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MODELING MALARIA AND ROTAVIRUS CO-INFECTION

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ABSTRACT: A mathematical model has been developed to explore the co-infection of rotavirus and malaria. A qualitative and comprehensive mathematical analysis has been carried out. A rotavirus only model is considered first. In its analysis, the basic reproduction number (R_0) is calculated. The existence of a disease free and a unique positive endemic equilibria is established and are proved to be both globally stable when $R_0 < 1$ and $R_0 > 1$ respectively. The basic reproduction number (R_{mr}) of the co-infection model has also been established. The disease free equilibrium is proved to be locally stable whenever $R_{mr} < 1$ but not globally stable due to co-infection. However, it has been observed that if maximum protection is given against co-infection, then global stability may be achieved. Analysis of co-infection model indicates that it may undergo a forward bifurcation. Numerical simulations using reasonable parameter values indicate that the co-infection persists whenever R_{mr} is greater than unity and dies out when R_{mr} is less than unity.

Key Words: basic reproduction number, co-infection, forward bifurcation, global stability

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1. INTRODUCTION

Humans acquire malaria following infective bites from infected female anopheles mosquitoes during blood feeding. Four parasite species account for most human malaria infections worldwide, with *Plasmodium falciparum* being the most common cause of malaria in Africa. In 2015, about 214 million cases of malaria were reported (range: 149-303 million) with the African region leading with 88%, followed by South-East Asia at 10% and Eastern Mediterranean region at 2%. The number of malaria deaths were reported to be 438, 000 (range:236,000-635,000), most of the deaths were children of under five years of age, that is, 306, 000 [1]. Malaria was the fourth cause of death in children in developing countries in 2002. In 2001, malaria was responsible for 22% of all hospital admissions, 26% of all outpatient visits and 28% of all hospital deaths in Malawi. In Kenya it accounts for 19% of all hospital admissions, 30% of all outpatient visits, with an estimate of 20% of all deaths in children less than five years of age being attributed to the disease [2, 3]. Rotavirus is a pathogen of the gastrointestinal tract that causes severe acute gastroenteritis and diarrhea in infants and young children [4]. Rotavirus is known as the main cause of diarrhoeal disease which is the second leading cause of deaths in children under five years old. Each year diarrhoea kills around 760, 000 children worldwide [5]. There are seven species of rotavirus, referred to as A, B, C, D, E, F and G. Humans are primarily infected by species A, B and C, most commonly by species A. All the seven species cause disease in other animals [6]. Rotavirus is transmitted by the faecal-oral route, via contact with contaminated hands, surfaces and objects [7] and possibly by the respiratory route [8]. Rotavirus disease incidence is similar worldwide, regardless of infrastructure and other levels of development [9], which suggests that traditional diarrheal disease control measures, such as safe water and improved hygienic standards, are inadequate. Once a child is infected by the virus, there is an incubation period of about two days before symptoms appear [10]. However, with each infection, immunity develops, subsequent infections are less severe [11]. Severe rotavirus infections occur most commonly in infants and children between 3 and 24 months of age. Rotavirus-related hospitalizations can account for as many as 2.5% of all hospitalizations of children. Some review analyses show that rotavirus accounted for 6% of diarrhea episodes and 20% of deaths caused by diarrhea in children less than five years of age in developing countries [9].

In industrialized counties, hospitalizations are often the most costly events associated with rotavirus disease and often constitute a major expense for national health budgets [12]. An outbreak of rotavirus diarrhea in a daycare center in Denmark demonstrated that even small outbreaks of rotavirus in childcare facilities can be associated with substantial expense on a personal and a public scale due to parental loss of work [13]. The results of a study on rotavirus infections among HIV-infected children in Nairobi, Kenya, indicate that rotavirus is an important viral etiological agent causing diarrhea in HIV-seropositive children [14].

