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Optimal Control Techniques for the Transmission Risk of Nipah Virus Disease with Awareness

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Abstract: Nipah virus is one of the life-threatening infectious diseases in South-East Asian regions. In this study, we developed a compartmental model of Nipah virus transmission using an ordinary differential equation. We find the disease-free equilibrium and compute basic reproduction number (R_0). The sensitivity analysis of the parameters of the basic reproduction number of the model is studied and identifies the most sensitive parameters which can control the transmission dynamics of the Nipah virus. The model is extended to the optimal control problem and is analyzed by using Pontryagin's Maximum Principle. Further, we analyze the cost-effective and three different time-dependent control strategies to minimize the number of infectives in during that period of time. Finally, compare the results of the optimal control models using numerical simulation.

Keywords: Nipah virus, Basic reproduction number, Sensitivity Analysis, Optimal Control Problem, Pontryagin's Maximum Principle.

1. INTRODUCTION

Nipah virus disease is a Zoonotic infection caused by Nipah virus, a paramyxovirus belonging to the genus Henipavirus of the family paramyxoviridae. Nipah Virus is one of the deadliest infectious diseases in South-East Asian regions since end of the century. It is transmitted to humans from infected bats, infected pigs, or contaminated fruits. Also it can be transmitted directly from human to human contact [1, 6]. The transmission of disease can be from bats to human, human to human and contaminated fruits to human. The symptoms of the Nipah Virus are fever, headache, dizziness, muscle pain, vomiting, drowsiness, and sore throat [5]. There is no medicine and vaccine available for either human or animals. The primary treatment for humans is supportive care. According WHO the case fatality rate is estimated at 40 $\%$ to 75 $\%$. This rate can very by outbreak depending on local capabilities for epidemiological surveillance and clinical management. In 1998, the first of Nipah virus case was recorded during Malaysian outbreak. In 1999, Nipah Virus was detected from an infected human of Sungai Nipah village in Malaysia [4]. In 1999, first largest Nipah virus outbreak was identified in Malaysia and Singapore among pig farmers. In Malaysia and Singapore outbreaks 276 cases were reported [1, 21] between 1998 to 1999. In that period most of the infected people had contact with sick pigs [16], and death rate infected people were 39% [7]. In India and Bangladesh, the evidence of Nipah Virus transmitted through raw date palm sap contaminated with infectious bat excretions. In 2001, Bangladesh Nipah outbreaks a total of 321 infection cases were reported [1, 16], and 161 of them deaths, accounting for a 70 percentage fatality rate. In India, the first Nipah outbreak was reported

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in Siliguri town in 2001, followed by the second outbreak in Nadia district in West Bengal state in 2007. In 2018, a Nipah outbreak In India and Bangaladesh human to human [9, 17], transmission is regularly reported according to CDC, but in Malaysia and Singapore there is no evidence of human to human transmission. In 2018, a Nipah Virus outbreak was reported in Kozhikode district and in 2019, another outbreak reported in Kochi district in Kerala. During this outbreak 17 Nipah infected people were dead. In 2021 also few Nipah virus suspected cases reported in Kozhikode district of Kerala. A 12-years old boy were infected and later the boy was death at a private hospital. The high risk of Nipah Virus infected countries other than above mention include Australia, Bhutan, Brunei, Cambodia, China, Indonesia, Laos, Madagascar, Myanmar, Nepal, Philippines, Papua New Guinea, Taiwan, Thailand, and Vietnam.

Many Nipah virus mathematical models are proposed and analysis in the literature to study the various aspects of transmission dynamics of disease. The study of Biswas [1] shows that the control strategy of deadly NiV in Bangladesh. Chua et. al. [6] studied Isolation of Nipah virus from Malaysian Island flying-fox. Chua et. al. [5] studied emergent of deadly Paramyxovitus of Nipah virus. Chua [4] discussed about Nipah virus outbreak in Malaysia. Mondal et. al. [7], studied controlling the spread of Nipah virus in Bangladesh through a mathematical model. Parashar et. al. [16], shows that the risk factors for human infection with a new zoonotic paramyxovirus and Nipah virus during the Malaysia outbreak in 1998-1999. Goh et. al. [9], shows that clinical features of Nipah virus encephalitis among pig farmers in Malaysia. Goswami [3], studied stability analysis of a mathematical model and discussed sensitivity analysis of basic reproduction number. Paton et.al. [17], shows that the outbreak of NiV infection among abattoir works in Singapore. Uppal [21], studied about emergence of Malaysia Nipha virus outbreak.

This paper is organized as follows: Section 2, formulates the model, analysis of the model includes positive invariant, boundedness. Section 3, compute the basic reproduction number using next-generation matrix method. Section 4, discuss sensitivity analysis of basic reproduction number and identify most sensitive parameter. Section 5, deals with the optimal control techniques using Pontryagin's Maximum Principal. Section 6, presents the numerical Results and discussion. Finally we concludes our the paper in Section 7.

2. MATHEMATICAL MODEL

A non-linear mathematical model is formulated for Nipah virus by considering the total population variable and the standard incident type interaction for transmission of the disease. We incorporate the awareness parameter in the model as media has a positive effect on controlling the transmission of any type of infectious disease. An extensive study suggests that any awareness program related to the disease can alert susceptible individuals and will not contact with infective. Also, due to the awareness program some infectives can take medical care and recover from the disease. This proposed study is an extension work of our previous mathematical model in [12], the mainly focuses of this study is on finding the optimal control strategies to reduce the Nipah virus transmission. The model is divided into seven mutually exclusive compartments viz., susceptible humans (S_h), exposed humans (E_h), infected humans (I_h), recovered humans (R_h), susceptible fruits (S_f), infected fruits (I_f), and infected bats (I_b). The model is a non-linear standard action type and considering logistic growth $bI_b\left(1-\dfrac{I_b}{K}\right)$ on the infected bat's population. Here, the incident rate $\dfrac{\beta_1 I_h}{N_h}$ is the average number contacts with infectives per unit time of one susceptible [20]. Although, $\left(\dfrac{\beta_1 I_h}{N_h}\right) S_h$ is the number of new cases per unit time among the susceptible. Nipah virus

Table 2.1. Description of biological parameters

Parameter	Description	Value
Λ_h	Rate of recruitment of human population	15
Λ_f	Rate of recruitment of fruits	20
β_1	Usual transmission probability between S_h and I_h	0.0541
β_2	Transmission probability between S_h and I_f	0.0521
β_3	Transmission probability between I_h and S_f	0.0631
δ_h	Contact rate between E_h and I_h	0.53
γ_h	Recovery rate of human population	0.009
μ_h	Natural mortality rate of human population	0.19
μ_1	Natural mortality rate of human population due to infection	0.09
μ_f	Natural mortality rate of fruits	0.095
μ_b	Natural mortality rate of bats	0.0123
b	Growth rate coefficient of infected bats	0.005
K	Carrying capacity of infected bats	100 - 500
a_h	Recovery rate of exposed humans due to effect of awareness	0.95

has been studied by many authors, most of the models are mass action type model but here we have formulated a standard incident type model. We have consider standard incidence type interaction between between human and fruits, which is more reasonable than mass action type model. This type of consideration is more suitable for many disease like Nipah virus, Zika virus, Dengue fever etc. It is well known that Nipah virus disease is one of the deadliest endemic, so long term study of the dynamics of disease is most significant. The biological interpretations of parameters and values of the parameters are shown in Table 1. The mathematical model of Nipah described as follows:

$$\begin{aligned}
S_h' &= \Lambda_h - \beta_1 S_h \frac{I_h}{N_h} - \beta_2 S_h \frac{I_f}{N_h} - \mu_h S_h \\
E_h' &= \beta_1 S_h \frac{I_h}{N_h} + \beta_2 S_h \frac{I_f}{N_h} - (\delta_h + a_h + \mu_h) E_h \\
I_h' &= \delta_h E_h - (\gamma_h + \mu_h + \mu_1) I_h \\
R_h' &= a_h E_h + \gamma_h I_h - \mu_h R_h \\
S_f' &= \Lambda_f - \beta_3 S_f \frac{I_b}{N_h} - \mu_f S_f \\
I_f' &= \beta_3 S_f \frac{I_b}{N_h} - \mu_f I_f \\
I_b' &= b I_b \left(1 - \frac{I_b}{K}\right) - \mu_b I_b
\end{aligned} \tag{2.1}$$

2.1. Positivity and Boundedness of the system

Here, we shall show that the positivity and boundedness of the population. From the system (2.1), we have

$$S_h'\Big|_{S_h=0} = \Lambda_h > 0,\ E_h'\Big|_{E_h=0} = \beta_1 S_h \frac{I_h}{N_h} + \beta_2 S_h \frac{I_f}{N_h} \geq 0,$$

$$I_h'\Big|_{I_h=0} = \delta_h E_h \geq 0,\ \ (R_h')_{R_h=0} = a_h E_h + \gamma_h I_h \geq 0,$$

$$S_f'\Big|_{S_f=0} = \Lambda_f > 0,\ I_f'\Big|_{I_f=0} = \beta_3 S_f \frac{I_b}{N_h} \geq 0,\ \ I_b'\Big|_{I_b=0} = 0$$

Here, all the rates are non-negative, so if we start in the interior of the non-negative bounding R^6, we shall always remain in this cone keeping mind of the fact that direction of the vector field is inward on all the bounding planes. We note the change rate of the total population $N_h = S_h + E_h + I_h + R_h$ and $N_f = S_f + I_f$ are given by the following differential equations.

$$\begin{aligned} N_h' &= \Lambda_h - \mu_h N_h - \mu_1 I_h \\ N_f' &= \Lambda_f - \mu_f N_f \end{aligned}$$

This gives $\limsup_{t\to\infty} N_h \leq \frac{\Lambda_h}{\mu_h}, \limsup_{t\to\infty} N_f \leq \frac{\Lambda_f}{\mu_f}$. Therefore, all $S_h(t), E_h(t), I_h(t), R_h(t)$ are bounded by $\frac{\Lambda_h}{\mu_h}$ and the solutions $S_f(t), I_f(t)$ are bounded by $\frac{\Lambda_f}{\mu_f}$. Hence, the biological feasible region of the proposed system (2.1) is given by the following positively invariant region:

$$\Omega = (S_h, E_h, I_h, R_h, S_f, I_f, I_b) \in R_+^7 : (S_h + E_h + I_h + R_h) \leq \frac{\Lambda_h}{\mu_h}, (S_f + I_f) \leq \frac{\Lambda_f}{\mu_f}$$

3. BASIC REPRODUCTION NUMBER $\mathcal{R}_0$

The disease-free equilibrium of the proposed model as E_0=$(N_h^0, E_h^0, I_h^0, R_h^0, N_f^0, I_f^0, I_b^0) = \left(\frac{\Lambda_h}{\mu_h}, 0, 0, 0, \frac{\Lambda_f}{\mu_f}, 0, 0\right)$.

To find the basic reproduction number $\mathcal{R}_0$, using the next-generation matrix method as described in [2, 8, 12, 13]. The matrix $\mathcal{F}$ and $\mathcal{V}$ as follows:

$$\mathcal{F} = \begin{pmatrix} \beta_1(N_h - E_h - I_h - R_h)\left(\frac{I_h + I_f}{N_h}\right) \\ 0 \\ \beta_3(N_f - I_f)\frac{I_b}{N_h} \\ 0 \end{pmatrix} \ and\, \mathcal{V} = \begin{pmatrix} (\delta_h + a_h + \mu_h)E_h \\ -\delta_h E_h + (\gamma_h + \mu_h + \mu_1)I_h \\ \mu_f I_f \\ -bI_b\left(1 - \frac{I_b}{K}\right) - \mu_b I_b \end{pmatrix}$$

Jacobian of $\mathcal{F}$ and $\mathcal{V}$ at E_0 as follows

$$\text{F=} \begin{pmatrix} 0 & \beta_1 & \beta_1 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \beta_3\frac{\mu_h\Lambda_f}{\mu_f\Lambda_h} \\ 0 & 0 & 0 & 0 \end{pmatrix} \ and\, V = \begin{pmatrix} \delta_h + \mu_h + a_h & 0 & 0 & 0 \\ -\delta_h & \gamma_h + \mu_h + \mu_1 & 0 & 0 \\ 0 & 0 & \mu_f & 0 \\ 0 & 0 & 0 & -b + \mu_b \end{pmatrix}$$

The largest eigenvalue of FV^{-1} is called the basic reproduction number $\mathcal{R}_0$ and is obtained as follows:

$$\mathcal{R}_0 = \frac{\beta_1\delta_h\mu_f\Lambda_h c_3 - \beta_3\mu_h\Lambda_f c_1 c_2}{2c_1c_2c_3\mu_f\Lambda_h} + \sqrt{\left(\frac{\beta_1\delta_h\mu_f\Lambda_h c_3 - \beta_3\mu_h\Lambda_f c_1 c_2}{2c_1c_2c_3\mu_f\Lambda_h}\right)^2 + \frac{\beta_1\beta_3\delta_h\mu_h\Lambda_f}{\mu_f\Lambda_h c_1 c_2 k_4}} \quad (3.2)$$

where,

$$c_1 = \delta_h + \mu_h + a_h; c_2 = \gamma_h + \mu_h + \mu_1, c_3 = \mu_b - b,$$

4. SENSITIVITY ANALYSIS OF REPRODUCTION NUMBER

In this section, we perform sensitivity analysis for the parameters involved in reproduction number R_0, which reflects that increase or decrease in these parameter causes increase or decrease in R_0 [3, 19]. The sensitivity of $\mathcal{R}_0$ to different parameters is shown in Figs. 4.1 to 4.7. It is used to discover the parameters that have a high impact on $\mathcal{R}_0$ and should be targeted by intervention strategies. Sensitivity indices allows to measure the relative change in a variable when parameter changes. For that we use the forward sensitivity index of a variable, with respect to a given parameter, which is defined as the ratio of the relative change in the variable to the relative change in the parameter. If such variable is differentiable with respect to the parameter, then the sensitivity index is defined using partial derivatives. The normalized forward sensitivity index of $\mathcal{R}_0$, which is differentiable with respect to a given parameter P, is defined by

$$Y_P^{\mathcal{R}_0} = \frac{P}{\mathcal{R}_0}\frac{\partial \mathcal{R}_0}{\partial P} \tag{4.3}$$

