambda_1}{dt} \leq 0$ for all $X, L, Y, I, V, Z, M > 0$. Moreover, $\frac{d\Lambda_1}{dt} = 0$ when $X = X_1$, $L = L_1$, $Y = Y_1$, $V = V_1$ and $I = Z = M = 0$. The solutions of system (2.1) tend to $\tilde{\Omega}_1$ where $I = 0$. Hence, $\dot{I} = 0$ and the fifth equation of system (2.1) gives

$$0 = \dot{I} = \delta_E E \Longrightarrow E(t) = 0, \text{ for all } t.$$

In addition, from the third equation of system (2.1) we get,

$$0 = \dot{E} = \beta_P X_1 P \Longrightarrow P(t) = 0, \text{ for all } t.$$

Hence, $\tilde{\Omega}_1 = \{\Xi_1\}$ and Ξ_1 is G.A.S by using L-LAST [61–63]. □

Theorem 3. *Let* $\mathfrak{R}_2 > 1$, $\mathfrak{R}_1/\mathfrak{R}_2 \leq 1$ *and* $\mathfrak{R}_4 \leq 1$, *then* Ξ_2 *is G.A.S.*

Proof. Consider

$$\begin{aligned}\Lambda_2 &= X_2 F\left(\frac{X}{X_2}\right) + L + E_2 F\left(\frac{E}{E_2}\right) + \frac{\eta_L + \delta_L}{\delta_L} Y + \frac{\eta_E + \delta_E}{\delta_E} I_2 F\left(\frac{I}{I_2}\right) \\ &\quad + \frac{\beta_V X_2}{\pi_V} V + \frac{\beta_P X_2}{\pi_P} P_2 F\left(\frac{P}{P_2}\right) + \beta_V X_2 \frac{\varkappa_V}{\sigma_Z \pi_V} Z + \beta_P X_2 \frac{\varkappa_P}{\sigma_M \pi_P} M.\end{aligned}$$

We calculate $\frac{d\Lambda_2}{dt}$ as:

$$\begin{aligned}\frac{d\Lambda_2}{dt} &= \left(1 - \frac{X_2}{X}\right)[\lambda - \alpha X - \beta_V X V - \beta_P X P] + \beta_V X V - (\eta_L + \delta_L) L \\ &\quad + \left(1 - \frac{E_2}{E}\right)[\beta_P X P - (\eta_E + \delta_E) E] + \frac{\eta_L + \delta_L}{\delta_L} [\delta_L L - \gamma_Y Y]\end{aligned}$$

$$+\frac{\eta_E+\delta_E}{\delta_E}\left(1-\frac{I_2}{I}\right)[\delta_E E-\gamma_I I]+\frac{\beta_V X_2}{\pi_V}[\kappa_V Y-\pi_V V-\varkappa_V VZ]$$
$$+\frac{\beta_P X_2}{\pi_P}\left(1-\frac{P_2}{P}\right)[\kappa_P I-\pi_P P-\varkappa_P PM]+\beta_V X_2\frac{\varkappa_V}{\sigma_Z\pi_V}[\sigma_Z VZ-\mu_Z Z]$$
$$+\beta_P X_2\frac{\varkappa_P}{\sigma_M\pi_P}[\sigma_M PM-\mu_M M]. \tag{5.4}$$

Then simplifying Eq (5.4), we get

$$\frac{d\Lambda_2}{dt}=\left(1-\frac{X_2}{X}\right)(\lambda-\alpha X)-\beta_P XP\frac{E_2}{E}+(\eta_E+\delta_E)E_2-\frac{\gamma_Y(\eta_L+\delta_L)}{\delta_L}Y$$
$$-\frac{\gamma_I(\eta_E+\delta_E)}{\delta_E}I-(\eta_E+\delta_E)E\frac{I_2}{I}+\frac{\gamma_I(\eta_E+\delta_E)}{\delta_E}I_2+\frac{\kappa_V}{\pi_V}\beta_V X_2 Y$$
$$+\frac{\kappa_P}{\pi_P}\beta_P X_2 I-\frac{\kappa_P}{\pi_P}\beta_P X_2 I\frac{P_2}{P}+\beta_P X_2 P_2+\frac{\varkappa_P}{\pi_P}\beta_P X_2 P_2 M-\frac{\varkappa_V\mu_Z}{\sigma_Z\pi_V}\beta_V X_2 Z$$
$$-\frac{\varkappa_P\mu_M}{\sigma_M\pi_P}\beta_P X_2 M.$$

Using the equilibrium conditions for Ξ_2:

$$\lambda=\alpha X_2+\beta_P X_2 P_2,\quad \beta_P X_2 P_2=(\eta_E+\delta_E)E_2,$$
$$E_2=\frac{\gamma_I}{\delta_E}I_2,\quad P_2=\frac{\kappa_P}{\pi_P}I_2,$$

we obtain,

$$\frac{d\Lambda_2}{dt}=\left(1-\frac{X_2}{X}\right)(\alpha X_2-\alpha X)+4\beta_P X_2 P_2-\beta_P X_2 P_2\frac{X_2}{X}-\beta_P X_2 P_2\frac{E_2 XP}{EX_2P_2}$$
$$-\beta_P X_2 P_2\frac{I_2 E}{IE_2}-\beta_P X_2 P_2\frac{P_2 I}{PI_2}+\frac{\gamma_Y(\eta_L+\delta_L)}{\delta_L}\left(\frac{\delta_L\kappa_V\beta_V X_2}{\gamma_Y\pi_V(\eta_L+\delta_L)}-1\right)Y$$
$$+\frac{\beta_P X_2\varkappa_P\mu_M}{\sigma_M\pi_P}\left(\frac{\sigma_M}{\mu_M}P_2-1\right)M-\frac{\beta_V X_2\varkappa_V\mu_Z}{\sigma_Z\pi_V}Z$$
$$=-\frac{\alpha(X-X_2)^2}{X}+\beta_P X_2 P_2\left(4-\frac{X_2}{X}-\frac{E_2 XP}{EX_2P_2}-\frac{I_2 E}{IE_2}-\frac{P_2 I}{PI_2}\right)$$
$$+\frac{\gamma_Y(\eta_L+\delta_L)}{\delta_L}\left(\frac{\mathfrak{R}_1}{\mathfrak{R}_2}-1\right)Y+\frac{X_2\varkappa_P(\alpha\sigma_M+\beta_P\mu_M)}{\pi_P\sigma_M}(\mathfrak{R}_4-1)M$$
$$-\frac{\beta_V X_2\varkappa_V\mu_Z}{\sigma_Z\pi_V}Z.$$

If $\mathfrak{R}_1/\mathfrak{R}_2\le 1$ and $\mathfrak{R}_4\le 1$, then employing inequality (5.1), we get $\frac{d\Lambda_2}{dt}\le 0$ for all $X,E,Y,I,P,Z,M>0$. Further, $\frac{d\Lambda_2}{dt}=0$ when $X=X_2$, $E=E_2$, $I=I_2$, $P=P_2$ and $Y=Z=M=0$. The solutions of system (2.1) tend to $\tilde{\Omega}_2$ which has $Y=0$, and gives $\dot{Y}=0$. The fourth equation of system (2.1) gives

$$0=\dot{Y}=\delta_L L\Longrightarrow L(t)=0,\ \text{for all } t.$$

In addition, from the second equation of system (2.1) gives

$$0=\dot{L}=\beta_V X_2 V\Longrightarrow V(t)=0,\ \text{for all } t.$$

Therefore, $\tilde{\Omega}_2=\{\Xi_2\}$. Applying L-LAST, we get Ξ_2 is G.A.S. □

Theorem 4. *Let* $\mathfrak{R}_3 > 1$ *and* $\mathfrak{R}_5 \leq 1$, *then* Ξ_3 *is G.A.S.*

Proof. Define

$$\Lambda_3 = X_3 F\left(\frac{X}{X_3}\right) + L_3 F\left(\frac{L}{L_3}\right) + E + \frac{\eta_L + \delta_L}{\delta_L} Y_3 F\left(\frac{Y}{Y_3}\right) + \frac{\eta_E + \delta_E}{\delta_E} I$$
$$+ \frac{\gamma_Y (\eta_L + \delta_L)}{\kappa_V \delta_L} V_3 F\left(\frac{V}{V_3}\right) + \frac{\gamma_I (\eta_E + \delta_E)}{\kappa_P \delta_E} P + \frac{\gamma_Y \varkappa_V (\eta_L + \delta_L)}{\kappa_V \delta_L \sigma_Z} Z_3 F\left(\frac{Z}{Z_3}\right) + \frac{\gamma_I \varkappa_P (\eta_E + \delta_E)}{\kappa_P \delta_E \sigma_M} M.$$

We calculate $\frac{d\Lambda_3}{dt}$ as:

$$\frac{d\Lambda_3}{dt} = \left(1 - \frac{X_3}{X}\right)[\lambda - \alpha X - \beta_V XV - \beta_P XP] + \left(1 - \frac{L_3}{L}\right)[\beta_V XV - (\eta_L + \delta_L) L] + \beta_P XP$$
$$- (\eta_E + \delta_E) E + \frac{\eta_L + \delta_L}{\delta_L}\left(1 - \frac{Y_3}{Y}\right)[\delta_L L - \gamma_Y Y] + \frac{\eta_E + \delta_E}{\delta_E}[\delta_E E - \gamma_I I]$$
$$+ \frac{\gamma_Y (\eta_L + \delta_L)}{\kappa_V \delta_L}\left(1 - \frac{V_3}{V}\right)[\kappa_V Y - \pi_V V - \varkappa_V VZ] + \frac{\gamma_I (\eta_E + \delta_E)}{\kappa_P \delta_E}[\kappa_P I - \pi_P P - \varkappa_P PM]$$
$$+ \frac{\gamma_Y \varkappa_V (\eta_L + \delta_L)}{\kappa_V \delta_L \sigma_Z}\left(1 - \frac{Z_3}{Z}\right)[\sigma_Z VZ - \mu_Z Z] + \frac{\gamma_I \varkappa_P (\eta_E + \delta_E)}{\kappa_P \delta_E \sigma_M}[\sigma_M PM - \mu_M M]. \tag{5.5}$$

Then simplifying Eq (5.5), we get

$$\frac{d\Lambda_3}{dt} = \left(1 - \frac{X_3}{X}\right)(\lambda - \alpha X) + \beta_V X_3 V + \beta_P X_3 P - \beta_V XV \frac{L_3}{L} + (\eta_L + \delta_L) L_3 - (\eta_L + \delta_L) L \frac{Y_3}{Y}$$
$$+ \frac{\gamma_Y (\eta_L + \delta_L)}{\delta_L} Y_3 - \frac{\pi_V \gamma_Y (\eta_L + \delta_L)}{\kappa_V \delta_L} V - \frac{\gamma_Y (\eta_L + \delta_L) YV_3}{\delta_L V} + \frac{\pi_V \gamma_Y (\eta_L + \delta_L)}{\kappa_V \delta_L} V_3$$
$$+ \frac{\varkappa_V \gamma_Y (\eta_L + \delta_L)}{\kappa_V \delta_L} ZV_3 - \frac{\pi_P \gamma_I (\eta_E + \delta_E)}{\kappa_P \delta_E} P - \frac{\varkappa_V \gamma_Y \mu_Z (\eta_L + \delta_L)}{\sigma_Z \kappa_V \delta_L} Z - \frac{\varkappa_V \gamma_Y (\eta_L + \delta_L)}{\kappa_V \delta_L} Z_3 V$$
$$+ \frac{\varkappa_V \gamma_Y \mu_Z (\eta_L + \delta_L)}{\sigma_Z \kappa_V \delta_L} Z_3 - \frac{\varkappa_P \gamma_I \mu_M (\eta_E + \delta_E)}{\sigma_M \kappa_P \delta_E} M.$$

Using the equilibrium conditions for Ξ_3:

$$\lambda = \alpha X_3 + \beta_V X_3 V_3, \quad \beta_V X_3 V_3 = (\eta_L + \delta_L) L_3,$$
$$L_3 = \frac{\gamma_Y}{\delta_L} Y_3, \quad \kappa_V Y_3 = \pi_V V_3 + \varkappa_V V_3 Z_3, \quad V_3 = \frac{\mu_Z}{\sigma_Z},$$

we obtain,

$$\frac{d\Lambda_3}{dt} = \left(1 - \frac{X_3}{X}\right)(\alpha X_3 - \alpha X) + 4\beta_V X_3 V_3 - \beta_V X_3 V_3 \frac{X_3}{X} - \beta_V X_3 V_3 \frac{L_3 XV}{LX_3 V_3}$$
$$- \beta_V X_3 V_3 \frac{Y_3 L}{YL_3} - \beta_V X_3 V_3 \frac{V_3 Y}{VY_3} + \frac{\pi_P \gamma_I (\eta_E + \delta_E)}{\kappa_P \delta_E}\left(\frac{\beta_P X_3 \kappa_P \delta_E}{\pi_P \gamma_I (\eta_E + \delta_E)} - 1\right) P$$
$$- \frac{\varkappa_P \gamma_I \mu_M (\eta_E + \delta_E)}{\sigma_M \kappa_P \delta_E} M$$
$$= -\frac{\alpha (X - X_3)^2}{X} + \beta_V X_3 V_3 \left(4 - \frac{X_3}{X} - \frac{L_3 XV}{LX_3 V_3} - \frac{Y_3 L}{YL_3} - \frac{V_3 Y}{VY_3}\right)$$

$$+\frac{\pi_P\gamma_I(\eta_E+\delta_E)}{\kappa_P\delta_E}(\Re_5-1)P-\frac{\varkappa_P\gamma_I\mu_M(\eta_E+\delta_E)}{\sigma_M\kappa_P\delta_E}M.$$

Using inequality (5.1) and $\Re_5 \leq 1$, we get $\frac{d\Lambda_3}{dt} \leq 0$ for all $X, L, Y, V, P, M > 0$. Further, $\frac{d\Lambda_3}{dt} = 0$ when $X = X_3$, $L = L_3$, $Y = Y_3$, $V = V_3$ and $P = M = 0$. Further, the trajectories of system (2.1) tend to $\tilde{\Omega}_3$ which has elements with $V = V_3$ and $P = 0$. Then $\dot{V} = 0$ and $\dot{P} = 0$. The sixth and seventh equations of system (2.1), provide

$$0 = \dot{V} = \kappa_V Y_3 - \pi_V V_3 - \varkappa_V V_3 Z \Longrightarrow Z(t) = Z_3, \text{ for all } t,$$
$$0 = \dot{P} = \kappa_P I \Longrightarrow I(t) = 0, \text{ for all } t.$$

In addition, from the fifth equation of system (2.1) gives

$$0 = \dot{I} = \delta_E E \Longrightarrow E(t) = 0, \text{ for all } t.$$

Consequently, $\tilde{\Omega}_3 = \{\Xi_3\}$. Applying L-LAST, we find that Ξ_3 is G.A.S. □

Theorem 5. *If* $\Re_4 > 1$ *and* $\Re_6 \leq 1$*, then* Ξ_4 *is G.A.S.*

Proof. Define a function Λ_4 as:

$$\Lambda_4 = X_4 F\left(\frac{X}{X_4}\right) + L + E_4 F\left(\frac{E}{E_4}\right) + \frac{\eta_L+\delta_L}{\delta_L}Y + \frac{\eta_E+\delta_E}{\delta_E}I_4 F\left(\frac{I}{I_4}\right) + \frac{\gamma_Y(\eta_L+\delta_L)}{\kappa_V\delta_L}V$$
$$+\frac{\gamma_I(\eta_E+\delta_E)}{\kappa_P\delta_E}P_4 F\left(\frac{P}{P_4}\right) + \frac{\gamma_Y\varkappa_V(\eta_L+\delta_L)}{\kappa_V\delta_L\sigma_Z}Z + \frac{\gamma_I\varkappa_P(\eta_E+\delta_E)}{\kappa_P\delta_E\sigma_M}M_4 F\left(\frac{M}{M_4}\right).$$

