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Local Asymptotic Stability and Sensitivity Analysis of a New Mathematical Epidemic Model Without Immunity

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Abstract
With this study it is aimed to introduce and analyze a new SIS epidemic model including vaccination effect. Vaccination considered in the model provides a temporary protection effect and is administered to both susceptible and new members of the population. The study provides a different aspect to the SIS models used to express, mathematically, some infectious diseases which are not eradicated by the immune system. The model given this study is designed by considering varying processes from person to person in the disease transmission, the recovery from disease (recovery without immunity) and in the loss of protective effect provided by the vaccine. The processes that change according to individuals are explained by distributed delays used in the relevant differential equations that provide the transition between compartments. The differences in the model are especially evident in these parts. In analyzing the model, firstly, the disease-free and endemic equilibrium points related to the model are determined. Then, the basic reproduction number $\mathcal{R}_0$ is calculated with the next generation matrix method. Next, the dynamics about locally asymptotically stable of the model at the disease-free and endemic equilibriums are examined according to the basic reproduction number $\mathcal{R}_0$. Attempts intended to reduce the spread of the disease are, of course, in the direction supporting the lowering the value $\mathcal{R}_0$. In this context, the reducing and enhancing effects of the parameters used in the model on the value $\mathcal{R}_0$ have been interpreted mathematically and suggestions were made to implement control measures in this direction. Also, in order to evaluate the support provided by the vaccine during the spread of the disease, the model has been examined as vaccinated and unvaccinated, and by some mathematical process, it has been seen that the vaccination has a crucial effect on disease control by decreasing the basic reproduction number. In other respects, by explored that the effect of parameters related to vaccination on the change of $\mathcal{R}_0$, a result about the minimum vaccination ratio of new members required for the elimination of the disease in the population within the scope of the target of $\mathcal{R}_0 < 1$ has been obtained.

Keywords: *Local Asymptotic Stability; Sensitivity Analysis; SIS model; Vaccine Effect; Disease-free equilibrium point; Endemic equilibrium point; Basic Reproduction Number.*

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1. Introduction

Mathematical modeling has been used to describe and analyze behaviors of many phenomena in the practical application areas such as theoretical ecology, mathematical epidemiology, economics, medicine, physics, chemical, biology, engineering and so on, [1–7]. Specially, the technique of compartmental modeling has become substantial tools in mathematical epidemiology for analyzing of the spread and control of infectious diseases. The modeling idea related to epidemic disease transmitted in a closed population consisting of susceptibles (S), infectives (I), and recovereds (R) were firstly considered by Kermack and McKendrick in 1927, [8]. Then, a lot of authors have dealt with various details to carry further forward this modeling technique. Along with, the historical adventure of compartmental modeling in mathematical epidemiology has proceeded from basic models to more detailed models. It is usually difficult or almost impossible the analytical examination of detailed models and so their usefulness for theoretical objectives is restricted, even though they may include substantial strategic values. On the other hand simple models may be inadequate for public health authorities who are faced with the need to make recommendations on strategies to deal with a particular situation. Therefore, the researches on the dynamics of basic but slightly more detailed models have folded day by day. Especially, it has been concentrated on seeing whether the variations in the models which are studied can lead to significant differences in behaviors related to qualitative and stability, with respect to models in classical type. Hereby, by using the general principles of modeling of epidemics, various models to describe the course of some epidemic diseases have been formulated, [9–18].

With the details studied in the epidemic models, specific principles including factors such as vaccination, quarantine, treatment; differences in systems reflecting transmission dynamics (such as being difference, differential, integral or integro-differential equations) or using of the delay element in the projected system ... etc. are meant. Vaccination appears as one of the significant factors between control measures for the dynamics in diseases transmission. Li and Ma studied on SIS epidemic model with vaccination in [19]. Cai and Li [20] examined the global stability of their $SEIV$ epidemic model with a nonlinear incidence rate.

In this paper, we formulate a new SIS model with distributed delays by adding the vaccination effect, too. To do this we use three distribute functions. Vaccination strategy in the model presented in this study base on administering to both susceptible and new members of the population. Also, in the model, we assume that the vaccinated individuals have temporary immunity and the losing of efficacy of vaccination varies from individual to individual depending on the fact that efficiency of any vaccine does not usually continue lifetime of the individual. On the other hand, it is thought that the infectiousness period in the transition from S to I and the recovery without immunity in transition from I to S vary from individual to individual. The fact that the system consists of integro-differential equations is originated from these effects varying according to individuals.

In the literature, there are studies that take into account the relative infectivity, [21–23], as well as the studies that assume that the immunity formed after vaccination is not permanent, [24].

On the other hand, by using nonlinear classical differential equations, models in which the delay period is the same and constant for all individuals can be made. However, nonlinear integro-differential equations are needed to express the delay process with distributed manner, provided that the delay process remains within a certain interval and varies according to individuals.

In the model introduced in this study, it is assumed that both the infectivity differs according to the individuals over time and the protection provided by the vaccination that does not create permanent immunity changes over time. In addition, the assumption that vaccinated individuals become relatively susceptible again with the loss of immunity is also reflected in the model. The study aims to contribute to the mathematical epidemiology literature with these novel aspects.

We continue this study to which we begin with introducing the model, with the qualitative and stability analysis of the model. In what follows, we evaluate the impact of vaccination on the model dynamics and discuss sensitivity analysis utilizing the normalized forward sensitivity index.

