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MATHEMATICAL MODEL FOR THE EFFECTS OF TREATMENT AND VACCINATION CONTROLS ON THE DYNAMICS OF ROTAVIRUS DISEASE WITH REFERENCE TO UGANDA

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Abstract. In this paper, while Rotavirus has been a recognised disease for a long time in developing countries like Uganda, the control of this endemic disease is still a challenge. We formulated a mathematical model for the dynamics of Rotavirus disease with both treatment and vaccination. The equilibrium points are determined. The disease free equilibrium points are shown to be locally and globally asymptotically stable. We analyzed different reproduction numbers at different doses of vaccination with treatment. Numerical results indicate that rotavirus can be reduced when one or both interventions are implemented. The study recommends that children should always be treated and also complete all their doses of rotavirus vaccines so as to reduce severe infections.

Keywords: rotavirus; treatment; vaccination; effective reproduction numbers; endemic disease.

2010 AMS Subject Classification: 37N30, 92B05, 93D20.

1. Introduction

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Like in most developing countries, like Uganda, rotavirus is the second major cause of severe gastroenteritis (diarrhea) in infants and young children (Tate *et al.*, 2012) leading to over 600,000 to 760,000 deaths annually worldwide (Clark *et al.*, 2004; WHO, 2012; Gavi Alliance, 2013). Different studies (WHO, 2009; CDC, 2009; WHO, 2012; CDC, 2013; Morrow *et al.*, 2004) have pointed out that, exclusive breast feeding could reduce gastrointestinal infection among infants, proper hygiene, access to clean water and sanitation but these measures have not yet been proved to be effective. Apart from the above measures, treatment has also been thought as a means of reducing rotavirus and this requires standard rehydration therapy (WHO, 1980; Heymann *et al.*, 2004). This is administered orally to children due to dehydration caused by severe diarrhea and vomiting (Dormitzer *et al.*, 2005; Matson *et al.*, 2003). Rotavirus vaccines have proved more effective than other measures and they have been recommended to prevent fatal and severe rotavirus disease (Vesikari *et al.*, 2007; WHO, 2009; Kim *et al.*, 2010; CDC, 2013). Thus, WHO has released a global recommendation that all countries especially developing ones to include infant rotavirus vaccination in their national immunization programmes and the GAVI Alliance has promised to provide financial support for rotavirus vaccination programmes to developing countries (Kim *et al.*, 2010a; WHO, 2009)

Basing on these facts, we formulate a mathematical model to understand the effect of both treatment and vaccination for rotavirus disease among children below five years with reference to Uganda. We compute the effective reproduction number, R_e , establish the existence and stability of equilibrium points, analyze the steady states and lastly discuss the results and then make conclusions.

2. Model formulation

We formulate our rotavirus model using the susceptible-infected-treated-recovered (SITR) basic model with four compartments at time t , namely: $S(t)$ denoting the number of susceptible children, $I(t)$ denoting the number of infectious children, $T(t)$ denoting the number of treated children, and $R(t)$ for those who have temporarily recovered from the disease.

In the development of the model we make the following assumptions: Constant recruitment rate Λ into the children group through birth by the adults, vaccination gives temporary immunity, and infected children if untreated may either recover or die.

Our model considers two modes of control strategies, that is, vaccination and treatment. The model is later modified with children population being divided into eleven classes at time t , namely: The susceptible class $S(t)$ has three compartments, $S_1(t)$ denoting number of susceptible recruited without vaccination, $S_2(t)$ denoting number of susceptible who lose immunity after the first dose of vaccination, and $S_3(t)$ denoting number of susceptible who lose immunity after the second dose of vaccination.

The vaccinated class $V(t)$ has three compartments, $V_1(t)$ denoting number of vaccinated children recruited for the first dose of vaccination, $V_2(t)$ denoting number of vaccinated children for the second dose of vaccination, and $V_3(t)$ denoting number of vaccinated children for the third dose of vaccination.

The infectious class $I(t)$ is divided into three compartments, $I_1(t)$ denoting number of infectious children without vaccination, $I_2(t)$ denoting number of infectious children who lost immunity after first dose of vaccination, and $I_3(t)$ denoting number of infectious children who lost immunity after second dose of vaccination. The treated class is represented by $T(t)$ denoting the number of treated children and $R(t)$ indicates number of recovered children. The concentration of rotavirus in the environment at time t infected with the virus is given by $E(t)$.

In this model, we assume constant recruitment Λ into the children group through birth by adults. A proportion $1 - \rho$ of the recruited to $S_1(t)$ is not vaccinated while the other proportion ρ of the recruited join the vaccinated subgroup $V_1(t)$. Rotavirus can be passed from one children to another through contaminated hands with the virus or by touching a contaminated surface or object (Buts *et al.*, 1993; Shim *et al.*, 2001). The primary mode of rotavirus transmission is fecal-oral (Hochwald *et al.*, 1999) and enters the body through the mouth (Parashar *et al.*, 1995). Children at $S_1(t)$ join the infectious class $I_1(t)$, when exposed to unhygienic environment or having close contact with an infected child. They can spread the virus before and after developing symptoms (Parashar *et al.*, 1995) within the incubation period of 1-3 days (Mastretta

et al., 2002; CDC, 2009). Thus they acquire infection at a rate $\psi(S_1(t), E, I_j(t))$, where

$$\psi(S_1(t), E, I_j(t)) = \varepsilon_1 S_1 \sum_{j=1}^3 (\theta_j I_j) + \frac{v_1 E S_1}{K + E}, \quad j = 1, 2, 3.$$

Here, ε_1 is the contact infection rate from infected children to susceptible children. The parameter v_1 is the contact infection rate from contaminated/hygienic environment to susceptible children, whose pathogen concentration is K .

Let us note from here that, the parameters ε_i and v_i , where, $i = 1, 2, 3$ measures the degree of susceptibility to disease. The S_i classes interact with I_j classes but the degree of susceptibility in each S_i varies and this can be achieved through $\varepsilon_1, \varepsilon_2, \& \varepsilon_3$ and $v_1, v_2, \& v_3$ with $\varepsilon_1 > \varepsilon_2 > \varepsilon_3$ and $v_1 > v_2 > v_3$. The degree of the infectiousness of $I_1, I_2, \& I_3$ can also be achieved when $\varepsilon_i S_i (I_1 + I_2 + I_3)$ is in the form $\varepsilon_i S_i (\theta_1 I_1 + \theta_2 I_2 + \theta_3 I_3)$ in which $\theta_1 > \theta_2 > \theta_3$ and $\theta_1 + \theta_2 + \theta_3 = 1$. Infected children experience symptoms which involve vomiting and diarrhea for 3-8 days, frequent fever and abdominal pain (CDC, 2009). A fraction r of children is treated at a rate ω_1 and they join the treated group $T(t)$, while the other fraction $1 - r$ is assumed to recovery naturally at a rate α_1 by other means like breast feeding (WHO, 2009), proper hygiene, sanitation, access to clean water among others (Buts *et al.*, 1993). Currently there are two rotavirus vaccines, RotaTeq and Rotarix. Both are given by mouth (orally) to young infants (CDC, 2012). RotaTeq is managed in a 3-dose successions, with doses managed at ages 2, 4, and 6 months and Rotarix is managed in a 2-dose successions, with doses administered at ages 2 and 4 months (Gavi Alliance report, 2013; CDC 2013; Robert *et al.*, 2010). The lowest age for dose 1 of rotavirus vaccine is 6 weeks, the highest age for dose 1 is 14 weeks and 6 days. Vaccination should not be started for infants aged 15 weeks and 0 days or older because of insufficient data on safety of dose 1 of rotavirus vaccine in older infants (CDC, 2013). The minimum interval between doses of rotavirus vaccine is 4 weeks, no maximum interval is set (CDC, 2012). All doses should be administered between age one and half months to 6 months only (CDC 2013; Robert *et al.*, 2010). Furthermore, a proportion ρ of children is recruited in the vaccinated class $V_1(t)$ for the first dose. After four weeks, these children should be taken back by their mothers or caretakers for the second dose. In Uganda, each dose of vaccine is approximately US\$36 at Kampala International Hospital and US\$38 at Nakasero Hospital as per May 2013. These two

hospitals are among the four centres where the vaccine is administered. Few mothers can afford this cost and many children, as a result, end up not getting the full dose of the vaccine. Children at $V_1(t)$ either go for the second dose or not. A fraction η of children from $V_1(t)$ are taken for the second dose and are vaccinated at a rate τ_1 and the other fraction $1 - \eta$ are not taken back so they lose the vaccine immunity and join the susceptible class $S_2(t)$ at a rate κ_1 . These children contract infection at a rate $\psi(S_2(t), E, I_j(t))$, where

$$\psi(S_2(t), E, I_j(t)) = \varepsilon_2 S_2 \sum_{j=1}^3 (\theta_j I_j) + \frac{v_2 E S_2}{K + E}, \quad j = 1, 2, 3$$

moving to the infectious class $I_2(t)$. At $I_2(t)$, a proportion a is treated at a rate ω_2 , while the other proportion $1 - a$ recovers by other means to the recovery class at a rate α_2 . The dynamics of rotavirus disease is summarised in the compartmental diagram in Figure 1. After the first

