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David A. Oluyori
Ahmadu Bello University

Helen O. Adebayo
Ahmadu Bello University

Ángel G.C. Pérez
Universidad Autónoma de Yucatán

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Global Analysis of an SEIRS Model for COVID-19 Capturing Saturated Incidence with Treatment Response

[1]David A. Oluyori, [2]Helen O. Adebayo, and [3*]Ángel G. C. Pérez

[1,2]Department of Mathematics, School of Physical Science
Ahmadu Bello University
Zaria, Kaduna State, Nigeria
[1]oluyoridavid@gmail.com, [2]helenlovejesus73@gmail.com

[3]Facultad de Matemáticas
Universidad Autónoma de Yucatán
Mérida, Yucatán, Mexico
angel.cervantes@correo.uady.mx

*Corresponding Author

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Abstract

In this work, a new SEIRS model with saturated incidence rate and piecewise linear treatment response is proposed to describe the dynamics of COVID-19. It is assumed that the treatment response is proportional to the number of infected people as long as the incidence cases are within the capacity of the healthcare system, after which the value becomes constant, when the number of confirmed cases exceeds the carrying capacity of the available medical facilities. Thus, the basic reproduction number of the model is obtained. It is proved that the disease-free equilibrium is globally asymptotically stable when the basic reproduction number is less than a critical value. Moreover, sufficient conditions are obtained to guarantee the local and global stability of the equilibrium points of the model. The numerical analysis reveals that multiple endemic equilibria may exist even when the basic reproduction number is less than one, and some interesting dynamics can be observed when the treatment parameter and immunity waning rate are varied.

Keywords: COVID-19; Saturated incidence; Treatment function; Routh-Hurwitz Criterion; Lozinskiĭ measure; Lyapunov function; Immunity waning rate

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1. Introduction

The novel coronavirus disease (COVID-19) was first confirmed in the Chinese city of Wuhan, late December 2019. The rapidity of its spread in many countries around the globe made the WHO declare it as a global pandemic and a public health emergency, raising concerns that if countries with robust healthcare systems to detect and control disease outbreak are having challenges managing the disease, then countries with weak healthcare system need to put adequate measures in place to contain the spread (World Health Organization (2020)). The Coronavirus disease is "novel" in the sense that it is a new strain of zoonotic origin, which has not been previously discovered to affect humans. Historically, the COVID-19 pandemic is a major human coronavirus epidemic in the last two decades aside SARS (Peiris et al. (2004)) and MERS (Zhou et al. (2020), Zaki et al. (2012)). Basically, there are three main transmission routes for the disease, which are droplet transmission, contact transmission, and aerosol transmission (Adhikari et al. (2020)).

According to Esteva and Matias (2001), *incidence* is the rate at which the susceptible population becomes infectious. Thus, if the unit of time is days, then the incidence is the number of new infections per day. The classical epidemic model by Kermack and McKendrick (1927) proposed a *bilinear incidence rate* for simple mass action that is proportional to the number of susceptible and infected individuals. The bilinear incidence has been extensively studied by various authors, such as Ma et al. (2004), Nakata and Kuniya (2010) and others. Sequel to the study of cholera epidemic that occurred in Bari, Capasso and Serio (1978) introduced the *saturated incidence rate*, which tends to a saturation level when the number of infected individuals becomes large; this kind of incidence takes into account the inhibitory effect from the behavioral change of the susceptible due to the crowding effect of the infectives. The saturation incidence seems more realistic than the bilinear incidence due to the inclusion of behavioral change and crowding effect of the infectives.

It is also a general assumption in classical epidemic models that the treatment rate of infection is proportional to the number of the infective individuals. However, the recovery rate may depend on the available medical resources, such as test kits, drugs, isolation centers, ventilators, and availability of trained medical personnel. Considering this, SIR models with continuous and differentiable saturated treatment functions were studied by Zhang and Liu (2008) and Zhou and Fan (2012). Later, Zhang et al. (2014) modified these models to obtain a SEIR model with saturated incidence and treatment functions. Agrawal et al. (2017) modified the work of Zhang et al. (2014) considering an SEIRS model with saturated incidence and treatment rate. Some other authors, such as Dubey et al. (2015), Liu (2019) and Pérez et al. (2019), have studied the stability and bifurcation of different models using this kind of treatment function. On the other hand, a piecewise linear treatment function was first proposed in Wang (2006) assuming that the treatment response is proportional to the number of infected as long as the incidence cases are within the capacity of the healthcare system, after which its value becomes constant. Epidemic models with the piecewise treatment function have been scarcely studied in literature, see, e.g., Hu et al. (2008), Al-Sheikh (2012) and Badole et al. (2018).

Since the beginning of the outbreak, many mathematical models have been proposed to study the dynamics of the COVID-19 epidemic. Some compartmental epidemiological models such as SIRD, SEIR, SEIRD and SEIRUS (Wu et al. (2020), Li et al. (2020), Russo et al. (2020), Ming et al. (2020), Okhuese (2020), Tanvi et al. (2020)) have been proposed to estimate epidemiological

parameters and study the stability of equilibria to provide insights for forecasting purposes. It is still an open question whether individuals who have recovered from COVID-19 can be infected with the virus again (Price and Propp (2020)) and there is uncertainty regarding the length of the immunity period for this disease, so some researchers have studied models for COVID-19 that include the possibility of becoming re-infected after a certain time (Malkov (2020), Mohd and Sulayman (2020)).

To date, no epidemic model for COVID-19 has been studied using the treatment function proposed in Wang (2006). Based on the motivation from Okhuese (2020), Wang (2006), Agrawal et al. (2017), Badole et al. (2018) and Al-Sheikh (2012), we propose a novel SEIRS model with saturated incidence and piecewise linear treatment rate that includes the possibility of reinfection, and we aim to perform a theoretical and numerical analysis of the dynamics of such model.

This rest of this paper is arranged as follows: in Section 2, we present the description of the SEIRS model and show that the system is epidemiologically well posed. In Section 3, we compute the basic reproduction number and discuss the local stability of the disease-free equilibrium. Section 4 states the necessary and sufficient conditions for the existence of endemic equilibria. Section 5 presents the global stability of the disease-free equilibrium using the Lyapunov function method. In Section 6, we consider the local stability of the endemic equilibria using the Routh-Hurwitz Criterion. Section 7 studies the global stability of the endemic equilibria using the geometric approach due to Li and Muldowney (1996). Section 8 presents the numerical simulations of the SEIRS model presented in Section 2. Finally, we present our conclusions in Section 9.

2. Model description

In this work, we propose a modified version of the models in Al-Sheikh (2012) and Badole et al. (2018) that includes the possibility of reinfection after recovery. We also introduce a parameter that represents the death rate of individuals in the R class. Hence, we propose the following SEIRS (Susceptible-Exposed-Infected-Recovered-Susceptible) model to study the dynamics of COVID-19:

$$\begin{aligned} S'(t) &= A - \mu S - \frac{\beta SI}{1 + \alpha I} + \delta R, \\ E'(t) &= \frac{\beta SI}{1 + \alpha I} - (\gamma + \mu)E, \\ I'(t) &= \gamma E - (\sigma + \mu + \varphi)I - T(I), \\ R'(t) &= \sigma I - (\delta + \mu + \varpi)R + T(I). \end{aligned} \tag{1}$$

Here, $S(t)$ is the number of susceptible individuals at time t, $E(t)$ is the number of the exposed individuals at time t, $I(t)$ is the number of the infectious individuals at time t, and $R(t)$ is the number of recovered individuals at time t. The parameter A is the recruitment rate of the population, μ is the natural death rate of the population per time, α is the saturation parameter that measures the inhibitory effect, β is the rate of transmission, δ is the rate of loss of immunity of the removed population that will subsequently move to the susceptible class, γ is the rate of developing infection after being exposed to the virus, σ is the natural recovery rate of infected population, φ

is the disease-induced death rate of the infected population not quarantined, and ϖ is the death rate of the infected population under observation. The saturated incidence rate is given by $\frac{\beta SI}{1+\alpha I}$, where $\frac{1}{1+\alpha I}$ represents the inhibitory parameter.

The treatment response $T(I)$ is given by the piecewise linear function proposed in Wang (2006), which is proportional the number of the infectious people when the number of infectious is less than or equal to a fixed value I_0. In the case when the infectious population is greater than I_0, the function takes a constant value (see equation (1.1) in Wang (2006)). This typifies an endemic situation where the number of the infectious has increased to a saturation point, the available medical facilities are stretched beyond capacity and death toll rises in an unprecedented manner.

All parameters are assumed positive, except δ, which is non-negative. The case $\delta = 0$ represents permanent immunity, that is, when reinfection by COVID-19 is not possible. The flow diagram of the model can be seen in Figure 1.

