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# MODELING THE IMPACT OF THREE DOSE VACCINATION AND TREATMENT STRATEGIES ON OPTIMAL CONTROL OF ROTAVIRUS DISEASE

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Abstract. In this paper, we derive and analyse a mathematical model to assess the impact of three dose vaccination and treament as control strategies on the transmission dynamics of rotavirus disease. We assume that at least every baby gets the first dose of vaccination and the infected ones are treated. By using the optimal control theory, we derive the conditions necessary for optimal control of the disease using the Pontryagin's maximum principle. Numerical results performed to illustrate our analytical results show that in case of an outbreak, with no control infection will disappear after 75 days, with treatment only, it will take 55 days, with vaccination only , it will take between 30 to 40 days and lastly in case both treatment and vaccination are implemented the infection will disappear within 10 days. Thus both treatment and vaccination should be used as controls to fight rotavirus disease since the infection takes less time to clear.

## 1. Introduction

Rotavirus is the most prevalent diarrheal pathogen in young children worldwide (Shim *et al.,* 2001). In fact, 95% of the children are infected with rotavirus disease by the time they reach age 5 with high incidence rate occurring between 4 months and 36 months (Parashar *et al.,* 1998). The disease kills an estimated 500,000 children each year and causes millions of hospital visits. It is responsible for about 40 percent of all diarrheal diseases serious enough to require hospitalizations in young children (Ruuska and Vesikari, 1990). The worst burden of rotavirus is in Africa, Asia, and Latin America were proper medical care is still a problem (CDC, 2009; CDC, 2010 ).

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Rotavirus spreads through secretions and person to person contact (Shim *et al.,* 2001). Contaminated environmental surfaces have also been identified as possible mechanism for spreading the disease (Parashar *et al.,* 1998). However the disease is curable and preventable. Improvements in sanitation and hygiene, health education camapigns, treatment to rehydrate children with severe rotavirus diarrhea can also help in the fight of rotavirus disease (Mastretta *et al.,* 2002).

Given the different control measures available, rotavirus vaccines have proved to be the most effective (CDC, 2013). There are two rotavirus vaccines on market, that is, RotaTeq and Rotarix (Molholland, 2004). Both vaccines have proved to be well much torelated, safe and immunogenic (Vesikari et al., 2004; CDC, 2010). In the United States, the introduction of rotavirus vaccines has dramatically reduced serious rotavirus infections. In 2008, after the introduction of RotaTeq, health care resource utilization for rotavirus disease was reduced by almost 90%. Thus, preventing some 50,000 hospital admissions each year (CDC, 2010).

Despite of the available control strategies for the disease, there is an urgent need for better understanding of unique parameters in rotavirus disease transmission and develop effective optimal strategies for the prevention and control of the spread of this disease.

Alkama *et al.* (2012) presents an approach that investigates a free terminal optimal time control of an SIR (Susceptible-Infected-Removed) epidemic model. In order to reduce the infected group and increase the number of recovered individuals, they present a control simulating vaccination program considering also the minimum duration of a vaccination campaign. The optimal control and the optimal final time is found using Pontryagin's maximum principle and the additional transversality condition for the terminal time.

Laarabi *et al.* (2013) considers a mathematical model of an SIR epidemic model with saturated incidence rate and saturated treatment function. They use an optimal vaccination strategies to minimize the susceptible and infected individuals as well as maximizing the number of recovered individuals.

Again Tunde and Benyah (2012) considered an SIR model with variable size population and formulated an optimal control problem subject to the model with vaccination and treatment as controls. Their aim was to find the optimal combination of vaccination and treatment strategies

that will minimize the cost of the two control measures as well as the number of infectives.

Basing on this studies we formulate an optimal control SIR model with vaccination and treatment in the transmission dynamics of rotavirus disease. The vaccination in our case is administered three times, that is at 2, 4 and 6 months. All doses must be administered not beyond 8 months. We assume that not all children get all the three booster doses however every baby must at least get the first dose.

1.1. **Model Formulation.** We develop our model from a SIR basic model. The model has seven compartments: $M(t)$ denoting the number of breast feeding infants at time t, $S(t)$ denoting the number of susceptible children at time t, $V_1(t)$ denoting the number of children vaccinated taking one dose between 2 to 8 months, $V_2(t)$ denoting the population of vaccinated twice between 4 and 8 months, $V_3(t)$ denoting the population vaccinated thrice, 3rd vaccine between 6 to 8 months, $I(t)$ denoting the number of infected children at time t and $R(t)$ denoting the number of recovered individuals. This is summarized in Table 1.

Table 1. Variables of the Model

| Variables | Description |
|---|---|
| $M(t)$ | Breast fed infants |
| $S(t)$ | Susceptible population at time t |
| $V_1(t)$ | The vaccinated population taking one dose between 2 to 8 months |
| $V_2(t)$ | The population vaccinated twice between 4 and 8 months |
| $V_3(t)$ | The population vaccinated thrice, 3rd vaccine between 6 to 8 months |
| $I(t)$ | Infectious population at time t |
| $R(t)$ | Recovered population at time t |

We consider both breast-fed and non-breast babies. Children are breast-fed between $0-6$ months. The proportion of infants that is breast-fed is denoted by $q$ while the birth rate is given by $b$. The non-breast fed fraction enters the susceptible class $S(t)$ at a rate $b(1-q)$. Maternal antibodies wane out at $\rho$ rate and babies from the breast-feeding class enter into susceptible class $S(t)$.

Let the probability of becoming infected per contact with an infectious baby be denoted by $\beta$. The mass infection rate is denoted by $\beta SI$. The daily rate of first dose vaccination between 2 to 8 months is administered at a rate $\phi$. Let $\tau$ be the daily rate at which children from $V_1$ are vaccinated the second time between 4 to 8 months and $\kappa$ is the

daily rate at which individuals from $V_2$ are vaccinated for the third time between 6 to 8 months.

Children in the different vaccination groups can come into contact with children in infected class, $I(t)$, but the risk between these groups is reduced at different rates, $\eta_1$ as the reduction in risk in case of first dose of vaccination $0 \leq \eta_1 \leq 1$ in $V_1$, $\eta_2$ as the reduction in risk for second dose of vaccination $0 \leq \eta_2 \leq 1$ in $V_2$ and lastly, $\eta_3$ as the reduction in risk in case third dose of vaccination $0 \leq \eta_3 \leq 1$ in $V_3$. Since the more times a baby is re-vaccinated the more resistant it becomes, we take $\eta_3 \geq \eta_2 \geq \eta_1$.