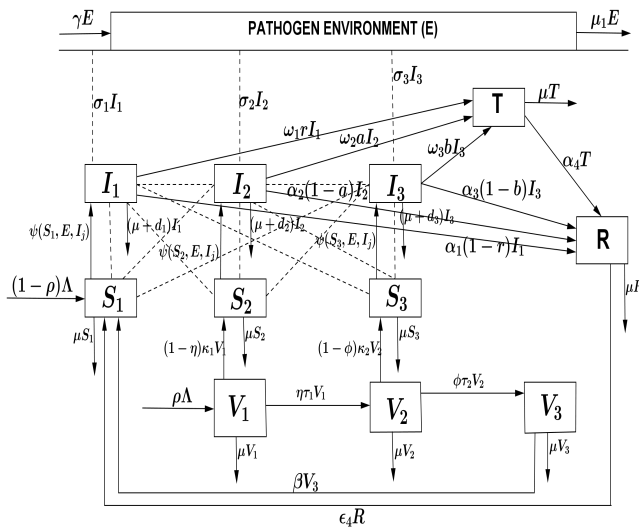


FIGURE 1. A schematic of rotavirus disease with both treatment and vaccination. Children are vaccinated with three different doses V_1, V_2 and V_3 , these doses are meant to be boosters such that the children have strong immunity. Where as infected children can be treated from disease at different rates whether they are vaccinated or unvaccinated.

dose, a proportion of children η joins $V_2(t)$ for the second dose. Again, children should be taken back for the third dose. A fraction ϕ is taken for the third dose at a rate τ_2 while the other remaining fraction $1 - \phi$ is not. These join the susceptible group $S_3(t)$ at a rate κ_2 . These

children become exposed and they acquire the virus at a rate $\psi(S_3(t), E, I_j(t))$, where

$$\psi(S_3(t), E, I_j(t)) = \varepsilon_3 S_3 \sum_{j=1}^3 (\theta_j I_j) + \frac{v_3 E S_3}{K + E}, \quad j = 1, 2, 3.$$

When these children become infectious, a proportion b is treated at a rate ω_3 , while the others $1 - b$ recovers naturally at a rate α_3 . Children who got a full dose of vaccination are assumed to have a very strong immunity compared to those who did not complete the dose. In Africa, the vaccine gives greatest protection during the first year and efficacy in the second year of life appears to be lower (Zaman *et al.*, 2010; Armah *et al.*, 2010; Madhi *et al.*, 2010), thus the waning rate of the vaccine is β from $V_3(t)$. All treated children at $T(t)$ join the recovery group at a rate α_4 . Since treatment can confer some immunity than when it is not given, we assume that $\alpha_4 > \alpha_3 > \alpha_2 > \alpha_1$. Furthermore, children at $R(t)$ can become susceptible again at a rate ε_4 . Infected individuals die due to rotavirus at a rate d and all human classes are assumed to experience natural death at a rate μ . A dirty environment contaminated with rotavirus can lead to the spread of the disease thus the free pathogen population is generated at a rate γ while infected children from $I_1(t)$, $I_2(t)$, and $I_3(t)$ can contribute to its enhancement through excretion at rates σ_1 , σ_2 , and σ_3 respectively. Rotavirus pathogens die naturally at the rate μ_1 . From the description of the dynamics of rotavirus and with the aid of the compartmental diagram in Figure 1, we have the following set of differential equations.

$$\frac{dS_1(t)}{dt} = (1 - \rho)\Lambda - \psi(S_1, E, I_j) + \varepsilon_4 R - \mu S_1 + \beta V_3,$$

$$\frac{dV_1(t)}{dt} = \rho\Lambda - (1 - \eta)\kappa_1 V_1 - \eta \tau_1 V_1 - \mu V_1,$$

$$\frac{dS_2(t)}{dt} = (1 - \eta)\kappa_1 V_1 - \psi(S_2, E, I_j) - \mu S_2,$$

$$\frac{dV_2(t)}{dt} = \eta \tau_1 V_1 - (1 - \phi)\kappa_2 V_2 - \phi \tau_2 V_2 - \mu V_2,$$

$$\begin{aligned}
\frac{dV_3(t)}{dt} &= \phi \tau_2 V_2 - \beta V_3 - \mu V_3, \\
\frac{dS_3(t)}{dt} &= (1 - \phi) \kappa_2 V_2 - \psi(S_3, E, I_j) - \mu S_3, \\
\frac{dI_1(t)}{dt} &= \psi(S_1, E, I_j) - \alpha_1(1 - r)I_1 - \omega_1 r I_1 - (\mu + d_1)I_1, \\
\frac{dI_2(t)}{dt} &= \psi(S_2, E, I_j) - \alpha_2(1 - a)I_2 - \omega_2 a I_2 - (\mu + d_2)I_2, \\
\frac{dI_3(t)}{dt} &= \psi(S_3, E, I_j) - \alpha_3(1 - b)I_3 - \omega_3 b I_3 - (\mu + d_3)I_3, \\
\frac{dT(t)}{dt} &= \omega_1 r I_1 + \omega_2 a I_2 + \omega_3 b I_3 - \alpha_4 T - \mu T, \\
\frac{dR(t)}{dt} &= \alpha_1(1 - r)I_1 + \alpha_2(1 - a)I_2 + \alpha_3(1 - b)I_3 + \alpha_4 T - \mu R - \varepsilon_4 R, \\
\frac{dE(t)}{dt} &= \gamma E - \mu_1 E + \sigma_1 I_1 + \sigma_2 I_2 + \sigma_3 I_3.
\end{aligned}
\tag{1}$$

where

$$\psi(S_i, E, I_j) = \varepsilon_i S_i \sum_{j=1}^3 (\theta_j I_j) + \frac{v_i E S_i}{K + E},$$

for $i = 1, 2, 3$, with initial conditions: $S_1(0) = S_{10}$, $V_1(0) = V_{10}$, $S_2(0) = S_{20}$, $V_2(0) = V_{20}$,

$V_3(0) = V_{30}$, $S_3(0) = S_{30}$, $I_1(0) = I_{10}$, $I_2(0) = I_{20}$, $I_3(0) = I_{30}$, $T(0) = T_0$, $R(0) = R_0$ and

$N(0) = N_0$.

2.1. Invariant Region

We assume that all the variables and parameters of the model are positive for all $t \geq 0$. The children population $N_C(t)$ can be determined by

$$\frac{dN_C(t)}{dt} = \Lambda - \mu N_C(t) - d(I_1 + I_2 + I_3)
\tag{2}$$

In absence of rotavirus, there is no death from rotavirus, that is, $d = 0$ then

$$(3) \quad \frac{dN_C(t)}{dt} \leq \Lambda - \mu N_C(t)$$

Integrating (3) on both sides and applying the initial conditions we obtain

$$(4) \quad \Lambda - \mu N_C(t) \geq (\Lambda - \mu N_0)e^{-\mu t}$$

Applying Birkhoff and Rota’s theorem (Birkhoff and Rota, 1985) and making $N_C(t)$ the subject in (4), we get

$$(5) \quad \begin{aligned} N_C(t) &\leq -\frac{1}{\mu}[(\Lambda - \mu N_0)e^{-\mu t} - \Lambda], \\ \Rightarrow N_C(t) &\leq \frac{\Lambda}{\mu} - \left(\frac{\Lambda - \mu N_0}{\mu}\right)e^{-\mu t} \end{aligned}$$

As $t \rightarrow \infty$ in (5), the children population size $N_C(t)$ approaches

$$(6) \quad 0 \leq N_C(t) \leq \frac{\Lambda}{\mu}, \Rightarrow N_C(t) \rightarrow \frac{\Lambda}{\mu}$$

This implies that, if there is no disease, $N_C^* = \frac{\Lambda}{\mu}$, meaning we have a steady state population which is globally asymptotically stable. Therefore, the feasible solution set of the children population of the system (1) enters the region

$$\Omega_C = \left\{ (S_1, V_1, S_2, V_2, S_3, V_3, I_1, I_2, I_3, T, R) \in \mathbf{R}_+^{11} \mid S_1 \geq 0, V_1 \geq 0, S_2 \geq 0, V_2 \geq 0, S_3 \geq 0, V_3 \geq 0, I_1 \geq 0, I_2 \geq 0, I_3 \geq 0, T \geq 0, R \geq 0, N_C(t) \leq \frac{\Lambda}{\mu} \right\}.$$

Similarly, considering the last differential equation in the system (1), that is,

$$\frac{dE(t)}{dt} = \gamma E - \mu_1 E + \sigma_1 I_1 + \sigma_2 I_2 + \sigma_3 I_3,$$

and letting the total pathogen population be $E(t)$, we have

$$(7) \quad \begin{aligned} \frac{dE(t)}{dt} &= (\gamma - \mu_1)E + \sigma_1 I_1 + \sigma_2 I_2 + \sigma_3 I_3 \leq (\gamma - \mu_1)E + (\sigma_1 + \sigma_2 + \sigma_3)N_C(t), \\ \Rightarrow \frac{dE(t)}{dt} &\leq (\gamma - \mu_1)E + (\sigma_1 + \sigma_2 + \sigma_3)N_C(t) \end{aligned}$$

But from (6), we have $N_C(t) \leq \frac{\Lambda}{\mu}$, which implies that

$$(8) \quad \frac{dE(t)}{dt} \leq (\gamma - \mu_1)E + (\sigma_1 + \sigma_2 + \sigma_3)N_C(t) \leq (\gamma - \mu_1)E + (\sigma_1 + \sigma_2 + \sigma_3)\frac{\Lambda}{\mu}$$

Integrating both sides of (8) gives

$$(9) \quad E(t) \leq \frac{(\sigma_1 + \sigma_2 + \sigma_3)\Lambda}{\mu(\mu_1 - \gamma)} [1 + Be^{-(\mu_1 - \gamma)t}]$$

where B is a constant. As $t \rightarrow \infty$ in (9), the pathogen population size $E(t)$ becomes

$$0 \leq E(t) \leq \frac{(\sigma_1 + \sigma_2 + \sigma_3)\Lambda}{\mu(\mu_1 - \gamma)}$$

and

$$\Rightarrow E(t) \rightarrow \frac{(\sigma_1 + \sigma_2 + \sigma_3)\Lambda}{\mu(\mu_1 - \gamma)}$$

provided $\mu_1 > \gamma$.

