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Study of Disease Dynamics of Co-infection of Rotavirus and Malaria with Control Strategies

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Abstract

This paper proposes a model that addresses the interaction and dynamics of malaria and rotavirus co-infection. The model incorporates various epidemiological and biological features of both the malaria and rotavirus. The mode of transmission of both the diseases is different as malaria is vector borne disease causing infection through infected arthropod and rotavirus is a contagious virus causing diarrhoea by the inflammation of intestines and stomach. It is being assumed in the model that humans are susceptible to malaria and rotavirus simultaneously. It is further assumed that the recovered population, whether naturally or through treatment is prone to the infection again. The co-infection dynamics of diseases is studied with different control measures in the form of treatments to both human and vector compartments. In order to visualize the effect of diverse control strategies, we studied three models, that is, one, in the absence of malaria disease, second, in the absence of rotavirus disease and third, for co-infection of both the diseases. To understand the dynamics of co-infection, the stability analysis of the full model for disease-free equilibrium and the threshold value, which is, the basic reproduction number is calculated. Bifurcation analysis is performed for full co-infection model along with that of malaria-only model. Both rotavirus-only model and malaria-only models are found to be globally asymptotically stable at disease-free equilibrium. Sensitivity indices have been calculated to study the effect of model parameters on the basic reproduction number. Results are illustrated with numerical simulation.

Keywords: malaria-rotavirus; stability analysis; next generation matrix; control measures; co-infection; basic reproduction number.

1 Introduction

There are various infections that may infect a host ([16], [17]) and that may altogether. There are many examples of them involving HIV and TB [37], HIV and hepatitis B [14], malaria and HIV [22], malaria and rotavirus [29], chikungunya and dengue, HIV-HBV co-infection [36] and many more ([18], [33]). Moreover, this infection may occur with different serotypes or various strains of same virus. Simultaneous infections may also occur even when it seems that there is no synergy between the two agents affecting the person. This dynamics of co-infection is important to study as the treatment of one infection affects the dynamics of the other infection. Disease, poverty, sanitation, health care, nutrition, access to facilities are various factors accountable for killing people with these infectious agents.

Malaria and rotavirus co-infection is the cause of big burden of public health worldwide. The co-infection with malaria is typically difficult to understand and diagnose as the main species responsible for it is Plasmodium falciparum which is unicellular protozoan parasite infecting humans and it is the lethal species of Plasmodium causing malaria in humans. The main mosquito species responsible for malaria are *Plasmodium ovale, Plasmodium vivax, Plasmodium malariae and Plasmodium falciparum* but *P. falciparum* is most fatal to human kind. *P. falciparum* can cause asymptomatic infections, chronic and sometimes repeated acute infection. Generally, an individual acquires a degree of immunity but if a febrile individual is co-infected with any other potential pathogen, it is hard to diagnose that *P. falciparum* is the sole cause of illness. It is the most important disease in the tropical regions with around 40% of world total population exposed to malaria in around 100 countries, it is a major health problem globally [41]. Its symptoms include severe headache, vomiting, nausea, fever, back pains, sweating and chills ([39], [45]). Malaria is responsible for about $700,00 - 2.7$ million causalities every year out of which 75% are African children under age of five years [7]. It is responsible for 30% of OPD, 19% of admissions to hospitals for various diseases and around 20% of deaths in children having age less than five years as seen in Kenya ([9], [46]). Prevention of malaria can be done through insect repellents, mosquito bed nets, draining of dirty water and spray of chemical insecticides etc. Many researchers have done a lot of work in the field of controlling the disease with different control measures.

On the other hand, the other infectious disease under study is rotavirus which is the most prevalent pathogen accountable for diarrhea among children [26]. It is transferred through fecal-oral route when person gets in contact with contaminated water, surface or object. It can also be transferred by respiratory route. Rotavirus causes severe infection of gastrointestinal tract and diarrhea in young children. It is the second main cause of mortality for children under five years [25]. Around the world, diarrhea claims $760,000$ deaths in children every year [29]. Over 2.5% of admissions to hospitals are because of rotavirus. It has been diagnosed clinically that 38% of the children gets protected against any rotavirus infection after first natural infection [30]. It has been observed that various factors associated with rotavirus infection are seasonality, breast feeding [5], hygiene, sanitation etc. [38]. The authors further probed by estimating number of deaths due to rotavirus infection for England and Wales. The data from Office for National Statistics of Deaths in children was taken into consideration. It was observed that there were 3.8 and 3.2 deaths due to rotavirus yearly when calculated by two different methods [15]. Further, the study was highlighted by understanding the effectiveness of vaccine for rotavirus on children with age less than 2 years in El Salvador [8]. It was concluded in [21] that vaccine efficacy gets reduced in low socio-economic settings population. The research was taken to the next level by Bishop et al. [4] in which clinical immunity after neonatal rotavirus infection was discussed. It was observed that it does not make children immune against reinfection but it protects them against clinically severe disease. Water and sanitation improvements, management of oral rehydration solution and vaccines were suggested as control measures by Mulholland et al. [23].

It was further observed that in Northern Ghana, rotavirus is the major cause in children of acute diarrhea. It was supported by a study conducted at Bulpeila health centre, that 15% of children with uncomplicated malaria has diarrhea. In Ghana, it was found that 11.8% of the total number of 243 children were tested co-infected with *P. falciparum* and enteropathogens, where in more than half of the infected persons rotavirus was common enteropathogen [34]. The study was further taken ahead by co-infection model for rotavirus and malaria by [29]. The work was progressed by another co-infection model for rotavirus and malaria developed by authors of [27]. In the work, effect of vaccination for rotavirus disease on co-infection dynamics was explored. It was further done by making SIR model for host (human) and SI model for vector (mosquito) for malaria disease with control measure as vaccination only for rotavirus. The effect of rotavirus vaccination on malaria and rotavirus co-infection was explored. It was found that rotavirus only model was globally asymptotically stable where co-infection model exhibits backward bifurcation. Further, it was concluded that rotavirus vaccination helps reduce co-infection.

A mathematical model on co-infection of malaria and cholera has been formulated and analyzed by [28]. The co-infection model was found to exhibit backward bifurcation. It was concluded that malaria infection can increase the risk of cholera but cholera infection does not accelerate risk of malaria. The impact of treatment of malaria on the dynamics of the infection of cholera has also been elaborately discussed. The work on co-infection of diseases has been taken to next level by researchers in [35] in which the conditions of optimal control for the co-infection of HIV-malaria are analyzed. Analysis of sub-models shows that malaria only model exhibits backward bifurcation. It was concluded that for optimal control of HIV-malaria, preventive control measures are the best form of strategy. To minimize the infection and cost associated with control measures, a dynamic model for the co-infection of measles and dysentery has been formulated and analyzed by Berhe et al. [3]. The controls like vaccination, treatment and sanitation of surroundings have been included. Further, the cost effectiveness analysis has been done using cost effectiveness ratio. Taking the work to next level, Tilahun et al. developed a mathematical model for Typhoid-Pneumonia co-infection [42]. Sensitivity index of the co-infection model and bifurcation analysis has been done to check the most sensitive parameters. It was concluded that Pneumonia treatment cost least with prevention of Typhoid fever. The necessary conditions for optimal control have been also derived along with an optimality system. A mathematical model on the co-infection of cancer and hepatitis has been formulated and studied by authors in [1].

Malaria and rotavirus models have been studied individually ([5], [38] and [41]) and some researchers have worked to calculate the key factor R_0. From the previous studies, it is quite clear that there are models that studied malaria-rotavirus co-infection ([27], [29]) but still there is scope in the field. In the work done by authors in [29], stability analysis of malaria-rotavirus co-infection model is done. Further, in the work done by [27], malaria-rotavirus co-infection is studied with treatment given only to rotavirus infected class.

The model developed in the present study represents co-infection dynamics of rotavirus and malaria disease that is complete enough to consider all the possible control measures not only on humans but also for mosquitoes responsible for the spread of malaria. Here, control measures are taken for rotavirus infected human population, malaria infected human population, co-infected human population and insecticide is taken as control measure for mosquito population. Taken together, these control measures gives a picture that is likely to produce better results of co-infection control.

