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Optimal Control of a Leptospirosis Epidemic Model

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ABSTRACT

In this paper, we extend the mathematical model of leptospirosis disease by considering the interaction of susceptible humans and susceptible vectors with both infected humans and infected vectors. Initially, we present the disease-free and endemic equilibrium points and also the basic reproduction number. Then, we introduce three control strategies by using Pontryagin's Maximum Principle to derive necessary conditions for the optimal control of the disease. Finally, we discuss the numerical results.

Keywords: Leptospirosis; Mathematical model; Basic reproduction number; Optimal control; Numerical-simulation

1. Introduction

Leptospirosis is an infectious disease of humans and animals that is caused by pathogenic spirochetes of the genus Leptospira. It is considered the most common zoonosis, a disease that can be spread from animals to humans, in the world [1]. Leptospirosis is distributed worldwide but is most common in the tropical climate.

Leptospirosis has been recognized as a re-emerging infectious disease among animals and humans and has the potential to become even more prevalent with advancing climate change and related trends [2]. Leptospira species infect a wide range of animals, including mammals, birds, amphibians, and reptiles. Humans are rarely chronic carriers and are therefore considered accidental hosts. The organism is typically transmitted via exposure of mucous membranes or abraded skin to the body fluid of an acutely infected animal or by exposure to soil or fresh water contaminated with the urine of an animal that is a chronic carrier [3].

In Southeast Asia, including Thailand, the epidemics of leptospirosis occur from July to October. Leptospirosis outbreaks continue to be predominantly an occupational disease related to wading through contaminated water; most cases occur among farmers, agricultural workers (notably rice producers), veterinarians,

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rescue workers and military personnel. In recent decades it has also increasingly been recognized as a disease of recreation. The outbreaks of the disease can also occur after storms, heavy rainfalls, or floods. Moreover, it may be acquired during adventure travel or outdoor activities such as swimming, hiking, canoeing or camping [4].

Most leptospirosis epidemic models use the susceptible-infective-removed (SIR) model [5-10] that has been used to describe the transmission dynamics of many infectious diseases without considering the exposed individuals who are infected but are not yet infectious. Besides, very little has been done in the area of applying optimal control theory to study and analyze the dynamics of leptospirosis. To do this, we introduce the optimal campaign by using three control variables. Our first control variable represents the standard precautions in health care including hand hygiene which is a major component of standard precautions and one of the most effective methods to prevent transmission of pathogens associated with health care. In addition to hand hygiene, the use of personal protective equipment (PPE) is important [11]. The second control variable represents the compliance of the patient in carrying out expected/instructed activities at home including monitoring the urine output and looking for symptoms and signs if a decision is made to manage a leptospirosis patient on an out-patient basis [12]. The third control variable represents a rodent control program in places [11].

In this paper, we considered the exposed class to human population and extend the model presented in [13] by considering both the interaction of susceptible humans and susceptible vectors with both infected humans and infected vectors in nonlinear terms which is different from the previous works. First, we present the equilibrium points and the basic reproduction number. Then, we derive the conditions under which it is optimal to control leptospirosis infection using Pontryagin's Maximum Principle. We also solve the optimality system numerically using the data presented for leptospirosis epidemic in Thailand [13]. Finally, we discuss the numerical results.

The structure of this paper is organized as follows. In Section 2, we will present the mathematical model of leptospirosis disease and obtain the basic reproduction number. In Section 3, we present the control problem and derive the necessary conditions for an optimal control. Section 4 is devoted to numerical solutions of the optimality system.

2. Materials and Methods

We know that leptospirosis is spread through the urine of infected animals, which gets into water or soil and can survive there for weeks to months. Animals become infected when they come into direct contact with this contaminated water or soil. The bacteria enter through cuts in the skin or through mucous membranes (eyes, nose or mouth). Animals can also become infected by drinking contaminated water [13]. According to this, we also extend by adding the interaction between susceptible vector and infected vector with the transmission rate.