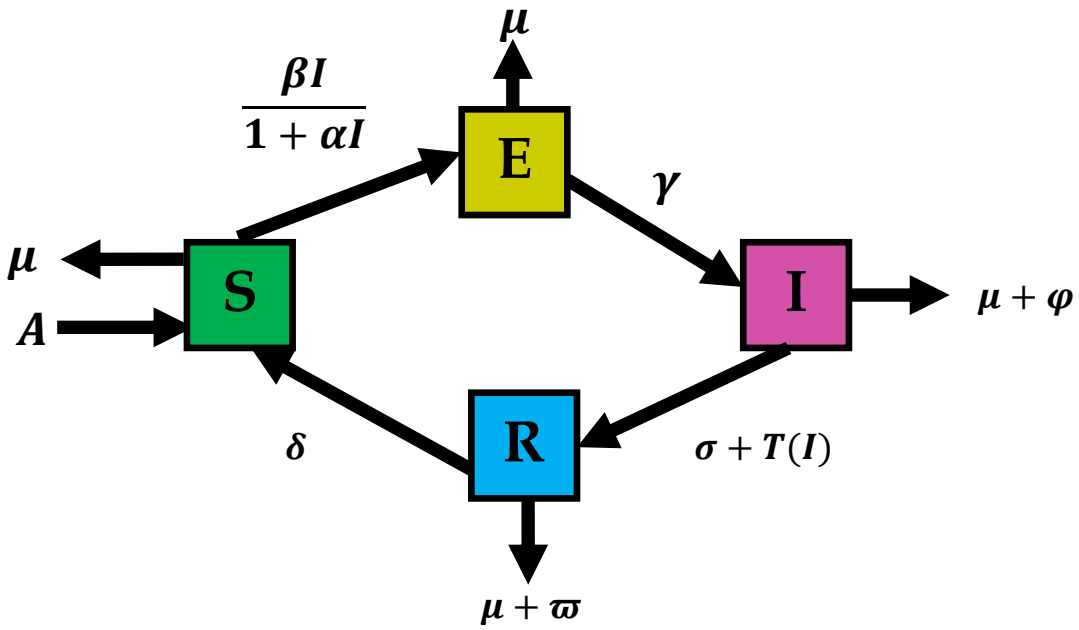

Figure 1. Schematic diagram of the model

We will now determine the feasible region for system (1). Summing up the three equations in (1) and letting $N = S + E + I + R$, we obtain

$$\begin{aligned} N' &= A - \mu(S + E + I + R) - \varphi I - \varpi R \\ &\leq A - \mu N. \end{aligned} \tag{2}$$

Then,

$$N(t) \leq N(0)e^{-\mu t} + \frac{A}{\mu}(1 - e^{-\mu t}).$$

From the above inequality, it follows that

$$\limsup_{t\to\infty} \big(S(t) + E(t) + I(t) + R(t)\big) = \limsup_{t\to\infty} N(t) \leq \frac{A}{\mu}. \tag{3}$$

Furthermore, $N^{'} < 0$ if $N > A/\mu$, so the solutions of the system are non-negative and bounded. This shows that the region

$$\Omega = \left\{(S, E, I, R) \in \mathbb{R}^4 : S + E + I + R \leq \frac{A}{\mu}, \qquad S \geq 0, E \geq 0, I \geq 0, R \geq 0\right\} \tag{4}$$

is positively invariant with respect to system (1). Therefore, the system is mathematically and epidemiologically well posed in Ω.

3. Dynamics near the disease-free equilibrium

We will now study the local dynamics of system (1) near the disease-free equilibrium. Thus, we will focus here on the case when $0 \leq I \leq I_0$, that is, when $T(I) = rI$. In that case, system (1) becomes

$$\begin{aligned} S^{'}(t) &= A - \mu S - \frac{\beta SI}{1 + \alpha I} + \delta R, \\ E^{'}(t) &= \frac{\beta SI}{1 + \alpha I} - (\gamma + \mu)E, \\ I^{'}(t) &= \gamma E - (\sigma + \mu + \varphi)I - rI, \\ R^{'}(t) &= \sigma I - (\delta + \mu + \varpi)R + rI. \end{aligned} \tag{5}$$

By simple calculation from the system (5), we obtain the equilibrium state where $S^{'}(t) = E^{'}(t) = I^{'}(t) = R^{'}(t) = 0$ (i.e., the left-hand side vanishes). Thus, any steady state (S^*, E^*, I^*, R^*) of system (5) satisfies the following algebraic system of equations:

$$\begin{aligned} S^* &= \frac{(A + \delta R^*)(1 + \alpha I^*)}{\mu(1 + \alpha I^*) + \beta I^*}, \qquad E^* = \frac{\beta I(A + \delta R^*)}{(\gamma + \mu)(\mu(1 + \alpha I^*) + \beta I^*)}, \\ I^* &= \frac{\gamma\beta I^*(A + \delta R^* - r)}{(\sigma + \mu + \varphi + r)(\gamma + \mu)(\mu(1 + \alpha I^*) + \beta I^*)}, \qquad R^* = \frac{(\sigma + r)I^*}{(\delta + \mu + \varpi)}. \end{aligned} \tag{6}$$

We can then obtain the following result.

Lemma 3.1.

The system (5) always has a disease-free equilibrium point $E^0 = \left(\frac{A}{\mu}, 0,0,0\right)$.

Proof:

At the disease-free equilibrium (DFE), when no disease outbreak occurs, no one is in the exposed or infected class and as such, no one is in the recovered class. Hence, we substitute $E^* = I^* = R^* = 0$ in the algebraic system (6), which reduces to $S^* = \frac{A}{\mu}$. Therefore, we conclude that $(S^*, E^*, I^*, R^*) = \left(\frac{A}{\mu}, 0,0,0\right) =: E^0$ is an equilibrium point of system (5).

3.1. Basic reproduction number

The basic reproduction number, denoted by R_0, represents the number of secondary cases that one infective individual generates over the course of its infectious period when introduced in a completely susceptible population. The threshold dynamics of R_0 helps epidemiologists to prove the following properties: (a) if $R_0 < 1$, the infection will die out with time, and (b) if $R_0 > 1$, the disease will become endemic in the population.

Next, we find the reproduction number R_0 of the system (1) by obtaining the Jacobian of the system and using the Next Generation Matrix Method (Driessche and Watmough (2002)).

The Jacobian of system (1) when $0 \le I \le I_0$ is given by

$$J(S^*, E^*, I^*, R^*) = \begin{bmatrix} -\left(\mu + \frac{\beta I}{1+\alpha I}\right) & 0 & -\frac{\beta S}{(1+\alpha I)^2} & \delta \\ \frac{\beta I}{1+\alpha I} & -(\gamma + \mu) & \frac{\beta S}{(1+\alpha I)^2} & 0 \\ 0 & \gamma & -(\sigma + \mu + \varphi + r) & 0 \\ 0 & 0 & \sigma + r & -(\delta + \mu + \varpi) \end{bmatrix}. \quad (7)$$

Evaluating the Jacobian matrix in the disease-free equilibrium $E^0 = \left(\frac{A}{\mu}, 0,0,0\right)$, we obtain

$$J\left(\frac{A}{\mu}, 0,0,0\right) = \begin{bmatrix} -\mu & 0 & -\frac{\beta A}{\mu} & \delta \\ 0 & -(\gamma + \mu) & \frac{\beta A}{\mu} & 0 \\ 0 & \gamma & -(\sigma + \mu + \varphi + r) & 0 \\ 0 & 0 & \sigma + r & -(\delta + \mu + \varpi) \end{bmatrix}. \quad (8)$$

The reproduction number R_0 can be computed as the spectral radius of the next generation matrix derived from the exposed and infected class, i.e.,

$$R_0 = \rho(K), \tag{9}$$

where $\rho(\cdot)$ denotes the spectral radius and $K = FV^{-1}$ is the next generation matrix, F is the matrix of new infections derived from the exposed and infected classes, and V is given by the remaining terms after F is taken.

Thus,

$$F = \begin{bmatrix} 0 & \frac{\beta A}{\mu} \\ 0 & 0 \end{bmatrix}, \qquad V = \begin{bmatrix} \gamma + \mu & 0 \\ -\gamma & \sigma + \mu + \varphi + r \end{bmatrix}.$$

Then,

$$V^{-1} = \begin{bmatrix} \frac{1}{\gamma + \mu} & 0 \\ \frac{\gamma}{(\gamma + \mu)(\sigma + \mu + \varphi + r)} & \frac{1}{\sigma + \mu + \varphi + r} \end{bmatrix},$$

and the next generation matrix of the system (1) is

$$K = FV^{-1} = \begin{bmatrix} \frac{\gamma\beta A}{\mu(\mu + \gamma)(\sigma + \mu + \varphi + r)} & \frac{\beta A}{\mu(\sigma + \mu + \varphi + r)} \\ 0 & 0 \end{bmatrix}.$$

The spectral radius is

$$\rho(K) = \frac{\gamma\beta A}{\mu(\mu + \gamma)(\sigma + \mu + \varphi + r)}.$$

Hence the basic reproduction number R_0 of system (1) is

$$R_0 = \frac{\gamma\beta A}{\mu(\mu + \gamma)(\sigma + \mu + \varphi + r)}. \tag{10}$$

3.2. Local stability analysis of the disease-free equilibrium

We will now examine the local stability of the DFE by the analysis of the eigenvalues of the Jacobian matrices of (1) at E^0 using the *Routh-Hurwitz Criterion*.

Theorem 3.2.

The disease-free equilibrium (E^0) is

(a) locally asymptotically stable if $R_0 < 1$;

(b) unstable if $R_0 > 1$.

