

Optimal Control Model of Haemorrhagic Conjunctivitis Disease

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Abstract

In this research article, a model for the transmission dynamics of haemorrhagic conjunctivitis disease is presented. The tool of dynamical system is employed in investigating the potency of the spreading of the epidemic. The analysis revealed the likelihood of the epidemic to spread when the basic reproduction number exceeds one. The model is reformulated as optimal control problem to assess the effectiveness of the proposed control strategy. Maximum Principle was employed to derive the necessary conditions for the existence of optimal control. Numerical solution of the optimality was derived and computed to investigate the optimum control strategy that would be efficacious to be implemented in reducing the number of exposed and infected individuals.

Keywords

Basic reproduction ratio; Pontryagin's maximum principle; Lagrangian; Hamiltonian; boundary conditions.

Introduction

Recent research has revealed a surge in the number of researchers interested in the modeling of infectious diseases. Factors behind this surge include the solid reputation of disease modeling to lay foundational structures such as the estimation of the threshold parameters, elucidation of the transmission dynamics of the disease, predicting the likelihood of the dying out of the epidemic or its ability to remain endemic in the population, combined with the fact that disease modeling has the ability to provide feasible control strategies [1].

Mathematical modeling of infectious diseases has been fruit-bearing soil where pragmatic therapeutic recommendations for treatment and prevention strategies of infectious diseases has been borne, and has been an alternative tool that has being in exploit in the approach of fighting infectious diseases [2].

Conjunctivitis or "Pink eye", is an acute condition characterized by redness of the eye(s). The infection is caused by both viral and bacterial. The disease is transmitted from an infected person to a susceptible individual through contact with discharge from conjunctivae or upper respiratory tracts of infected persons, contact with contaminated foreign bodies of clothing, fingers, and other articles, especially those in contact with the eyes such as make-up applicators and allergies may cause the condition. The disease can also be transmitted vertically to newly born babies due its direct relation between maternal gonococcal and chlamydial infection. The incubation period of bacteria conjunctivitis ranges from 1-3 days. Symptoms of the disease includes tearing, irritation, photophobia; which usually results in swelling of the lids or a purulent discharge [3].

According to Medecins Sans Frontieres, Conjunctivitis is highly contagious among children and endemic in the poorest rural areas of Africa, Asia, Central and South America and the Middle East, and is increasingly becoming serious health problem in communities where the appropriate drugs for treatment are not readily available [4]. Conjunctivitis infection is commonly contracted in the early ages of children either by direct or indirect contact with contaminated materials. The burden of the disease includes; loss in contact hours of pupils, as a results of isolation of the infected persons until examination and treatment has been provided by health care provider, loss of savings through treatment and drug cost, loss in worker productivity due to exclusion from active work environment until treatment has been provided. Gonococcal Conjunctivitis in newly born babies may lead to severe corneal lesions and blindness. Recommended control measures of the disease include prevention of direct contact with towel, clothing, discharge of the infected persons, encouragement of frequent hand-washing, isolation of newborns for 24 to 45 hours, cleaning of eyes 4 to 6 times with boiled water, avoidance of cosmetics during the acute phase, application of antihistamines.