To formulate the Leptospirosis model that, we develop from the model presented in [13] we assume that, the human population is divided into four compartments: susceptible human (S_h), exposed human (E_h), infected human (I_h) and recovered human (R_h). For the vector population, we assume that it is divided into three compartments: susceptible vector (S_v), exposed vector (E_v) and infected vector (I_v). Thus the total human population is $N_h = S_h + E_h + I_h + R_h$, and the total vector population is $N_v = S_v + E_v + I_v$. The interaction between the seven categories of population of the model is presented in the flow diagram in Fig. 1.

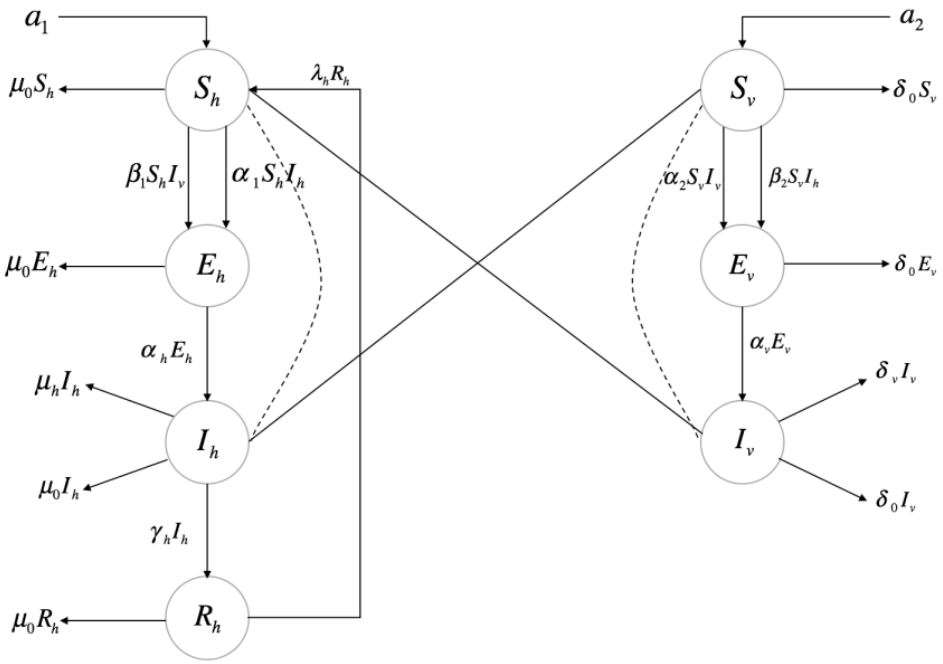

Fig. 1. The flow diagram interaction of human and vector.

The model presented in Fig. 1 is represented by the following system of nonlinear differential equations given by:

$$\frac{dS_h}{dt} = a_1 - \mu_0 S_h - \beta_1 S_h I_v - \alpha_1 S_h I_h + \lambda_h R_h, \quad (2.1)$$

$$\frac{dE_h}{dt} = \beta_1 S_h I_v + \alpha_1 S_h I_h - \mu_0 E_h - \alpha_h E_h, \quad (2.2)$$

$$\frac{dI_h}{dt} = \alpha_h E_h - \mu_0 I_h - \mu_h I_h - \gamma_h I_h, \quad (2.3)$$

$$\frac{dR_h}{dt} = \gamma_h I_h - \mu_0 R_h - \lambda_h R_h, \quad (2.4)$$

$$\frac{dS_v}{dt} = a_2 - \delta_0 S_v - \beta_2 S_v I_h - \alpha_2 S_v I_v, \quad (2.5)$$

$$\frac{dE_v}{dt} = \beta_2 S_v I_h + \alpha_2 S_v I_v - \delta_0 E_v - \alpha_v E_v, \quad (2.6)$$

$$\frac{dI_v}{dt} = \alpha_v E_v - \delta_0 I_v - \delta_v I_v, \quad (2.7)$$

with initial conditions,

$$S_h \geq 0,\ E_h \geq 0,\ I_h \geq 0,\ R_h \geq 0,\ S_v \geq 0,\ E_v \geq 0,\ I_v \geq 0.$$

