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A Mathematical Modeling of the Vaccination Effect on the SARS-CoV-2 Transmission: Analysis and Simulation

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Abstract

Several illustrative studies on the mathematical modeling and analysis of the Coronavirus have been carried out in a short period of time. There is not enough work that accounts for the vaccination campaign's two stages. In this work, a mathematical model is created to show the impact of the recent two-stage vaccination treatment on the Coronavirus. In the proposed model, five compartments are constructed, namely the susceptible individuals $S(t)$, the first dose of vaccination $V_1(t)$, the second dose of vaccination $V_2(t)$, infected $I(t)$ and recovered population $R(t)$. The uniqueness, boundedness and existence of the solutions of this model have been discussed. All potential model equilibrium points are determined. The local as well as global stability of the system in terms of the basic reproduction number is investigated. Numerical simulation is also carried out to investigate the influence of parameters affecting the dynamics of the model and to support the gathered analytical findings of the model.

Keywords: SARS-CoV-2, Vaccination, Mathematical model, Stability.

نمذجة رياضية لتأثير التطعيم على انتقال فيروس كوفيد 19: التحليل والمحاكاة

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الخلاصة

هناك العديد من النماذج الرياضية لدراسة انتشار وباء فيروس كورونا في الفترة التي مضت . لا يوجد عمل كافا فسر وجود مرحلتين من التطعيم. في هذا العمل، تم إنشاء نموذج رياضي لمناقشة تأثير التطعيم على مرحلتين للتحكم بانتشار الفيروس. تم بناء النموذج المقترح من خمسة مكونات تدعى الافراد المعرضين للإصابة، الافراد الملقحين بالجرعة الاولى، الافراد الملقحين بالجرعة الثانية، الافراد المصابين واخيرا المتعافين. تمت مناقشة وحدانية وجود الحل. تم ايجاد جميع نقاط التوازن المحتملة للنموذج. اقترحنا الاستقرار المحلي والكللي للنظام بواسطة رقم الاستنتاج الاساسي. وأخيرا، تم إجراء المحاكاة العددية لدراسة تأثير المعلمات على ديناميات النموذج المقترح ودعم النتائج التحليلية.

1. Introduction

There is a great interest in mathematical epidemiological models due to the important tools for understanding and studying the spread of epidemics such as HIV, HBV, Ebola, H1N1 and malaria. It is also employed to control the spread of outbreaks in the population is a major challenge. On the other hand, the world continues are to fight existing infectious diseases, while the changing world conditions lead to the emergence of different types of viruses. The newest of these viruses, and the most effective in recent two years, is the new type of coronavirus which is called COVID-19 a contagious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The first known case was identified in Wuhan, China, in December 2019 [1]. The disease has spread worldwide, and leading to an ongoing pandemic. Symptoms of COVID-19 are variable but often include fever, cough, headache, fatigue, breathing difficulties, and loss of smell and taste. Symptoms may begin one to fourteen days after exposure to the virus. At least, a third of people who are infected do not develop noticeable symptoms. For those people who develop symptoms noticeable enough to be classed as patients, most (81%) develop mild to moderate symptoms (up to mild pneumonia), while 14% of them develop severe symptoms (dyspnea, hypoxia, or more than 50% lung involvement on imaging), and 5% suffer critical symptoms (respiratory failure, shock) [2]. Older people are at a higher risk of developing severe symptoms. Some people continue to experience a range of effects (long COVID) which is a condition characterized by long-term consequences persisting or appearing after the typical convalescence period of COVID-19. It is also known as post-COVID-19 syndrome, a post-COVID-19 condition for months after recovery, and damage to organs have been observed. Multi-studies yearly are underway to further investigate the long-term effects of the disease. The World Health Organization instructed all citizens in the world to take precautions and measures, it repeatedly stressed to take the vaccine in order to reduce infection with the virus. This is because vaccines save millions of lives each year [3]. The idea of mathematical modeling has risen in importance during the past few years. Nowadays, mathematics is very closely linked to daily life, and this connection gives significance to the embodiment of this abstract science [4] , [5] . Numerous academic investigations into the mathematical model of the COVID-19 pandemic have been completed in a short time. Among these studies, Mohsen et al. [6] studied a mathematical model for the dynamics of the COVID-19 pandemic involving infective immigrants. Mohsen et al. [7] studied the global stability of the COVID-19 model involving the quarantine strategy and media coverage effects. Zu, J. et al. [8] examined the COVID-19 transmission patterns in mainland China and the effectiveness of various control measures. Tang et al. [9] studied the effectiveness of quarantine and isolation to determine the trend of the COVID-19 epidemic in the final phase of the current outbreak in china. Ahmed et al. [10] studied the analysis coronavirus model using a numerical and logistic model. Hattaf et al. [11] studied modeling the dynamics of COVID-19 with carrier effect and environmental contamination. Yavuz et al. [12] studied the vaccination and mathematical modeling of COVID-19. In addition, a number of modeling studies have been conducted in relation to COVID-19 and other significant infectious diseases, see [13 - 25].

In this work, a mathematical model involves two stages of vaccination and the dynamics of the COVID-19 pandemic are also presented and analyzed. This work is organized as follows; section 2 illustrates the mathematical modeling of the novel coronavirus and two stages of the vaccination. Section 3 discusses the boundedness of the solution and the existence of equilibrium points of the model among other fundamental characteristics. In section 4, the local stability analysis is investigated utilizing Gersgorin's theorem. In section 5, the global stability of the proposed model at all equilibrium points is analyzed by using the Lyapunov function. Finally, section 6 uses numerical simulation to assess the effects of altering all system parameters.

2. Mathematical Model

In this part, we formulate a mathematical model of the COVID-19 pandemic that describes the dynamics of two stages of vaccination, namely infection of individuals and recovery of those infected by the virus. The rest of the parameters are shown in the following table.

Table 1: Parameters description utilized in the system (1)

Parameters	Interpretation
$S(t)$	Susceptible population
$V_i(t), i = 1, 2.$	Individuals vaccinated of the susceptible population
$I(t)$	infected population
$R(t)$	Recovered population
Λ	Birth rate.
n	Fear rate of the vaccine.
α, γ	The vaccination rates.
β_1	The contact rate between the susceptible and infected population.
μ	Natural death rate.
β_2	The contact rate between the vaccinated individuals of the first dose with infected population.
β_3	The contact rate between the vaccinated individuals of the second dose with infected population. $\beta_3 < \beta_2 < \beta_1.$
μ_1	Death rate due to disease.
θ	Recovery rate from the disease.

Therefore, the dynamics of the above proposed model can be represented by the following set of the first order non-linear differential equations. The block diagram of this model system can be illustrated in Figure 1.

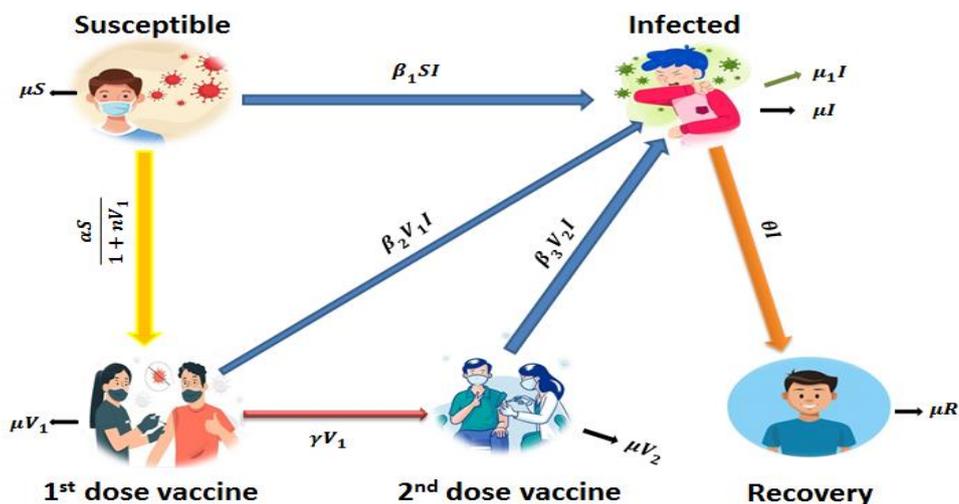


Figure 1: the block diagram of system (1).

$$\begin{aligned}
\frac{dS}{dt} &= \Lambda - \frac{\alpha S}{1+nV_1} - \beta_1 SI - \mu S \\
\frac{dV_1}{dt} &= \frac{\alpha S}{1+nV_1} - \gamma V_1 - \beta_2 V_1 I - \mu V_1 \\
\frac{dV_2}{dt} &= \gamma V_1 - \beta_3 V_2 I - \mu V_2 \\
\frac{dI}{dt} &= \beta_1 SI + \beta_2 V_1 I + \beta_3 V_2 I - (\mu + \mu_1)I - \theta I \\
\frac{dR}{dt} &= \theta I - \mu R
\end{aligned}
\tag{1}$$

with the initial conditions,

$$S(0) > 0, V_1(0) \geq 0, V_2(0) \geq 0, I(0) \geq 0, R(0) \geq 0.$$

Where $(S(t), V_1(t), V_2(t), I(t), R(t)) \in R_+^5$. Suppose that the functions $S(t), V_1(t), V_2(t), I(t), R(t)$ and their derivatives are continuous for all $t \geq 0$. Therefore, these functions are Lipschitzain on R_+^5 , and the solution of the system (1) exists and unique. In the next theorem, the bounds of the solution of the system (1) in R_+^5 have been established.

Theorem (1): All solutions of system (1) that are initial in R_+^5 are uniformly bounded.

Proof:

Let $(S(t), V_1(t), V_2(t), I(t), R(t))$ be solutions of the system (1) with non(-ve) initial conditions $(S(0), V_1(0), V_2(0), I(0), R(0))$, and let

$$\begin{aligned}
H(t) &= S(t) + V_1(t) + V_2(t) + I(t) + R(t), \text{ then} \\
\frac{dH}{dt} &= \frac{dS}{dt} + \frac{dV_1}{dt} + \frac{dV_2}{dt} + \frac{dI}{dt} + \frac{dR}{dt}.
\end{aligned}$$

Therefore, we can easily get:

$$\frac{dH}{dt} \leq \Lambda - \mu H$$

By using Gronwall's lemma [26], we obtain the following

$$H(t) \leq \frac{\Lambda}{\mu} + \left(H_0 - \frac{\Lambda}{\mu}\right) e^{-\mu t}.$$

Where $H_0 = (S(0), V_1(0), V_2(0), I(0), R(0))$.

Therefore, $(t) \leq \frac{\Lambda}{\mu}$, as $t \rightarrow \infty$.

3. Existence of the equilibrium points and basic reproduction number

We note that the variable R , which represents the recovery rate, does not appear in the first four equations of the system (1), thus one can solve the following system instead of the system (1), and then substitute the solution value of I in the fifth equation of the system (1) to solving it separately as a linear differential equation with respect to the variable R , we got the solution of the fifth equation at $t \rightarrow \infty$, can be written as

$$R(t) = \frac{\theta \check{I}}{\mu}, \tag{2}$$

where \check{I} represents the solution values of the system (3) that is given below.