The intrusion of mathematics into the modeling of infectious disease has been an

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alternative means of providing empirical and insightful explanations to the transmission dynamics of infectious disease and has provided feasible control intervention strategies [5]. Unyong and Naowarat [6], proposed a simple SEIR model of conjunctivitis that considers a nonlinear incidence term. The local stability of the model was performed. It was deduced that an increase in the infected humans was dependent on the decrease in the fraction of the infected individuals. Suratchata et al. [7], formulated a deterministic mathematical model for the dynamics of conjunctivitis disease that assessed the effect of educational campaign on the spread of the disease. The model ascertained that an effective educational campaign has the effect of decreasing the number of infectives. Hurtado [8], presented and analyzed a mathematical model of the vertebrate immune response of conjunctivitis in wild passerine birds. The model was used to investigate which pathogen and host immune characteristics drive patterns of *Mycoplasma gallisepticum* infections is observed by house finch and other passerine birds. Chowell et al [9], modelled an outbreak of acute haemorrhagic conjunctivitis by considering a model that was categorized into susceptible, infectious, reported and recovered compartments respectively. They investigated the impact of underreporting and behavior changes on the transmission rate in Mexico. Optimal control models have produced another dimension in the modeling of infectious diseases, as it has come with insightful models that focus on variant control strategies for quality decision making on control intervention strategies with minimal cost [10-12]. Even though an imperative contributions have been made by researchers in explaining the bacteria interaction with human and their biology, the complexities in the life cycle of the bacteria, highly environmental factors that to a larger extent affects the transmission dynamics of the disease, coupled with the evolutionary challenge posed by the bacteria in drug resistance has thrown a challenge to researchers and modelers to come up with a combination of different methodologies, rather than the single type of deterministic models which have been applied in the attempt to eliminate the epidemic. It is felt that a combination of different methodologies may bring the most laudable and long term feasible control strategies which could be applied by public health professionals in finding a lasting solution to the disease. In this research article, we formulate an optimal control model for bacteria conjunctivitis disease as studies in section 2. The section 3 deduces an optimal control problem that assesses the impact of prevention and treatment control strategies by using time dependent control functions. The necessary conditions for an optimal and the corresponding states are then derived by employing the Pontryagin's Maximum Principle. Finally, in section 4, the resulting optimality system is numerically solved and computed to investigate the optimum control strategy that would be efficacious to be implemented in reducing the number of exposed and infected.

Epidemic Model Formulation

This section presents a model for conjunctivitis disease with nonlinear incidence rate. The population at time t is categorized into four compartments: susceptible individuals $S(t)$, exposed individuals $E(t)$, infected individuals

$I(t)$ and recovered individuals $R(t)$. Hence the total population at any time t is given by $N = S(t) + E(t) + I(t) + R(t)$. The model assumed that people enter the susceptible class either through birth or immigration at a recruitment rate pN . When an infectious individual makes a contact with a susceptible individual, there is some finite likelihood that the bacteria will be passed on to the susceptible at the rate $\frac{bI}{N}$ and the person will move to the exposed class. Individuals from the exposed class enter the infectious class at a rate τ . Recovered individuals move to the recovery class at a rate γ and die from the infection at a rate δ . Further, it is assumed that recovered individuals have temporary immunity that can be lost and are again susceptible to reinfection at a rate σ . All individual classes leave the population through the same natural death rate μ . The mathematical differential equations of the dynamics of the conjunctivitis model are:

$$\begin{aligned}\frac{dS}{dt} &= pN + sR - b\frac{SI}{N} - mS \\ \frac{dE}{dt} &= b\frac{SI}{N} - (t + m)E \\ \frac{dI}{dt} &= tE - (g + d + m)I \\ \frac{dR}{dt} &= gI - (s + m)R\end{aligned}\quad (1)$$

The basic Reproduction Ratio and the Stability of the Disease-free Equilibrium

The conjunctivitis model (1) has a unique Disease-Free Equilibrium (DFE).

$$E_0 = \left(\frac{pN}{m}, 0, 0, 0 \right)$$

The basic reproduction ratio R_0 , which is defined as infection sourcing from an infected pathogen in the midst of uninfected population, is determined by the next generation matrix approach [13]. Here, the matrices F and V evaluated at

$$E_0 = \left(\frac{pN}{m}, 0, 0, 0 \right) \text{ are}$$

$$F = \begin{pmatrix} \frac{bp}{m} & 0 \\ 0 & 0 \end{pmatrix} \text{ and}$$

$$V = \begin{pmatrix} t + m & 0 \\ -t & (g + d + m) \end{pmatrix}$$

$$\text{Hence } R_0 = r(FV^{-1}) = \frac{bpt}{m(t + m)(g + d + m)} \quad (2)$$

The disease-free equilibrium (DFE), is locally asymptotically stable if $R_0 < 1$ and unstable if $R_0 > 1$.