Therefore, the feasible solution set of the pathogen population of the system (1) enters the region

$$\Omega_C = \left\{ (E(t) \in \mathbf{R}_+ | E(t) \leq \frac{(\sigma_1 + \sigma_2 + \sigma_3)\Lambda}{\mu(\mu_1 - \gamma)}) \right\}$$

Thus, the feasible set for our model system (1) is given by

(10)

$$\Omega = \left\{ (S_1, V_1, S_2, V_2, S_3, V_3, I_1, I_2, I_3, T, R, E) \in \mathbf{R}_+^{12} | (S_1, V_1, S_2, V_2, S_3, V_3, I_1, I_2, I_3, T, R, E) \geq 0; N_C(t) \leq \frac{\Lambda}{\mu}; E(t) \leq \frac{(\sigma_1 + \sigma_2 + \sigma_3)\Lambda}{\mu(\mu_1 - \gamma)} \right\}.$$

which is a positively invariant set under the flow induced by the model system (1). Hence the system is biologically meaningful and mathematically well-posed in the domain Ω .

2.1.1. Positivity of Solutions

Lemma 2.1. *Let the initial data be*

$$\{(S_1(0), V_1(0), S_2(0), V_2(0), S_3(0), V_3(0), I_1(0), I_2(0), I_3(0), T(0), R(0), E(0)) \geq 0\} \in \mathbf{R}_+^{12}.$$

Then, the solution set

$$\{S_1(t), V_1(t), S_2(t), V_2(t), S_3(t), V_3(t), I_1(t), I_2(t), I_3(t), T(t), R(t), E(t)\}$$

of the system (1) is non-negative for all $t > 0$.

Proof. From the first equation of the model system (1)

$$\begin{aligned}\frac{dS_1(t)}{dt} &= (1 - \rho)\Lambda - \psi(S_1, E, I_j) + \varepsilon_4 R - \mu S_1 + \beta V_3. \\ \frac{dS_1(t)}{dt} &\geq -\mu S_1.\end{aligned}$$

By integrating on both sides, we get,

$$\int \frac{dS_1(t)}{S_1} \geq \int -\mu dt$$

this gives

$$S_1(t) \geq S_1(0)e^{-\int \mu dt} \geq 0,$$

and using initial conditions $S_1(0) = S_{10}$, we get

$$S_1(t) \geq S_{10}e^{-\mu t} \geq 0, \text{ since } \mu > 0$$

Considering the second equation of model system (1)

$$\frac{dV_1(t)}{dt} = \rho\Lambda - (1 - \eta)\kappa_1 V_1 - \eta\tau_1 V_1 - \mu V_1.$$

$$\frac{dV_1(t)}{dt} \geq -((1 - \eta)\kappa_1 + \eta\tau_1 + \mu)V_1.$$

Integrating on both sides,

we get,

$$\int \frac{dV_1(t)}{V_1} \geq \int -((1 - \eta)\kappa_1 + \eta\tau_1 + \mu)dt$$

this gives

$$V_1(t) \geq V_1(0)e^{-\int ((1 - \eta)\kappa_1 + \eta\tau_1 + \mu)dt} \geq 0 \text{ since } ((1 - \eta)\kappa_1 + \eta\tau_1 + \mu) \geq 0$$

Similarly the other are derived.

$$S_2(t) \geq S_2(0)e^{-\int \mu dt} \geq 0, \text{ since } \mu > 0$$

$$V_2(t) \geq V_2(0)e^{-\int ((1-\phi)\kappa_2 + \phi\tau_2 + \mu) dt} \geq 0, \text{ since } ((1-\phi)\kappa_2 + \phi\tau_2 + \mu) \geq 0$$

$$V_3(t) \geq V_3(0)e^{-\int (\beta + \mu) dt} \geq 0, \text{ since } (\beta + \mu) \geq 0$$

$$S_3(t) \geq S_3(0)e^{-\int \mu dt} \geq 0, \text{ since } \mu > 0$$

$$I_1(t) \geq I_1(0)e^{-\int (\alpha_1(1-r) + \omega_1 r + (\mu + d_1)) dt} \geq 0, \text{ since } (\alpha_1(1-r) + \omega_1 r + (\mu + d_1)) > 0$$

$$I_2(t) \geq I_2(0)e^{-\int (\alpha_2(1-a) + \omega_2 a + (\mu + d_2)) dt} \geq 0, \text{ since } (\alpha_2(1-a) + \omega_2 a + (\mu + d_2)) > 0$$

$$I_3(t) \geq I_3(0)e^{-\int (\alpha_3(1-b) + \omega_3 b + (\mu + d_3)) dt} \geq 0, \text{ since } (\alpha_3(1-b) + \omega_3 b + (\mu + d_3)) > 0$$

$$T(t) \geq T(0)e^{-\int (\alpha_4 + \mu) dt} \geq 0, \text{ since } (\alpha_4 + \mu) \geq 0$$

$$R(t) \geq R(0)e^{-\int (\varepsilon_1 + \mu) dt} \geq 0, \text{ since } (\varepsilon_1 + \mu) \geq 0$$

$$E(t) \geq E(0)e^{\int (\gamma - \mu_1) dt} \geq 0, \text{ since } (\gamma - \mu_1) \geq 0.$$

2.2. Disease Free Equilibrium Point for Treatment and Vaccination, P^0

Let the disease free equilibrium point, P^0 with treatment and vaccination be given by

$$P^0 = (S_1^0, V_1^0, S_2^0, V_2^0, V_3^0, S_3^0, I_1^0, I_2^0, I_3^0, T^0, R^0, E^0)$$

Thus

$$(11) \quad \begin{aligned} S_1^0 &= \frac{(1-\rho)\Lambda}{\mu} + \frac{\beta}{\mu} \frac{\phi\tau_2}{(\beta + \mu)} \frac{\eta\tau_1}{((1-\phi)\kappa_2 + \phi\tau_2 + \mu)} \frac{\rho\Lambda}{((1-\eta)\kappa_1 + \eta\tau_1 + \mu)} \\ V_1^0 &= \frac{\rho\Lambda}{((1-\eta)\kappa_1 + \eta\tau_1 + \mu)} \\ S_2^0 &= \frac{(1-\eta)\kappa_1}{\mu} \frac{\rho\Lambda}{((1-\eta)\kappa_1 + \eta\tau_1 + \mu)} \\ V_2^0 &= \frac{\eta\tau_1}{((1-\phi)\kappa_2 + \phi\tau_2 + \mu)} \frac{\rho\Lambda}{((1-\eta)\kappa_1 + \eta\tau_1 + \mu)} \\ V_3^0 &= \frac{\phi\tau_2}{(\beta + \mu)} \frac{\eta\tau_1}{((1-\phi)\kappa_2 + \phi\tau_2 + \mu)} \frac{\rho\Lambda}{((1-\eta)\kappa_1 + \eta\tau_1 + \mu)} \\ S_3^0 &= \frac{(1-\phi)\kappa_2}{\mu} \frac{\eta\tau_1}{((1-\phi)\kappa_2 + \phi\tau_2 + \mu)} \frac{\rho\Lambda}{((1-\eta)\kappa_1 + \eta\tau_1 + \mu)} \end{aligned}$$

Therefore

$$(12) \quad P^0 = (S_1^0, V_1^0, S_2^0, V_2^0, V_3^0, S_3^0, 0, 0, 0, 0, 0, 0)$$

2.2.1. The Effective Reproduction Number for Treatment and Vaccination, R_e

The effective reproduction number R_e is the average number of infectious individuals resulting from a single infective introduced at time t into the population, given an intervention and naturally acquired immunity at that time. This is calculated using the next generation operator approach as described by Van den Driessche and Watmough (2002) as follows.

Let

- (i) $\mathcal{F}_i(x)$ be the rate of appearance of new infections in compartment i .
- (ii) $\mathcal{V}_i^+(x)$ be the rate of transfer of individuals into compartment i by all other means, other than the epidemic.
- (iii) $\mathcal{V}_i^-(x)$ be the transfer of individuals out of the compartment i .

The disease transmission model consists of the system of equations

$$x_i' = f_i(x) = \mathcal{F}_i(x) - \mathcal{V}_i(x)$$

where

$$\mathcal{V}_i = \mathcal{V}_i^-(x) - \mathcal{V}_i^+.$$

The next important step is to obtain the disease-free equilibrium point P^0 . We then compute matrices F and V which are $m \times m$ matrices, where m represents the infected classes, defined by

$$F = \left[\frac{\partial \mathcal{F}_i}{\partial x_j}(P^0) \right]$$

and

$$V = \left[\frac{\partial \mathcal{V}_i}{\partial x_j}(P^0) \right] \text{ with } 1 \leq i, j \leq m,$$

and F is nonnegative and V is a nonsingular M -matrix (a matrix with inverse, belonging to the class of positive matrices). Since F is nonnegative and V is nonsingular, then V^{-1} is nonnegative and also FV^{-1} is nonnegative.