Mathematical models for the co-infection of *P. falciparum* and rotavirus in children are rare, yet review shows a number of reported cases where the two coexist. In a study carried out in Ghana , it was observed that 11.8% of the 243 children examined were

co-infected with *P. falciparum* and enteropathogens, where rotavirus was also found to be common enteropathogens present in more than half of the patients [15]. Although a rapid antigen stool test is available, the diagnosis of a rotavirus infection is typically made clinically, which means without testing and based on your symptoms, especially if rotavirus infections are going around in a community. This work is organized as follows. The model is formulated in section 2, in section 3 we analyze rotavirus only model while in section 4 we analyze the co-infection model. In Section 5, we present numerical simulations, discussions and made concluding remarks in Section 6.

2. MODEL FORMULATION

To formulate this model, we assume that all malaria-negative and rotavirus-negative children are susceptible, although it is possible to have some level of immunity to rotavirus infection due to breastfeeding[16]. The total human population, N_H, is subdivided into the classes, namely susceptible S_H, infectious with malaria I_M, latently infected with rotavirus L_R, symptomatically infected with rotavirus I_R, infectious with both malaria and latently with rotavirus L_{MR} and symptomatically infected with both malaria and rotavirus I_{MR} [8, 17]. By considering the latent stage of rotavirus disease, we have taken care of the fact that exposed individuals are capable of transmitting the disease before and after they have developed symptoms[8, 17]. We have also considered the mosquito population N_v and subdivided it into the susceptible S_V and infectious I_V classes. These two different classes of population therefore gives us the following equations:

$$N_H = S_H + I_M + L_R + I_R + L_{MR} + I_{MR} \tag{1}$$

and

$$N_V = S_V + I_V. \tag{2}$$

We denote the rates of infection of susceptible humans with malaria and rotavirus by λ_M and λ_R respectively while susceptible vector is given by λ_v. The constant per capita recruitment rate into susceptible human and vector population is denoted by Λ_H and Λ_v respectively. The rate at which humans progress from the L_R class to the I_R class is ψ. Finally, we let $\vartheta = \vartheta_M + \vartheta_R$ be the disease induced mortality in humans, μ_H and μ_v be the rates at which natural deaths occur in all human and vector sub-populations respectively. Malarial infection has a depressant effect on the immune system. Acute malarial parasitemia has a profound immunosuppressant effect, probably through the activation of suppressor T cells. In a malaria endemic area, young children may suffer from severe infections (bacterial or protozoal diseases) as either super-infections or co-infections due to this immunosuppression [18]. We thus define the parameter $\theta > 1$ to account for the increased susceptibility to infection with rotavirus for individuals infected with malaria. The expected decrease in contact due to ill health as a result of rotavirus disease is accounted for by the parameter $0 < \rho < 1$. We also define $\epsilon > 1$ as modification parameter accounting for assumed increased rate of progression from latent to active rotavirus infection for those infected with malaria.

The individuals displaying symptoms of both malaria and rotavirus suffer malaria-induced mortality at the rate $\delta\vartheta_M$, where the parameter $\delta > 1$ accounts for the assumed increase in malaria-related mortality due to the dual infection with rotavirus and also suffer rotavirus-induced mortality at the rate $\kappa\vartheta_R$, where the parameter $\kappa > 1$ accounts for the assumed increase in rotavirus-related mortality due to the dual infection with malaria. The rates of recovery back into the susceptible class from malaria, symptomatic rotavirus and symptomatic dual infections are given by γ_1, γ_2 and γ_3 respectively.

The force of infection associated with malaria infection in humans is

$$\lambda_M = \frac{\beta_m b_m I_V}{N_H} \tag{3}$$

where β_m is the transmission probability of malaria in humans and b_m is the per capita biting rate of mosquitoes.
The force of infection associated with malaria infection in vectors is

$$\lambda_v = \beta_v b_m \frac{(I_M + L_{MR} + \alpha I_{MR})}{N_H} \tag{4}$$

where β_v is the transmission probability of malaria in vectors and $\alpha \geq 1$ is a modification parameter accounting for the increased likelihood of infection of vectors from humans with dual malaria-rotavirus infection as compared to acquiring infection from humans with malaria only [18].