Calculating $\frac{d\Lambda_4}{dt}$ as:

$$\frac{d\Lambda_4}{dt} = \left(1-\frac{X_4}{X}\right)[\lambda-\alpha X-\beta_V XV-\beta_P XP]+\beta_V XV-(\eta_L+\delta_L)L$$
$$+\left(1-\frac{E_4}{E}\right)[\beta_P XP-(\eta_E+\delta_E)E]+\frac{\eta_L+\delta_L}{\delta_L}[\delta_L L-\gamma_Y Y]$$
$$+\frac{\eta_E+\delta_E}{\delta_E}\left(1-\frac{I_4}{I}\right)[\delta_E E-\gamma_I I]+\frac{\gamma_Y(\eta_L+\delta_L)}{\kappa_V\delta_L}[\kappa_V Y-\pi_V V-\varkappa_V VZ]$$
$$+\frac{\gamma_I(\eta_E+\delta_E)}{\kappa_P\delta_E}\left(1-\frac{P_4}{P}\right)[\kappa_P I-\pi_P P-\varkappa_P PM]+\frac{\gamma_Y\varkappa_V(\eta_L+\delta_L)}{\kappa_V\delta_L\sigma_Z}[\sigma_Z VZ-\mu_Z Z]$$
$$+\frac{\gamma_I\varkappa_P(\eta_E+\delta_E)}{\kappa_P\delta_E\sigma_M}\left(1-\frac{M_4}{M}\right)[\sigma_M PM-\mu_M M]. \tag{5.6}$$

Equation (5.6) can be written as:

$$\frac{d\Lambda_4}{dt} = \left(1-\frac{X_4}{X}\right)(\lambda-\alpha X)+\beta_V X_4 V+\beta_P X_4 P-\beta_P XP\frac{E_4}{E}+(\eta_E+\delta_E)E_4-(\eta_E+\delta_E)E\frac{I_4}{I}$$
$$+\frac{\gamma_I(\eta_E+\delta_E)}{\delta_E}I_4-\frac{\pi_V\gamma_Y(\eta_L+\delta_L)}{\kappa_V\delta_L}V-\frac{\pi_P\gamma_I(\eta_E+\delta_E)}{\kappa_P\delta_E}P-\frac{\gamma_I(\eta_E+\delta_E)P_4}{\delta_E P}I$$
$$+\frac{\pi_P\gamma_I(\eta_E+\delta_E)}{\kappa_P\delta_E}P_4+\frac{\varkappa_P\gamma_I(\eta_E+\delta_E)}{\kappa_P\delta_E}MP_4-\frac{\varkappa_V\gamma_Y\mu_Z(\eta_L+\delta_L)}{\kappa_V\delta_L\sigma_Z}Z-\frac{\varkappa_P\gamma_I\mu_M(\eta_E+\delta_E)}{\kappa_P\delta_E\sigma_M}M$$

$$- \frac{\varkappa_P \gamma_I (\eta_E + \delta_E)}{\kappa_P \delta_E} M_4 P + \frac{\varkappa_P \gamma_I \mu_M (\eta_E + \delta_E)}{\sigma_M \kappa_P \delta_E} M_4.$$

Using the equilibrium conditions for Ξ_4:

$$\lambda = \alpha X_4 + \beta_P X_4 P_4, \quad \beta_P X_4 P_4 = (\eta_E + \delta_E) E_4,$$
$$\kappa_P I_4 = \pi_P P_4 + \varkappa_P P_4 M_4, \quad E_4 = \frac{\gamma_I}{\delta_E} I_4, \quad P_4 = \frac{\mu_M}{\sigma_M},$$

we obtain,

$$\begin{aligned}
\frac{d\Lambda_4}{dt} &= \left(1 - \frac{X_4}{X}\right)(\alpha X_4 - \alpha X) + 4\beta_P X_4 P_4 - \beta_P X_4 P_4 \frac{X_4}{X} - \beta_P X_4 P_4 \frac{E_4 X P}{E X_4 P_4} \\
&\quad - \beta_P X_4 P_4 \frac{I_4 E}{I E_4} - \beta_P X_4 P_4 \frac{P_4 I}{P I_4} - \frac{\varkappa_V \gamma_Y \mu_Z (\eta_L + \delta_L)}{\kappa_V \delta_L \sigma_Z} Z + \frac{\pi_V \gamma_Y (\eta_L + \delta_L)}{\kappa_V \delta_L} \left(\frac{\beta_V X_4 \kappa_V \delta_L}{\pi_V \gamma_Y (\eta_L + \delta_L)} - 1\right) V \\
&= -\frac{\alpha (X - X_4)^2}{X} + \beta_P X_4 P_4 \left(4 - \frac{X_4}{X} - \frac{E_4 X P}{E X_4 P_4} - \frac{I_4 E}{I E_4} - \frac{P_4 I}{P I_4}\right) \\
&\quad + \frac{\pi_V \gamma_Y (\eta_L + \delta_L)}{\kappa_V \delta_L} (\mathfrak{R}_6 - 1) V - \frac{\varkappa_V \gamma_Y \mu_Z (\eta_L + \delta_L)}{\kappa_V \delta_L \sigma_Z} Z.
\end{aligned}$$

Since $\mathfrak{R}_6 \leq 1$, then employing inequality (5.1), we get $\frac{d\Lambda_4}{dt} \leq 0$ for all $X, E, I, V, P, Z > 0$. Further, $\frac{d\Lambda_4}{dt} = 0$ when $X = X_4$, $E = E_4$, $I = I_4$, $P = P_4$ and $V = Z = 0$. The solutions of system (2.1) tend to $\tilde{\Omega}_4$ which contains elements with $P = P_4$ and $V = 0$, then $\dot{V} = \dot{P} = 0$. The sixth and seventh equations of system (2.1) imply

$$0 = \dot{V} = \kappa_V Y \Longrightarrow Y(t) = 0, \text{ for all } t,$$
$$0 = \dot{P} = \kappa_P I_4 - \pi_P P_4 - \varkappa_P P_4 M \Longrightarrow M(t) = M_4, \text{ for all } t.$$

In addition, since $Y = 0$, then $\dot{Y} = 0$. The fourth equation of system (2.1) gives

$$0 = \dot{Y} = \delta_L L \Longrightarrow L(t) = 0, \text{ for all } t.$$

Therefore, $\tilde{\Omega}_4 = \{\Xi_4\}$. Applying L-LAST, we get Ξ_4 is G.A.S. □

Theorem 6. *If* $\mathfrak{R}_5 > 1$, $\mathfrak{R}_1/\mathfrak{R}_2 > 1$ *and* $\mathfrak{R}_8 \leq 1$, *then* Ξ_5 *is G.A.S.*

Proof. Define

$$\begin{aligned}
\Lambda_5 &= X_5 F\left(\frac{X}{X_5}\right) + L_5 F\left(\frac{L}{L_5}\right) + E_5 F\left(\frac{E}{E_5}\right) + \frac{\eta_L + \delta_L}{\delta_L} Y_5 F\left(\frac{Y}{Y_5}\right) \\
&\quad + \frac{\eta_E + \delta_E}{\delta_E} I_5 F\left(\frac{I}{I_5}\right) + \frac{\gamma_Y (\eta_L + \delta_L)}{\kappa_V \delta_L} V_5 F\left(\frac{V}{V_5}\right) + \frac{\gamma_I (\eta_E + \delta_E)}{\kappa_P \delta_E} P_5 F\left(\frac{P}{P_5}\right) \\
&\quad + \frac{\gamma_Y \varkappa_V (\eta_L + \delta_L)}{\kappa_V \delta_L \sigma_Z} Z_5 F\left(\frac{Z}{Z_5}\right) + \frac{\gamma_I \varkappa_P (\eta_E + \delta_E)}{\kappa_P \delta_E \sigma_M} M.
\end{aligned}$$

Calculating $\frac{d\Lambda_5}{dt}$ as:

$$\frac{d\Lambda_5}{dt} = \left(1 - \frac{X_5}{X}\right)[\lambda - \alpha X - \beta_V X V - \beta_P X P] + \left(1 - \frac{L_5}{L}\right)[\beta_V X V - (\eta_L + \delta_L) L]$$

$$+\left(1-\frac{E_5}{E}\right)[\beta_P XP-(\eta_E+\delta_E)E]+\frac{\eta_L+\delta_L}{\delta_L}\left(1-\frac{Y_5}{Y}\right)[\delta_L L-\gamma_Y Y]$$
$$+\frac{\eta_E+\delta_E}{\delta_E}\left(1-\frac{I_5}{I}\right)[\delta_E E-\gamma_I I]+\frac{\gamma_Y(\eta_L+\delta_L)}{\kappa_V\delta_L}\left(1-\frac{V_5}{V}\right)[\kappa_V Y-\pi_V V-\varkappa_V VZ]$$
$$+\frac{\gamma_I(\eta_E+\delta_E)}{\kappa_P\delta_E}\left(1-\frac{P_5}{P}\right)[\kappa_P I-\pi_P P-\varkappa_P PM]+\frac{\gamma_Y\varkappa_V(\eta_L+\delta_L)}{\kappa_V\delta_L\sigma_Z}\left(1-\frac{Z_5}{Z}\right)[\sigma_Z VZ-\mu_Z Z]$$
$$+\frac{\gamma_I\varkappa_P(\eta_E+\delta_E)}{\kappa_P\delta_E\sigma_M}[\sigma_M PM-\mu_M M]. \tag{5.7}$$

Equation (5.7) can be simplified as:

$$\frac{d\Lambda_5}{dt}=\left(1-\frac{X_5}{X}\right)(\lambda-\alpha X)+\beta_V X_5 V+\beta_P X_5 P-\beta_V XV\frac{L_5}{L}+(\eta_L+\delta_L)L_5-\beta_P XP\frac{E_5}{E}$$
$$+(\eta_E+\delta_E)E_5-(\eta_L+\delta_L)L\frac{Y_5}{Y}+\frac{\gamma_Y(\eta_L+\delta_L)}{\delta_L}Y_5-(\eta_E+\delta_E)E\frac{I_5}{I}+\frac{\gamma_I(\eta_E+\delta_E)}{\delta_E}I_5$$
$$-\frac{\pi_V\gamma_Y(\eta_L+\delta_L)}{\kappa_V\delta_L}V-\frac{\gamma_Y(\eta_L+\delta_L)V_5}{\delta_L V}Y+\frac{\pi_V\gamma_Y(\eta_L+\delta_L)}{\kappa_V\delta_L}V_5+\frac{\varkappa_V\gamma_Y(\eta_L+\delta_L)}{\kappa_V\delta_L}V_5Z$$
$$-\frac{\pi_P\gamma_I(\eta_E+\delta_E)}{\kappa_P\delta_E}P-\frac{\gamma_I(\eta_E+\delta_E)P_5}{\delta_E P}I+\frac{\pi_P\gamma_I(\eta_E+\delta_E)}{\kappa_P\delta_E}P_5+\frac{\varkappa_P\gamma_I(\eta_E+\delta_E)}{\kappa_P\delta_E}MP_5$$
$$-\frac{\varkappa_V\gamma_Y\mu_Z(\eta_L+\delta_L)}{\kappa_V\delta_L\sigma_Z}Z-\frac{\varkappa_V\gamma_Y(\eta_L+\delta_L)}{\kappa_V\delta_L}VZ_5+\frac{\varkappa_V\gamma_Y\mu_Z(\eta_L+\delta_L)}{\kappa_V\delta_L\sigma_Z}Z_5$$
$$-\frac{\varkappa_P\gamma_I\mu_M(\eta_E+\delta_E)}{\kappa_P\delta_E\sigma_M}M.$$

Using the equilibrium conditions for Ξ_5:

$$\lambda=\alpha X_5+\beta_V X_5V_5+\beta_P X_5P_5,\quad \beta_V X_5V_5=(\eta_L+\delta_L)L_5,$$
$$\beta_P X_5P_5=(\eta_E+\delta_E)E_5,\quad \kappa_V Y_5=\pi_V V_5+\varkappa_V V_5Z_5,$$
$$\kappa_P I_5=\pi_P P_5,\quad V_5=\frac{\mu_Z}{\sigma_Z},$$
$$L_5=\frac{\gamma_Y}{\delta_L}Y_5,\quad E_5=\frac{\gamma_I}{\delta_E}I_5,$$

we obtain,

$$\frac{d\Lambda_5}{dt}=\left(1-\frac{X_5}{X}\right)(\alpha X_5-\alpha X)+4\beta_V X_5V_5+4\beta_P X_5P_5-\beta_V X_5V_5\frac{X_5}{X}-\beta_P X_5P_5\frac{X_5}{X}$$
$$-\beta_V X_5V_5\frac{L_5XV}{LX_5V_5}-\beta_P X_5P_5\frac{E_5XP}{EX_5P_5}-\beta_V X_5V_5\frac{Y_5L}{YL_5}-\beta_P X_5P_5\frac{I_5E}{IE_5}$$
$$-\beta_V X_5V_5\frac{V_5Y}{VY_5}-\beta_P X_5P_5\frac{P_5I}{PI_5}+\frac{\varkappa_P\gamma_I\mu_M(\eta_E+\delta_E)}{\kappa_P\delta_E\sigma_M}\left(\frac{\sigma_M}{\mu_M}P_5-1\right)M$$
$$=-\frac{\alpha(X-X_5)^2}{X}+\beta_V X_5V_5\left(4-\frac{X_5}{X}-\frac{L_5XV}{LX_5V_5}-\frac{Y_5L}{YL_5}-\frac{V_5Y}{VY_5}\right)$$
$$+\beta_P X_5P_5\left(4-\frac{X_5}{X}-\frac{E_5XP}{EX_5P_5}-\frac{I_5E}{IE_5}-\frac{P_5I}{PI_5}\right)$$

$$+\frac{\varkappa_P\gamma_I\left(\eta_E+\delta_E\right)\left(\alpha\sigma_Z\sigma_M+\beta_V\mu_Z\sigma_M+\beta_P\mu_M\sigma_Z\right)}{\kappa_P\delta_E\beta_P\sigma_Z\sigma_M}\left(\mathfrak{R}_8-1\right)M.$$

Since $\mathfrak{R}_8 \leq 1$, then employing inequality (5.1), we get $\frac{d\Lambda_5}{dt} \leq 0$ for all $X, L, E, Y, I, V, P, M > 0$. Moreover, we have $\frac{d\Lambda_5}{dt} = 0$, when $X = X_5$, $L = L_5$, $E = E_5$, $Y = Y_5$, $I = I_5$, $V = V_5$, $P = P_5$ and $M = 0$. The trajectories of system (2.1) converge to $\tilde{\Omega}_5$ which comprises elements with $Y = Y_5$ and $V = V_5$, then $\dot{V} = 0$. The sixth equation of system (2.1) implies that

$$0 = \dot{V} = \kappa_V Y_5 - \pi_V V_5 - \varkappa_V V_5 Z \Longrightarrow Z(t) = Z_5, \text{ for all } t.$$

Consequently, $\tilde{\Omega}_5 = \{\Xi_5\}$. and by applying L-LAST, we get Ξ_5 is G.A.S. □

Theorem 7. *Let* $\mathfrak{R}_6 > 1$, $\mathfrak{R}_7 \leq 1$ *and* $\mathfrak{R}_2/\mathfrak{R}_1 > 1$, *then* Ξ_6 *is G.A.S.*

Proof. Consider a function Λ_6 as:

$$\begin{aligned}\Lambda_6 = {} & X_6 F\left(\frac{X}{X_6}\right) + L_6 F\left(\frac{L}{L_6}\right) + E_6 F\left(\frac{E}{E_6}\right) + \frac{\eta_L+\delta_L}{\delta_L} Y_6 F\left(\frac{Y}{Y_6}\right) \\ & + \frac{\eta_E+\delta_E}{\delta_E} I_6 F\left(\frac{I}{I_6}\right) + \frac{\gamma_Y\left(\eta_L+\delta_L\right)}{\kappa_V\delta_L} V_6 F\left(\frac{V}{V_6}\right) + \frac{\gamma_I\left(\eta_E+\delta_E\right)}{\kappa_P\delta_E} P_6 F\left(\frac{P}{P_6}\right) \\ & + \frac{\gamma_Y\varkappa_V\left(\eta_L+\delta_L\right)}{\kappa_V\delta_L\sigma_Z} Z + \frac{\gamma_I\varkappa_P\left(\eta_E+\delta_E\right)}{\kappa_P\delta_E\sigma_M} M_6 F\left(\frac{M}{M_6}\right).\end{aligned}$$