2. The Main Results Related to Research

The model which have been constructed by using the distribution function in three directions of transmission and adding vaccination effect is governed by a system of nonlinear integro-differential equations below.

$$\frac{dS}{dt} = (1-p)\,b - \beta S(t)\int_0^{h_1} f(\tau)\,I(t-\tau)\,d\tau - \sigma S(t) - \mu S(t) + \xi\int_0^{h_2} g(\theta)\,V(t-\theta)\,d\theta + \eta\int_0^{h_3} k(\gamma)\,I(t-\gamma)\,d\gamma,$$

$$\begin{aligned} \frac{dI}{dt} &= \beta S(t) \int_0^{h_1} f(\tau) I(t-\tau) d\tau - \eta \int_0^{h_3} k(\gamma) I(t-\gamma) d\gamma - \delta I(t) - \mu I(t), \\ \frac{dV}{dt} &= pb + \sigma S(t) - \xi \int_0^{h_2} g(\theta) V(t-\theta) d\theta - \mu V(t). \end{aligned} \tag{2.1}$$

According to the model, the population was divided into three categories: Susceptible (S), Vaccinated (V), and Infectious (I) individuals.

The susceptible class consists the individuals who are susceptible to the disease and have not any immunity. By infectious individuals, it is meant the individuals who are infected by the disease and are able to spread the disease to susceptible individuals.

Here $S(t)$, $I(t)$ and $V(t)$ represent the numbers of susceptible, infectious and vaccinated individuals at time t, respectively. The total population size at time t is $N(t)$ and for all $t \geq 0$, $N(t) = S(t) + I(t) + V(t)$. Also it is assumed that all functions and parameters used in the model are nonnegative. The inclusion of all newborn individuals into the population is provided by giving input to the susceptible and vaccinated classes with the constant rate b in total. The rates of natural death and the disease induced death are represented by μ and δ, respectively. β denotes the effective contact rate between infectious and susceptible individuals.

h_1 is maximum infectiousness period and τ indicates the period of time for each individual becomes infectious such that $0 \leq \tau \leq h_1$. By using f which is first distribution function used in the model, the density of individuals whose infectious period τ is indicated with $f(\tau)$. Classically, it is supposed that f is non-negative and continuous on $[0, h_1]$. Also f satisfies $\int_0^{h_1} f(\tau) d\tau = 1$. The term $f(\tau) I(t-\tau)$ corresponds to number of surviving individuals at time t who infected at time $t-\tau$ and have infectiousness period τ. The integral $\beta S(t) \int_0^{h_1} f(\tau) I(t-\tau) d\tau$ is expression that reflects transition of individuals to the compartment I as a result of effective contact between the susceptible and infectious individuals within their infectiousness period.

The model envisions a vaccination strategy in which the vaccine is effective on all individuals and vaccinated individuals are not become infected during their protection period. But the effectiveness of the vaccination loses over time. p shows the vaccination rate of newborns while $(1-p)\, b$ represents the inclusion rate of newborns without vaccination to the susceptibles. Also σ is the vaccination rate of individuals in susceptible group and ξ is the losing rate of effectiveness of the vaccine.

Besides these, g is the second distribution function such that $g(\theta)$ shows the ratio of individuals whose protection period provided by the vaccine is θ. h_2 is the maximum protection period provided by vaccination. So $\theta = 0$ means that the vaccine is completely ineffective. Also, $0 < \theta \leq h_2$ means that the vaccinated individuals gain only a finite protection period (partial protection). Classically it is supposed that g is non-negative and continuous on $[0, h_2]$ in addition that g satisfies $\int_0^{h_2} g(\theta) d\theta = 1$. The term $g(\theta) V(t-\theta)$ corresponds to number of surviving individuals at time t who have been vaccinated at time $t-\theta$ and whose protection period is θ.

According to this model, the vaccination does not provide a protective effect that will last forever. So, when the protection period is finished, the vaccinated individuals who no longer has any protection turns again to the susceptible compartment. To reflect this transition, we have used the expression $\xi \int_0^{h_2} g(\theta) V(t-\theta) d\theta$ in the model.

On the other hand, with entering the individuals to the recovery process, the amount of pathogens in the host individual's body become sufficiently low in the rate that the individual is no longer capable of transmitting the disease. Individuals who complete the recovery process return to class S because they have not acquire any immunity to the disease. η indicates the recovery rate of infectious individuals (recovery without immunity) and h_3 is maximum recovery period. γ indicates the time of recovery period of each individual with $0 \leq \gamma \leq h_3$. k is third distribution function used in the model such that $k(\gamma)$ denotes the density of individuals whose their recovery period is γ. Again, classically, it is supposed that k denotes non-negative and k is continuous on $[0, h_3]$, such that k satisfies $\int_0^{h_3} k(\gamma) d\gamma = 1$. The term $k(\gamma) I(t-\gamma)$ represents the number of surviving individuals at time t who have been infectious at time $t-\gamma$ and whose recovery period is γ. According to our model the recovery period is also a process that varies according to the individuals, just like the infectiousness period. Thus we use the

mathematical expression $\eta \int_0^{h_3} k(\gamma) I(t-\gamma)\, d\gamma$ in the transition from I to S to reflect the changing of the recovery process according to individuals.

2.1 The Qualitative Analysis Results

Before moving on to the analysis of the model, we have to be sure that solutions of the system (2.1) remain in a biologically feasible region for all parameters t belong to time. After preparation to this particular, we determine the equilibrium points and basic reproduction number of the model.

2.1.1 Feasible Positive Invariant Region for the Model

Theorem 2.1. *The bounded set*

$$\Theta = \left\{ (S,I,V) : S \in C(\mathbb{R}_+, \mathbb{R}_+),\ I \in C([-\max\{\tau,\gamma\}, \infty), \mathbb{R}_+),\ V \in C([-\theta,\infty), \mathbb{R}_+) : N(t) \leq \frac{b}{\mu} \right\} \tag{2.2}$$

is positively invariant for the model, where $\mathbb{R}_+ = [0,\infty)$.