Again individuals from $I(t)$ can recover naturally at a rate $\theta$. The natural death rate from all the seven classes is denoted by $\mu$. In our model, we assume that primary vaccination is available but at very low levels. Hence we consider both vaccination and treatment campaigns as our control strategies. Vaccination campaigns are considered such that more children are being vaccinated and the infected ones are being treated from the disease. We introduce vaccination as control such that the number of susceptible children increase and few become exposed to disease.

We consider $u_1$ as the fraction of susceptibles being vaccinated per unit time for first dose, $u_2$ as fraction of being vaccinated for the second dose from $V_1$, $u_3$ is the fraction of babies vaccinated for the third dose from $V_2$. We assume that every child gets the first dose of vaccination. We further assume that the vaccine is very effective such that all vaccinated children who complete the three doses become immune and they join the recovered class $R$. We again bound our controls with $0 \leq u_i \leq 0.9$, for $i = 1, 2, 3$ since the entire susceptible population is not vaccinated. Children in the infected class are treated at a rate $u_4$ who thereafter join the recovery class with $0 \leq u_4 \leq 1$ . In case of no controls, all the control parameters are set to zero, that is, $u_1 = u_2 = u_3 = u_4 = 0$.

The model flow diagram is described as shown in Figure 1.1

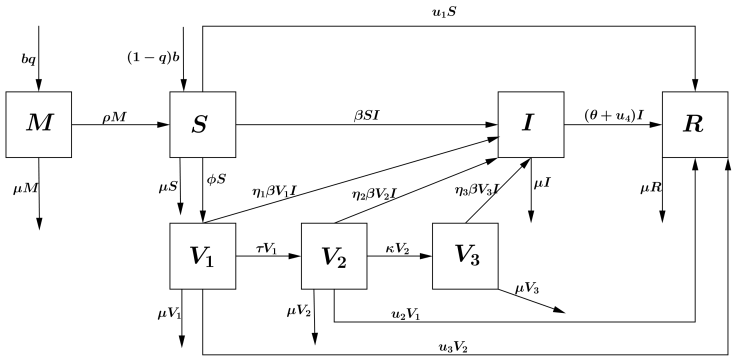



FIGURE 1.1. The flow chart describing our model with and without controls

The parameters are summarized in Table 2.

Table 2. parameters of the Model

| Parameters | Description |
|---|---|
| $b$ | Birth rate |
| $\mu$ | Death rate |
| $q$ | Proportion of breast feeding infants |
| $\rho$ | Rate of departure from breast feeding into susceptible class |
| $\beta$ | Probability of becoming infected per contact with an infectious individuals |
| $\phi$ | The daily rate of first dose vaccination |
| $\tau$ | The daily rate of second dose of vaccination |
| $\kappa$ | The daily rate of third dose of vaccination |
| $\eta_1$ | Reduction in risk from first vaccine $(0 \leq \eta_1 \leq 1)$ from $V_1$ to $I$ |
| $\eta_2$ | Reduction in risk from second vaccine $(0 \leq \eta_2 \leq 1)$ from $V_2$ to $I$ |
| $\eta_3$ | Reduction in risk from third vaccine $(0 \leq \eta_3 \leq 1)$ from $V_3$ to $I$ |
| $\theta$ | Natural recovery rate |

In this model, we derive the best optimal control strategy such that the total infection burden is reduced at low minimum cost within a period of 100 days thus we have the following set of ordinary differential

systems.

$$
\begin{aligned}
\frac{dM}{dt} &= bq - \rho M - \mu M \\
\frac{dS}{dt} &= \rho M + (1-q)b - \phi S - \beta SI - \mu S - u_1 S \\
\frac{dV_1}{dt} &= \phi S - \eta_1 \beta V_1 I - \tau V_1 - \mu V_1 - u_2 V_1 \\
\frac{dV_2}{dt} &= \tau V_1 - \eta_2 \beta V_2 I - u_3 V_2 - \kappa V_2 - \mu V_2 \\
\frac{dV_3}{dt} &= \kappa V_2 - \eta_3 \beta V_3 I - \mu V_3 \\
\frac{dI}{dt} &= \beta SI + (\eta_1 V_1 + \eta_2 V_2 + \eta_3 V_3)\beta I - (\theta + \mu) I - u_4 I \\
\frac{dR}{dt} &= \theta I + u_4 I - \mu R + u_1 S + u_2 V_1 + u_3 V_2
\end{aligned} \tag{1.1}
$$

with intial conditions
$M(0) = M_0, \quad S(0) = S_0, \quad V_1(0) = V_{10}, \quad V_2(0) = V_{20}, \quad V_3(0) = V_{30}, \quad I(0) = I_0, \quad R(0) = R_0.$

1.2. **Optimal Control Analysis.** Under this Section, we investigate the optimal control efforts needed to control rotavirus disease. Controls are represented as functions of time and assigned reasonable upper and lower bounds. Vaccination with three booster doses is implemented at rate $u_1(t), u_2(t), u_3(t)$ for one dose, two and three doses and $u_4$ is the percentage of infected individuals being treated per unit time. Our main goal is to minimize the total infectious burden and costs of the different controls (vaccination and treatment). The objective functional $J$ is given as

$$\mathcal{J}(u_1, u_2, u_3, u_4) = \min_{(u_1,\ u_2,\ u_3,\ u_4)} \int_0^T \{I + B_0(u_1 S + u_1^2) + B_1(u_2 V_1 + u_2^2) + B_2(u_3 V_2 + u_3^2) + B_3(u_4 I + u_4^2)\} dt \tag{1.2}$$

where $B_0, B_1, B_2, B_3$ are balancing coefficients or weight constants transforming the integral into dollars expended over a finite time period of $T$ days. We consider an integrand convex on the set of control parameters to indicate non-linear costs potentially arising in case of high treatment or vaccination levels. Furthermore we assume unlimited control measures and the set of optimal controls $(u_1^*(t), u_2^*(t), u_3^*(t), u_4^*(t)) \in \Omega$ such that

$$\mathcal{J}(u_1^*, u_2^*, u_3^*, u_4^*, ) = \min_{\Omega} \mathcal{J}(u_1(t), u_2(t), u_3(t), u_4(t)) \tag{1.3}$$

is Lebesgue measurable and is defined as

$$\Omega = \{(u_1(t), u_2(t), u_3(t), u_4(t)) | 0 \leq u_1(t) \leq u_{1_{max}} \leq 0.9, 0 \leq u_2(t) \leq u_{2_{max}} \leq 0.9, 0 \leq u_3(t) \leq u_{3_{max}} \leq 0.9, 0 \leq u_4(t) \leq u_{4_{max}} \leq 1, t \in [0, T]\} \tag{1.4}$$

Since our goal is to characterize an optimal control $(u_1^*, u_2^*, u_3^*, u_4^*) \in \Omega$ which minimizes the cost of vaccination and the cost of the treatment over the specified time interval as well as minimizes the number of infectives in a unlimited vaccination scenario. The problem is stated as follows: we have to characterize $(u_1^*, u_2^*, u_3^*, u_4^*) \in \Omega$ so that it satisfies

$$\mathcal{J}(u_1^*, u_2^*, u_3^*, u_4^*) = \min_{(u_1,\ u_2,\ u_3,\ u_4)} \int_0^T \{I + B_0(u_1 S + u_1^2) + B_1(u_2 V_1 + u_2^2) + B_2(u_3 V_2 + u_3^2) + B_3(u_4 I + u_4^2)\} dt \tag{1.5}$$

where $\Omega$ is defined in (1.4) subject to system (1.1).