We then compute matrix FV^{-1} , defined as the next generation matrix (Diekmann *et al.*, 1990). The effective reproductive number with treatment and vaccination R_e is then defined as

$$R_e = \rho(FV^{-1})$$

where $\rho(A)$ is the spectral radius of matrix A (or the maximum modulus of the eigenvalues of A). By using the method described above, we can compute the effective reproduction number for treatment and vaccination (R_e) as follows:

We rearrange the equations of model system (1) with the infected classes, $I_1(t)$, $I_2(t)$, $I_3(t)$ first, environment class, $E(t)$ second, susceptible classes, $S_1(t)$, $S_2(t)$, $S_3(t)$ third, vaccination classes, $V_1(t)$, $V_2(t)$, $V_3(t)$ fourth, treatment class, $T(t)$ fifth and recovered class, $R(t)$ last.

Let

$$(13) \quad \mathcal{F}_i = \begin{bmatrix} \varepsilon_1 S_1 (\theta_1 I_1 + \theta_2 I_2 + \theta_3 I_3) + \frac{v_1 E S_1}{K+E} \\ \varepsilon_2 S_2 (\theta_1 I_1 + \theta_2 I_2 + \theta_3 I_3) + \frac{v_2 E S_2}{K+E} \\ \varepsilon_3 S_3 (\theta_1 I_1 + \theta_2 I_2 + \theta_3 I_3) + \frac{v_3 E S_3}{K+E} \\ 0 \end{bmatrix}$$

and

$$(14) \quad \mathcal{V}_i = \begin{bmatrix} (\alpha_1(1-r) + \omega_1 r + (\mu + d))I_1 \\ (\alpha_2(1-a) + \omega_1 a + (\mu + d))I_2 \\ (\alpha_3(1-b) + \omega_1 b + (\mu + d))I_3 \\ \mu_1 E - \gamma E - \sigma_1 I_1 - \sigma_2 I_2 - \sigma_3 I_3 \end{bmatrix}$$

Evaluating the partial derivative of (13) at disease free, P^0 gives

$$(15) \quad F = \begin{bmatrix} \varepsilon_1 \theta_1 S_1 & \varepsilon_1 \theta_2 S_1 & \varepsilon_1 \theta_3 S_1 & \frac{v_1 S_1}{K} \\ \varepsilon_2 \theta_1 S_2 & \varepsilon_2 \theta_2 S_2 & \varepsilon_2 \theta_3 S_2 & \frac{v_2 S_2}{K} \\ \varepsilon_3 \theta_1 S_3 & \varepsilon_3 \theta_2 S_3 & \varepsilon_3 \theta_3 S_3 & \frac{v_3 S_3}{K} \\ 0 & 0 & 0 & 0 \end{bmatrix}$$

Similarly, the Jacobian matrix of \mathcal{V} , is found by partial differentiation of (14) gives

$$(16) \quad V = \begin{bmatrix} \xi_1 & 0 & 0 & 0 \\ 0 & \xi_2 & 0 & 0 \\ 0 & 0 & \xi_3 & 0 \\ -\sigma_1 & -\sigma_2 & -\sigma_3 & (\mu_1 - \gamma) \end{bmatrix}$$

with

$$\xi_1 = (\alpha_1(1 - r) + \omega_1 r + (\mu + d)), \quad \xi_2 = (\alpha_2(1 - a) + \omega_2 a + (\mu + d)),$$

$$\xi_3 = (\alpha_3(1 - b) + \omega_3 b + (\mu + d))$$

The inverse of the Jacobian matrix (16), will be

$$(17) \quad V^{-1} = \begin{bmatrix} \frac{1}{\xi_1} & 0 & 0 & 0 \\ 0 & \frac{1}{\xi_2} & 0 & 0 \\ 0 & 0 & \frac{1}{\xi_3} & 0 \\ \frac{\sigma_1}{\xi_1(\mu_1 - \gamma)} & \frac{\sigma_2}{\xi_2(\mu_1 - \gamma)} & \frac{\sigma_3}{\xi_3(\mu_1 - \gamma)} & \frac{1}{(\mu_1 - \gamma)} \end{bmatrix}$$

By computing the product of (15) and (16) we get

$$(18) \quad FV^{-1} = \begin{bmatrix} \varepsilon_1 \theta_1 S_1 & \varepsilon_1 \theta_2 S_1 & \varepsilon_1 \theta_3 S_1 & \frac{v_1 S_1}{K} \\ \varepsilon_2 \theta_1 S_2 & \varepsilon_2 \theta_2 S_2 & \varepsilon_2 \theta_3 S_2 & \frac{v_2 S_2}{K} \\ \varepsilon_3 \theta_1 S_3 & \varepsilon_3 \theta_2 S_3 & \varepsilon_3 \theta_3 S_3 & \frac{v_3 S_3}{K} \\ 0 & 0 & 0 & 0 \end{bmatrix} \begin{bmatrix} \frac{1}{\xi_1} & 0 & 0 & 0 \\ 0 & \frac{1}{\xi_2} & 0 & 0 \\ 0 & 0 & \frac{1}{\xi_3} & 0 \\ \frac{\sigma_1}{\xi_1(\mu_1 - \gamma)} & \frac{\sigma_2}{\xi_2(\mu_1 - \gamma)} & \frac{\sigma_3}{\xi_3(\mu_1 - \gamma)} & \frac{1}{(\mu_1 - \gamma)} \end{bmatrix}$$

This gives

$$(19) \quad FV^{-1} = \begin{bmatrix} \frac{\varepsilon_1 \theta_1 S_1}{\xi_1} + \frac{v_1 S_1 \sigma_1}{K \xi_1 (\mu_1 - \gamma)} & \frac{\varepsilon_1 \theta_2 S_2}{\xi_2} + \frac{v_1 S_1 \sigma_2}{K \xi_2 (\mu_1 - \gamma)} & \frac{\varepsilon_1 \theta_3 S_3}{\xi_3} + \frac{v_1 S_1 \sigma_3}{K \xi_3 (\mu_1 - \gamma)} & \frac{v_1 S_1}{K(\mu_1 - \gamma)} \\ \frac{\varepsilon_2 \theta_1 S_2}{\xi_1} + \frac{v_2 S_2 \sigma_1}{K \xi_1 (\mu_1 - \gamma)} & \frac{\varepsilon_2 \theta_2 S_2}{\xi_2} + \frac{v_2 S_2 \sigma_2}{K \xi_2 (\mu_1 - \gamma)} & \frac{\varepsilon_2 \theta_3 S_3}{\xi_3} + \frac{v_2 S_2 \sigma_3}{K \xi_3 (\mu_1 - \gamma)} & \frac{v_2 S_2}{K(\mu_1 - \gamma)} \\ \frac{\varepsilon_3 \theta_1 S_3}{\xi_1} + \frac{v_3 S_3 \sigma_1}{K \xi_1 (\mu_1 - \gamma)} & \frac{\varepsilon_3 \theta_2 S_3}{\xi_2} + \frac{v_3 S_3 \sigma_2}{K \xi_2 (\mu_1 - \gamma)} & \frac{\varepsilon_3 \theta_3 S_3}{\xi_3} + \frac{v_3 S_3 \sigma_3}{K \xi_3 (\mu_1 - \gamma)} & \frac{v_3 S_3}{K(\mu_1 - \gamma)} \\ 0 & 0 & 0 & 0 \end{bmatrix}$$

Basing on matrix (19), the dominant eigenvalue will be the trace of (19), that is,

$$(20) \quad \lambda = \left(\frac{\varepsilon_1 \theta_1 S_1}{\xi_1} + \frac{v_1 S_1 \sigma_1}{K \xi_1 (\mu_1 - \gamma)} \right) + \left(\frac{\varepsilon_2 \theta_2 S_2}{\xi_2} + \frac{v_2 S_2 \sigma_2}{K \xi_2 (\mu_1 - \gamma)} \right) + \left(\frac{\varepsilon_3 \theta_3 S_3}{\xi_3} + \frac{v_3 S_3 \sigma_3}{K \xi_3 (\mu_1 - \gamma)} \right)$$

Therefore, λ in equation (20) evaluated at P^0 will be our effective reproduction number, R_e . That is,

$$(21) \quad R_e = \left(\frac{\varepsilon_1 \theta_1 S_1^0}{\xi_1} + \frac{v_1 S_1^0 \sigma_1}{K \xi_1 (\mu_1 - \gamma)} \right) + \left(\frac{\varepsilon_2 \theta_2 S_2^0}{\xi_2} + \frac{v_2 S_2^0 \sigma_2}{K \xi_2 (\mu_1 - \gamma)} \right) + \left(\frac{\varepsilon_3 \theta_3 S_3^0}{\xi_3} + \frac{v_3 S_3^0 \sigma_3}{K \xi_3 (\mu_1 - \gamma)} \right)$$

Let

$$\begin{aligned} \Delta_1 &= \frac{\varepsilon_1 \theta_1 S_1^0}{\xi_1} + \frac{v_1 S_1^0 \sigma_1}{K \xi_1 (\mu_1 - \gamma)} \\ &= \frac{S_1^0}{\xi_1} \left(\varepsilon_1 \theta_1 + \frac{v_1 \sigma_1}{K(\mu_1 - \gamma)} \right) \end{aligned}$$

where

$$S_1^0 = \frac{(1 - \rho)\Lambda}{\mu} + \frac{\beta}{\mu} \frac{\phi \tau_2}{(\beta + \mu)} \frac{\eta \tau_1}{((1 - \phi)\kappa_2 + \phi \tau_2 + \mu)} \frac{\rho \Lambda}{((1 - \eta)\kappa_1 + \eta \tau_1 + \mu)}$$

We note that:

- (i) S_1^0 contains number of children who are unvaccinated and those who became susceptible after the third dose when the vaccine worn out.

