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Effects of isolation by taking sick leaves of conjunctivitis infected individuals and treatment control on stability of mathematical modeling of conjunctivitis

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ABSTRACT

Conjunctivitis or pink eye is an inflammation of the conjunctiva which can cause the eye to become red. It can be found in patients of all ages and, in particular, half of them are young children and school age children. The disease is often found in rainy season and in tropical countries. For better understanding of conjunctivitis infection, in this study, we have constructed and analyzed mathematical model involving isolation by taking sick leaves of infected individuals. Both theoretical and numerical analysis is performed. In addition, the basic reproduction number, R_0, is calculated and used as the threshold to indicate model equilibrium points' stability. Further, the model is extended to be optimal control model by adding the treatment control variable. The results suggest that isolation by taking sick leaves of infected individuals together with treatment control should be encouraged as strategy to reduce overall conjunctivitis patients.

Keywords: basic reproduction number; conjunctivitis; numerical analysis; optimal control; sensitivity

1. INTRODUCTION

Conjunctivitis, or it is sometimes called "pink eye", is an inflammation of the conjunctiva which is the thin clear tissue that lies over the white part of the eye and the inner side of the eyelid. It is caused by some bacteria, viruses and sometimes by allergies like pollen, dust or toxic substances or by irritants such as dirt and shampoos. In this study, we focus on the conjunctivitis caused by viruses. The symptoms of conjunctivitis may include redness in the white of the eye inner eyelid, itchy eyes, blurred vision and increased amount of tears. In general, the signs and symptoms can last for about 5-7 days and they are resolved in approximately 2 weeks (Chowell et al., 2006). The viral conjunctivitis is highly contagious and it is transmitted by direct contact from infected person, e.g., by touching hand-to-infected eye or contaminated object with the infectious virus, sharing spaces, and contacting with infectious tears. It can also spread via large respiratory droplets. The incubation period of susceptible individuals who get virus infected is about 1-2 days.

Further, this disease is usually seen during rainy season when the weather is humid and suitable for the growth of the virus (Sangsawang et al., 2012). It is often found in tropical countries (Ghazali et al., 2003) including Thailand (Chansaenroj et al., 2015). To prevent further transmission of this disease, an isolation of infected individuals is recommended (Chowell et al., 2006). Sick leave for home isolation helps speeding the recovery and reducing frequency and duration of infectious public contact (Chowell

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et al., 2006). In addition, American Academy of Pediatrics suggests that isolation of students by refraining from attending school to avoid close contact with other students which results in the spread of infection faster should be encouraged (David et al., 2015).

Mathematical models have been constructed and analyzed to better understand of conjunctivitis infection. Some examples of models are the work by Chowell et al., 2006, Suksawat and Naowarat, 2014, Unyong and Naowarat, 2014 and Sangthongjeen et al., 2015. Therefore, in this study, we extend the Chowell et al., 2006 conjunctivitis mathematical model by adding the isolation term (both sick leaves of workers and school sick leaves of children) of infected individuals and adding the reversion of recovered individuals who do not go see the doctor to susceptible individuals group. This is to investigate the impact of patients' isolation and the role of recovered individuals, who are not educated enough by the doctor to protect themselves from the disease in the future. Our model is analyzed and both theoretical and numerical studies are performed. The basic reproduction number and its sensitivity are calculated. Finally, we extend our model to gain the optimal model by adding the treatment control to seek for strategies in controlling the spread of conjunctivitis.

2. MODEL FORMULATION

Mathematical model involving the effects of isolation by taking sick leaves of infected individuals on the transmission of conjunctivitis is proposed.

The model is modified from the work of Chowell et al., 2006 by adding the term relating to percentage of isolation by taking sick leaves of infected individuals efficiency and the reverse dynamics of the recovery from conjunctivitis individuals who do not go see the doctor to susceptible individuals. This is because they are not educated by the doctors of how to prevent the disease in the future.

In this model, we assume that the recovered individuals who go see the doctor will not move to susceptible individuals group again due to the knowledge of prevention that the doctor gives, therefore their contribution to further disease transmission is negligible. The schematic diagram of this model is shown in Figure 1.