Optimal Control Strategies

In this section, the state system (1) is modified to assess the impact of some control strategies: prevention and treatment. The associated force of infection is reduced by a factor $1 - w_1(t)$, where $w_1(t)$ denotes the effort to prevent contact between susceptible and infected individuals. The control variable $w_2(t)$ denotes the rate at which infected individuals are treated at each time of infection. Further, we assume that w_2I individuals at any time (t) are removed from the infective class and added to the removed class. With regards to these underlying assumptions, an optimal control model for conjunctivitis disease is formulated that deduces prevention and treatment strategies with a minimal cost of implementation. Hence, the dynamics of system (1) are modified to the following system of equations:

$$\frac{dS}{dt} = pN + sR - (1 - w_1(t))b\frac{SI}{N} - mS$$

$$\begin{aligned}\frac{dE}{dt} &= (1 - w_1(t))b \frac{SI}{N} - (t + m)E \\ \frac{dI}{dt} &= tE - (g + d + m + w_2)I \\ \frac{dR}{dt} &= gI + w_2I - (s + m)R\end{aligned}\quad (3)$$

The objective of our work is to minimize the number of exposed and infected individuals and treatment of infected individuals through preventive and treatment strategies, by employing feasible minimal time dependent control variables $w_1(t)$ and $w_2(t)$ respectively.

With appropriate initial conditions, we consider an optimal control problem to minimize the objective functional given by

$$J(w_1, w_2) = \int_0^{t_f} [A_1 E + A_2 I + \frac{1}{2}(a_1 w_1^2 + a_2 w_2^2)] dt \quad (4)$$

The quantities A_1 and A_2 represent the weight constant of the exposed and infected individuals. Further, the quantities w_1 and w_2 are weight constant for minimizing the number of exposed and infected individuals and treatment of the infected. Again, the terms

$$\frac{1}{2} a_1 w_1^2 \text{ and } \frac{1}{2} a_2 w_2^2$$

represent the cost associated with the minimizing the exposed and infected and treatment of infected individuals.

We choose a quadratic cost on the controls as a reflection of what is in other literature on epidemic control models [14-16]. Now, we seek an optimal control w_1^* and w_2^* such that

$$J(w_1^*, w_2^*) = \min \{J(w_1, w_2 \mid w_1, w_2 \in W)\} \quad (5)$$

where

$$\{w_1, w_2 \mid w_i(t) \text{ is lebesgue measurable with, } 0 \leq w_i(t) \leq 1, i = 1, 2\} \quad (6)$$

Applying the Pontryagin's Maximum Principle [17], the system (3) and (4) are converted into minimizing the Hamiltonian H , with respect to w_1 and w_2 where

$$H(S, E, I, R, w_1, w_2, \lambda_1, \lambda_2, \lambda_3, \lambda_4, t) = A_1 E + A_2 I + \frac{1}{2} a_1 w_1^2 + \frac{1}{2} a_2 w_2^2 + \lambda_1 \frac{dS}{dt} + \lambda_2 \frac{dE}{dt} + \lambda_3 \frac{dI}{dt} + \lambda_4 \frac{dR}{dt} \quad (7)$$

Where λ_i for $i=1,2,3,\dots$, adjoint variables to be determined.

Theorem 3.1: There exist an optimal control $W^* = (w_1^*, w_2^*) \in WW^*$ such that

$$J(w_1^*, w_2^*) = \min_{(w_1, w_2) \in W} J(w_1, w_2)$$

subject to the control system (3) with initial conditions at $t=0$.

Proof: The existence of an optimal control is proved by applying the result in [18]. It is evidence that the control and state variables are nonnegative values. Hence, the necessary convexity of the objective functional in w_1 and w_2 are satisfied in this minimizing problem. The set of all control variables $(w_1^*, w_2^*) \in W$ is also convex and closed by definition. The optimal control system is bounded which determines the compactness needed for the existence of the optimal control. In addition, the integrand in the functional

$$A_1 E + A_2 I + \frac{1}{2}(a_1 w_1^2 + a_2 w_2^2)$$

is convex on the set W . Also, we can easily see that there exist a constant $\rho > 1$ and positive numbers V_1, V_2 such that

$$J(w_1, w_2) \geq V_1 (\|w_1\|^2 + \|w_2\|^2)^{\rho/2} - V_2,$$

because, the state variables are bounded, which completes the existence of an optimal control.