The parameters involved in the model are as follows:

a_1 is the recruitment rate of human population,

a_2 is the recruitment rate of vector population,

β_1 is the transmission coefficient between susceptible human and infected vector,

β_2 is the transmission coefficient between susceptible vector and infected human,

α_1 is the transmission coefficient between susceptible human and infected human,

α_2 is the transmission coefficient between susceptible vector and infected vector,

α_h is the rate at which exposed human transfer to infected class,

α_v is the rate at which exposed vector transfer to infected class,

μ_0 is the natural mortality rate of human,

μ_h is the disease death rate of infected human,

δ_0 is the natural mortality rate of vector,

δ_v is the disease death rate of infected vector,

γ_h is the rate at which infected human move to recovered class,

λ_h is the constant proportionality where the recovered human becomes susceptible again.

To find the equilibrium states, we set the right-hand side of Eq. (2.1) to (2.7) equal to zero. So, the equilibrium states are

I. Disease Free State

$$E_0\left(\frac{a_1}{\mu_0},0,0,0,\frac{a_2}{\delta_0},0,0\right)$$

II. Endemic State

$$E^*\left(S_h^*,E_h^*,I_h^*,R_h^*,S_v^*,E_v^*,I_v^*\right),$$

where

$$S_h^* = \frac{a_1}{\mu_0}+\frac{1}{\mu_0}\left(\frac{\lambda_h\gamma_h}{T_3}-\frac{T_1T_2}{\alpha_h}\right)I_h^*,$$

$$E_h^* = \frac{T_2I_h^*}{\alpha_h},$$

$$I_h^* = \frac{\left[\mu_0\alpha_h\lambda_h\gamma_h\left(1-T_3\right)-\alpha_h\alpha_1a_1T_3\left(\beta_1+1\right)\right]}{\left[\alpha_h\alpha_1\lambda_h\gamma_h\left(\beta_1+1\right)-\alpha_1T_1T_2T_3\left(\beta_1+1\right)\right]},$$

$$I_v^* = \frac{T_1E_h^*}{\beta_1S_h^*}-\alpha_1I_h^*,$$

and

$$T_1 = (\mu_0+\alpha_h),\ T_2 = (\mu_0+\mu_h+\gamma_h),$$
$$T_3 = (\mu_0+\lambda_h),\ T_4 = (\delta_0+\alpha_v),\ T_5 = (\delta_0+\delta_v).$$

The basic reproduction number of this model is

$$R_0 = \frac{1}{2}\left(\frac{\alpha_1\alpha_ha_1}{\mu_0T_1T_2}+\frac{\alpha_2\alpha_va_2}{\delta_0T_4T_5}\right) + \sqrt{\frac{1}{2}\left(\frac{\alpha_1\alpha_ha_1}{\mu_0T_1T_2}+\frac{\alpha_2\alpha_va_2}{\delta_0T_4T_5}\right)^2-\left(\frac{\alpha_1\alpha_2\alpha_h\alpha_va_1a_2-\beta_1\beta_2a_1a_2\alpha_h\alpha_v}{\mu_0\delta_0T_1T_2T_4T_5}\right)} \quad (2.8)$$

3. Optimal Control Problem

Optimal control is one of the techniques to minimize the infection in the human class and vector class. Several papers have been published on different epidemic models by applying the optimal control strategies to reduce the infection. In this section, we present an optimal control technique by using three control variables to reduce the spread of leptospirosis infection in a community [13]. Our campaign consists of the following control variables:

- $u_1(t)$ represents the control with personal hygiene and personal protective equipment (PPE),
- $u_2(t)$ represents the control by medical monitoring and records,
- $u_3(t)$ represents the control by using rodenticide and resource reduction.