2 Formulation and Description of the Model

We propose a model for co-infection of rotavirus and malaria with various control measures. Since, we are dealing with vector-host interaction, there are separate compartments for host and vector in the formulation of model. In the model, it is being assumed that a person can recover from malaria disease only, rotavirus disease only and also from the co-infection once co-infected with the diseases. It is also being assumed that all rotavirus recovered humans, malaria recovered humans and humans recovered from both the diseases are not permanently recovered. Therefore, they are susceptible to the diseases again. The total human population (N_h) is divided into different compartments namely susceptible class (S_h), class infected with rotavirus only (I_r), class infected with malaria only (I_m), class infected with both rotavirus and malaria (I_{mr}), only malaria recovered class (R_m), only rotavirus recovered class (R_r), malaria-rotavirus recovered or removed class (R_{mr}). Similarly, the total mosquito/vector population (N_v) is divided in two compartments namely susceptible vector (S_v) and infected vector (I_v).

In the model, A is the recruitment of susceptible human population and B is recruitment of susceptible mosquito population. It is being assumed that susceptible humans gets infected with malaria after the bite of malaria infected mosquito at biting rate a per day. So, susceptible person gets infection of malaria with a force $\lambda_m = \frac{abI_v}{N_h}$. Malaria infected individuals (I_m) recover naturally at a rate η_m and by treatment t_1. Malaria infected population gets reduced by disease death rate α_1 and natural death μ_h. Further, malaria recovered population become susceptible again at a rate β. Again, malaria is transmitted to susceptible vector population after coming in contact with malaria infected individual through biting. So, a susceptible mosquito gets infected at a rate $\lambda_v = \frac{ac(I_m+\theta_1 I_{mr})}{N_v}$. Mosquito population is reduced naturally at rate μ_v and by pesticide at a rate q. It is being assumed that there are no disease deaths in mosquitoes and also they do not recover from malaria once infected. So, there is no recovered compartment for mosquitoes.

Susceptible humans gets infected with rotavirus at a rate $\lambda_r = \frac{r(I_r+\theta_2 I_{mr})}{N_h}$ after coming in contact with rotavirus infectious human. Here, r is taken to be the effective contact rate of susceptible humans with rotavirus infected humans. Rotavirus infected population is decreased by natural recovery rate η_r and through treatment at rate t_2. It is also dwindled by disease death with rate α_2 and natural death rate μ_h. Here θ_2 models that humans co-infected with malaria-rotavirus both are more infectious than only-rotavirus infected [11]. Malaria infected individuals gets infected with rotavirus at rate $\delta\lambda_r$ and gets transferred to co-infected compartment. The parameter $\delta > 1$ is for increased susceptibility of individual getting infected with rotavirus than those who already have malaria. According to the authors in [2], there are chances of co-infection as malaria causes immunosuppression especially in young children. In the same way, humans having rotavirus infection gets infected with malaria at rate $\xi\lambda_m$ shifting the individual to co-infected compartment I_{mr}. Again, $\xi > 1$ accounts for increased susceptibility of malaria infection in human having weak immune system due to rotavirus. Co-infected humans recover from rotavirus at rate α_r and gets transferred to malaria infected compartment. Similarly, co-infected individuals recover from malaria and gets transferred to rotavirus-only infected compartment at rate α_m.

2.1 Model equations

The model describes malaria-rotavirus co-infection with treatments for both malaria and rotavirus as control measures for humans and usage of insecticide for vector population to control

malaria. The model equations are given as:

$$\begin{aligned}
\dot{S_h}(t) &= A - (\lambda_m + \lambda_r + \mu_h)S_h + \beta R_m + \beta R_r + \beta R_{mr},\\
\dot{I_m}(t) &= \lambda_m S_h + \alpha_r I_{mr} - (\delta\lambda_r + \eta_m + t_1 + \alpha_1 + \mu_h)I_m,\\
\dot{I_r}(t) &= \lambda_r S_h + \alpha_m I_{mr} - (\xi\lambda_m + \eta_r + t_2 + \alpha_2 + \mu_h)I_r,\\
\dot{I_{mr}}(t) &= \delta\lambda_r I_m + \xi\lambda_m I_r - (\alpha_3 + \eta_{mr} + \alpha_r + \alpha_m + t_3 + \mu_h)I_{mr},\\
\dot{R_m}(t) &= (\eta_m + t_1)I_m - (\mu_h + \beta)R_m,\\
\dot{R_r}(t) &= (\eta_r + t_2)I_r - (\mu_h + \beta)R_r,\\
\dot{R_{mr}}(t) &= (\eta_{mr} + t_3)I_{mr} - (\mu_h + \beta)R_{rm},\\
\dot{S_v}(t) &= B - \lambda_v S_v - (\mu_v + q)S_v,\\
\dot{I_v}(t) &= \lambda_v S_v - (\mu_v + q)I_v.
\end{aligned} \tag{1}$$

With initial conditions as $S_h(0) > 0, I_m(0) > 0, I_r(0) > 0, I_{mr}(0) > 0, S_v(0) > 0, I_v(0) > 0$.

Here, the total population $N_h(t)$ and $N_v(t)$ satisfies

$$N_h(t) = S_h(t) + I_m(t) + I_r(t) + I_{mr}(t) + R_m(t) + R_r(t) + R_{mr}(t), N_v(t) = S_v(t) + I_v(t).$$

Upon adding the equations in (1) separately for humans and vectors, we get

$$\begin{aligned}
\dot{N_h} &= A - \mu_h N_h - \alpha_1 I_m - \alpha_2 I_r - \alpha_3 I_{mr},\\
\dot{N_v} &= B - \mu_v N_v - qN_v.
\end{aligned} \tag{2}$$

It is evident from equation (2), that when there is no disease in the population,

$$\dot{N_h} \leq A - \mu_h N_h.$$

After solving above equation and calculating as time approaches infinity, we have

$$\Omega_1 = \{(S_h, I_m, I_r, I_{mr}, R_m, R_r, R_{mr}, S_v, I_v) \in R_+^9 : 0 \leq N_h \leq \frac{A}{\mu_h}\}.$$

Similarly, for vector population, in case of no death due to insecticide

$$\dot{N_v} \leq B - \mu_v N_v.$$

After solving this equation as time tends to infinity, we get,

$$\Omega_2 = \{(S_v, I_v) \in R_+^2 : 0 \leq N_v \leq \frac{B}{\mu_v}\}.$$

The solution set of the system is bounded in $\Omega = \Omega_1 \times \Omega_2$.

2.2 Notations and parameters in the model

The terms used in the model are given in the tabular form below:

Table 1: Description of parameters.

Parameters	Description
r	Effective contact rate of susceptible human with rotavirus infected human
β	The rate at which recovered population becomes susceptible again
η_m	Natural recovery rates from malaria
η_r	Natural recovery rates from rotavirus
η_{mr}	Natural recovery rates from malaria-rotavirus both
t_1	Effective treatment control on malaria
t_2	Effective treatment control on rotavirus
t_3	Effective treatment control on malaria-rotavirus both
α_r	Rate at which co-infected recover from rotavirus and transfer to malaria infected
α_m	Rate at which co-infected recover from malaria and transfer to rotavirus infected
α_1	Disease deaths due to malaria
α_2	Disease deaths due to rotavirus
α_3	Disease deaths due to malaria and rotavirus both
a	The average bites by mosquito on humans
b	Transmission rates per bite from malaria infected mosquito to susceptible human
c	Transmission rates per bite from malaria infected human to susceptible vector
μ_h	Natural mortality rates of humans
μ_v	Natural mortality rates of mosquitoes
q	Mortality rate of mosquitoes due to insecticide
δ	For increase in human susceptible to rotavirus infection who is already malaria infected
ξ	Models increase in human susceptible to infection with malaria already infected with rotavirus
θ_1	For increase in probability of infection in vector from co-infected human [29]
θ_2	Models that co-infected are more contagious than that infected with only rotavirus [11]

*Table for parameters

Here,

$$\lambda_m = \frac{abI_v}{N_h}, \qquad \lambda_v = \frac{ac(I_m + \theta_1 I_{mr})}{N_v}, \qquad \lambda_r = \frac{r(I_r + \theta_2 I_{mr})}{N_h}.$$

3 Positivity and Boundedness of Solution of Co-infection Model

To perform the analysis of the model given by (1), it is very important to see the positivity and boundedness of the solutions of all variables involved in the model. As the model proposed is for dynamics of mosquito and human, it is being assumed that all the parameters taken in the model are positive.

Theorem 3.1. *With the initial conditions proposed in the model to lie in T, where*

$$T = \{(S_h, I_m, I_r, I_{mr}, R_m, R_r, R_{mr}, S_v, I_v) \in R_+^9 : S_h \geq 0, I_m \geq 0, I_r \geq 0, I_{mr} \geq 0, \\ R_m \geq 0, R_r \geq 0, R_{mr} \geq 0, S_v \geq 0, I_v \geq 0\}.$$

then there exists a unique solution for system of equations given by (1) and solution of above model remain in T for all time $t \geq 0$.