Calculating $\frac{d\Lambda_6}{dt}$ as:

$$\begin{aligned}\frac{d\Lambda_6}{dt} = {} & \left(1-\frac{X_6}{X}\right)\left[\lambda-\alpha X-\beta_V XV-\beta_P XP\right] + \left(1-\frac{L_6}{L}\right)\left[\beta_V XV-\left(\eta_L+\delta_L\right)L\right] \\ & + \left(1-\frac{E_6}{E}\right)\left[\beta_P XP-\left(\eta_E+\delta_E\right)E\right] + \frac{\eta_L+\delta_L}{\delta_L}\left(1-\frac{Y_6}{Y}\right)\left[\delta_L L-\gamma_Y Y\right] \\ & + \frac{\eta_E+\delta_E}{\delta_E}\left(1-\frac{I_6}{I}\right)\left[\delta_E E-\gamma_I I\right] + \frac{\gamma_Y\left(\eta_L+\delta_L\right)}{\kappa_V\delta_L}\left(1-\frac{V_6}{V}\right)\left[\kappa_V Y-\pi_V V-\varkappa_V VZ\right] \\ & + \frac{\gamma_I\left(\eta_E+\delta_E\right)}{\kappa_P\delta_E}\left(1-\frac{P_6}{P}\right)\left[\kappa_P I-\pi_P P-\varkappa_P PM\right] + \frac{\gamma_Y\varkappa_V\left(\eta_L+\delta_L\right)}{\kappa_V\delta_L\sigma_Z}\left[\sigma_Z VZ-\mu_Z Z\right] \\ & + \frac{\gamma_I\varkappa_P\left(\eta_E+\delta_E\right)}{\kappa_P\delta_E\sigma_M}\left(1-\frac{M_6}{M}\right)\left[\sigma_M PM-\mu_M M\right]. \qquad (5.8)\end{aligned}$$

We collect the terms of Eq (5.8) as:

$$\begin{aligned}\frac{d\Lambda_6}{dt} = {} & \left(1-\frac{X_6}{X}\right)\left(\lambda-\alpha X\right) + \beta_V X_6 V + \beta_P X_6 P - \beta_V XV\frac{L_6}{L} + \left(\eta_L+\delta_L\right)L_6 - \beta_P XP\frac{E_6}{E} \\ & + \left(\eta_E+\delta_E\right)E_6 - \left(\eta_L+\delta_L\right)L\frac{Y_6}{Y} + \frac{\gamma_Y\left(\eta_L+\delta_L\right)}{\delta_L}Y_6 - \left(\eta_E+\delta_E\right)E\frac{I_6}{I} + \frac{\gamma_I\left(\eta_E+\delta_E\right)}{\delta_E}I_6 \\ & - \frac{\pi_V\gamma_Y\left(\eta_L+\delta_L\right)}{\kappa_V\delta_L}V - \frac{\gamma_Y\left(\eta_L+\delta_L\right)V_6}{\delta_L V}Y + \frac{\pi_V\gamma_Y\left(\eta_L+\delta_L\right)}{\kappa_V\delta_L}V_6 + \frac{\varkappa_V\gamma_Y\left(\eta_L+\delta_L\right)}{\kappa_V\delta_L}V_6 Z \\ & - \frac{\pi_P\gamma_I\left(\eta_E+\delta_E\right)}{\kappa_P\delta_E}P - \frac{\gamma_I\left(\eta_E+\delta_E\right)P_6}{\delta_E P}I + \frac{\pi_P\gamma_I\left(\eta_E+\delta_E\right)}{\kappa_P\delta_E}P_6 + \frac{\varkappa_P\gamma_I\left(\eta_E+\delta_E\right)}{\kappa_P\delta_E}MP_6 \\ & - \frac{\varkappa_V\gamma_Y\mu_Z\left(\eta_L+\delta_L\right)}{\kappa_V\delta_L\sigma_Z}Z - \frac{\varkappa_P\gamma_I\mu_M\left(\eta_E+\delta_E\right)}{\kappa_P\delta_E\sigma_M}M - \frac{\varkappa_P\gamma_I\left(\eta_E+\delta_E\right)}{\kappa_P\delta_E}PM_6 + \frac{\varkappa_P\gamma_I\mu_M\left(\eta_E+\delta_E\right)}{\kappa_P\delta_E\sigma_M}M_6.\end{aligned}$$

Using the equilibrium conditions for Ξ_6:

$$\lambda = \alpha X_6 + \beta_V X_6 V_6 + \beta_P X_6 P_6, \quad \beta_V X_6 V_6 = (\eta_L + \delta_L) L_6, \quad \beta_P X_6 P_6 = (\eta_E + \delta_E) E_6,$$
$$L_6 = \frac{\gamma_Y}{\delta_L} Y_6, \quad E_6 = \frac{\gamma_I}{\delta_E} I_6, \quad Y_6 = \frac{\pi_V}{\kappa_V} V_6,$$
$$I_6 = \frac{\pi_P}{\kappa_P} P_6 + \frac{\varkappa_P}{\kappa_P} P_6 M_6, \quad P_6 = \frac{\mu_M}{\sigma_M},$$

we obtain,

$$\begin{aligned}
\frac{d\Lambda_6}{dt} &= \left(1 - \frac{X_6}{X}\right)(\alpha X_6 - \alpha X) + 4\beta_V X_6 V_6 + 4\beta_P X_6 P_6 - \beta_V X_6 V_6 \frac{X_6}{X} - \beta_P X_6 P_6 \frac{X_6}{X} \\
&\quad - \beta_V X_6 V_6 \frac{L_6 X V}{L X_6 V_6} - \beta_P X_6 P_6 \frac{E_6 X P}{E X_6 P_6} - \beta_V X_6 V_6 \frac{Y_6 L}{Y L_6} - \beta_P X_6 P_6 \frac{I_6 E}{I E_6} \\
&\quad - \beta_V X_6 V_6 \frac{V_6 Y}{V Y_6} - \beta_P X_6 P_6 \frac{P_6 I}{P I_6} + \frac{\varkappa_V \gamma_Y \mu_Z (\eta_L + \delta_L)}{\kappa_V \delta_L \sigma_Z} \left(\frac{\sigma_Z}{\mu_Z} V_6 - 1\right) Z \\
&= -\frac{\alpha (X - X_6)^2}{X} + \beta_V X_6 V_6 \left(4 - \frac{X_6}{X} - \frac{L_6 X V}{L X_6 V_6} - \frac{Y_6 L}{Y L_6} - \frac{V_6 Y}{V Y_6}\right) \\
&\quad + \beta_P X_6 P_6 \left(4 - \frac{X_6}{X} - \frac{E_6 X P}{E X_6 P_6} - \frac{I_6 E}{I E_6} - \frac{P_6 I}{P I_6}\right) \\
&\quad + \frac{\varkappa_V \gamma_Y (\eta_L + \delta_L)(\alpha \sigma_Z \sigma_M + \beta_V \mu_Z \sigma_M + \beta_P \mu_M \sigma_Z)}{\kappa_V \delta_L \sigma_M \beta_V \sigma_Z} (\mathfrak{R}_7 - 1) Z.
\end{aligned}$$

Since $\mathfrak{R}_7 \leq 1$, then employing inequality (5.1), we get $\frac{d\Lambda_6}{dt} \leq 0$ for all $X, L, E, Y, I, V, P, Z > 0$. Moreover, $\frac{d\Lambda_6}{dt} = 0$ when $X = X_6$, $L = L_6$, $E = E_6$, $Y = Y_6$, $I = I_6$, $V = V_6$, $P = P_6$ and $Z = 0$. The solutions of system (2.1) tend to $\tilde{\Omega}_6$ which contains elements with $P = P_6$ then, $\dot{P} = 0$. The seven equation of system (2.1) implies that

$$0 = \dot{P} = \kappa_P I_6 - \pi_P P_6 - \varkappa_P P_6 M \Longrightarrow M(t) = M_6, \text{ for all } t.$$

Consequently, $\tilde{\Omega}_6 = \{\Xi_6\}$. Using L-LAST we deduce that Ξ_6 is G.A.S. □

Theorem 8. *If $\mathfrak{R}_7 > 1$ and $\mathfrak{R}_8 > 1$, then Ξ_7 is G.A.S.*

Proof. Define a function Λ_7 as:

$$\begin{aligned}
\Lambda_7 &= X_7 F\left(\frac{X}{X_7}\right) + L_7 F\left(\frac{L}{L_7}\right) + E_7 F\left(\frac{E}{E_7}\right) + \frac{\eta_L + \delta_L}{\delta_L} Y_7 F\left(\frac{Y}{Y_7}\right) \\
&\quad + \frac{\eta_E + \delta_E}{\delta_E} I_7 F\left(\frac{I}{I_7}\right) + \frac{\gamma_Y (\eta_L + \delta_L)}{\kappa_V \delta_L} V_7 F\left(\frac{V}{V_7}\right) + \frac{\gamma_I (\eta_E + \delta_E)}{\kappa_P \delta_E} P_7 F\left(\frac{P}{P_7}\right) \\
&\quad + \frac{\gamma_Y \varkappa_V (\eta_L + \delta_L)}{\kappa_V \delta_L \sigma_Z} Z_7 F\left(\frac{Z}{Z_7}\right) + \frac{\gamma_I \varkappa_P (\eta_E + \delta_E)}{\kappa_P \delta_E \sigma_M} M_7 F\left(\frac{M}{M_7}\right).
\end{aligned}$$

Calculating $\frac{d\Lambda_7}{dt}$ as:

$$\frac{d\Lambda_7}{dt} = \left(1 - \frac{X_7}{X}\right)[\lambda - \alpha X - \beta_V X V - \beta_P X P] + \left(1 - \frac{L_7}{L}\right)[\beta_V X V - (\eta_L + \delta_L) L]$$

$$+\left(1-\frac{E_7}{E}\right)[\beta_P XP-(\eta_E+\delta_E)E]+\frac{\eta_L+\delta_L}{\delta_L}\left(1-\frac{Y_7}{Y}\right)[\delta_L L-\gamma_Y Y]$$
$$+\frac{\eta_E+\delta_E}{\delta_E}\left(1-\frac{I_7}{I}\right)[\delta_E E-\gamma_I I]+\frac{\gamma_Y(\eta_L+\delta_L)}{\kappa_V\delta_L}\left(1-\frac{V_7}{V}\right)[\kappa_V Y-\pi_V V-\varkappa_V VZ]$$
$$+\frac{\gamma_I(\eta_E+\delta_E)}{\kappa_P\delta_E}\left(1-\frac{P_7}{P}\right)[\kappa_P I-\pi_P P-\varkappa_P PM]+\frac{\gamma_Y\varkappa_V(\eta_L+\delta_L)}{\kappa_V\delta_L\sigma_Z}\left(1-\frac{Z_7}{Z}\right)[\sigma_Z VZ-\mu_Z Z]$$
$$+\frac{\gamma_I\varkappa_P(\eta_E+\delta_E)}{\kappa_P\delta_E\sigma_M}\left(1-\frac{M_7}{M}\right)[\sigma_M PM-\mu_M M]. \tag{5.9}$$

We collect the terms of Eq (5.9) as:

$$\frac{d\Lambda_7}{dt}=\left(1-\frac{X_7}{X}\right)(\lambda-\alpha X)+\beta_V X_7 V+\beta_P X_7 P-\beta_V XV\frac{L_7}{L}+(\eta_L+\delta_L)L_7-\beta_P XP\frac{E_7}{E}$$
$$+(\eta_E+\delta_E)E_7-(\eta_L+\delta_L)L\frac{Y_7}{Y}+\frac{\gamma_Y(\eta_L+\delta_L)}{\delta_L}Y_7-(\eta_E+\delta_E)E\frac{I_7}{I}+\frac{\gamma_I(\eta_E+\delta_E)}{\delta_E}I_7$$
$$-\frac{\pi_V\gamma_Y(\eta_L+\delta_L)}{\kappa_V\delta_L}V-\frac{\gamma_Y(\eta_L+\delta_L)V_7}{\delta_L V}Y+\frac{\pi_V\gamma_Y(\eta_L+\delta_L)}{\kappa_V\delta_L}V_7+\frac{\varkappa_V\gamma_Y(\eta_L+\delta_L)}{\kappa_V\delta_L}V_7 Z$$
$$-\frac{\pi_P\gamma_I(\eta_E+\delta_E)}{\kappa_P\delta_E}P-\frac{\gamma_I(\eta_E+\delta_E)P_7}{\delta_E P}I+\frac{\pi_P\gamma_I(\eta_E+\delta_E)}{\kappa_P\delta_E}P_7+\frac{\varkappa_P\gamma_I(\eta_E+\delta_E)}{\kappa_P\delta_E}MP_7$$
$$-\frac{\varkappa_V\gamma_Y\mu_Z(\eta_L+\delta_L)}{\kappa_V\delta_L\sigma_Z}Z-\frac{\varkappa_V\gamma_Y(\eta_L+\delta_L)}{\kappa_V\delta_L}VZ_7+\frac{\varkappa_V\gamma_Y\mu_Z(\eta_L+\delta_L)}{\kappa_V\delta_L\sigma_Z}Z_7-\frac{\varkappa_P\gamma_I\mu_M(\eta_E+\delta_E)}{\kappa_P\delta_E\sigma_M}M$$
$$-\frac{\varkappa_P\gamma_I(\eta_E+\delta_E)}{\kappa_P\delta_E}PM_7+\frac{\varkappa_P\gamma_I\mu_M(\eta_E+\delta_E)}{\kappa_P\delta_E\sigma_M}M_7.$$

Using the equilibrium conditions for Ξ_7:

$$\lambda=\alpha X_7+\beta_V X_7V_7+\beta_P X_7P_7,\qquad \beta_V X_7V_7=(\eta_L+\delta_L)L_7,$$
$$\beta_P X_7P_7=(\eta_E+\delta_E)E_7,\quad L_7=\frac{\gamma_Y}{\delta_L}Y_7,\quad E_7=\frac{\gamma_I}{\delta_E}I_7,$$
$$Y_7=\frac{\pi_V}{\kappa_V}V_7+\frac{\varkappa_V}{\kappa_V}V_7Z_7,\quad I_7=\frac{\pi_P}{\kappa_P}P_7+\frac{\varkappa_P}{\kappa_P}P_7M_7,$$
$$V_7=\frac{\mu_Z}{\sigma_Z},\quad P_7=\frac{\mu_M}{\sigma_M},$$

we obtain,

$$\frac{d\Lambda_7}{dt}=\left(1-\frac{X_7}{X}\right)(\alpha X_7-\alpha X)+4\beta_V X_7V_7+4\beta_P X_7P_7-\beta_V X_7V_7\frac{X_7}{X}-\beta_P X_7P_7\frac{X_7}{X}$$
$$-\beta_V X_7V_7\frac{L_7XV}{LX_7V_7}-\beta_P X_7P_7\frac{E_7XP}{EX_7P_7}-\beta_V X_7V_7\frac{Y_7L}{YL_7}-\beta_P X_7P_7\frac{I_7E}{IE_7}$$
$$-\beta_V X_7V_7\frac{V_7Y}{VY_7}-\beta_P X_7P_7\frac{P_7I}{PI_7}$$
$$=-\frac{\alpha(X-X_7)^2}{X}+\beta_V X_7V_7\left(4-\frac{X_7}{X}-\frac{L_7XV}{LX_7V_7}-\frac{Y_7L}{YL_7}-\frac{V_7Y}{VY_7}\right)$$
$$+\beta_P X_7P_7\left(4-\frac{X_7}{X}-\frac{E_7XP}{EX_7P_7}-\frac{I_7E}{IE_7}-\frac{P_7I}{PI_7}\right).$$

Using inequality (5.1), we get $\frac{d\Lambda_7}{dt} \leq 0$ for all $X, L, E, Y, I, V, P > 0$, where $\frac{d\Lambda_7}{dt} = 0$ when $X = X_7$, $L = L_7$, $E = E_7$, $Y = Y_7$, $I = I_7$, $V = V_7$ and $P = P_7$. The solutions of system (2.1) tend to $\tilde{\Omega}_7$ which includes element with $V = V_7$ and $P = P_7$ which gives $\dot{V} = \dot{P} = 0$ and from the sixth and seventh equations of system (2.1) we get

$$0 = \dot{V} = \kappa_V Y_7 - \pi_V V_7 - \varkappa_V V_7 Z \Longrightarrow Z(t) = Z_7, \text{ for all } t,$$
$$0 = \dot{P} = \kappa_P I_7 - \pi_P P_7 - \varkappa_P P_7 M \Longrightarrow M(t) = M_7, \text{ for all } t.$$

Therefore, $\tilde{\Omega}_7 = \{\Xi_7\}$ and by employing L-LAST, we get Ξ_7 is G.A.S. □

Based on the above findings, we summarize the existence and global stability conditions for all equilibrium points in Table 1.

