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OPTIMAL CONTROL ANALYSIS OF THE MALARIA MODEL WITH SATURATED TREATMENT

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Abstract. Malaria is a disease which is transmitted through the bite of an infected Anopheles mosquito. According to WHO report, 400.000 people die worldwide from malaria disease annually. We extend a Susceptible-Infective-Susceptible (SIS) model of malaria transmission with saturated treatment to optimal control problem. Pontryagin's Maximum Principle is used to study this optimal control problem and to derive the necessary conditions for the time dependent optimal control. In this paper we discuss different types of strategies to find the suitable cost-effective strategy to reduce the number of malaria infectives in a desired interval of time.

Keywords: Malaria Model, Optimal Control, Pontryagin's Maximum Principle, Numerical Simulation.

AMS Subject Classification: 92B05, 49J15.

1. Introduction

Malaria is a life-threatening mosquito-borne disease. The malaria parasites are transmitted to the human host through a bite by an infected female anopheles mosquito. When an infected female mosquito bites to human, clinical symptoms such as fever, pain, chills and sweats occur after few days. It can be fatal if not treated properly. In 2019, near about 229 million cases and in 2017, approximately 219 million malaria cases were reported in 87 countries. As per WHO, 92% of malaria cases and 93 % of malaria deaths were reported in African countries alone. Half of the malaria cases were found in 5 countries, Nigeria (25 %), Democratic Republic of Congo (11 %), Mozambique (5 %), India (4 %) and Uganda (4 %). [1]

In India controlling the malaria was a very big challenge but after implementation of "The National Strategic Plan (NSP)" malaria cases have consistently declined from 2.08 million in 2001 to about 4 lakhs in 2018. NSP is developed by National Vector Borne

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Disease Control Programme, Ministry of Health and Family Welfare, Government of India with the help of WHO. They have developed some strategies to control the malaria in India such as Early case detection and prompt treatment (EDPT), Vector control where Mosquito population is controlled in the community with the combination of multiple activities such as chemical and biological control. Also people use of liquids, mosquito repellent creams, coils, mats etc. and cover full body when they go out. Government of India is also promoting "Swachh Bharat Mission" to have clean India, [2, 3].

In [4] proposed and analyzed mathematical models for malaria with human reservoir. The model is analyzed for two different cases: (i) when the rate of environmental discharge is constant; (ii) when the rate of environmental discharge is population dependent. Many researchers extended the ODE's models for malaria to the optimal control problem, [5, 6, 7, 8]. In [9], authors discussed malaria model with optimal control using bed nets strategy. In [10], authors used malaria data from 2000 to 2015 to study the impact of malaria control on Plasmodium falciparum.

Treatment plays an important role in controlling any infectious disease. Different types of treatment functions are explored to understand the disease dynamics. The present work is the extension of the model investigated in [11] where authors formulated and analyzed a mathematical model for malaria by considering saturated treatment function for infected individuals and logistic growth of mosquito population. Here we extend this model to optimal control problem. The remaining of this paper is organized as follows: Section 2 describes the mathematical model with optimal control, Section 3 is optimal control problem, Section 4 deals with simulation results of the optimal control model and Section 5 concludes the paper.

2. Optimal Control Model

Here we extend the mathematical model discussed in [11] to optimal control problem. The whole The whole human population is divided into three disjoint compartments and these compartments are Susceptible Individuals $S(t)$, Malaria infected individuals $I(t)$ and Recovered individuals $R(t)$. Similarly, the total female Aedes mosquitoes $(N_v(t))$ is divided into Susceptible mosquitoes $S_v(t)$ and Infected mosquitoes $I_v(t)$. The interaction between human and mosquitoes is of criss-cross type that leads to transmission of malaria. This model includes saturated treatment function $T(I) = \dfrac{\alpha I}{1+\alpha_1 I}$ where α is cure rate, [12, 13]. When the number of infectives I is small this treatment function approaches to αI i.e. it is proportional to number of infectives. When I is large this treatment function approaches to $\dfrac{\alpha}{\alpha_1}$. And when $\alpha = 0$, this treatment function becomes linear one. Basically this kind of treatment function implies that resources for treatment are limited and are not enough in case the number of infectives is very very large. Here we incorporate two types of control parameters, namely, $u_1(t)$ and $u_2(t)$ to the model proposed by Srivastav and Ghosh in [11]. The control variable $u_1(t)$ shows that use of repulsive lotion, bed-nets and electronic devices, to reduce mosquito biting rate and transmission between human and mosquito. The control variable $u_2(t)$ shows the increase in the death rate of Aedes Mosquito. If u_1 and u_2 are equal to zero, then there is no effort being placed in these controls at time t and if they are equal to one then maximum effort is applied. Keeping