Pontryagin's maximum principle, introduces adjoint functions that allow us to attach our state system i.e. $M, S, V_1, V_2, V_3, I, R$ differential equations (1.1) to our objective functional. The existence of optimal controls is guaranteed by standard results in control theory (the integrand of $\mathcal{J}$ is a convex function of the control parameters and the state

system satisfies the Lipschitz property with respect to the state variables (Fleming and Rishel, 1975; Lenhart and Workman, 2007). The necessary conditions that optimal solutions must satisfy are derived using Pontryagin's maximum principle.

This principle is used to obtain the differential equations for the adjoint variables, corresponding boundary conditions and the characterization of an optimal control set $(u_1^*, u_2^*, u_3^*, u_4^*)$. This characterization gives a representation of an optimal control in terms of state and adjoint functions. Also this principle converts the problem of minimizing the objective functional subject to the state system into minimizing the Hamiltonian with respect to the controls (bounded measurable functions) at each time $t$.

According to (1.1) and (1.2) the Hamiltonian for our optimal control problem is:

(1.6)

$$\begin{aligned} H =& I + B_0(u_1 S + u_1^2) + B_1(u_2 V_1 + u_2^2) + B_2(u_3 V_2 + u_3^2) + B_3(u_4 I + u_4^2) + \\ & \lambda_M(t)(bq - \rho M(t) - \mu M(t)) + \\ & \lambda_S(t)(\rho M + (1-q)b - \phi S - \beta SI - \mu S - u_1 S) + \\ & \lambda_{V_1}(t)(\phi S - \eta_1 \beta V_1 I - \tau V_1 - \mu V_1 - u_2 V_1) + \\ & \lambda_{V_2}(t)(\tau V_1 - \eta_2 \beta V_2 I - u_3 V_2 - \kappa V_2 - \mu V_2) + \\ & \lambda_{V_3}(t)(\kappa V_2 - \eta_3 \beta V_3 I - \mu V_3) + \\ & \lambda_I(t)(\beta SI + (\eta_1 V_1 + \eta_2 V_2 + \eta_3 V_3)\beta I - (\theta + \mu) I - u_4 I) + \\ & \lambda_R(t)(\theta I + u_4 I - \mu R + u_1 S + u_2 V_1 + u_3 V_2). \end{aligned}$$

where $\lambda_M, \lambda_S, \lambda_{V_1}, \lambda_{V_2}, \lambda_{V_3}, \lambda_I, \lambda_R$ are the adjoint functions associated with their respective states. Note that, in $H$, each adjoint function multiplies the right-hand side of the differential equation of its corresponding state function. The first term in $H$ comes from the integrand of the objective functional.

Given an optimal control set $(u_1^*, u_2^*, u_3^*, u_4^*)$ and corresponding states $(M^*, S^*, V_1^*, V_2^*, V_3^*, I^*, R^*)$, there exist adjoint functions $\lambda_M, \lambda_S, \lambda_{V_1}, \lambda_{V_2}, \lambda_{V_3}, \lambda_I, \lambda_R$ satisfying

$$\frac{d\lambda_M}{dt} = -\frac{\partial H}{\partial M}, \quad \frac{d\lambda_S}{dt} = -\frac{\partial H}{\partial S}, \quad \frac{d\lambda_{V_1}}{dt} = -\frac{\partial H}{\partial V_1}, \quad \frac{d\lambda_{V_2}}{dt} = -\frac{\partial H}{\partial V_2}, \quad \frac{d\lambda_{V_3}}{dt} = -\frac{\partial H}{\partial V_3},$$

$\frac{d\lambda_I}{dt} = -\frac{\partial H}{\partial I}$, $\frac{d\lambda_R}{dt} = -\frac{\partial H}{\partial R}\frac{d\lambda_{X_1}}{dt} = -\frac{\partial H}{\partial X_1}$, $\frac{d\lambda_{X_2}}{dt} = -\frac{\partial H}{\partial X_2}$, $\frac{d\lambda_{X_3}}{dt} = -\frac{\partial H}{\partial X_3}$.

That is

$$\begin{aligned}
\frac{d\lambda_{_M}}{dt} &= \lambda_{_M}(\rho+\mu) - \lambda_{_S}\rho \\
\frac{d\lambda_{_S}}{dt} &= \lambda_{_S}(\phi+\beta I(t)+\mu+u_1(t)) - \lambda_{_{V_1}}\phi - \lambda_{_I}\beta I(t) - B_0u_{_1}(t) - \lambda_{_R}u_1(t) \\
\frac{d\lambda_{_{V_1}}}{dt} &= \lambda_{_{V_1}}(\eta_1\beta I(t)+\tau+\mu+u_{_2}(t)) - \lambda_{_{V_2}}\tau - \lambda_{_I}\eta_1\beta I(t) - B_{_1}u_{_2}(t) - \lambda_{_R}u_2 \\
\frac{d\lambda_{_{V_2}}}{dt} &= \lambda_{_{V_2}}(\eta_2\beta I(t)+\kappa+\mu+u_{_3}(t)) - \lambda_{_{V_3}}\kappa - \lambda_{_I}\eta_2\beta I(t) - B_{_2}u_{_3}(t) - \lambda_{_R}u_3 \\
\frac{d\lambda_{_{V_3}}}{dt} &= \lambda_{_{V_3}}(\eta_3\beta I(t)+\mu) - \lambda_{_I}\eta_3\beta I(t) \\
\frac{d\lambda_{_I}}{dt} &= \lambda_{_S}\beta S(t) + \lambda_{_{V_1}}\eta_1\beta V_{_1}(t) + \lambda_{_{V_2}}\eta_2\beta V_{_2}(t) + \lambda_{_{V_3}}\eta_3\beta V_{_3}(t) - 1- \\
&\quad \lambda_{_I}((S(t)+\eta_1V_{_1}(t)+\eta_2V_{_2}(t)+\eta_3V_{_3}(t))\beta - \theta - u_4 - \mu) - \lambda_{_R}(\theta+u_4) \\
&-B_3u_4 \\
\frac{d\lambda_{_R}}{dt} &= \lambda_R\mu
\end{aligned}$$

with the transversality conditions

(1.7)
$$\lambda_{_M}(T)=0, \lambda_{_S}(T)=0, \lambda_{_{V_1}}(T)=0, \lambda_{_{V_2}}(T)=0, \lambda_{_{V_3}}(T)=0, \lambda_{_I}(T)=0, \lambda_{_R}(T)=0$$

The transversality conditions i.e. the final time boundary conditions for the adjoint variables $\lambda_M, \lambda_S, \lambda_{V_1}, \lambda_{V_2}, \lambda_{V_3}, \lambda_I, \lambda_R$ are zero since there is no dependence on the states at the final time in the objective functional.