Table 1. Conditions of existence and global stability of the system's equilibria.

Equilibrium point	Existence conditions	Global stability conditions
$\Xi_0 = (X_0, 0, 0, 0, 0, 0, 0, 0, 0)$	None	$\mathfrak{R}_1 \leq 1$ and $\mathfrak{R}_2 \leq 1$
$\Xi_1 = (X_1, L_1, 0, Y_1, 0, V_1, 0, 0, 0)$	$\mathfrak{R}_1 > 1$	$\mathfrak{R}_1 > 1$, $\mathfrak{R}_2/\mathfrak{R}_1 \leq 1$ and $\mathfrak{R}_3 \leq 1$
$\Xi_2 = (X_2, 0, E_2, 0, I_2, 0, P_2, 0, 0)$	$\mathfrak{R}_2 > 1$	$\mathfrak{R}_2 > 1$, $\mathfrak{R}_1/\mathfrak{R}_2 \leq 1$ and $\mathfrak{R}_4 \leq 1$
$\Xi_3 = (X_3, L_3, 0, Y_3, 0, V_3, 0, Z_3, 0)$	$\mathfrak{R}_3 > 1$	$\mathfrak{R}_3 > 1$ and $\mathfrak{R}_5 \leq 1$
$\Xi_4 = (X_4, 0, E_4, 0, I_4, 0, P_4, 0, M_4)$	$\mathfrak{R}_4 > 1$	$\mathfrak{R}_4 > 1$ and $\mathfrak{R}_6 \leq 1$
$\Xi_5 = (X_5, L_5, E_5, Y_5, I_5, V_5, P_5, Z_5, 0)$	$\mathfrak{R}_5 > 1$ and $\mathfrak{R}_1/\mathfrak{R}_2 > 1$	$\mathfrak{R}_5 > 1$, $\mathfrak{R}_8 \leq 1$ and $\mathfrak{R}_1/\mathfrak{R}_2 > 1$
$\Xi_6 = (X_6, L_6, E_6, Y_6, I_6, V_6, P_6, 0, M_6)$	$\mathfrak{R}_6 > 1$ and $\mathfrak{R}_2/\mathfrak{R}_1 > 1$	$\mathfrak{R}_6 > 1$, $\mathfrak{R}_7 \leq 1$ and $\mathfrak{R}_2/\mathfrak{R}_1 > 1$
$\Xi_7 = (X_7, L_7, E_7, Y_7, I_7, V_7, P_7, Z_7, M_7)$	$\mathfrak{R}_7 > 1$ and $\mathfrak{R}_8 > 1$	$\mathfrak{R}_7 > 1$ and $\mathfrak{R}_8 > 1$

6. Effect of the antibody immunity on the IAV/SARS-CoV-2 coinfection dynamics

We noted that system (2.1) has eight equilibria for which the coexistence case of IAV and SARS-CoV-2 can only be occurred if at least one type of the specific antibody immunities is active. Now, we discuss the importance of considering the antibody immune response in the IAV/SARS-CoV-2

dynamics model. If the antibody immune response is neglected then system (2.1) becomes:

$$\begin{cases} \dot{X} = \lambda - \alpha X - \beta_V XV - \beta_P XP, \\ \dot{L} = \beta_V XV - (\eta_L + \delta_L)L, \\ \dot{E} = \beta_P XP - (\eta_E + \delta_E)E, \\ \dot{Y} = \delta_L L - \gamma_Y Y, \\ \dot{I} = \delta_E E - \gamma_I I, \\ \dot{V} = \kappa_V Y - \pi_V V, \\ \dot{P} = \kappa_P I - \pi_P P. \end{cases} \tag{6.1}$$

We can see that system (6.1) describes the competition between IAV and SARS-CoV-2 on one source of target cells, epithelial cells. The model admits only three equilibria:

(i) Infection-free equilibrium, $\tilde{\Xi}_0 = (\tilde{X}_0, 0, 0, 0, 0, 0, 0)$, where both IAV and SARS-CoV-2 are cleared,

(ii) SARS-CoV-2 single-infection equilibrium $\tilde{\Xi}_1 = (\tilde{X}_1, \tilde{L}_1, 0, \tilde{Y}_1, 0, \tilde{V}_1, 0)$, where the IAV is blocked,

(iii) IAV single-infection equilibrium, $\tilde{\Xi}_2 = (\tilde{X}_2, 0, \tilde{E}_2, 0, \tilde{I}_2, 0, \tilde{P}_2)$, where the SARS-CoV-2 is blocked, where $\tilde{X}_i = X_i$, $i = 0, 1, 2$, $\tilde{L}_1 = L_1$, $\tilde{Y}_1 = Y_1$, $\tilde{V}_1 = V_1$, $\tilde{E}_2 = E_2$, $\tilde{I}_2 = I_2$, and $\tilde{P}_2 = P_2$.

We note that the case of IAV and SARS-CoV-2 coexistence does not appear. In the recent studies presented in [5, 9, 11, 12], it was recorded that some COVID-19 patients were detected to be coinfected with IAV. Therefore, neglecting the immune response may not describe the coinfection dynamics accurately. This supports the idea of including the immune response into the IAV/SARS-CoV-2 coinfection model, where the case of IAV and SARS-CoV-2 coexistence is observed.

7. Numerical simulations

The global stability of the system's equilibria will be illustrated numerically. We use the values of the parameters presented in Table 2. In addition, we make a comparison between single-infection and coinfection.

Table 2. Model parameters.

Parameter	Value	Parameter	Value	Parameter	Value	Parameter	Value
λ	0.5	γ_I	0.2	$\varkappa_V$	0.05	μ_M	0.04
α	0.05	κ_V	0.2	$\varkappa_P$	0.04	η_L	0.05
β_V	Varied	κ_P	0.4	σ_Z	Varied	η_E	0.06
β_P	Varied	π_V	0.2	σ_M	Varied	δ_L	0.05
γ_Y	0.11	π_P	0.1	μ_Z	0.05	δ_E	0.06

7.1. Stability of the equilibria

Now, we solve system (2.1) with three different initial conditions (states) as:

$$\text{C1} : (X(0), L(0), E(0), Y(0), I(0), V(0), P(0), Z(0), M(0)) = (8, 0.5, 1, 1, 0.5, 1, 0.5, 1, 4),$$
$$\text{C2} : (X(0), L(0), E(0), Y(0), I(0), V(0), P(0), Z(0), M(0)) = (7, 1, 1.5, 1.5, 0.7, 1.5, 0.8, 2, 6),$$
$$\text{C3} : (X(0), L(0), E(0), Y(0), I(0), V(0), P(0), Z(0), M(0)) = (6, 1.5, 2, 2, 1, 2, 1.4, 3, 8).$$

Selecting the values of β_V, β_P, σ_Z and σ_M leads to the following situations:

Situation 1 (Stability of Ξ_0): $\beta_V = 0.001$, $\beta_P = 0.001$, $\sigma_Z = 0.01$ and $\sigma_M = 0.02$. For these values of parameters, we have $\mathfrak{R}_1 = 0.0455 < 1$ and $\mathfrak{R}_2 = 0.1 < 1$. Figure 2 shows that the trajectories tend to the equilibrium $\Xi_0 = (10, 0, 0, 0, 0, 0, 0, 0, 0)$ for all initials C1-C3. This demonstrates that, Ξ_0 is G.A.S based on Theorem 1. In this situation, both SARS-CoV-2 and IAV will be removed.

Situation 2 (Stability of Ξ_1): $\beta_V = 0.05$, $\beta_P = 0.001$, $\sigma_Z = 0.002$ and $\sigma_M = 0.02$. With such selection we obtain $\mathfrak{R}_1 = 2.2727 > 1$, $\mathfrak{R}_3 = 0.0874 < 1$ and hence $\mathfrak{R}_2/\mathfrak{R}_1 = 0.044 < 1$. The equilibrium point Ξ_1 exists with $\Xi_1 = (4.4, 2.8, 0, 1.27, 0, 1.27, 0, 0, 0)$. It is clear from Figure 3 that, the trajectories tend to Ξ_1 for all initials C1-C3. Thus, the numerical results agree with Theorem 2. This case simulates a SARS-CoV-2 single-infection without antibody immunity.

Situation 3 (Stability of Ξ_2): $\beta_V = 0.005$, $\beta_P = 0.03$, $\sigma_Z = 0.01$ and $\sigma_M = 0.001$. This gives $\mathfrak{R}_2 = 3 > 1$, $\mathfrak{R}_4 = 0.12 < 1$ and then $\mathfrak{R}_1/\mathfrak{R}_2 = 0.0758 < 1$. The numerical results show that, $\Xi_2 = (3.33, 0, 2.78, 0, 0.83, 0, 3.33, 0, 0)$ exists. We can observe from Figure 4 that, the trajectories converge to Ξ_2 regardless of the initial states. This result supports the result of Theorem 3. This situation represents an IAV single-infection without antibody immunity.

Situation 4 (Stability of Ξ_3): $\beta_V = 0.09$, $\beta_P = 0.002$, $\sigma_Z = 0.05$ and $\sigma_M = 0.05$. This yields $\mathfrak{R}_3 = 1.461 > 1$ and $\mathfrak{R}_5 = 0.0714 < 1$. Figure 5 shows that the trajectories tend to $\Xi_3 = (3.57, 3.21, 0, 1.46, 0, 1, 0, 1.84, 0)$ regardless of the initial states. Therefore, Ξ_3 is G.A.S and this supports Theorem 4. Hence, a SARS-CoV-2 single-infection with stimulated SARS-CoV-2-specific antibody is attained.

Situation 5 (Stability of Ξ_4): $\beta_V = 0.01$, $\beta_P = 0.1$, $\sigma_Z = 0.01$ and $\sigma_M = 0.02$. The values of $\mathfrak{R}_4$ and $\mathfrak{R}_6$ are computed as $\mathfrak{R}_4 = 2 > 1$ and $\mathfrak{R}_6 = 0.0909 < 1$. Thus, Ξ_4 exists with $\Xi_4 = (2, 0, 3.33, 0, 1, 0, 2, 0, 2.5)$. In Figure 6 we see that the trajectories tend to Ξ_4 regardless of the initial states. It follows that Ξ_4 is G.A.S according to Theorem 5. Hence, an IAV single-infection with activated IAV-specific antibody is achieved.

Situation 6 (Stability of Ξ_5): $\beta_V = 0.09$, $\beta_P = 0.02$, $\sigma_Z = 0.095$ and $\sigma_M = 0.009$. Then, we calculate $\mathfrak{R}_5 = 1.027 > 1$, $\mathfrak{R}_8 = 0.5369 < 1$ and $\mathfrak{R}_1/\mathfrak{R}_2 = 2.0455 > 1$ The numerical results drawn in Figure 7 show that $\Xi_5 = (5, 2.37, 0.11, 1.08, 0.03, 0.53, 0.13, 4.18, 0)$ exists and it is G.A.S and this is consistent with Theorem 6. As a result, a coinfection with SARS-CoV-2 and IAV is attained where only SARS-CoV-2-specific antibody is stimulated.

Situation 7 (Stability of Ξ_6): $\beta_V = 0.09$, $\beta_P = 0.09$, $\sigma_Z = 0.03$ and $\sigma_M = 0.03$. We compute $\mathfrak{R}_6 = 1.2032 > 1$, $\mathfrak{R}_7 = 0.6392 < 1$ and $\mathfrak{R}_2/\mathfrak{R}_1 = 2.2 > 1$. We find that, the equilibrium $\Xi_6 = (2.44, 0.84, 2.44, 0.38, 0.73, 0.38, 1.33, 0, 3)$ exists. Further, the numerical solutions outlined in Figure 8 show that, Ξ_6 is G.A.S and this boosts the result of Theorem 7. In this situation, a coinfection with SARS-CoV-2 and IAV are attained where only IAV-specific antibody is activated.

Situation 8 (Stability of Ξ_7): $\beta_V = 0.09$, $\beta_P = 0.09$, $\sigma_Z = 0.5$ and $\sigma_M = 0.5$. This selection yields $\mathfrak{R}_7 = 3.0898 > 1$ and $\mathfrak{R}_8 = 6.7976 > 1$. Figure 9 shows that

$\Xi_7 = (7.55, 0.68, 0.45, 0.31, 0.14, 0.1, 0.08, 8.36, 14.49)$ exists and it is G.A.S based on Theorem 8. In this situation, a coinfection with SARS-CoV-2 and IAV is established regardless of the initial states. In this case, both SARS-CoV-2-specific antibodies and IAV-specific antibodies are working against the coinfection.

For more confirmation, we investigate the local stability of the system's equilibria. Calculating the Jacobian matrix $J = J(X, L, E, Y, I, V, P, Z, M)$ of system (2.1) as:

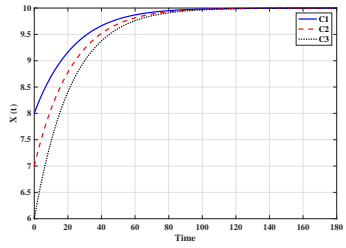
$$J = \begin{pmatrix} J\_11 & 0 & 0 & 0 & 0 & -\beta\_VX & -\beta\_PX & 0 & 0 \\ \beta\_VV & J_{22} & 0 & 0 & 0 & \beta\_VX & 0 & 0 & 0 \\ \beta\_PP & 0 & J_{33} & 0 & 0 & 0 & \beta\_PX & 0 & 0 \\ 0 & \delta\_L & 0 & -\gamma\_Y & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \delta\_E & 0 & -\gamma\_I & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \kappa\_V & 0 & J_{66} & 0 & -\varkappa\_VV & 0 \\ 0 & 0 & 0 & 0 & \kappa\_P & 0 & J_{77} & 0 & -\varkappa\_PP \\ 0 & 0 & 0 & 0 & 0 & \sigma\_ZZ & 0 & J_{88} & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \sigma\_MM & 0 & J_{99} \end{pmatrix},$$

where $J_{11} = -(\alpha + \beta_V V + \beta_P P)$, $J_{22} = -(\eta_L + \delta_L)$, $J_{33} = -(\eta_E + \delta_E)$, $J_{66} = -(\pi_V + \varkappa_V Z)$, $J_{77} = -(\pi_P + \varkappa_P M)$, $J_{88} = \sigma_Z V - \mu_Z$, $J_{99} = \sigma_M P - \mu_M$.

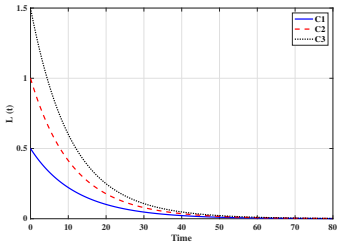
At each equilibrium, we compute the eigenvalues λ_j, $j = 1, 2, ..., 9$ of J. If $\mathrm{Re}(\lambda_j) < 0$, $i = 1, 2, ..., 9$, then the equilibrium point is locally stable. We select the parameters β_V, β_P, σ_Z and σ_M as given in situations 1-8, then we compute all nonnegative equilibria and the accompanying eigenvalues. Table 3 outlined the nonnegative equilibria, the real parts of the eigenvalues and whether or not the equilibrium point is stable.

Table 3. Local stability of nonnegative equilibria Ξ_i, $i = 0, 1, ..., 9$.