Proof. By the sum of the differential equations that make up the system (2.1), the differential inequality

$$\begin{aligned} N'(t) &= \frac{dS}{dt} + \frac{dI}{dt} + \frac{dV}{dt} \\ &= b - \mu(S(t) + I(t) + V(t)) - \delta I(t) \\ &\leq b - \mu(N(t)) \end{aligned} \tag{2.3}$$

is obtained. The solution of this differential inequality is achieved from solving the differential equation

$$N'(t) + \mu N(t) = b.$$

Then, we get the solution

$$N(t) = N(0)e^{-\mu t} + \frac{b}{\mu}\left(1 - e^{-\mu t}\right) \tag{2.4}$$

for the initial condition $t = 0$. Standard Comparison Theorem [25] says that the right side of the equality (2.4) is the maximal solution of inequality (2.3). Thus we write

$$N(t) \leq N(0)e^{-\mu t} + \frac{b}{\mu}\left(1 - e^{-\mu t}\right)$$

for all $t \geq 0$.

It is obvious that $N(t) \leq b/\mu$ for all $t > 0$ when $N(0) \leq b/\mu$. Hence, Θ is positively invariant for the system (2.1).

On the other hand, it can be derived that $N(t)$ is bounded above with b/μ.

Consequently Θ is an asymptotic global attractor for all solutions of (2.1). Thus examining of the dynamics of (2.1) in the region Θ would be appropriate epidemiologically. □

2.1.2 Disease-Free Equilibrium Point

Since an equilibrium point of the system (2.1) is a constant solution of the system, it holds the equations constituting the system and so it is written as:

$$\begin{aligned} 0 &= (1-p)b - \beta S_0 I_0 - \sigma S_0 - \mu S_0 + \xi V_0 + \eta I_0, \\ 0 &= pb + \sigma S_0 - \xi V_0 - \mu V_0. \end{aligned}$$

From first and second equations, it is obtained respectively that

$$S_0 = \frac{(1-p)b + \xi V_0}{\sigma + \mu} \tag{2.5}$$

and

$$V_0 = \frac{pb + \sigma S_0}{\xi + \mu}, \tag{2.6}$$

for $I_0 \neq 0$. Substituting the equality (2.6) into (2.5), we get

$$S_0\left[\sigma\xi + \sigma\mu + \mu\xi + \mu^2 - \sigma\xi\right] = b\xi + b\mu\left(1-p\right)$$

and so

$$S_0 = \frac{b\left(\xi + \mu\left(1-p\right)\right)}{\mu\left(\xi + \mu + \sigma\right)}.$$

If this value is rewritten in (2.6), it is obtained that

$$V_0 = \frac{b\left(p\mu + \sigma\right)}{\mu\left(\xi + \mu + \sigma\right)}.$$

Hence, the disease-free equilibrium point of the model is

$$DFE = (S_0, I_0, V_0) = \left(\frac{b\left(\xi + \mu\left(1-p\right)\right)}{\mu\left(\xi + \mu + \sigma\right)}, 0, \frac{b\left(p\mu + \sigma\right)}{\mu\left(\xi + \mu + \sigma\right)}\right). \tag{2.7}$$

2.1.3 Basic Reproduction Number

The basic reproduction number denoted by $\mathcal{R}_0$ is described as the average number of new cases (secondary infections) created from one infectious individual in the wholly susceptible population through the entire length of him/her infectiousness period.

In this part, we determine the basic reproduction number of the model by using the next generation matrix approach, [26].

The dynamic system given by (2.1) can be written in matrix form as

$$\frac{dW}{dt} = \begin{bmatrix} \dot{I} \\ \dot{S} \\ \dot{V} \end{bmatrix},$$

where $W = (I, S, V)^T$.

For the system written in the form

$$\frac{dW}{dt} = \mathcal{Y}(W) - \mathcal{Z}(W),$$

$\mathcal{Y}(W)$ and $\mathcal{Z}(W)$ are the following matrices, respectively:

$$\mathcal{Y}(W) = \begin{bmatrix} \beta S\left(t\right) \int\limits_0^{h_1} f\left(\tau\right) I\left(t-\tau\right) d\tau \\ 0 \\ 0 \end{bmatrix}$$

and

$$\mathcal{Z}(W) = \begin{bmatrix} \mathcal{Z}(W)_{11} \\ \mathcal{Z}(W)_{21} \\ \mathcal{Z}(W)_{31} \end{bmatrix},$$

where

$$\begin{aligned}
\mathcal{Z}(W)_{11} &= \eta \int\limits_0^{h_3} k\left(\gamma\right) I\left(t-\gamma\right) d\gamma + \left(\delta + \mu\right) I\left(t\right), \\
\mathcal{Z}(W)_{21} &= \beta S\left(t\right) \int\limits_0^{h_1} f\left(\tau\right) I\left(t-\tau\right) d\tau + \sigma S\left(t\right) - \xi \int\limits_0^{h_2} g\left(\theta\right) V\left(t-\theta\right) d\theta - \eta \int\limits_0^{h_3} k\left(\gamma\right) I\left(t-\gamma\right) d\gamma + \mu S\left(t\right) - \left(1-p\right) b, \\
\mathcal{Z}(W)_{31} &= \xi \int\limits_0^{h_2} g\left(\theta\right) V\left(t-\theta\right) d\theta + \mu V\left(t\right) - \sigma S\left(t\right) - pb.
\end{aligned}$$

In this splitting, $\mathcal{Y}(W)$ is the matrix formed by writing of the partitionings in which new infections appear in compartments I, S and V, respectively; and $\mathcal{Z}(W)$ is the matrix formed by writing of the partitionings in which other transitions between compartments I, S, V, and other compartments, respectively.