The above formula can be used to compute the analytical expression for the sensitivity of $\mathcal{R}_0$ to each parameter that it includes. Accordingly, the sensitivity indexes of the model (2.1) are illustrate in Fig. 4.1. Consequently, the value of $\mathcal{R}_0$ increases with increase in the values of all positive indices parameters $\beta_1,\ \beta_3,\ \delta_h,\ \mu_f,\ \mu_b$, and Λ_f with $\mathcal{R}_0$. Also, the parameters $a_h,\ \gamma_h,\ \mu_h,\ \mu_1,\ b$, and Λ_h have negative index with $\mathcal{R}_0$. It is clearly observed that the effect of the parameter Λ_h is the maximum and hence it is the most sensitive parameter of $\mathcal{R}_0$. It means that small change (increase or decrease) in the parameters Λ_h will significant change in the value of $\mathcal{R}_0$. Other sensitive parameter $\mathcal{R}_0$ are β_1, δ_h, μ_h as small change in these parameters can cause large change in the value of R_0. So correct estimation of these parameters is very important to predict transmission of this disease. It is obvious that phenomenon of a lower value of $\mathcal{R}_0$ will boost to prevent the disease prevalence. Thus, to control the disease from the population, we have to control the increase of parameters having positive indices with $\mathcal{R}_0$, whereas parameters with negative indices should be maintained.

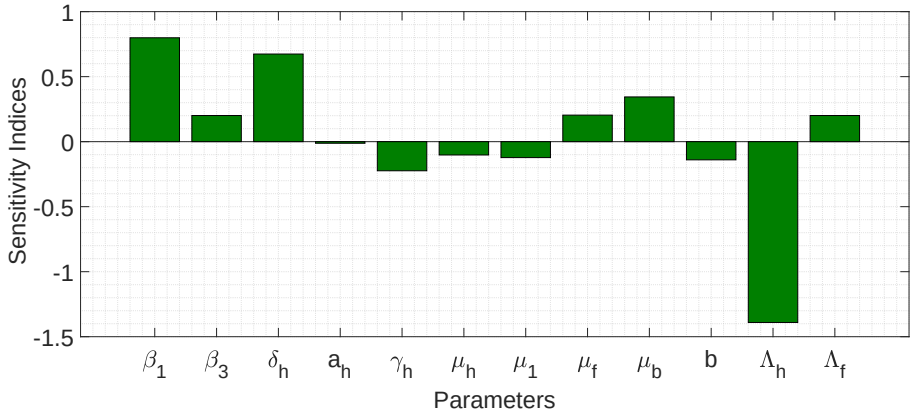

Fig. 4.1. Forward sensitivity of R_0 for the parameters as $\beta_1 = 0.0541$; $\beta_3 = 0.0631$; $\delta_h = 0.53$; $a_h = 0.95$; $\gamma_h = 0.009$; $\mu_h = 0.19$; $\mu_f = 0.095$; $\mu_1 = 0.09$; $\mu_b = 0.0123$; $b = 0.005$; $\Lambda_h = 15$; $\Lambda_f = 20$.

5. THE OPTIMAL CONTROL MODEL

In this section, three different types of control intervention viz., $u_1(t), u_2(t), and u_3(t)$ are incorporated into the model system (2.1) and extended to optimal control problem.

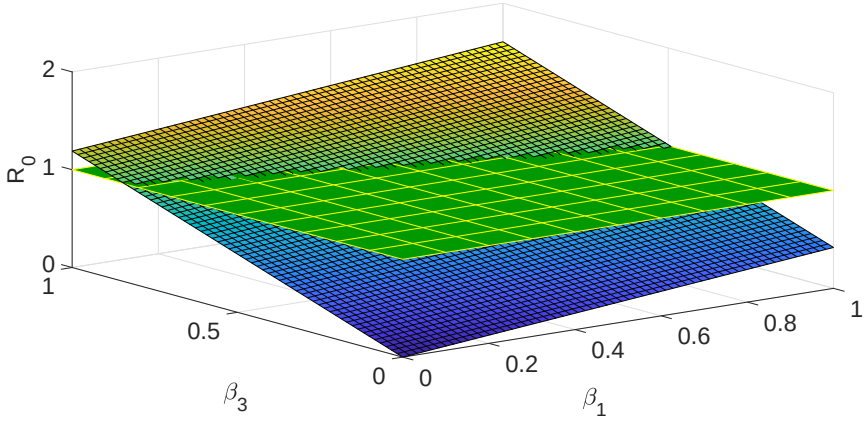

Fig. 4.2. Influence of β_1 and β_3 on $\mathcal{R}_0$.

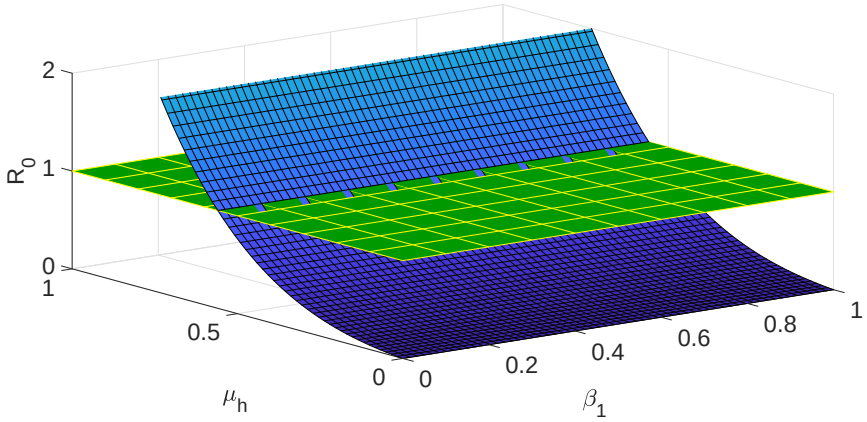

Fig. 4.3. Influence of β_1 and μ_h on $\mathcal{R}_0$.

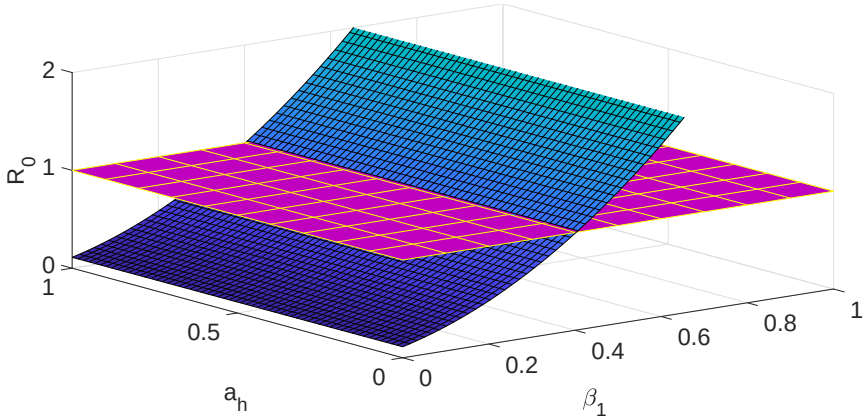

Fig. 4.4. Influence of β_1 and a on $\mathcal{R}_0$.