The Hamiltonian is minimized with respect to the control (at the optimal control set) thus we differentiate $H$ with respect to $u_{_1}, u_{_2}, u_{_3}, u_{_4}$ respectively in the interior of $\Omega$ to obtain the optimality conditions that

follows:

$$
\begin{aligned}
\frac{\partial H}{\partial u_1} &= B_0(S + 2u_1) - \lambda_S S + \lambda_R S = 0 \\
\frac{\partial H}{\partial u_2} &= B_1(V_1 + 2u_2) - \lambda_{V_1} V_1 + \lambda_R V_1 = 0 \\
\frac{\partial H}{\partial u_3} &= B_2(V_2 + 2u_3) - \lambda_{V_2} V_2 + \lambda_R V_2 = 0 \\
\frac{\partial H}{\partial u_4} &= B_3(I + 2u_4) - \lambda_I I + \lambda_R I = 0
\end{aligned} \tag{1.8}
$$

Solving for $u_1 = \hat{u}_1, u_2 = \hat{u}_2, u_3 = \hat{u}_3, u_4 = \hat{u}_4$ from the above set of equations, the optimality conditions are obtained as follows:

$$
\begin{aligned}
\hat{u}_1 &= \frac{(\lambda_S - \lambda_R - B_0)S}{2B_0} \\
\hat{u}_2 &= \frac{(\lambda_{V_1} - \lambda_R - B_1)V_1}{2B_1} \\
\hat{u}_3 &= \frac{(\lambda_{V_2} - \lambda_R - B_2)V_2}{2B_2} \\
\hat{u}_4 &= \frac{(\lambda_I - \lambda_R - B_3)I}{2B_3}
\end{aligned} \tag{1.9}
$$

Using the standard argument for control bounds, we arrive at the following expression for the optimal control function:

$$
\begin{aligned}
u_1^*(t) &= min\{max\{0, \hat{u}_1(t)\}, u_{1_{max}}\} \\
u_2^*(t) &= min\{max\{0, \hat{u}_2(t)\}, u_{2_{max}}\} \\
u_3^*(t) &= min\{max\{0, \hat{u}_3(t)\}, u_{3_{max}}\} \\
u_4^*(t) &= min\{max\{0, \hat{u}_4(t)\}, u_{4_{max}}\}
\end{aligned} \tag{1.10}
$$

From (1.10) the following optimality system is obtained.

$$\frac{dM}{dt} = bq - \rho M - \mu M,$$

$$\frac{dS}{dt} = \rho M + (1-q)b - \phi S - \beta SI - \mu S - min\{max\{0, \hat{u}_1(t)\}, u_{1_{max}}\}S,$$

$$\frac{dV_1}{dt} = \phi S - \eta_1 \beta V_1 I - \tau V_1 - \mu V_1 - min\{max\{0, \hat{u}_2(t)\}, u_{2_{max}}\}V_1,$$

$$\frac{dV_2}{dt} = \tau V_1 - \eta_2 \beta V_2 I - min\{max\{0, \hat{u}_3(t)\}, u_{3_{max}}\}V_2 - \kappa V_2 - \mu V_2$$

$$\frac{dV_3}{dt} = \kappa V_2 - \eta_3 \beta V_3 I - \mu V_3$$

$$\frac{dI}{dt} = \beta SI + (\eta_1 V_1 + \eta_2 V_2 + \eta_3 V_3)\beta I - (\theta + \mu)I - min\{max\{0, \hat{u}_4(t)\}, u_{4_{max}}\}I,$$

$$\frac{dR}{dt} = \theta I + min\{max\{0, \hat{u}_4(t)\}, u_{4_{max}}\}I - \mu R + min\{max\{0, \hat{u}_1(t)\}, u_{1_{max}}\}S +$$
$$min\{max\{0, \hat{u}_2(t)\}, u_{2_{max}}\}V_1 + min\{max\{0, \hat{u}_3(t)\}, u_{3_{max}}\}V_2$$

(1.11)

$$\frac{d\lambda_M}{dt} = \lambda_M(\rho + \mu) - \lambda_S \rho$$

$$\frac{d\lambda_S}{dt} = \lambda_S(\phi + \beta I(t) + \mu + min\{max\{0, \hat{u}_1(t)\}, u_{1_{max}}\}) - \lambda_{V_1}\phi - \lambda_I \beta I(t) -$$
$$B_0 min\{max\{0, \hat{u}_1(t)\}, u_{1_{max}}\} - \lambda_R min\{max\{0, \hat{u}_1(t)\}, u_{1_{max}}\}$$

$$\frac{d\lambda_{V_1}}{dt} = \lambda_{V_1}(\eta_1 \beta I(t) + \tau + \mu + min\{max\{0, \hat{u}_2(t)\}, u_{2_{max}}\}) - \lambda_{V_2}\tau -$$
$$\lambda_I \eta_1 \beta I(t) - B_1 min\{max\{0, \hat{u}_2(t)\}, u_{2_{max}}\} - \lambda_R min\{max\{0, \hat{u}_2(t)\}, u_{2_{max}}\}$$

$$\frac{d\lambda_{V_2}}{dt} = \lambda_{V_2}(\eta_2 \beta I(t) + \kappa + \mu + min\{max\{0, \hat{u}_3(t)\}, u_{3_{max}}\}) - \lambda_{V_3}\kappa -$$
$$\lambda_I \eta_2 \beta I(t) - B_2 min\{max\{0, \hat{u}_3(t)\}, u_{3_{max}}\} - \lambda_R min\{max\{0, \hat{u}_3(t)\}, u_{3_{max}}\}$$

$$\frac{d\lambda_{V_3}}{dt} = \lambda_{V_3}(\eta_3 \beta I(t) + \mu) - \lambda_I \eta_3 \beta I(t)$$