Accordingly, the following system will be study instead of the system (1).

$$\begin{aligned}
\frac{dS}{dt} &= \Lambda - \frac{\alpha S}{1+nV_1} - \beta_1 SI - \mu S \\
\frac{dV_1}{dt} &= \frac{\alpha S}{1+nV_1} - \gamma V_1 - \beta_2 V_1 I - \mu V_1 \\
\frac{dV_2}{dt} &= \gamma V_1 - \beta_3 V_2 I - \mu V_2 \\
\frac{dI}{dt} &= \beta_1 SI + \beta_2 V_1 I + \beta_3 V_2 I - (\mu + \mu_1)I - \theta I
\end{aligned}
\tag{3}$$

System (3) has six equilibrium points which are as follows:

- The first equilibrium point (FEP) which is denoted by $E_0 = (\bar{S}, 0, 0, 0)$, when $\alpha = 0$,

where

$$\bar{S} = \Lambda/\mu \quad (4)$$

• The second equilibrium point (SEP) which is denoted by $E_1 = (\bar{S}, \bar{V}_1, 0, 0)$ when $\gamma = 0$, where

$$\bar{S} = \frac{\Lambda(1+n\bar{V}_1)}{\alpha+\mu(1+n\bar{V}_1)} \quad (5)$$

while \bar{V}_1 represents a non-negative root of the following polynomial.

$$W_1V_1^2 + W_2V_1 + W_3 = 0 \quad (6)$$

Where

$$V_1 = \frac{-W_2 + \sqrt{W_2^2 - 4W_1W_3}}{2W_1}$$

$$W_1 = n\mu^2 > 0,$$

$$W_2 = \mu^2 + \alpha\mu,$$

$$W_3 = -\alpha\Lambda < 0.$$

• The third equilibrium point (TEP) which is denoted by $E_2 = (\hat{S}, 0, 0, \hat{I})$ when $\alpha = 0$,

Where

$$\hat{S} = \frac{\Lambda}{\beta_1\hat{I} + \mu} \quad (7)$$

$$\hat{I} = \frac{\beta_1\Lambda - u_1}{u_2} \quad (8)$$

with $u_1 = \mu(\mu + \mu_1 + \theta)$ and $u_2 = \beta_1(\mu + \mu_1 + \theta)$ exists under the following condition:
 $u_1 < \beta_1\Lambda$. (9)

• The fourth equilibrium point (FOEP) which is denoted by $E_3 = (\check{S}, \check{V}_1, \check{V}_2, 0)$,

where

$$\check{S} = \frac{\Lambda(1+n\check{V}_1)}{\alpha+\mu(1+n\check{V}_1)} \quad (10)$$

$$\check{V}_2 = \frac{\gamma\check{V}_1}{\mu} \quad (11)$$

while \check{V}_1 represents a non-negative root of the following polynomial

$$Q_1V_1^2 + Q_2V_1 + Q_3 = 0 \quad (12)$$

Where

$$V_1 = \frac{-Q_2 + \sqrt{Q_2^2 - 4Q_1Q_3}}{2Q_1}$$

$$Q_1 = n\mu(\gamma + \mu) > 0,$$

$$Q_2 = \gamma\alpha + \mu(\gamma + \alpha + \mu),$$

$$Q_3 = -\alpha\Lambda < 0.$$

• The fifth equilibrium point (FIEP) which is denoted by $E_4 = (\tilde{S}, \tilde{V}_1, 0, \tilde{I})$ where $\gamma = 0$

and

$$\tilde{S} = \frac{-\beta_2\tilde{V}_1 + \mu + \mu_1 + \theta}{\beta_1} \quad (13)$$

while, the point (\tilde{V}_1, \tilde{I}) represents a unique intersection point of two isoclines in the interior of the first quadrant of the V_1I - plane :

$$f(V_1, I) = r_1V_1^2 + r_2V_1^2I + r_3V_1 + r_4V_1I + r_5 = 0 \quad (14a)$$

$$g(V_1, I) = k_1V_1^2 + k_2V_1^2I + k_3V_1 + k_4V_1I + k_5I + k_6 = 0 \quad (14b)$$

where

$r_1 = -\beta_1 n \mu$, $r_2 = -\beta_1 \beta_2 n$, $r_3 = -(\beta_1 \mu + \beta_2 \alpha)$, $r_4 = -\beta_1 \beta_2$, $r_5 = \alpha(\mu + \mu_1 + \theta)$
 $k_1 = \mu n \beta_2$, $k_2 = n \beta_1 \beta_2$, $k_3 = \Lambda n \beta_1 + \beta_2(\alpha + \mu) - \mu n(\mu + \mu_1 + \theta)$,
 $k_4 = \beta_1[\beta_2 - n(\mu + \mu_1 + \theta)]$, $k_5 = -\beta_1(\mu + \mu_1 + \theta)$, $k_6 = \Lambda \beta_1 - [(\alpha + \mu)(\mu + \mu_1 + \theta)]$.
 Clearly, as $I = 0$ the two isoclines become:

$$f(V_1, 0) = r_1 V_1^2 + r_3 V_1 + r_5 = 0, \tag{15a}$$

$$g(V_1, 0) = k_1 V_1^2 + k_3 V_1 + k_6 = 0. \tag{15b}$$

According to the polynomial equations (15a) and (15b), each one has a unique positive root designated by V_1 and I if and only if the following sufficient condition is met:

$$\Lambda \beta_1 < (\alpha + \mu)(\mu + \mu_1 + \theta) \tag{16}$$

Keeping the above in mind, the fifth equilibrium point $E_4 = (\tilde{S}, \tilde{V}_1, 0, \tilde{I})$ exists uniquely if the condition (16) and the following sufficient conditions are met:

$$\frac{\partial I}{\partial V_1} = - \left(\frac{\partial f(V_1, I)}{\partial V_1} \right) / \left(\frac{\partial f(V_1, I)}{\partial I} \right) > 0 \tag{17a}$$

$$\frac{\partial I}{\partial V_1} = - \left(\frac{\partial g(V_1, I)}{\partial V_1} \right) / \left(\frac{\partial g(V_1, I)}{\partial I} \right) < 0 \tag{17b}$$

$$\beta_2 \tilde{V}_1 < \mu + \mu_1 + \theta \tag{17c}$$

• The sixth equilibrium point (SIEP) can be obtained for the system (3) which is denoted by

$$E_5 = (S^*, V_1^*, V_2^*, I^*),$$

where

$$S^* = \frac{-V_2^*(\beta_2 \beta_3 I^* + \mu \beta_2 + \gamma \beta_3) + \gamma(\mu + \mu_1 + \theta)}{\gamma \beta_1}, \tag{18}$$

$$V_1^* = \frac{V_2^*(\beta_3 I^* + \mu)}{\gamma}, \tag{19}$$

while, the point (V_2^*, I^*) signifies a unique intersection point of two isoclines in the interior of the first quadrant of the $V_2 I$ - plane :

$$f(V_2, I) = h_1 V_2^2 I^3 + h_2 V_2^2 + h_3 V_2^2 I^2 + h_4 V_2^2 I + h_5 V_2 I + h_6 V_2 I^2 + h_7 V_2 + h_8 I + h_9 = 0, \tag{20a}$$

$$g(V_2, I) = L_1 V_2^3 I^2 + L_2 V_2^2 I^2 + L_3 V_2^2 I + L_4 V_2 I^2 + L_5 V_2 I + L_6 V_2^2 + L_7 V_2 + L_8 = 0, \tag{20b}$$

where

$$\begin{aligned}
 h_1 &= n \beta_1 \beta_2 \beta_3^2, & h_2 &= n \mu^2 (\mu \beta_2 + \gamma \beta_3), & h_3 &= n \beta_3 [\mu \beta_2 (2 \beta_1 + \beta_3) + \gamma \beta_1 \beta_3], \\
 h_4 &= n \mu [\mu \beta_2 (3 \beta_3 + \beta_1) + \gamma (\beta_3^2 + \beta_1 \beta_2)], \\
 h_5 &= \gamma [\Lambda n \beta_1 \beta_3 + \alpha \beta_2 \beta_3 + \mu \beta_1 \beta_2 + \gamma \beta_1 \beta_3 + \mu \beta_2 \beta_3 - n \mu (\beta_1 + \beta_3) (\mu + \mu_1 + \theta)], \\
 h_6 &= \gamma \beta_1 \beta_3 [\beta_2 - n (\mu + \mu_1 + \theta)], \\
 h_7 &= \gamma [\mu (\Lambda n \beta_1 + \alpha \beta_2 + \mu \beta_2 + \gamma \beta_3) + \gamma \alpha \beta_3 - n \mu^2 (\mu + \mu_1 + \theta)], \\
 h_8 &= -\gamma^2 \beta_1 (\mu + \mu_1 + \theta), & h_9 &= \gamma^2 [\Lambda \beta_1 - (\alpha + \mu) (\mu + \mu_1 + \theta)], \\
 L_1 &= -n \beta_1 \beta_2 \beta_3^2, & L_2 &= -\beta_1 \beta_3 [\mu (\beta_2 + n \beta_2 + n \beta_3) + n \gamma \beta_3], \\
 L_3 &= -n \mu \beta_1 [\beta_3 (2 \gamma + \mu + 1) + \mu \beta_2], & L_4 &= -\gamma \beta_1 \beta_2 \beta_3, \\
 L_5 &= -\gamma [\beta_3 (\alpha \beta_2 + \gamma \beta_1) + \mu \beta_1 (\beta_2 + \beta_3)], & L_6 &= -n \mu^2 \beta_1 (\gamma + \mu), \\
 L_7 &= -\gamma [\mu (\alpha \beta_2 + \gamma \beta_1 + \mu \beta_1) + \gamma \alpha \beta_3], & L_8 &= \gamma (\mu + \mu_1 + \theta).
 \end{aligned}$$

Clearly, as $I = 0$ the two isoclines become:

$$f(V_2, 0) = h_2 V_2^2 + h_7 V_2 + h_9 = 0 \tag{21a}$$

$$g(V_2, 0) = L_6 V_2^2 + L_7 V_2 + L_8 = 0 \tag{21b}$$

According to the polynomial equations (21a) and (21b), each one has a unique positive root designated by V_2 and I , respectively, if and only if condition (16) is met.

Keeping the above in mind, the sixth equilibrium point $E_5 = (S^*, V_1^*, V_2^*, I^*)$ exists uniquely if the condition (16) and the following sufficient conditions are met:

$$\frac{\partial I}{\partial V_2} = - \left(\frac{\partial f(V_2, I)}{\partial V_2} \right) / \left(\frac{\partial f(V_2, I)}{\partial I} \right) > 0 \tag{22a}$$

$$\frac{\partial I}{\partial V_2} = - \left(\frac{\partial g(V_2, I)}{\partial V_2} \right) / \left(\frac{\partial g(V_2, I)}{\partial I} \right) < 0 \tag{22b}$$

$$V_2(\beta_2\beta_3I + \mu\beta_2 + \gamma\beta_3) < \gamma(\mu + \mu_1 + \theta). \quad (22c)$$

It is well known that the basic reproduction number which is denoted by \mathcal{R}_0 is an expected number of secondary cases produced by a typical infective individual in a completely susceptible population. Indeed, if $\mathcal{R}_0 < 1$, then the average of an infected individual produces less than one new infected individual over the course of its infectious period, and the infection cannot grow. Conversely, if $\mathcal{R}_0 > 1$, then each infected individual produces more than one new infection, and the disease can invade the population.