- (ii) Δ_1 represents the basic reproduction number of unvaccinated children and the effective reproduction number of children whose vaccine worn out.
- (iii) $\frac{\beta}{\mu} \frac{\phi \tau_2}{(\beta + \mu)} \frac{\eta \tau_1}{((1 - \phi)\kappa_2 + \phi \tau_2 + \mu)} \frac{\rho \Lambda}{((1 - \eta)\kappa_1 + \eta \tau_1 + \mu)}$, represents number of children who got the three doses and after the waning out of the vaccine they became susceptible again.
- (iv) $\frac{(1 - \rho)\Lambda}{\mu}$, number of unvaccinated children.

Let also

$$\begin{aligned} \Delta_2 &= \frac{\varepsilon_2 \theta_2 S_2^0}{\xi_2} + \frac{v_2 S_2^0 \sigma_2}{K \xi_2 (\mu_1 - \gamma)} \\ &= \frac{S_2^0}{\xi_2} \left(\varepsilon_2 \theta_2 + \frac{v_2 \sigma_2}{K(\mu_1 - \gamma)} \right) \end{aligned}$$

where

$$S_2^0 = \frac{(1 - \eta)\kappa_1}{\mu} \frac{\rho \Lambda}{((1 - \eta)\kappa_1 + \eta \tau_1 + \mu)}$$

We note that,

- (i) Δ_2 , represents the effective reproduction number of children who got the first dose of vaccination and were never taken for the second dose.
- (ii) $\frac{\rho \Lambda}{((1 - \eta)\kappa_1 + \eta \tau_1 + \mu)}$, represents number of children who received the first dose of vaccination
- (iii) $\frac{(1 - \eta)\kappa_1}{\mu} \frac{\rho \Lambda}{((1 - \eta)\kappa_1 + \eta \tau_1 + \mu)}$, represents number of children who did not go for the second dose of vaccination when they had received the first one.

And again let

$$\begin{aligned} \Delta_3 &= \frac{\varepsilon_3 \theta_3 S_3^0}{\xi_3} + \frac{v_3 S_3^0 \sigma_3}{K \xi_3 (\mu_1 - \gamma)} \\ &= \frac{S_3^0}{\xi_3} \left(\varepsilon_3 \theta_3 + \frac{v_3 \sigma_3}{K(\mu_1 - \gamma)} \right) \end{aligned}$$

where

$$S_3^0 = \frac{(1-\phi)\kappa_2}{\mu} \frac{\eta\tau_1}{((1-\phi)\kappa_2 + \phi\tau_2 + \mu)} \frac{\rho\Lambda}{((1-\eta)\kappa_1 + \eta\tau_1 + \mu)}$$

We further note that,

- (i) Δ_3 , represents the effective reproduction number of children who got both the first and second doses of vaccination but were not taken for the third dose.
- (ii) $\frac{(1-\phi)\kappa_2}{\mu} \frac{\eta\tau_1}{((1-\phi)\kappa_2 + \phi\tau_2 + \mu)} \frac{\rho\Lambda}{((1-\eta)\kappa_1 + \eta\tau_1 + \mu)}$, number of children that got two doses of the vaccine only and they are not taken back for the third dose.

Therefore

$$R_e = \Delta_1 + \Delta_2 + \Delta_3$$

2.2.2. Analysis of the Effective Reproduction Number with Treatment and Vaccination, R_e

From (21), we are able to analyze our effective reproduction number R_e as follows:

The basic reproduction number R_0 of our model will be obtained when $\beta = \omega_1 = \rho = \tau_1 = \tau_2 = 0$ and is given by

$$R_0 = \frac{\Lambda}{\mu(\alpha_1 + \mu + d)} \left(\varepsilon_1\theta_1 + \frac{v_1\sigma_1}{K(\mu_1 - d)} \right)$$

The effective reproduction number with treatment R_T is given by

$$R_T = \frac{\varepsilon_1\theta_1\Lambda}{\mu(\alpha_1(1-r) + \omega_1r + (\mu + d))} + \frac{\sigma_1v_1\Lambda}{\mu K(\alpha_1(1-r) + \omega_1r + (\mu + d))(\mu_1 - \gamma)}$$

The effective reproduction number with first dose of vaccination and treatment R_{1TV} is given by

$$R_{1TV} = \frac{(1-\eta)\kappa_1}{\mu((1-a) + \omega_2a + (\mu + d))} \frac{\rho\Lambda}{((1-\eta)\kappa_1 + \eta\tau_1 + \mu)} \left(\varepsilon_2\theta_2 + \frac{v_2\sigma_2}{K(\mu_1 - \gamma)} \right)$$

The effective reproduction number with treatment and second dose of vaccination R_{2TV} is given by

$$R_{2TV} = \frac{(1-\phi)\kappa_2}{\mu(1-b) + \omega_3b + (\mu + d)} \frac{\eta\tau_1}{((1-\phi)\kappa_2 + \phi\tau_2 + \mu)} \frac{\rho\Lambda}{((1-\eta)\kappa_1 + \eta\tau_1 + \mu)} k,$$

where $k = \varepsilon_3\theta_3 + \frac{v_3\sigma_3}{K(\mu_1 - \gamma)}$. From the above analysis, the following theorem holds without proof:

Theorem 2.1. *The disease free equilibrium point P^0 of the rotavirus model (1) with treatment and vaccination is locally asymptotically stable if $R_e < 1$ and unstable if $R_e > 1$.*

2.2.3. Global Stability of a Disease Free Equilibrium point, P^0

Theorem 2.2. *The disease free equilibrium point, P^0 is globally asymptotically stable if $R_0 < 1$ and unstable if $R_0 > 1$.*

Proof. To establish global stability of the disease free equilibrium point P_0 when $R_0 < 1$, we employ the comparison approach by (Diekmann *et al.*, 1990). Here, we consider the variables representing the infected components and their rates of change. It follows that at disease free equilibrium point P_0 , $I_1 = I_2 = I_3 = 0$ thus

$$(22) \quad \begin{bmatrix} \frac{dI_1(t)}{dt} \\ \frac{dI_2(t)}{dt} \\ \frac{dI_3(t)}{dt} \\ \frac{dE(t)}{dt} \end{bmatrix} = (F - V) \begin{bmatrix} I_1(t) \\ I_2(t) \\ I_3(t) \\ E(t) \end{bmatrix}$$

$$- \begin{bmatrix} v_1 E \left(\frac{(1-\rho)\Lambda}{\mu K} + \frac{\beta}{\mu} \frac{\phi \tau_2}{(\beta+\mu)} \frac{\eta \tau_1}{((1-\phi)\kappa_2 + \phi \tau_2 + \mu)} \frac{\rho \Lambda}{((1-\eta)\kappa_1 + \eta \tau_1 + \mu)} - \frac{S_1}{K+E} \right) \\ v_2 E \left(\frac{(1-\eta)\kappa_1}{\mu K} \frac{\rho \Lambda}{((1-\eta)\kappa_1 + \eta \tau_1 + \mu)} - \frac{S_2}{K+E} \right) \\ v_3 E \left(\frac{(1-\phi)\kappa_2}{\mu K} \frac{\eta \tau_1}{((1-\phi)\kappa_2 + \phi \tau_2 + \mu)} \frac{\rho \Lambda}{((1-\eta)\kappa_1 + \eta \tau_1 + \mu)} - \frac{S_3}{K+E} \right) \\ 0 \end{bmatrix},$$

where the matrices F and V are defined in equations (15) and (16) respectively.

At disease free equilibrium point $S_1 \leq \left(\frac{(1-\rho)\Lambda}{\mu} + \frac{\beta}{\mu} \frac{\phi \tau_2}{(\beta+\mu)} \frac{\eta \tau_1}{((1-\phi)\kappa_2 + \phi \tau_2 + \mu)} \frac{\rho \Lambda}{((1-\eta)\kappa_1 + \eta \tau_1 + \mu)} \right)$ which implies $\frac{S_1}{K+E} \leq \left(\frac{(1-\rho)\Lambda}{\mu} + \frac{\beta}{\mu} \frac{\phi \tau_2}{(\beta+\mu)} \frac{\eta \tau_1}{((1-\phi)\kappa_2 + \phi \tau_2 + \mu)} \frac{\rho \Lambda}{((1-\eta)\kappa_1 + \eta \tau_1 + \mu)} \right)$ for all $t \geq 0$.

Similarly, $S_2 \leq \frac{(1-\eta)\kappa_1}{\mu} \frac{\rho \Lambda}{((1-\eta)\kappa_1 + \eta \tau_1 + \mu)}$ which implies $\frac{S_2}{K+E} \leq \frac{(1-\eta)\kappa_1}{\mu} \frac{\rho \Lambda}{((1-\eta)\kappa_1 + \eta \tau_1 + \mu)}$. Again

$S_3 \leq \frac{(1-\phi)\tau_2}{\mu} \frac{\eta \tau_1}{(\tau_2 + \mu)} \frac{\rho \Lambda}{(\tau_1 + \mu)}$, which implies $\frac{S_3}{K+E} \leq \frac{(1-\phi)\tau_2}{\mu} \frac{\eta \tau_1}{(\tau_2 + \mu)} \frac{\rho \Lambda}{(\tau_1 + \mu)}$ for all $t \geq 0$ in Ω .