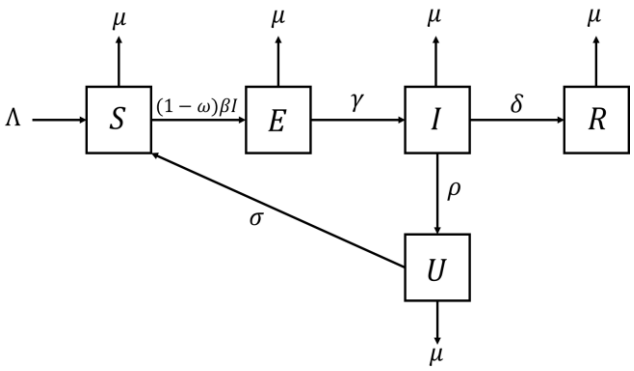

Figure 1 A schematic diagram of conjunctivitis dynamics involving isolation by taking sick leaves

The system of differential equations of this model is written by

$$\frac{dS}{dt} = \Lambda - (1-\omega)\beta SI + \sigma U - \mu S \tag{1}$$

$$\frac{dE}{dt} = (1-\omega)\beta SI - \gamma E - \mu E \tag{2}$$

$$\frac{dI}{dt} = \gamma E - \delta I - \rho I - \mu I \tag{3}$$

$$\frac{dU}{dt} = \rho I - \mu U - \sigma U \tag{4}$$

$$\frac{dR}{dt} = \delta I - \mu R, \tag{5}$$

with initial conditions

$$S(0) > 0, E(0) > 0, I(0) > 0, U(0) > 0, R(0) > 0.$$

In this model, the population is divided into five subgroups at time t : S is the number of susceptible individuals, E is the number of exposed individuals, I

is the number of conjunctivitis infected individuals, R is the number of recovered individuals who go see the doctor, U is the number of recovered individuals who do not go see the doctor, with the population size $N(t)$ where $N = S + E + I + U + R$. The parameters used in this model are defined as Λ is the recruitment rate, μ is the natural mortality rate, β the transmission rate of conjunctivitis, δ is the rate of infected individuals who go to the doctor, γ is the incubation rate of conjunctivitis, ρ is the rate of infected individuals who do not go to the doctor, σ is the rate at which recovered individuals who do not go see the doctor become susceptible individual and ω is the percentage of an isolation by taking sick leaves of infected individuals efficiency.

2.1 Boundary of solution

In this section, we determine the boundary of solutions of the system of equations. In this section, we determine the boundary of solutions of the system of equations (1)-(5). The total population in this model is $N = S + E + I + U + R$, therefore we have

$$\frac{dN}{dt} = \Lambda - \mu N.$$

Hence, $$N_t = \frac{\Lambda}{\mu} - \left[\frac{\Lambda}{\mu} - N_0\right]e^{-\mu t} \quad .$$

As $t \to \infty$, then $N_t \to \frac{\Lambda}{\mu}$, implying that $0 \le N \le \frac{\Lambda}{\mu}$,

therefore, all solutions of this model are bounded and enter the region

$$\Gamma = \left\{(S, E, I, U, R) \in \Re_+^5 : N \le \frac{\Lambda}{\mu}\right\}.$$

Hence, Γ is a positively invariant. That is every solution of this model remains within the region for all $t > 0$.

2.2 Equilibrium point

There are two main equilibrium points in this model which are:

1. Disease-free equilibrium point is

$$E_0 = (\frac{\Lambda}{\mu}, 0, 0, 0) \quad \text{and}$$

2. Endemic equilibrium point is

$$E_1 = (S_1^*, E_1^*, I_1^*, U_1^*) \quad \text{where}$$

$$S_1^* = \frac{(\delta + \rho + \mu)(\mu + \gamma)}{\gamma\beta(1-\omega)}, E_1^* = \frac{(\delta + \rho + \mu)I_1^*}{\gamma},$$

$$I_1^* = \frac{(\mu + \sigma)U_1^*}{\rho}, U_1^* = \frac{\Lambda - \mu S_1^*}{(1-\omega)\beta S_1^* \frac{(\mu+\sigma)}{\rho} - \sigma}.$$