Proof. Taking the first equation of co-infection model (1),

$$\dot{S_h}(t) = A + \beta R_m + \beta R_r + \beta R_{mr} - (\lambda_m + \lambda_r + \mu_h)S_h,$$
$$\dot{S_h}(t) \geq -(\lambda_m + \lambda_r + \mu_h)S_h.$$

Integrating above equation with respect to t, we get

$$S_h(t) \geq S_h(0)e^{-\int(\lambda_m+\lambda_r+\mu_h)dt} \geq 0.$$

Since $\lambda_m + \lambda_r + \mu_h > 0$ and by the initial condition $S_h(0) > 0$. This implies that $S_h(t) > 0$.

Similarly, taking second equation of co-infection model (1),

$$\dot{I_m}(t) = \lambda_m S_h + \alpha_r I_{mr} - \delta\lambda_r I_m - \eta_m I_m - t_1 I_m - \alpha_1 I_m - \mu_h I_m,$$
$$\dot{I_m}(t) \geq -(\delta\lambda_r + \eta_m + t_1 + \alpha_1 + \mu_h)I_m.$$

Integrating above equation w.r.t to t, we get,

$$I_m(t) \geq I_m(0)e^{-\int(\delta\lambda_r+\eta_m+t_1+\alpha_1+\mu_h)dt} \geq 0.$$

Since $(\delta\lambda_r + \eta_m + t_1 + \alpha_1 + \mu_h) > 0$ and by the initial condition $I_m(0) > 0$. This implies $I_m(t) > 0$.

Similarly, $R_m(t) \geq 0 \, \forall \, t > 0$. Now, taking second last equation of co-infection model (1),

$$\dot{S_v}(t) = B - \lambda_v S_v - (\mu_v + q)S_v,$$
$$\dot{S_v}(t) \geq -(\lambda_v + q + \mu_v)S_v.$$

Integrating above equation w.r.t to t, we get,

$$S_v(t) \geq S_v(0)e^{-\int(\lambda_v+q+\mu_v)dt} \geq 0.$$

Since $(\lambda_v + q + \mu_v) > 0$ and by the initial conditions $S_v(0) > 0$. This implies that $S_v(t) > 0$. Similarly, we can prove that other variables are also positive and this proves the theorem. □

To proceed further, it is important to study and analyse the disease transmission of both the diseases individually. For this, we will study the co-infection model (1) in the absence of malaria disease (rotavirus model) and the same model in the absence of rotavirus (malaria model) separately. The individual models for both the diseases are given in the following section.

4 Models for Rotavirus and Malaria

We will study the individual models for rotavirus and malaria separately.

4.1 Model to study disease dynamics of rotavirus only

By excluding terms related to malaria from the co-infection model given by (1), the single rotavirus-only model is given by

$$\begin{aligned} \dot{S_h}(t) &= A - \lambda_r S_h - \mu_h S_h + \beta R_r, \\ \dot{I_r}(t) &= \lambda_r S_h - \eta_r I_r - t_2 I_r - \alpha_2 I_r - \mu_h I_r, \\ \dot{R_r}(t) &= \eta_r I_r + t_2 I_r - \mu_h R_r - \beta R_r. \end{aligned} \tag{3}$$

4.2 Model to study disease dynamics of malaria only

Leaving out the terms related to rotavirus in the co-infection model given by (1), we get malaria-only model

$$\begin{aligned} \dot{S_h}(t) &= A - \lambda_m S_h - \mu_h S_h + \beta R_m, \\ \dot{I_m}(t) &= \lambda_m S_h - \eta_m I_m - t_1 I_m - \alpha_1 I_m - \mu_h I_m, \\ \dot{R_m}(t) &= \eta_m I_m + t_1 I_m - \mu_h R_m - \beta R_m, \\ \dot{S_v}(t) &= B - \lambda_v S_v - (\mu_v + q) S_v, \\ \dot{I_v}(t) &= \lambda_v S_v - (\mu_v + q) I_v. \end{aligned} \tag{4}$$

In the next section, the analysis of the main model given by (1) will be studied by performing analysis of the two models given by equations (3) and (4).

4.3 Analysis of individual models

In this section, we analyse the individual models by calculating their disease-free equilibrium points, basic reproduction numbers and stability at these points.

4.3.1 Analysis of the model considering rotavirus disease only

First, we will start by calculating disease-free equilibrium of model (3) for rotavirus disease. Disease-free equilibrium of model dealing with rotavirus disease only is given by $E_{0r} = \left(\frac{A}{\mu_h}, 0, 0\right)$.

4.3.2 Basic reproduction number

The stability of disease-free equilibrium point of rotavirus-only model is checked by basic reproduction number. It is very important factor for dynamics of the model. It is defined as the total number of secondary infections produced by a single infective in a totally naive population. We apply next generation matrix method given by Driessche [43]. We separate the transition terms and transmission terms from the infected compartment. Here, all the new infections are taken in the matrix named F and all other transitions are taken in the matrix named V. Let $F = [r]$ and

$V = [-(\eta_r + t_2 + \mu_h + \alpha_2)]$. Then we calculate the matrix FV^{-1}. The spectral radius of the matrix FV^{-1} is denoted by R_0 and is called basic reproduction number. It is given by

$$R_0 = \rho(FV^{-1}).$$

$$R_{0r} = \frac{r}{\eta_r + t_2 + \mu_h + \alpha_2}, \tag{5}$$

here, $R_{0r} < 1$ implies that $r < \eta_r + t_2 + \mu_h + \alpha_2$, which means that effective contact rate of rotavirus from rotavirus infected human with susceptible human is less than total recovery rate (natural as well as with treatment) and death rate of human (natural death as well as disease death). This justifies the disease-free state that if transmission rate of any disease is less than its recovery, that disease will definitely die out .

In the upcoming sections, the local stability analysis and global stability analysis at disease-free equilibrium of rotavirus has been performed.

4.3.3 Local stability analysis of disease-free equilibrium of rotavirus model

The above result of disease-free equilibrium of rotavirus-only model can be written as:

Theorem 4.1. *The disease-free equilibrium of rotavirus-only model is locally asymptotically stable if* $R_{0r} < 1$ *and is unstable for* $R_{0r} > 1$.

Proof. We will find the stability conditions at disease-free equilibrium by calculating the variational matrix. The condition for stability of DFE is attained by applying Routh-Hurwitz criteria for stability at required points. The Jacobian matrix of the system (3) at disease-free equilibrium $E_{0r} = \left(\frac{A}{\mu_h}, 0, 0\right)$ is given as

$$J_0 = \begin{pmatrix} -\mu_h & -r & \beta \\ 0 & r - M & 0 \\ 0 & \eta_r + t_2 & -\mu_h - \beta \end{pmatrix},$$

where $M = \eta_r + t_2 + \mu_h + \alpha_2$.

The eigenvalues are $\lambda = -\mu_h, -\mu_h - \beta, r - M$. First two eigenvalues are negative. For third eigenvalue to be negative, $r - M < 0$, which implies $\frac{r}{M} < 1$,

$$R_{0r} < 1.$$

□

4.3.4 Global stability analysis of disease-free equilibrium of rotavirus model

The global stability analysis of rotavirus model is performed by considering a suitable Lyapunov function [19] and La Salle invariant principle [20].

Theorem 4.2. *The disease-free equilibrium* E_{0r} *of the sub-model* (3) *is globally asymptotically stable in* Ω *if* $R_{0r} < 1$.

Proof. Consider a Lyapunov function for the system (3):

$$V(t) = (\eta_r + t_2 + \mu_h + \alpha_2)\, I_r.$$

Let $(\eta_r + t_2 + \mu_h + \alpha_2) = M$, differentiating with respect to time, we get,

$$\begin{aligned} \dot{V(t)} &= (\eta_r + t_2 + \mu_h + \alpha_2)\dot{I_r}, \\ &= M(\frac{rI_rS_h}{N_h} - MI_r), \\ &\leq M(r - M)I_r, \\ &= M^2(R_{0r} - 1)I_r, \\ &\leq 0. \end{aligned}$$

If $R_{0r} \leq 1$. It follows that $\dot{V(t)} \leq 0$ for $R_{0r} \leq 1$.