There interventions are implementing either pharmaceutical(treatment) or non-pharmaceutical(effect of information). The main goal of this research is to investigate the best control strategies with minimum cost of implementation as well as financial loss generated. Since there is no proper vaccination and appropriate medicines for Nipah virus infections, so in the model we introduce three control strategies, viz, creating awareness $u_1(t)$, estimation of novel technologies $u_2(t)$, and the treatment $u_3(t)$. If $u_1(t)$, $u_2(t)$, and

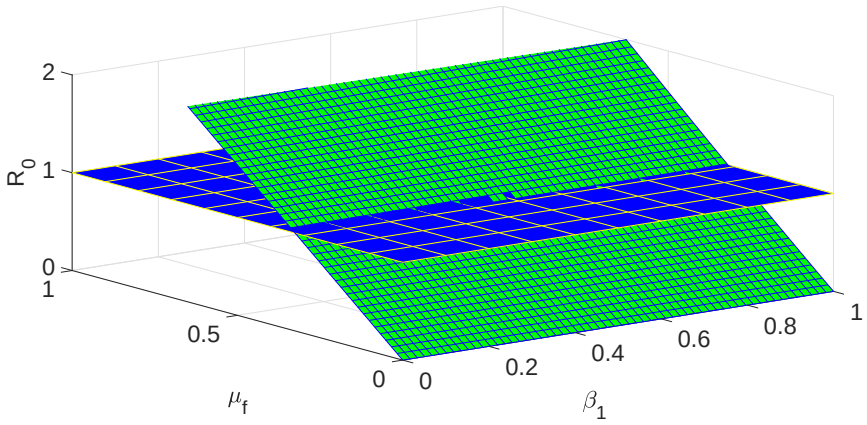

Fig. 4.5. Influence of β_1 and μ_f on $\mathcal{R}_0$.

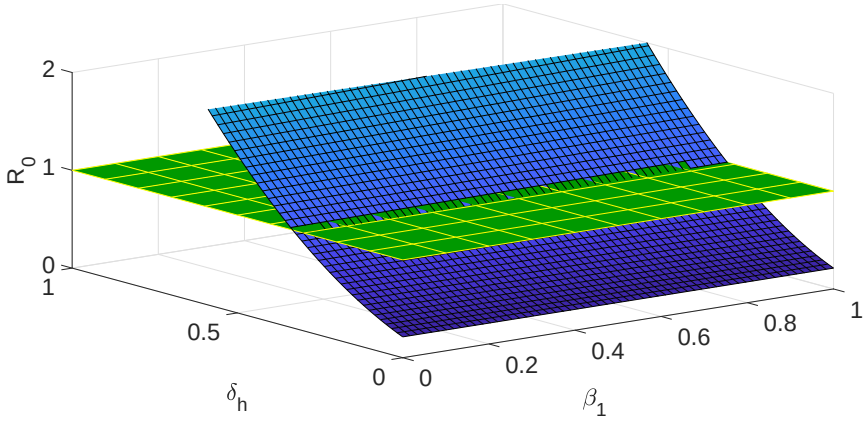

Fig. 4.6. Influence of β_1 and δ_h on $\mathcal{R}_0$.

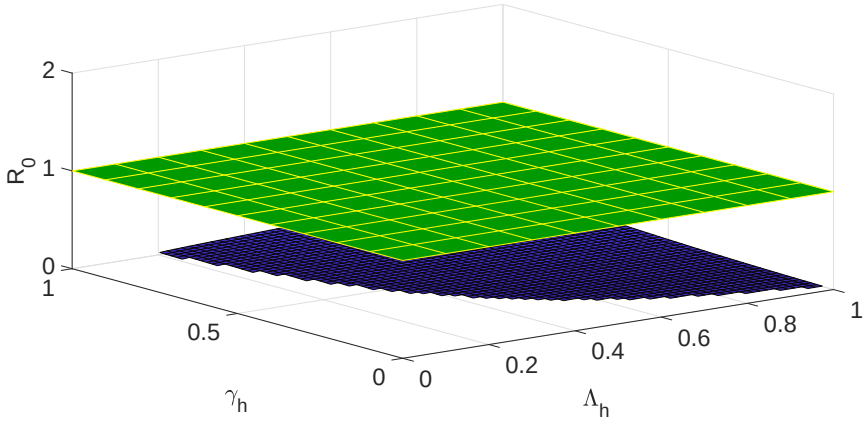

Fig. 4.7. Influence of Λ_h and γ_h on $\mathcal{R}_0$.

$u_3(t)$ 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 the maximum effort is applied. The details of each intervention are described as follows:

- **Control variable** $u_1(t)$: The force of Nipah Virus infections is reduce by (1-$u_1(t)$), where the effect control measures $u_1(t)$ increase awareness in the population which results in the reduction of the transmission rate β_1 and the control measures the effort required for giving health cares for the infected people to reduce the infected individuals. Creating awareness activity among the community about the risky areas before outbreak of the disease is more effective. Personal care should be taken in order to avoid direct contact with the person infected by Nipah virus. Also, using masks, gloves and glasses will help in prevention and control effectively potential outbreaks.
- **Control variable** $u_2(t)$: The control variable $u_2(t)$ is estimation of novel technologies or methods to minimize spread of the virus within bat or pig population. Controlling bat is associated with a reduction in human cases. This is an effective intervention but requires considerable amount of money. Thus, our main objective is to minimize the disease effect in pig or bat population with minimum cost.
- **Control variable** $u_3(t)$: The control variable $u_3(t)$ is the use of effective medicines for the treatment measure of infectious humans and insecticide to the Nipah virus infection causing species. η is the modification parameter in control $u_3(t)$. Due to the expensive nature of the antibody drugs, in this effective intervention requires large amount of money. Thus, the main objective of this intervention is to minimize the disease effect in human population with minimum cost.

$$\begin{aligned}
\frac{dS_h}{dt} &= \Lambda_h - (1-u_1(t))\beta_1 S_h \frac{I_h}{N_h} - (1-u_2(t))\beta_2 S_h \frac{I_f}{N_h} - \mu_h S_h \\
\frac{dE_h}{dt} &= (1-u_1(t))\beta_1 S_h \frac{I_h}{N_h} + (1-u_2(t))\beta_2 S_h \frac{I_f}{N_h} - (\delta_h + a_h + \mu_h)E_h \\
\frac{dI_h}{dt} &= \delta_h E_h - (\gamma_h + \eta u_3(t) + \mu_h + \mu_1)I_h \\
\frac{dR_h}{dt} &= a_h E_h + (\eta u_3(t) + \gamma_h)I_h - \mu_h R_h \\
\frac{dS_f}{dt} &= \Lambda_f - (1-u_2(t))\beta_3 S_f \frac{I_b}{N_h} - \mu_f S_f \\
\frac{dI_f}{dt} &= (1-u_2(t))\beta_3 S_f \frac{I_b}{N_h} - \mu_f I_f \\
\frac{dI_b}{dt} &= bI_b\left(1 - \frac{I_b}{K}\right) - \mu_b I_b
\end{aligned} \tag{5.4}$$

Consider $u_1(t) = u_1$, $u_2(t) = u_2$, and $u_3(t) = u_3$ for further analysis.

5.1. COST CONSTRUCTION AND CHARACTERIZATION OF OPTIMAL CONTROLS

This particular section devotes into two parts which include determination of the total cost generated due to applied controls as well as diseases itself. Whereas the second part determines the analytical forms of the controls.