$$\frac{d\lambda_I}{dt} = \lambda_S \beta S(t) + \lambda_{V_1}\eta_1 \beta V_1(t) + \lambda_{V_2}\eta_2 \beta V_2(t) + \lambda_{V_3}\eta_3 \beta V_3(t) - 1 -$$
$$\lambda_I((S(t) + \eta_1 V_1(t) + \eta_2 V_2(t) + \eta_3 V_3(t))\beta - \theta - min\{max\{0, \hat{u}_4(t)\}, u_{4_{max}}\} - \mu) -$$

$$\lambda_{_R}(\theta + min\{max\{0, \hat{u}_{_4}(t)\}, u_{_{4_{max}}}\}) - B_3 min\{max\{0, \hat{u}_{_4}(t)\}, u_{_{4_{max}}}\}$$

$$\frac{d\lambda_{_R}}{dt} = \lambda_R \mu$$

with initial conditions

$M(0) = M_0, \quad S(0) = S_0, \quad V_1(0) = V_{10}, \quad V_2(0) = V_{20}, \quad V_3(0) = V_{30}, \quad I(0) = I_0, \quad R(0) = R_0$

and $\lambda_{_M}(T) = 0, \quad \lambda_{_S}(T) = 0, \quad \lambda_{_{V_1}}(T) = 0, \lambda_{_{V_2}}(T) = 0, \quad \lambda_{_{V_3}}(T) = 0, \quad \lambda_{_I}(T) = 0, \quad \lambda_{_R}(T) = 0.$

Now, the state system of differential equations and the adjoint system of differential equations together with the control characterization above form the optimality system to be solved numerically. Since the state equations have initial conditions and the adjoint equations have final time conditions, we cannot solve the optimality system directly by only sweeping forward in time. Thus an iterative algorithm " forward-backward sweep method " is used. An initial estimate for the control is made. The state system is then solved forward in time from the dynamics using RK4 method. Resulting state values are placed in the right hand side of the adjoint differential equations. Then the adjoint system with given final conditions is solved backward in time, again employing RK4. Both state and adjoint values are used to update the control using characterization and then the process is repeated. This iterative process terminates when current state, adjoint and control values converge sufficiently.

## 2. Numerical Analysis of the Model

In this Section, we study the optimal control model (1.1) numerically. We solve the model using the forward backward sweep method (Lenhart and Workman, 2007). Using the iterative method, we solve the optimality system derived in (1.11). We examine the model with three doses of vaccination controls, $u_1$, $u_2$, $u_3$ and treatment $u_4$ on the spread of rotavirus. In our numerical analysis, we investigate and compare numerical results with different scenarios, and these include:

(i) When treatment is optimized and vaccination is set to zero, that is, $u_1 = u_2 = u_3 = 0$
(ii) When controls $u_1$, $u_2$, $u_3$, that is, vaccination is optimized while treatment is set to zero.

(iii) When both controls are optimized, that is, when both treatment and vaccination are optimized.
(iv) Effect of no control, with treatment only, with vaccination only, and both controls on the infected class.

We further assume the weight factors for vaccination is the same for all doses and treatment is slightly lower. The cost factors associated with treatment include, oral rehydration drugs, medical examinations and hospitalization. The parameter values used in the simulation of the model are stated in Table 3a and Table 3b.

Table 3a. State variables and parameters of the Model

| State variables | Description | Value | Reference |
|---|---|---|---|
| $M(0)$ | Infants with maternal immunity at time $t = 0$ | 290 | Assumed |
| $S(0)$ | Number of susceptibles at time $t = 0$ | 800 | Assumed |
| $V_1(0)$ | Vaccinated population taking one dose at time $t = 0$ | 300 | Assumed |
| $V_2(0)$ | Vaccinated population taking second dose at time $t = 0$ | 150 | Assumed |
| $V_3(0)$ | Vaccinated population taking third dose at time $t = 0$ | 100 | Assumed |
| $I(0)$ | Number of infected children at time $t = 0$ | 100 | Assumed |
| $R(0)$ | Number of recovered children at time $t = 0$ | 50 | Assumed |
| Parameters | | | |
| $b$ | Birth rate | 0.0018 per day | [18] |
| $\mu$ | Natural death rate | 0.0018 per day | [18] |
| $q$ | Proportion of infants with maternal immunity | 0.6 | [14] |
| $\rho$ | Rate of departure from breast feeding | 0.0111 | [2] |
| $\beta$ | Contact transmission rate | 0.00025 | [6] |
| $\eta_1$ | Reduction in risk from first vaccine | 0.4 | Assumed |
| $\eta_2$ | Reduction in risk from second vaccine | 0.7 | Assumed |
| $\eta_3$ | Reduction in risk from third vaccine | 0.85 | Assumed |
| $\theta$ | Recovery rate | 0.1818 per day | [8, 15] |
| $\phi$ | The daily rate of first dose vaccination | 0.01667 | Assumed |
| $\tau$ | The daily rate of second dose of vaccination | 0.00833 | Assumed |
| $\kappa$ | The daily rate of third dose of vaccination | 0.00556 | Assumed |

Table 3b. Weight parameters of the Model

| Parameters | Description | Value | Reference |
|---|---|---|---|
| $B_0$ | Weight parameter for first dose | 40 | Assumed |
| $B_1$ | Weight parameter for second dose | 40 | Assumed |
| $B_2$ | Weight parameter for third dose | 40 | Assumed |
| $B_3$ | Weight parameter for treatment | 5 | Assumed |

2.1. **No control strategies.** Under no strategy, Figures 2.1 and 2.2, shows the dynamics of rotavirus disease without treatment and vaccination. We consider a case where some of the children are breastfed while other are not. In Figure 2.1, breast-fed children move to class (a) and after a period of three months they join the susceptible class (b). Children that are not breastfed go directly to (b) class. At (b) children are vaccinated for first dose of rotavirus and they move to (c). We notice an initial increase in this class since they are coming from (b) and later a decrease because they are moving to class (d) for second dose of

vaccination. Again from (d) children are vaccinated for the third dose and they move to class (e) as seen in Figure 2.2. Again from Figure 2.2 (f), we notice an increase in number of infected individuals who later decrease in number but after a long time, almost when $t = 75$ days. We lastly notice that children in the recovered class (g) take sometime to recover completely. This is due to the fact that, in absence of controls, the recovery level tends to be slow than in the presence of controls.