Proof:

We recall that the Jacobian matrix of the system (1) at the disease-free equilibrium is given by (8). Hence, the characteristic equation of the system (1) at E^0 is

$$(\mu+\lambda)(\delta+\mu+\varpi+\lambda)\left[\lambda^2+(\gamma+\sigma+\varphi+r+2\mu)\lambda+(\sigma+\mu+\varphi+r)(\gamma+\ \mu)-\frac{\gamma\beta A}{\mu}\right] = 0. \tag{11}$$

We can see that $\lambda_1 = -\mu$ and $\lambda_2 = -(\delta+\mu+\varpi)$ are two roots of (11). The other roots of (11) are determined by the equation

$$\lambda^2+(\gamma+\sigma+\varphi+r+2\mu)\lambda+(\sigma+\mu+\varphi+r)(\gamma+\ \mu)-\frac{\gamma\beta A}{\mu}=0,$$

which has negative roots if and only if $(\sigma+\mu+\varphi+r)(\gamma+\ \mu)-\frac{\gamma\beta A}{\mu}>0$, and this is equivalent to the reproduction number R_0 being less than one. This implies that the disease-free equilibrium E^0 is locally asymptotically stable when $R_0<1$ and unstable when $R_0>1$. Hence, the proof is complete.

4. Existence of endemic equilibria

In this section, we consider the endemic equilibria of system (1). An endemic equilibrium of (1) satisfies the system

$$E=\frac{(\sigma+\mu+\varphi)I+T(I)}{\gamma},$$
$$R=\frac{\sigma I+T(I)}{\delta+\mu+\varpi},$$
$$S=\frac{(1+\alpha I)(\gamma+\mu)E}{\beta I},$$
$$A-\mu S+\delta R-(\gamma+\mu)E=0.$$

Suppose that $P^*(S^*,E^*,I^*,R^*)$ is an endemic equilibrium of (1). We consider first the case when $0<I^*\le I_0$. In this case, we have $T(I^*)=rI^*$, so P^* satisfies

$$E^*=\frac{(\sigma+\mu+\varphi+r)I^*}{\gamma},$$
$$R^*=\frac{(\sigma+r)I^*}{\delta+\mu+\varpi},$$
$$S^*=\frac{(1+\alpha I^*)(\gamma+\mu)(\sigma+\mu+\varphi+r)}{\beta\gamma}.$$

We substitute the above expressions in the equation $A - \mu S + \delta R - (\gamma + \mu)E = 0$ and obtain a linear equation in I, whose solution can be written as

$$I^* = \frac{\mu(\mu+\gamma)(\sigma+\mu+\varphi+r)(\delta+\mu+\varpi)(R_0-1)}{(\alpha\mu+\beta)(\mu+\gamma)(\delta+\mu+\varpi)(\sigma+\mu+\varphi+r) - \beta\gamma\delta(\sigma+r)}.$$

The denominator of the expression for I^* is always positive, while the numerator is positive if and only if $R_0 > 1$. The condition $I^* \leq I_0$ is equivalent to $R_0 \leq 1 + \frac{q_0}{p_0} I_0$, where

$$\begin{aligned} p_0 &= \mu(\mu+\gamma)(\sigma+\mu+\varphi+r)(\delta+\mu+\varpi), \\ q_0 &= (\alpha\mu+\beta)(\mu+\gamma)(\delta+\mu+\varpi)(\sigma+\mu+\varphi+r) - \beta\gamma\delta(\sigma+r). \end{aligned} \tag{12}$$

Hence, an endemic equilibrium $P^*(S^*, E^*, I^*, R^*)$ with $0 < I^* \leq I_0$ exists under the conditions $R_0 > 1$ and $R_0 \leq 1 + \frac{q_0}{p_0} I_0$.

We summarize this in the following result.

Theorem 4.1.

Assume that

$$1 < R_0 \leq 1 + \frac{q_0}{p_0} I_0,$$

where p_0 and q_0 are given by (12). Then system (1) has an endemic equilibrium $P^*(S^*, E^*, I^*, R^*)$ with $0 < I^* \leq I_0$.

Next, we study the endemic equilibria of (1) when $I > I_0$ and hence $T(I) = k$.
An endemic equilibrium (S, E, I, R) with $I > I_0$ satisfies

$$\begin{aligned} E &= \frac{(\sigma+\mu+\varphi)I + k}{\gamma}, \\ R &= \frac{\sigma I + k}{\delta+\mu+\varpi}, \\ S &= \frac{(1+\alpha I)(\gamma+\mu)\big((\sigma+\mu+\varphi)I + k\big)}{\beta\gamma I}. \end{aligned}$$

Substituting these expressions in the equation $A - \mu S + \delta R - (\gamma + \mu)E = 0$, we obtain the quadratic equation

$$A_1 I^2 + B_1 I + C_1 = 0, \tag{13}$$

where

$$A_1 = (\alpha\mu + \beta)(\delta + \mu + \varpi)(\sigma + \mu + \varphi)(\mu + \gamma) - \beta\gamma\delta\sigma > 0,$$
$$B_1 = \big(\alpha\mu k + \beta k + \mu(\sigma + \mu + \varphi)\big)(\delta + \mu + \varpi)(\mu + \gamma) - \beta\gamma A(\delta + \mu + \varpi) - \beta\gamma\delta k, \quad (14)$$
$$C_1 = \mu k(\delta + \mu + \varpi)(\mu + \gamma) > 0.$$

If $B_1 \geq 0$, then (13) does not have any positive solutions. Consider the case when $B_1 < 0$. Let $\Delta = {B_1}^2 - 4A_1C_1$. The solutions are given by

$$I_1 = \frac{-B_1 - \sqrt{\Delta}}{2A_1}, \qquad I_2 = \frac{-B_1 + \sqrt{\Delta}}{2A_1}.$$

These solutions are positive and distinct only when $\Delta > 0$. The two solutions coalesce into a double positive root when $\Delta = 0$. Lastly, (13) has no real solutions when $\Delta < 0$. Hence, we obtain the following result.

Theorem 4.2.

Let A_1, B_1 and C_1 be given by (14). Define $\Delta = {B_1}^2 - 4A_1C_1$,

$$I_1 = \frac{-B_1 - \sqrt{\Delta}}{2A_1}, \qquad I_2 = \frac{-B_1 + \sqrt{\Delta}}{2A_1},$$

and

$$S_i = \frac{(1 + \alpha I_i)(\gamma + \mu)\big((\sigma + \mu + \varphi)I_i + k\big)}{\beta\gamma I_i}, \qquad E_i = \frac{(\sigma + \mu + \varphi)I_i + k}{\gamma}, \qquad R_i = \frac{\sigma I_i + k}{\delta + \mu + \varpi}$$

for $i = 1,2$. Then $P_i(S_i, E_i, I_i, R_i)$ is an endemic equilibrium of (1) if and only if $B_1 < 0$, $\Delta \geq 0$ and $I_i > I_0$. Moreover, P_1 and P_2 coalesce into a single endemic equilibrium when $B_1 < 0$, $\Delta = 0$ and $I_1 = I_2 > I_0$.

5. Global stability of the disease-free equilibrium

In this section, we analyze the global stability of the disease-free equilibrium for system (1) using the method of Lyapunov functions, similar to Agrawal et al. (2017) and Badole et al. (2018).

Theorem 5.1.

Let

$$R_1 := 1 - \frac{r}{\sigma + \mu + \varphi + r}.$$

If $R_0 < R_1$, then the disease-free state equilibrium E^0 is globally asymptotically stable.

***Proof*:**

From the system of equations in (5), we have $\frac{dS}{dt} \leq A - \mu S$. A solution of the equation $\frac{dy}{dt} \leq A - \mu y$ is a maximal solution of $S(t)$. We recall that $y \to \frac{A}{\mu}$ as $t \to \infty$. By applying the comparison theorem, we obtain $S(t) \leq \frac{A}{\mu}$, also from the set

$$\Omega = \left\{(S, E, I, R) \in \mathbb{R}^4 : S + E + I + R \leq \frac{A}{\mu}, \qquad S \geq 0, E \geq 0, I \geq 0, R \geq 0\right\}$$

we have $I(t) \leq \frac{A}{\mu}$.

Define the Lyapunov function

$$L = \gamma E + (\gamma + \mu) I. \tag{15}$$

From $R_0 < 1 - \frac{r}{\sigma+\mu+\varphi+r}$, we have $\frac{\gamma\beta A}{\mu(\mu+\gamma)(\sigma+\mu+\varphi+r)} < \frac{\sigma+\mu+\varphi}{\sigma+\mu+\varphi+r}$, and then $\gamma\beta\left(\frac{A}{\mu}\right) - (\gamma + \mu)(\sigma + \mu + \varphi) < 0$.