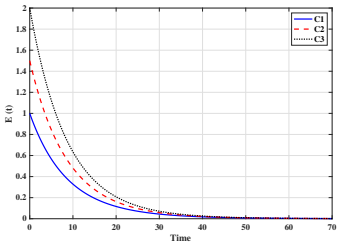
Situation	The equilibria	$\mathrm{Re}(\lambda_j)$, $j = 1, 2, ..., 9$	Stability
1	$\Xi_0 = (10, 0, 0, 0, 0, 0, 0, 0, 0)$	$(-0.18, -0.18, -0.18, -0.15, -0.08, -0.07, -0.05, -0.05, -0.04)$	stable
2	$\Xi_0 = (10, 0, 0, 0, 0, 0, 0, 0, 0)$	$(-0.22, -0.22, -0.18, -0.18, -0.07, -0.05, -0.05, -0.04, 0.04)$	unstable
	$\Xi_1 = (4.4, 2.8, 01.27, 0, 1.27, 0, 0, 0)$	$(-0.22, -0.22, -0.17, -0.17, -0.08, -0.04, -0.04, -0.05, -0.04)$	stable
3	$\Xi_0 = (10, 0, 0, 0, 0, 0, 0, 0, 0)$	$(-0.24, -0.24, -0.18, -0.18, 0.06, -0.05, -0.05, -0.05, -0.04)$	unstable
	$\Xi_2 = (3.33, 0, 2.78, 0, 0.83, 0, 3.33, 0, 0)$	$(-0.24, -0.24, -0.17, -0.17, -0.07, -0.05, -0.05, -0.05, -0.04)$	stable
4	$\Xi_0 = (10, 0, 0, 0, 0, 0, 0, 0, 0)$	$(-0.24, -0.24, -0.18, -0.18, 0.08, -0.05, -0.05, -0.05, -0.04)$	unstable
	$\Xi_1 = (2.44, 3.78, 0, 1.27, 0, 1.27, 0, 0, 0)$	$(-0.25, -0.25, -0.17, -0.17, -0.08, -0.06, -0.06, -0.04, 0.04)$	unstable
	$\Xi_3 = (3.57, 3.21, 0, 1.46, 0, 1, 0, 1.84, 0)$	$(-0.27, -0.27, -0.17, -0.17, -0.07, -0.04, -0.04, -0.04, -0.03)$	stable
5	$\Xi_0 = (10, 0, 0, 0, 0, 0, 0, 0, 0)$	$(-0.29, -0.29, -0.19, -0.19, 0.15, -0.05, -0.05, -0.04, -0.03)$	unstable
	$\Xi_2 = (1, 0, 3.75, 0, 1.13, 0, 4.5, 0, 0)$	$(-0.47, -0.29, -0.18, -0.15, -0.08, -0.08, -0.08, -0.05, 0.05)$	unstable
	$\Xi_4 = (2, 0, 3.33, 0, 1, 0, 2, 0, 2.5)$	$(-0.31, -0.31, -0.17, -0.17, -0.06, -0.06, -0.07, -0.05, -0.03)$	stable
6	$\Xi_0 = (10, 0, 0, 0, 0, 0, 0, 0, 0)$	$(-0.24, -0.24, -0.23, -0.23, 0.08, -0.05, -0.05, -0.04, 0.03)$	unstable
	$\Xi_1 = (2.44, 3.78, 0, 1.72, 0, 1.72, 0, 0, 0)$	$(-0.25, -0.25, -0.2, -0.2, 0.11, -0.06, -0.06, -0.04, -0.03)$	unstable
	$\Xi_2 = (5, 0, 2.08, 0, 0.63, 0, 2.5, 0, 0)$	$(-0.22, -0.22, -0.22, -0.22, -0.05, -0.04, -0.04, 0.04, -0.02)$	unstable
	$\Xi_3 = (5.14, 2.43, 0, 1.11, 0, 0.53, 0, 4.4, 0)$	$(-0.32, -0.32, -0.21, -0.21, -0.02, -0.02, -0.04, -0.04, 0.001)$	unstable
	$\Xi_5 = (5, 2.37, 0.11, 1.08, 0.03, 0.53, 0.13, 4.18, 0)$	$(-0.31, -0.31, -0.21, -0.21, -0.02, -0.02, -0.04, -0.03, -0.001)$	stable
7	$\Xi_0 = (10, 0, 0, 0, 0, 0, 0, 0, 0)$	$(-0.28, -0.28, -0.24, -0.24, 0.14, 0.07, -0.05, -0.05, -0.04)$	unstable
	$\Xi_1 = (2.44, 3.78, 0, 1.72, 0, 1.72, 0, 0, 0)$	$(-0.25, -0.25, -0.23, -0.23, -0.06, -0.06, -0.04, 0.04, 0.002)$	unstable
	$\Xi_2 = (1.11, 0, 3.71, 0, 1.11, 0, 4.44, 0, 0)$	$(-0.4, -0.31, -0.19, -0.19, 0.09, -0.08, -0.08, -0.05, -0.03)$	unstable
	$\Xi_3 = (2.5, 3.75, 0, 1.7, 0, 1.67, 0, 0.09, 0)$	$(-0.25, -0.25, -0.23, -0.23, -0.06, -0.06, 0.04, -0.04, -0.001)$	unstable
	$\Xi_4 = (2.94, 0, 2.94, 0, 0.88, 0, 1.33, 0, 4.12)$	$(-0.32, -0.32, -0.21, -0.21, -0.04, -0.04, -0.05, -0.04, 0.008)$	unstable
	$\Xi_6 = (2.44, 0.84, 2.44, 0.38, 0.73, 0.38, 1.33, 0, 3)$	$(-0.3, -0.3, -0.21, -0.21, -0.05, -0.05, -0.04, -0.02, -0.02)$	stable
8	$\Xi_0 = (10, 0, 0, 0, 0, 0, 0, 0, 0)$	$(-0.28, -0.28, -0.24, -0.24, 0.14, 0.08, -0.05, -0.05, -0.04)$	unstable
	$\Xi_1 = (2.44, 3.78, 0, 1.72, 0, 1.72, 0, 0, 0)$	$(0.81, -0.25, -0.25, -0.23, -0.23, -0.06, -0.06, -0.04, 0.04)$	unstable
	$\Xi_2 = (1.11, 0, 3.7, 0, 1.11, 0, 4.44, 0, 0)$	$(2.18, -0.4, -0.31, -0.19, -0.19, -0.08, -0.08, -0.05, -0.03)$	unstable
	$\Xi_3 = (8.47, 0.76, 0, 0.35, 0, 0.1, 0, 9.87, 0)$	$(-0.63, -0.27, -0.27, -0.26, 0.13, -0.05, -0.01, -0.01, -0.04)$	unstable
	$\Xi_4 = (8.74, 0, 0.52, 0, 0.16, 0, 0.08, 0, 17.17)$	$(-0.67, -0.41, -0.24, -0.24, 0.07, -0.01, -0.01, -0.05, -0.05)$	unstable
	$\Xi_6 = (2.44, 9.27, 0.15, 1.64, 0.04, 1.64, 0.08, 0, 3)$	$(0.77, -0.27, -0.27, -0.25, -0.25, -0.06, -0.06, -0.006, -0.006)$	unstable
	$\Xi_7 = (7.55, 0.68, 0.45, 0.31, 0.14, 0.1, 0.08, 8.36, 14.49)$	$(-0.54, -0.49, -0.49, -0.27, -0.02, -0.02, -0.05, -0.01, -0.01)$	stable



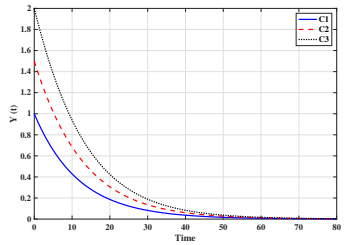
(a) Uninfected epithelial cells



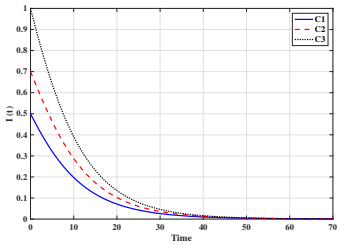
(b) Latent SARS-CoV-2-infected cells



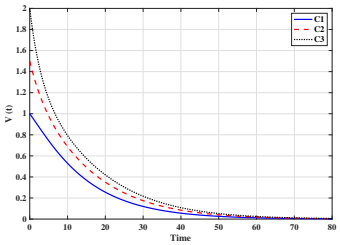
(c) Latent IAV-infected cells



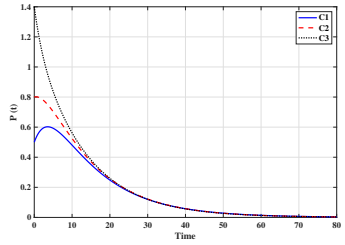
(d) Active SARS-CoV-2-infected cells



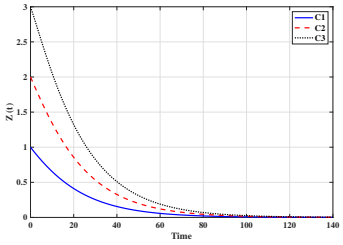
(e) Active IAV-infected cells



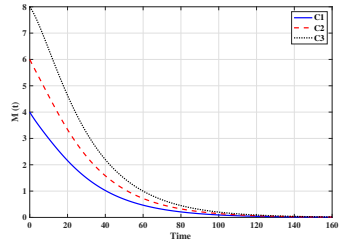
(f) Free SARS-CoV-2 particles



(g) Free IAV particles

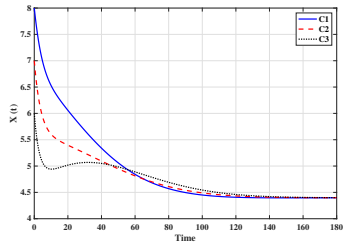


(h) SARS-CoV-2-specific antibodies

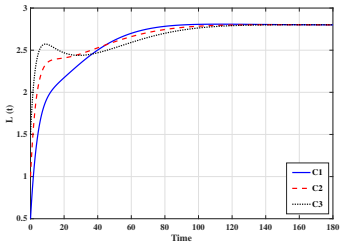


(i) IAV-specific antibodies

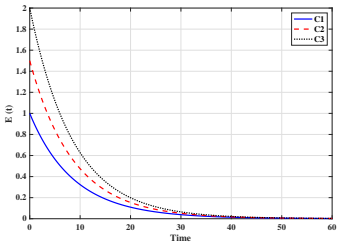
Figure 2. Solutions of system (2.1) when $\mathfrak{R}_1 \leq 1$ and $\mathfrak{R}_2 \leq 1$.



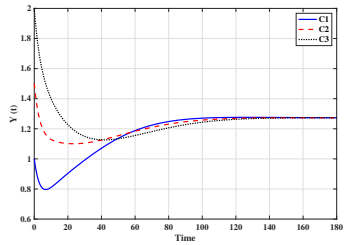
(a) Uninfected epithelial cells



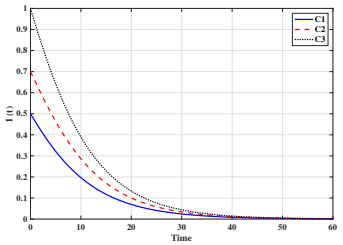
(b) Latent SARS-CoV-2-infected cells



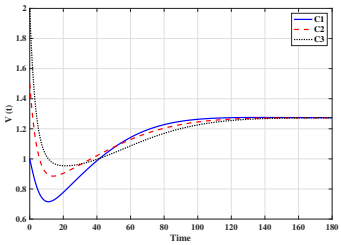
(c) Latent IAV-infected cells



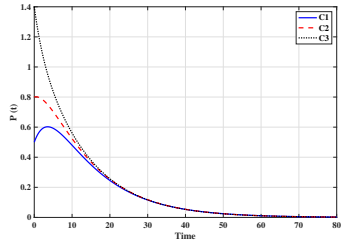
(d) Active SARS-CoV-2-infected cells



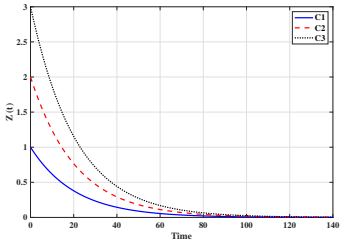
(e) Active IAV-infected cells



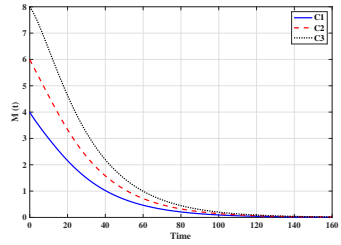
(f) Free SARS-CoV-2 particles



(g) Free IAV particles

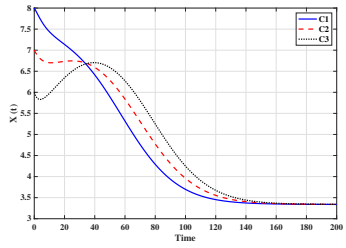


(h) SARS-CoV-2-specific antibodies

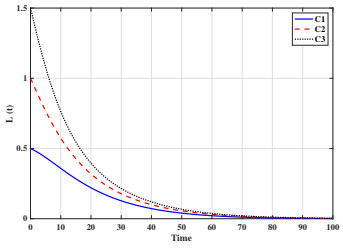


(i) IAV-specific antibodies

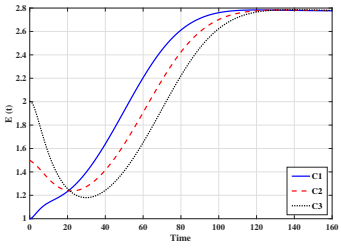
Figure 3. Solutions of system (2.1) when $\mathfrak{R}_1 > 1$, $\mathfrak{R}_2/\mathfrak{R}_1 \leq 1$ and $\mathfrak{R}_3 \leq 1$.



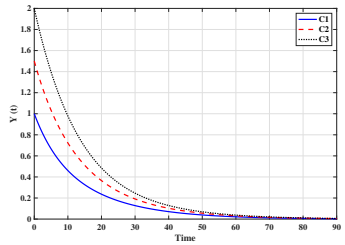
(a) Uninfected epithelial cells



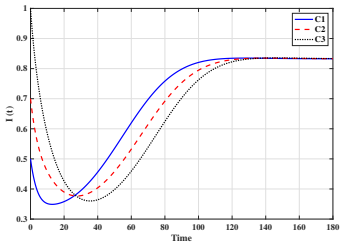
(b) Latent SARS-CoV-2-infected cells



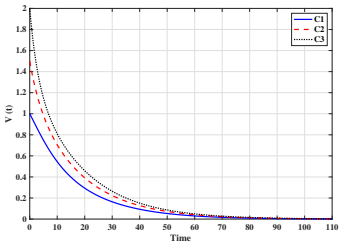
(c) Latent IAV-infected cells



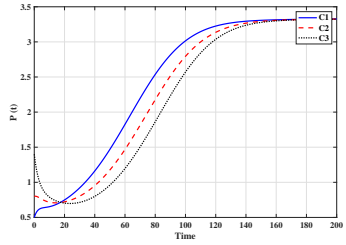
(d) Active SARS-CoV-2-infected cells



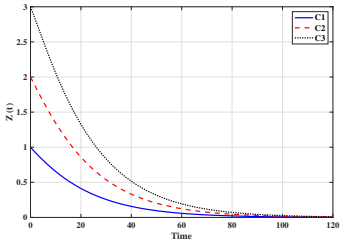
(e) Active IAV-infected cells



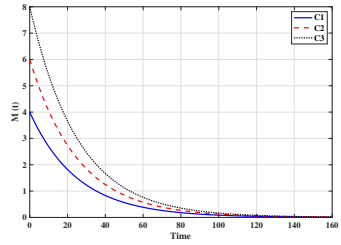
(f) Free SARS-CoV-2 particles



(g) Free IAV particles

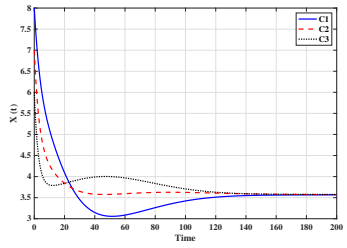


(h) SARS-CoV-2-specific antibodies

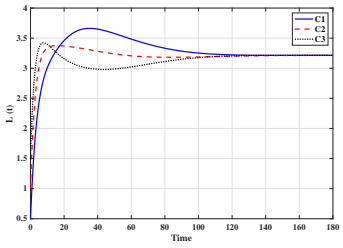


(i) IAV-specific antibodies

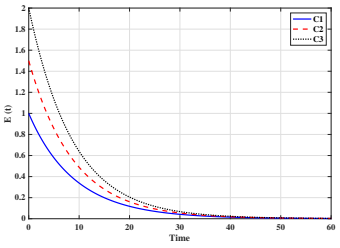
Figure 4. Solutions of system (2.1) when $\mathfrak{R}_2 > 1$, $\mathfrak{R}_1/\mathfrak{R}_2 \leq 1$ and $\mathfrak{R}_4 \leq 1$.