Clearly, $\dot{V} = 0$ is true if and only if $R_{0r} = 1$ or $I_r = 0$. Therefore, by Lyapunov LaSalle Principle [20], every solution of the system (3) in the feasible region approaches E_{0r} as time approaches infinity. □

4.3.5 Analysis of the model considering malaria disease only

To understand the dynamics of malaria in the absence of rotavirus disease, we will perform stability analysis at disease-free equilibrium of the model given by (4). Disease-free equilibrium is denoted as $E_{0m}\left(S_h^0, I_m^0, R_m^0, S_v^0, I_v^0\right)$ i.e $\left(\frac{A}{\mu_h}, 0, 0, \frac{B}{\mu_v+q}, 0\right)$.

4.3.6 Basic reproduction number

To see the disease dynamics, we need to calculate basic reproduction number by next generation matrix method given by Driessche [43]. We divide the coefficient matrix of infected compartment I_m and I_v of the system (4) into two matrices F and V. The matrix F is for transmission, that is, new infections and V is for transition terms, which are given below

$$F = \begin{pmatrix} 0 & ab \\ ac & 0 \end{pmatrix},$$

and

$$V = \begin{pmatrix} -(\eta_m + t_1 + \alpha_1 + \mu_h) & 0 \\ 0 & -(\mu_v + q) \end{pmatrix}.$$

Calculating the matrix $J = FV^{-1}$, we get,

$$J = FV^{-1} = \begin{pmatrix} 0 & -\frac{ab}{(\mu_v+q)} \\ -\frac{ac}{\eta_m+t_1+\alpha_1+\mu_h} & 0 \end{pmatrix}.$$

The eigenvalues of the above determinant are calculated by

$$J - \lambda I = 0,$$

where,

$$J - \lambda I = \begin{pmatrix} -\lambda & -\frac{ab}{(\mu_v+q)} \\ -\frac{ac}{\eta_m+t_1+\alpha_1+\mu_h} & -\lambda \end{pmatrix}.$$

Now, the spectral radius of the matrix FV^{-1} denoted by R_{0m} is called basic reproduction number, that is

$$R_{0m} = \rho(FV^{-1}),$$

which implies

$$R_{0m} = \sqrt{\frac{a^2bc}{(\eta_m + t_1 + \alpha_1 + \mu_h)(\mu_v + q)}}. \tag{6}$$

$R_{0m} < 1$ implies $a^2bc < (\eta_m + t_1 + \alpha_1 + \mu_h)(\mu_v + q)$. This can be interpreted that the collective transmission rate of malaria disease from infected human to susceptible mosquito and from infected mosquito to susceptible human along with mosquito biting rate is less than the cumulative recovery rate (natural as well as with treatment) and death rate (natural as well as with disease) which in turn justifies the disease-free state as transmission of any disease should be less than its recovery and death. Also, it is noteworthy that in case of vector-host models when an infectious mosquito or an infectious human is introduced in a completely naive population, the basic reproduction number is always in the form of square, that is, R_0^2. This is interpreted in a way that it takes two generations for infectious host/vector to reproduce itself [44]. In the upcoming section, local stability analysis is performed at disease-free equilibrium points.

4.3.7 Local stability analysis of malaria model at disease-free equilibrium

By applying theorem 2 of Driessche and Watmough [44], the following result is stated:

Theorem 4.3. *The disease-free equilibrium of the model (4) for malaria disease only is locally asymptotically stable if $R_{0m} < 1$ and unstable if $R_{0m} > 1$.*

Proof. Firstly, we will calculate the variational matrix to see the local stability of disease-free equilibrium. Further, to calculate that, we need to find the eigenvalues of the system. The Jacobian matrix at disease-free equilibrium $E_{0m}\left(S_h^0, I_m^0, R_m^0, S_v^0, I_v^0\right)$ i.e $E_{0m}\left(\frac{A}{\mu_h}, 0, 0, \frac{B}{\mu_v+q}, 0\right)$ is

$$J_0 = \begin{pmatrix} -\mu_h & 0 & \beta & 0 & -ab \\ 0 & -L & 0 & 0 & ab \\ 0 & -(\eta_m + t_1) & -\mu_h - \beta & 0 & 0 \\ 0 & -ac & 0 & (\mu_v + q) & 0 \\ 0 & ac & 0 & 0 & -(\mu_v + q) \end{pmatrix},$$

where $L = \eta_m + t_1 + \alpha_1 + \mu_h$.

The eigenvalues are $\lambda = -\mu_h, -(\mu_v + q), -\mu_h - \beta$. Other eigenvalues are given by

$$\lambda^2 + \lambda(L + \mu_v + q) + L(\mu_v + q) - a^2bc = 0.$$

It can be rewritten as

$$\lambda^2 + l_1\lambda + l_2 = 0,$$

where $l_1 = (L + \mu_v + q)$ and $l_2 = L(\mu_v + q) - a^2bc$.

According to Routh-Hurwitz criteria l_1 and l_2 should be both positive for the equilibrium to be stable. It is quite clear that $l_1 > 0$.

Now, $l_2 > 0$ implies $L(\mu_v + q) > a^2bc$, implying

$$\frac{a^2bc}{(\eta_m + t_1 + \alpha_1 + \mu_h)(\mu_v + q)} < 1,$$

which implies

$$R_{0m}^2 < 1.$$

□

4.3.8 Bifurcation analysis of malaria model

The phenomenon of bifurcation is proved by applying centre manifold criteria for the system (4). Applying the Centre Manifold Theorem [6] along with [28], bifurcation analysis is carried out. Let us consider b^* as bifurcation parameter so that $R_{0m} = 1$. Here

$$b^* = \frac{L(\mu_v + q)}{a^2c}.$$

Now, we transform the variables in the system (1) as:

$$S_h = x_1, \quad I_m = x_2, \quad R_m = x_3, \quad S_v = x_4, \quad I_v = x_5.$$

The system takes the form:

$$\begin{aligned}
\dot{x_1} &= A - (\lambda_m + \mu_h)x_1 + \beta x_3,\\
\dot{x_2} &= \lambda_m x_1 - (\eta_m + t_1 + \alpha_1 + \mu_h)x_2,\\
\dot{x_3} &= (\eta_m + t_1)x_2 - (\mu_h + \beta)x_3,\\
\dot{x_4} &= B - \lambda_v x_4 - (\mu_v + q)x_4,\\
\dot{x_5} &= \lambda_v x_4 - (\mu_v + q)x_5,
\end{aligned} \tag{7}$$

where

$$\lambda_m = \frac{abx_5}{N_h}, \qquad \lambda_v = \frac{acx_2}{N_v}.$$

Firstly, the Jacobian of the system (7) is calculated at E_{0m}, which is given by

$$J_{0m} = \begin{pmatrix} -\mu_h & 0 & \beta & 0 & -p_1 \\ 0 & -L & 0 & 0 & p_1 \\ 0 & p_2 & -p_3 & 0 & 0 \\ 0 & -p_4 & 0 & -p_5 & 0 \\ 0 & p_4 & 0 & 0 & -p_5 \end{pmatrix},$$

where

$$p_1 = ab, \qquad p_2 = \eta_m + t_1, \qquad p_3 = \mu_h + \beta, \qquad p_4 = ac, \qquad p_5 = \mu_v + q.$$

Now, we will calculate the left and right eigenvectors of the Jacobian J_{0m}. Let us denote the left and right eigenvectors v and w, where $v = [v_1, v_2, v_3, v_4, v_5]^T$ and $w = [w_1, w_2, w_3, w_4, w_5]^T$. We get,

$$w_1 = \left(\frac{w_2}{\mu_h}\right)\left(\frac{\beta p_2}{p_3} - \frac{p_1 p_4}{p_5}\right), \qquad w_2 = w_2, \qquad w_3 = \frac{p_2 w_2}{p_3}, \qquad w_4 = \frac{-p_4 w_2}{p_5}, \qquad w_5 = \frac{p_4 w_2}{p_5},$$

and

$$v_1 = v_3 = v_4 = 0, \qquad v_2 = v_2, \qquad v_5 = \frac{p_1 v_2}{p_5}.$$

After rigorous calculation and calculating the coefficients l and m from the theorem in [6], we have,

$$l = -w_5 \left[\frac{v_2 w_2 a b^* \mu_h}{A} + \frac{v_2 w_3 a b^* \mu_h}{A} + \frac{v_5 w_2 a c (\mu_v + q)}{A} \right],$$

and

$$m = a v_2 w_5.$$

As the coefficient m is positive definite and $l < 0$. From the theorem in [6], the system undergoes forward bifurcation.

4.3.9 Global stability analysis of malaria model at disease-free equilibrium

The global stability analysis of malaria model is performed by considering a suitable Lyapunov function [19] and La Salle invariant principle [20].