2.3 Basic reproduction number R_0

Next, the basic reproduction number is determined by using next generation method (van den Driessche and Watmough, 2002). From our model, we have

$$R_0 = \frac{(1-\omega)\gamma\beta\Lambda}{\mu(\gamma + \mu)(\delta + \rho + \mu)}.$$

2.4 Stability analysis

The local stability of each equilibrium point within this model is determined from the Jacobian matrix at that equilibrium point of the system of equations (1)-(4), which is

$$J(S,E,I,U) = \begin{bmatrix} -(1-\omega)\beta I - \mu & 0 & -(1-\omega)\beta S & \sigma \\ (1-\omega)\beta I & -\gamma - \mu & (1-\omega)\beta S & 0 \\ 0 & \gamma & -\delta - \rho - \mu & 0 \\ 0 & 0 & \rho & -\mu - \sigma \end{bmatrix}.$$

Theorem 2.1 (local stability at E_0) If $R_0 < 1$, the disease-free equilibrium point E_0 is locally asymptotically stable. If $R_0 > 1$, then the disease-free equilibrium point E_0 is unstable.

Proof. The Jacobian matrix of the disease-free equilibrium point is

$$J(\frac{\Lambda}{\mu}, 0, 0, 0) = \begin{bmatrix} -\mu & 0 & -(1-\omega)\beta S_0^* & \sigma \\ 0 & -\gamma - \mu & (1-\omega)\beta S_0^* & 0 \\ 0 & \gamma & -\delta - \rho - \mu & 0 \\ 0 & 0 & \rho & -\mu - \sigma \end{bmatrix}.$$

From Jacobian matrix above, we set det $(J - \lambda I) = 0$ to find eigenvalues, then we obtain

$(-\mu-\lambda)(-\mu-\sigma-\lambda)\{(-\gamma-\mu-\lambda)(-\delta-\rho-\mu-\lambda) - \gamma\beta S_0^*(1-\omega)\}=0.$

Thus, $\lambda_1=-\mu<0$, $\lambda_2=-\mu-\sigma<0$ and $\lambda^2+(\gamma+2\mu+\delta+\rho)\lambda+\{(\gamma+\mu)(\delta+\rho+\mu)-\gamma\beta S_0^*(1-\omega)\}=0$ which is considered in the form of $\lambda^2+a_1\lambda+a_2=0$.

Therefore, we have

$$(i)\quad a_1=\gamma+2\mu+\delta+\rho>0,$$

$$(ii)\quad a_2=(\gamma+\mu)(\delta+\rho+\mu)-\gamma\beta\frac{\Lambda}{\mu}(1-\omega)$$
$$=(\gamma+\mu)(\delta+\rho+\mu)(1-R_0).$$

Hence, by the criteria of Routh-Hurwitz, E_0 is locally asymptotically stable when $a_2 > 0$, i.e., $R_0 < 1$ and when $R_0 > 1$, resulting in $a_2 < 0$, i.e., the disease-free equilibrium point E_0 is unstable. This completes the proof.

Theorem 2.2 (local stability at E_1) When $R_0 > 1$, the endemic equilibrium point E_1 is stable if it satisfies the Routh-Hurwitz criteria.

Proof. Considering Jacobian matrix of endemic equilibrium point, we have

$$J(S_1^*,E_1^*,I_1^*,U_1^*)=\begin{bmatrix} -(1-\omega)\beta I_1^*-\mu & 0 & -(1-\omega)\beta S_1^* & \sigma \\ (1-\omega)\beta I_1^* & -\gamma-\mu & (1-\omega)\beta S_1^* & 0 \\ 0 & \gamma & -\delta-\rho-\mu & 0 \\ 0 & 0 & \rho & -\mu-\sigma \end{bmatrix}.$$