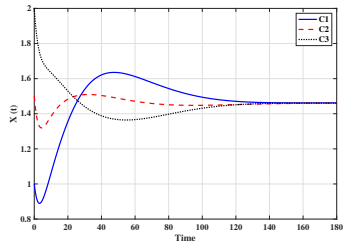
(a) Uninfected epithelial cells



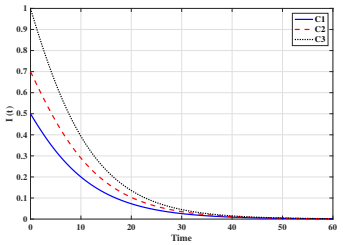
(b) Latent SARS-CoV-2-infected cells



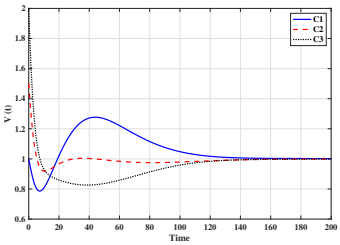
(c) Latent IAV-infected cells



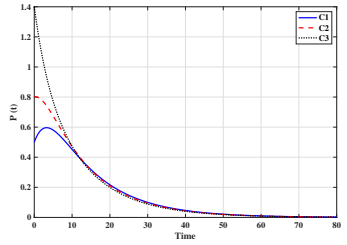
(d) Active SARS-CoV-2-infected cells



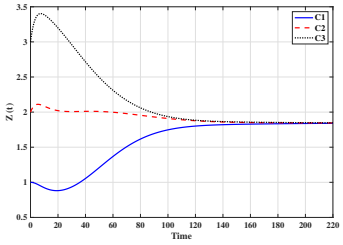
(e) Active IAV-infected cells



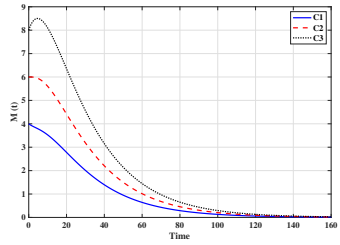
(f) Free SARS-CoV-2 particles



(g) Free IAV particles

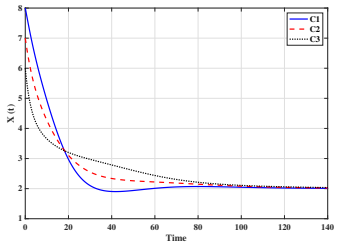


(h) SARS-CoV-2-specific antibodies

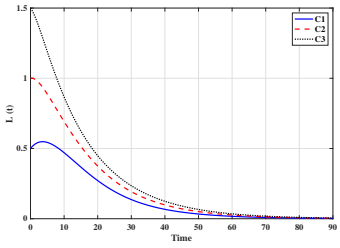


(i) IAV-specific antibodies

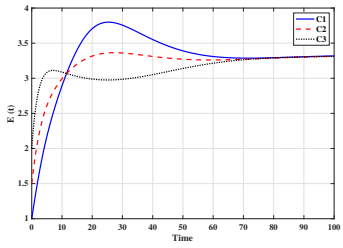
Figure 5. Solutions of system (2.1) when $\mathfrak{R}_3 > 1$ and $\mathfrak{R}_5 \leq 1$.



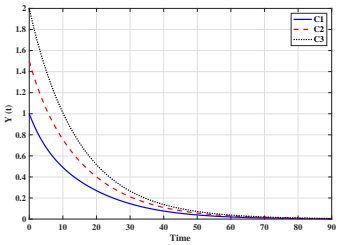
(a) Uninfected epithelial cells



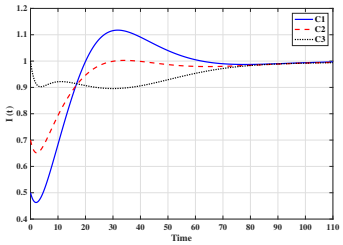
(b) Latent SARS-CoV-2-infected cells



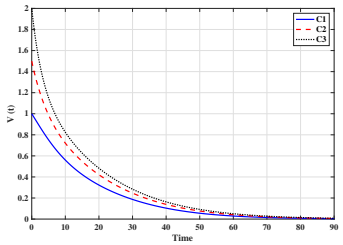
(c) Latent IAV-infected cells



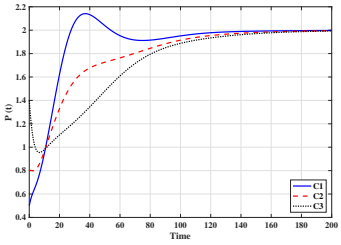
(d) Active SARS-CoV-2-infected cells



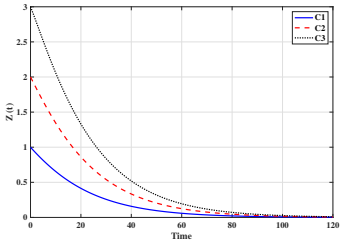
(e) Active IAV-infected cells



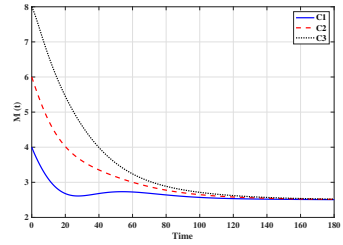
(f) Free SARS-CoV-2 particles



(g) Free IAV particles

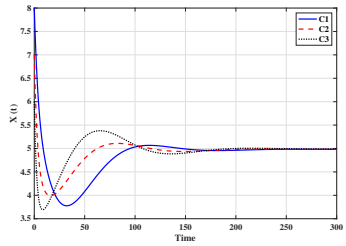


(h) SARS-CoV-2-specific antibodies

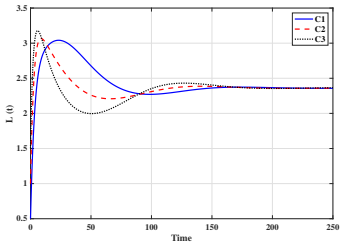


(i) IAV-specific antibodies

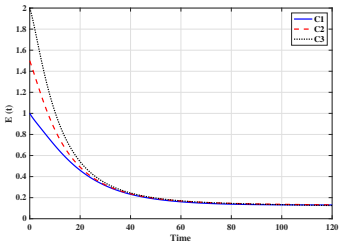
Figure 6. Solutions of system (2.1) when $\mathfrak{R}_4 > 1$ and $\mathfrak{R}_6 \leq 1$.



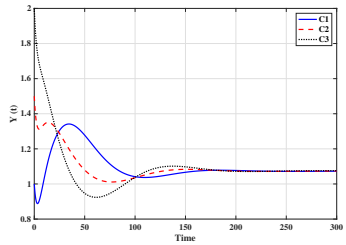
(a) Uninfected epithelial cells



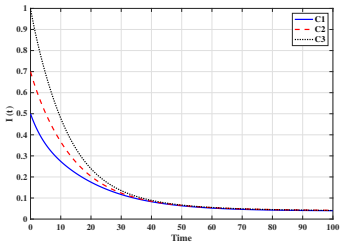
(b) Latent SARS-CoV-2-infected cells



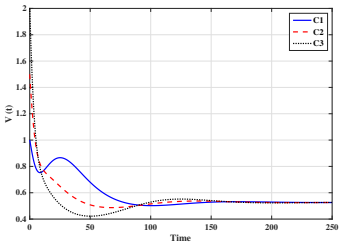
(c) Latent IAV-infected cells



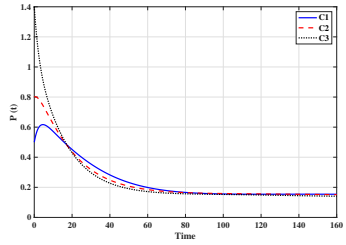
(d) Active SARS-CoV-2-infected cells



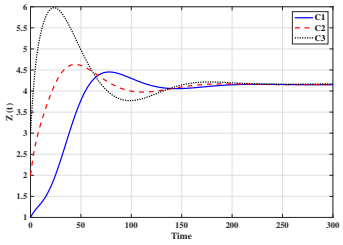
(e) Active IAV-infected cells



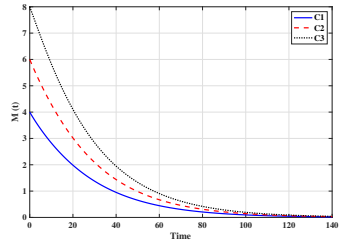
(f) Free SARS-CoV-2 particles



(g) Free IAV particles

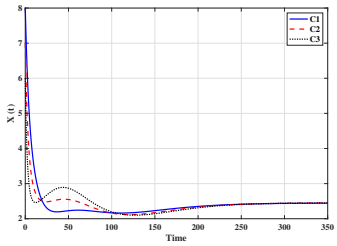


(h) SARS-CoV-2-specific antibodies

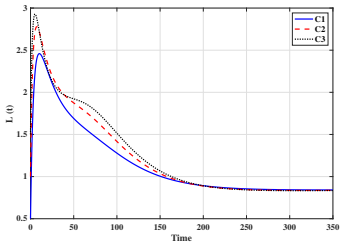


(i) IAV-specific antibodies

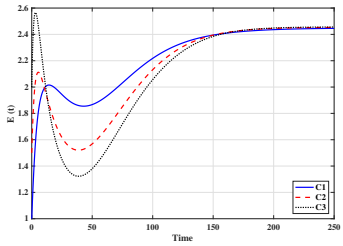
Figure 7. Solutions of system (2.1) when $\mathfrak{R}_5 > 1$, $\mathfrak{R}_1/\mathfrak{R}_2 > 1$ and $\mathfrak{R}_8 \leq 1$.



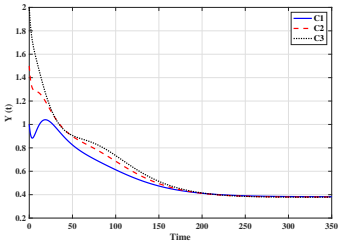
(a) Uninfected epithelial cells



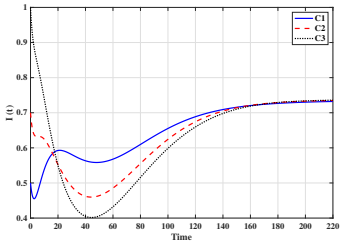
(b) Latent SARS-CoV-2-infected cells



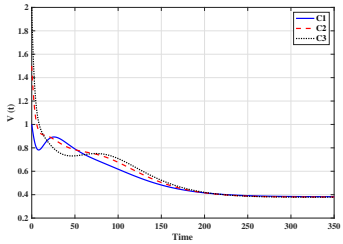
(c) Latent IAV-infected cells



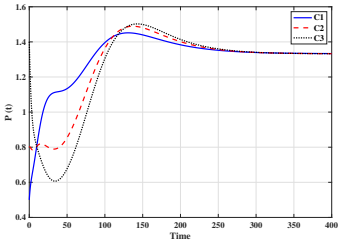
(d) Active SARS-CoV-2-infected cells



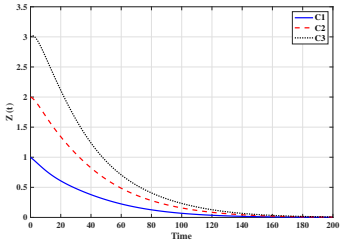
(e) Active IAV-infected cells



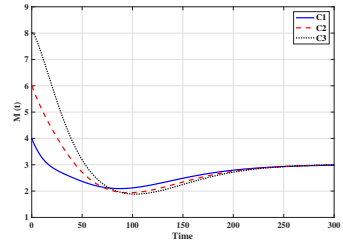
(f) Free SARS-CoV-2 particles



(g) Free IAV particles

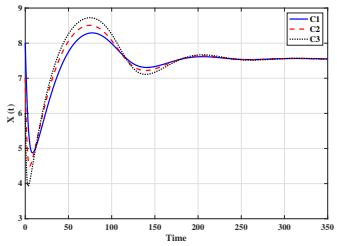


(h) SARS-CoV-2-specific antibodies

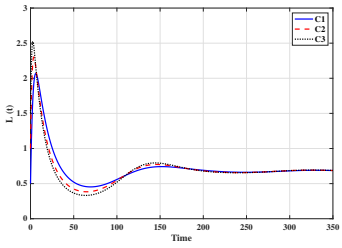


(i) IAV-specific antibodies

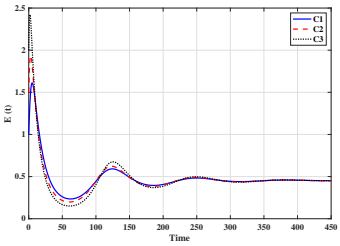
Figure 8. Solutions of system (2.1) when $\mathfrak{R}_6 > 1$, $\mathfrak{R}_2/\mathfrak{R}_1 > 1$ and $\mathfrak{R}_7 \leq 1$.



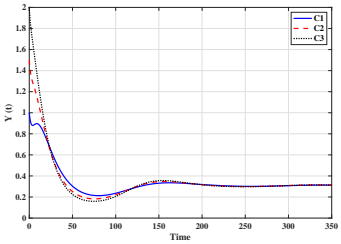
(a) Uninfected epithelial cells



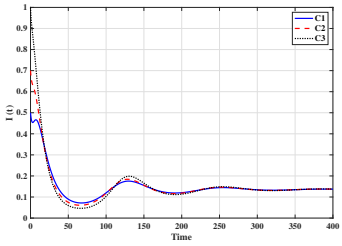
(b) Latent SARS-CoV-2-infected cells



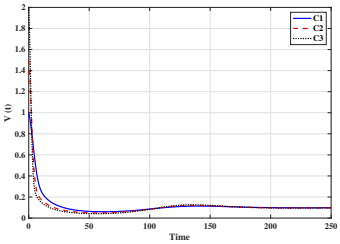
(c) Latent IAV-infected cells



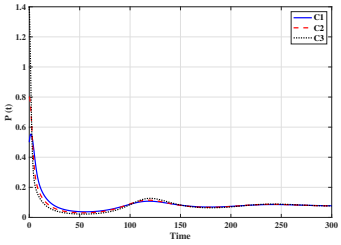
(d) Active SARS-CoV-2-infected cells



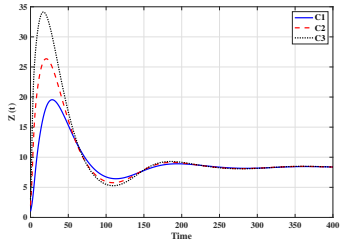
(e) Active IAV-infected cells



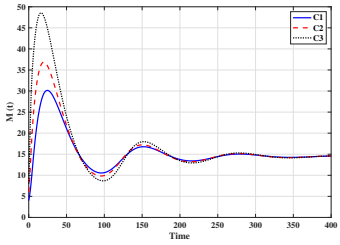
(f) Free SARS-CoV-2 particles



(g) Free IAV particles



(h) SARS-CoV-2-specific antibodies



(i) IAV-specific antibodies

Figure 9. Solutions of system (2.1) when $\mathfrak{R}_7 > 1$ and $\mathfrak{R}_8 > 1$.

7.2. Comparison results

In this subsection, we present a comparison between the single-infection and coinfection.