In order to find an optimal solution, we apply Pontryagin's Maximum Principle [19] as follows:

Given that (x, w) is an optimal solution of an optimal control problem, then there exist a non-trivial vector function $\lambda = \lambda_1 + \lambda_2 + \lambda_3 + \dots + \lambda_n$ which satisfies the inequalities

$$\begin{aligned}\frac{dx}{dt} &= \nabla_x H(t, x, w, \lambda) \\ 0 &= \nabla_w H(t, x, w, \lambda) \\ \lambda' &= -\nabla_x H(t, x, w, \lambda)\end{aligned}\quad (8)$$

Now, we apply the necessary conditions to the Hamiltonian H in (7).

Theorem 3.2: Given that (S^*, E^*, I^*, R^*) are optimal state solutions and (w_1^*, w_2^*) are associated optimal control variable for the optimal control problem (3)-(4), then, there exists adjoint variables λ_i , for $i=1,2,\dots,4$, which satisfies

$$\begin{aligned}\lambda_1' &= (1 - w_1)(\lambda_1 - \lambda_2)bI \frac{(E + I + R)}{N^2} + \lambda_1 m \\ \lambda_2' &= -A_1 + (\lambda_2 - \lambda_3)t + \lambda_2 m \\ \lambda_3' &= -A_2 + (1 - w_1)(\lambda_1 - \lambda_2)bS \frac{(E + I + R)}{N^2} + (\lambda_3 - \lambda_4)g + (\lambda_3 - \lambda_4)w_2 + \lambda_3(d + m) \\ \lambda_4' &= (\lambda_4 - \lambda_1)s + \lambda_4 m\end{aligned}\quad (9)$$

with the boundary conditions

$$\lambda_i(t_f) = 0 \text{ for } i = 1, 2, \dots, 4. \quad (10)$$

Furthermore, optimal controls w_1^* and w_2^* are given by

$$w_1^* = \max \left\{ \min \left\{ \frac{(\lambda_2 - \lambda_1)bS^*I^*}{a_1 N}, 1 \right\}, 0 \right\} \quad (11)$$

$$w_2^* = \max \left\{ \min \left\{ \frac{(\lambda_4 - \lambda_3)I^*}{a_2}, 1 \right\}, 0 \right\} \quad (12)$$

Proof: The adjoint equations and the transversality conditions are determined by using the Hamiltonian (7). By putting $S=S^*(t)$, $E=E^*(t)$, $I=I^*(t)$, $R=R^*(t)$ and differentiating the Hamiltonian with respect to S, E, I and R respectively, we obtain (9). Further, by solving the equations

$$\frac{\partial H}{\partial w_1} = 0, \text{ and } \frac{\partial H}{\partial w_2} = 0$$

on the interior of the control set and using the optimality condition and the property of the control space W , we obtain (11)-(12).

Here, we empty the formulas (11)-(12) for $w^* = (w_1^*, w_2^*)$ the characteristic of the optimal control. The optimal control and the state are found by solving the optimality system, which consists of the state system (3), the adjoint (9), initial condition at $t=0$, boundary conditions (10), and the characterization of the optimal control (11)-(12). To solve the optimality system, we use the initial and transversality conditions together with the characterization of the optimal control (w_1^*, w_2^*) given by (11)-(12). In addition, the second derivative of the Lagrangian with respect to w_1 and w_2 respectively, are positive, which shows that the optimal problem is

minimum at controls W_1^* and W_2^* .

By substituting the values of W_1^* and W_2^* into the control system, we deduce the following system of equations.

$$\begin{aligned}\frac{dS}{dt} &= pN + sR - \beta \left[\max \left\{ \min \left\{ \frac{(I_2 - I_1) b S^* I^*}{a_1 N}, \frac{I_2}{N} \right\}, 0 \right\} \right] - mS \\ \frac{dE}{dt} &= \beta \left[\max \left\{ \min \left\{ \frac{(I_2 - I_1) b S^* I^*}{a_1 N}, \frac{I_2}{N} \right\}, 0 \right\} \right] - (t + m)E \\ \frac{dI}{dt} &= tE - gI + d + m + \max \left\{ \min \left\{ \frac{(I_4 - I_3) I^*}{a_1}, \frac{I_4}{I} \right\}, 0 \right\} \\ \frac{dR}{dt} &= gI + \max \left\{ \min \left\{ \frac{(I_4 - I_3) I^*}{a_2}, \frac{I_4}{I} \right\}, 0 \right\} - (s + m)R\end{aligned}\quad (13)$$