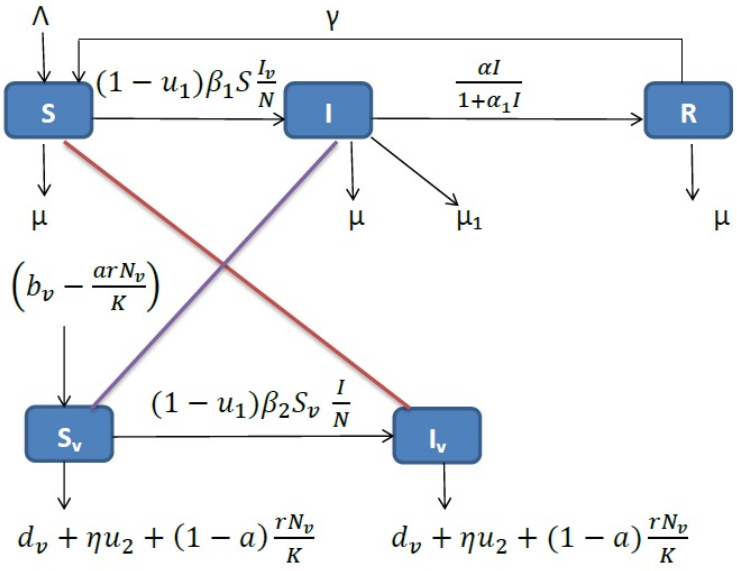

FIGURE 1. Flow chart of the model

in view of the above assumptions, the optimal control model is formulated as follows:

$$\begin{aligned}
\frac{dS}{dt} &= \Lambda-(1-u_1(t))\beta_1 S\frac{I_v}{N}-\mu S+\gamma R\\
\frac{dI}{dt} &= (1-u_1(t))\beta_1 S\frac{I_v}{N}-(\mu+\mu_1)I-\frac{\alpha I}{1+\alpha_1 I}\\
\frac{dR}{dt} &= \frac{\alpha I}{1+\alpha_1 I}-\mu R-\gamma R\\
\frac{dS_v}{dt} &= \left(b_v-\frac{arN_v}{K}\right)N_v-(1-u_1(t))\beta_2 S_v\frac{I}{N}-\left(d_v+\eta u_2(t)+(1-a)\frac{rN_v}{K}\right)S_v\\
\frac{dI_v}{dt} &= (1-u_1(t))\beta_2 S_v\frac{I}{N}-\left(d_v+\eta u_2(t)+(1-a)\frac{rN_v}{K}\right)I_v
\end{aligned} \tag{1}$$

The biologically feasible region of the model system (1) is given by the following positive invariant set:

$$\Omega=\left\{(S,I,R)\in R^3 \text{ and } (S_v,I_v)\in R^2 | 0\le S,I,R\le\frac{\Lambda}{\mu}, S_v+I_v\le K\right\}.$$

The basic reproduction number for this model is computed in [11] ands is given by

$$R_0=\sqrt{\frac{\beta_1\beta_2 K\mu}{(d_v+(1-a)r)(\alpha+\mu+\mu_1)\Lambda}}$$

This model without optimal control exhibits backward bifurcation which implies that there exist two endemic equilibria when the basic reproduction number R_0 is less than one. For the details about the disease-free and endemic equilibrium point one can refer [11].