Theorem 4.4. *The disease-free equilibrium E_{0m} of the sub-model (4) is globally asymptotically stable in Ω if $R_{0m} < 1$.*

Proof. Consider a Lyapunov function for the system (4):

$$V(t) = acI_m + (\eta_m + t_1 + \mu_h + \alpha_1) I_v.$$

Here $(\eta_m + t_1 + \mu_h + \alpha_1) = L$, differentiating with respect to time, we get,

$$\begin{aligned}
\dot{V(t)} &= ac\dot{I_m} + L\dot{I_v}, \\
&= ac \left(\frac{abI_v S_h}{N_h} - LI_m \right) + L \left(\frac{acI_m S_v}{N_v} - (\mu_v + q) I_v \right), \\
&\leq a^2 bcI_v - acLI_m + acLI_m - (\mu_v + q) LI_v, \\
&= a^2 bcI_v - (\mu_v + q) LI_v, \\
&= (\mu_v + q) LI_v \left[\frac{a^2 bc}{(\mu_v + q) L} - 1 \right], \\
&= (\mu_v + q) LI_v \left[R_{0m}^2 - 1 \right], \\
&\leq 0,
\end{aligned}$$

if $R_{0m} \leq 1$. It follows that $\dot{V(t)} \leq 0$ for $R_{0m} \leq 1$.

Clearly, $\dot{V} = 0$ is true if and only if $R_{0m} = 1$ or $I_v = 0$. Therefore, by Lyapunov Lasalle Principle [20], every solution of the system (4) in the feasible region approaches E_{0m} as time approaches infinity. Therefore, the disease-free equilibrium E_{0m} of the sub-model (4) is globally asymptotically stable in Ω if $R_{0m} < 1$. Hence the theorem is proved. □

5 Analysis of Co-infection Model

The disease-free equilibrium of co-infection model is given by (1)

$$E_{0rm}\left(S_h^0,\, I_m^0,\, I_r^0,\, I_{mr}^0,\, R_m^0,\, R_r^0,\, R_{rm}^0,\, S_v^0,\, I_v^0\right) = E_{0rm}\left(\frac{A}{\mu_h},\, 0,\, 0,\, 0,\, 0,\, 0,\, 0,\, \frac{B}{\mu_v+q},\, 0\right).$$

In the coming section, we will find the basic reproduction number of the main model given by (1) as it is the threshold value that help us to decides the dynamics of the disease. Also, the global stability analysis will be performed along with bifurcation analysis of the model. There may be some parameters for which system may be sensitive. It will be checked through sensitivity analysis.

5.1 Basic reproduction number of co-infection model

The basic reproduction number of co-infection model (1) is given by

$$R_0 = max\{R_{0r}, R_{0m}\},$$

where R_{0r} and R_{0m} are given by equations 5 and 6.

5.2 Global stability analysis of co-infection model

We study the global asymptotic stability of the model (1) by Castillo-Chavez et al. approach in [6]. For that, we express the system of the equations given by (1) in the form:

$$\dot{X} = F(X, Z),$$

$$\dot{Z} = G(X, Z), G(X, 0) = 0,$$

where X and Z stands for uninfected and infected populations. Here, $X = (S_h,\, R_m,\, R_r,\, R_{mr},\, S_v)$ and $Z = (I_m, I_r, I_{mr}, I_v)$. Let the disease-free equilibrium of the model be $E_0 = (X_0, 0)$, where $X_0 = \left(\frac{A}{\mu_h},\, \frac{B}{\mu_v+q}\right)$. To make sure, the system is globally asymptotically stable, the conditions given by C_1 and C_2 must be satisfied.

(C_1): For $\dot{X} = F(X, 0), X_0$ is globally asymptotically stable.

$(C_2) : G(X, Z) = BZ - \hat{G}(X, Z), \hat{G}(X, Z) \geq 0$ for $(X, Z) \in \Omega$, where $B = \dfrac{\partial}{\partial Z} G(X_0, 0)$.

If the model (1) satisfies above two conditions, following results holds.

Theorem 5.1. *The disease-free equilibrium of the model given by* (1) *is globally asymptotically stable for* $R_0 < 1$ *and conditions* C_1 *and* C_2 *are satisfied.*

Proof. For the model (1), $F(X,Z)$ and $G(X,Z)$ are given as:

$$F(X,Z) = \begin{pmatrix} A-(\lambda_m+\lambda_r+\mu_h)S_h+\beta(R_m+R_r+R_{mr}) \\ (\eta_m+t_1)I_m-(\mu_h+\beta)R_m \\ (\eta_r+t_2)I_r-(\mu_h+\beta)R_r \\ (\eta_{mr}+t_3)I_{mr}-(\mu_h+\beta)R_{mr} \\ B-\lambda_v S_v-(\mu_v+q)S_v \end{pmatrix},$$

and

$$G(X,Z) = \begin{pmatrix} \lambda_m S_h+\alpha_r I_{mr}-(\delta\lambda_r+\eta_m+t_1+\alpha_1+\mu_h)I_m \\ \lambda_r S_h+\alpha_m I_{mr}-(\xi\lambda_m+\eta_r+t_2+\alpha_2+\mu_h)I_r \\ \delta\lambda_r I_m+\xi\lambda_m I_r-(\alpha_r+\eta_{mr}+t_3+\alpha_3+\alpha_m+\mu_h)I_{mr} \\ \lambda_v S_v-(\mu_v+q)I_v \end{pmatrix}.$$

Consider the system

$$F(X,0) = \begin{pmatrix} A-\mu_h S_h \\ 0 \\ 0 \\ 0 \\ B-(\mu_v+q)S_v \end{pmatrix}.$$

It is clear that $X_0 = (\frac{A}{\mu_h}, \frac{B}{\mu_v+q})$ is globally asymptotically stable point of above equation of $F(X,0)$.

This can be verified as the solution of above equation $S_h = \frac{A}{\mu_h} + (S_h(0) - \frac{A}{\mu_h})e^{-\mu_h t}$ and $S_v = \frac{B}{\mu_v+q} + (S_v(0) - \frac{B}{\mu_v+q})e^{-(\mu_v+q)t}$ approaches X_0 as time approaches infinity which implies global convergence of solution of system (1) in Ω,

$$B = \begin{pmatrix} -(\eta_m+t_1+\alpha_1+\mu_h) & 0 & \alpha_r & ab \\ 0 & r-(\eta_r+t_2+\alpha_2+\mu_h) & r\theta_2+\alpha_m & 0 \\ 0 & 0 & -(\eta_{mr}+t_3+\alpha_3+\alpha_m+\alpha_r+\mu_h) & 0 \\ ac & 0 & ac\theta_1 & -(\mu_v+q) \end{pmatrix}.$$

Then $G(X,Z)$ can be written as $G(X,Z) = BZ - \hat{G}(X,Z)$, where

$$\hat{G}(X,Z) = \begin{pmatrix} \hat{G}_1(X,Z) \\ \hat{G}_2(X,Z) \\ \hat{G}_3(X,Z) \\ \hat{G}_4(X,Z) \end{pmatrix},$$

$$= \begin{pmatrix} abI_v(1-\frac{S_h}{N_h})+\delta\lambda_r I_m \\ \lambda_r(N_h-S_h)+\xi\lambda_m I_r \\ -(\delta\lambda_r I_m+\xi\lambda_m I_r) \\ \lambda_v(N_v-S_v) \end{pmatrix}.$$

Clearly $\hat{G}_3(X,Z) < 0$, which implies $\hat{G}(X,Z) < 0$. Hence, condition C_2 is not satisfied. Therefore, $E_0(X_0,0)$ may not be globally asymptotically stable for $R_0 < 1$. □

5.3 Bifurcation analysis

We use method based on using Center Manifold Theory [6]. For such theorem as mentioned in [6] (see also [42]), there are two main quantities say a and b which decides the direction of bifurcation. In particular, if $a < 0$ and $b > 0$, then system undergoes forward bifurcation and if $a > 0$ and $b > 0$, then the system exhibits backward bifurcation . Using this theorem, the following results can be concluded.

Theorem 5.2. *If* $a_0 = \frac{\beta k_9}{k_7} - \frac{k_3 k_{10}}{k_{12}} > 0$, *the system* (1) *undergoes backward bifurcation at* $R_0 = 1$. *If the inequality is reversed, then the system undergoes forward bifurcation at* $R_0 = 1$.