7.2.1. Influence of IAV infection on the dynamics of SARS-CoV-2 single-infection

Here, we compare the solutions of model (2.1) and the following SARS-CoV-2 single-infection model:

$$\begin{cases} \dot{X} = \lambda - \alpha X - \beta_V XV, \\ \dot{L} = \beta_V XV - (\eta_L + \delta_L) L, \\ \dot{Y} = \delta_L L - \gamma_Y Y, \\ \dot{V} = \kappa_V Y - \pi_V V - \varkappa_V VZ, \\ \dot{Z} = \sigma_Z VZ - \mu_Z Z. \end{cases} \tag{7.1}$$

We fix parameters $\beta_V = 0.09$, $\beta_P = 0.05$, $\sigma_Z = 0.5$, and $\sigma_M = 0.9$ and select the initial state as:

$$\text{C4} : (X(0), L(0), E(0), Y(0), I(0), V(0), P(0), Z(0), M(0)) = (7.5, 0.3, 5, 0.5, 0.4, 0.05, 0.04, 9, 9.5).$$

From Figure 10 we observe that when the SARS-CoV-2 single-infected individual is coinfected with IAV, then the concentrations of uninfected epithelial cells, latent SARS-CoV-2-infected cells, active SARS-CoV-2-infected cells and SARS-CoV-2-specific antibodies are reduced. However, the concentration of free SARS-CoV-2 particles tends to be the same value in both SARS-CoV-2 single-infection and IAV/SARS-CoV-2 coinfection. This result agrees with the observation of Ding et al. [11] which said that "*IAV/SARS-CoV-2 coinfection did not result in worse clinical outcomes in comparison with SARS-CoV-2 single-infection*".

7.2.2. Influence of SARS-CoV-2 infection on the dynamics IAV single-infection

To examine the impact of SARS-CoV-2 infection on IAV single-infection, we compare the solutions of model (2.1) and the following IAV single-infection model:

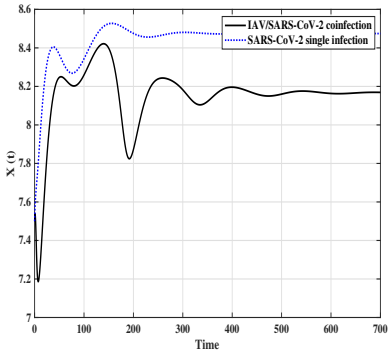
$$\begin{cases} \dot{X} = \lambda - \alpha X - \beta_P XP, \\ \dot{E} = \beta_P XV - (\eta_E + \delta_E) E, \\ \dot{I} = \delta_E E - \gamma_I I, \\ \dot{P} = \kappa_P I - \pi_P P - \varkappa_P PM, \\ \dot{M} = \sigma_M PM - \mu_M M. \end{cases} \tag{7.2}$$

We fix parameters $\beta_V = 0.09$, $\beta_P = 0.08$, $\sigma_Z = 0.07$ and $\sigma_M = 0.05$ and consider the following initial condition:

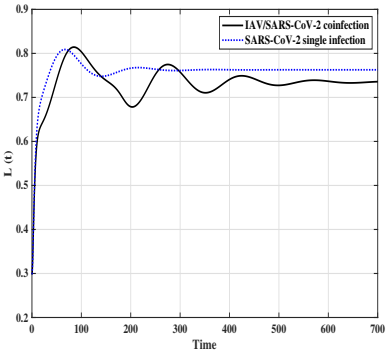
$$\text{C5} : (X(0), L(0), E(0), Y(0), I(0), V(0), P(0), Z(0), M(0)) = (4, 1, 5, 0.6, 0.5, 0.2, 0.05, 3, 8).$$

It can be observed from Figure 11 that, when the IAV single-infected individual is coinfected with SARS-CoV-2 then the concentrations of uninfected epithelial cells, latent IAV-infected cells, active

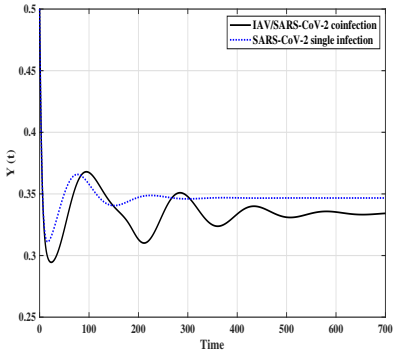
IAV-infected cells and IAV-specific antibodies are decreased. However, the concentration of free IAV particles tend to the same value in both IAV single-infection and IAV/SARS-CoV-2 coinfection.



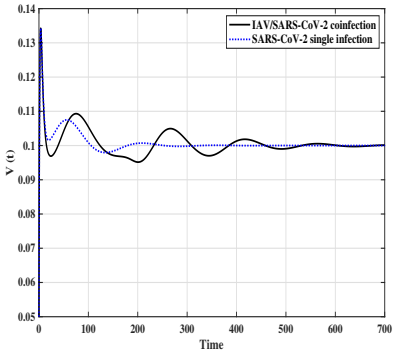
(a) Uninfected epithelial cells



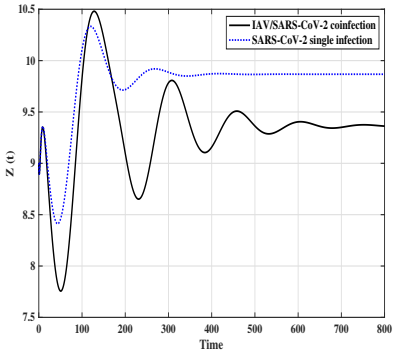
(b) Latent SARS-CoV-2-infected cells



(c) Active SARS-CoV-2-infected cells

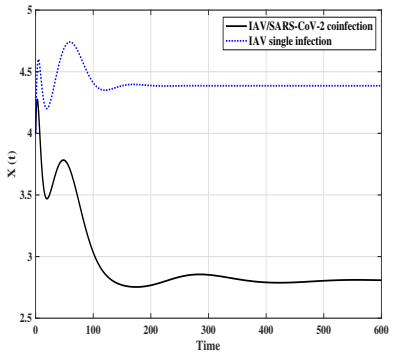


(d) Free SARS-CoV-2 particles

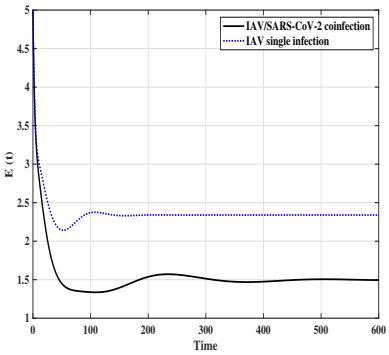


(e) SARS-CoV-2-specific antibodies

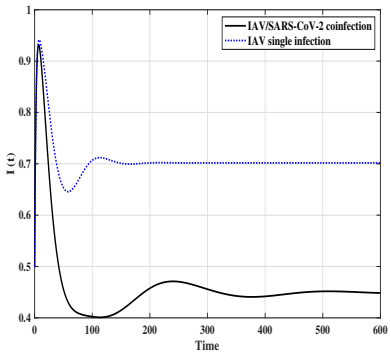
Figure 10. Comparison between the solutions of SARS-CoV-2-single infection model and IAV/SARS-CoV-2 coinfection model.



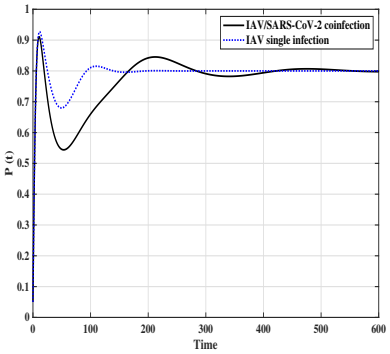
(a) Uninfected epithelial cells



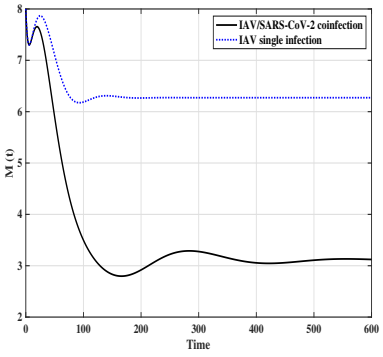
(b) Latent IAV-infected cells



(c) Active IAV-infected cells



(d) Free IAV particles



(e) IAV-specific antibodies

Figure 11. Comparison between the solutions of IAV-single infection model and IAV/SARS-CoV-2 coinfection model.

8. Discussion

IAV and SARS-CoV-2 coinfection cases were reported in some works (see [5, 9, 11, 12]). Therefore, it is important to understand the within-host dynamics of this coinfection. In this paper, we develop and examine a within-host IAV/SARS-CoV-2 coinfection model. The model considered the interactions between uninfected epithelial cells, latent SARS-CoV-2-infected cells, latent IAV-infected cells, active SARS-CoV-2-infected cells, active IAV-infected cells, free SARS-CoV-2 particles, free IAV particles, SARS-CoV-2-specific antibodies and IAV-specific antibodies. We examined the nonnegativity and boundedness of the solutions. We found that the system has eight equilibria and we proved the following:

(I) The infection-free equilibrium Ξ_0 always exists. It is G.A.S when $\mathfrak{R}_1 \leq 1$ and $\mathfrak{R}_2 \leq 1$. In this case, the patient is recovered from both IAV and SARS-CoV-2.

(II) The SARS-CoV-2 single-infection equilibrium without antibody immunity Ξ_1 exists if $\mathfrak{R}_1 > 1$. It is G.A.S when $\mathfrak{R}_1 > 1$, $\mathfrak{R}_2/\mathfrak{R}_1 \leq 1$ and $\mathfrak{R}_3 \leq 1$. This case leads to the situation of the patient only infected by SARS-CoV-2 with an inactive immune response. As we will see below that if both SARS-CoV-2-specific antibody and IAV-specific antibody immunities are not activated against the two viruses, then according to the competition between the two viruses, SARS-CoV-2 may be able to block the IAV.

(III)- The IAV single-infection equilibrium without antibody immunity Ξ_2 exists if $\mathfrak{R}_2 > 1$. It is G.A.S when $\mathfrak{R}_2 > 1$, $\mathfrak{R}_1/\mathfrak{R}_2 \leq 1$ and $\mathfrak{R}_4 \leq 1$. This case leads to the situation of the patient only infected by IAV with an unstimulated immune response. Then, IAV may be able to block the SARS-CoV-2.

(IV) The SARS-CoV-2 single-infection equilibrium with stimulated SARS-CoV-2-specific antibody immunity Ξ_3 exists if $\mathfrak{R}_3 > 1$. It is G.A.S when $\mathfrak{R}_3 > 1$ and $\mathfrak{R}_5 \leq 1$. This point represents the situation of SARS-CoV-2 single-infection patient with active SARS-CoV-2-specific antibody immunity.

(V) The IAV single-infection equilibrium with stimulated IAV-specific antibody immunity Ξ_4 exists if $\mathfrak{R}_4 > 1$. It is G.A.S when $\mathfrak{R}_4 > 1$ and $\mathfrak{R}_6 \leq 1$. This point represents the case of IAV single-infection patient with active IAV-specific antibody immunity.

(VI) The IAV/SARS-CoV-2 coinfection equilibrium with only stimulated SARS-CoV-2-specific antibody immunity Ξ_5 exists if $\mathfrak{R}_5 > 1$ and $\mathfrak{R}_1/\mathfrak{R}_2 > 1$. It is G.A.S when $\mathfrak{R}_5 > 1$, $\mathfrak{R}_8 \leq 1$ and $\mathfrak{R}_1/\mathfrak{R}_2 > 1$. Here, the IAV/SARS-CoV-2 coinfection occurs with only stimulated SARS-CoV-2-specific antibody immunity.

(VII) The IAV/SARS-CoV-2 coinfection equilibrium with only stimulated IAV-specific antibody immunity Ξ_6 exists if $\mathfrak{R}_6 > 1$ and $\mathfrak{R}_2/\mathfrak{R}_1 > 1$. It is G.A.S when $\mathfrak{R}_6 > 1$, $\mathfrak{R}_7 \leq 1$ and $\mathfrak{R}_2/\mathfrak{R}_1 > 1$. It means that the IAV/SARS-CoV-2 coinfection occurs with only stimulated IAV-specific antibody immunity.

(VIII) The IAV/SARS-CoV-2 coinfection equilibrium with stimulated both SARS-CoV-2-specific antibodies and IAV-specific antibody immunities Ξ_7 exists and it is G.A.S if $\mathfrak{R}_7 > 1$ and $\mathfrak{R}_8 > 1$. It means that, the IAV/SARS-CoV-2 coinfection occurs with both SARS-CoV-2-specific antibodies and IAV-specific antibody immunities are activated.

The global stability of equilibria was established using the Lyapunov method. We performed numerical simulations and demonstrated that they are in good agreement with the theoretical results. We discussed the influence of IAV infection on SARS-CoV-2 single-infection dynamics and vice

versa. We found that the concentration of free IAV or SARS-CoV-2 particles cells tends to be the same value in both single-infection and coinfection. This agrees with the work of Ding et al. [11] which reported that IAV/SARS-CoV-2 coinfection did not result in worse clinical outcomes. In addition, the spread of seasonal influenza can increase the likelihood of coinfection in patients with COVID-19 [9].

The model developed in this work can be improved by (i) utilizing real data to find a good estimation of the parameters' values, (ii) studying the effect of time delays that occur during infection or production of IAV and SARS-CoV-2 particles, (iii) considering viral mutations [64, 65], (iv) considering the effect of treatments on the progression of both viruses, and (v) including the influence of CTLs in killing SARS-CoV-2-infected and IAV-infected cells. Memory is an important characteristic of viral infections and immune response. It will be important to address the effect of memory on the dynamics of IAV/SARS-CoV-2 coinfection by formulation of the model via fractional differential equations [66–68].

The innate immune response is one of the major antiviral responses to explain host-pathogen interaction. Also, it is a trigger to induce adaptive immunity which is the major focus of our proposed model. Model (2.1) can be extended to include the effect of IFN response as:

$$
\begin{aligned}
\dot{X} &= \lambda - \alpha X - \beta_V XV - \beta_P XP,\\
\dot{L} &= \beta_V XV - \eta_L L - \frac{\delta_L L}{1+\epsilon_L F},\\
\dot{E} &= \beta_P XP - \eta_E E - \frac{\delta_E E}{1+\epsilon_E F},\\
\dot{Y} &= \frac{\delta_L L}{1+\epsilon_L F} - \gamma_Y Y,\\
\dot{I} &= \frac{\delta_E E}{1+\epsilon_E F} - \gamma_I I,\\
\dot{V} &= \frac{\kappa_V Y}{1+\epsilon_V F} - \pi_V V - \varkappa_V VZ,\\
\dot{P} &= \frac{\kappa_P I}{1+\epsilon_P F} - \pi_P P - \varkappa_P PM,\\
\dot{Z} &= \sigma_Z VZ - \mu_Z Z,\\
\dot{M} &= \sigma_M PM - \mu_M M,\\
\dot{F} &= \varpi_F(Y(t-\tau) + I(t-\tau)) - \mu_F F.
\end{aligned}
$$

where ϵ_L, ϵ_E, ϵ_V and ϵ_P are the efficiencies of the IFN effects. These research points need further investigations so we leave them to future works.

Acknowledgment

This research work was funded by Institutional Fund Projects under grant no. (IFPIP:69-130-1443). The authors gratefully acknowledge technical and financial support provided by the Ministry of Education and King Abdulaziz University, DSR, Jeddah, Saudi Arabia.