Now we find the correspondences at the DFE of the derivative matrices of $\mathcal{Y}(W)$ and $\mathcal{Z}(W)$ with respect to I, S and V, respectively.

$$d\mathcal{Y}(DFE) = \begin{bmatrix} \beta S_0 & \beta I_0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}$$

and

$$d\mathcal{Z}(DFE) = \begin{bmatrix} \eta+\delta+\mu & 0 & 0 \\ \beta S_0 - \eta & \beta I_0 + \sigma + \mu & -\xi \\ 0 & -\sigma & \xi+\mu \end{bmatrix}.$$

Now, considering that the infection can only exist in compartment I, let us constitute the block matrices Y and Z as

$$Y = \mathcal{Y}_{11} = [\beta S_0]$$

and

$$Z = \mathcal{Z}_{11} = [\eta+\delta+\mu].$$

Hence

$$YZ^{-1} = \left[\frac{\beta S_0}{\eta+\mu+\delta}\right].$$

From the biological meanings of Y and Z, it follows that Y is entrywise non-negative and Z is a non-singular M-matrix, so Z^{-1} is entrywise non-negative. Let $\phi(0)$ shows the number of initially infected individuals. Then $YZ^{-1}\phi(0)$ is an entrywise non-negative vector giving the expected number of new infections. The matrix YZ^{-1} has $(1;1)$ entry equal to the expected number of secondary infections in compartments I produced by an infected individual introduced in compartments I. Thus YZ^{-1} is the next generation matrix and $\mathcal{R}_0 = \rho\left(YZ^{-1}\right)$; where ρ denotes the spectral radius.

Considering the component

$$S_0 = \frac{b(\xi+\mu(1-p))}{\mu(\xi+\mu+\sigma)}$$

of the DFE, the basic reproduction number of the system (2.1) is obtained as

$$\begin{aligned} \mathcal{R}_0 &= \rho\left(YZ^{-1}\right) \\ &= \frac{\beta S_0}{\eta+\mu+\delta} \\ &= \frac{b\beta(\xi+\mu(1-p))}{\mu(\xi+\mu+\sigma)(\eta+\mu+\delta)}. \end{aligned}$$

2.1.4 Existence and Uniqueness of Endemic Equilibrium Point

Now, we handle the problem of existence and uniqueness of endemic equilibrium point of the presented model. The endemic equilibrium $EE(S^*, I^*, V^*)$ which is a constant solution of differential equations constituting the system (2.1) satisfies the algebraic equations

$$\begin{aligned} 0 &= (1-p)b - \beta S^* I^* - \sigma S^* - \mu S^* + \xi V^* + \eta I^*, \\ 0 &= \beta S^* I^* - \eta I^* - (\mu+\delta) I^*, \\ 0 &= pb + \sigma S^* - \xi V^* - \mu V^*, \end{aligned} \tag{2.8}$$

such that $I^* \neq 0$. From second equation of this algebraic system, we write

$$I^*(\beta S^* - \eta - (\mu+\delta)) = 0.$$

So, it must be

$$\beta S^* - \eta - (\mu+\delta) = 0.$$

Then

$$S^* = \frac{\eta + \mu + \delta}{\beta}. \tag{2.9}$$

If S^* obtained in (2.9) is written in third equation of (2.8), V^* is found as

$$V^* = \frac{pb\beta + \sigma(\eta + \mu + \delta)}{\beta(\xi + \mu)}.$$

On the other hand, by considering $\mathcal{R}_0$, S^* and V^* are written as

$$S^* = \frac{b(\xi + \mu(1-p))}{\mu(\xi + \mu + \sigma)\mathcal{R}_0}$$

and

$$V^* = \frac{pb\mu(\xi + \mu + \sigma)\mathcal{R}_0 + \sigma b(\xi + \mu(1-p))}{\mu(\xi + \mu)(\xi + \mu + \sigma)\mathcal{R}_0}.$$

Now, by using these equalities we have obtained, we will focus on the first equation of the system (2.8).

$$\left[\beta\frac{b(\xi + \mu(1-p))}{\mu(\xi + \mu + \sigma)\mathcal{R}_0} - \eta\right] I^* = (1-p)b - (\sigma + \mu)\frac{b(\xi + \mu(1-p))}{\mu(\xi + \mu + \sigma)\mathcal{R}_0} + \xi\frac{pb\mu(\xi + \mu + \sigma)\mathcal{R}_0 + \sigma b(\xi + \mu(1-p))}{\mu(\xi + \mu)(\xi + \mu + \sigma)\mathcal{R}_0}.$$

After regulations, we write

$$I^* = \frac{\begin{array}{c}(1-p)b\mu(\xi + \mu + \sigma)(\xi + \mu)\mathcal{R}_0 - b(\sigma + \mu)(\xi + \mu(1-p))(\xi + \mu) \\ +\xi[pb\mu(\xi + \mu + \sigma)\mathcal{R}_0 + \sigma b(\xi + \mu(1-p))]\end{array}}{(\xi + \mu)[b\beta(\xi + \mu(1-p)) - \eta\mu(\xi + \mu + \sigma)\mathcal{R}_0]}.$$

Precisely in this part, it has great importance to regulate the numerator of this fraction with careful operations. The numerator part of I^* can be written as

$$(1-p)b\mu(\xi + \mu + \sigma)(\xi + \mu)\mathcal{R}_0 - b(\sigma + \mu)\xi(\xi + \mu) - b\mu(1-p)(\sigma + \mu)(\xi + \mu) + \xi pb\mu(\xi + \mu + \sigma)\mathcal{R}_0 + \xi\sigma b(\xi + \mu(1-p)).$$

If the first and fourth terms of the numerator consisting of five sums are taken into the common factor ($(\xi + \mu + \sigma)\mathcal{R}_0$) parenthesis, it is obtained the term $(\xi + \mu + \sigma)\mathcal{R}_0 b\mu(\xi + \mu(1-p))$. From second and third terms, it comes $-b(\xi + \mu)(\sigma + \mu)(\xi + \mu(1-p))$. If this last term and the fifth term of the sum are considered together, it is obtained that $-b\mu(\xi + \sigma + \mu)(\xi + \mu(1-p))$.