Proof. To apply this theory, we consider two important coefficients b and r to be bifurcation parameters for $R_{0r} = 1$ and $R_{0m} = 1$ iff $r = r^*$ and $b = b^*$, where

$$r = r^* = \eta_r + t_2 + \mu_h + \alpha_2,$$

and

$$b = b^* = \frac{(\mu_v + q)(\eta_m + t_1 + \alpha_1 + \mu_h)}{a^2 c}.$$

Now, we transform the variables in the system (1) as:

$$S_h = x_1, \quad I_m = x_2, \quad I_r = x_3, \quad I_{mr} = x_4, \quad R_m = x_5, \quad R_r = x_6, \quad R_{mr} = x_7, \quad S_v = x_8, \quad I_v = x_9.$$

Let $x = (x_1, x_2, x_3, x_4, x_5, x_6, x_7, x_8, x_9)^T$ and $F = (f_1, f_2, f_3, f_4, f_5, f_6, f_7, f_8, f_9)^T$, then the system given by (1) takes the form

$$\dot{dx} = F(x), \tag{8}$$

can be presented as:

$$\begin{aligned}
\dot{x_1} &= A - (\lambda_m + \lambda_r + \mu_h)x_1 + \beta x_5 + \beta x_6 + \beta x_7,\\
\dot{x_2} &= \lambda_m x_1 + \alpha_r x_4 - (\delta\lambda_r + \eta_m + t_1 + \alpha_1 + \mu_h)x_2,\\
\dot{x_3} &= \lambda_r x_1 + \alpha_m x_4 - (\xi\lambda_m + \eta_r + t_2 + \alpha_2 + \mu_h)x_3,\\
\dot{x_4} &= \delta\lambda_r x_2 + \xi\lambda_m x_3 - (\alpha_3 + \eta_{mr} + \alpha_r + \alpha_m + t_3 + \mu_h)x_4,\\
\dot{x_5} &= (\eta_m + t_1)x_2 - (\mu_h + \beta)x_5,\\
\dot{x_6} &= (\eta_r + t_2)x_3 - (\mu_h + \beta)x_6,\\
\dot{x_7} &= (\eta_{mr} + t_3)x_4 - (\mu_h + \beta)x_7,\\
\dot{x_8} &= B - \lambda_v x_8 - (\mu_v + q)x_8,\\
\dot{x_9} &= \lambda_v x_8 - (\mu_v + q)x_9,
\end{aligned} \tag{9}$$

where $\lambda_m = \frac{abI_v}{N_h}$, $\lambda_v = \frac{ac(I_m + \theta_1 I_{mr})}{N_v}$ and $\lambda_r = \frac{r(I_r + \theta_2 I_{mr})}{N_h}$. The Jacobian of the system (9) at disease-free equilibrium $(\frac{A}{\mu_h}, 0, 0, 0, 0, 0, 0, \frac{B}{\mu_v + q}, 0)$ is

$$J_2 = \begin{pmatrix}
-\mu_h & 0 & -k_1 & -k_2 & \beta & \beta & \beta & 0 & -k_3\\
0 & -L & 0 & \alpha_r & 0 & 0 & 0 & 0 & k_3\\
0 & 0 & k_4 & k_5 & 0 & 0 & 0 & 0 & 0\\
0 & 0 & 0 & -N & 0 & 0 & 0 & 0 & 0\\
0 & k_6 & 0 & 0 & -k_7 & 0 & 0 & 0 & 0\\
0 & 0 & k_8 & 0 & 0 & -k_7 & 0 & 0 & 0\\
0 & 0 & 0 & k_9 & 0 & 0 & -k_7 & 0 & 0\\
0 & -k_{10} & 0 & -k_{11} & 0 & 0 & 0 & -k_{12} & 0\\
0 & k_{10} & 0 & k_{11} & 0 & 0 & 0 & 0 & -k_{12}
\end{pmatrix},$$

where,

$$\begin{aligned}
&k_1 = r, \quad k_2 = r\theta_2, \quad k_3 = ab, \quad k_4 = r - M, \quad k_5 = r\theta_2 + \alpha_m, \quad k_6 = \eta_m + t_1,\\
&k_7 = \mu_h + \beta, \quad k_8 = \eta_r + t_2, \quad k_9 = \eta_{mr} + t_3, \quad k_{10} = ac, \quad k_{11} = ac\theta_1,\\
&k_{12} = \mu_v + q, \quad N = (\alpha_3 + \eta_{mr} + \alpha_r + \alpha_m + t_3 + \mu_h).
\end{aligned}$$

Now, we will calculate the right eigenvector of the Jacobian J_2.

Let it be denoted by $w = [w_1, w_2, w_3, w_4, w_5, w_6, w_7, w_8, w_9]^T$. After calculation, we get,

$$\begin{aligned}
-\mu_h w_1 - k_1 w_3 - k_2 w_4 + \beta w_5 + \beta w_6 + \beta w_7 - k_3 w_9 &= 0,\\
-L w_2 + \alpha_r w_4 + k_3 w_9 &= 0,\\
k_4 w_3 + k_5 w_4 &= 0,\\
-N w_4 &= 0,\\
k_6 w_2 - k_7 w_5 &= 0,\\
k_8 w_3 - k_7 w_6 &= 0,\\
k_9 w_4 - k_7 w_7 &= 0,\\
-k_{10} w_2 - k_{11} w_4 - k_{12} w_8 &= 0,\\
k_{10} w_2 + k_{11} w_4 - k_{12} w_9 &= 0.
\end{aligned} \tag{10}$$

From above set of equations (10), we get,

$$w_1 = \frac{w_2}{\mu_h}\left(\frac{\beta k_6}{k_7} - \frac{k_3 k_{10}}{k_{12}}\right), \quad w_2 = w_2, \quad w_3 = w_4 = 0, \quad w_5 = \frac{k_6 w_2}{k_7},$$
$$w_6 = w_7 = 0, \quad w_8 = -\frac{k_{10} w_2}{k_{12}}, \quad w_9 = \frac{k_{10} w_2}{k_{12}}.$$

Let the left eigenvector of Jacobian J_2 associated with zero eigenvalue is denoted by

$$v = [v_1, v_2, v_3, v_4, v_5, v_6, v_7, v_8, v_9]^T.$$

After calculation, we get,

$$\begin{aligned}
-\mu_h v_1 &= 0,\\
-L v_2 + K_6 v_5 - k_{10} v_8 + k_{10} v_9 &= 0,\\
-k_1 v_1 + k_4 v_3 + k_8 v_6 &= 0,\\
-k_2 v_1 + \alpha_2 v_2 + k_5 v_3 - N v_4 + k_9 v_7 - k_{11} v_8 + k_{11} v_9 &= 0,\\
\beta v_1 - k_7 v_5 &= 0,\\
\beta v_1 - k_7 v_6 &= 0,\\
\beta v_1 - k_7 v_7 &= 0,\\
-k_{12} v_8 &= 0,\\
-k_3 v_1 + k_3 v_2 - k_{12} v_9 &= 0.
\end{aligned} \tag{11}$$

Here $L = \eta_m + t_1 + \alpha_1 + \mu_h$, $M = \eta_r + t_2 + \alpha_2 + \mu_h$ and $N = \eta_{mr} + t_3 + \alpha_m + \alpha_r + \alpha_3 + \mu_h$.

Solving the above equations in (11), we get,

$$v_1 = 0, \quad v_2 = v_2, \quad v_3 = 0, \quad v_4 = \frac{v_2}{N}\left(\alpha_r + \frac{L k_{11}}{k_{10}}\right), \quad v_5 = v_6 = v_7 = v_8 = 0, \quad v_9 = \frac{L v_2}{k_{10}},$$

where v_2 can be calculated satisfying the condition for eigenvectors v and w such that $v.w = 1$. The coefficients l and m are defined in the equations given below :

$$l = \sum_{k=i=j=1}^{n} v_k w_i w_j \frac{\partial^2 f_k}{\partial x_i \partial x_j}(s_h^0, 0, 0, 0, 0, 0, 0, s_v^0, 0), \tag{12}$$

$$m = \sum_{k=i=1}^{n} v_k w_i \frac{\partial^2 f_k}{\partial x_i \partial b^*}(s_h^0, 0, 0, 0, 0, 0, 0, s_v^0, 0). \tag{13}$$

Here, $f_i's$ denote the right side of the system of equations given by (9). Considering the system (9) and taking into account only non-zero components of v, it follows that:

$$l = \frac{v_2 w_2^2 k_{10} a b^* a_0}{\mu_h k_{12}}, \quad m = a v_2 w_9,$$

where

$$a_0 = \frac{\beta k_9}{k_7} - \frac{k_3 k_{10}}{k_{12}}. \tag{14}$$

Since, the coefficient m is always positive. Hence, the bifurcation of the system (9) at $b = b^*$ depends on the value of l. From the equation (14), it can be clearly seen that $l > 0$ iff $a_0 > 0$, that is, $\frac{\beta k_9}{k_7} > \frac{k_3 k_{10}}{k_{12}}$. Hence, for $l > 0$, the system exhibits backward bifurcation and for $l < 0$, it undergoes forward bifurcation at disease-free equilibrium at $R_0 = 1$. □

5.4 Sensitivity analysis

We performed sensitivity analysis of the model parameters. With the help of this, we can identify those parameters having greater influence on R_0, that is, the basic reproduction number. The technique used by [7] have been applied. Sensitivity index of a function R_0 with respect to any parameter say p is defined as

$$\Upsilon_p^{R_0} = \frac{\partial R_0}{\partial p} \frac{p}{R_0}.$$

Since, $R_0 = \max[R_{0m}, R_{0r}]$, we have performed the sensitivity analysis for both R_{0r} and R_{0m} separately.