We have thus $L' = \gamma E' + (\gamma + \mu) I'$, that is,

$$\begin{aligned} L' &= \gamma\left[\frac{\beta S I}{1 + \alpha I} - (\gamma + \mu) E\right] + (\gamma + \mu)[\gamma E - (\sigma + \mu + \varphi) I + T(I)] \\ &= \left[\frac{\gamma\beta S}{1+\alpha I} - (\gamma + \mu)(\sigma + \mu + \varphi)\right] I - (\gamma + \mu) T(I) \\ &\leq [\gamma\beta S - (\gamma + \mu)(\sigma + \mu + \varphi + r)] I. \end{aligned}$$

Recall that $S \leq \frac{A}{\mu}$. Therefore,

$$L' \leq \left[\gamma\beta\left(\frac{A}{\mu}\right) - (\gamma + \mu)(\sigma + \mu + \varphi)\right] I \leq 0$$

and $L' = 0$ if and only if $I = 0$. Thus, the largest compact invariant set contained in $\{(S, E, I, R) \in \Omega, L' = 0\}$ is the singleton $\{E^0\}$. Therefore, by Lasalle-Lyapunov Theorem, every solution that starts in Ω approaches E^0 as $t \to \infty$ and the proof is complete.

6. Local stability of endemic equilibria

We consider the local stability of the endemic equilibrium point $P^*(S^*, E^*, I^*, R^*)$ by analyzing the eigenvalues of the Jacobian matrices of (1) at the endemic equilibrium point using the *Routh-Hurwitz Criterion*.

Theorem 6.1.

Let $P^*(S^*, E^*, I^*, R^*)$ be an endemic equilibrium of (1) with $I^* \leq I_0$. Then P^* is locally asymptotically stable if and only if $a_3 > 0$, $a_4 > 0$ and $a_1 a_2 a_3 > {a_3}^2 + {a_1}^2 a_4$, where a_1, a_2, a_3 and a_4 are given in (17).

Proof:

When $I^* \leq I_0$, system (1) can be written as (5). The Jacobian of system (5) at the endemic state P^* is

$$J(S^*, E^*, I^*, R^*) = \begin{bmatrix} -\left(\mu + \frac{\beta I^*}{1+\alpha I^*}\right) & 0 & -\frac{\beta S^*}{(1+\alpha I^*)^2} & \delta \\ \frac{\beta I^*}{1+\alpha I^*} & -(\gamma + \mu) & \frac{\beta S^*}{(1+\alpha I^*)^2} & 0 \\ 0 & \gamma & -(\sigma+\mu+\varphi+r) & 0 \\ 0 & 0 & \sigma + r & -(\delta+\mu+\varpi) \end{bmatrix},$$

from which we obtain the characteristic equation

$$\lambda^4 + a_1\lambda^3 + a_2\lambda^2 + a_3\lambda + a_4 = 0, \tag{16}$$

where a_1, a_2, a_3, and a_4 are as defined below:

$$\begin{aligned} a_1 &= (\gamma + \sigma + \varphi + r + \delta + \varpi + 4\mu) + \frac{\beta I^*}{1+\alpha I^*}, \\ a_2 &= (\delta + \mu + \varpi)\left(\mu + \frac{\beta I^*}{1+\alpha I^*}\right) + (\gamma + \mu)\left(\delta + \varpi + 2\mu + \frac{\beta I^*}{1+\alpha I^*}\right) \\ &\quad + (\sigma + \mu + \varphi + r)\left(\gamma + \delta + \varpi + 3\mu + \frac{\beta I^*}{1+\alpha I^*}\right) - \frac{\gamma\beta S^*}{(1+\alpha I^*)^2}, \\ a_3 &= \left(\mu + \frac{\beta I^*}{1+\alpha I^*}\right)[(\delta + \mu + \varpi)(\gamma + \sigma + \varphi + r + 2\mu)] \\ &\quad + (\gamma + \mu)\left(\delta + \varpi + 2\mu + \frac{\beta S^*}{(1+\alpha I^*)^2}\right)(\sigma + \mu + \varphi + r) \\ &\quad - \frac{\gamma\beta S^*}{(1+\alpha I^*)^2}(\delta + \varpi + 2\mu), \\ a_4 &= \left(\mu + \frac{\beta I^*}{1+\alpha I^*}\right)(\gamma + \mu)(\delta + \mu + \varpi)(\sigma + \mu + \varphi + r) \\ &\quad + \frac{\gamma\beta}{1+\alpha I^*}\left[\frac{(\delta + \mu + \varpi)S^* I^*}{(1+\alpha I^*)^2}\right. \\ &\quad \left. - \left\{\frac{(\delta + \mu + \varpi)S^*}{1+\alpha I^*}\left(\mu + \frac{\beta I^*}{1+\alpha I^*}\right) + \rho(\gamma + \mu)I^*\right\}\right]. \end{aligned} \tag{17}$$

Notice that a_1 is always positive. Thus, by the Routh-Hurwitz criterion, we have that the endemic equilibrium $P^*(S^*, E^*, I^*, R^*)$ of (1) is locally asymptotically stable if and only if $a_3 > 0$, $a_4 > 0$ and $a_1 a_2 a_3 > {a_3}^2 + {a_1}^2 a_4$. Hence, the theorem follows.

Next, we discuss the local stability for the second case of the treatment function, that is, when $T(I) = k$, which corresponds to an equilibrium with $I^* > I_0$. In this case, we have the system

$$\begin{aligned} S'(t) &= A - \mu S - \frac{\beta SI}{1 + \alpha I} + \delta R, \\ E'(t) &= \frac{\beta SI}{1 + \alpha I} - (\gamma + \mu)E, \\ I'(t) &= \gamma E - (\sigma + \mu + \varphi)I - k, \\ R'(t) &= \sigma I - (\delta + \mu + \varpi)R + k. \end{aligned} \tag{18}$$

Theorem 6.2.

Let $P^*(S^*, E^*, I^*, R^*)$ be an endemic equilibrium of (1) with $I^* > I_0$. Then P^* is locally asymptotically stable if and only if $b_3 > 0$, $b_4 > 0$ and $b_1 b_2 b_3 > {b_3}^2 + {b_1}^2 b_4$, where b_1, b_2, b_3 and b_4 are given in (21).

Proof:

The Jacobian matrix of system (18) at P^* is

$$J = \begin{bmatrix} -\left(\mu + \frac{\beta I^*}{1 + \alpha I^*}\right) & 0 & -\frac{\beta S^*}{(1 + \alpha I^*)^2} & \delta \\ \frac{\beta I^*}{1 + \alpha I^*} & -(\gamma + \mu) & \frac{\beta S^*}{(1 + \alpha I^*)^2} & 0 \\ 0 & \gamma & -(\sigma + \mu + \varphi) & 0 \\ 0 & 0 & \sigma & -(\delta + \mu + \varpi) \end{bmatrix}, \tag{19}$$

from which we obtain the characteristic equation

$$\lambda^4 + b_1\lambda^3 + b_2\lambda^2 + b_3\lambda + b_4 = 0, \tag{20}$$

where b_1, b_2, b_3, and b_4 are as defined below:

$$\begin{aligned} b_1 &= (\gamma + \sigma + \varphi + \delta + \varpi + 4\mu) + \frac{\beta I^*}{1 + \alpha I^*}, \\ b_2 &= (\delta + \mu + \varpi)\left(\mu + \frac{\beta I^*}{1 + \alpha I^*}\right) + (\gamma + \mu)\left(\delta + \varpi + 2\mu + \frac{\beta I^*}{1 + \alpha I^*}\right) \\ &\quad + (\sigma + \mu + \varphi)\left(\gamma + \delta + \varpi + 3\mu + \frac{\beta I^*}{1 + \alpha I^*}\right) - \frac{\gamma\beta S^*}{(1 + \alpha I^*)^2}, \end{aligned} \tag{21}$$

$$b_3 = \left(\mu + \frac{\beta I^*}{1+\alpha I^*}\right)[(\delta+\mu+\varpi)\,(\gamma+\sigma+\varphi+2\mu)] + (\gamma+\mu)\left(\delta+\varpi+2\mu+\frac{\beta S^*}{(1+\alpha I^*)^2}\right)(\sigma+\mu+\varphi) - \frac{\gamma\beta S^*}{(1+\alpha I^*)^2}(\delta+\varpi+2\mu),$$

$$b_4 = \left(\mu + \frac{\beta I^*}{1+\alpha I^*}\right)(\gamma+\mu)(\delta+\mu+\varpi)\,(\sigma+\mu+\varphi) + \frac{\gamma\beta}{1+\alpha I^*}\left[\frac{(\delta+\mu+\varpi)S^*I^*}{(1+\alpha I^*)^2} - \left\{\frac{(\delta+\mu+\varpi)S^*}{1+\alpha I^*}\left(\mu+\frac{\beta I^*}{1+\alpha I^*}\right)+\rho(\gamma+\mu)I^*\right\}\right].$$

It follows from the above expression that b_1 is always positive. Thus, by the Routh-Hurwitz criterion, we have that the endemic equilibrium $P^*(S^*, E^*, I^*, R^*)$ of (1) is locally asymptotically stable if and only if $b_3 > 0$, $b_4 > 0$ and $b_1 b_2 b_3 > {b_3}^2 + {b_1}^2 b_4$. Hence, the theorem follows.

7. Global stability of endemic equilibria

In this following, we analyze the global stability of the endemic equilibria of system (1). For that, we need to prove first the following result on the uniform persistence of the model.

Lemma 7.1.