So with the last rearrangement of the numerator part, we obtain

$$\begin{aligned} I^* &= \frac{b\mu(\xi + \mu(1-p))(\xi + \mu + \sigma)[\mathcal{R}_0 - 1]}{(\xi + \mu)\left[\underbrace{b\beta(\xi + \mu(1-p))}_{\mu(\xi+\mu+\sigma)(\eta+\mu+\delta)\mathcal{R}_0} - \eta\mu(\xi + \mu + \sigma)\mathcal{R}_0\right]} \\ &= \frac{b(\xi + \mu(1-p))(\mathcal{R}_0 - 1)}{(\mu + \delta)(\xi + \mu)\mathcal{R}_0}. \end{aligned}$$

Hence I^* is meaningful for only $\mathcal{R}_0 > 1$. Thus, we say that the system (2.1) has a unique endemic equilibrium point formulated by equality

$$\begin{aligned} EE &= (S^*, I^*, V^*) \\ &= \left(\frac{b(\xi + \mu(1-p))}{\mu(\xi + \mu + \sigma)\mathcal{R}_0}, \frac{b(\xi + \mu(1-p))(\mathcal{R}_0 - 1)}{(\mu + \delta)(\xi + \mu)\mathcal{R}_0}, \frac{pb\mu(\xi + \mu + \sigma)\mathcal{R}_0 + \sigma b(\xi + \mu(1-p))}{\mu(\xi + \mu)(\xi + \mu + \sigma)\mathcal{R}_0}\right), \end{aligned}$$

when $\mathcal{R}_0 > 1$.

2.2 The Stability Analysis Results

In this section, we explore the asymptotic behaviors of the equilibrium points for the model (2.1).

Theorem 2.2. *The disease-free equilibrium point DFE is locally asymptotically stable in Θ for $\mathcal{R}_0 < 1$.*

Proof. For the system (2.1), the Jacobian matrix at $DFE = (S_0, I_0, V_0)$ is

$$J(DFE) = \begin{bmatrix} -\beta I_0 - \sigma - \mu & -\beta S_0 + \eta & \xi \\ \beta I_0 & \beta S_0 - \eta - \mu - \delta & 0 \\ \sigma & 0 & -\xi - \mu \end{bmatrix}.$$

Since $I_0 = 0$, the characteristic equation which is correspond to this Jacobian matrix is

$$\begin{aligned} \det(J(DFE) - \lambda I_3) &= \begin{vmatrix} -(\sigma+\mu) - \lambda & -\beta S_0 + \eta & \xi \\ 0 & \beta S_0 - \eta - \mu - \delta - \lambda & 0 \\ \sigma & 0 & -\xi - \mu - \lambda \end{vmatrix} \\ &= (\beta S_0 - \eta - \mu - \delta - \lambda)\left[(\sigma + \mu + \lambda)(\xi + \mu + \lambda) - \sigma\xi\right] \\ &= 0. \end{aligned} \tag{2.10}$$

From hence, for the roots of characteristic equation given by (2.10), we write

$$\begin{aligned} \lambda_1 &= \beta S_0 - (\eta + \mu + \delta) \\ &= (\eta + \mu + \delta)(\mathcal{R}_0 - 1). \end{aligned}$$

The remaining roots are obtained from the equation

$$\lambda^2 + (\xi + \sigma + 2\mu)\lambda + \mu\xi + \sigma\mu + \mu^2 = 0.$$

For this quadratic equation,

$$\lambda_2 + \lambda_3 = -(\xi + \sigma + 2\mu) < 0$$

and

$$\lambda_2\lambda_3 = \mu(\xi + \sigma + \mu) > 0.$$

While $\mathcal{R}_0 < 1$, all roots of the characteristic equation always have the negative sign. Therefore DFE is locally asymptotically stable for $\mathcal{R}_0 < 1$. □

To prove that the EE is locally asymptotically stable when $\mathcal{R}_0 > 1$, we will use the criteria which is well known in the literature and given by Routh and Hurwitz.

Theorem 2.3. *The endemic equilibrium point EE is locally asymptotically stable in Θ for $\mathcal{R}_0 > 1$.*

Proof. The Jacobian matrix of system (2.1) at $EE = (S^*, I^*, V^*)$ is

$$J(EE) = \begin{bmatrix} -\beta I^* - \sigma - \mu & -\beta S^* + \eta & \xi \\ \beta I^* & \beta S^* - \eta - \mu - \delta & 0 \\ \sigma & 0 & -\xi - \mu \end{bmatrix}.$$

Thus, the characteristic equation which is correspond to $J(EE)$ is

$$\lambda^3 + C_1\lambda^2 + C_2\lambda + C_3 = 0, \tag{2.11}$$

where

$$C_1 = \beta I^* + \xi + \sigma + 2\mu,$$

$$C_2 = \mu\beta I^* + \delta\beta I^* + \mu\xi + \sigma\xi + \beta\xi I^* + \mu^2 + \mu\sigma + \mu\beta I^*$$

and

$$C_3 = \mu\beta\xi I^* + \delta\beta\xi I^* + \mu^2\beta I^* + \mu\delta\beta I^*.$$