The force of infection associated with rotavirus infection is

$$\lambda_R = \beta_R \frac{L_R + L_{MR} + \phi(I_R + I_{MR})}{N_H} \tag{5}$$

where β_R is the effective contact rate for rotavirus infection and the modification parameter $\phi > 1$ accounts for the the fact that individuals displaying rotavirus symptoms are more infectious than individuals latently infected with rotavirus. The model flow diagrams for both human and mosquito populations are show in Figure1 below. From the above definitions, formulations and variables, we have developed the following model

$$\begin{aligned}
\frac{dS_H}{dt} &= \Lambda_H - \frac{\beta_m b_m I_V}{N_H} S_H - \beta_R \frac{L_R + L_{MR} + \phi(I_R + I_{MR})}{N_H} S_H - \mu_H S_H \\
&\quad + \gamma_1 I_M + \gamma_2 I_R + \gamma_3 I_{MR} \\
\frac{dI_M}{dt} &= \frac{\beta_m b_m I_V}{N_H} S_H - \theta\beta_R \frac{L_R + L_{MR} + \phi(I_R + I_{MR})}{N_H} I_M - \gamma_1 I_M \\
&\quad - \vartheta_M I_M - \mu_H I_M \\
\frac{dL_R}{dt} &= \beta_R \frac{L_R + L_{MR} + \phi(I_R + I_{MR})}{N_H} S_H - \frac{\beta_m b_m I_V}{N_H} L_R - \psi L_R - \mu_H L_R \\
\frac{dI_R}{dt} &= \psi L_R - \rho \frac{\beta_m b_m I_V}{N_H} I_R - \vartheta_R I_R - \gamma_2 I_R - \mu_H I_R \\
\frac{dL_{MR}}{dt} &= \frac{\beta_m b_m I_V}{N_H} L_R + \theta\beta_R \frac{L_R + L_{MR} + \phi(I_R + I_{MR})}{N_H} I_M
\end{aligned} \tag{6}$$

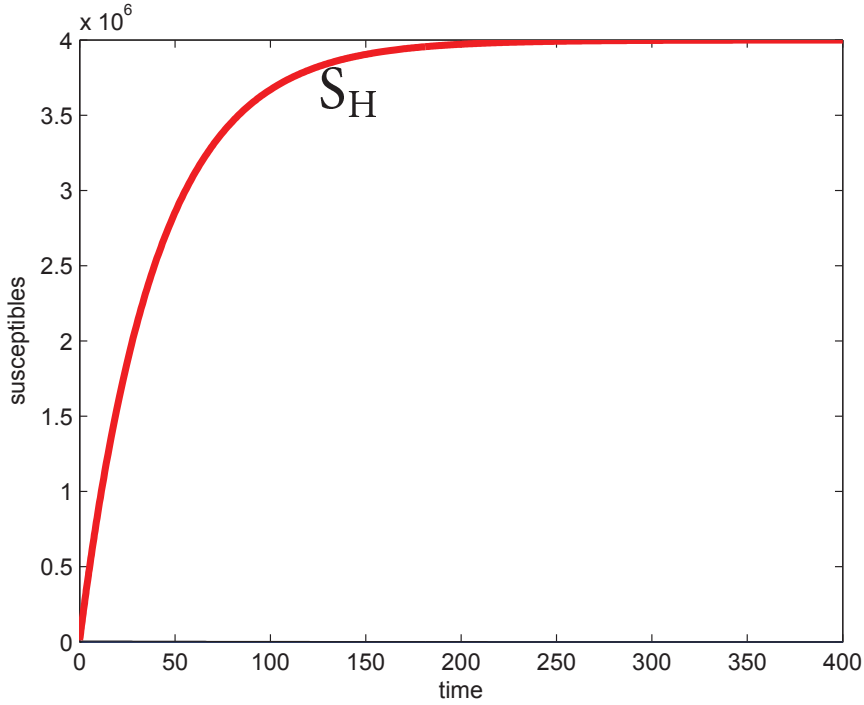


Figure 1: Model flow for (a) human population and (b) mosquito population.