Assume that $R_0 > 1$. Then system (1) is uniformly persistent in the sense that there exists a positive constant C such that every solution (S, E, I, R) of (1) with initial condition $\big(S(0), E(0), I(0), R(0)\big) \in \Omega \setminus \partial\Omega$ satisfies

$$\liminf_{t\to\infty} S(t) \geq C, \qquad \liminf_{t\to\infty} E(t) \geq C, \qquad \liminf_{t\to\infty} I(t) \geq C, \qquad \liminf_{t\to\infty} R(t) \geq C,$$

where C is independent of the initial data.

Proof:

From Theorem 3.2, we know that the disease-free equilibrium E^0 is unstable when $R_0 > 1$. By Theorem 4.3 in Freedman et al. (1994), combined with the fact that $E^0 \in \partial\Omega$, we can see that the uniform persistence of the system is equivalent to instability of E^0. Hence, when $R_0 > 1$, system (1) is uniformly persistent. This completes the proof.

Now we will consider the global stability of the endemic equilibrium when $I^* \leq I_0$. To do this, we reduce the system of equations in (5) using $R(t) = \frac{A}{\mu} - S(t) - E(t) - I(t)$ to eliminate the $R(t)$ component from the first equation of system (5) to obtain a three-dimensional system given below:

(22)

$$S'(t) = \frac{A}{\mu}(\mu + \delta) - (\mu + \delta)S - \delta E - \delta I - \frac{\beta SI}{1 + \alpha I},$$
$$E'(t) = \frac{\beta SI}{1 + \alpha I} - (\gamma + \mu)E,$$
$$I'(t) = \gamma E - (\sigma + \mu + \varphi + r)I,$$

with initial conditions $S \geq 0$, $E \geq 0$, $I \geq 0$.

We consider the geometric approach due to Li and Muldowney **(**1996) to obtain the global stability of the endemic equilibrium and find the sufficient conditions for which the endemic equilibrium is globally asymptotically stable. We describe the geometric approach as follows.

We consider

$$x' = f(x), \tag{23}$$

where $f: D \to R^n$, $D \subset R^n$ is a simply connected open set and $f \in C^1(D)$.

Let x^* be an equilibrium of the equation (23), i.e., $f(x^*) = 0$. Assume that the following hypotheses hold.

$(Y1)$: There exists a compact absorbing set $K \subset D$.

$(Y2)$: Equation (23) has a unique equilibrium $x^* \in D$.

Let $P(x)$ be an $\binom{n}{2} \times \binom{n}{2}$ matrix valued function that is C^1 on D and consider

$$B = P_f P^{-1} + PJ^{[2]}P^{-1}, \tag{24}$$

where the matrix P_f is defined by

$$\left(p_{ij}(x)\right)_f = \left(\nabla p_{ij} \cdot f(x)\right), \tag{25}$$

$J(x) = Df(x)$ is the Jacobian matrix of system (23), and $J^{[2]}$ denotes the second additive compound matrix of J. Generally speaking, for an $n \times n$ matrix $J = (J_{ij})$, $J^{[2]}$ is an $\binom{n}{2} \times \binom{n}{2}$ matrix, and in the special case $n = 3$ one has

$$J^{[2]} = \begin{pmatrix} J_{11} + J_{22} & J_{23} & -J_{13} \\ J_{32} & J_{11} + J_{33} & J_{12} \\ -J_{31} & J_{21} & J_{22} + J_{33} \end{pmatrix}. \tag{26}$$

Consider the Lozinskiĭ measure $\mu(B)$ of B with respect of a vector norm $\|.\|$ in R^N, $N = \binom{n}{2}$, defined by

$$\mu(B) = \lim_{h\to 0^+} \frac{\|I + hB\| - 1}{h}. \tag{27}$$

Suppose that $(Y1)$ and $(Y2)$ hold and consider the condition

$$q := \lim_{t\to\infty} \sup \sup_{x_0 \in K} \frac{1}{t} \int_0^t \mu(B(x(s, x_0)))\, ds < 0. \tag{28}$$

It is shown in Li and Muldowney (1996) that, if D is simply connected, the condition $q < 0$ rules out the presence of any orbit that gives rise to a simple closed rectifiable curve that is invariant for (23), such as periodic orbits, homoclinic orbits and heteroclinic cycles. Moreover, it is robust under C^1 local perturbations of f near any non-equilibrium point that is non-wandering. In particular, it follows from Theorem 3.5 by Li and Muldowney **(**1996) that, if D is simply connected and assumptions $(Y1)$ and $(Y2)$ are satisfied, then the unique equilibrium x^* of (23) is globally asymptotically stable in D when $q < 0$.

For applying these results to our model, we will take $D = \Omega \setminus \partial\Omega$ (the interior of Ω). Lemma 7.1 guarantees the existence of a compact absorbing set $K \subset D$, so the assumption (Y1) always holds. Having established the above, we study the global stability of the endemic equilibrium P^* and obtain the following result.

Theorem 7.2.

Assume that $P^*(S^*, E^*, I^*, R^*)$ is an endemic equilibrium of (1), which is unique and satisfies $I^* \leq I_0$. Let

$$w_1 = \max\left\{\delta\frac{A}{\mu C} - (\delta + \mu), \quad -\delta, \quad -\gamma\right\}.$$

If $\mu - w_1 > 0$, then the endemic equilibrium P^* is globally asymptotically stable in $\Omega \setminus \partial\Omega$.

Proof:

See Appendix A.

We will now analyze the global stability of the endemic steady states when $I^* > I_0$. After reducing the system of equations in (18) using $R(t) = \frac{A}{\mu} - S(t) - E(t) - I(t)$, we eliminate the $R(t)$ component from the first equation of system (18) to obtain the three-dimensional model

$$\begin{aligned} S'(t) &= \frac{A}{\mu}(\mu + \delta) - (\mu + \delta)S - \delta E - \delta I - \frac{\beta SI}{1 + \alpha I}, \\ E'(t) &= \frac{\beta SI}{1 + \alpha I} - (\gamma + \mu)E, \end{aligned} \tag{29}$$

$$I^{'}(t) = \gamma E - (\sigma + \mu + \varphi)I - k,$$

with initial conditions $S \geq 0$, $E \geq 0$, $I \geq 0$. In this case, we obtain the following theorem.

Theorem 7.3.

Assume that $Q^*(S^*, E^*, I^*, R^*)$ is an endemic equilibrium of (1), which is unique and satisfies $I^* > I_0$. Let

$$w_2 = \max\left\{\delta\frac{A}{\mu C} - (\delta + \mu),\ \frac{k}{C} - \delta,\ \frac{k}{C} - \gamma\right\}.$$

If $\mu - w_2 > 0$, then the endemic equilibrium Q^* is globally asymptotically stable in $\Omega \setminus \partial\Omega$.

Proof:

See Appendix B.

8. Numerical simulations

In this section, we perform numerical simulations to determine how the dynamics of our model changes when some of the parameters are varied.

We will consider first the set of parameter values

$$A = 2000, \quad \mu = 2.4 \times 10^{-5}, \quad \sigma = \frac{1}{10}, \quad \gamma = \frac{1}{4}, \quad \alpha = \frac{1}{20000}, \quad r = 0.04,$$
$$\varphi = 0.01, \quad \varpi = 0.008, \quad \delta = \frac{1}{100}, \tag{30}$$

while β and I_0 are variable.

First, we consider the case when $I_0 = 400$. As the parameter β varies between 1.4404×10^{-9} and 3.2408×10^{-9}, the basic reproduction number R_0 varies between 0.8 and 1.8. The bifurcation diagram is shown in Figure 2. We can see that an endemic equilibrium P^* with less than 400 infected individuals appears for $R_0 \in (1, 1.03)$. Moreover, two other endemic equilibria, P_1 and P_2, may also appear, and they exist also for values of R_0 less than 1. The equilibria P_1 and P_2 coalesce into a single point at $R_0 = 0.9$.

If we keep the same parameter values as above but increase the treatment capacity by taking $I_0 = 2000$, we obtain the bifurcation diagram shown in Figure 3. In this case, there are no endemic equilibria for R_0 less than 1. An interesting feature that can be seen in the diagram is that there is a range of values ($1.16 < R_0 < 1.18$) where three endemic equilibria coexist: an endemic equilibrium P^* with less than 2000 infected individuals and two endemic equilibria (P_1 and P_2) with more than 2000 infected individuals.