References

1. *World Health Organization (WHO)*, Coronavirus disease (COVID-19), weekly epidemiological update (2 October 2022), 2022. Available from: https://www.who.int/publications/m/item/weekly-epidemiological-update-on-covid-19—5-october-2022 .
2. A. D. Iuliano, K. M. Roguski, H. H. Chang, D. J. Muscatello, R. Palekar, S. Tempia, et al., Estimates of global seasonal influenza-associated respiratory mortality: A modelling study, *Lancet*, **391** (2018), 1285–1300. https://doi.org/10.1016/S0140-6736(17)33293-2
3. B. Hancioglu, D. Swigon, G. Clermont, A dynamical model of human immune response to influenza A virus infection, *J. Theor. Biol.*, **246** (2007), 70–86. https://doi.org/10.1016/j.jtbi.2006.12.015
4. Z. Varga, A. J. Flammer, P. Steiger, M. Haberecker, R. Andermatt, A. S. Zinkernagel, et al., Endothelial cell infection and endotheliitis in COVID-19, *Lancet*, **395** (2020), 1417–1418. https://doi.org/10.1016/S0140-6736(20)30937-5
5. R. Ozaras, Influenza and COVID-19 coinfection: Report of six cases and review of the literature, *J. Med. Virol*, **92** (2020), 2657–2665. https://doi.org/10.1002/jmv.26125
6. *World Health Organization (WHO)*, Influenza Update No. 428, (19 September 2022), 2022. Available from: https://www.who.int/publications/m/item/influenza-update-n-428 .
7. *World Health Organization (WHO)*, Coronavirus disease (COVID-19), Vaccine tracker, 2022. Available from: https://covid19.trackvaccines.org/agency/who/ .
8. R. F. Nuwarda, A. A. Alharbi, V. Kayser, An overview of influenza viruses and vaccines, *Vaccines*, **9** (2021), 1032. https://doi.org/10.3390/vaccines9091032
9. X. Zhu, Y. Gea, T. Wua, K. Zhaoa, Y. Chena, B. Wu, et al., Co-infection with respiratory pathogens among COVID-2019 cases, *Virus Research*, **285** (2020), 198005. https://doi.org/10.1016/j.virusres.2020.198005
10. P. S. Aghbash, N. Eslami, M. Shirvaliloo, H. B. Baghi, Viral coinfections in COVID-19, *J. Med. Virol.*, **93** (2021), 5310–5322. https://doi.org/10.1002/jmv.27102
11. Q. Ding, P. Lu, Y. Fan, Y. Xia, M. Liu, The clinical characteristics of pneumonia patients coinfected with 2019 novel coronavirus and influenza virus in Wuhan, China, *J. Med. Virol.*, **92** (2020), 1549–1555. https://doi.org/10.1002/jmv.25781
12. G. Wang, M. Xie, J. Ma, J. Guan, Y. Song, Y. Wen, et al., Is co-infection with influenza virus a protective factor of COVID-19?, 2020.
13. M. Wang, Q. Wu, W. Xu, B. Qiao, J. Wang, H. Zheng, et al., Clinical diagnosis of 8274 samples with 2019-novel coronavirus in Wuhan, *MedRxiv*, (2020). https://doi.org/10.1101/2020.02.12.20022327
14. L. Lansbury, B. Lim, V. Baskaran, W. S. Lim, Co-infections in people with COVID-19: A systematic review and meta-analysis, *J. Infect.*, **81** (2020), 266–275. https://doi.org/10.1016/j.jinf.2020.05.046
15. T. L. Dao, P. Colson, M. Million, P. Gautret, Co-infection of SARS-CoV-2 and influenza viruses: A systematic review and meta-analysis, *J. Clin. Virol.*, **1** (2021), 100036. https://doi.org/10.1016/j.jcvp.2021.100036

16. H. Ghaznavi, M. Shirvaliloo, S. Sargazi, Z. Mohammadghasemipour, Z. Shams, Z. Hesari, et al., SARS-CoV-2 and influenza viruses: Strategies to cope with coinfection and bioinformatics perspective, *CBI*, **46** (2022), 1009–1020. https://doi.org/10.1002/cbin.11800

17. H. Khorramdelazada, M. H. Kazemib, A. Najafib, M. Keykhaeee, R. Z. Emameh, R. Falak, Immunopathological similarities between COVID-19 and influenza: Investigating the consequences of co-infection, *Microb. Pathog.*, **152** (2021), 104554. https://doi.org/10.1016/j.micpath.2020.104554

18. X. Xiang, Z. Wang, L. Ye, X. He, X. Wei, Y. Ma, et al., Co-infection of SARS-COV-2 and influenza A virus: A case series and fast review, *Curr. Med. Sci.***41** (2021), 51–57. https://doi.org/10.1007/s11596-021-2317-2

19. H. Yue, M. Zhang, L. Xing, K. Wang, X. Rao, H. Liu, et al., The epidemiology and clinical characteristics of co-infection of SARS-CoV-2 and influenza viruses in patients during COVID-19 outbreak, *J. Med. Virol.*,**92** (2020), 2870–2873. https://doi.org/10.1002/jmv.26163

20. A. J. Zhang, A. C. Lee, J. F. Chan, F. Liu, C. Li, Y. Chen, H. Chu, et al., Coinfection by severe acute respiratory syndrome coronavirus 2 and influenza A (H1N1) pdm09 virus enhances the severity of pneumonia in golden Syrian hamsters, *Clin. Infect. Dis.*, **72** (2021), e978–e992. https://doi.org/10.1093/cid/ciaa1747

21. M. D. Nowak, E. M. Sordillo, M. R. Gitman, A. E. P. Mondolfi, Coinfection in SARS-CoV-2 infected patients: Where are influenza virus and rhinovirus/enterovirus?, *J. Med. Virol.*, **92** (2020), 1699. https://doi.org/10.1002/jmv.25953

22. P. J. Halfmann, N. Nakajima, Y. Sato, K. Takahashi, M. Accola, S. Chiba, et al., SARS-CoV-2 interference of influenza virus replication in Syrian hamsters, *JID*, **225** (2022), 282–286. https://doi.org/10.1093/infdis/jiab587

23. K. Oishi, S. Horiuchi, J. M. Minkoff, B. R. tenOever, The host response to influenza A virus interferes with SARS-CoV-2 replication during coinfection, *J. Virol.*, **96** (2022), e0076522. https://doi.org/10.1128/jvi.00765-22

24. L. Pinky, H. M. Dobrovolny, SARS-CoV-2 coinfections: Could influenza and the common cold be beneficial?, *J. Med. Virol.*, **92** (2020), 2623–2630. https://doi.org/10.1002/jmv.26098

25. A. M. Smith, R. M. Ribeiro, Modeling the viral dynamics of influenza A virus infection, *Crit. Rev. Immunol.*, **30** (2010), 291–298. https://doi.org/10.1615/critrevimmunol.v30.i3.60

26. C. A. Beauchemin, A. Handel, A review of mathematical models of influenza A infections within a host or cell culture: Lessons learned and challenges ahead, *BMC public health*, **11** (2011), 1–15. https://doi.org/10.1186/1471-2458-11-S1-S7

27. L. Canini, A. S. Perelson, Viral kinetic modeling: state of the art, *J. Pharmacokinet*, **41** (2014), 431–443. https://doi.org/10.1007/s10928-014-9363-3

28. A. Handel, L. E. Liao, C. A. Beauchemin, Progress and trends in mathematical modelling of influenza A virus infections, *Curr. Opin. Syst. Biol.*, **12** (2018), 30–36. https://doi.org/10.1016/j.coisb.2018.08.009

29. A. Boianelli, V. K. Nguyen, T. Ebensen, K. Schulze, E. Wilk, N. Sharma, et al., Modeling influenza virus infection: a roadmap for influenza research, *Viruses*, **7** (2015), 5274–5304. https://doi.org/10.3390/v7102875
30. P. Baccam, C. Beauchemin, C. A. Macken, F. G. Hayden, A. S. Perelson, Kinetics of influenza A virus infection in humans, *J. Virol.*, **80** (2006), 7590–7599. https://doi.org/10.1128/JVI.01623-05
31. A. M. Smith, A. S. Perelson, Influenza A virus infection kinetics: quantitative data and models, *WIREs Systems Biology and Medicine*, **3** (2011), 429–445. https://doi.org/10.1002/wsbm.129
32. R. A. Saenz, M. Quinlivan, D. Elton, S. MacRae, A. S. Blunden, J. A. Mumford, et al., Dynamics of influenza virus infection and pathology, *J. Virol.* **84** (2010), 3974–3983. https://doi.org/10.1128/JVI.02078-09
33. A. Tridane, Y. Kuang, Modeling the interaction of cytotoxic T lymphocytes and influenza virus infected epithelial cells, *AIMS*, **7** (2010), 171–185. https://doi.org/10.3934/mbe.2010.7.171
34. H. Y. Lee, D. J. Topham, S. Y. Park, J. Hollenbaugh, J. Treanor, T. R. Mosmann, et al., Simulation and prediction of the adaptive immune response to influenza A virus infection, *J. Virol.*, **83** (2009), 7151–7165. https://doi.org/10.1128/JVI.00098-09
35. E. A. Hernandez-Vargas, E. Wilk, L. Canini, F. R. Toapanta, S. C. Binder, A. Uvarovskii, et al., Effects of aging on influenza virus infection dynamics, *J. Virol.* **88** (2014), 4123–4131. http://dx.doi.org/10.1128/JVI.03644-13
36. K. Li, J. M. McCaw, P. Cao, Modelling within-host macrophage dynamics in influenza virus infection, *J. Theor. Biol.*, **508** (2021), 110492. https://doi.org/10.1016/j.jtbi.2020.110492
37. D. B. Chang, C. S. Young, Simple scaling laws for influenza A rise time, duration, and severity, *J. Theor. Biol.*, **246** (2007), 621–635. https://doi.org/10.1016/j.jtbi.2007.02.004
38. A. Handel, I. M. Longini Jr, R. Antia, Towards a quantitative understanding of the within-host dynamics of influenza A infections, *J. R. Soc. Interface*, **7** (2010), 35–47. https://doi.org/10.1098/rsif.2009.0067
39. C. A. Beauchemin, J. J.McSharry, G. L.Drusano, J. T.Nguyen, G. T.Went, R. M.Ribeiro, et al., Modeling amantadine treatment of influenza A virus in vitro, *J. Theor. Biol.*, **254** (2008), 439–451. https://doi.org/10.1016/j.jtbi.2008.05.031
40. A. Handel, I. M. Longini Jr, R. Antia, Neuraminidase inhibitor resistance in influenza: Assessing the danger of its generation and spread, *PLoS Comput. Biol.*, **3** (2007), e240. https://doi.org/10.1371/journal.pcbi.0030240
41. B. Emerenini, R. Williams, R. N. G. R. Grimaldo, K. Wurscher, R. Ijioma, Mathematical modeling and analysis of influenza in-host infection dynamics, *Lett. Biomath.*, **8** (2021), 229–253. https://doi.org/10.30707/LiB8.1.1647878866.124006
42. M. Barik, C. Swarup, T. Singh, S. Habbi, S. Chauhan, Dynamical analysis, optimal control and spatial pattern in an influenza model with adaptive immunity in two stratified population, *AIMS Math.*, **7**(4) (2022), 4898–4935. http://dx.doi.org/10.3934/math.2022273
43. E. A. Hernandez-Vargas, J. X. Velasco-Hernandez, In-host mathematical modelling of COVID-19 in humans, *Annu. Rev. Control*, **50** (2020), 448–456. https://doi.org/10.1016/j.arcontrol.2020.09.006

44. R. Ke, C. Zitzmann, D. D. Ho, R. M. Ribeiro, A. S. Perelson, In vivo kinetics of SARS-CoV-2 infection and its relationship with a person's infectiousness, *PNAS*, **118** (2021), e2111477118. https://doi.org/10.1073/pnas.2111477118

45. S. Wang, Y. Pan, Q. Wang, H. Miao, A. N. Brown, L. Rong, Modeling the viral dynamics of SARS-CoV-2 infection, *Math. Biosci.*, **328**(2020), 108438. https://doi.org/10.1016/j.mbs.2020.108438

46. C. Li, J. Xu, J. Liu, Y. Zhou, The within-host viral kinetics of SARS-CoV-2, *Math. Biosci. Engi.*, **17** (2020), 2853–2861. https://doi.org/10.1101/2020.02.29.965418

47. M. Sadria, A. T. Layton, Modeling within-host SARS-CoV-2 infection dynamics and potential treatments, *Viruses*, **13** (2021), 1141. https://doi.org/10.3390/v13061141

48. 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** (2020), 1615–1628. https://doi.org/10.1002/jmv.25866

49. K. Hattaf, N. Yousfi, Dynamics of SARS-CoV-2 infection model with two modes of transmission and immune response, *Math. Biosci. Engi.*, **17** (2020), 5326–5340. https://doi.org/10.3934/mbe.2020288

50. J. Mondal, P. Samui, A. N. Chatterjee, Dynamical demeanour of SARS-CoV-2 virus undergoing immune response mechanism in COVID-19 pandemic, *Eur. Phys. J. Spec. Top.*, (2022). https://doi.org/10.1140/epjs/s11734-022-00437-5 .

51. A. E. S. Almoceraa, G. Quiroz, E. A. Hernandez-Vargas, Stability analysis in COVID-19 within-host model with immune response, *Commun. Nonlinear Sci. Numer. Simulat.*, **95** (2021), 105584. https://doi.org/10.1016/j.cnsns.2020.105584

52. A. Gonçalves, J. Bertrand, R. Ke, E. Comets, X. Lamballerie, D. Malvy, et al., Timing of antiviral treatment initiation is critical to reduce SARS-CoV-2 viral load, *J. PSP*, **9** (2020), 509–514. https://doi.org/10.1002/psp4.12543

53. P. Abuin, A. Anderson, A. Ferramosca, E. A. Hernandez-Vargas, A. H. Gonzalez, Characterization of SARS-CoV-2 dynamics in the host, *Annu. Rev. Control*, **50** (2020), 457–468. https://doi.org/10.1016/j.arcontrol.2020.09.008

54. A. M. Elaiw, A. J. Alsaedi, A. D. Al Agha, A. D. Hobiny, Global stability of a humoral immunity COVID-19 model with logistic growth and delays, *Mathematics*, **10** (2022), 1857. https://doi.org/10.3390/math10111857

55. B. J. Nath, K. Dehingia, V. N. Mishra, Y.-M. Chu, H. K. Sarmah, Mathematical analysis of a within-host model of SARS-CoV-2, *Adv. Differ. Equ.*, **2021** (2021), 113. https://doi.org/10.1186/s13662-021-03276-1

56. A. M. Elaiw, A. D. Hobiny, A. D. Al Agha, Global dynamics of SARS-CoV-2/cancer model with immune responses, *Applied Mathematics and Computation*, **408** (2021), 126364. https://doi.org/10.1016/j.amc.2021.126364

57. A. D. Al Agha, A. M. Elaiw, S. A. Azoz, E. Ramadan, Stability analysis of within-host SARS-CoV-2/HIV coinfection model, *Math. Methods Appl. Sci.*, (2022), 1–20, https://doi.org/10.1002/mma.8457 .

58. A.D. Al Agha, A.M. Elaiw, Global dynamics of SARS-CoV-2/malaria model with antibody immune response, *Math. Biosci. Engi.*, **19** (2022), 8380–8410. http://dx.doi.org/10.3934/mbe.2022390

59. A. Korobeinikov, Global properties of basic virus dynamics models, *Bull. Math. Biol.*, **66** (2004), 879–883. https://doi.org/10.1016/j.bulm.2004.02.001

60. J. K. Hale, S. V. Lunel, *Introduction to functional differential equations*, Springer-Verlag, New York, (1993). http://dx.doi.org/10.1007/978-1-4612-4342-7

61. E. A. Barbashin, *Introduction to the theory of stability*, Wolters-Noordhoff, Groningen, 1970. https://doi.org/10.1007/978-1-4612-4046-4

62. J. P. LaSalle, The Stability of Dynamical Systems, *SIAM*, Philadelphia, 1976. https://doi.org/10.1137/1021079

63. A. M. Lyapunov, *The general problem of the stability of motion*,Taylor Francis, Ltd., London, 1992. https://doi.org/10.1080/00207179208934253

64. N. Bellomo, D. Burini, N. Outada, Multiscale models of Covid-19 with mutations and variants, *Netw. Heterog. Media.*, **17** (2022), 293–310. https://doi.org/10.3934/nhm.2022008 .

65. N. Bellomo, D. Burini, N. Outada, Pandemics of mutating virus and society: a multi-scale active particles approach, *Philos. Trans. Math. Phys. Eng. Sci.*, **380** (2022), 1–14. https://doi.org/10.1098/rsta.2021.0161 .

66. K. Hattaf, A new generalized definition of fractional derivative with non-singular kernel, *Computation*, **8** (2020), 49. https://doi.org/10.3390/computation8020049

67. K. Hattaf, On the stability and numerical scheme of fractional differential equations with application to biology, *Computation*, **10**(6) (2022), 97. https://doi.org/10.3390/computation10060097

68. A. N. Chatterjee, F. Al Basir, M.A. Almuqrin, J. Mondal, I. Khan, SARS-CoV-2 infection with lytic and nonlytic immune responses: a fractional order optimal control theoretical study, *Results Phys.*, **26**, (2021), 104260. https://doi.org/10.1016/j.rinp.2021.104260

AIMS Press