It is easy to verify that the basic reproduction number of the system (3) is given by

$$\mathcal{R}_0 = \text{Max.} \{ \mathcal{R}_{01}, \mathcal{R}_{02}, \mathcal{R}_{03} \}, \quad (23a)$$

where

$$\left. \begin{aligned} \mathcal{R}_{01} &= \frac{\beta_1 \bar{S}}{\mu + \mu_1 + \theta} \\ \mathcal{R}_{02} &= \frac{\beta_1 \bar{S} + \beta_2 \bar{V}_1}{\mu + \mu_1 + \theta} \\ \mathcal{R}_{03} &= \frac{\beta_1 \bar{S} + \beta_2 \bar{V}_1 + \beta_3 \bar{V}_2}{\mu + \mu_1 + \theta} \end{aligned} \right\} \quad (23b)$$

4. Local stability analysis

In this section, the local stability of the system (3) is studied by using the linearization method. The Jacobian matrix of the system (3) at (S, V_1, V_2, I) is $J = (a_{ij})_{4 \times 4}$; $i, j = 1, 2, 3, 4$, where

$$\begin{aligned} a_{11} &= -\frac{\alpha}{1+nV_1} - \beta_1 I - \mu, \quad a_{12} = \frac{n\alpha S}{(1+nV_1)^2}, \quad a_{14} = -\beta_1 S, \quad a_{21} = \frac{\alpha}{1+nV_1}, \\ a_{22} &= -\frac{n\alpha S}{(1+nV_1)^2} - \gamma - \beta_2 I - \mu, \quad a_{24} = -\beta_2 V_1, \quad a_{32} = \gamma, \quad a_{33} = -\beta_3 I - \mu, \\ a_{34} &= -\beta_3 V_2, \quad a_{41} = \beta_1 I, \quad a_{42} = \beta_2 I, \quad a_{43} = \beta_3 I, \quad a_{13} = a_{23} = a_{31} = 0, \\ a_{44} &= \beta_1 S + \beta_2 V_1 + \beta_3 V_2 - (\mu + \mu_1) - \theta \end{aligned}$$

Theorem 2: The FEP is locally asymptotically stable (L.A.S.) if the following sufficient condition is satisfied:

$$\mathcal{R}_{01} < 1 \quad (24)$$

Proof: The Jacobian matrix at FEP is

$$J(E_0) = \begin{bmatrix} -\mu & 0 & 0 & -\beta_1 \bar{S} \\ 0 & -\gamma - \mu & 0 & 0 \\ 0 & \gamma & -\mu & 0 \\ 0 & 0 & 0 & \beta_1 \bar{S} - (\mu + \mu_1 + \theta) \end{bmatrix} \quad (25)$$

The characteristic equation of $J(E_0)$ is given by

$$(\beta_1 \bar{S} - (\mu + \mu_1 + \theta) - \lambda)(-\mu - \lambda)(-\gamma - \mu - \lambda)(-\mu - \lambda) = 0. \quad (26a)$$

Consequently, the equation (26a) has four roots that represent the eigenvalues of $J(E_0)$:

$$\left. \begin{aligned} \lambda_1 &= \beta_1 \bar{S} - (\mu + \mu_1 + \theta) \\ \lambda_2 &= -\mu \\ \lambda_3 &= -(\gamma + \mu) \\ \lambda_4 &= -\mu \end{aligned} \right\} \quad (26b)$$

Therefore, all the eigenvalues will be negative and hence the FEP is L.A.S. if and only if $\mathcal{R}_{01} < 1$ or equivalently $\lambda_1 < 0$. However, it is an unstable saddle point if and only if $\mathcal{R}_{01} > 1$ or equivalently $\lambda_1 > 0$. Hence, the proof is finished.

Theorem 3: The SEP is L.A.S. if the following sufficient condition is satisfied:

$$\mathcal{R}_{02} < 1 . \tag{27}$$

Proof: The Jacobian matrix at SEP is

$$J(E_1) = \begin{bmatrix} -\frac{\alpha}{1+n\bar{v}_1} - \mu & \frac{n\alpha\bar{s}}{(1+n\bar{v}_1)^2} & 0 & -\beta_1\bar{s} \\ \frac{\alpha}{1+n\bar{v}_1} & \frac{-n\alpha\bar{s}}{(1+n\bar{v}_1)^2} - \mu & 0 & -\beta_2\bar{v}_1 \\ 0 & 0 & -\mu & 0 \\ 0 & 0 & 0 & \beta_1\bar{s} + \beta_2\bar{v}_1 - (\mu + \mu_1 + \theta) \end{bmatrix} \tag{28}$$

The equation of $J(E_1)$ is

$$[\lambda^2 + A_1\lambda + A_2][-\mu - \lambda][\beta_1\bar{s} + \beta_2\bar{v}_1 - (\mu + \mu_1 + \theta) - \lambda] = 0 . \tag{29a}$$

Here

$$A_1 = \frac{\alpha}{1+n\bar{v}_1} + \frac{n\alpha\bar{s}}{(1+n\bar{v}_1)^2} + 2\mu .$$

$$A_2 = \mu \left(\frac{n\alpha\bar{s}}{(1+n\bar{v}_1)^2} + \frac{\alpha}{1+n\bar{v}_1} + \mu \right) .$$

Consequently, the equation (29a) has four roots that represent the eigenvalues of $J(E_1)$:

$$\left. \begin{aligned} \lambda_{1,2} &= -\frac{A_1}{2} \mp \frac{1}{2}\sqrt{A_1^2 - 4A_2} \\ \lambda_3 &= -\mu \\ \lambda_4 &= \beta_1\bar{s} + \beta_2\bar{v}_1 - (\mu + \mu_1 + \theta) \end{aligned} \right\} \tag{29b}$$

Therefore, all the eigenvalues will be negative and hence the SEP is L.A.S. if and only if $\mathcal{R}_{02} < 1$ or equivalently $\lambda_4 < 0$. However, it is an unstable saddle point if and only if $\mathcal{R}_{02} > 1$ or equivalently $\lambda_4 > 0$. Hence, the proof is finished.

Theorem 4: The TEP is L.A.S. if the following sufficient conditions are satisfied:

$$\beta_1\hat{s} < \beta_1\hat{l} + 2\mu + \mu_1 + \theta , \tag{30a}$$

$$\mu\beta_1\hat{s} < (\beta_1\hat{l} + \mu)(\mu + \mu_1 + \theta) . \tag{30b}$$

Proof: The Jacobian matrix at TEP is

$$J(E_2) = \begin{bmatrix} -\beta_1\hat{l} - \mu & 0 & 0 & -\beta_1\hat{s} \\ 0 & -\gamma - \beta_2\hat{l} - \mu & 0 & 0 \\ 0 & \gamma & -\beta_3\hat{l} - \mu & 0 \\ \beta_1\hat{l} & \beta_2\hat{l} & \beta_3\hat{l} & \beta_1\hat{s} - (\mu + \mu_1 + \theta) \end{bmatrix} \tag{31}$$

The equation of $J(E_2)$ is

$$[\lambda^2 + B_1\lambda + B_2][-\gamma - \beta_2\hat{l} - \mu - \lambda][-\beta_3\hat{l} - \mu - \lambda] = 0 . \tag{32a}$$

Here

$$B_1 = \beta_1\hat{l} + 2\mu + \mu_1 + \theta - \beta_1\hat{s}$$

$$B_2 = (\beta_1\hat{l} + \mu)(\mu + \mu_1 + \theta) - \mu\beta_1\hat{s}$$

Consequently, the equation (32a) has four roots that represent the eigenvalues of $J(E_2)$:

$$\left. \begin{aligned} \lambda_{1,4} &= -\frac{B_1}{2} \mp \frac{1}{2}\sqrt{B_1^2 - 4B_2} \\ \lambda_2 &= -\gamma - \beta_2\hat{l} - \mu \\ \lambda_3 &= -\beta_3\hat{l} - \mu \end{aligned} \right\} \tag{32b}$$

So, all the above eigenvalues will be negative and hence the TEP is L.A.S. if the conditions (30a) - (30b) hold.

Theorem 5: The FOEP is L.A.S. if the following sufficient condition is satisfied:

$$\mathcal{R}_{03} < 1 \tag{33}$$

Proof: The Jacobian matrix at FOEP is

$$J(E_3) = \begin{bmatrix} -\frac{\alpha}{1+n\check{V}_1} - \mu & \frac{n\alpha\check{S}}{(1+n\check{V}_1)^2} & 0 & -\beta_1\check{S} \\ \frac{\alpha}{1+n\check{V}_1} & \frac{-n\alpha\check{S}}{(1+n\check{V}_1)^2} - \gamma - \mu & 0 & -\beta_2\check{V}_1 \\ 0 & \gamma & -\mu & -\beta_3\check{V}_2 \\ 0 & 0 & 0 & \beta_1\check{S} + \beta_2\check{V}_1 + \beta_3\check{V}_2 - (\mu + \mu_1 + \theta) \end{bmatrix} \tag{34}$$

The equation of $J(E_3)$ is

$$[\lambda^2 + C_1\lambda + C_2][-\mu - \lambda][\beta_1\check{S} + \beta_2\check{V}_1 + \beta_3\check{V}_2 - (\mu + \mu_1 + \theta) - \lambda] = 0. \tag{35a}$$

Here

$$C_1 = \frac{\alpha}{1+n\check{V}_1} \left(1 + \frac{n\check{S}}{1+n\check{V}_1} \right) + \gamma + 2\mu.$$

$$C_2 = \frac{\alpha}{1+n\check{V}_1} \left(\frac{n\mu\check{S}}{1+n\check{V}_1} + \gamma + \mu \right) + \mu(\gamma + \mu).$$

Consequently, the equation (35a) has four roots that represent the eigenvalues of $J(E_3)$:

$$\left. \begin{aligned} \lambda_{1,2} &= -\frac{C_1}{2} \mp \frac{1}{2} \sqrt{C_1^2 - 4C_2} \\ \lambda_3 &= -\mu \\ \lambda_4 &= \beta_1\check{S} + \beta_2\check{V}_1 + \beta_3\check{V}_2 - (\mu + \mu_1 + \theta) \end{aligned} \right\} \tag{35b}$$

Therefore, all the eigenvalues will be negative and hence the FOEP is L.A.S. if and only if

$\mathcal{R}_{03} < 1$ or equivalently $\lambda_4 < 0$. However, it is an unstable saddle point if and only if

$\mathcal{R}_{03} > 1$ or equivalently $\lambda_4 > 0$. Hence, the proof is finished.