TABLE 1. Description of parameters and its values

Parameter		Description	Value	Reference
Λ	:	Rate of recruitment in human population	20	assumed
β_1	:	Transmission coefficient due to interaction of S and I_v,	0.00162	[11]
β_2	:	Transmission coefficient due to interaction	0.062	[11]
	:	of S_v and I,		
α	:	Cure rate,	0.6	[11]
μ	:	Natural death rate of human population,	0.0000426	demographic
μ_1	:	Disease-related death rate of human population,	0.0042	assumed
γ	:	Rate at which individuals move from recovered class to susceptible class	0.01	assumed
$r\ (b_v - d_v)$	:	Intrinsic growth rate of the mosquito population,	0.013	[11]
K	:	Carrying capacity of mosquito population,	1000	[11]
d_v	:	Natural death rate of the mosquito population,	0.015	[11]
α_1	:	Saturation factor that measures the effect of the infected being delayed for treatment	0.02	[12]

3. The Optimal Control Problem

Using the optimal control theory, we analyze the behavior of the model (1).The cost functional corresponding to total cost incurred, for fixed time t_f, which need to be minimized is given by:

$$J = \int_0^{t_f} (D_1 I + D_2(S_v + I_v) + \frac{1}{2} D_3 {u_1}^2 + \frac{1}{2} D_4 {u_2}^2). \tag{2}$$

Here the parameters $D_1 \geq 0$, $D_2 \geq 0$, $D_3 \geq 0$, $D_4 \geq 0$ and it show the weight constants of the variable includes in the objective functional. Our objective is to find the control ${u_1}^*$ and ${u_2}^*$, such that

$$J({u_1}^*, {u_2}^*) = \min_{u_1, u_2 \in \Omega} J(u_1, u_2), \tag{3}$$

where U is the control set and is defined as

$U = \{u_1, u_2 : \text{measurable and } 0 \leq u_1, u_2 \leq 1\}$ and $t \in [0, t_f]$.

3.1. **Existence and characterization of optimal controls.** Here we shall first establish the existence of such control functions that minimize the cost functional J. The Lagrangian of this problem is defined as:

$$L(I, S_v, I_v, u_1, u_2) = D_1 I + D_2(S_v + I_v) + \frac{1}{2} D_3 {u_1}^2 + \frac{1}{2} D_4 {u_2}^2$$

Theorem 3.1. *There exist optimal controls ${u_1}^*, {u_2}^* \in U$ such that*

$$J({u_1}^*, {u_2}^*) = \min J({u_1}^*, {u_2}^*)$$

subject to system (1).

Proof. To establish this result, we follow the Theorem 3.1 mentioned in [17] for the existence of optimal controls. As discussed above the state variables (populations) are bounded for each bounded control coming from the control set U. Furthermore, Lipschitz condition with respect to state variables is satisfied by the right hand part of the model system (1).

The control variable set U is also convex and closed by the definition and the model system (1) is linear in control variables. The integrand of the functional $L = D_1 I + D_2(S_v + I_v) + \frac{1}{2}D_3{u_1}^2 + \frac{1}{2}D_4{u_2}^2$ is convex on the control set U due to quadratic nature of control variables. Moreover, $L = D_1 I + D_2(S_v + I_v) + \frac{1}{2}D_3{u_1}^2 + \frac{1}{2}D_4{u_2}^2 \geq \frac{1}{2}D_3{u_1}^2 + \frac{1}{2}D_4{u_2}^2$. Now, consider $c_1 = min(D_1, D_2, D_3, D_4) > 0$ and $g(u_1, u_2,) = c_1(\frac{1}{2}D_3{u_1}^2 + \frac{1}{2}D_4{u_2}^2)$. Thus, $L \geq g(u_1, u_2)$ holds true and g is continuous. Also, g satisfies the condition $\mid (u_1, u_2) \mid^{-1} g(u_1, u_2) \to \infty$ whenever $\mid (u_1, u_2) \mid \to \infty$. Thus, all the conditions for the existence of controls are fulfilled (for more details one cam follow [17, 18]. Hence the result. □

Now, we shall use Pontryagin's maximum principle for necessary conditions for optimal controls. For that the associated Hamiltonian $\mathcal{H}$ is given by

$$\mathcal{H} = L(I, S_v, I_v, u_1, u_2) + \lambda_1 \frac{dS}{dt} + \lambda_2 \frac{dI}{dt} + \lambda_3 \frac{dR}{dt} + \lambda_4 \frac{dS_v}{dt} + \lambda_5 \frac{dI_v}{dt},$$

where λ_i, $i = 1 \ldots 5$ are the adjoint variables. Now adjoint variables in the form of differential equation can be written as follows:

Theorem 3.2. *Let u_i^*, $1 \leq i \leq 2$, be optimal control functions and $S^*, I^*, R^*, S_v^*, I_v^*$, are the corresponding state variables of the optimal control problem (1)-(2). Then there exists adjoint variable $\lambda = (\lambda_1, \lambda_2, \ldots, \lambda_5)^T \in \mathbb{R}^5$, which satisfies the following equations:*

$$\begin{aligned}
\frac{d\lambda_1}{dt} = -\frac{\partial H}{\partial S} &= \lambda_1\mu + \beta_1 I_v(1-u_1)\left(\frac{I+R}{N^2}\right)(\lambda_1 - \lambda_2) \\
\frac{d\lambda_2}{dt} = -\frac{\partial H}{\partial I} &= -D_1 + \lambda_2(\mu + \mu_1) + (1-u_1)\beta_1\frac{I_v}{N^2}(\lambda_2 - \lambda_1) + \frac{\alpha}{(1+\alpha_1 I)^2}(\lambda_1 - \lambda_2) \\
&\quad + (1-u_1)\beta_2 S_v\left(\frac{S+R}{N^2}\right)(\lambda_4 - \lambda_5) \\
\frac{d\lambda_3}{dt} = -\frac{\partial H}{\partial R} &= \lambda_3\mu + (1-u_1)\beta_1 S\frac{I_v}{N^2}(\lambda_2 - \lambda_1) + (1-u_1)\beta_2 S_v\left(\frac{I}{N^2}\right)(\lambda_5 - \lambda_4) \\
&\quad + \gamma(\lambda_3 - \lambda_1) \\
\frac{d\lambda_4}{dt} = -\frac{\partial H}{\partial S_v} &= -D_2 + \lambda_4\left(2N_v\frac{ar}{K} - b_v + d_v + \eta u_2 + (1-a)(2S_v + I_v)\frac{r}{K}\right) \\
&\quad + (1-u_1)\beta_2\frac{I}{N}(\lambda_4 - \lambda_5) \\
\frac{d\lambda_5}{dt} = -\frac{\partial H}{\partial I_v} &= -D_3 + (1-u_1)\beta_1\frac{S}{N}(\lambda_1 - \lambda_2) + \lambda_4\left(2N_v\frac{ar}{K} + (1-a)S_v\frac{r}{K}\right) \\
&\quad + \lambda_5\left(d_v + \eta u_2 + (1-a)(2I_v + S_v)\frac{r}{K}\right)
\end{aligned}$$

Let $\widetilde{S}$, $\widetilde{I}$, $\widetilde{R}$, $\widetilde{S_v}$, $\widetilde{I_v}$, be the optimum values of S, I, R, S_v, I_v respectively, and $\widetilde{\lambda_1}$, $\widetilde{\lambda_2}$, $\widetilde{\lambda_3}$, $\widetilde{\lambda_4}$, $\widetilde{\lambda_5}$ be the solution of the above system of differential equations.

Proof. By using [17, 18], we prove this theorem where the transversality conditions are given by

$$\lambda_i(t_f) = 0, \; i = 1 \ldots 5, . \tag{5}$$

Let $u_i^*,\ 1 \leq i \leq 2$, be the optimal control functions and $S^*, I^*, R^*, S_v^*, I_v^*$, are the corresponding state variables. Then, Pontryagin's Maximum Principle ensures the existence of the following adjoint variable $\lambda = (\lambda_1, \lambda_2, \ldots, \lambda_5)^T \in \mathbb{R}^5$, which satisfies the following canonical equations:

$$\frac{d\lambda_1}{dt} = -\frac{\partial H}{\partial S},\ \frac{d\lambda_2}{dt} = -\frac{\partial H}{\partial I},\ \frac{d\lambda_3}{dt} = -\frac{\partial H}{\partial R},\ \frac{d\lambda_4}{dt} = -\frac{\partial H}{\partial S_v},\ \frac{d\lambda_5}{dt} = -\frac{\partial H}{\partial I_v},$$

with transversality conditions (5). Where $\mathcal{H}$ is the Hamiltonian defined as above. Thus, the adjoint system can be obtained. □