By setting $\det(J-\lambda I)=0$; we have

$$\lambda^4+[(((1-\omega)\beta I_1^*+\mu)+(\gamma+\delta+\rho+2\mu))+(\mu+\sigma)]\lambda^3+(((\mu+\sigma)((1-\omega)\beta I_1^*+\mu)+(\mu+\sigma)(\gamma+\delta+\rho+2\mu)+((1-\omega)\beta I_1^*+\mu)(\gamma+\delta+\rho+2\mu)+(\gamma+\mu)(\delta+\rho+\mu)-\gamma(1-\omega)\beta S_1^*)\lambda^2+((\mu+\sigma)((1-\omega)\beta I_1^*+\mu)(\gamma+\delta+\rho+2\mu)+(\mu+\sigma)(\gamma+\mu)(\delta+\rho+\mu)-(\mu+\sigma)(1-\omega)\beta S_1^*\gamma+((1-\omega)\beta I_1^*+\mu)(\gamma+\mu)(\gamma+\mu)(\delta+\rho+\mu)-\mu(1-\omega)\beta S_1^*\gamma)\lambda+(\mu+\sigma)((1-\omega)\beta S_1^*+\mu)(\gamma+\mu)(\delta+\rho+\mu)-\mu(\mu+\sigma)(1-\omega)\beta S_1^*\gamma-\sigma(1-\omega)\beta I_1^*\gamma\rho=0.$$

Considering the above equation in the form of, $\lambda^4+a_1\lambda^3+a_2\lambda^2+a_3\lambda+a_4$ we have

$$a_1=((1-\omega)\beta I_1^*+\mu)+(\gamma+\delta+\rho+2\mu)+(\mu+\sigma)$$

$$a_2=(\mu+\sigma)((1-\omega)\beta I_1^*+\mu)+(\mu+\sigma)(\gamma+\delta+\rho+2\mu)+((1-\omega)\beta I_1^*+\mu)(\gamma+\delta+\rho+2\mu)+(\gamma+\mu)(\delta+\rho+\mu)-\gamma(1-\omega)\beta S_1^*$$

$$a_3=((\mu+\sigma)((1-\omega)\beta I_1^*+\mu)(\gamma+\delta+\rho+2\mu)+(\mu+\sigma)(\gamma+\mu)(\delta+\rho+\mu)-(\mu+\sigma)(1-\omega)\beta S_1^*\gamma)+((1-\omega)\beta I_1^*+\mu)(\gamma+\mu)(\delta+\rho+\mu)-\mu((1-\omega)\beta S_1^*\gamma)$$

$$a_4=(\mu+\sigma)((1-\omega)\beta I_1^*+\mu)(\gamma+\mu)(\delta+\rho+\mu)-\mu(\mu+\sigma)(1-\omega)\beta S_1^*\gamma-\sigma(1-\omega)\beta I_1^*\gamma\rho.$$

By using Routh-Hurwitz criteria for $n=4$, this endemic equilibrium point is stable if

$$(i)=a_1>0,\ (ii)=a_3>0,\ (iii)=a_4>0$$
$$\text{and}\ (iv)=\ a_1a_2a_3>a_3^2+a_1^2a_4.$$

2.5 Global stability analysis of disease-free equilibrium point

Theorem 2.3 (global stability of E_0) If $R_0 <1$, then E_0 is globally asymptotically stable.

Proof. Let the Lyapunov function be as follows:

$$L=\gamma E+(\gamma+\mu)I$$

$$\frac{dL}{dt}=(1-\omega)\beta\gamma SI-\gamma^2E-\gamma\mu E+(\gamma+\mu)\gamma E-(\gamma+\mu)(\delta+\mu+\rho)I$$
$$=(\gamma+\mu)(\delta+\mu+\rho)(R_0-1)I.$$

Thus, $\frac{dL}{dt}<0$ when $R_0<1$ and $\frac{dL}{dt}=0$ at I_0. Therefore, when $R_0<1$, then E_0 is globally asymptotically stable.

2.6 Sensitivity analysis

The sensitivity indices of the model reproduction number are determined to seek for the best strategies to reduce the conjunctivitis patients. They are calculated by using the technique of the normalized forward sensitivity index (Ngoteya and Gyekye, 2015; Samsuzzoha et al., 2013). Therefore, by using the parameters value from Table 2, the sensitivity indices are given in Table 1.

Table 1 Numerical values of sensitivity indices of R_0

Parameters	Index at Parameter Value	Sign
Λ	+1.000	positive
μ	-0.1681	negative
γ	+0.1445	positive
ω	-0.1628	negative
β	+1.000	positive
δ	-0.7049	negative
ρ	-0.1880	negative

The result in Table 1 shows that in order to reduce the value of R_0, we may try to increase the value of δ, ρ, μ and ω, respectively and decrease the value of Λ, β and γ, respectively.