$$\begin{aligned}H^* &= AE + AI + \frac{1}{2} a_1 \max \left\{ \min \left\{ \frac{(I_2 - I_1) b S^* I^*}{a_1 N}, \frac{I_2}{N} \right\}, 0 \right\} + \frac{1}{2} a_2 \max \left\{ \min \left\{ \frac{(I_4 - I_3) I^*}{a_2}, \frac{I_4}{I} \right\}, 0 \right\} \\ I_1 \frac{dS}{dt} + I_2 \frac{dE}{dt} + I_3 \frac{dI}{dt} + I_4 \frac{dR}{dt}\end{aligned}\quad (14)$$

Numerical Examples and Discussion

In this section, we assess numerically by investigating the effect of control strategies on the transmission dynamics of conjunctivitis disease. The optimal control is deduced by solving the optimality system; state system and adjoint system. We then employ an iterative scheme in solving the optimality system. First, we solve the state systems of equations with a guess for the controls over the simulated time frame using fourth order Runge-Kutta scheme. Due to the boundary conditions (10), the adjoint system is solved by backwards fourth order Runge-Kutta by employing the current iterative solutions of the state equation. The controls are then updated by means of a convex combination of the previous controls as well as the characterizations (11) and (12). The whole process is repeated until the values of the unknowns at the previous iterations are closed to the one at the current iterations.

The model investigates the transmission dynamics of Conjunctivitis disease by using the tool of optimal control. We study the control effects of prevention of the interaction between the susceptible and the infected individuals and treatment control on the spread of the disease. We ascertain the effects of the control strategies by comparing numerically the results of the stated scenarios with simulated values taken from [7], and $S(0)=1000$, $E(0)=50$, $I(0)=10$, $R(0)=5$.

Further, we assume that the weight factor, a_1 , associated with

control w_2 is greater than A_1 , A_2 and a_2 respectively, which are association of control w_2 . This is due to the fact that the cost of implementing w_1 includes, the cost of health education and training of personnel on screening and surveillance techniques and educational campaign of educating the general public against practices extensive make-ups application, preventing the eye from becoming contact with foreign contaminated bodies or materials and the need to avoid if possible, becoming exposed to various eye fluids of infected persons and the need of pregnant women having safe sex with outsiders and even long term partners to avoid vertical transmission of the disease to new born babies, as sexually transmitted diseases such as gonococcal and chlamydial infection in pregnancy may cause neonatal conjunctivitis. The cost of treatment includes hospitalization, medical examination and the logistics supply of antibiotic drugs to the infected person. Here, we illustrate the effect of various optimal control strategies on the spread of Conjunctivitis epidemic model in an endemic population.

The parameter values used in the simulations are estimated based on the Conjunctivitis disease as provided in Table 1. Other parameters were chosen arbitrary for the purpose of the numerical simulation.

Figures 1-2 represent the number of susceptible individuals (S) without and with controls for $a_1=1000$ and $a_2=50$. In the absence of control, the susceptible (dashed curve) decreases sharply in the first thirty days until all the susceptible population are infected with the disease and leaves no population of susceptible. In the presence of controls, the susceptible (solid curve) decreases sharply in the first thirty days. This could be possible in the early days of the implementation of the control strategies, as there could be errors and ineffective implementation. However, when these errors are checked, the situation is reversed and the susceptible population never degenerated due to the presence of control strategy.

Similarly, Figures 3-4 represent the number of Exposed individuals (E) without and with controls for $a_1=1000$ and $a_2=50$. When there are no controls, the exposed (dashed curve) increases steadily in the first twenty-five days, and maintained the level for the rest of the days. In the presence of control, the number of (E) (solid curve) decreases gradually, but are not entirely removed from the population for the rest of the days, even though it is drastically decreased from the population.