Our control system considering the above three control variables can be easily implemented to reduce the spread of Leptospirosis in the community by using Pontryagin's Maximum Principle to derive necessary conditions for the optimal control of the disease. The objective here is to minimize the number of exposed human and infected human individuals and the number of vectors; thus, the objective functional that we consider is given by

$$F(u_1,u_2,u_3) = \int_0^T A_1E_h + A_2I_h + A_3\left(S_v+E_v+I_v\right) + \frac{1}{2}\left(D_1u_1^2+D_2u_2^2+D_3u_3^2\right)dt. \quad (3.1)$$

The constants A_i and D_i for $i=1,2,3$ are the constant weight or balance factors to keep the balancing of individuals in the objective functional.

The necessary conditions that an optimal control must satisfy come from the Pontryagin's Maximum Principle. This principle converts the system of equations (2.1)-(2.7) with controls and (3.1) into a problem of minimizing pointwise a Hamiltonian H with respect to (u_1,u_2,u_3):

$$
\begin{aligned}
&H\left(N_h,N_v,u\right)=A_1E_h+A_2I_h+A_3\left(S_v+E_v+I_v\right)\\
&+\frac{1}{2}\left(D_1u_1^2+D_2u_2^2+D_3u_3^2\right)\\
&+\lambda_1(t)\Big[a_1-\mu_0S_h-\beta_1\left(1-u_1(t)\right)S_hI_v\\
&\qquad-\alpha_1\left(1-u_1(t)\right)S_hI_h+\lambda_hR_h\Big]\\
&+\lambda_2(t)\Big[\beta_1\left(1-u_1(t)\right)S_hI_v+\alpha_1\left(1-u_1(t)\right)S_hI_h\\
&\qquad-\mu_0E_h-\alpha_h\left(1-u_2(t)\right)E_h\Big]\\
&+\lambda_3(t)\Big[\alpha_h\left(1-u_2(t)\right)E_h-\mu_0I_h-\mu_hI_h-\gamma_hI_h\Big]\\
&+\lambda_4(t)\Big[\gamma_hI_h-\mu_0R_h-\lambda_hR_h\Big]\\
&+\lambda_5(t)\Big[a_2-\delta_0S_v-\beta_2S_vI_h-\alpha_2S_vI_v-u_3(t)S_v\Big]\\
&+\lambda_6(t)\Big[\beta_2S_vI_h+\alpha_2S_vI_v-\delta_0E_v-\alpha_vE_v-u_3(t)E_v\Big]\\
&+\lambda_7(t)\Big[\alpha_vE_v-\delta_0I_v-\delta_vI_v-u_3(t)I_v\Big].
\end{aligned}
\tag{3.2}
$$

To achieve the optimal control, the adjoint functions, must satisfy

$$\lambda_1^{'}=(\beta_1I_v-\alpha_1I_h)(1-u_1(t))(\lambda_1-\lambda_2)+\mu_0\lambda_1-A_1, \tag{3.3}$$

$$\lambda_2^{'}=\alpha_h(1-u_2(t))(\lambda_2-\lambda_3)+\mu_0\lambda_2-A_2, \tag{3.4}$$

$$\begin{aligned}\lambda_3^{'}=&\alpha_1S_h(1-u_1(t))(\lambda_1-\lambda_2)+(\mu_0+\mu_h)\lambda_3\\&+\gamma_h(\lambda_3-\lambda_4)+\beta_2S_v(\lambda_5-\lambda_6),\end{aligned} \tag{3.5}$$

$$\lambda_4^{'}=\lambda_h(\lambda_4-\lambda_1)+\mu_0\lambda_4, \tag{3.6}$$

$$\lambda_5^{'}=(\delta_0+u_3(t))\lambda_5+(\beta_2I_h+\alpha_2I_v)(\lambda_5-\lambda_6)-A_3, \tag{3.7}$$

$$\lambda_6^{'}=(\delta_0+u_3(t))\lambda_6+\alpha_v(\lambda_6-\lambda_7)-A_3, \tag{3.8}$$

$$\begin{aligned}\lambda_7^{'}=&\beta_1S_h(1-u_1(t))(\lambda_1-\lambda_2)+\alpha_2S_v(\lambda_5-\lambda_6)\\&+(\delta_0+\delta_v+u_3(t))\lambda_7-A_3,\end{aligned} \tag{3.9}$$

subject to the constraints $0\le u_1^{\,*}\le u_{1max}$, $0\le u_2^{\,*}\le u_{2max}$ and $0\le u_3^{\,*}\le u_{3max}$.