5.1.1. Total cost determination Here, the total cost is determined for the applied control interventions and disease as well, which need to be minimized.

- **Cost due to disease:** The cumulative cost incurred due to the disease burden is modeled as follows:

$$\int_0^t A_1(E_h + I_h) + A_2(S_f + I_f)dt$$

This cost consists of various components such as cost due to loss of manpower, opportunity loss and significant economic losses for farmers.

- **Cost incurred due to health care awareness :** The total cost involved in reducing the transmission between human to human is given as

$$\int_0^t A_3 u_1^2 dt.$$

- **Cost incurred due to novel technologies:** The total cost involved in reducing bat or pig infection is defined as

$$\int_0^t A_5 u_2^2 dt.$$

- **Cost incurred in treatment for infected human population:** The cumulative cost in process of treating infected human is defined by

$$\int_0^t A_5 u_3^2 dt.$$

The cost functional corresponding to total cost incurred, for fixed time t, which need to be minimized is given by

$$J(u_1, u_2, u_3) = \int_0^t \left[A_1(E_h + I_h) + A_2(S_f + I_f) + A_3 I_b + \frac{1}{2}(A_4 u_1^2 + A_5 u_2^2 + A_6 u_3^2) \right] dt \tag{5.5}$$

subject to the model system (5.4). The parameter $A_1 \geq 0$, $A_2 \geq 0$, $A_3 \geq 0$, $A_4 \geq 0$, $A_5 \geq 0$, $A_6 \geq 0$ are the weight and balancing constants, which measure the respective cost involvement over the interval $[0, t]$. In order to find an optimal control, ${u_1}^*$, ${u_2}^*$, and ${u_3}^*$ such that

$$J({u_1}^*, {u_2}^*, {u_3}^*) = \min_{(u_1, u_2, u_3) \in \mathcal{U}} J(u_1, u_2, u_3), \tag{5.6}$$

where $\mathcal{U}$ is the control set and is defined as

$$\mathcal{U} = \{(u_1, u_2, u_3) : 0 \leq u_1, u_2, u_3 \leq 1,\ t \in [0, t]\}$$

Here, all the controls are bounded and measurable.

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

$$\begin{aligned} L(E_h, I_h, S_f, I_f, I_b, u_1, u_2, u_3) &= A_1(E_h + I_h) + A_2(S_f + I_f) + A_3 I_b + \frac{1}{2} A_4 {u_1}^2 \\ &\quad + \frac{1}{2} A_5 u_2^2 + \frac{1}{2} A_6 u_3^2 \end{aligned}$$

Now, we shall use Pontryagin's maximum principle [18] for necessary conditions for optimal controls system (5.4). For that by choosing $X = (S_h, E_h I_h, R_h, S_f, I_f, I_b)$, $\mathcal{U} = (u_1, u_2, u_3)$ and $\lambda = (\lambda_1, \lambda_2, \lambda_3, \lambda_4, \lambda_5, \lambda_6)$, the associated Hamiltonian $\mathcal{H}$ can be written as

$$\begin{aligned} \mathcal{H}(X, \mathcal{U}, \lambda) &= L(E_h, I_h, S_f, I_f, I_b, u_1, u_2, u_3) + \lambda_1 \frac{dS_h}{dt} + \lambda_2 \frac{dE_h}{dt} + \lambda_3 \frac{dI_h}{dt} + \lambda_4 \frac{dR_h}{dt} \\ &\quad + \lambda_5 \frac{dS_f}{dt} + \lambda_6 \frac{dI_f}{dt} + \lambda_7 \frac{dI_b}{dt} \end{aligned} \tag{5.7}$$

Since u_1^*,u_2^*, u_3^* are solutions to the control problem (5.4), there exists the adjoint variables $\lambda_1, \lambda_2, \lambda_3, \lambda_4, \lambda_5, \lambda_6$ satisfying the following conditions.

$$\begin{aligned} \frac{dx}{dt} &= \frac{\partial H(t, x, u_1^*, u_2^*, u_3^*, \lambda_1, \lambda_2, \lambda_3.\lambda_4, \lambda_5, \lambda_6, \lambda_7)}{\partial \lambda} \\ 0 &= \frac{\partial H(t, x, u_1^*, u_2^*, u_3^*, \lambda_1, \lambda_2, \lambda_3.\lambda_4, \lambda_5, \lambda_6, \lambda_6, \lambda_7)}{\partial u} \\ \frac{d\lambda}{dt} &= -\frac{\partial H(t, x, u_1^*, u_2^*, u_3^*, \lambda_1, \lambda_2, \lambda_3.\lambda_4, \lambda_5, \lambda_7)}{\partial x} \end{aligned} \tag{5.8}$$

Theorem 5.1:
For the objective functional (5.5) and the control set (5.8) subject to control system (5.4) there exists an optimal control $u^* = ({u_1}^*, {u_2}^*, {u_3}^*) \in \mathcal{U}$ *such that*

$$J({u_1}^*, {u_2}^*, {u_3}^*) = \min_{\mathcal{U}} J(u_1, u_2, u_3).$$

Proof
To prove this theorem, we use [14]. As, we have discussed above that all the state variables (population) are bounded for each bounded controls coming from the control set $\mathcal{U}$. Furthermore, Lipschitz condition with respect to state variables is satisfied by the right hand side functions of the model system (5.4). The control variable set $\mathcal{U}$ is also convex and closed by the definition and the model system (5.4) is linear in control variables u_1,u_2 and u_3 with coefficients depending on state variables. The integrand of the function $L = A_1(E_h + I_h) + A_2(S_f + I_f) + A_3 I_b + \frac{1}{2}A_4 {u_1}^2 + \frac{1}{2}A_5 u_2^2 + \frac{1}{2}A_6 u_3^2$ is convex on the control set $\mathcal{U}$ due to quadratic nature of control variables u_1,u_2 and u_3 respectively. Moreover, $L = A_1(E_h + I_h) + A_2(S_f + I_f) + A_3 I_b + \frac{1}{2}A_4 {u_1}^2 + \frac{1}{2}A_5 u_2^2 + \frac{1}{2}A_6 u_3^2 \geq \frac{1}{2}A_4 {u_1}^2 + \frac{1}{2}A_5 u_2^2 + \frac{1}{2}A_6 u_3^2$. Now consider $c_1 = min(A_1, A_2, A_3) > 0$ and $g(u_1, u_2, u_3) = c_1({u_1}^2 + {u_2}^2 + {u_3}^2)$. Thus, $L \geq g(u_1, u_2, u_3)$ holds true and g is continuous. Also, g satisfies the condition $|(u_1, u_2, u_3)|^{-1} g(u_1, u_2, u_3) \to \infty$ whenever $|(u_1, u_2, u_3)| \to \infty$. Thus, all the conditions for the existence of controls are fulfilled. Hence from result [10, 14, 15, 18], we conclude that there is a control pair u_1^*, u_2^*, u_3^* such that $J({u_1}^*, {u_2}^*, {u_3}^*) = \min_{\mathcal{U}} J(u_1, u_2, u_3)$. □