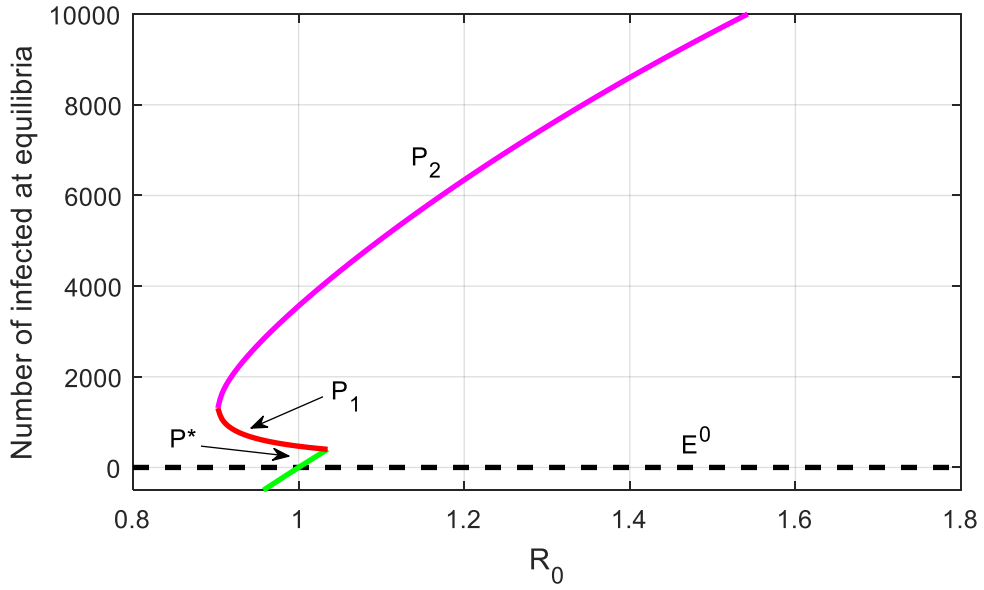

Figure 2. Bifurcation diagram of system (1) when the parameter values are given by (30) and $I_0 = 400$

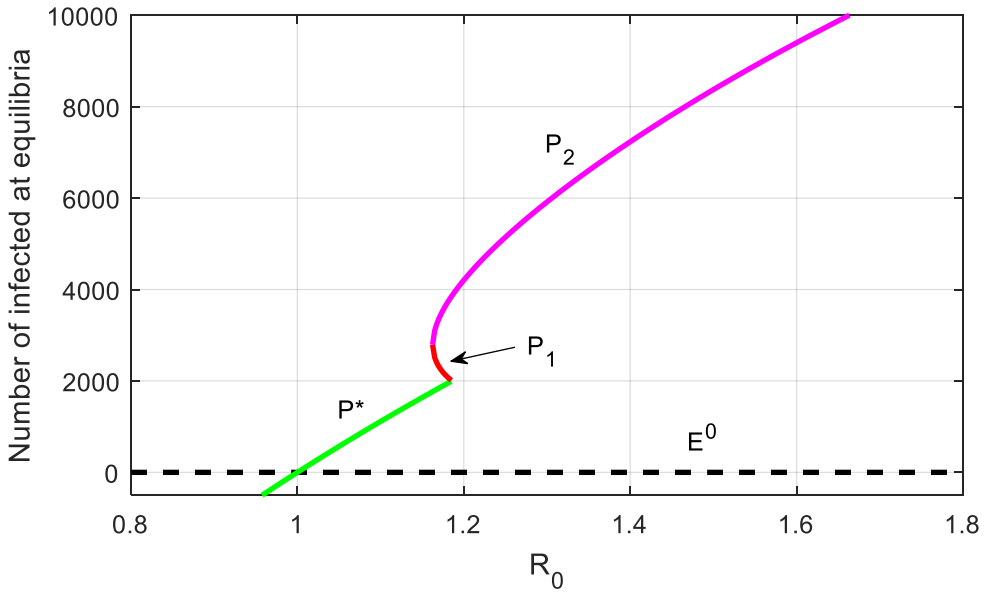

Figure 3. Bifurcation diagram of system (1) when the parameter values are given by (30) and $I_0 = 2000$

8.1 Effect of varying the treatment capacity

We will now carry out some simulations to show the importance of treatment capacity in the epidemic dynamics. We consider here the parameter values given by (30) with $\beta = 2.1 \times 10^{-9}$ and several values for the parameter I_0.

We integrate numerically the solutions of model (1) using the initial conditions

$$S(0) = 8 \times 10^7, \qquad E(0) = 100, \qquad I(0) = 100, \qquad R(0) = 0. \tag{31}$$

The resulting dynamics for the number of infected individuals $I(t)$ are shown in Figure 4. We can see that the infected population increases slowly at first, but then there is a sudden increase in infectious cases at the time when $I(t)$ reaches the value I_0. Moreover, the peak of the epidemic curve becomes higher when the treatment capacity is reduced.

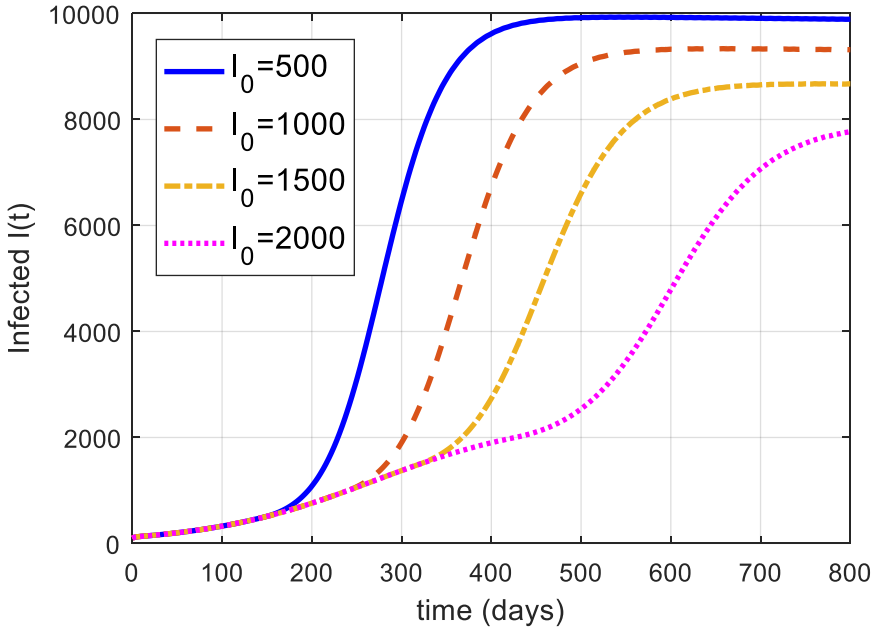

Figure 4. Solutions of system (1) with parameter values (30), $\beta = 2.1 \times 10^{-9}$, initial condition (31) and several values for the treatment capacity I_0

8.2 Effect of varying the immunity waning rate

Finally, we study the effect of varying the parameter δ, which represents the rate at which recovered individuals lose their immunity against COVID-19. The case $\delta = 0$ implies that immunity is permanent. When δ is positive, we can interpret $1/\delta$ as the duration of the immunity period.

For this section, we consider

(32)

$$A = 2000, \quad \mu = 2.4 \times 10^{-5}, \quad \sigma = \frac{1}{10}, \quad \gamma = \frac{1}{4}, \quad \alpha = \frac{1}{20000}, \quad r = 0.04,$$
$$\varphi = 0.01, \quad \varpi = 0.008, \quad \beta = 2.1 \times 10^{-9}, \quad I_0 \in \{500, 2000\}$$

and $\delta = 1/50, 1/100, 1/200, 0$ (days^{-1}).

Figure 5 shows the simulations for the infected population $I(t)$ when $I_0 = 500$ (left) and $I_0 = 2000$ (right). In both cases, the variations in the graphs are unnoticeable at the beginning of the epidemic, when $I(t)$ is still increasing. Once the epidemic curve reaches its peak and $I(t)$ starts to decrease, we can see that the number of infections becomes lower as the immunity period becomes longer (that is, for lower values of δ).

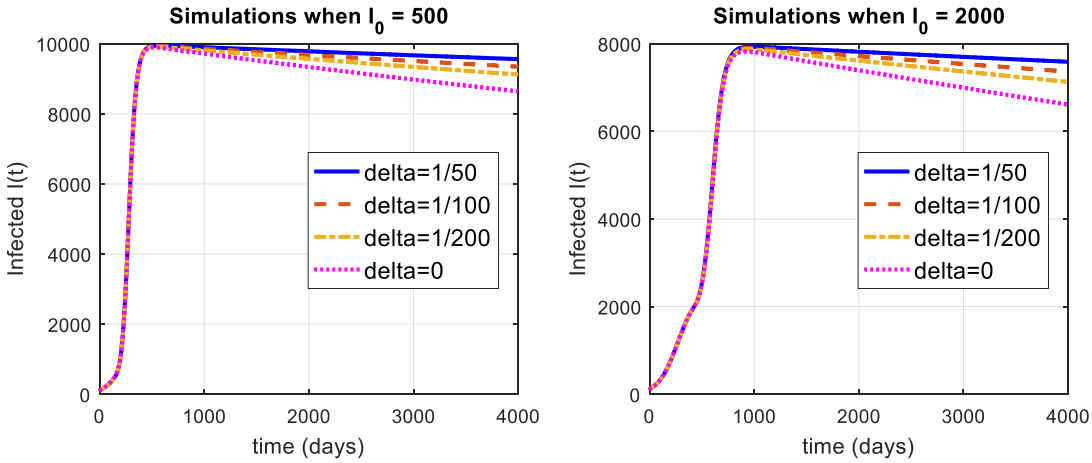

Figure 5. Solutions of system (1) with parameter values (32), initial condition (31) and several values for the immunity waning rate δ

9. Conclusion

The SEIRS model proposed in this work is novel, as it has not been previously studied. It is an extension of previous works: the major difference is that, while the SEIR and SEIRS models with piecewise linear treatment rate studied in the literature were not very specific on the dynamics of any disease, ours was focused on the novel coronavirus (COVID-19), and we include some parameters that are reflective of the dynamics of COVID-19, such as the disease-induced death rate and the death rate of the population under observation in various health facilities. We also generate new results on the numerical validation of our model such as bifurcation analysis to study factors that may favor an increase in cases and cause an overstretched healthcare system and how prompt response can save more lives when the available healthcare resources are in short supply.