3. RESULTS

3.1 Numerical simulation

In this section, the system of equations (1)-(5) is solved numerically with the use of parameters values in Table 2. Figure 2 shows the dynamics of exposed and infected individuals when the percentage of isolation efficiency by taking sick leaves of infected individuals is (ω) varied.

Figure 2 shows the changes in dynamics of exposed and infected individuals when the percentage of isolation efficiency by taking sick leaves of infected individuals is (ω) varied. It can be seen from Figure 2(a) that when the ω increases, the number of exposed individuals decreases with the slower time for the peak to occur whereas the dynamics is reaching the same equilibrium value when time goes by. However, Figure 2(b) shows that the number of infected individuals would decrease when the number of ω is high enough (> 80%) with slightly slower time for the peak to occur.

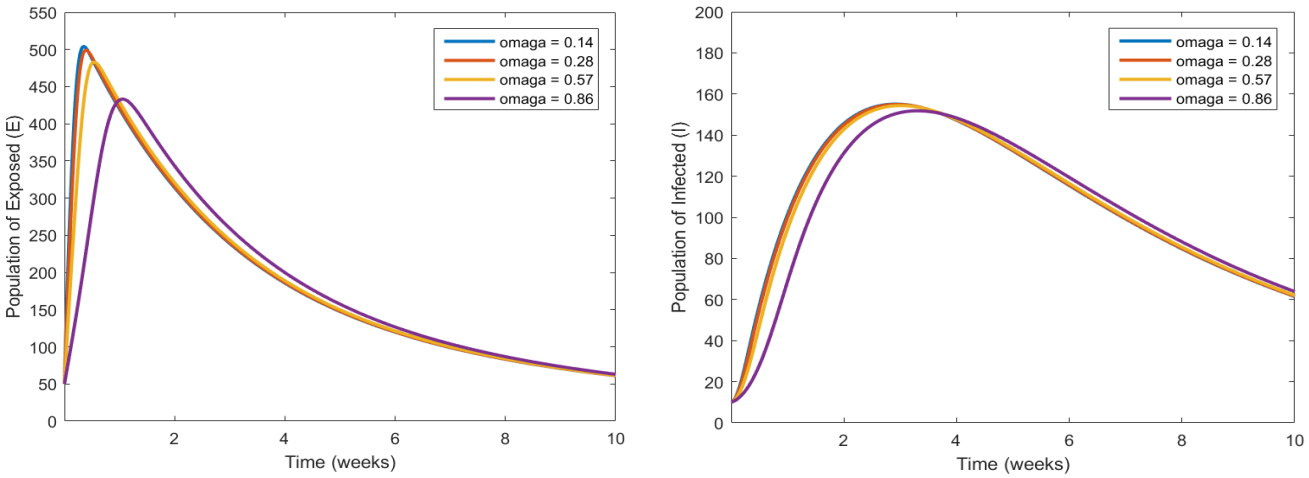

Figure 2 Numerical solution of system of equations (1)-(5) obtained using parameters: λ =4.56, γ =0.27, μ=0.0456, σ =0.5, ρ =0.08, β =0.63, δ =0.30 where (*a*) is the number of exposed individuals *E*, (*b*) is the number of conjunctivitis infected individuals I when ω varies

Table 2 Parameters values used in numerical study

Parameter	Description	Value	Reference
Λ	The birth rate.	4.56 per week	Suksawat and Naowarat, 2014
μ	The natural mortality rate.	0.0456 per week	Unyong and Naowarat 2014
γ	The incubation rate of conjunctivitis.	0.27 per week	Chowell et al., 2006
ω	The percentage of an isolation by taking sick leaves of infected individuals efficiency.	0.1400 per week	Assume
β	The transmission rate of conjunctivitis.	0.63 per week	Chowell et al., 2006
δ	The rate of recovered individuals who go see the doctor.	0.30 per week	Chowell et al., 2006
ρ	The rate of recovered individuals who don't go see the doctor.	0.08 per week	Chowell et al., 2006
σ	The rate at which recovered individuals who do not go see doctor become susceptible individuals.	0.5 per week	Assume