Table 2: Table for sensitivity indices.

Symbol	Sensitivity index
R_{0r}	Basic reproduction number for rotavirus-only model
r	1.0000
μ_h	−1.0002
η_r	−0.4543
t_2	−0.4998
α_2	−0.0004
R_{0m}	Basic reproduction number for malaria-only model
a	1.0000
b	0.5000
c	0.5000
μ_h	−0.5000
μ_v	−0.0001
q	−0.0001
η_m	−0.2498
t_1	−0.2498
α_1	−0.2498

*Table for sensitivity indices

Positive value of sensitivity index means that corresponding to an increase in given parameter, there will be increase in basic reproduction number. Whereas a negative value of sensitivity index

implies that an increase in the parameter value will reflect in the form of decrease in value of basic reproduction number. From the table 2, it has been observed that the parameters r, a, b and c have great impact in spreading the disease if their values are increased thereby increasing basic reproduction number provided other parameters are fixed. This can be clearly verified as the parameters r, a, b and c are the rates of transmission of disease. So, increase in the values of these will definitely increase the basic reproduction number and that in turn increases the spread of these diseases. The parameters having negative sensitivity indices like η_m, η_r, t_1, t_2 and q will decrease the value of basic reproduction number if their values are increased thereby controlling the disease. This is biologically true that increase in recovery naturally or by treatment will control the spread of disease along with the increased usage of insecticide.

6 Numerical Simulation and Discussion

We simulate the model (1) for different values of treatment in each case. Here, four types of control strategies are applied: (1) malaria-treatment for malaria infected (2) rotavirus treatment for rotavirus infected (3) malaria-rotavirus treatment for co-infected (4) insecticide treatment for vectors (5) all treatments combined.

6.1 Parameter values in the model

Table 3: Values of parameters.

Parameters	Description	Value	Source
a	Average number of bites by mosquitoes on humans	4×10^{-1}	[32]
b	Transmission rate of malaria from infected mosquito to human	$0.83333\ \text{day}^{-1}$	[7]
c	Transmission rate of malaria from infected human to mosquito	$7.2 \times 10^{-2}\ \text{day}^{-1}$	[40]
β	Rate at which human recovered from co-infection transfer to susceptible class (S_h)	$0.0027\ \text{day}^{-1}$	[25]
μ_h	Natural mortality rate of humans	$2.537 \times 10^{-5}\ \text{day}^{-1}$	[24]
μ_v	Natural mortality rate of mosquitoes	$4 \times 10^{-5}\ \text{day}^{-1}$	[12]
η_m	Natural recovery rate from malaria	$0.5\ \text{day}^{-1}$	[10]
η_r	Natural recovery rate from rotavirus	$0.5\ \text{day}^{-1}$	Assumed
η_{mr}	Natural recovery rate from malaria-rotavirus co-infection	$5.75 \times 10^{-4}\ \text{day}^{-1}$	Assumed
t_1	Effective treatment control for malaria	$0.5\ \text{day}^{-1}$	Assumed
t_2	Effective treatment control for rotavirus	$0.5\ \text{day}^{-1}$	Assumed
t_3	Effective treatment control for malaria-rotavirus co-infection	$0.5\ \text{day}^{-1}$	Assumed
α_1	Disease death due to malaria	$4.49312 \times 10^{-4}\ \text{day}^{-1}$	[13]
α_2	Disease death due to rotavirus	$4.466 \times 10^{-4}\ \text{day}^{-1}$	[31]
α_3	Disease death due to malaria-rotavirus co-infection	$5.0 \times 10^{-2}\ \text{day}^{-1}$	Assumed
q	Mortality rate of mosquitoes due to insecticide	$0.2\ \text{day}^{-1}$	Assumed

*Table for values of parameters

Figures 1 and 2 show the impact of insecticide in eradicating co-infection in the population. It is verified that co-infection decreases sharply as we apply all the treatments and it takes longer if we apply insecticide treatment only on vector compartment. It can seen in Figure 1 that it takes 40 days for the infection to die out with only insecticide treatment where as it takes only 10 days for the infection to vanish with all treatments as can be seen in Figure 2.

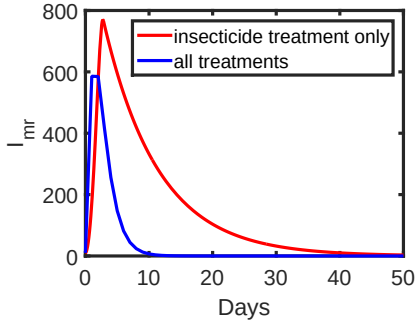

Figure 1: Co-infected population I_{mr} under the effect of insecticide treatment.

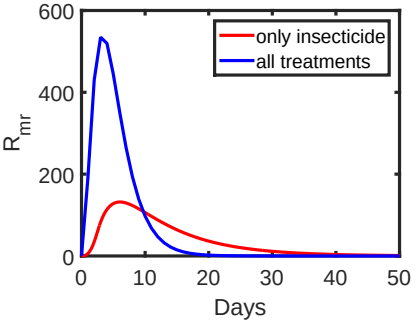

Figure 2: Recovered from both malaria and rotavirus I_{mr} under the effect of insecticide treatment.

Similarly, in Figure 3, it can be seen that with malaria treatment only, the co-infection dies out in around 40 days while it takes around 10 days for the same to happen with all treatments. Also, it is evident from the Figure 4 that the recovered population is high when all the treatments given. Similarly, it is apparent from Figure 5 that co-infection dies out in 10 days with all treatments whereas it takes about 30 days with rotavirus treatment only.

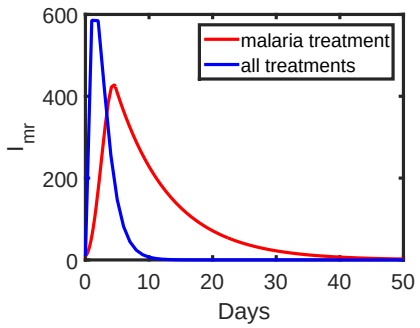

Figure 3: Co-infected population I_{mr} under the effect of malaria treatment only.

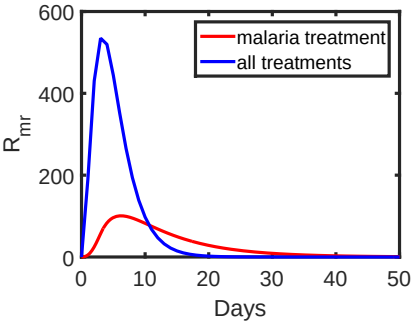

Figure 4: Recovered from both malaria and rotavirus R_{mr} under the effect of malaria treatment only.

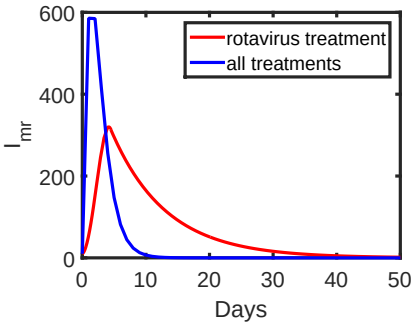

Figure 5: Co-infected population I_{mr} under the effect of rotavirus treatment only.

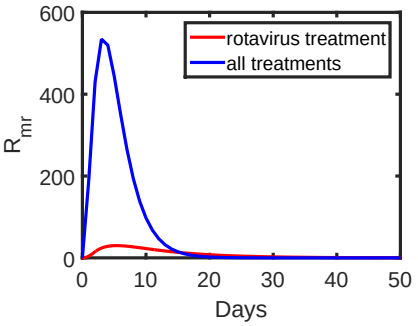

Figure 6: Recovered from both malaria and rotavirus R_{mr} under the effect of rotavirus treatment only.