Therefore

$$(23) \quad \begin{bmatrix} \frac{dI_1(t)}{dt} \\ \frac{dI_2(t)}{dt} \\ \frac{dI_3(t)}{dt} \\ \frac{dE(t)}{dt} \end{bmatrix} \leq (F - V) \begin{bmatrix} I_1(t) \\ I_2(t) \\ I_3(t) \\ E(t) \end{bmatrix}$$

Since all the eigenvalues of the matrix $(F - V)$ have negative real parts, it implies that the (23) is stable if $R_0 < 1$ and as $t \rightarrow \infty$, we will have $I_1 \rightarrow 0$, $I_2 \rightarrow 0$, $I_3 \rightarrow 0$, and $E \rightarrow 0$. Therefore by comparison theorem in Lakshmikantham *et al.* (1989), it follows that $(I_1, I_2, I_3, E) \rightarrow (0, 0, 0, 0)$ and the three remaining equations of model system (1) gives us

$$S_1 = \left(\frac{(1-\rho)\Lambda}{\mu} + \frac{\beta}{\mu} \frac{\phi \tau_2}{(\beta+\mu)} \frac{\eta \tau_1}{((1-\phi)\kappa_2 + \phi \tau_2 + \mu)} \frac{\rho \Lambda}{((1-\eta)\kappa_1 + \eta \tau_1 + \mu)} \right), S_2 = \frac{(1-\eta)\kappa_1}{\mu} \frac{\rho \Lambda}{((1-\eta)\kappa_1 + \eta \tau_1 + \mu)} \text{ and}$$

$$S_3 = \frac{(1-\phi)\tau_2}{\mu} \frac{\eta \tau_1}{(\tau_2 + \mu)} \frac{\rho \Lambda}{(\tau_1 + \mu)} \text{ whenever } I_1 = I_2 = I_3 = E = 0.$$

Thus $(S_1, V_1, S_2, V_2, V_3, S_3, I_1, I_2, I_3, R, E) \rightarrow P_0$ as $t \rightarrow \infty$ for $R_0 < 1$, so P_0 is globally asymptotically stable. Hence the following theorem holds.

2.3. Existence and Stability of the Endemic Equilibrium Point with Treatment and Vaccination, P^*

The endemic equilibrium point with treatment and vaccination, P^* , is obtained by setting our model system (1) to zero. This is done by expressing all our state variables in terms of the force of infection, $\psi^*(S_1^*, S_2^*, S_3^*, E^*, I_1^*, I_2^*, I_3^*)$. We note that the force of infection is defined as

$$(24) \quad \psi^*(S_1^*, S_2^*, S_3^*, E^*, I_1^*, I_2^*, I_3^*) = \left(\varepsilon_i S_i \sum_j^3 (\theta_j I_j) + \frac{v_i S_i E}{K + E} \right), \quad i = 1, 2, 3.$$

thus $\psi^*(S_1^*, S_2^*, S_3^*, E^*, I_1^*, I_2^*, I_3^*) = \psi_1^* + \psi_2^* + \psi_3^*$, where

$$(25) \quad \psi_1^* = \left(\varepsilon_1 S_1^* (\theta_1 I_1^* + \theta_2 I_2^* + \theta_3 I_3^*) + \frac{v_1 S_1^* E^*}{K + E^*} \right)$$

$$(26) \quad \psi_2^* = \left(\varepsilon_2 S_2^* (\theta_1 I_1^* + \theta_2 I_2^* + \theta_3 I_3^*) + \frac{v_2 S_2^* E^*}{K + E^*} \right)$$

$$(27) \quad \psi_3^* = \left(\varepsilon_3 S_3^* (\theta_1 I_1^* + \theta_2 I_2^* + \theta_3 I_3^*) + \frac{v_3 S_3^* E^*}{K + E^*} \right)$$

After computation, we get the following expressions:

$$(28) \quad \begin{aligned} S_1^* &= \frac{1}{\mu} [(1 - \rho)\Lambda - \psi_1^* + \varepsilon_4 R^* + \beta V_3^*] \\ V_1^* &= \frac{\rho\Lambda}{((1 - \eta)\kappa_1 + \eta\tau_1 + \mu)} \\ S_2^* &= \frac{(1 - \eta)\kappa_1}{\mu} \frac{\rho\Lambda}{((1 - \eta)\kappa_1 + \eta\tau_1 + \mu)} - \frac{\psi_2^*}{\mu} \\ V_2^* &= \frac{\eta\tau_1}{((1 - \phi)\kappa_2 + \phi\tau_2 + \mu)} \frac{\rho\Lambda}{((1 - \eta)\kappa_1 + \eta\tau_1 + \mu)} \\ V_3^* &= \frac{\phi\tau_2}{(\beta + \mu)} \frac{\eta\tau_1}{((1 - \phi)\kappa_2 + \phi\tau_2 + \mu)} \frac{\rho\Lambda}{((1 - \eta)\kappa_1 + \eta\tau_1 + \mu)} \\ S_3^* &= \frac{(1 - \phi)\kappa_2}{\mu} \frac{\eta\tau_1}{((1 - \phi)\kappa_2 + \phi\tau_2 + \mu)} \frac{\rho\Lambda}{((1 - \eta)\kappa_1 + \eta\tau_1 + \mu)} - \frac{\psi_3^*}{\mu} \\ I_1^* &= \frac{\psi_1^*}{\xi_1} \\ I_2^* &= \frac{\psi_2^*}{\xi_2} \\ I_3^* &= \frac{\psi_3^*}{\xi_3} \\ T^* &= \frac{\left(\omega_1 r \frac{\psi_1^*}{\xi_1} + \omega_2 a \frac{\psi_2^*}{\xi_2} + \omega_3 b \frac{\psi_3^*}{\xi_3} \right)}{(\alpha_4 + \mu)} \\ R^* &= \frac{\alpha_1 (1 - r) \frac{\psi_1^*}{\xi_1} + \alpha_2 (1 - a) \frac{\psi_2^*}{\xi_2} + \alpha_3 (1 - b) \frac{\psi_3^*}{\xi_3} + \alpha_4 T^*}{(\mu + \varepsilon_4)} \\ E^* &= \frac{\left(\sigma_1 \frac{\psi_1^*}{\xi_1} + \sigma_2 \frac{\psi_2^*}{\xi_2} + \sigma_3 \frac{\psi_3^*}{\xi_3} \right)}{(\mu_1 - \gamma)} \end{aligned}$$

Recall that: $\xi_1 = (\alpha_1(1 - r) + \omega_1 r + (\mu + d_1))$, $\xi_2 = (\alpha_2(1 - a) + \omega_2 a + (\mu + d_2))$,

and $\xi_3 = (\alpha_3(1 - b) + \omega_3 b + (\mu + d_3))$.

To establish the existence and stability of the endemic equilibrium point with treatment and vaccination, P^* , of (1), we will examine only two cases, that is, with treatment and first dose of vaccination and with treatment and second dose of vaccination since the methods is the same for others.

2.3.1. Case one: Endemic Equilibrium Point with Treatment and First Dose of Vaccination, R_{1TV}

The endemic equilibrium point with treatment and first dose of vaccination, P_{1TV} , will be obtained when $\psi_1^* = \psi_3^* = 0$. This is because ψ_1^* is the force of transmission without treatment and vaccination. And ψ_3^* is the force of transmission under treatment and second dose of vaccination.

This means that (24) will be reduced to (25), that is,

$$\psi_2^* = \varepsilon_2 S_2^* (\theta_2 I_2^*) + \frac{v_2 S_2^* E^*}{K + E^*}$$

substituting the expressions for S_2^* , I_2^* , and E^* from (28), the endemic equilibrium satisfy the following equation

$$(29) \quad \psi_2^* f(\psi_2^*) = \psi_2^* (A \psi_2^{*2} + B \psi_2^* + C) = 0$$

where

$$A = \varepsilon_2 \theta_2 \sigma_2$$

$$B = \mu \xi_2 \sigma_2 - (\mu \varepsilon_2 \sigma_2 S_2 \sigma_2 - \varepsilon_2 \theta_2 K \xi_2 (\mu_1 - \gamma) - \mu \xi_2 v_2 \sigma_2)$$

$$S_2 = \frac{(1 - \eta) \kappa_1}{\mu} \frac{\rho \Lambda}{((1 - \eta) \kappa_1 + \eta \tau_1 + \mu)}$$

$$C = \mu \xi_2 K \xi_2 (\mu_1 - \gamma) - (\mu \varepsilon_2 \theta_2 S_2 K \xi_2 (\mu_1 - \gamma) + \mu \xi_2 v_2 S_2 \sigma_2)$$

C can further be reduced to $1 - R_{1TV}$ as follows:

$$\begin{aligned}
 C &= \mu \xi_2 K \xi_2 (\mu_1 - \gamma) - (\mu \varepsilon_2 \theta_2 S_2 K \xi_2 (\mu_1 - \gamma) + \mu \xi_2 v_2 S_2 \sigma_2) \\
 &= 1 - \left(\frac{\varepsilon_2 \theta_2 S_2}{\xi_2} + \frac{v_2 \sigma_2 S_2}{K \xi_2 (\mu_1 - \gamma)} \right) \\
 &= 1 - \frac{S_2}{\xi_2} \left(\varepsilon_2 \theta_2 + \frac{v_2 \sigma_2}{K (\mu_1 - \gamma)} \right) \\
 &= 1 - \frac{(1 - \eta) \kappa_1}{(\alpha_2 (1 - a) + \omega_2 a + (\mu + d)) \mu} \frac{\rho \Lambda}{((1 - \eta) \kappa_1 + \eta \tau_1 + \mu)} \left(\varepsilon_2 \theta_2 + \frac{v_2 \sigma_2}{K (\mu_1 - \gamma)} \right) \\
 &= 1 - R_{1TV}
 \end{aligned}$$

Solutions of (29) are $\psi_2^* = 0$ and $f(\psi_2^*) = 0$. $\psi_2^* = 0$ corresponds to disease free equilibrium point (DFE) whose stability has been established under subsection 2.2.2 and $f(\psi_2^*) = 0$ corresponds to a situation when the disease persists (endemic). In case of backward bifurcation, multiple endemic equilibrium must exist. This implies that equation (29) indicates that there are three cases we have to consider of $f(\psi_2^*) = 0$ depending on the signs of B and C since A is always positive. That is,

- (1) If $B < 0$ and $C = 0$ or $B^2 - 4AC = 0$, then equation (29) has a unique endemic equilibrium point (one positive root) and no backward bifurcation possibility.
- (2) If $C > 0$, $B > 0$ and $B^2 - 4AC > 0$, then equation (29) has two endemic equilibria (two positive roots), and therefore its possible for backward bifurcation to occur.