Theorem 6: The FIEP is L.A.S. if the following sufficient conditions are satisfied:

$$\beta_1\check{\check{S}} + \beta_2\check{\check{V}}_1 < \mu + \mu_1 + \theta \tag{36a}$$

$$\frac{n\alpha^2\check{\check{S}}}{(1+n\check{\check{V}}_1)^3} < \left(\frac{\alpha}{1+n\check{\check{V}}_1} + \beta_1\check{\check{I}} + \mu \right) \left(\frac{n\alpha\check{\check{S}}}{(1+n\check{\check{V}}_1)^2} + \beta_2\check{\check{I}} + \mu \right) \tag{36b}$$

$$\frac{n\beta_1\alpha\check{\check{S}}}{(1+n\check{\check{V}}_1)^2} < \left(\frac{n\alpha\check{\check{S}}}{(1+n\check{\check{V}}_1)^2} + \beta_2\check{\check{I}} + \mu \right) \beta_2 \tag{36c}$$

$$\beta_2\check{\check{V}}_1 \left(\beta_1\check{\check{S}} + \beta_2\check{\check{V}}_1 \right) + \frac{\beta_1\alpha\check{\check{S}}}{1+n\check{\check{V}}_1} < \beta_2\check{\check{V}}_1(\mu + \mu_1 + \theta). \tag{36d}$$

Proof: The Jacobian matrix at FIEP is

$$J(E_4) = (d_{ij})_{4 \times 4} ; i, j = 1, 2, 3, 4$$

here

$$\begin{aligned} d_{11} &= -\frac{\alpha}{1+n\check{\check{V}}_1} - \beta_1\check{\check{I}} - \mu, d_{12} = \frac{n\alpha\check{\check{S}}}{(1+n\check{\check{V}}_1)^2}, d_{14} = -\beta_1\check{\check{S}}, \\ d_{21} &= \frac{\alpha}{1+n\check{\check{V}}_1}, d_{22} = \frac{-n\alpha\check{\check{S}}}{(1+n\check{\check{V}}_1)^2} - \beta_2\check{\check{I}} - \mu, d_{24} = -\beta_2\check{\check{V}}_1, \\ d_{33} &= -\beta_3\check{\check{I}} - \mu, d_{41} = \beta_1\check{\check{I}}, d_{42} = \beta_2\check{\check{I}}, d_{43} = \beta_3\check{\check{I}}, \\ d_{44} &= \beta_1\check{\check{S}} + \beta_2\check{\check{V}}_1 - (\mu + \mu_1 + \theta), d_{13} = d_{23} = d_{31} = d_{32} = d_{34} = 0. \end{aligned} \tag{37}$$

The equation of $J(E_4)$ is

$$[-\beta_3\check{\check{I}} - \mu - \lambda][\lambda^3 + D_1\lambda^2 + D_2\lambda + D_3] = 0, \tag{38}$$

where

$$\begin{aligned}
 D_1 &= -(d_{11} + d_{22} + d_{44}), \\
 D_2 &= (d_{11}d_{22} - d_{12}d_{21}) + (d_{11}d_{44} - d_{14}d_{41}) + (d_{22}d_{44} - d_{24}d_{42}), \\
 D_3 &= d_{44}(d_{12}d_{21} - d_{11}d_{22}) - d_{12}d_{24}d_{41} - d_{14}d_{21}d_{42} + d_{14}d_{22}d_{41} + d_{11}d_{24}d_{42}.
 \end{aligned}$$

While

$$\begin{aligned}
 \Delta &= D_1D_2 - D_3, \text{ that is} \\
 \Delta &= (d_{11} + d_{22})(d_{12}d_{21} - d_{11}d_{22}) + (d_{11} + d_{44})(d_{14}d_{41} - d_{11}d_{44}) - \\
 &\quad d_{22}d_{44}(2d_{11} + d_{22} + d_{44}) + d_{24}(d_{12}d_{41} + d_{22}d_{42}) + d_{42}(d_{44}d_{24} + d_{14}d_{21})
 \end{aligned}$$

So, either

$$\left[-\beta_3 \tilde{I} - \mu - \lambda \right] = 0, \tag{39a}$$

or

$$[\lambda^3 + D_1\lambda^2 + D_2\lambda + D_3] = 0, \tag{39b}$$

from equation (39a), we obtain that $\lambda_3 = -\beta_3 \tilde{I} - \mu < 0$ which is always a negative eigenvalue. On the other hand, it is easy to verify that $D_1 > 0$ and $D_3 > 0$ under the condition (36a) - (36b).

While $\Delta > 0$ under the conditions (36c) - (36d). Then all the eigenvalues λ_1, λ_2 and λ_4 of Eq.(39b) have negative real parts. So, FIEP is L.A.S. if the conditions (36a-36d) are holds.

Theorem 7: The SIEP of the system (3) is L.A.S. in the subregion $\Omega \in R_+^4$ which satisfies the condition:

$$2(\beta_1S^* + \beta_2V_1^* + \beta_3V_2^*) < \mu + \mu_1 + \theta. \tag{40}$$

Proof: The Jacobian matrix at SIEP is

$$J(E_5) = (r_{ij})_{4 \times 4}; \quad i, j = 1, 2, 3, 4$$

here

$$\begin{aligned}
 r_{11} &= -\frac{\alpha}{1+nV_1^*} - \beta_1I^* - \mu, \quad r_{12} = \frac{n\alpha S^*}{(1+nV_1^*)^2}, \quad r_{14} = -\beta_1S^*, \\
 r_{21} &= \frac{\alpha}{1+nV_1^*}, \quad r_{22} = \frac{-n\alpha S^*}{(1+nV_1^*)^2} - \gamma - \beta_2I^* - \mu, \quad r_{24} = -\beta_2V_1^*, \\
 r_{32} &= \gamma, \quad r_{33} = -\beta_3I^* - \mu, \quad r_{34} = -\beta_3V_2^*, \quad r_{41} = \beta_1I^*, \\
 r_{42} &= \beta_2I^*, \quad r_{43} = \beta_3I^*, \quad r_{44} = \beta_1S^* + \beta_2V_1^* + \beta_3V_2^* - (\mu + \mu_1 + \theta), \\
 r_{13} &= r_{31} = r_{23} = 0.
 \end{aligned}$$

.....(41)

By using the Gersgorin theorem [27], if the following condition is satisfied,

$$|r_{ii}| > \sum_{\substack{i=1 \\ i \neq j}}^4 |r_{ij}|.$$

Therefore, all the eigenvalues of the Jacobian matrix at (E_5) exist in the sub region Ω , where

$$\Omega = \cup \left\{ U^* \in C: |U^* - r_{ij}| < \sum_{\substack{i=1 \\ i \neq j}}^4 |r_{ij}| \right\}$$

Therefore, all the eigenvalues of $J(E_5)$ exist in the disc centered at r_{ii} . Thus, if the diagonal elements are negative and condition (40) holds, then all the eigenvalues will exist in the left half plane and the SIEP is L.A.S.

5. Global stability analysis

In this part, the global stability of all equilibrium points of the system (3) has been presented as shown in the following theorems.

Theorem 8: Assume that the FEP is L.A.S. in R_+^4 . Then it is globally asymptotically stable (G.A.S.) provided that the following conditions hold:

$$\mathcal{R}_{01} < 1, \tag{42a}$$

$$\bar{S} < S. \tag{42b}$$

Proof: We define the function

$$U_1(S, V_1, V_2, I) = \frac{(S-\bar{S})^2}{2} + V_1 + V_2 + I.$$

Clearly, U_1 is a positive definite function and $U_1: R_+^4 \rightarrow R$ is a continuously differentiable function such that

$$U_1(\bar{S}, 0, 0, 0) = 0 \text{ and } U_1(S, V_1, V_2, I) > 0, \forall (S, V_1, V_2, I) \neq (\bar{S}, 0, 0, 0).$$

Further,

$$\begin{aligned} \frac{dU_1}{dt} &= (S - \bar{S})[\Lambda - \beta_1 SI - \mu S] - \gamma V_1 - \beta_2 V_1 I - \mu V_1 + \gamma V_1 - \beta_3 V_2 I - \mu V_2 \\ &\quad + \beta_1 SI + \beta_2 V_1 I + \beta_3 V_2 I - (\mu + \mu_1 + \theta)I \end{aligned}$$

$$\begin{aligned} \frac{dU_1}{dt} &= (S - \bar{S})[-\beta_1 SI - \mu(S - \bar{S})] - \beta_2 V_1 I - \mu V_1 - \beta_3 V_2 I - \mu V_2 \\ &\quad + \left[\frac{\beta_1 S + \beta_2 V_1 + \beta_3 V_2}{\mu + \mu_1 + \theta} - 1 \right] I \end{aligned}$$

$$\frac{dU_1}{dt} = -\beta_1 SI(S - \bar{S}) - \mu(S - \bar{S})^2 - \beta_2 V_1 I - \mu V_1 - \beta_3 V_2 I - \mu V_2 + [\mathcal{R}_{01} - 1]I$$

Consequently, by using the conditions (42a – 42b), we get that:

$$\frac{dU_1}{dt} \leq -\beta_1 SI(S - \bar{S}) - \mu[(S - \bar{S})^2 + V_1 + V_2] - \beta_2 V_1 I - \beta_3 V_2 I - I$$

Obviously, $\frac{dU_1}{dt} \leq 0$, hence U_1 is a Lyapunov function. Thus, FEP is a G.A.S.

Theorem 9: Assume that the SEP is L.A.S. Then it is a G.A.S. in the subregion of R_+^4 that satisfies the following conditions:

$$\mathcal{R}_{02} < 1, \tag{43a}$$

$$\bar{S} < S, \tag{43b}$$

$$\bar{V}_1 < V_1, \tag{43c}$$

$$q_{12}^2 < 4q_{11}q_{22}. \tag{43d}$$

Where the symbols $q_{ij}, i, j = 1, 2$ are given in the proof

Proof: We define the function

$$U_2(S, V_1, V_2, I) = \frac{(S-\bar{S})^2}{2} + \frac{(V_1-\bar{V}_1)^2}{2} + V_2 + I.$$

Clearly, U_2 is the positive definite function and $U_2: R_+^4 \rightarrow R$ is a continuously differentiable function such that

$$U_2(\bar{S}, \bar{V}_1, 0, 0) = 0 \text{ and } U_2(S, V_1, V_2, I) > 0, \forall (S, V_1, V_2, I) \neq (\bar{S}, \bar{V}_1, 0, 0).$$

Additionally, get that taking the derivative in terms of time and simplifying the resulting terms

$$\begin{aligned} \frac{dU_2}{dt} &= (S - \bar{S}) \left[\Lambda - \frac{\alpha S}{1+nV_1} - \beta_1 SI - \mu S \right] + (V_1 - \bar{V}_1) \left[\frac{\alpha S}{1+nV_1} - \beta_2 V_1 I - \mu V_1 \right] \\ &\quad - \beta_3 V_2 I - \mu V_2 + \beta_1 SI + \beta_2 V_1 I + \beta_3 V_2 I - (\mu + \mu_1 + \theta)I. \end{aligned}$$

$$\begin{aligned} \frac{dU_2}{dt} &= - \left[q_{11}(S - \bar{S})^2 - q_{12}(S - \bar{S})(V_1 - \bar{V}_1) + q_{22}(V_1 - \bar{V}_1)^2 \right] - \beta_1 SI(S - \bar{S}) \\ &\quad - \beta_2 V_1 I(V_1 - \bar{V}_1) - \beta_3 V_2 I - \mu V_2 + \left[\frac{\beta_1 S + \beta_2 V_1 + \beta_3 V_2}{\mu + \mu_1 + \theta} - 1 \right] I. \end{aligned}$$

$$\begin{aligned} \frac{dU_2}{dt} &= - \left[q_{11}(S - \bar{S})^2 - q_{12}(S - \bar{S})(V_1 - \bar{V}_1) + q_{22}(V_1 - \bar{V}_1)^2 \right] - \beta_1 SI(S - \bar{S}) \\ &\quad - \beta_2 V_1 I(V_1 - \bar{V}_1) - \beta_3 V_2 I - \mu V_2 + [\mathcal{R}_{02} - 1]I. \end{aligned}$$

Consequently, by using the conditions (43a – 43d), we get that:

$$\begin{aligned} \frac{dU_2}{dt} &\leq - \left[\sqrt{q_{11}}(S - \bar{S}) - \sqrt{q_{22}}(V_1 - \bar{V}_1) \right]^2 - \mu V_2 \\ &\quad - \beta_1 SI(S - \bar{S}) - \beta_2 V_1 I(V_1 - \bar{V}_1) - \beta_3 V_2 I - I. \end{aligned}$$

Where ,

$$q_{11} = \frac{\alpha + \mu(1+nV_1)}{(1+nV_1)}, q_{12} = \frac{\alpha(n\bar{S} + n\bar{V}_1 + 1)}{(1+nV_1)(1+n\bar{V}_1)}, q_{22} = \frac{n\alpha\bar{S} + \mu(1+nV_1)(1+n\bar{V}_1)}{(1+nV_1)(1+n\bar{V}_1)}$$

Obviously, $\frac{dU_2}{dt} \leq 0$, hence U_2 is the Lyapunov function. Thus, SEP is a G.A.S.