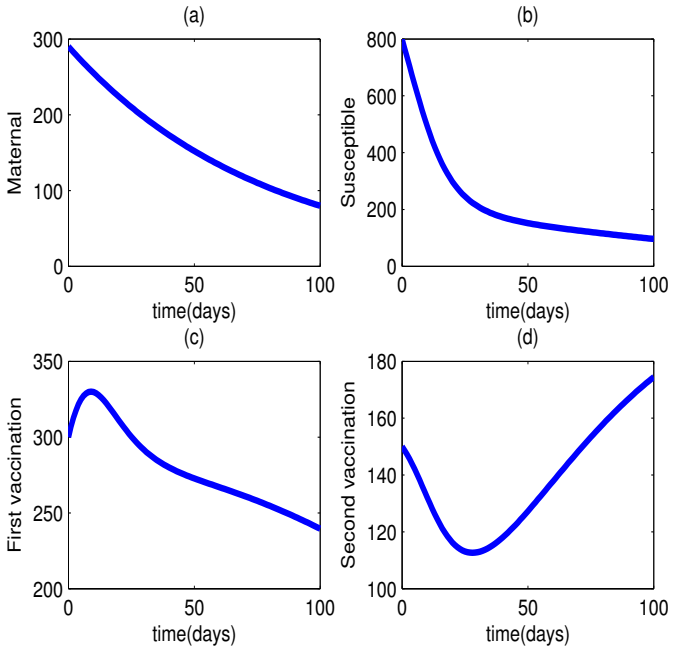



FIGURE 2.1. Profile (a) of the dynamics of rotavirus without controls

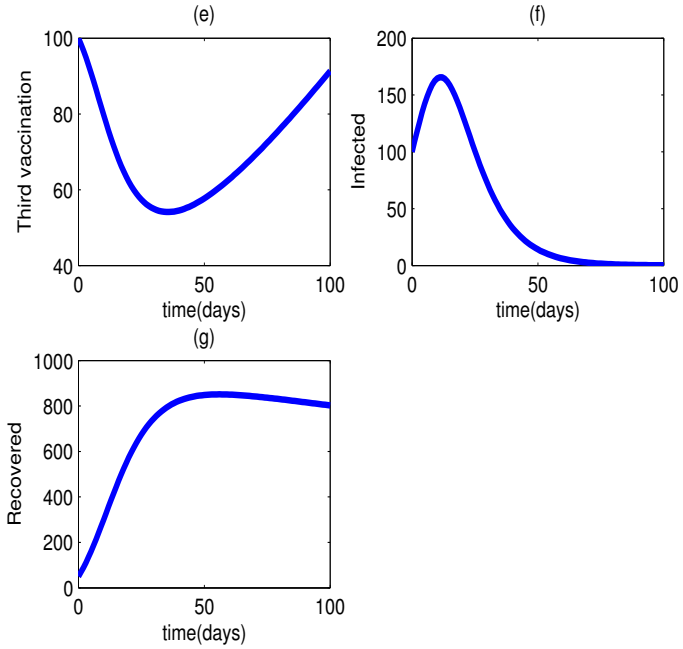
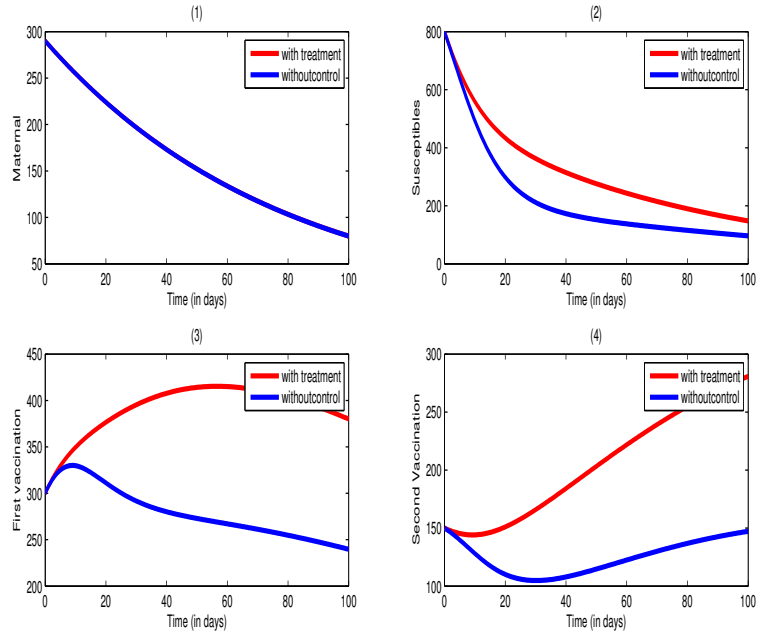
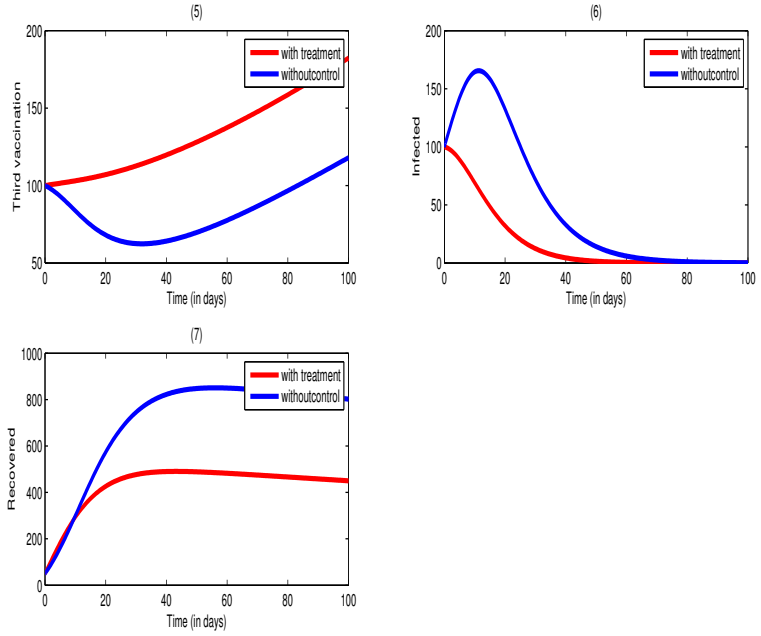