Although the information regarding the immunity waning rate for COVID-19 varies, our simulations reveal that the value of such parameter does not affect the disease dynamics at the beginning of the epidemic, but its effect is only noticeable once the epidemic curve hits the peak and the population of the infectious decreases. Conclusively, our results show that, if the infected

population size exceeds the capacity of available medical facilities, the number of new infections will increase very rapidly and have a devastating effect in the population. The best way to prevent this is to reduce the contact rate between individuals through various interventions so that the reproduction number becomes sufficiently small. Hence, how long COVID-19 pandemic stays with us depends on how much we are willing to take responsibility as individuals and government.

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APPENDICES

Appendix A: Proof of Theorem 7.2

Since $I^* \leq I_0$, (S^*, E^*, I^*) is an equilibrium for system (22). The Jacobian matrix of system (22) is given as

$$J = \begin{pmatrix} -(\mu+\delta) - \frac{\beta I}{1+\alpha I} & -\delta & -\frac{\beta S}{(1+\alpha I)^2} - \delta \\ \frac{\beta I}{1+\alpha I} & -(\gamma+\mu) & \frac{\beta S}{(1+\alpha I)^2} \\ 0 & \gamma & -(\sigma+\mu+\varphi+r) \end{pmatrix}$$

and its second additive matrix is

$$J^{[2]} = \begin{pmatrix} -\left(\gamma+\delta+2\mu+\frac{\beta I}{1+\alpha I}\right) & \frac{\beta S}{(1+\alpha I)^2} & \frac{\beta S}{(1+\alpha I)^2}+\delta \\ \gamma & -\left(2\mu+\delta+\sigma+\varphi+r+\frac{\beta I}{1+\alpha I}\right) & -\delta \\ 0 & \frac{\beta I}{1+\alpha I} & -(\gamma+\sigma+\varphi+r+2\mu) \end{pmatrix}.$$

Choose the function $P = P(S,E,I) = \text{diag}\left(1, \frac{E}{I}, \frac{E}{I}\right)$. Then $P^{-1} = \text{diag}\left(1, \frac{I}{E}, \frac{I}{E}\right)$ and $P_f = \text{diag}\left(0, \frac{E'I - I'E}{I^2}, \frac{E'I - I'E}{I^2}\right)$.

Then,

$$P_f P^{-1} = \text{diag}\left(0, \frac{E'}{E} - \frac{I'}{I}, \frac{E'}{E} - \frac{I'}{I}\right),$$

$$PJ^{[2]}P^{-1} = \begin{pmatrix} -\left(\gamma+\delta+2\mu+\frac{\beta I}{1+\alpha I}\right) & \frac{\beta SI}{(1+\alpha I)^2E} & \frac{\beta SI}{(1+\alpha I)^2E}+\delta\frac{I}{E} \\ \frac{\gamma E}{I} & -\left(2\mu+\delta+\sigma+\varphi+r+\frac{\beta I}{1+\alpha I}\right) & -\delta \\ 0 & \frac{\beta I}{1+\alpha I} & -(\gamma+\sigma+\varphi+r+2\mu) \end{pmatrix}.$$

The matrix $B = P_f P^{-1} + PJ^{[2]}P^{-1}$ can be written in block form as

$$B = \begin{pmatrix} B_{11} & B_{12} \\ B_{21} & B_{22} \end{pmatrix},$$

where

$$B_{11} = -\left(\gamma+\delta+2\mu+\frac{\beta I}{1+\alpha I}\right), \qquad B_{12} = \left(\frac{\beta SI}{(1+\alpha I)^2E}, \ \frac{\beta SI}{(1+\alpha I)^2E}+\delta\frac{I}{E}\right),$$

$$B_{21} = \left(\frac{\gamma E}{I}, \quad 0\right)^T,$$

$$B_{22} = \begin{pmatrix} -\left(2\mu+\delta+\sigma+\varphi+r+\frac{\beta I}{1+\alpha I}\right)+\frac{E'}{E}-\frac{I'}{I} & -\delta \\ \frac{\beta I}{1+\alpha I} & -(\gamma+\sigma+\varphi+r+2\mu)+\frac{E'}{E}-\frac{I'}{I} \end{pmatrix}.$$

Let (u, v, w) be a vector in $\mathbb{R}^3$, its norm $\|\cdot\|$ is defined as

$$\|(u, v, w)\| = \max\{|u|, |v| + |w|\}.$$

Let $\mu(B)$ be the Lozinskiĭ measure with respect to this norm. Thus, we have

$$\mu(B) \leq \sup\{g_1, g_2\},$$

where $g_1 = \mu_1(B_{11}) + |B_{12}|$ and $g_2 = \mu_2(B_{22}) + |B_{21}|$. Here, $\mu_1(B_{11}) = B_{11}$, $|B_{12}|$ and $|B_{21}|$ are matrix norms with respect to l_1 vector norm, and μ_2 denotes the Lozinskiĭ measure with respect to l_1 vector norm. Then,

$$\mu_1(B_{11}) = -\left(\gamma+\delta+2\mu+\frac{\beta I}{1+\alpha I}\right),$$

$$|B_{12}| = \max\left(\frac{\beta SI}{(1+\alpha I)^2E}, \quad \frac{\beta SI}{(1+\alpha I)^2E}+\delta\frac{I}{E}\right) = \frac{\beta SI}{(1+\alpha I)^2E}+\delta\frac{I}{E},$$

$$|B_{21}| = \frac{\gamma E}{I}.$$

Note that since B_{11} is a scalar, its Lozinskiĭ measure with respect to any vector norm μ_1 is equal to B_{11}. Now, we calculate $\mu_2(B_{22})$ by taking the maximum of the two diagonal elements of B_{22}, that is,

$$\mu_2(B_{22}) = \max\left\{-\left(2\mu + \delta + \sigma + \varphi + r + \frac{\beta I}{1+\alpha I}\right) + \frac{E'}{E} - \frac{I'}{I}, \right.$$
$$\left. -(\gamma + \sigma + \varphi + r + 2\mu) + \frac{E'}{E} - \frac{I'}{I}\right\}$$
$$= \frac{E'}{E} - \frac{I'}{I} - (2\mu + \sigma + \varphi + r) + \max\{-\delta, -\gamma\}.$$

Therefore, we have

$$g_1 = \mu_1(B_{11}) + |B_{12}| = -\left(\gamma + \delta + 2\mu + \frac{\beta I}{1+\alpha I}\right) + \frac{\beta SI}{(1+\alpha I)^2 E} + \delta\frac{I}{E},$$
$$g_2 = \mu_2(B_{22}) + |B_{21}| = \frac{E'}{E} - \frac{I'}{I} - (2\mu + \sigma + \varphi + r) + \max\{-\delta, -\gamma\} + \frac{\gamma E}{I}.$$

From the system of equations in (5), we have

$$\frac{E'}{E} = \frac{\beta SI}{(1+\alpha I)E} - (\gamma + \mu) \quad \text{and} \quad \frac{I'}{I} = \frac{\gamma E}{I} - (\sigma + \mu + \varphi + r).$$

Then

$$g_1 \le \frac{\beta SI}{(1+\alpha I)E} - (\gamma + \mu) - \left(\delta + \mu + \frac{\beta I}{1+\alpha I}\right) + \delta\frac{I}{E}$$
$$= \frac{E'}{E} - \left(\delta + \mu + \frac{\beta I}{1+\alpha I}\right) + \delta\frac{I}{E},$$
$$g_2 = \frac{E'}{E} - \mu + \max\{-\delta, -\gamma\},$$

From this and $\mu(B) \le \sup\{g_1, g_2\}$, we obtain

$$\mu(B) \le \sup\left\{\frac{E'}{E} - \left(\delta + \mu + \frac{\beta I}{1+\alpha I}\right) + \delta\frac{I}{E}, \quad \frac{E'}{E} - \mu + \max\{-\delta, -\gamma\}\right\}$$
$$= \frac{E'}{E} - \mu + \max\left\{\delta\frac{I}{E} - \left(\delta + \mu + \frac{\beta I}{1+\alpha I}\right), \quad -\delta, \quad -\gamma\right\}$$
$$\le \frac{E'}{E} - \mu + \max\left\{\delta\frac{A}{\mu C} - (\delta + \mu), \quad -\delta, \quad -\gamma\right\},$$

where we have used that $0 < I \le A/\mu$ and $\liminf_{t\to\infty} E(t) \ge C$.

Set $w_1 = \max\left\{\delta\frac{A}{\mu C} - (\delta + \mu),\ -\delta,\ -\gamma\right\}$. Then,

$$\mu(B) \leq \frac{E'}{E} - (\mu - w_1).$$

Integrating both sides simultaneously, we have

$$\frac{1}{t}\int_0^t \mu(B)\,ds \;\leq\; \frac{1}{t}\ln\frac{E(t)}{E(0)} - (\mu - w_1),$$

so

$$\lim_{t\to\infty}\sup\sup_{x_0\in K}\frac{1}{t}\int_0^t \mu(B)\,ds \leq\; -(\mu - w_1) < 0$$

by the hypothesis $\mu - w_1 > 0$. Thus, by Theorem 3.5 in Li and Muldowney **(**1996), we conclude that P^* is globally asymptotically stable in $D = \Omega \setminus \partial\Omega$.