Specifically, where

$$u_1^*(t)=max(0,min(u_1(t),u_{1max}))\,,$$
$$u_2^*(t)=max(0,min(u_2(t),u_{2max}))\,,$$
$$u_3^*(t)=max(0,min(u_3(t),u_{3max}))\,.$$

Considered by $\frac{\partial H}{\partial u_i}=0$ for $i=1,2,3$, then we have

$$u_1(t)=\frac{(\lambda_2-\lambda_1)\beta_1S_h^*I_v^*+(\lambda_2-\lambda_1)\alpha_1S_h^*I_h^*}{D_1},$$

$$u_2(t)=\frac{\alpha_hE_h^*(\lambda_3-\lambda_2)}{D_2},$$

and $u_3(t)=\dfrac{S_v^*\lambda_5+E_v^*\lambda_6+I_v^*\lambda_7}{D_3}$.

4. Numerical Results

In this section, we present the numerical simulation of the proposed model. The optimal problem is solved numerically by using the mathematical program MATLAB. We consider parameter values presented in Table 1., where some of them we assumed to correspond to the analytic results.

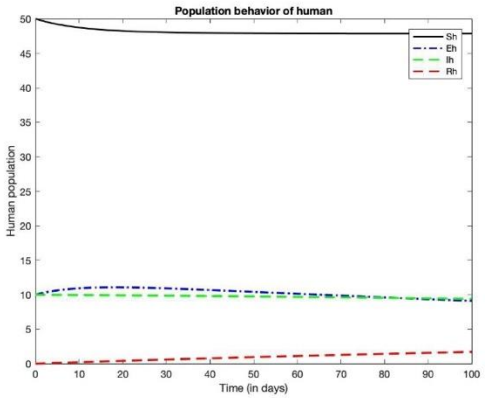

Fig. 2. The plot represents the dynamical behavior of human population for $R_0<1$.

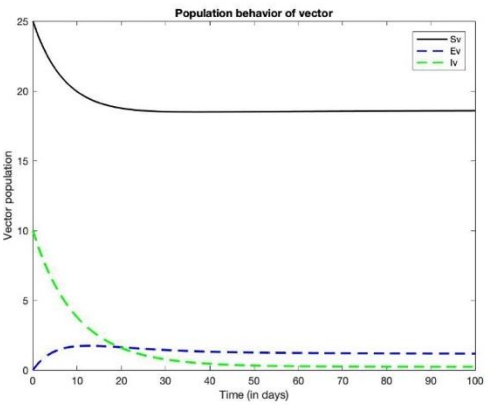

Fig. 3. The plot represents the dynamical behavior of vector population for $R_0<1$.

Table 1. Parameters values in the numerical simulation.

Parameter	Symbol	Value	Reference
Total population of humans	N_h	100	Assumed
Total population of vectors	N_v	500	Assumed
The recruitment rate of human population	a_1	5×10^{-2}	[13]
The recruitment rate of vector population	a_2	2	[13]
The transmission coefficient between susceptible human and infected vector	β_1	4×10^{-4}	Assumed
The transmission coefficient between susceptible vector and infected human	β_2	7.8×10^{-4}	Assumed
The transmission coefficient between susceptible human and infected human	α_1	1.5×10^{-5}	Assumed
The transmission coefficient between susceptible vector and infected vector	α_2	1×10^{-3}	Assumed
The rate at which exposed human transfers to infected class	α_h	3×10^{-3}	[13]
The rate at which exposed vector transfers to infected class	α_v	5×10^{-2}	Assumed
The natural mortality rate of human	μ_0	9×10^{-4}	[13]
The disease death rate of infected human	μ_h	8×10^{-4}	[13]
The natural mortality rate of vector	δ_0	1×10^{-1}	[13]
The disease death rate of infected vector	δ_v	1×10^{-3}	[13]
The rate at which infected human moves to recovered class	γ_h	2.1×10^{-3}	[13]
The constant proportionality where the recovered human becomes susceptible again	λ_h	2.85×10^{-3}	[13]