Theorem 3.3. *The optimal controls* $({u_1}^*, {u_2}^*)$ *which minimizes* J *over the region* Ω *given by*

$${u_1}^* = min\{1, max(0, \widetilde{u_1})\}, {u_2}^* = min\{1, max(0, \widetilde{u_2})\},$$

where

$$\widetilde{u_1} = \frac{\beta_1 S\frac{I_v}{N}(\lambda_2 - \lambda_1) + \beta_2 S_v\frac{I}{N}(\lambda_5 - \lambda_4)}{D_3},$$
$$\widetilde{u_2} = \frac{\eta(S_v\lambda_4 + I_v\lambda_5)}{D_4}.$$

Proof. : Using optimally condition :

$$\frac{\partial \mathcal{H}}{\partial u_1} = 0, \frac{\partial \mathcal{H}}{\partial u_2} = 0.$$

we get,

$$\frac{\partial \mathcal{H}}{\partial u_1} = D_3 u_1 + \beta_1 S\frac{I_v}{N}(\lambda_1 - \lambda_2) + \beta_2 S_v\frac{I}{N}(\lambda_4 - \lambda_5) = 0.$$

This implies

$$u_1 = \frac{\beta_1 S\frac{I_v}{N}(\lambda_2 - \lambda_1) + \beta_2 S_v\frac{I}{N}(\lambda_5 - \lambda_4)}{D_3} = \widetilde{u_1},$$

And,

$$\frac{\partial \mathcal{H}}{\partial u_2} = u_2 D_4 - \lambda_4\eta S_v - \lambda_5\eta I_v = 0,$$

gives

$$u_2 = \frac{\eta(S_v\lambda_4 + I_v\lambda_5)}{D_4} = \widetilde{u_2}.$$

Again upper and lower bounds for these control are 0 and 1 respectively. i.e. $u_1 = u_2 = 0$ if $u_1 < 0$ and $u_2 < 0$, and $u_1 = u_2 = 1$ if $\widetilde{u_1} > 1$ and $\widetilde{u_2} > 1$, otherwise $u_1 = \widetilde{u_1}$ and $u_2 = \widetilde{u_2}$. Hence for these controls ${u_1}^*, {u_2}^*$ we get optimum value of the function J. □

4. Simulation

We simulate our optimal control model (1) using MATLAB software. We used the parameter values given in the Table 1, which is corresponding to the endemic equilibrium. The value of weight constants for the problem are given as $D_1 = 1, D_2 = 1, D_3 = 45, D_4 = 65$. We solve the optimality system by iterative method with the help of forward and backward difference approximations (see [17]). Total time interval [0, 200] is consider for our study. First we solve the state equations by the forward difference approximation method then we use the backward difference approximation method to solve the adjoint equations.

Strategy I: When both controls are applied

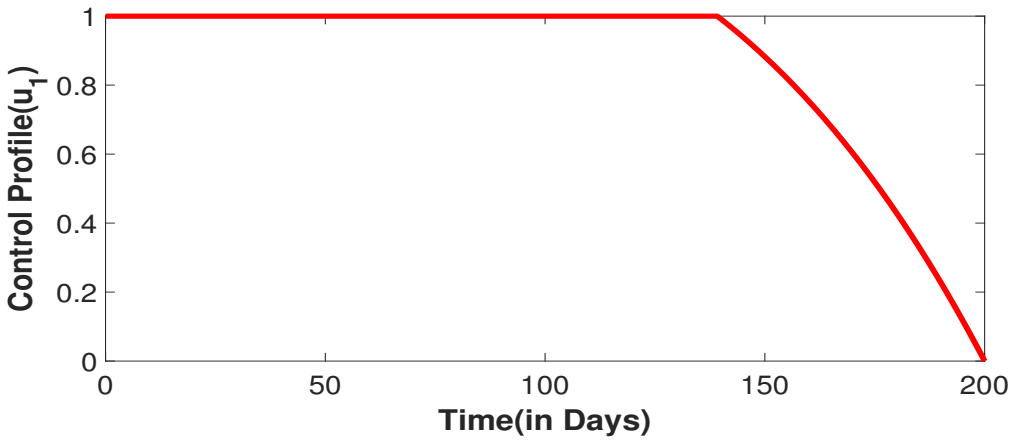

FIGURE 2. Optimal Control profile of u_1 when both the controls are applied simultaneously.

Here all the control mechanism (u_1, u_2) are used to optimize the objective function J. Figures 2-3 show the control profiles of u_1 and u_2. The variation of total infected human (I) with time is shown in Figure 4. Here it is easy to observe that there is a significant decrease in the total number of infectives in the case when both optimal controls are applied simultaneously.