Theorem 10: Assume that, the TEP is L.A.S. Then it is a G.A.S. in the subregion of R_+^4 that satisfies the following conditions:

$$\max\{1, \hat{S}\} < S, \quad (44a)$$

$$\hat{I} < I. \quad (44b)$$

Proof: We define the function

$$U_3(S, V_1, V_2, I) = \frac{(S-\hat{S})^2}{2} + V_1 + V_2 + \left(I - \hat{I} - \hat{I} \ln \frac{I}{\hat{I}}\right).$$

Clearly, U_3 is the positive definite function and $U_3: R_+^4 \rightarrow R$ is a continuously differentiable function such that $U_3(\hat{S}, 0, 0, \hat{I}) = 0$ and $U_3(S, V_1, V_2, I) > 0, \forall (S, V_1, V_2, I) \neq (\hat{S}, 0, 0, \hat{I})$.

Further,

$$\begin{aligned} \frac{dU_3}{dt} = (S - \hat{S})[\Lambda - \beta_1 S I - \mu S] - \gamma V_1 - \beta_2 V_1 I - \mu V_1 + \gamma V_1 - \beta_3 V_2 I - \mu V_2 \\ + (I - \hat{I})[\beta_1 S + \beta_2 V_1 + \beta_3 V_2 - (\mu + \mu_1 + \theta)]. \end{aligned}$$

From conditions (44a) and (44b), we get:

$$\frac{dU_3}{dt} \leq -(\beta_1 \hat{I} + \mu)(S - \hat{S})^2 - (\beta_2 \hat{I} + \mu)V_1 - (\beta_3 \hat{I} + \mu)V_2.$$

Consequently, due to conditions (44a) - (44b) $\frac{dU_3}{dt} \leq 0$, we have U_3 is the Lyapunov function.

Thus, the TEP is a G.A.S.

Theorem 11: Assume that the FOEP is L.A.S. Then it is a G.A.S. in the subregion of R_+^4 that satisfies the following conditions:

$$\mathcal{R}_{03} < 1, \quad (45a)$$

$$\check{S} < S, \quad (45b)$$

$$\check{V}_1 < V_1, \quad (45c)$$

$$\check{V}_2 < V_2, \quad (45d)$$

$$k_{12}^2 < 2k_{11}k_{22}, \quad (45e)$$

$$k_{23}^2 < 2k_{22}k_{33}. \quad (45f)$$

Where the symbols $k_{ij}, i, j = 1, 2, 3$ are given in the proof

Proof: We define the function

$$U_4(S, V_1, V_2, I) = \frac{(S-\check{S})^2}{2} + \frac{(V_1-\check{V}_1)^2}{2} + \frac{(V_2-\check{V}_2)^2}{2} + I.$$

Clearly, U_4 is the positive definite function and $U_4: R_+^4 \rightarrow R$ is a continuously differentiable function such that $U_4(\check{S}, \check{V}_1, \check{V}_2, 0) = 0$ and $U_4(S, V_1, V_2, I) > 0, \forall (S, V_1, V_2, I) \neq (\check{S}, \check{V}_1, \check{V}_2, 0)$.

Additionally,

$$\begin{aligned} \frac{dU_4}{dt} = (S - \check{S}) \left[\Lambda - \frac{\alpha S}{1+nV_1} - \beta_1 S I - \mu S \right] + (V_1 - \check{V}_1) \left[\frac{\alpha S}{1+nV_1} - \gamma V_1 - \beta_2 V_1 I - \mu V_1 \right] \\ + (V_2 - \check{V}_2) [\gamma V_1 - \beta_3 V_2 I - \mu V_2] + \beta_1 S I + \beta_2 V_1 I + \beta_3 V_2 I - (\mu + \mu_1 + \theta) I. \end{aligned}$$

$$\begin{aligned} \frac{dU_4}{dt} = - \left[k_{11}(S - \check{S})^2 - k_{12}(S - \check{S})(V_1 - \check{V}_1) + \frac{k_{22}}{2}(V_1 - \check{V}_1)^2 \right] \\ - \left[\frac{k_{22}}{2}(V_1 - \check{V}_1)^2 - k_{23}(V_1 - \check{V}_1)(V_2 - \check{V}_2) + k_{33}(V_2 - \check{V}_2)^2 \right] \\ - \beta_1 S I (S - \check{S}) - \beta_2 V_1 I (V_1 - \check{V}_1) - \beta_3 V_2 I (V_2 - \check{V}_2) + \left[\frac{\beta_1 S + \beta_2 V_1 + \beta_3 V_2}{\mu + \mu_1 + \theta} - 1 \right] I. \end{aligned}$$

$$\begin{aligned} \frac{dU_4}{dt} = & - \left[k_{11}(S - \check{S})^2 - k_{12}(S - \check{S})(V_1 - \check{V}_1) + \frac{k_{22}}{2}(V_1 - \check{V}_1)^2 \right] \\ & - \left[\frac{k_{22}}{2}(V_1 - \check{V}_1)^2 - k_{23}(V_1 - \check{V}_1)(V_2 - \check{V}_2) + k_{33}(V_2 - \check{V}_2)^2 \right] \\ & - \beta_1 S I (S - \check{S}) - \beta_2 V_1 I (V_1 - \check{V}_1) - \beta_3 V_2 I (V_2 - \check{V}_2) + [\mathcal{R}_{03} - 1] I. \end{aligned}$$

Consequently, by using the conditions (45a – 45f), we get that:

$$\begin{aligned} \frac{dU_4}{dt} \leq & - \left[\sqrt{k_{11}}(S - \check{S}) - \sqrt{\frac{k_{22}}{2}}(V_1 - \check{V}_1) \right]^2 - \left[\sqrt{\frac{k_{22}}{2}}(V_1 - \check{V}_1) - \sqrt{k_{33}}(V_2 - \check{V}_2) \right]^2 \\ & - \beta_1 S I (S - \check{S}) - \beta_2 V_1 I (V_1 - \check{V}_1) - \beta_3 V_2 I (V_2 - \check{V}_2) - I . \end{aligned}$$

Where, $k_{11} = \frac{\alpha + \mu(1+nV_1)}{(1+nV_1)}$, $k_{12} = \frac{\alpha(n\check{S} + n\check{V}_1 + 1)}{(1+nV_1)(1+n\check{V}_1)}$, $k_{22} = \frac{n\alpha\check{S} + (\mu + \gamma)(1+nV_1)(1+n\check{V}_1)}{(1+nV_1)(1+n\check{V}_1)}$.
 $k_{23} = \gamma$, $k_{33} = \mu$.

Obviously, $\frac{dU_4}{dt} \leq 0$, hence U_4 is the Lyapunov function with respect to E_3 . Thus, the FOEP is a G.A.S.

Theorem 12: Assume that the FIEP is L.A.S. Then it is a G.A.S. in the subregion of R_+^4 that satisfies the following conditions:

$$\max \{1, \check{S}\} < S, \tag{46a}$$

$$\check{I} < I, \tag{46b}$$

$$\max \{1, \check{V}_1\} < V_1, \tag{46c}$$

$$R_{12}^2 < 4R_{11}R_{22}. \tag{46d}$$

Where the symbols R_{ij} , $i, j = 1, 2$ are given in the proof.

Proof: We define the function

$$U_5(S, V_1, V_2, I) = \frac{(S - \check{S})^2}{2} + \frac{(V_1 - \check{V}_1)^2}{2} + V_2 + \left(I - \check{I} - \check{I} \ln \frac{I}{\check{I}} \right).$$

Clearly, U_5 is a positive definite function and $U_5: R_+^4 \rightarrow R$ is a continuously differentiable function such that

$$U_5(\check{S}, \check{V}_1, 0, \check{I}) = 0 \text{ and } U_5(S, V_1, V_2, I) > 0, \forall (S, V_1, V_2, I) \neq (\check{S}, \check{V}_1, 0, \check{I}).$$

Additionally, we have

$$\begin{aligned} \frac{dU_5}{dt} = & (S - \check{S}) \left[\Lambda - \frac{\alpha S}{1+nV_1} - \beta_1 S I - \mu S \right] + (V_1 - \check{V}_1) \left[\frac{\alpha S}{1+nV_1} - \beta_2 V_1 I - \mu V_1 \right] \\ & - \beta_3 V_2 I - \mu V_2 + (I - \check{I}) [\beta_1 S + \beta_2 V_1 + \beta_3 V_2 - (\mu + \mu_1 + \theta)] . \end{aligned}$$

$$\begin{aligned} \frac{dU_5}{dt} = & - \left[R_{11}(S - \check{S})^2 - R_{12}(S - \check{S})(V_1 - \check{V}_1) + R_{22}(V_1 - \check{V}_1)^2 \right] \\ & - \beta_1 (S - \check{S})(I - \check{I})[S - 1] - \beta_2 (V_1 - \check{V}_1)(I - \check{I})[V_1 - 1] - \mu V_2 - \beta_3 V_2 \check{I} . \end{aligned}$$

Consequently, by using the conditions (46a - 46d), we get that:

$$\begin{aligned} \frac{dU_5}{dt} \leq & - \left[\sqrt{R_{11}}(S - \check{S}) - \sqrt{R_{22}}(V_1 - \check{V}_1) \right]^2 - \beta_1 (S - \check{S})(I - \check{I})[S - 1] \\ & - \beta_2 (V_1 - \check{V}_1)(I - \check{I})[V_1 - 1] - (\mu + \beta_3 \check{I})V_2. \end{aligned}$$

Where,

$$R_{11} = \frac{\alpha + (\mu + \beta_1 \tilde{I})(1 + nV_1)}{(1 + nV_1)}, R_{12} = \frac{\alpha(n\tilde{S} + n\tilde{V}_1 + 1)}{(1 + nV_1)(1 + n\tilde{V}_1)}, R_{22} = \frac{n\alpha\tilde{S} + (\mu + \beta_2 \tilde{I})(1 + nV_1)(1 + n\tilde{V}_1)}{(1 + nV_1)(1 + n\tilde{V}_1)}.$$

Consequently, due to the conditions above $\frac{dU_5}{dt} \leq 0$, then U_5 is Lyapunov function with respect to E_4 in the region that satisfies the given condition Thus, the FIEP is a G.A.S.