FIGURE 2.2. Profile (b) of the dynamics of rotavirus without controls

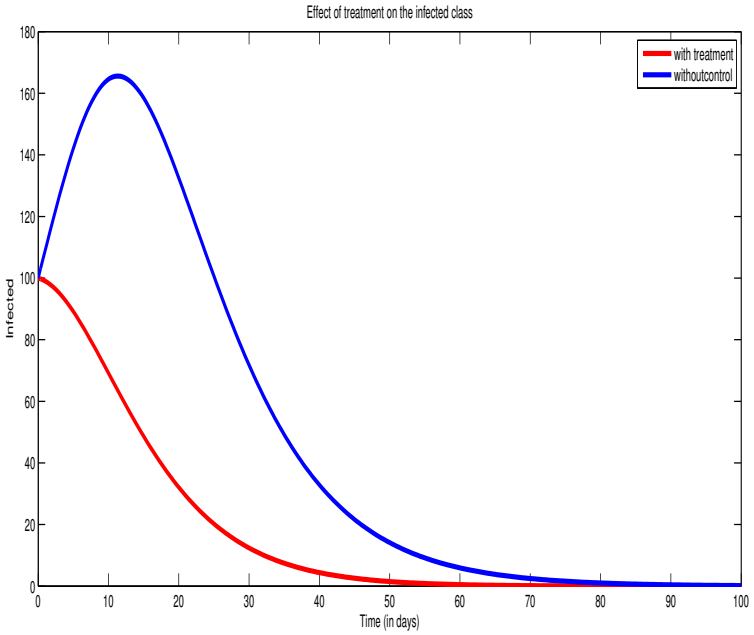
2.2. **Optimal Treatment Only.** Under this strategy, we optimize only treatment and all vaccination doses are put to zero, that is, $u_1 = u_2 = u_3 = 0$. When treatment is optimized, we do not see any effect in the maternal class (Figure 2.3(a)-(1)), a slight increase in the number of susceptibles leaving this class but treatment has no direct effect on this class (Figure 2.3(a)-(2)). We notice an increase in the number of vaccinated children within Figure 2.3(a)-(3),(4), and Figure 2.3(b)-(5). Since treatment has a direct effect on the infected class (Figure 2.3(b)-(6)) we notice that infection starts to decrease up to when $t = 55$ days. This is well shown in Figure 2.3(c) where in absence of treatment infection takes longer to clear, that is, $t = 75$ days than in presence of treatment where it takes less time, $t = 55$ days.




(a) $u_4$ profile



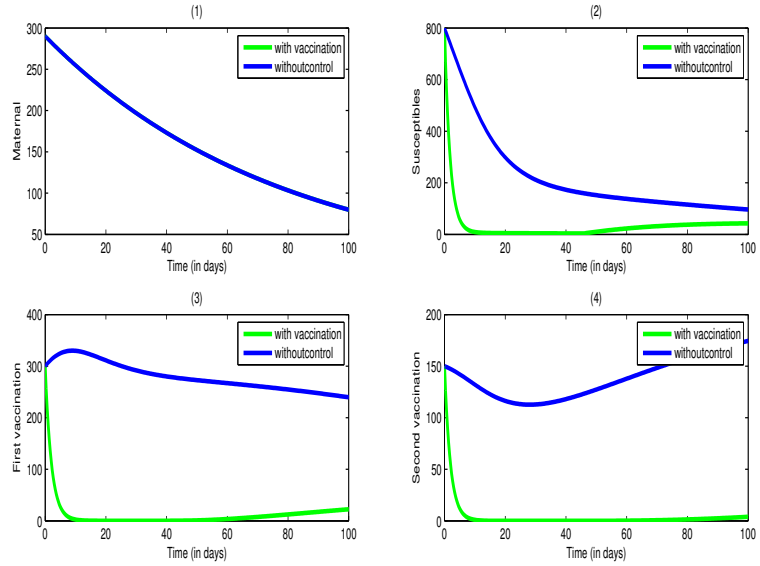

(b) $u_4$ profile



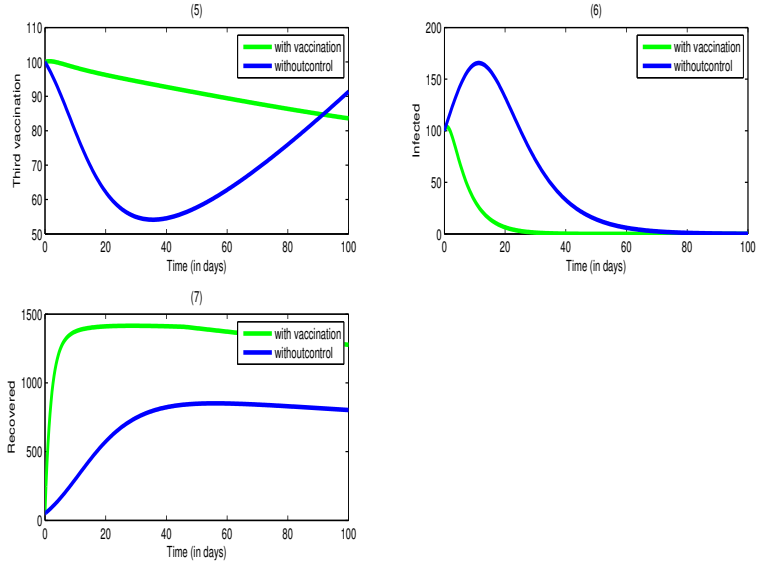

(c) Infected class with treatment only (red curve) and no treatment (blue curve)

FIGURE 2.3. Plots (a) and (b) shows $u_4$ profile where optimal control of treatment is indicated by the red curve and the blue shows no control while (c) shows the effect of treatment on the infected class (red curve) and no control (blue curve)

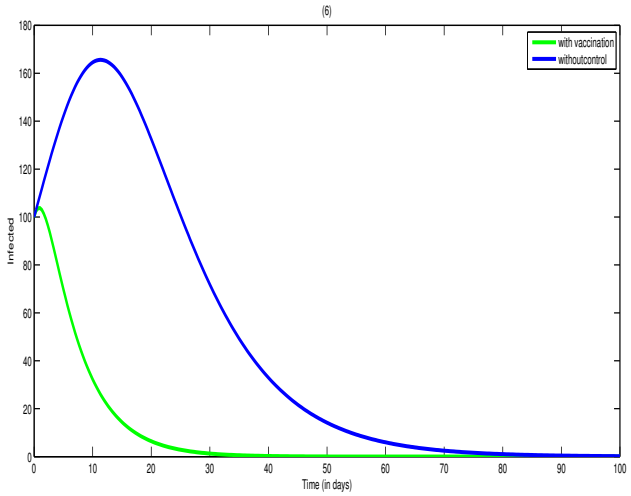
2.3. **Optimal Vaccination only.** Under this strategy, in Figure 2.4, we optimize vaccination, considering all the three doses, that is, $u_1$, $u_2$, and $u_3$ setting the treatment control variable $u_4 = 0$. When vaccination is optimized, susceptibes take much longer in the susceptible class, that is, 50 days and in case of no vaccination, they take between 15 to 20 days to move from this class. We further note that, vaccination has an indirect effect on the infected class, as shown in Figure 2.4(c), the disease disappear within the first 30 days, that is, at $t = 30$ and in absence of vaccination the disease takes 75 days to disappear. Again recovery takes 10 days when vaccination is implemented and without it, it takes 40 days for full recovery to take place.