Strategy II: When only one control is used at a time
Here we try to find which type of optimal control is more effective in reducing the infective population. So we consider each type of control one by one.
In Fig. 5 and 7, the control profiles of different types of optimal control when they are applied alone are shown and corresponding effects on total number of infectives (I) is shown in Figure 6 and Figure 8. It shows that if controls (u_1) and (u_2) are applied one at a time, then the control (u_2) is more effective than the control (u_1).

From above figures we conclude that strategy I when both the controls are applied simultaneously is more effective than strategy I where only one control is applied at a time. Next we try to see the impact of the some of the parameters on total number of infected human when strategy I is followed. We consider the parameters α and d_v which are cure rate of infected human and death rate of mosquito population. These parameters may vary depending upon availability of medical resources and proper implementation of vector control methods. Here Figure 9 demonstrate the impact of these parameters on the number of infectives. It is observed that increase in these parameters causes significant decrease in the total number of infected human. From this plot, it is noticed that if infected human population can get better treatment then number of infectives can be reduced significantly.

5. Conclusion

This paper presents optimal control analysis of a non-linear mathematical model for malaria with saturated treatment. The presented model incorporates two types of optimal controls, namely $u_1(t)$ associated with the transmission between human and mosquito and $u_2(t)$ associated with the increase in the death rate of mosquito population. Numerical simulation of our model indicates the fact that the number of infected human decreases significantly when both the controls are applied simultaneously. When only one of the

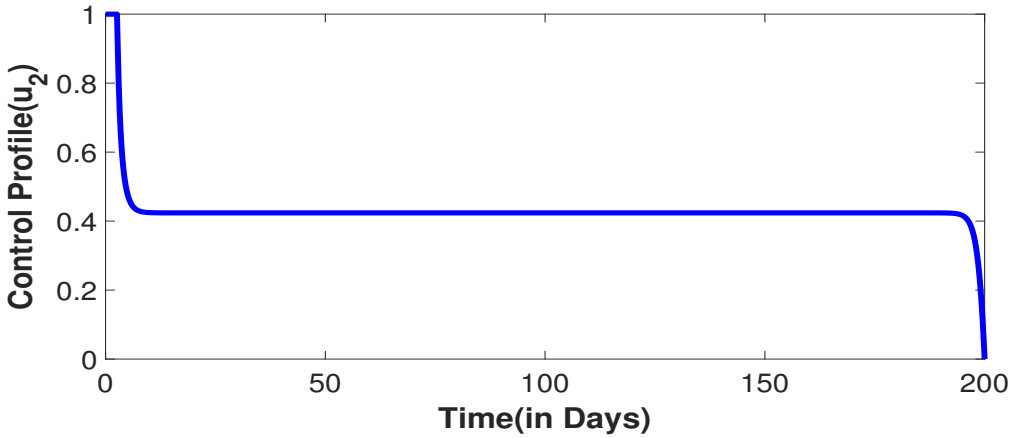

FIGURE 3. Optimal Control profile of u_2 when both the controls are applied simultaneously.

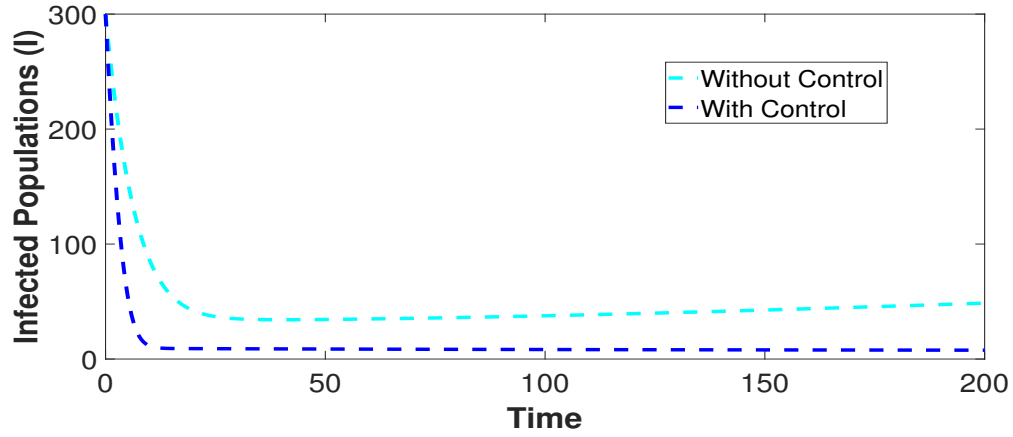

FIGURE 4. Time series of I with and without control when both the controls are applied simultaneously.