Theorem 13: Assume that the SIEP is L.A.S. Then it is a G.A.S. in the subregion of R_+^4 that satisfies the following conditions:

$$\beta_1 S + \beta_2 V_1 + \beta_3 V_2 < \mu + \mu_1 + \theta, \tag{47a}$$

$$W_{12}^2 < \frac{4}{6} W_{11} W_{22}, \tag{47b}$$

$$W_{23}^2 < \frac{4}{6} W_{22} W_{33}, \tag{47c}$$

$$W_{14}^2 < \frac{4}{6} W_{11} W_{44}, \tag{47d}$$

$$W_{24}^2 < \frac{4}{9} W_{22} W_{44}, \tag{47e}$$

$$W_{34}^2 < \frac{4}{6} W_{33} W_{44}. \tag{47f}$$

Where the symbols W_{ij} , $i, j = 1, 2, 3, 4$ are given in the proof.

Proof: We define the function

$$U_6(S, V_1, V_2, I) = \frac{(S - S^*)^2}{2} + \frac{(V_1 - V_1^*)^2}{2} + \frac{(V_2 - V_2^*)^2}{2} + \frac{(I - I^*)^2}{2}.$$

Clearly, U_6 is the positive definite function and $U_6: R_+^4 \rightarrow R$ is a continuously differentiable function such that

$$U_6(S^*, V_1^*, V_2^*, I^*) = 0 \text{ and } U_6(S, V_1, V_2, I) > 0, \forall (S, V_1, V_2, I) \neq (S^*, V_1^*, V_2^*, I^*).$$

Additionally, we have

$$\begin{aligned} \frac{dU_6}{dt} = & (S - S^*) \left[\Lambda - \frac{\alpha S}{1 + nV_1} - \beta_1 SI - \mu S \right] + (V_1 - V_1^*) \left[\frac{\alpha S}{1 + nV_1} - \gamma V_1 - \beta_2 V_1 I - \mu V_1 \right] \\ & + (V_2 - V_2^*) [\gamma V_1 - \beta_3 V_2 I - \mu V_2] + (I - I^*) [\beta_1 SI + \beta_2 V_1 I + \beta_3 V_2 I - (\mu + \mu_1 + \theta) I]. \end{aligned}$$

$$\begin{aligned} \frac{dU_6}{dt} = & - \left[\frac{W_{11}}{2} (S - S^*)^2 - W_{12} (S - S^*) (V_1 - V_1^*) + \frac{W_{22}}{3} (V_1 - V_1^*)^2 \right] \\ & - \left[\frac{W_{11}}{2} (S - S^*)^2 - W_{14} (S - S^*) (I - I^*) + \frac{W_{44}}{3} (I - I^*)^2 \right] \\ & - \left[\frac{W_{22}}{3} (V_1 - V_1^*)^2 - W_{23} (V_1 - V_1^*) (V_2 - V_2^*) + \frac{W_{33}}{2} (V_2 - V_2^*)^2 \right] \\ & - \left[\frac{W_{22}}{3} (V_1 - V_1^*)^2 + W_{24} (V_1 - V_1^*) (I - I^*) + \frac{W_{44}}{3} (I - I^*)^2 \right] \\ & - \left[\frac{W_{33}}{2} (V_2 - V_2^*)^2 + W_{34} (V_2 - V_2^*) (I - I^*) + \frac{W_{44}}{3} (I - I^*)^2 \right]. \end{aligned}$$

Consequently, by using the conditions (47a - 47f), we get that:

$$\begin{aligned} \frac{dU_6}{dt} \leq & - \left[\sqrt{\frac{W_{11}}{2}} (S - S^*) - \sqrt{\frac{W_{22}}{3}} (V_1 - V_1^*) \right]^2 - \left[\sqrt{\frac{W_{11}}{2}} (S - S^*) + \sqrt{\frac{W_{44}}{3}} (I - I^*) \right]^2 \\ & - \left[\sqrt{\frac{W_{22}}{3}} (V_1 - V_1^*) - \sqrt{\frac{W_{33}}{2}} (V_2 - V_2^*) \right]^2 - \left[\sqrt{\frac{W_{22}}{3}} (V_1 - V_1^*) + \sqrt{\frac{W_{44}}{3}} (I - I^*) \right]^2 \\ & - \left[\sqrt{\frac{W_{33}}{2}} (V_2 - V_2^*) + \sqrt{\frac{W_{44}}{3}} (I - I^*) \right]^2. \end{aligned}$$

Where,

$$\begin{aligned} W_{11} &= \frac{\alpha + (\mu + \beta_1 I^*)(1 + nV_1)}{(1 + nV_1)}, W_{12} = \frac{\alpha(nS^* + nV_1^* + 1)}{(1 + nV_1)(1 + nV_1^*)} \\ W_{22} &= \frac{n\alpha\tilde{S} + (\beta_2 I^* + \mu + \gamma)(1 + nV_1)(1 + nV_1^*)}{(1 + nV_1)(1 + nV_1^*)}, W_{14} = \beta_1 (S - I^*), W_{23} = \gamma \\ W_{44} &= \mu + \mu_1 + \theta - (\beta_1 S + \beta_2 V_1 + \beta_3 V_2) \end{aligned}$$

$$W_{33} = \beta_3 I^* + \mu, W_{24} = \beta_2 (V_1 - I^*), W_{34} = \beta_3 (V_2 - I^*)$$

Consequently, due to the conditions above $\frac{dU_6}{dt} \leq 0$, then U_6 is the Lyapunov function with respect to E_5 in the region that satisfies the given condition. Thus, the SIEP is a G.A.S.

6. Numerical simulation

In this part, In order to verify our findings and comprehend how changing parameter values affect the system dynamics, numerical simulations are run. The following hypothetical parameter values are used, and the system is numerically solved. We begin with the various initial conditions. The obtained trajectories are drawn using Matlab 2014a.

$$\Lambda = 5000, \beta_1 = 0.0003, \beta_2 = 0.00002, \beta_3 = 0.000002, \alpha = 0.5, \\ n = 0.00005, \theta = 0.003, \gamma = 0.4, \mu_1 = 0.3, \mu = 0.01. \tag{48}$$

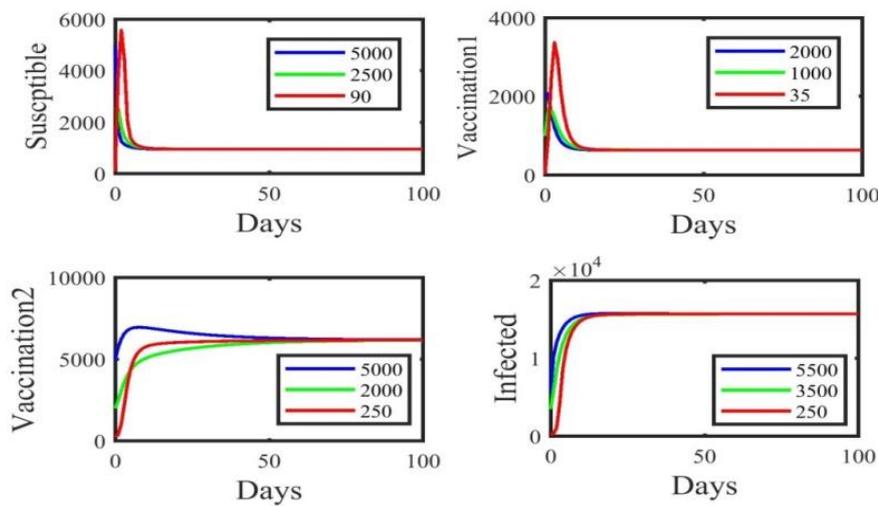


Figure 2: Time series of the trajectories of the system (3) for the sets of data as given in Eq.(48) which approaches to $E_5 = (0.0959, 0.0641, 0.6186, 1.5725)$ and $\mathcal{R}_0 = 3.298$.

Obviously, the phase plot that is given by Figure 2 shows the SIEP of the system (3) that is given by $E_5 = (0.0959, 0.0641, 0.6186, 1.5725)$ is a G.A.S. and this confirms our obtained analytical results.

Now, in order to discuss the effect of the parameter values of the system (3) on the dynamical behavior of the system, the system is numerically solved for the data that are given in Eq.(48) with varying one or more parameters each time. It is observed that for the rest of the data as given in Eq.(48) with changing the parameters $\alpha = 0, \beta_1 = 0.0000003$ and $\beta_3 = 0.0002$, the solution of the system (3) approaches asymptotically to $E_0 = (3.161, 0, 0, 0)$ as shown in Figure 3.

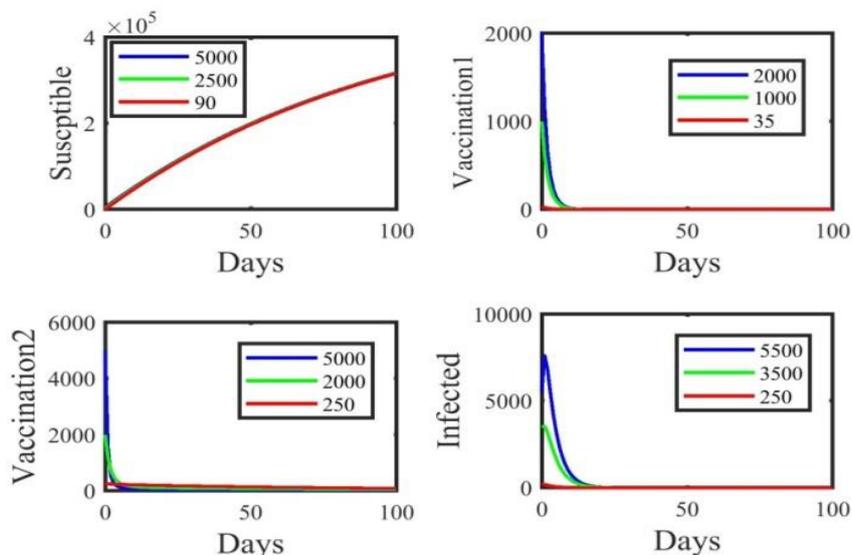


Figure 3: Time series of the trajectories of the system (3) for the rest of the data as given in Eq.(48) with changing the parameters $\alpha = 0, \beta_1 = 0.0000003$ and $\beta_3 = 0.0002$, which approaches to $E_0 = (3.161, 0, 0, 0)$ and $\mathcal{R}_{01} = 0.03$.

By changing the parameters $\gamma = 0, \beta_1 = 0.0000003, \beta_2 = 0.000002$ and $\beta_3 = 0.02$ with keeping the rest of parameter values as in Eq.(48), then the trajectories of the system (3) approaches asymptotically to $E_1 = (0.8930, 2.2677, 0, 0)$ as shown in Figure 4.