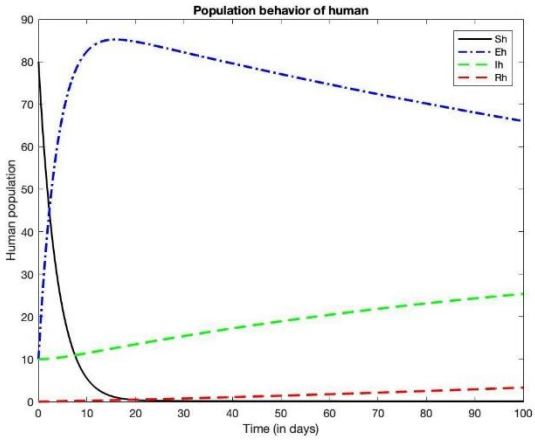

Fig. 4. The plot represents the dynamical behavior of human population for $R_0 > 1$.

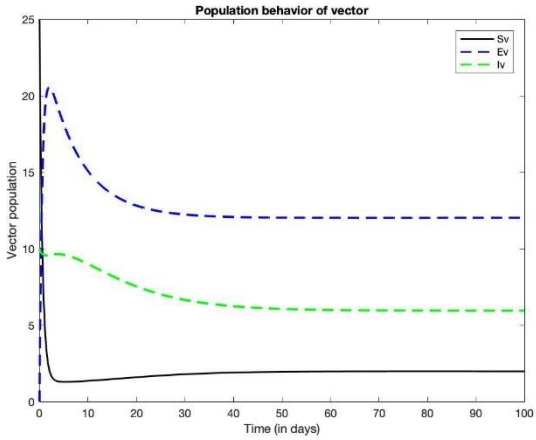

Fig. 5. The plot represents the dynamical behavior of vector population for $R_0 > 1$.

Fig. 2 and Fig. 3 show the evolutions of the four classes of human population and the three classes of vector population when the parameter values that the most effect to the basic reproduction number $\alpha_1 = 1.5\times10^{-5}$ that given $R_0 < 1$, respectively.

Fig. 4 and Fig. 5 show the evolutions of the four classes of human population and the three classes of vector population when the parameter values that the most effect to the basic reproduction number $\alpha_1 = 1.5\times10^{-4}$ that given $R_0 > 1$, respectively.

Figs. 6-11 show the population of each individual in the system. The bold lines show the evolution without control and the dashed lines show the evolution with three controls in the system. In Fig. 6 and Fig. 7, we can see that the control is effective, with the increase in susceptible population in both human and vector. In Figs. 8-11 we can see that the exposed and infected individuals in both human and vector population in control system are less than without control system.

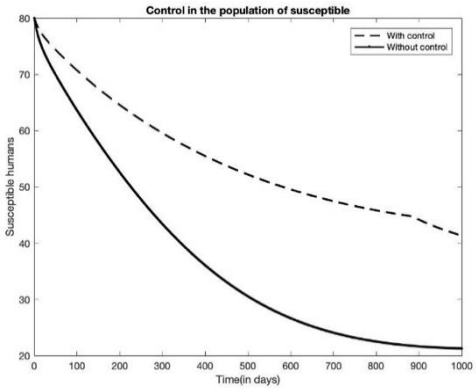

Fig. 6. The plot represents the population of susceptible human individuals.

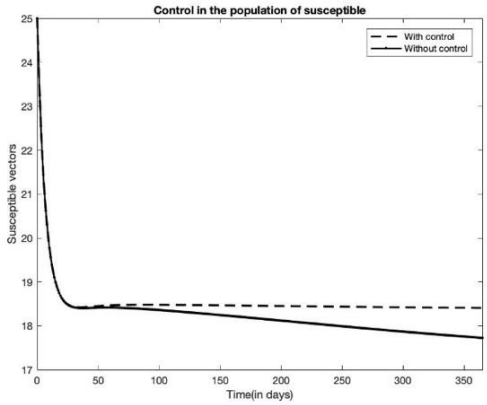

Fig. 7. The plot represents the population of susceptible vector individuals.