Since C_1, C_2, C_3 are positive, we can determine stability of the system (2.1) by using Routh-Hurwitz Criteria. According to this criteria,

$$H_1 = C_1 > 0$$

and

$$H_2 = \frac{C_1 C_2 - C_3}{C_1}.$$

After required simplifications, the numerator part of the value H_2 is obtained as

$$\begin{aligned} C_1C_2 - C_3 &= \mu(\beta I^*)^2 + \delta(\beta I^*)^2 + \mu\xi\beta I^* + \sigma\xi\beta I^* + \xi(\beta I^*)^2 + \mu^2\beta I^* + \mu\sigma\beta I^* + \mu(\beta I^*)^2 + \sigma\mu\beta I^* + \sigma\delta\beta I^* \\ &\quad + \sigma\mu\xi + \sigma^2\xi + \sigma\xi\beta I^* + \sigma\mu^2 + \mu\sigma^2 + \sigma\mu\beta I^* + \mu^2\beta I^* + \mu\delta\beta I^* + 2\mu^2\xi + 2\mu\sigma\xi + 2\mu\beta\xi I^* \\ &\quad + 2\mu^3 + 2\mu^2\sigma + 2\mu^2\beta I^* + \mu\beta\xi I^* + \mu\xi^2 + \sigma\xi^2 + \xi^2\beta I^* + \mu^2\xi + \sigma\mu\xi \\ &> 0. \end{aligned}$$

and so

$$H_2 > 0.$$

Finally,

$$H_3 = C_3 > 0.$$

Thus, according to Routh-Hurwitz stability criteria, all eigenvalues of the Jacobian matrix of system (2.1) at the endemic equilibrium point EE, that is, each of the roots of equation (2.11) have negative real parts. Consequently, if $\mathcal{R}_0 > 1$ then the endemic equilibrium $EE = (S^*, I^*, V^*)$, which is unique equilibria for the system (2.1), is locally asymptotically stable. □

2.3 The Effect of Vaccination on the Spread of Disease

When the model is considered without vaccine (in this case, $\sigma = p = 0$ and so $\xi = 0$)) it transforms to SIS epidemic model in the following form:

$$\begin{aligned} \frac{dS}{dt} &= b - \beta S(t)\int_0^{h_1} f(\tau) I(t-\tau)\, d\tau + \eta\int_0^{h_3} k(\gamma) I(t-\gamma)\, d\gamma - \mu S(t), \\ \frac{dI}{dt} &= \beta S(t)\int_0^{h_1} f(\tau) I(t-\tau)\, d\tau - \eta\int_0^{h_3} k(\gamma) I(t-\gamma)\, d\gamma - \delta I(t) - \mu I(t) \end{aligned}$$

and for this model, the basic reproduction number is

$$\breve{\mathcal{R}}_0 = \frac{b\beta}{\mu(\eta + \mu + \delta)}.$$

It can be easily seen that there exists the relationship

$$\mathcal{R}_0 = \left(1 - \frac{\mu p + \sigma}{\xi + \mu + \sigma}\right)\breve{\mathcal{R}}_0$$

between $\mathcal{R}_0$ and $\breve{\mathcal{R}}_0$. Here $\mathcal{R}_0 < \breve{\mathcal{R}}_0$ and this mathematical result indicates that, obviously, vaccination has a crucial effect on disease control by decreasing the basic reproduction number. Thus, with the appropriate vaccination strategy, the disease can be eradicated in the population by keeping the value $\mathcal{R}_0$ below 1.

Several mathematical operations give us:

$$\begin{aligned} \mathcal{R}_0 &< 1 \\ &\Leftrightarrow \left(\breve{\mathcal{R}}_0 - \frac{(\mu p + \sigma)\breve{\mathcal{R}}_0}{\xi + \mu + \sigma}\right) < 1 \\ &\Leftrightarrow (\xi + \mu)\left(\breve{\mathcal{R}}_0 - 1\right) < \sigma + \mu p\breve{\mathcal{R}}_0. \end{aligned}$$

Thus, within the scope of the target of $\mathcal{R}_0 < 1$, the value $p_{\min}$ that comes with the inequality

$$p_{\min} > \frac{(\xi+\mu)\left(\breve{\mathcal{R}}_0 - 1\right) - \sigma}{\mu\breve{\mathcal{R}}_0} \tag{2.12}$$

is the minimum vaccination ratio of new members required for the elimination of the disease in the population. We note obviously that the parameters which define $p_{\min}$ in (2.12) should be chosen such that $0 < p_{\min} < 1$. Also, since the other parameter determined the number of vaccinated individuals is σ, the choosing of parameters $p_{\min}$ and σ should be considered together in (2.12). The result obtained about $p_{\min}$ means that, with increasing of σ and with decreasing of ξ, $\mathcal{R}_0$ decreases and so the spread of the disease gradually decreases in the population. Therefore it is meaningful that the efforts to increasing σ or decreasing ξ. This result will be seen again from the mathematical explanations in a different perspective in the following part.