Further, Figures 5-6 gives the dynamics of the infected individuals (I) without and with controls for

$a_1=1000$ and $a_2=50$. In the absence of controls, the infected (dashed curve) increases steadily for the first forty days, and maintains that level for the rest of the days. However, the population of infected remains in the population. The presence of control is witnessed by the number of infected I (solid curve) decreasing sharply in the early days of the infection and decreasing gradually

Parameter	Description	Estimated Value	Reference
β	Transmission rate	0.08	[Assumed]
π	Rate at which individuals are recruited into the susceptible compartment	0.000456	[7]
γ	Recovery rate	0.033	[Assumed]
δ	Death rate of infected individuals	0.09	[7]
σ	Rate at which recovered individuals become Reinfected	0.01	[7]
μ	Natural death rate	0.0004	[7]
τ	Rate at which exposed individuals enter infected compartment	0.08333	[Assumed]

Table 1: Description of variables and parameters of the Conjunctivitis model [1]

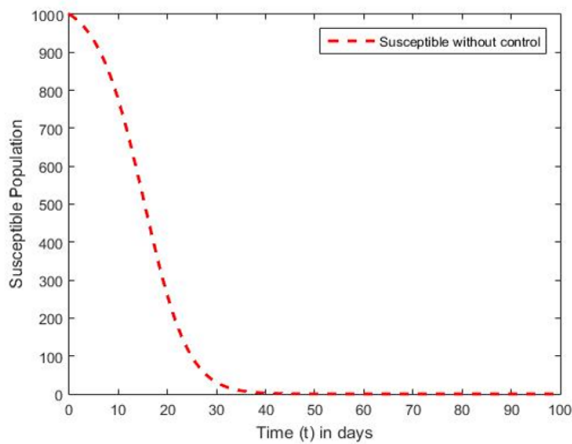


Figure 1: The plot represents population of susceptible without control

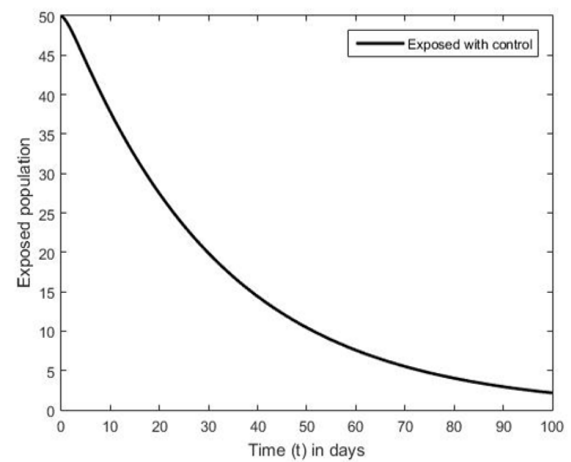


Figure 4: The plot represents population of Exposed with control

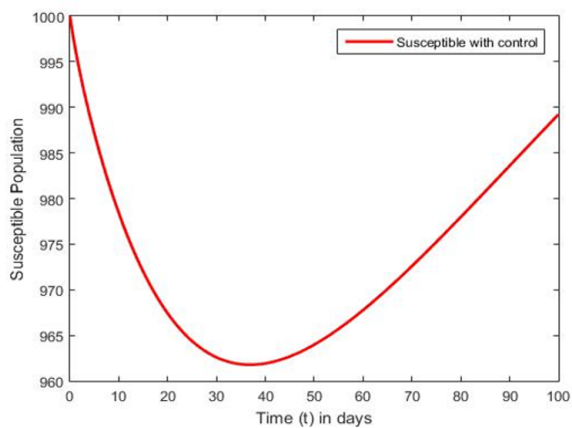


Figure 2: The plot represents population of susceptible with control

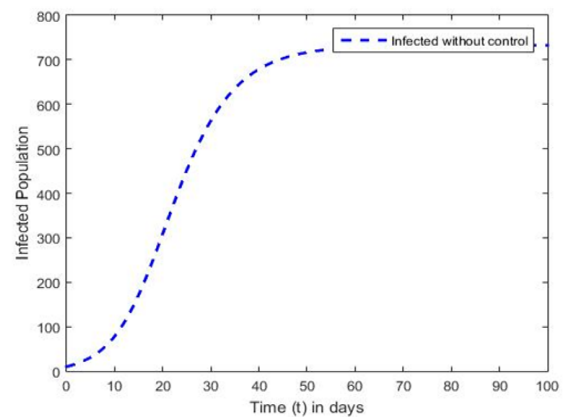


Figure 5: The plot represents population of Infected without control

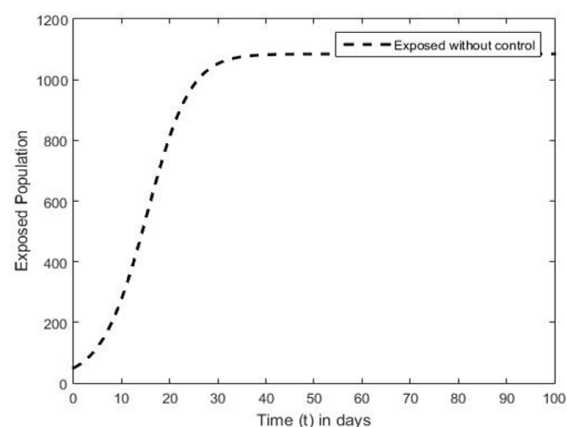


Figure 3: The plot represents population of Exposed without control

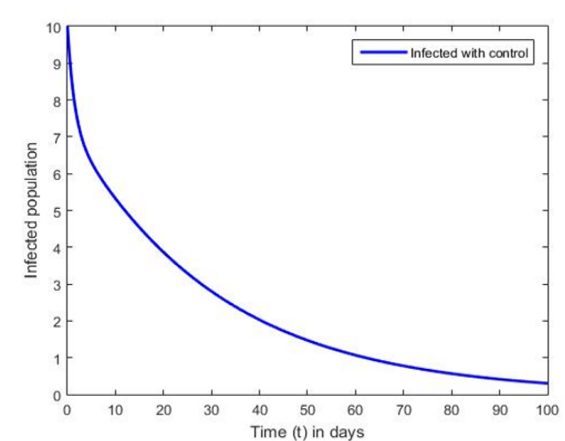


Figure 6: The plot represents population of Infected with control

for the rest of the time frame of hundred days. This is due to the fact that the control strategies proposed were effective in reducing the infected population drastically.

Figure 7 presents the optimal control plots of the effort to prevent contact between susceptible and infected individuals w_1 , and