Theorem 5.2:
For optimal controls measures u_1^*, u_2^*, u_3^* *and the state solutions* $S_h^*, E_h^*, I_h^*, R_h^*, S_f^*, I_f^*$, I_b^* *of the state system (5.4), there exists adjoint variables* $\lambda = (\lambda_i)^t \in \mathbb{R}^7, i = 1, 2, 3, 4, 5, 6, 7$ *such that*

$$\frac{d\lambda_i}{dt} = -\frac{\partial \mathcal{H}}{\partial u_i} \tag{5.9}$$

with transversality conditions

$$\lambda_1(t) = \lambda_2(t) = \lambda_3(t) = \lambda_4(t) = \lambda_5(t) = \lambda_6(t) = \lambda_7(t) = 0 \tag{5.10}$$

Further, the optimal controls $({u_1}^*, {u_2}^*), {u_3}^*$ *which minimizes J over the region* $\mathcal{U}$ *given by*

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

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

$$u_3{}^* = min\{1, max(0, \widetilde{u_3})\}$$

where,

$$\begin{aligned} \widetilde{u_1} &= \frac{\beta_1 I_h}{(S_h + E_h + I_h + R_h)A_4} \\ \widetilde{u_2} &= \frac{\left(4\beta_3 \frac{S_f I_b}{N_h^2} + \frac{I_b}{N_h} + \frac{S_f}{N_h}\right)(\lambda_6 - \lambda_5)}{A_5} \\ \widetilde{u_3} &= \frac{(\gamma_h + \eta)(\lambda_3 - \lambda_4)}{A_6} \end{aligned} \tag{5.11}$$

Proof
Let u_1^*, u_2^*, u_3^* be the optimal control functions and $S_h^*, E_h^*, I_h^*, R_h^*,\ S_f^*, I_f^*, I_b^*$ are the corresponding state variables. Then, Pontryagin's Maximum Principle ensures the existence of the following adjoint variable $\lambda_i (i = 1, 2, 3, 4, 5, 6, 7) \in \mathbb{R}^6$, which satisfies the following canonical equations:

$$\frac{d\lambda_1}{dt} = -\frac{\partial H}{\partial S_h},\ \frac{d\lambda_2}{dt} = -\frac{\partial H}{\partial E_h},\ \frac{d\lambda_3}{dt} = -\frac{\partial H}{\partial I_h},\ \frac{d\lambda_4}{dt} = -\frac{\partial H}{\partial R_h},\ \frac{d\lambda_5}{dt} = -\frac{\partial H}{\partial S_f},$$

$$\frac{d\lambda_6}{dt} = -\frac{\partial H}{\partial I_f},\ \frac{d\lambda_7}{dt} = -\frac{\partial H}{\partial I_b}$$

with transversality conditions (5.10) and the Hamiltonian (5.7) .

To establish the adjoint system (5.9) and the transversality conditions in (5.10), we use Hamiltonian $\mathcal{H}$ in (5.7).

By using third condition of (5.6), we get (5.11), as follows

$$\begin{aligned} -\frac{d\lambda_1}{dt} &= (1-u_1)\beta_1 \frac{(E_h + I_h + R_h)I_h}{N_h^2}(\lambda_1 - \lambda_2) + (1-u_2)\beta_2 \frac{(E_h + I_h + R_h)I_f}{N_h^2}(\lambda_1 - \lambda_2) \\ &\quad + (1-u_2)\beta_3 \frac{S_f I_b}{N_h^2}(\lambda_6 - \lambda_5) + \mu_h \lambda_1 \\ \frac{d\lambda_2}{dt} &= -A_1 + (1-u_1)\beta_1 \frac{S_h I_h}{N_h^2}(\lambda_2 - \lambda_1) + (1-u_2)\beta_2 \frac{S_h I_f}{N_h^2}(\lambda_2 - \lambda_1) \\ &\quad + (1-u_2)\beta_3 \frac{S_f I_b}{N_h^2}(\lambda_6 - \lambda_5) + (a_h + \mu_h)\lambda_2 \\ \frac{d\lambda_3}{dt} &= -A_1 + (1-u_1)\beta_1 \frac{S_h(S_h + E_h + R_h)}{N_h^2}(\lambda_2 - \lambda_1) + (1-u_2)\beta_2 \frac{S_h I_f}{N_h^2}(\lambda_2 - \lambda_1) \\ &\quad + (1-u_2)\beta_3 \frac{S_f I_b}{N_h^2}(\lambda_6 - \lambda_5) + (\gamma_h + \eta u_3)(\lambda_3 - \lambda_4) + (\mu_h + \mu_1)\lambda_3 \\ \frac{d\lambda_4}{dt} &= (1-u_1)\beta_1 \frac{S_h I_h}{N_h^2}(\lambda_2 - \lambda_1) + (1-u_2)\beta_2 \frac{S_h I_f}{N_h^2}(\lambda_2 - \lambda_1) \end{aligned}$$

$$
\begin{aligned}
&+(1-u_2)\beta_3\frac{S_f I_b}{N_h^2}(\lambda_6-\lambda_5)+\mu_h\lambda_4\\
\frac{d\lambda_5}{dt} &= -A_2+(1-u_2)\beta_3\frac{I_b}{N_h}(\lambda_6-\lambda_5)+\mu_f\lambda_5\\
\frac{d\lambda_6}{dt} &= -A_2+(1-u_2)\beta_2\frac{S_h}{N_h}(\lambda_1-\lambda_2)+\mu_f\lambda_6\\
\frac{d\lambda_7}{dt} &= -A_3+(1-u_2)\beta_3\frac{S_f}{N_h}(\lambda_5-\lambda_6)+\mu_b\lambda_7-(b-\frac{2bI_b}{K})\lambda_7
\end{aligned}
$$

Using the second condition of (5.6), we get (5.11), as follows

$$\frac{\partial\mathcal{H}}{\partial u_1}=A_4u_1+\frac{\beta_1 I_h(\lambda_1-\lambda_2)}{S_h+E_h+I_h+R_h}=0$$

This implies,

$$u_1=\frac{\beta_1 I_h(\lambda_2-\lambda_1)}{(S_h+E_h+I_h+R_h)A_4}$$

$$\frac{\partial\mathcal{H}}{\partial u_2}=A_5u_2+\left(4\beta_3\frac{S_f I_b}{N_h^2}+\frac{I_b}{N_h}+\frac{S_f}{N_h}\right)(\lambda_5-\lambda_6)=0$$

This implies,

$$u_2=\frac{\left(4\beta_3\frac{S_f I_b}{N_h^2}+\frac{I_b}{N_h}+\frac{S_f}{N_h}\right)(\lambda_6-\lambda_5)}{A_5}$$

And,

$$\frac{\partial\mathcal{H}}{\partial u_3}=A_6u_3+(\gamma_h+\eta)(\lambda_3-\lambda_4)=0$$

This implies,

$$u_3=\frac{(\gamma_h+\eta)(\lambda_3-\lambda_4)}{A_6}$$

Moreover, lower and upper bounds of these control are 0 and 1 respectively. Thus, if $\widetilde{u_1}>1,\ \widetilde{u_2}>1,\ \widetilde{u_3}>1$, then

$$u_1=u_2=u_3=1.$$

Also, $\widetilde{u_1}<0,\ \widetilde{u_2}<0\ ,\widetilde{u_3}<0$, then

$$u_1=u_2=u_3=0.$$

Otherwise, we have

$$u_1=\widetilde{u_1},\ u_2=\widetilde{u_2},\ and\ u_3=\widetilde{u_3}$$

Hence, for these controls $u_1^*,\ u_2^*,\ u_3^*$ we get optimum value of the function J. □

6. NUMERICAL RESULTS AND DISCUSSION

With the help of MATLAB, the optimal control model is simulated. We simulate our optimal control model by using the parameters shown in Table 1. Most of the values of Table 1 are taking from [10]. The weight constants for the optimal control problem are taken as $A_1 = 1, A_2 = 1, A_3 = 1, A_4 = 55, A_5 = 75, A_6 = 85$. We solve the optimality system (5.4) by iterative method with the help of forward and backward difference approximations [14]. We consider the time interval as [0, 150]. 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. It is observed that from Fig. 6.15, the optimal control model gives a better result as compacted to the model without the optimal control model as it reduces the number of infectives significantly in a desired interval of time. Following are the different types of control strategies to see the impact of optimal control in the total number of human infectives.