2.4 Sensitivity Analysis

One of the main objectives of the epidemic investigations is to suggest strategies such that it will ensure that the necessary control measures are taken to stop the epidemic and to prevent possible outbreaks in the future. Attempts intended to reduce the spread of the disease are, of course, in the direction supporting the lowering the value $\mathcal{R}_0$. Considering that there are many negative conditions brought about by the disease, together with the difficulty of completely eliminating the epidemic in a population in a short time, attempts to reduce the spread of the disease are very important. In this sense, with various control measures which will be implemented; lowering the value $\mathcal{R}_0$ is one of the most fundamental issues. Thus, it has a major significance to explore the effect of parameters on the change of $\mathcal{R}_0$ and to apply control measures in this direction. To this, in the followings, we will evaluate the influence aspects of the parameters that affect $\mathcal{R}_0$ by determining the normalized forward sensitivity index of it. The normalized forward sensitivity index of the variable $\mathcal{R}_0$ with respect to the parameter ϑ is defined as

$$\mathcal{Q}_{\vartheta}^{\mathcal{R}_0} = \frac{\partial \mathcal{R}_0}{\partial \vartheta} \times \frac{\vartheta}{\mathcal{R}_0},$$

by using partial derivative. Where ϑ represents the basic parameters constituting $\mathcal{R}_0$. In that case,

$$\mathcal{Q}_{\beta}^{\mathcal{R}_0} = \frac{\partial \mathcal{R}_0}{\partial \beta} \times \frac{\beta}{\mathcal{R}_0} = 1 > 0$$

and

$$\begin{aligned} \mathcal{Q}_{\xi}^{\mathcal{R}_0} &= \frac{\partial \mathcal{R}_0}{\partial \xi} \times \frac{\xi}{\mathcal{R}_0} \\ &= \frac{(\sigma+\mu p)\,\xi}{(\xi+\mu+\sigma)\,(\xi+\mu\,(1-p))} > 0. \end{aligned}$$

By increasing of these parameters that have additive effect on the spread of disease, $\mathcal{R}_0$ increases and so the disease gets out of control in the population. Therefore, the control measures which will be established should be aimed at reducing of the parameters β and ξ.

Now let us concentrate to the effect of parameters related to vaccine on $\mathcal{R}_0$. If we calculate, the normalized forward sensitivity index taking account of the derivatives of $\mathcal{R}_0$ with respect to p and σ, we get

$$\begin{aligned} \mathcal{Q}_{p}^{\mathcal{R}_0} &= \frac{\partial \mathcal{R}_0}{\partial p} \times \frac{p}{\mathcal{R}_0} \\ &= -\frac{\mu p}{\xi+\mu\,(1-p)} < 0 \end{aligned}$$

and

$$\begin{aligned} \mathcal{Q}_{\sigma}^{\mathcal{R}_0} &= \frac{\partial \mathcal{R}_0}{\partial \sigma} \times \frac{\sigma}{\mathcal{R}_0} \\ &= -\frac{\sigma}{\xi+\mu+\sigma} < 0. \end{aligned}$$

Thus the disease can be eliminated with some favorable and adequate vaccination strategies. For example, one of the necessary conditions for disease elimination is given in the result of mathematical calculation in (2.12). Improvements in these two parameters that depend on the efficacy of vaccines may lead to disease eradication.

On the other hand

$$\begin{aligned} \mathcal{Q}_{\eta}^{\mathcal{R}_0} &= \frac{\partial \mathcal{R}_0}{\partial \eta} \times \frac{\eta}{\mathcal{R}_0} \\ &= -\frac{\eta}{\eta+\mu+\delta} < 0 \end{aligned}$$

and

$$\begin{aligned} \mathcal{Q}_{\delta}^{\mathcal{R}_0} &= \frac{\partial \mathcal{R}_0}{\partial \delta} \times \frac{\delta}{\mathcal{R}_0} \\ &= -\frac{\delta}{\eta+\mu+\delta} < 0. \end{aligned}$$

The parameters η and δ that its sensitivity indices are negative will bring about the decrease in $\mathcal{R}_0$. Therefore, strategies and actions developed on these two parameters will be useful in order that the spread of disease enters a downward course.

3. Concluding Remarks

While expressing dynamic systems mathematically, nonlinear and moreover delayed differential equations are needed to construct closer models to reality in the expression of complex phenomena. Because of the fact that nonlinearity and the existence of delay in a system may lead to being much more complex of analysis and control of the system, in particular, studying with nonlinear differential equations with delays is quite coercive mathematically.

All these difficulties aside, the dynamic analysis of nonlinear systems is often examined by looking at the local stability of the system. To reach conclusions related to local stabilities, it is needed to look at the linearized equivalent of any equilibrium point of the nonlinear system. Thus it can be reached a conclusion about the local dynamics of the system.

In this paper, a new mathematical epidemic model under the vaccine effect is constructed. Also asymptotic behaviors of solutions by evaluating the local stabilities of equilibrium points for mentioned model are examined.

Subsequently, in order to evaluate the support provided by the vaccine during the spread of the disease, the model has been considered as vaccinated and unvaccinated, and it has been seen that the vaccination has a crucial effect on disease control by decreasing the basic reproduction number with several mathematical operations. Thus, with the appropriate vaccination strategy, the disease can be eradicated in the population by keeping the value $\mathcal{R}_0$ below 1. Also, within the scope of the target of $\mathcal{R}_0 < 1$, a result about the minimum vaccination ratio of new members required for the elimination of the disease in the population has been obtained.

Also in this part, the effects on $\mathcal{R}_0$ of the parameters σ and p which represents the vaccination rate of susceptible individuals and of the parameter ξ which the losing rate of protective effect provided by the vaccine have been determined; and the control measures which will can be applied on these parameters have been interpreted.

One of the main objectives of the epidemic investigations is to suggest strategies such that it will ensure that the necessary control measures are taken to decrease and if it is possible to stop the epidemic and to prevent possible outbreaks in the future. Attempts intended to reduce the spread of the disease are, of course, in the direction supporting the lowering the value $\mathcal{R}_0$. In this context, the reducing and enhancing effects of the parameters used in the model on the value $\mathcal{R}_0$ have been interpreted mathematically and suggestions were made to implement control measures in this direction.