(a) $u_1$, $u_2$ *and* $u_3$ profile



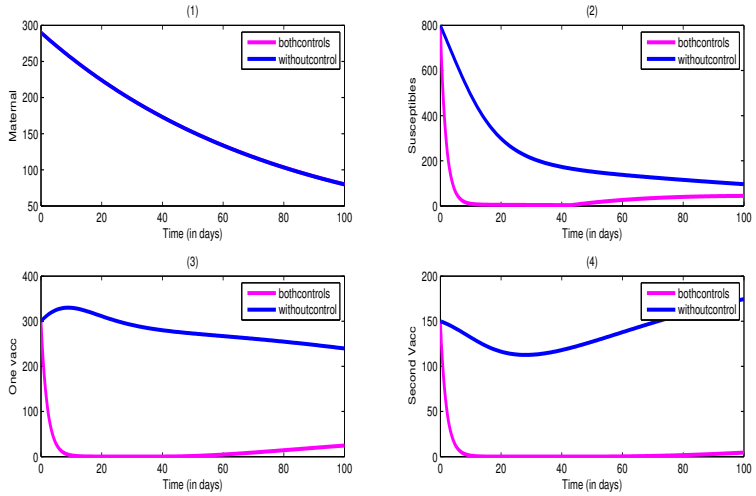

(b) $u_1$, $u_2$ *and* $u_3$ profile



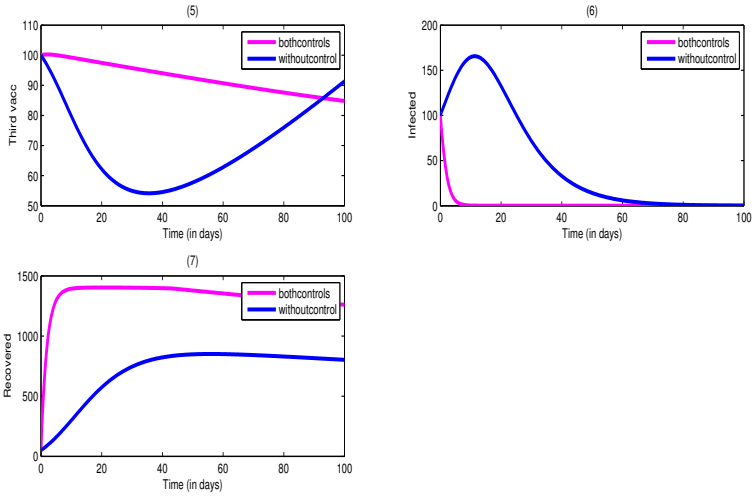

(c) Infected class with vaccination only (green curve) and non-vaccinated (blue curve)

FIGURE 2.4. A plot represents optimal vaccination only.

2.4. **Optimal Vaccination and Treatment.** Under this strategy, in Figure 2.5 (a) and (b) we optimize both vaccination and treatment. When both treatment and vaccination are implemented, infection is controlled within the first 10 days as shown in Figure 2.5(c).

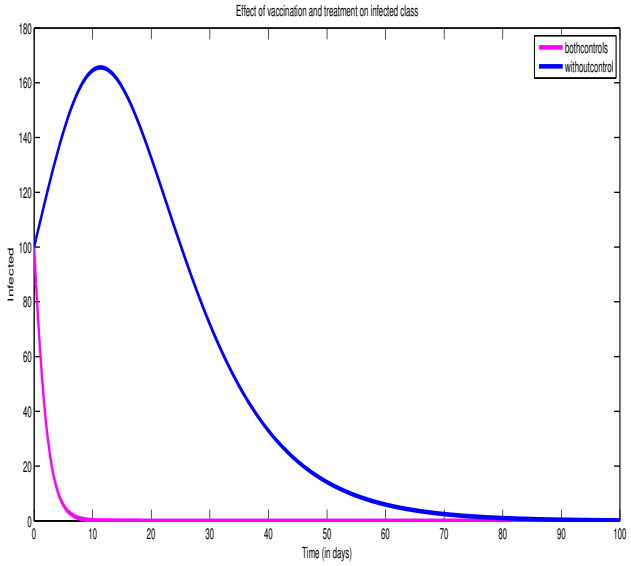



(a) $u_1$, $u_2$, $u_3$ *and* $u_4$ profile




(b) $u_1$, $u_2$, $u_3$ *and* $u_4$ profile

2.5. **Optimal without control, with treatment only, vaccination only, and both treatment and vaccination.** In Figure 2.6, we deduce the effect of different control scenarios on the infected class since our aim is to reduce the level of infected class. Without controls, infection takes t=75 days for the infection to clear, with treatment only, $t = 55$ days, with vaccination only $t = 30 - 40$ days and in




(c) Infected class with both treatment and vaccination (pink curve) and no vaccination, no treatment (blue curve)

FIGURE 2.5. A plot represents optimal of both vaccination and treatment.

presence of both treatment and vaccination, $t = 10$ days. Thus we recommend both treatment and vaccination since infection disappears within a short time.

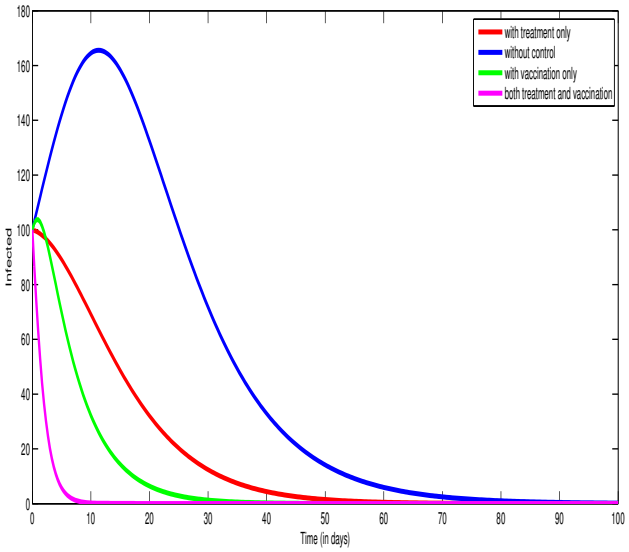



FIGURE 2.6. A plot represents optimal without control (blue curve), with treatment only(red curve), with vaccination only(green curve), and with both treatment and treatment (pink curve)

## 3. Conclusion

We derived and analyzed a mathematical model for the transmission dynamics of rotavirus disease that includes vaccination administered as three booster doses and treatment as our control strategies. We performed optimal control analysis of the model by applying the conditions necessary for optimal control of the disease derived using the Pontryagin's maximum principle. The numerical results show that in case of a disease outbreak we should used both control measures to reduce the infection burden within the first 10 days, otherwise, if we treat only, the infection will take 55 days to clear, if we vaccinate, the infection will take between 30 to 40 days to clear and if we do not control at all, the infection will take much longer time to clear, that is, 75 days. The later is very dangerous because if do not control the infection burden will increase hence making more children to become infected.

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