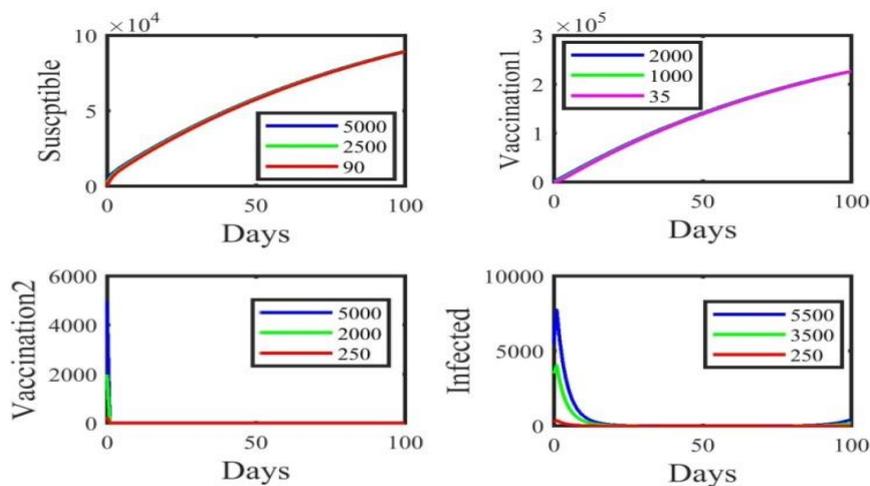


Figure 4: Time series of the trajectories of the system (3) for the rest of the data as given in Eq.(48) with changing the parameters $\gamma = 0, \beta_1 = 0.0000003, \beta_2 = 0.000002$ and $\beta_3 = 0.02$, which approaches to $E_1 = (0.8930, 2.2677, 0, 0)$ and $\mathcal{R}_{02} = 0.153$.

For Eq.(48) with changing the parameter $\alpha = 0$, then the trajectories of the system (3) approach asymptotically to $E_2 = (0.1043, 0, 0, 1.5942)$ as shown in Figure 5.

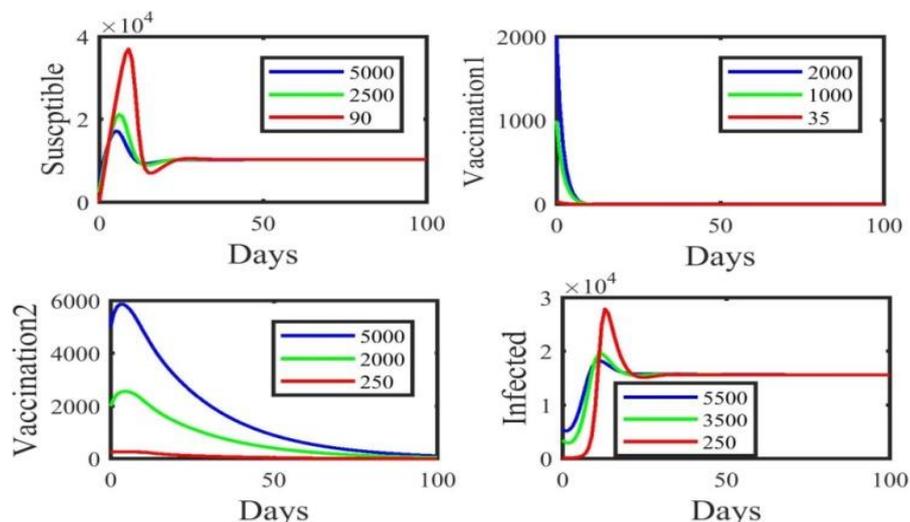


Figure 5: Time series of the trajectories of the system(3) for the rest of the data as given in Eq.(48) with changing the parameters $\alpha = 0$, which approaches to $E_2 = (0.1043, 0, 0, 1.5942)$ and $\mathcal{R}_0 = 1.68$.

By changing the parameters $\beta_1 = 0.0000003$, and $\beta_3 = 0.0000002$ and keeping the rest of parameters values as in Eq.(48), , then the trajectories of the system (3) approach asymptotically to $E_3 = (0.1542, 0.1182, 2.8885, 0)$ as shown in Figure 6.

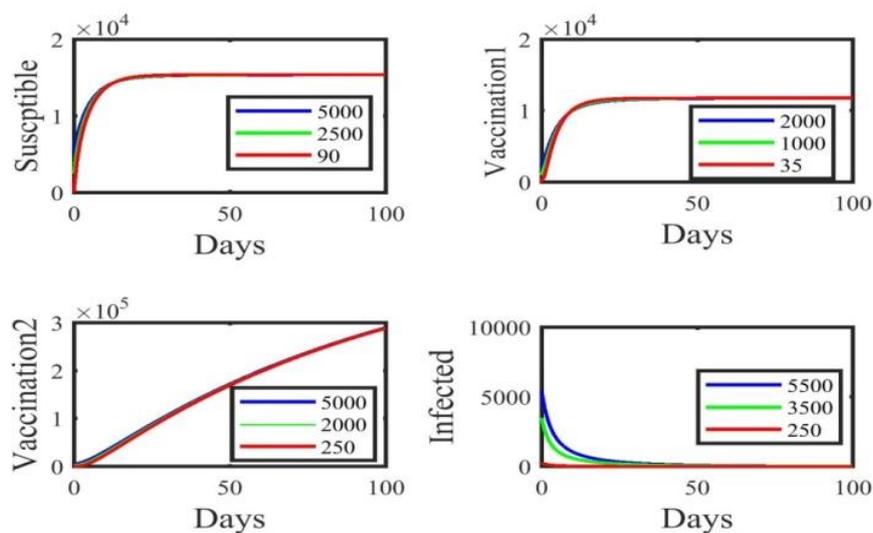


Figure 6: Time series of the trajectories of the system (3) for the rest of the data as given in Eq.(48) with changing the parameters $\beta_1 = 0.0000003$, and $\beta_3 = 0.0000002$, which approaches to $E_3 = (0.1542, 0.1182, 2.8885, 0)$ and $\mathcal{R}_{03} = 0.95463$

For Eq.(48) with changing the parameter $\gamma = 0$, then the trajectories of the system (3) approach asymptotically to $E_4 = (0.0953, 0.1360, 0, 1.5901)$ as shown in Figure 7.

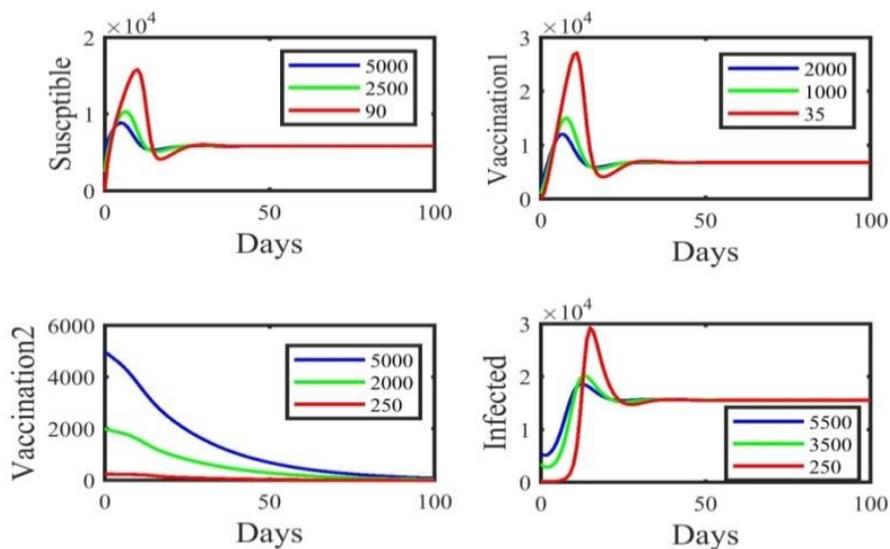


Figure 7: Time series of the trajectories of the system (3) for the rest of the data as given in Eq.(48) with changing the parameters $\gamma = 0$, which approaches to $E_4 = (0.0953, 0.1360, 0, 1.5901)$.

Now, we discuss the effect of the vaccination rate α , for Eq.(48) with different values of vaccination rate α given by the values of the parameters $\alpha = 0.5 \times 10^{-6}$, the trajectories of system (3) approach to TEP as shown in Figure 8.

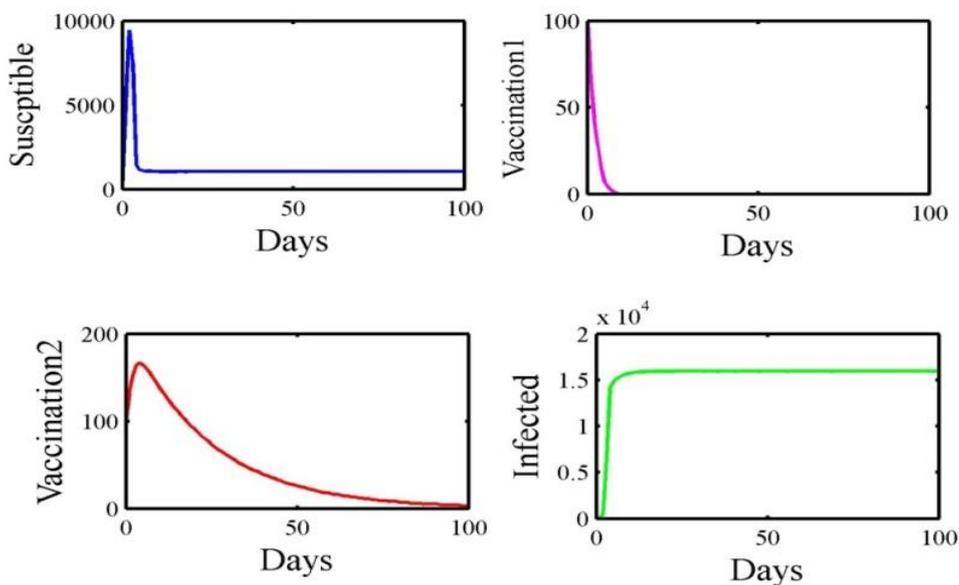


Figure 8: Time series of the trajectories of the system (3) for the rest of the data as given in Eq.(48) with changing the parameters $\alpha = 0.5 \times 10^{-6}$, which approaches to (TEP).

On the other hand, however, for Eq.(48) with different values of vaccination rate α given by the values of the parameters $\alpha = 50$, the trajectories of system (3) approach to SIEP as shown in Figure 9.

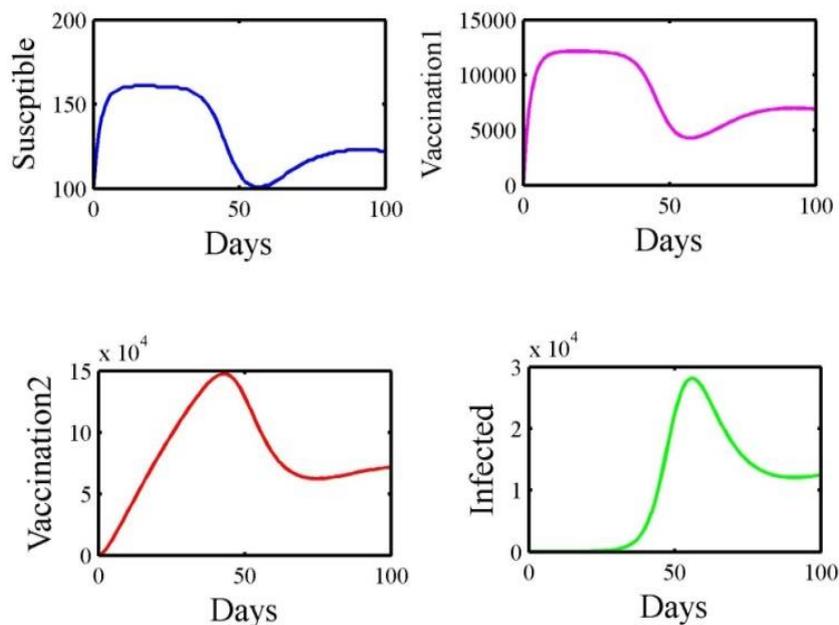


Figure- 9 Time series of the trajectories of the system (3) for the rest of the data as given in Eq.(48) with changing the parameters $\alpha = 50$, which approaches to (SIEP).