However its important to note that C is always positive if $R_{1TV} < 1$ and negative if $R_{1TV} > 1$.

Theorem 2.3. *The rotavirus model with treatment and first dose of vaccination has,*

- (i) *Precisely one unique endemic equilibrium if $C < 0 \iff R_{1TV} > 1$.*
- (ii) *Precisely two endemic equilibrium if $C > 0$, $B < 0$ and $B^2 - 4AC > 0$.*

By this result, Theorem 2.3 gives a condition for existence of endemic equilibrium point with treatment and first dose of vaccination.

Theorem 2.4. *The endemic equilibrium P_{1TV} , with treatment and first dose of vaccination exists if and only if $R_{1TV} > 1$.*

2.3.2. Case two: Endemic Equilibrium Point with Treatment and Second Dose of Vaccination, R_{2TV}

The endemic equilibrium point with treatment and second dose of vaccination, P_{2TV} will be obtained when $\psi_1^* = \psi_2^* = 0$. This is because ψ_1^* is the force of transmission without treatment and vaccination. And ψ_2^* is the force of transmission under treatment and first dose of vaccination. This means that (24) is reduced to (27), that is,

$$\psi_3^* = \varepsilon_3 S_3^* (\theta_3 I_3^*) + \frac{v_3 S_3^* E^*}{K + E^*}$$

substituting the expressions for S_3^* , I_3^* , and E^* from (28), the endemic equilibrium satisfy the following equation

$$(30) \quad \psi_3^* f(\psi_3^*) = \psi_3^* (A \psi_3^{*2} + B \psi_3^* + C) = 0$$

where

$$\begin{aligned} A &= \varepsilon_3 \theta_3 \sigma_3 \\ B &= \mu \xi_3 \sigma_3 - (\mu \varepsilon_3 \sigma_3 S_3 \sigma_3 - \varepsilon_3 \theta_3 K \xi_3 (\mu_1 - \gamma) - \mu \xi_3 v_3 \sigma_3) \\ S_3 &= \frac{(1 - \phi) \kappa_2}{\mu} \frac{\eta \tau_1}{((1 - \phi) \kappa_2 + \phi \tau_2 + \mu)} \frac{\rho \Lambda}{((1 - \eta) \kappa_1 + \eta \tau_1 + \mu)} \\ C &= \mu \xi_3 K \xi_3 (\mu_1 - \gamma) - (\mu \varepsilon_3 \theta_3 S_3 K \xi_3 (\mu_1 - \gamma) + \mu \xi_3 v_2 S_3 \sigma_3) \end{aligned}$$

C can further be reduced to $1 - R_{2TV}$ as follows:

$$\begin{aligned} C &= 1 - \left(\frac{\varepsilon_3 \theta_3 S_3}{\xi_3} + \frac{v_3 \sigma_3 S_3}{K \xi_3 (\mu_1 - \gamma)} \right) \\ &= 1 - \frac{S_3}{\xi_3} \left(\varepsilon_3 \theta_3 + \frac{v_3 \sigma_3}{K (\mu_1 - \gamma)} \right) \\ &= 1 - R_{2TV} \end{aligned}$$

Applying the same procedure used in analysing (29) to (30), we note that C is always positive if $R_{2TV} < 1$ and negative if $R_{2TV} > 1$. Thus Theorem 2.5.

Theorem 2.5. *The rotavirus model with treatment and second dose of vaccination has,*

- (i) *Precisely one unique endemic equilibrium if $C < 0 \iff R_{2TV} > 1$.*

- (ii) *Precisely two endemic equilibrium if $C > 0$, $B < 0$ and $B^2 - 4AC > 0$.*
- (iii) *None otherwise.*

Depending on this result, Theorem 2.5 gives a condition for existence of endemic equilibrium point with treatment and second dose of vaccination as stated.

Theorem 2.6. *The endemic equilibrium P_{2TV} , with treatment and second dose of vaccination exists if and only if $R_{2TV} > 1$.*

We note that the endemic equilibrium point with treatment, R_T and endemic equilibrium point with treatment and third dose of Vaccination, R_{3TV} , uses the same procedure as above. Thus Theorem 2.7 holds.

Theorem 2.7. *The endemic equilibrium P^* , with treatment and vaccination exists if and only if $R_e > 1$.*

3. Numerical Results and Discussion

Here, we verify some of the analytical results of the model (1) numerically. The values of the parameters used are mainly from literature as well as assumptions. Some of the data used was obtained from different hospitals of Kampala District and depict the Ugandan situation. We simulated the model using both Matlab ODE solvers and R programming language. The following initial conditions were considered:

$$S_1(0) = 10000, V_1(0) = 5000, S_2(0) = 4000, V_2(0) = 1500, V_3(0) = 500,$$

$$S_3(0) = 3000, I_1(0) = 100, I_2(0) = 50, I_3(0) = 10, T(0) = 0, R(0) = 0 \text{ and } E(0) = 0.$$

Tables 1 and 2 shows the description of parameters and corresponding values used in the simulation of the model (1).

3.1. Impact of treatment

Table 1 : Parameters of the model (1)

Parameters	Description	Value	Source
ρ	proportion of vaccinated	0.4	Assumed
Λ	per capital birth rate	0.0018 per day	[40]
ε_1	degree of susceptibility between S_1 & I_i	0.0002	Assumed
ε_2	degree of susceptibility between S_2 & I_i	0.0002	[29]
ε_3	degree of susceptibility between S_3 & I_i	0.0001	[20,26]
θ_1	degree of infectiousness between S_1 & I_i	0.5	Assumed
θ_2	degree of infectiousness between S_2 & I_i	0.4	Assumed
θ_3	degree of infectiousness between S_3 & I_i	0.1	Assumed
ν_1	degree of susceptibility between S_1 & E	0.002	[13, 29]
ν_2	degree of susceptibility between S_2 & E	0.001	[21, 29]
ν_3	degree of susceptibility between S_3 & E	0.001	[13, 38]
ε_4	natural immunity waning rate	0.0027 per day	[32, 35]
μ	natural per capital death rate	0.0018 per day	[40]
β	vaccine waning rate	0.01667 per day	[25, 26, 47]
σ_1	shedding rate of I_1	10 – 100 $cellsL^{-1}$	[4, 12]
σ_2	shedding rate of I_2	5 – 100 $cellsL^{-1}$	[27, 30]
σ_3	shedding rate of I_3	0 – 100 $cellsL^{-1}$	[4,38]
τ_1	rate of second dose vaccination	0.0059 per day	Assumed
τ_2	rate of third dose of vaccination	0.0018 per day	Assumed
K	pathogen concentration	10000 $cellsL^{-1}$	[32]
γ	pathogen contribution from environment	0.0001 per day	[27]
d_1	death rate due to rotavirus from I_1	0.00004466 per day	[31]
d_2	death rate due to rotavirus from I_2	0.000004466 per day	Assumed
d_3	death rate due to rotavirus from I_3	0.0000004466 per day	Assumed
μ_1	rotavirus pathogen death rate	0.0667 per day	[32]

Table 2 : Parameters of the model (1)

Parameters	Description	Value	Source
α_1	recovery rate from I_1	0.2 per day	[30, 31]
α_2	recovery rate from I_2	0.5 per day	[30, 31]
α_3	recovery rate from I_3	0.9091 per day	[30, 31]
ω_1	treatment rate of I_1	0.2554 per day	Assumed
ω_2	treatment rate of I_1	0.1783 per day	Assumed
ω_3	treatment rate of I_1	0.1116 per day	Assumed
r	proportion of I_1 treated	0.4	Assumed
a	proportion of I_2 treated	0.3	Assumed
b	proportion of I_3 treated	0.2	Assumed
α_4	recovery rate of treated	0.5 per day	[12,31]
κ_1	progression rate from V_1 to S_2	0.0201 per day	Assumed
κ_2	progression rate from V_2 to S_2	0.0384 per day	Assumed
η	proportion of vaccinated for second dose	0.3	Assumed
ϕ	proportion of vaccinated for third dose	0.1	Assumed

Here, we consider the unvaccinated group S_1I_1TRE to show the impact of treatment on the infected class and the indirect effect of treatment on the environment in an attempt to understand the dynamics of rotavirus disease.

3.1.1. Impact of treatment on infected class

Figure 2 (a) shows the population of infected children with rotavirus disease with no treatment to be very high. However when the treatment is considered, Figure 2 (b), we see a decline in the infected population. We use different treatment rates for different coverages. When $\omega_1 = 0.2554$, our treatment coverage is 40% of the infected children, $\omega_1 = 0.34567$ our treatment coverage is 50% of the infected children. Similarly $\omega_1 = 0.4581$ (60%) and $\omega_1 = 0.6020$ (70%). This implies that as more infected children are treated, this decreases the level of infection hence reduction in spread of rotavirus disease.