Nowadays, with the advancement of science, the desires and efforts of individuals have been increased in solving and analyzing more complex problems. In this sense, the various nonlinear dynamic systems have been formed to explain the more complex mechanisms in the struggle against epidemics and it have been examined the stability behaviors of these new models. As a matter of course, the several details such as adding some different compartments (exposed, asymptomatic infectious, etc.) or adding some parameters reflecting various control measures (isolation etc.) may be considered to carry forward this model.

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References

[1] Şekerci Fırat, Y.: *Climate change forces plankton species to move to get rid of extinction: mathematical modeling approach*. Eur. Phys. J. Plus. **135**:794, 1-20 (2020).

[2] Özarslan, R., Şekerci Fırat, Y.: *Fractional order oxygen plankton system under climate change*, Chaos. **30**(3), 33131 (2020).

[3] Şekerci Fırat, Y., Özarslan, R.: *Dynamic analysis of time fractional order oxygen in a plankton system*. Eur. Phys. J. Plus. **135**(1), 1-13 (2020).

[4] Daşbaşı, B., Boztosun, D.: *Stability analysis of the palomba model in economy by fractional-order differential equations with multi-orders.* The Journal of International Social Research. **11** (59), 1-7 (2018).

[5] Yavuz, M., Sene, N.: *Stability analysis and numerical computation of the fractional predator-prey model with the harvesting rate*. Fractal Fract. **4(3)**, 35 1-22 (2020).

[6] Yavuz, M., Özdemir N.: *Analysis of an epidemic spreading model with exponential decay law*. Mathematical Sciences and Applications E-Notes. **8**(1), 142-154 (2020).

[7] Yavuz, M., Bonyah E.: *New approaches to the fractional dynamics of schistosomiasis disease model*. Physica A: Statistical Mechanics and its Applications. **525**, 373-393 (2019).

[8] Kermack, W. O., McKendrick, A. G.: *A contributions to the mathematical theory of epidemics*. Proc. Roy. Soc. A. **115,** 700-721 (1927)**.**

[9] Çakan, S.: *Dynamic analysis of a mathematical model with health care capacity for COVID-19 pandemic*. Chaos, Solitons and Fractals. **139**, 110033, (2020).

[10] Aghdaoui, H., Alaoui A. L., Nisar K. S., Tilioua, M.: *On analysis and optimal control of a SEIRI epidemic model with general incidence rate*, Results in Physics, **20**, 103681 1-9 (2021).

[11] Gölgeli, M., Atay F. M.: *Analysis of an epidemic model for transmitted diseases in a group of adults and an extension to two age classes*. Hacet. J. Math. Stat. **49** (3), 921-934 (2020).

[12] Naik, P. A.: *Global dynamics of a fractional-order SIR epidemic model with memory*. Int J Biomath. **13**(8), 2050071 (2020).

[13] Naik, P. A., Zu, J., Owolabi M.K.: *Modeling the mechanics of viral kinetics under immune control during primary infection of HIV-1 with treatment in fractional order*. Physica A. **545**, 123816 (2020).

[14] Naik, P. A., Zu, J., Ghoreishi, M.: *Stability analysis and approximate solution of SIR epidemic model with Crowley-Martin type functional response and holling type-II treatment rate by using homotopy analysis method*. J Appl Anal Comput. **10**(4), 1482-1515 (2020).

[15] Naik, P. A., Yavuz, M., Qureshi, S., Zu, J., Townley, S.: *Modeling and analysis of COVID-19 epidemics with treatment in fractional derivatives using real data from Pakistan*. Eur. Phys. J. Plus. **135**(10), 795 (2020).

[16] Naik, P. A., Yavuz, M., Zu, J.: *The role of prostitution on HIV transmission with memory: A modeling approach*. Alexandria Eng J. **59**(4), 2513-2531 (2020).

[17] Naik, P. A., Owolabi M. K., Yavuz, M., Zu, J.: *Chaotic dynamics of a fractional order HIV-1 model involving AIDS-related cancer cells*. Chaos Solitons & Fractals. **140**, 110272 (2020).

[18] Yavuz, M., Coşar, F. Ö., Günay, F., Özdemir, F. N.: *A new mathematical modeling of the COVID-19 pandemic including the vaccination campaign*. Open Journal of Modelling and Simulation. **9**(3), 299-321 (2021).

[19] Li, J., Ma, Z.: *Qualitative analyses of SIS epidemic model with vaccination and varying total population size*. Math. Comput. Model. **35,** 1235-1243 (2002).

[20] Cai, L. M., Li, X. Z.: *Analysis of a SEIV epidemic model with a nonlinear incidence rate*. Applied Mathematical Modelling. **33** (5), 2919-2926 (2009).

[21] McCluskey C. C.: *Complete global stability for an SIR epidemic model with delay-Distributed or discrete*, Nonlinear Anal. Real World Appl., **11** (1), 55-59 (2010).

[22] Elazzouzi, A., Alaoui, A. L., Tilioua, M., Torres, D. F. M.: *Analysis of a SIRI Epidemic Model with Distributed Delay and Relapse*. Statistics, Optimization and Information Computing, **7**(3), 545-557 (2019).

[23] Elazzouzi, A., Alaoui A. L., Tilioua, M., Tridane, A.: *Global stability analysis for a generalized delayed SIR model with vaccination and treatment*, Adv. Difference Equ., **532**, 1-19 (2019).

[24] Li, J., Ma, Z.: *Global analysis of SIS epidemic models with variable total population size*. Math. Comput. Model. **39**, 1231-1242 (2004).

[25] Lakshmikantham, S., Leela, S., Martynyuk, A. A.: Stability analysis of nonlinear systems. Marcel Dekker, Inc., New York (1989).

[26] Driessche, P. V. D., Watmough J.: *Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission*, Math.Biosci. **180**, 29-48 (2002).

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