3.2 Optimal control

The model in section 2 is further extended by adding the control variable ϕ which is the treatment of conjunctivitis infected individuals control. The control model diagram is shown in Figure 3 and its system of differential equations is shown below.

$$\frac{dS}{dt} = \Lambda - (1-\omega)\beta SI + \sigma U - \mu S \tag{6}$$

$$\frac{dE}{dt} = (1-\omega)\beta SI - \gamma E - \mu S \tag{7}$$

$$\frac{dI}{dt} = \gamma E - \phi(t) I - \rho I - \mu I \tag{8}$$

$$\frac{dU}{dt} = \rho I - \sigma U - \mu U \tag{9}$$

$$\frac{dR}{dt} = \phi(t) I - \mu R, \tag{10}$$

where all parameters definitions are the same as in section 2.

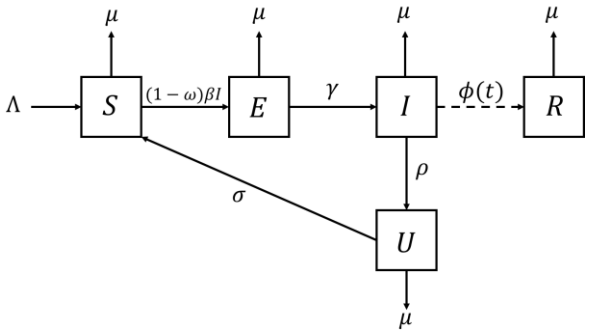

Figure 3 A schematic diagram of control model of conjunctivitis dynamics

For the optimal control model, the objective of the model is to minimize the number of exposed and conjunctivitis infected individuals at a minimal cost of control over the time interval [0,*T*]. The objective function is given by

$$J(\phi) = \min \int_0^T \left[(A_1 I + \frac{1}{2} A_2 \phi^2(t)) \right] dt \tag{11}$$

with initial conditions

$$S(0) \geq 0, E(0) \geq 0, I(0) \geq 0, U(0) \geq 0, R(0) \geq 0.$$

Here the constants A_1 and A_2 are weight constants and the term $A_2\phi^2$ represents the cost associated with treatment for conjunctivitis infected individuals. We can find an optimal solution of this optimal control problem by considering the Lagrangian and the Hamiltonian for the problem. The Lagrangian of the optimal control problem is given by

$$J(I, \phi_1) = A_1 I + \frac{1}{2} A_2 \phi^2(t). \quad (12)$$

By applying Pontryagin's Maximum Principle (PMP) [12], we form the Hamiltonian and derive the optimality system as follows:

$$H = (A_1 I + \frac{1}{2} A_2 \phi^2(t)) + \lambda_S(\Lambda - (1-\omega)\beta SI - \sigma U - \mu S)$$
$$+ \lambda_E\left((1-\omega)\beta SI - \gamma E - \mu E\right) + \lambda_I(\gamma E - \phi(t)I - \rho I - \mu I)$$
$$+ \lambda_U(\rho I - \sigma U - \mu U) + \lambda_R(\phi(t)I - \mu R), \quad (13)$$

where $\lambda_S, \lambda_E, \lambda_I, \lambda_U, \lambda_R$ are the adjoint functions associated with the state equations for *S*, *E*, *I*, *U* and *R*, respectively. Next, we obtain the adjoint equations as

$$\lambda_S^{'} = -\frac{\partial H}{\partial S} = -\left[-\lambda_S(1-\omega)\beta I - \lambda_E \mu + \lambda_E(1-\omega)\beta I\right]$$
$$\lambda_E^{'} = -\frac{\partial H}{\partial E} = -\left[\lambda_E(-\gamma - \mu) + \lambda_I(\gamma)\right]$$
$$\lambda_I^{'} = -\frac{\partial H}{\partial I} = -\left[A_1 + \lambda_S(-(1-\omega)\beta S) + \lambda_E(1-\omega)\right.$$
$$\left.\beta S + \lambda_I(-\phi(t) - \rho - \mu) + \lambda_R(\phi(t)) + \lambda_U \rho\right]$$
$$\lambda_U^{'} = -\frac{\partial H}{\partial U} = -\left[\lambda_S \sigma + \lambda_U(-\sigma - \mu)\right]$$
$$\lambda_R^{'} = -\frac{\partial H}{\partial R} = -\left[\lambda_R(-\mu)\right]. \quad (14)$$