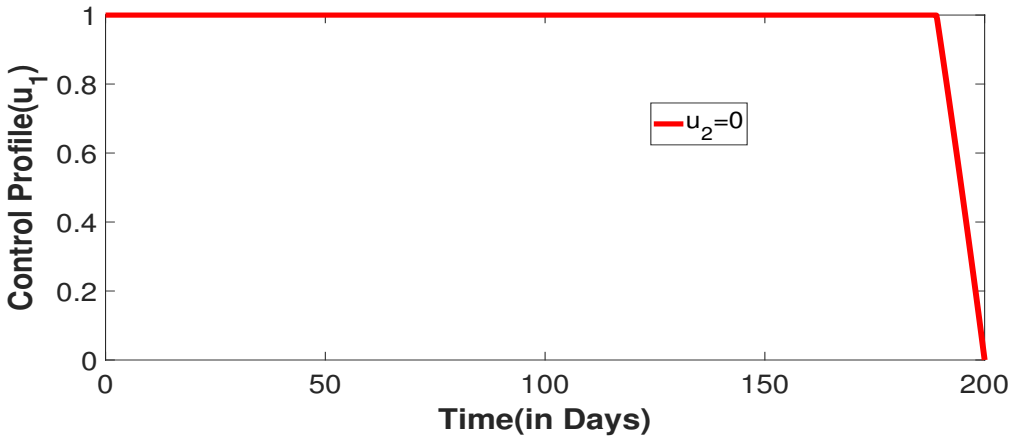

FIGURE 5. Optimal Control profile of u_1 when the control u_2 is zero.

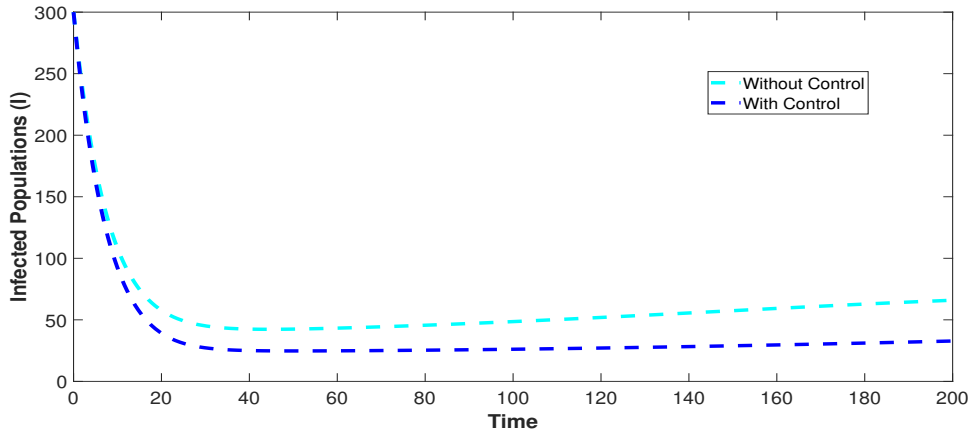

FIGURE 6. Time series of I with and without control when only control u_1 is applied.