the treatment control w_2 for $a_1=50000$. We see that the preventive control (magenta solid curve) is at the upper bound at $t=2$, and then slowly drops to the lower bound at $t=100$, while the optimal treatment (green solid curve) is at the lower bound throughout the time frame of $t=100$.

Similarly, Figure 8 presents the optimal control plots of the effort to prevent contact between susceptible and infected individuals w_1 , and the treatment control w_2 for $a_1=50000$. We see that the preventive control (magenta solid curve) is at the upper bound at $t=2$, and then slowly drops to the lower bound at $t=100$, while the optimal treatment (green solid curve) is at the lower bound throughout the time frame of $t=100$.

Further, Figure 9 presents the optimal control plots of the effort to prevent contact between susceptible and infected individuals w_1 and the treatment control w_2 for $a_2=500000$. We observe that the preventive control (magenta solid curve) is at the peak of 100% for $t=68$, and then drops sharply to the lower bound at $t=100$, while the optimal treatment (green solid curve) is at the lower bound throughout the whole time frame of $t=100$. This implies that least effort would be required in employing the strategy of preventive control for $a_2=50000$.

Finally, Figure 10 presents the optimal control plots of the effort to prevent contact between susceptible and infected individuals w_1 , and the treatment control w_2 , for $a_2=500000$. We observe that the preventive control (magenta solid curve) is at the upper bound until $t=68$, and then drops sharply to the lower bound at $t=100$, while the optimal treatment (green solid curve) is at the lower bound throughout the whole time frame of $t=100$. This implies that least effort would be required in employing the strategy of preventive control for $a_2=500000$.