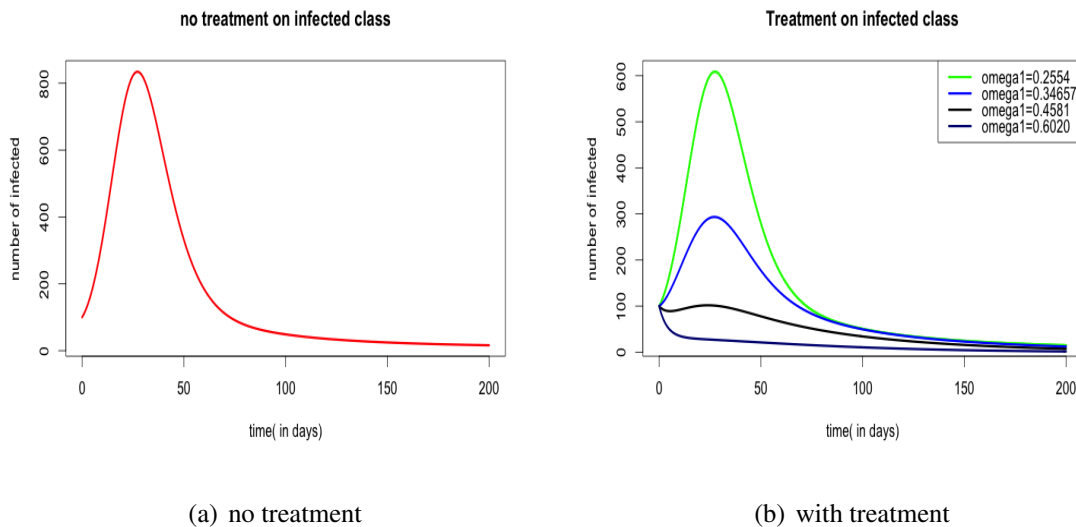


FIGURE 2. A plot represents the effects of no treatment and treatment on the infected class (I_1).

3.1.2. Indirect impact of treatment on environment class

Figure 3 (a) shows a high number of pathogens within the environment. This is due to the fact that, in presence of rotavirus disease, there is high shedding rate from infected children, pathogen growth from infected environment, for example, unhygienic/contaminated water contribute. In the presence of treated individuals, there shedding rate is low or there no shedding from infected individuals and this indirectly reduces the pathogen growth from environment as seen in Figure 3 (b). Thus high treatment coverage reduces indirectly the spread of rotavirus infection from the environment.

3.2. Both treatment and vaccination

Under this Section, we numerically understand the effect of both treatment and vaccination on the transmission dynamics of rotavirus disease.

3.2.1. Presence of treatment and indirect impact of vaccination on infected class

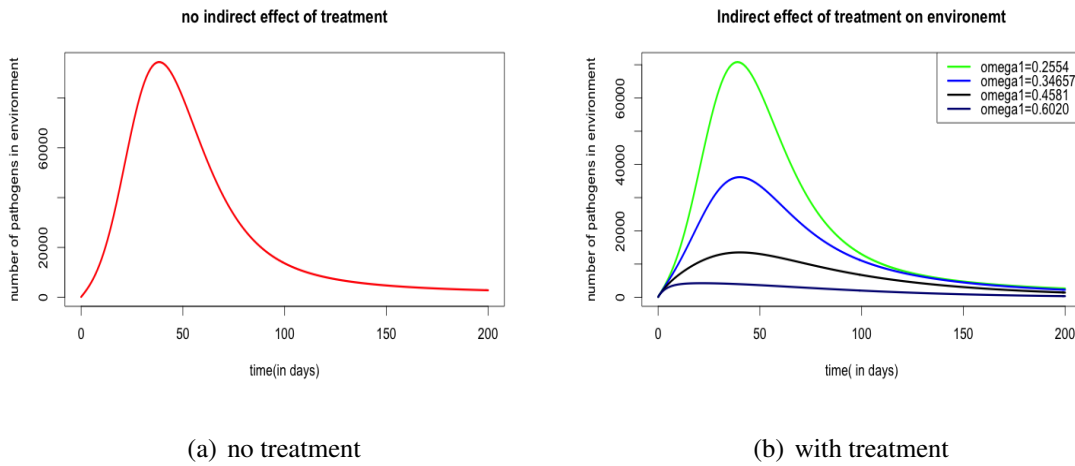


FIGURE 3. A plot represents the effects of no treatment and indirect impact of treatment on the environment class (E).

Figure 4: Shows the indirect impact of vaccination on the infected children as well as the direct impact of treatment. We note that in the presence of no treatment and vaccination the infected number of children is very high, but after first dose of vaccination and treatment, the infected levels decrease to much more low levels. And when a second dose of vaccination is administered with treatment, the number of infected children even decrease more compare to first dose vaccination and treatment. This trend predicts that in the presence of third vaccination and treatment, the rotavirus infection will even decrease to almost few or low endemic state. Thus both controls can help in the reduction of rotavirus disease among children.

3.3. Stucture of vaccination of different doses

Figure 5: Shows the frequency of children vaccinated for rotavirus disease. Since the vaccine is a repeated dose, many children are vaccinated for the first dose only, almost 50%, and only 30% of children who took the first dose of vaccination take the second dose and of these only 10% of children take the third dose. This confirms with the data we collected, due to the fact that the vaccination is very expensive only certain class of parents (of good economic status) can afford to take their children for all the three doses of vaccination.

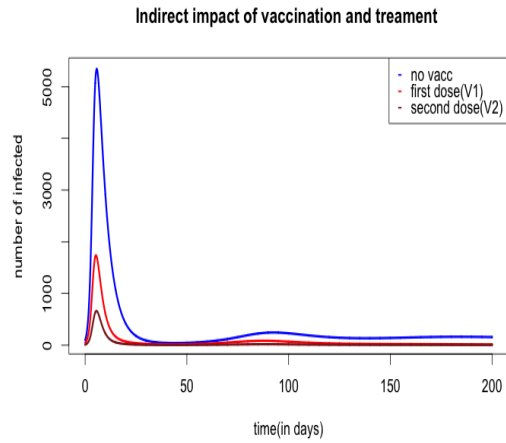


FIGURE 4. indirect impact of vaccination with two doses with the presence of treatment on the infected class.

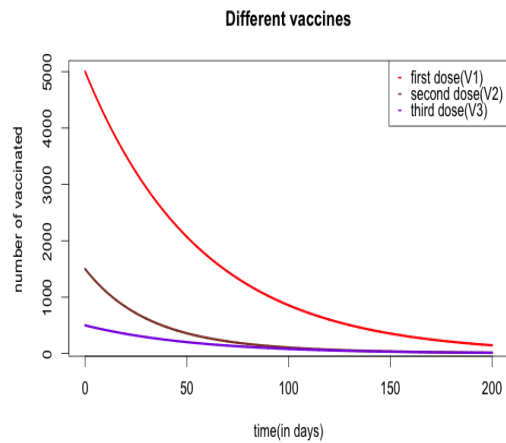


FIGURE 5. structure of vaccination of different doses.

3.4. Effect of vaccination on susceptibles.

Figure 6: Shows the impact of vaccination on the susceptible classes, S_1, S_2, S_3 . S_1 is the class of the unvaccinated susceptible and we note that in this class, because of no vaccination a lot of children are susceptible to rotavirus and they quickly leave this class to join I_1 . S_2 represents susceptible children who are vaccinated for the first dose. We note that, in the presence of vaccination, the degree of susceptibility is low compared to S_1 where there is no vaccination.

And in case a second dose is taken, we still note that, the degree of being less susceptible is even more lower than when only one dose is taken. Thus vaccination can help to reduce the number of susceptible children from being exposed to rotavirus disease hence reduction in infection.

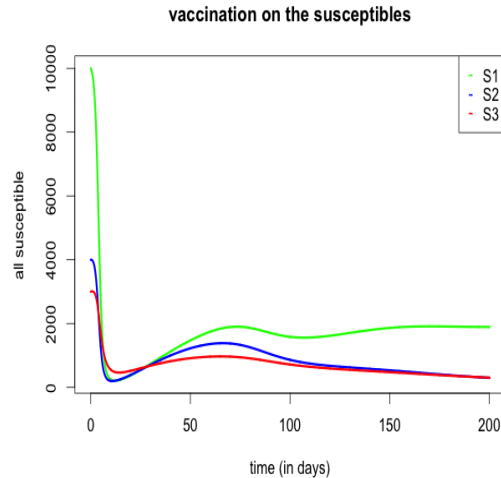


FIGURE 6. Impact of vaccination on the different susceptible classes

4. Conclusions

The rotavirus model with treatment and vaccination have been formulated with the aim of assessing the impact of treatment and vaccination on the disease. Existence and stability of the steady points have been computed. Four cases were taken into consideration during the analysis: treatment with first dose of vaccination, treatment with the second dose of vaccination, treatment only and finally when both interventions are considered.

It has been shown that the disease free equilibrium point is both locally asymptotically stable and globally stable. Existence of the endemic equilibrium point was established in relation to the two cases, that is, with treatment and first dose of vaccination and with treatment and second dose of vaccination.

Results showed that, in all cases the endemic equilibrium point exists whenever $R_{1TV} > 1$, $R_{2TV} > 1$, $R_{3TV} > 1$, $R_T > 1$ and $R_e > 1$. This study recommends to either use treatment or vaccination or both in the fight of rotavirus disease as well as further research using age

structured models to study the impact of vaccination at different ages, that is, 2 months, 4 months and 6 months.

Conflict of Interests

The authors declare that there is no conflict of interests.

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