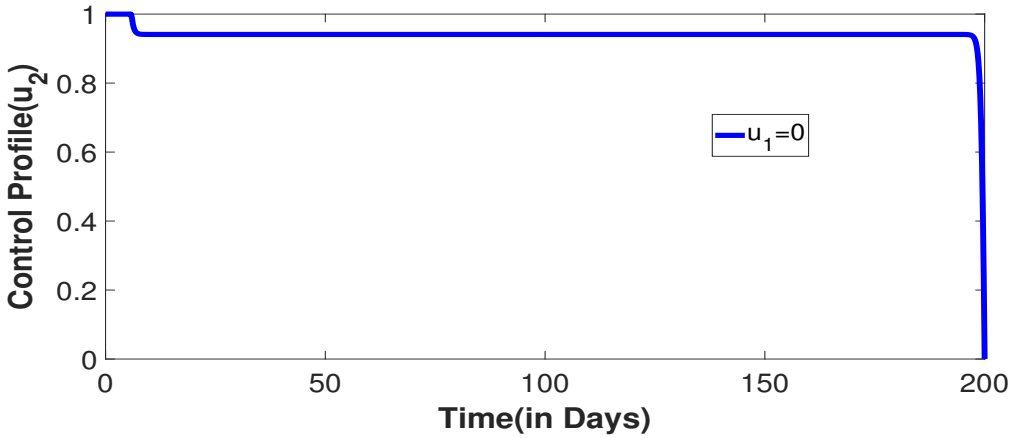

FIGURE 7. Optimal Control profile of u_2 when the control u_2 is zero.

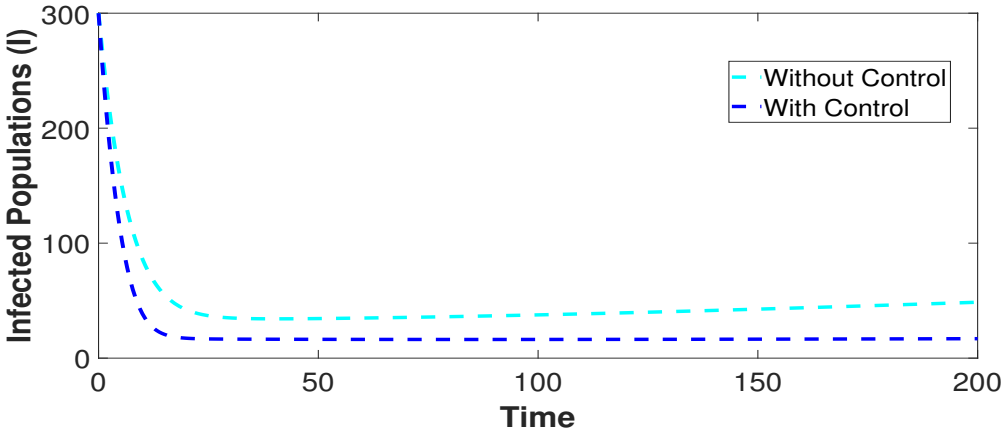

FIGURE 8. Plot of I with and without control only control u_2 is applied.

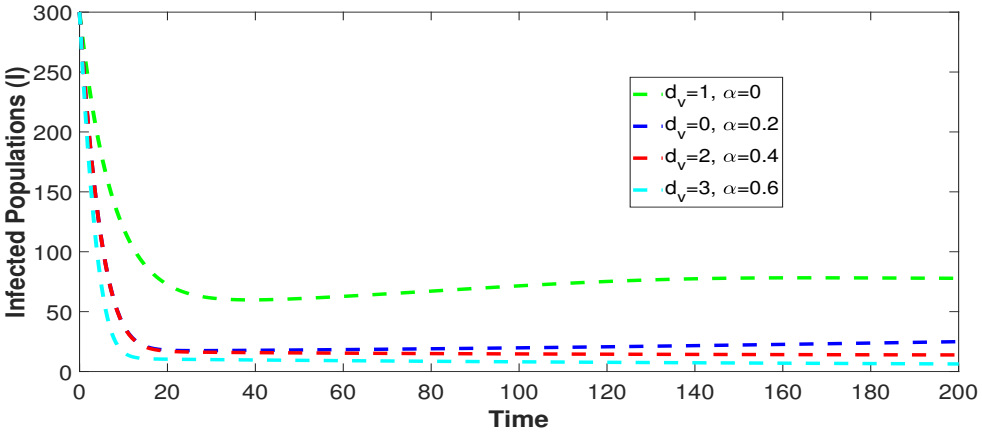

FIGURE 9. Variation of I with time for different value of d_v and α in presence of both the controls.

controls is applied then too there is decrease in the number of infected human but this decease is much less compared to the decrease in presence of both the controls. Our results reveal that optimal control offers better result compared to the model without optimal control. Numerical simulation indicates that the treatment of infectives and vector-control are also very important factors in the control of malaria. Increase in these two parameters reduces the number of malaria infected human. This study may help policy makers in planning suitable control strategies for the control of malaria in endemic regions.

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