Strategy I: When only one control is used at a time

(i) Employing only control measure u_1 to optimize the objective function J, while control intervention $u_2 = u_3 = 0$, were not employed. The influence of u_1 is shown in the Fig. 6.8, to minimize the objective function, the optimal control u_1 is maintained at the maximum level. A single preventive measure can influence the spread of Nipah virus in the population. From the figures, it is clear that the control intervention u_1 is more effective compared to other types of controls.

(ii) Employing only control measure u_2 is used to optimize the objective function J, while control intervention $u_1 = u_3 = 0$, were not employed. The influence of u_2 is demonstrated in Fig. 6.9,to minimizing cost as well as infection of Nipah virus.

(iii) Employing only control measure u_3 is used to optimize the objective function J, while control intervention $u_2 = u_3 = 0$, were not employed. The influence of u_3 is demonstrated in Fig. 6.10, to minimize the disease effect in human population with minimum cost.

Strategy II: When two controls are used

Employing double control interventions (u_1, u_2) when $u_3 = 0$, (u_1, u_3) when $u_2 = 0$, and (u_2, u_3) when $u_1 = 0$, to optimize the objective function J. The control intervention are demonstrated in Figs. 6.11, 6.12, and 6.13. It is observed that combination of two control intervention is most effective then using signal control intervention. Significant number of Nipah virus infective cases reduce.

Strategy III: When all three controls are used

Employing all three control interventions (u_1, u_2, u_3) to optimize the objective function J. This control intervention is demonstrated in Fig. 6.14. It is easy to say that the total number of infectious individuals decreases significantly if we combine all three optimal controls u_1, u_2, and u_3. The three optimal control application is the best control strategy to minimize the number of infectives, and will definitely reduce the spread of Nipah virus.

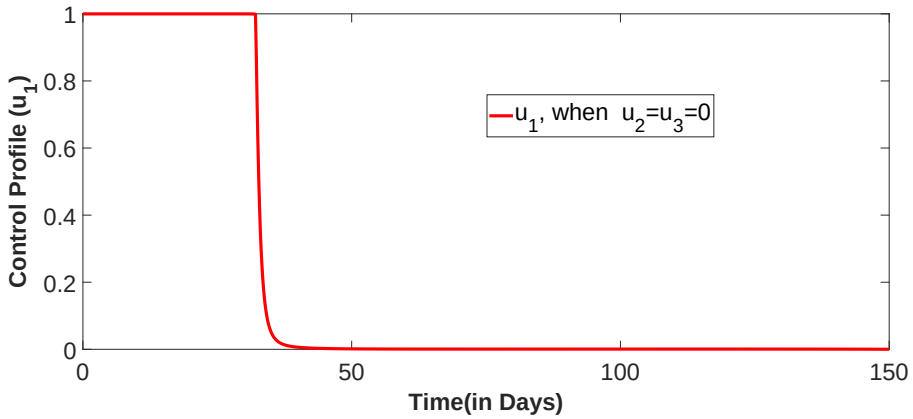

Fig. 6.8. Control profile of u_1, when $u_2 = u_3 = 0$.

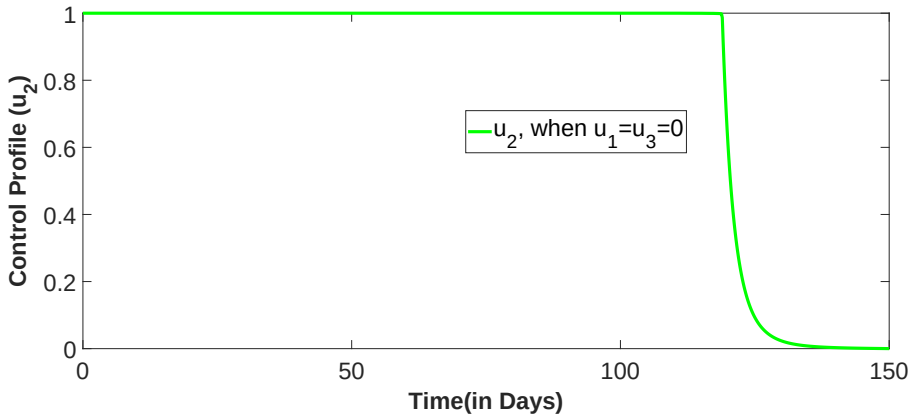

Fig. 6.9. Control profile of u_2, when $u_1 = u_3 = 0$.

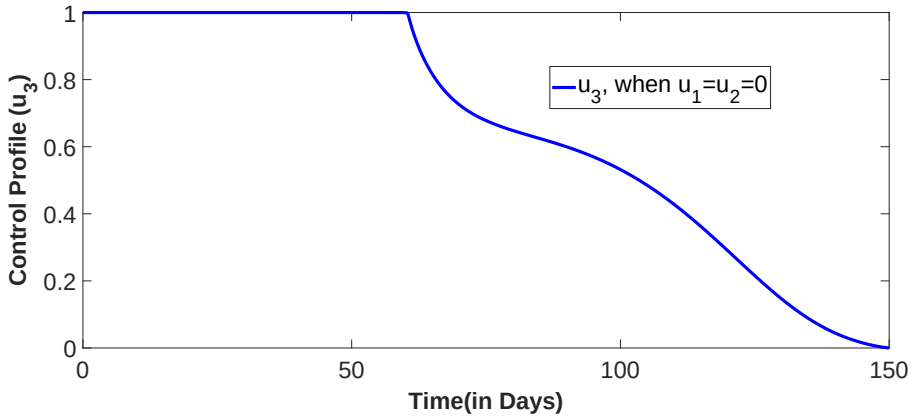

Fig. 6.10. Control profile of u_3, when $u_2 = u_3 = 0$.