Appendix B: Proof of Theorem 7.3

Since $I^* > I_0$, Q^* is an equilibrium for system (29). The Jacobian matrix of system (29) is given as

$$J = \begin{pmatrix} -(\mu+\delta) - \dfrac{\beta I}{1+\alpha I} & -\delta & -\dfrac{\beta S}{(1+\alpha I)^2} - \delta \\ \dfrac{\beta I}{1+\alpha I} & -(\gamma+\mu) & \dfrac{\beta S}{(1+\alpha I)^2} \\ 0 & \gamma & -(\sigma+\mu+\varphi) \end{pmatrix}$$

and its second additive matrix is

$$J^{[2]} = \begin{pmatrix} -\left(\gamma+\delta+2\mu+\dfrac{\beta I}{1+\alpha I}\right) & \dfrac{\beta S}{(1+\alpha I)^2} & \dfrac{\beta S}{(1+\alpha I)^2} + \delta \\ \gamma & -\left(2\mu+\delta+\sigma+\varphi+\dfrac{\beta I}{1+\alpha I}\right) & -\delta \\ 0 & \dfrac{\beta I}{1+\alpha I} & -(\gamma+\sigma+\varphi+2\mu) \end{pmatrix}.$$

Choose the function $Q = Q(S,E,I) = \operatorname{diag}\left(1, \frac{E}{I}, \frac{E}{I}\right)$. Then $Q^{-1} = \operatorname{diag}\left(1, \frac{I}{E}, \frac{I}{E}\right)$ and $Q_f = \operatorname{diag}\left(0, \frac{E'I - I'E}{I^2}, \frac{E'I - I'E}{I^2}\right)$.

Then,

$$Q_f Q^{-1} = \operatorname{diag}\left(0, \frac{E'}{E} - \frac{I'}{I}, \frac{E'}{E} - \frac{I'}{I}\right),$$

$$PJ^{[2]}P^{-1} = \begin{pmatrix} -\left(\gamma + \delta + 2\mu + \frac{\beta I}{1+\alpha I}\right) & \frac{\beta SI}{(1+\alpha I)^2 E} & \frac{\beta SI}{(1+\alpha I)^2 E} + \delta\frac{I}{E} \\ \frac{\gamma E}{I} & -\left(2\mu + \delta + \sigma + \varphi + \frac{\beta I}{1+\alpha I}\right) & -\delta \\ 0 & \frac{\beta I}{1+\alpha I} & -(\gamma + \sigma + \varphi + 2\mu) \end{pmatrix}.$$

The matrix $C = Q_f Q^{-1} + QJ^{[2]}Q^{-1}$ can be written in block form as

$$C = \begin{pmatrix} C_{11} & C_{12} \\ C_{21} & C_{22} \end{pmatrix},$$

where

$$C_{11} = -\left(\gamma + \delta + 2\mu + \frac{\beta I}{1+\alpha I}\right), \qquad C_{12} = \left(\frac{\beta SI}{(1+\alpha I)^2 E}, \frac{\beta SI}{(1+\alpha I)^2 E} + \delta\frac{I}{E}\right),$$

$$C_{21} = \left(\frac{\gamma E}{I}, 0\right)^T,$$

$$C_{22} = \begin{pmatrix} -\left(2\mu + \delta + \sigma + \varphi + \frac{\beta I}{1+\alpha I}\right) + \frac{E'}{E} - \frac{I'}{I} & -\delta \\ \frac{\beta I}{1+\alpha I} & -(\gamma + \sigma + \varphi + 2\mu) + \frac{E'}{E} - \frac{I'}{I} \end{pmatrix}.$$

Let (u, v, w) be a vector in $\mathbb{R}^3$, its norm $\|\cdot\|$ is defined as

$$\|(u, v, w)\| = \max\{|u|, |v| + |w|\}.$$

Let $\mu(C)$ be the Lozinskiĭ measure with respect to this norm. Thus, we have

$$\mu(C) \leq \sup\{f_1, f_2\},$$

where $f_1 = \mu_1(C_{11}) + |C_{12}|$ and $f_2 = \mu_2(C_{22}) + |C_{21}|$. Here, $\mu_1(C_{11}) = C_{11}$, $|C_{12}|$ and $|C_{21}|$ are matrix norms with respect to l_1 vector norm, and μ_2 denotes the Lozinskiĭ measure with respect to l_1 vector norm. Then,

$$\mu_1(C_{11}) = -\left(\gamma + \delta + 2\mu + \frac{\beta I}{1+\alpha I}\right),$$

$$|C_{12}| = \max\left(\frac{\beta SI}{(1+\alpha I)^2 E}, \quad \frac{\beta SI}{(1+\alpha I)^2 E} + \delta\frac{I}{E}\right) = \frac{\beta SI}{(1+\alpha I)^2 E} + \delta\frac{I}{E},$$

$$|C_{21}| = \frac{\gamma E}{I}.$$

Note that since C_{11} is a scalar, its Lozinskiĭ measure with respect to any vector norm μ_1 is equal to C_{11}. Now, we calculate $\mu_2(C_{22})$, by taking the maximum of the two diagonal elements of C_{22}, that is,

$$\mu_2(C_{22}) = \max\left\{-\left(2\mu+\delta+\sigma+\varphi+\frac{\beta I}{1+\alpha I}\right)+\frac{E'}{E}-\frac{I'}{I}, \quad -(\gamma+\sigma+\varphi+2\mu)+\frac{E'}{E}-\frac{I'}{I}\right\}$$
$$= \frac{E'}{E}-\frac{I'}{I}-(2\mu+\sigma+\varphi)+\max\{-\delta,-\gamma\}.$$

Therefore, we have

$$f_1 = \mu_1(C_{11}) + |C_{12}| = -\left(\gamma+\delta+2\mu+\frac{\beta I}{1+\alpha I}\right)+\frac{\beta SI}{(1+\alpha I)^2 E}+\delta\frac{I}{E},$$
$$f_2 = \mu_2(C_{22}) + |C_{21}| = \frac{E'}{E}-\frac{I'}{I}-(2\mu+\sigma+\varphi)+\max\{-\delta,-\gamma\}+\frac{\gamma E}{I}.$$

From the system of equations in (18), we have

$$\frac{E'}{E} = \frac{\beta SI}{(1+\alpha I)E}-(\gamma+\mu) \quad \text{and} \quad \frac{I'}{I} = \frac{\gamma E}{I}-(\sigma+\mu+\varphi)-\frac{k}{I}.$$

Then,

$$f_1 \le \frac{\beta SI}{(1+\alpha I)E}-(\gamma+\mu)-\left(\delta+\mu+\frac{\beta I}{1+\alpha I}\right)+\delta\frac{I}{E}$$
$$= \frac{E'}{E}-\left(\delta+\mu+\frac{\beta I}{1+\alpha I}\right)+\delta\frac{I}{E},$$
$$f_2 = \frac{E'}{E}-\mu+\max\{-\delta,-\gamma\}+\frac{k}{I},$$

From this and $\mu(C) \le \sup\{f_1, f_2\}$, we obtain

$$\mu(C) \le \sup\left\{\frac{E'}{E}-\left(\delta+\mu+\frac{\beta I}{1+\alpha I}\right)+\delta\frac{I}{E}, \quad \frac{E'}{E}-\mu+\max\{-\delta,-\gamma\}+\frac{k}{I}\right\}$$
$$= \frac{E'}{E}-\mu+\max\left\{\delta\frac{I}{E}-\left(\delta+\mu+\frac{\beta I}{1+\alpha I}\right), \quad \frac{k}{I}-\delta, \quad \frac{k}{I}-\gamma\right\}$$
$$\le \frac{E'}{E}-\mu+\max\left\{\delta\frac{A}{\mu C}-(\delta+\mu), \quad \frac{k}{C}-\delta, \quad \frac{k}{C}-\gamma\right\},$$

where we have used that $0 < I \le A/\mu$, $\liminf_{t\to\infty} E(t) \ge C$ and $\liminf_{t\to\infty} I(t) \ge C$.

Set $w_2 = \max\left\{\delta\frac{A}{\mu C}-(\delta+\mu), \ \frac{k}{C}-\delta, \ \frac{k}{C}-\gamma\right\}$. Then,

$$\mu(C) \leq \frac{E'}{E} - (\mu - w_2).$$

Integrating both sides simultaneously, we have

$$\frac{1}{t}\int_0^t \mu(C)\,ds \;\leq\; \frac{1}{t}\ln\frac{E(t)}{E(0)} - (\mu - w_2),$$

so

$$\lim_{t\to\infty}\sup\sup_{x_0\in K}\frac{1}{t}\int_0^t \mu(C)\,ds \leq\; -(\mu - w_1) < 0$$

by the hypothesis $\mu - w_2 > 0$. Thus, by Theorem 3.5 in Li and Muldowney **(**1996), we conclude that Q^* is globally asymptotically stable in $D = \Omega \setminus \partial\Omega$.