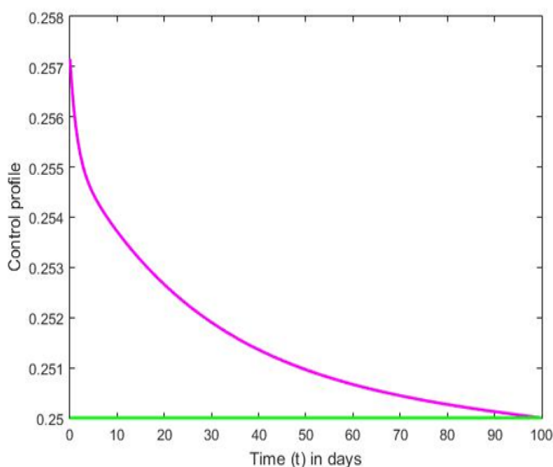


Figure 7: The plot represents Optimal control w_1 and w_2 with $a_1=50000$

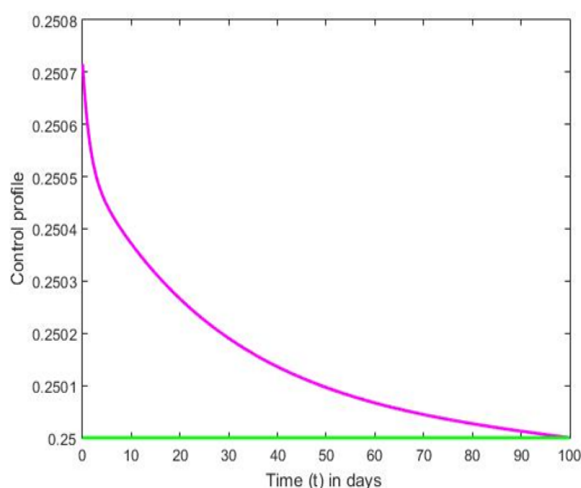


Figure 8: The plot represents Optimal control w_1 and w_2 with $a_1=50000$

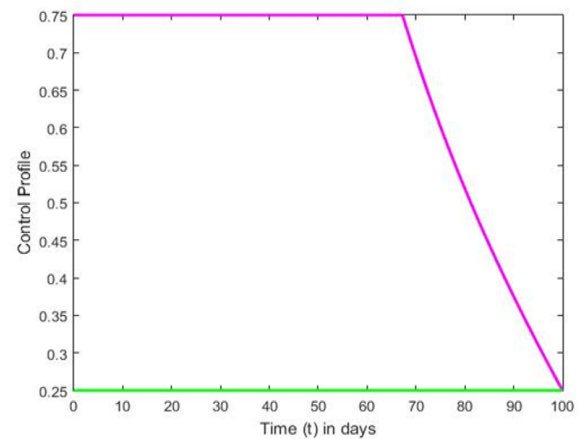


Figure 9: The plot represents Optimal control w_1 and w_2 with $a_2=50000$

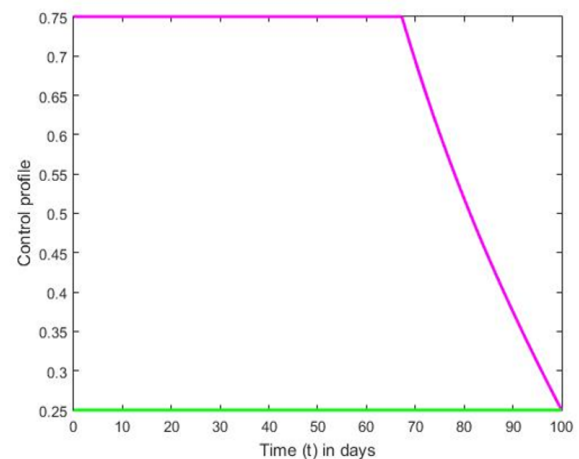


Figure 10: The plot represents Optimal control w_1 and w_2 with $a_2=50000$

Conclusion

In this research article, an optimal control model of haemorrhagic conjunctivitis disease was mathematically formulated to study the transmission dynamics of the disease in order to analyze the optimum control strategy that would be efficacious to be implemented to control the disease at a minimal cost. Two control functions were introduced to assess and measure empirically the efficacy of the efforts to prevent contact between susceptible and infected individuals and the treatment control of giving therapeutic treatment to the infected individuals. The analysis proved that the optimal control strategies considered have an optimum and incomparable results on the reduction of the number of exposed and infected individuals as compared to the model without control as illustrated in the plot of figures for the models with and without controls. The numerical examples showed that the proposed strategies are effective in the reduction of the number of the exposed and infected individuals of the conjunctivitis disease.

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