7. CONCLUSION

The transmission dynamics of Nipah virus mathematical model is proposed and analyzed. Disease-free equilibrium and the basic reproduction number (R_0) is computed. The sensitivity of different parameters of (R_0) is presented and it is clear that from the forward sensitivity indices figure that $\Lambda_h, \beta_1, \delta_h$, and μ_h are very sensitive parameter. Its shows that

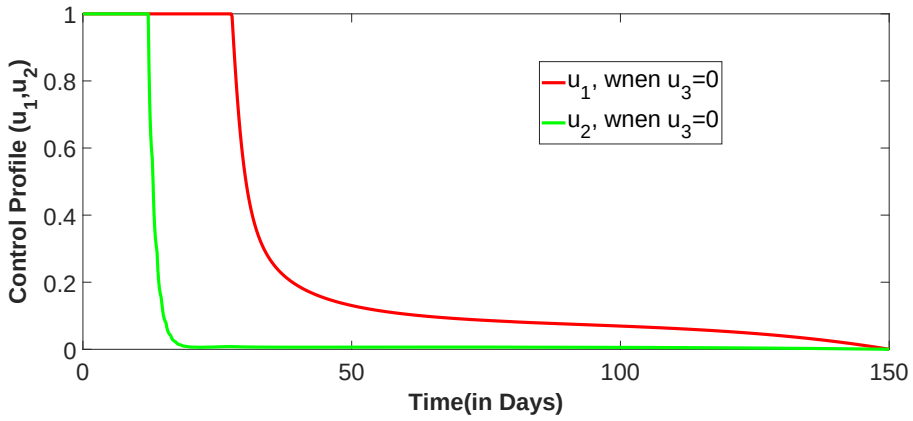

Fig. 6.11. Control profile of u_1, u_2, when $u_3 = 0$.

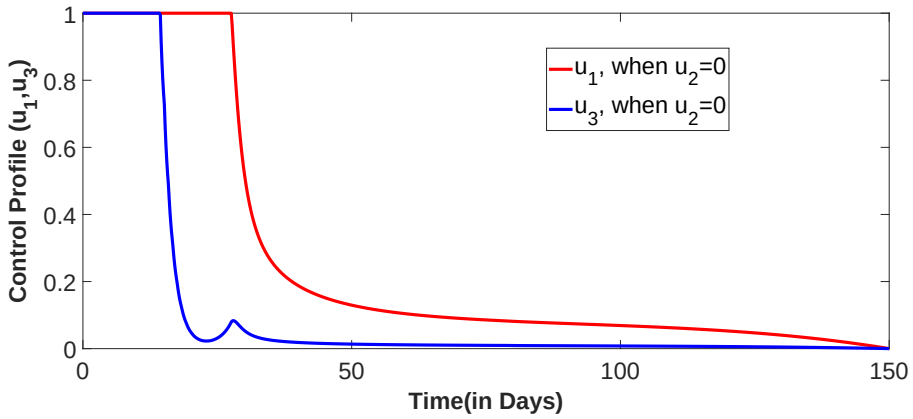

Fig. 6.12. Control profile of u_1, u_3, when $u_2 = 0$.

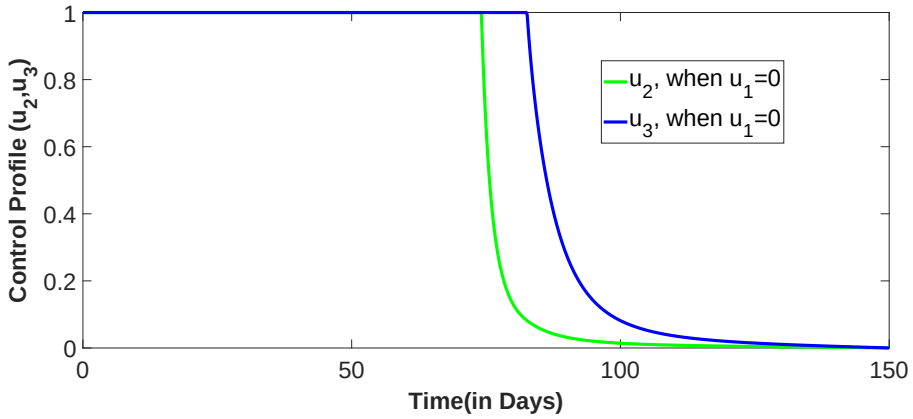

Fig. 6.13. Control profile of u_2, u_3, when $u_1 = 0$.

small change in these parameters can cause huge change in the value of basic reproduction number R_0. The parameter a_h corresponds effects of awareness and it is the fact that due to awareness programs by media, the equilibrium level of the infected population decreases significantly. The proposed mathematical model is extended to optimal control problem by incorporating three time-dependent optimal control parameters to reducing transmission and cost duo to Nipah virus outbreak by using Pontryagin's Maximum Principal. The

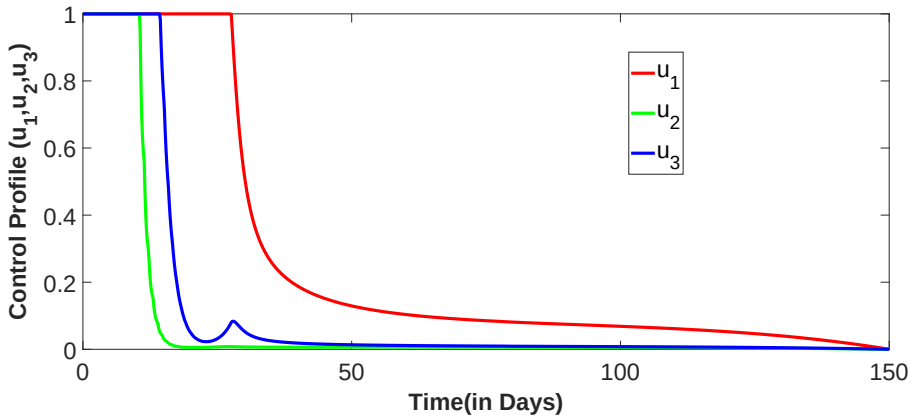

Fig. 6.14. Control profile of u_1, u_2, and u_3.

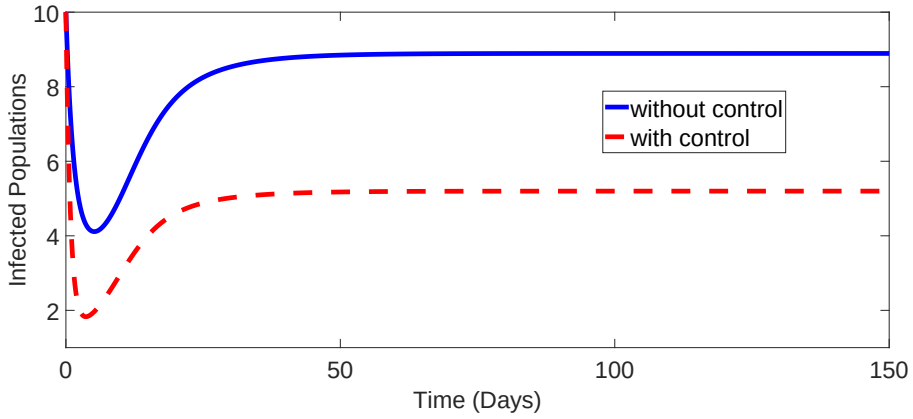

Fig. 6.15. Variation of infected human populations against time with and without optimal control.

optimal control model provides a more reliable result as compacted to the model without the optimal control model. This control strategy reduces the number of infectives significantly in a desired interval of time. Numerical simulation is performed to support our analytical findings. The fact of the control strategies are demonstrated with the help of Matlab and it is observed that combining all three optimal controls give significant effect. The simulation result indicates the effectiveness of optimal control strategies in reducing the number of infectives.

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