It can be seen in Figure 7 that co-infection dies off in 10 days with all treatment effects where as it takes 20 days for the disease to terminate with malaria-rotavirus treatment. Figure 8 shows that all treatments have better effect on disease progression in comparison to malaria-rotavirus treatment.

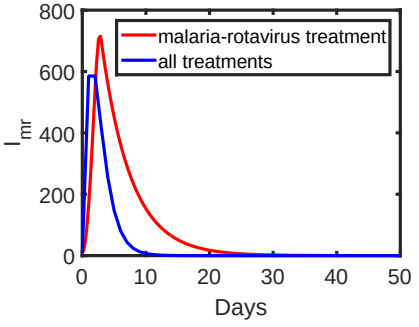

Figure 7: Co-infected population I_{mr} under the effect of malaria-rotavirus treatment only.

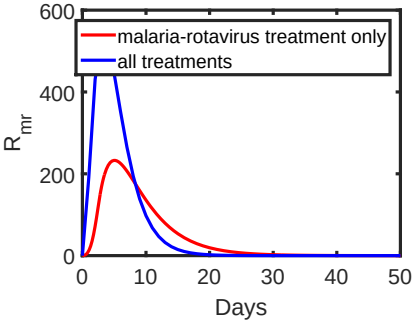

Figure 8: Recovered from both malaria and rotavirus R_{mr} under effect of malaria-rotavirus treatment only.

We simulated the model for various values of treatments and studied the co-infected and recovered population. It is being seen in the Figures 9 and 10 that increase in the value of t_3, that is, malaria-rotavirus treatment decreases the number of days in which co-infection dies off and it also reduces the amplitude of co-infection.

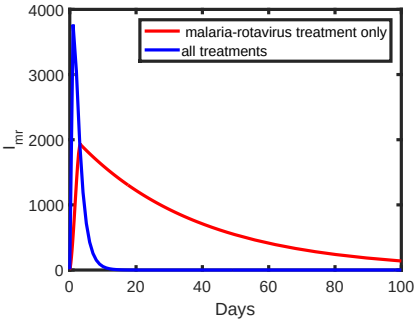

Figure 9: Dynamics of co-infected population I_{mr} with $t_3 = 0.01$.

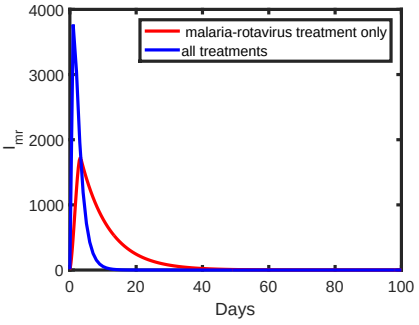

Figure 10: Dynamics of co-infected population I_{mr} with $t_3 = 0.1$.

We simulated the model for different values of rotavirus treatment and then malaria treatment. Figures 11, 12, 13 and 14 show the effect of increasing the value of treatments for rotavirus and malaria i.e. t_2 and t_1 in decreasing the co-infection.

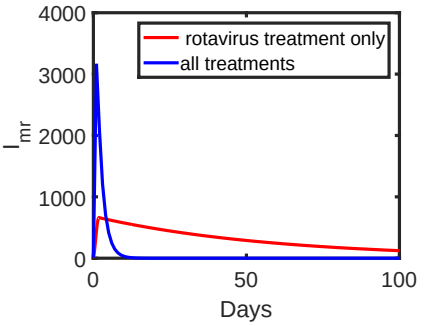

Figure 11: Dynamics of co-infected population I_{mr} with $t_2 = 0.1$.

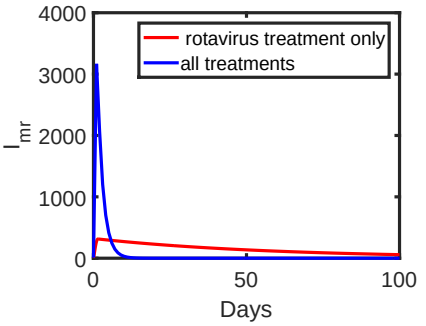

Figure 12: Dynamics of co-infected population I_{mr} with $t_2 = 0.5$.

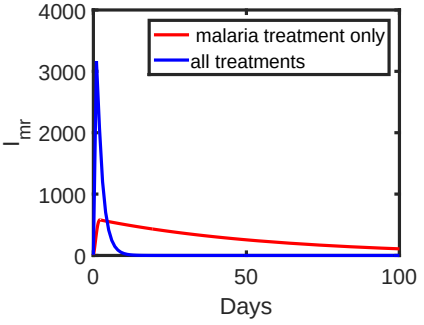

Figure 13: Dynamics of co-infected population I_{mr} with $t_1 = 1$.

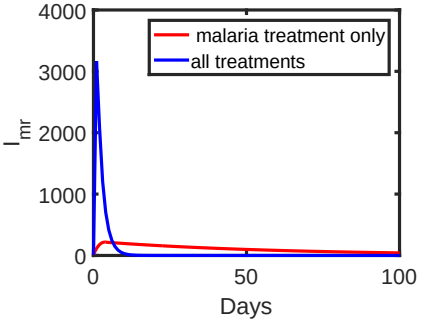

Figure 14: Dynamics of co-infected population I_{mr} with $t_1 = 10$.

Figure 15 shows the collective impact of different treatments for all the susceptible population and Figure 16 shows the collective impact of different treatments on co-infected population.

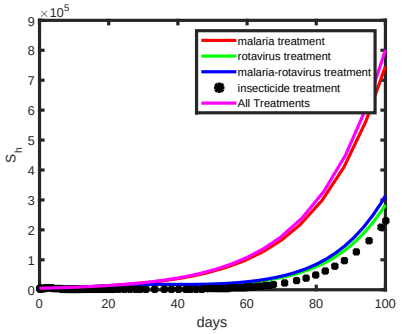

Figure 15: Susceptible population S_h under the effect of different treatments.

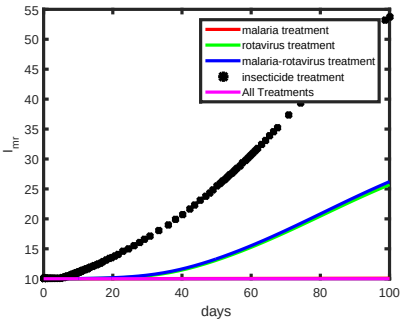

Figure 16: Co-infected population I_{mr} under the effect of different treatments.

It is evident that all treatments have better results than any other treatment. When we compare malaria-rotavirus treatment with all treatments, the results are better with all treatments which means that the additional treatment factor of insecticide gives additional control on disease transmission. In vector borne diseases, vector control helps in eradicating the disease. As a result, it can be interpreted that vector control is a major factor in controlling the co-infection along with other control strategies in reduction of co-infected individuals.

7 Conclusion

A compartmental model for transmission of malaria and rotavirus is formulated and studied for various control measures/treatments. The effect of various control strategies namely treatment for humans infected with rotavirus, treatment for humans infected with malaria, treatment for humans co-infected with malaria-rotavirus and insecticide control for mosquito population is studied. Since, the results are based on theoretical and numerical analysis, they offer some very important insights about the dynamics of diseases. The underlying relationship of two diseases under different control scenario is quite clear from the analysis.

Firstly, we studied single disease models and performed the disease-free stability analysis. It is found that the dynamics of disease is determined by threshold value R_{0r} and R_{0m} in case of rotavirus and malaria respectively. According to analysis, disease-free equilibrium is locally asymptotically stable as well as globally asymptotically stable for rotavirus-only model and malaria-only model if $R_{0r} < 1$ and $R_{0m} < 1$ respectively. We derived the basic reproduction number for co-infection model $R_{mr} = max\{R_{0r}, R_{0m}\}$. Sensitivity analysis of the model indicates that the parameters a, b and c have positive value creating great influence on the spread of malaria whereas the basic reproduction number of rotavirus-only model is most sensitive to r. Bifurcation analysis of the full co-infection model is done. The full co-infection model is found to be globally asymptotically unstable at disease-free equilibrium. It is evident that single control measure takes longer to control or eradicate the infection from the system. It is observed that only insecticide treatment also takes longer to control the infection in human population. It is clear that when all treatments namely malaria-rotavirus treatment and insecticide treatment to mosquitoes are applied collectively, the infection dies out in much lesser time. This means that the combined strategy saves more accumulative cases of co-infection than any other strategy of treatment.

As a conclusion, the study indicates that the possibility of controlling the co-infection of rotavirus and malaria using effective strategies for treatment/controls for both the diseases is bright.

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Conflicts of Interest The authors declare no conflict of interest.

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