The characterization of the optimal control variables $\phi(t)$ can be calculated as follows:

$$\frac{\partial H}{\partial \phi(t)} = A_2\phi(t) + \lambda_I(-I) + \lambda_R(I) = 0$$

$$\phi(t) = \frac{(\lambda_I - \lambda_R)I}{A_2}, \quad (15)$$

where it is subject to the constant $0 \leq \phi(t) \leq \phi(t)_{\max}$. Therefore, the optimal control variable $\phi^*(t)$ are

$$\phi^*(t) = \min\{0, \max\{\phi(t), \phi(t)_{\max}\}\}$$

$$= \min\{\max\{\frac{(\lambda_I - \lambda_R)I^*}{A_2}, \phi_{\max}\}, 0\}. \quad (16)$$

The numerical solution of equations (6)-(10) is performed continuously for 100 days using the parameters values in Table 2 where we assume the weight function as A_1 = 0.07 and A_2 = 0.2. The results are shown in Figure 4.

Figure 4 shows that by keeping the treatment control of the conjunctivitis infected at of $\phi_{\max}$ of 70% for about 97 days would give a dramatically decrease in the number of conjunctivitis infected with lower equilibrium point value. Hence, it is suggested that treatment control is essential in reducing overall conjunctivitis transmission.

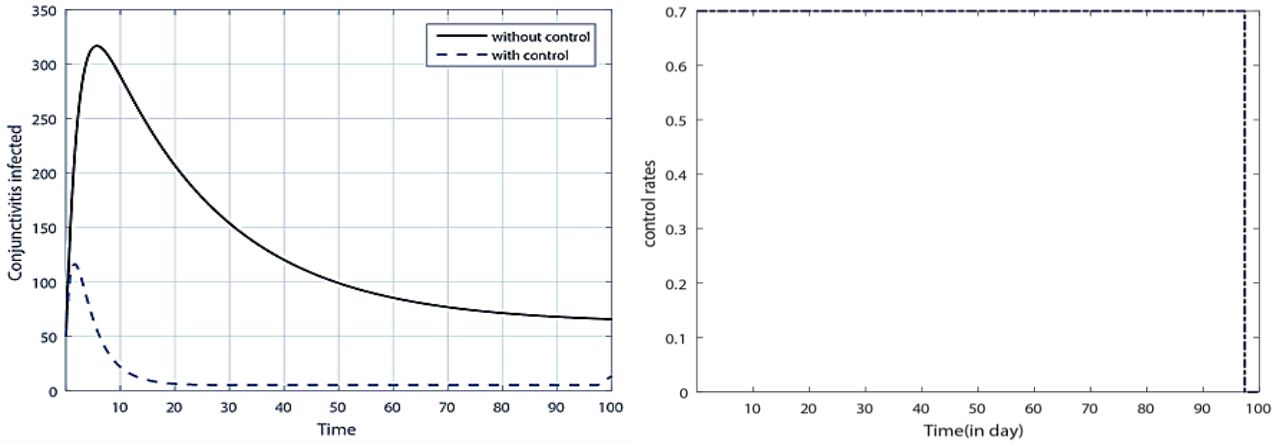

Figure 4 Numerical simulation of control conjunctivitis model

4. CONCLUSION

In this paper, the model involving the effects of isolation by taking sick leaves of infected individuals on the spreading of conjunctivitis is developed. We obtain two main equilibrium points, the disease-free and the endemic ones. The basic reproduction number is $R_0 = \frac{(1-\omega)\gamma\beta\Lambda}{\mu(\gamma+\mu)(\delta+\rho+\mu)}$. The stability of each equilibrium point depends on the condition of R_0. If $R_0 < 1$, then the disease-free equilibrium point is locally and globally stable whereas when $R_0 > 1$, the endemic equilibrium point exists and is locally stable if it satisfies the Routh-Hurwitz criteria. The numerical simulations indicate that the percentage of isolation efficiency by taking sick leaves of infected individuals plays a key role in reducing the number of conjunctivitis patients and the optimal control model results suggest that the treatment control also gives a strong impact on overall conjunctivitis spread reduction.

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