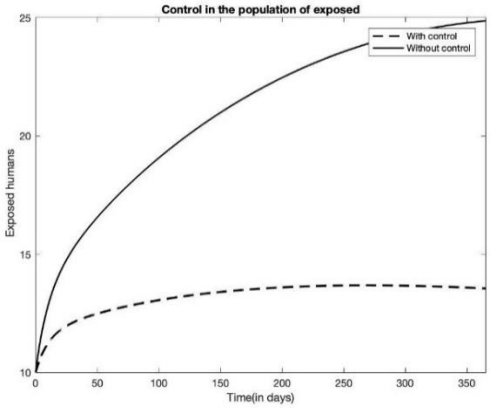

Fig. 8. The plot represents the population of exposed human individuals.

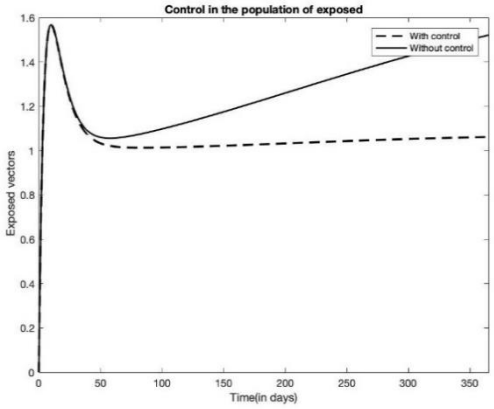

Fig. 9. The plot represents the population of exposed vector individuals.

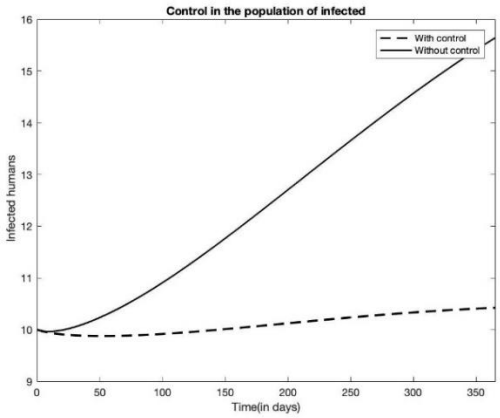

Fig. 10. The plot represents the population of infected human individuals.

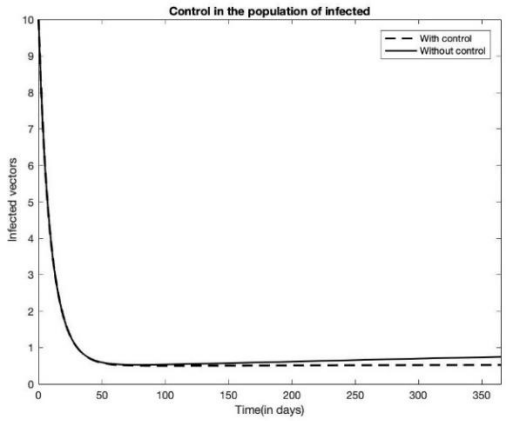

Fig. 11. The plot represents the population of infected vector individuals.

5. Conclusion

In this paper, we modified a deterministic model for the transmission of Leptospirosis by considering the interaction of susceptible humans and susceptible vectors with both infected humans and infected vectors in the term of nonlinear. We presented the disease-free equilibrium and the endemic equilibrium and also investigated the basic reproduction number. Moreover, we introduced the mathematical model by applying the optimal control strategies to the model to maximize the susceptible population. We have defined the control variables $u_1(t)$, $u_2(t)$ and $u_3(t)$ as in detail in section 3. Then the control problem and the objective functional were defined. Finally, the numerical results at both systems were analyzed for comparison by using the optimal control technique.

Acknowledgements

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