Now, we discuss the effect of the vaccination rate γ , for Eq.(48) with different values of vaccination rate γ given by the values of the parameters $\gamma = 0.4 \times 10^{-6}$, the trajectories of the system (3) approach to FIEP as shown in Figure 10.

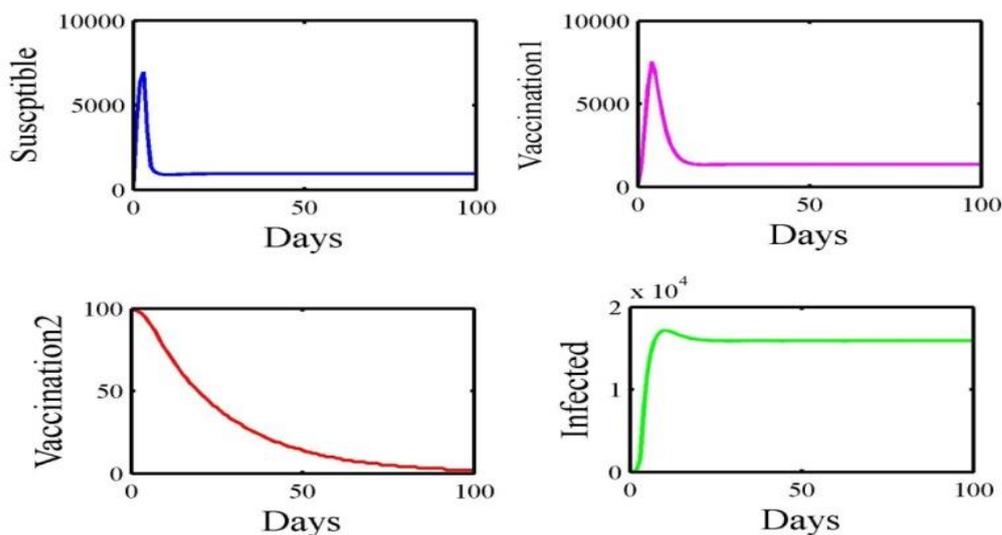


Figure 10: Time series of the trajectories of the system (3) for the rest of the data as given in Eq.(48) with changing the parameters $\gamma = 0.4 \times 10^{-6}$, which approaches to (FIEP).

On the other hand, however, for Eq.(48) with different values of vaccination rate γ given by the values of the parameters $\gamma = 50$, the trajectories of the system (3) approach to SIEP as shown in Figure 11.

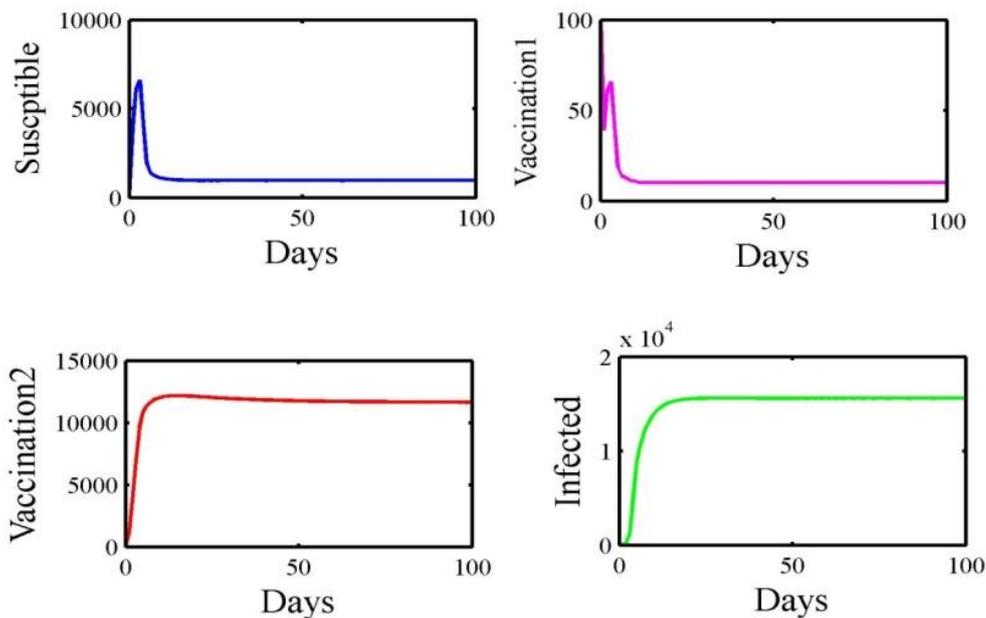


Figure 11: Time series of the trajectories of the system (3) for the rest of the data as given in Eq.(48) with changing the parameters $\gamma = 50$, which approaches to (SIEP).

Now, we discuss the effect of the fear rate of the vaccine, for Eq.(48) with different values of fear rate n given by the values of the parameters $n = 0.5 \times 10^{-6}$, the trajectories of the system (3) approach SIEP as shown in Figure 12.

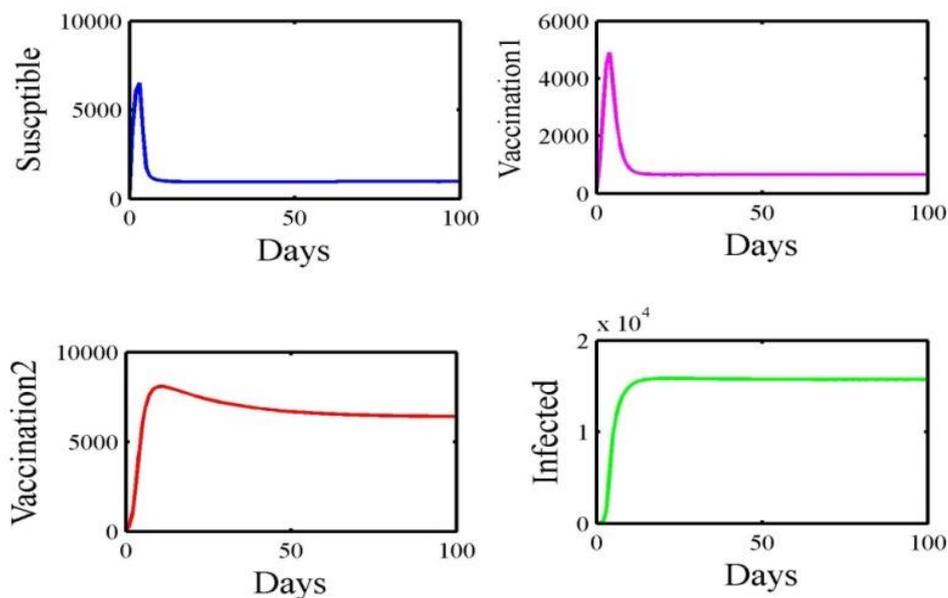


Figure 12: Time series of the trajectories of the system (3) for the rest of the data as given in Eq.(48) with changing the parameter $n = 50$, which approaches to (SIEP).

On the other hand, however, for Eq.(48) with different values of fear rate n given by the parameter value $n = 50$, the trajectories of the system (3) approach as shown in Figure 13.

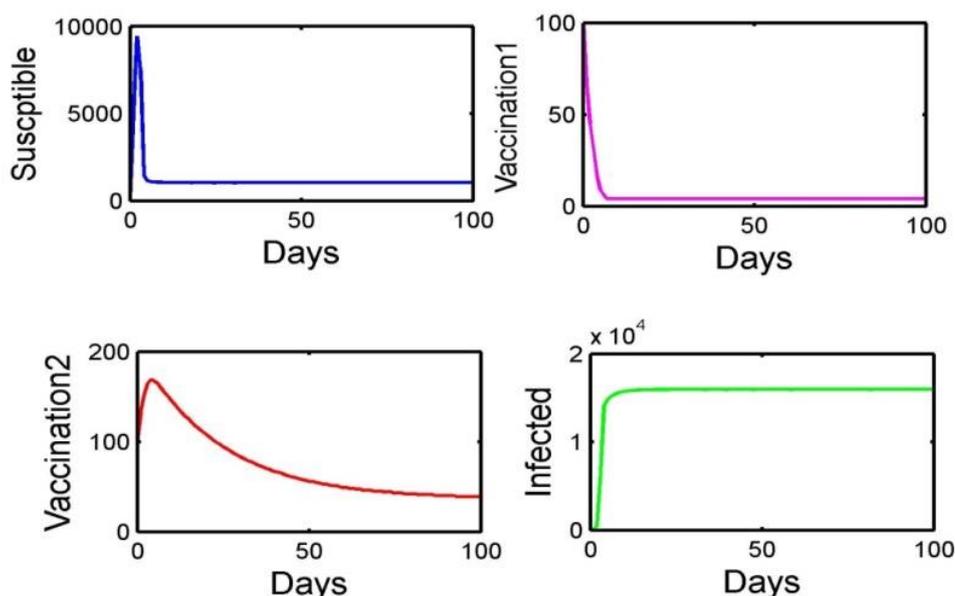


Figure 13: Time series of the trajectories of the system (3) for the rest of the data as given in Eq.(48) with changing the parameter $n = 50$.

7. Conclusion and discussion

In this section, we have looked at the impact of the COVID-19 disease on the two stages of the vaccination process which are explored mathematically and analytically. Understanding the impacts of vaccination on the populace is the study's goal. The system's boundedness has been studied. All potential system equilibrium points and their existence conditions are established. All feasible equilibrium points are studied for local and global stability. Both analytical and numerical methods are used to study the qualitative dynamical behavior as a result of changing the parameter values. Finally, system (3) is numerically solved for the hypothetical data set that is biologically plausible as given in Eq. (48). The results are explained in some common graphics. The results are summed up as follows:

- 1- Hypothetical parameters values are given by Eq.(48), and the system (3) has a globally asymptotically stable equilibrium point $E_5 = (S^*, V_1^*, V_2^*, I^*)$.
- 2- For the existence condition the vaccination rate $= 0$, it decreases the contacts rate between the susceptible with infected population β_1 below the specific value and increases the contacts rate between the vaccinated individuals of the second dose with infected population β_3 more than the particular value destabilizes the vaccination equilibrium point and the asymptotic trajectory to the FEP of the system (3).
- 3- For the existence condition the vaccination rate $\gamma = 0$, decreases both the contacts rate between the susceptible with infected population β_1 , the contacts rate between the vaccinated individuals of the first dose with infected population β_2 below the specific value and increasing the contacts rate between the vaccinated individuals of the second dose with infected population β_3 more than the specified value leads the endemic and vaccine to become destabilizing from the second dosage equilibrium point, and the trajectories of the system (3) approach asymptotically to the equilibrium point SEP.
- 4- Decreasing the contacts rate between the susceptible with infected population β_1 below the specific value and decreasing the contacts rate between the vaccinated individuals of the second dose with infected population β_3 lowering the particular value results in the endemic

equilibrium point becoming unstable, and the trajectories of system (3) approach to the equilibrium point (FOEP) .

5- It is observed that the proportion of caution and the vaccine and commitment to prevention factor only isn't enough to reduce the epidemic. But can reduce the epidemic dangers by applying all of it together.

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