$$\begin{aligned}
& -\epsilon\psi L_{MR} - (\vartheta_M + \mu_H)L_{MR} \\
\frac{dI_{MR}}{dt} &= \rho\frac{\beta_m b_m I_V}{N_H} I_R + \epsilon\psi L_{MR} - (\delta\vartheta_M + \kappa\vartheta_R + \gamma_3 + \mu_H)I_{MR} \\
\frac{dS_V}{dt} &= \Lambda_v - \beta_v b_m \frac{(I_M + L_{MR} + \alpha I_{MR})}{N_H} S_V - \mu_v S_V \\
\frac{dI_V}{dt} &= \beta_v b_m \frac{(I_M + L_{MR} + \alpha I_{MR})}{N_H} S_V - \mu_v I_V
\end{aligned}$$

3. ANALYSIS OF MALARIA FREE MODEL (ROTAVIRUS ONLY)

In the absence of malaria, that is, $I_V = L_{MR} = I_M = S_V = I_{MR} = 0$, we obtain rotavirus only model given by

$$\begin{aligned}
\frac{dS_H}{dt} &= \Lambda_H - \beta_R \left(\frac{L_R + \phi I_R}{N_H}\right) S_H - \mu_H S_H + \gamma_2 I_R \\
\frac{dL_R}{dt} &= \beta_R \left(\frac{L_R + \phi I_R}{N_H}\right) S_H - (\psi + \mu_H)L_R \\
\frac{dI_R}{dt} &= \psi L_R - (\vartheta_R + \gamma_2 + \mu_H)I_R,
\end{aligned} \tag{7}$$

where $N_H = S_H + L_R + I_R$.
Consider the region

$$\Omega = \{(S_H, L_R, I_R) \in \mathbb{R}^3_+ : N_H \leq \frac{\Lambda_H}{\mu_H}$$

It can be verified (see,[19, 20]) that all solutions of system (7) of Ω remains in Ω for all time $t \geq 0$. Thus, Ω is positively invariant hence we analyze system (7) in Ω.
System (7) has a disease free equilibrium given by $E^0 = \left(\frac{\Lambda_H}{\mu_H}, 0, 0\right)$. Using the next generation operator matrix as used in [21, 22, 23], we obtain the basic reproduction number as

$$R_0 = \frac{\beta_R(\vartheta_R + \gamma_2 + \mu_H + \phi\psi)}{(\psi + \mu_H)(\vartheta_R + \gamma_2 + \mu_H)} \tag{8}$$

For more details on the use of the next generation matrix, see Section 4.4.

If we let $\beta_R < (\psi + \mu_H)$, then the following theorem holds;

Theorem 1. *Whenever $\beta_R < (\psi + \mu_H)$, the disease free equilibrium (E^0) of system (7) is globally asymptotically stable when $R_0 \leq 1$ and unstable when $R_0 > 1$.*

Proof. We start by proving the local asymptotic stability of the E^0. The Jacobian matrix of system (7) at $E^0 = \left(\frac{\Lambda_H}{\mu_H}, 0, 0\right)$ is given as

$$J_{(E^0)} = \begin{pmatrix} -\mu_H & -\beta_R & -\phi\beta_R + \gamma_2 \\ 0 & \beta_R - (\psi + \mu_H) & \phi\beta_R \\ 0 & \psi & -(\vartheta_R + \gamma_2 + \mu_H) \end{pmatrix} \tag{9}$$

The Jacobian matrix (9) has one of its eigen values give by $\lambda_1 = -\mu_H < 0$. To obtain the remaining eigenvalues, we express (9) as a 2×2 block matrix A defined by

$$A = \begin{pmatrix} \beta_R - (\psi + \mu_H) & \phi\beta_R \\ \psi & -(\vartheta_R + \gamma_2 + \mu_H) \end{pmatrix} \tag{10}$$

If $\beta_R < (\psi + \mu_H)$, then we can see clearly that the trace of A is negative. The determinant of matrix A is given as

$$DetA = -\beta_R(\vartheta_R + \gamma_2 + \mu_H + \psi\phi) + (\psi + \mu_H)(\vartheta_R + \gamma_2 + \mu_H)$$

From equation (8), we see that if $R_0 < 1$, then $(\psi+\mu_H)(\vartheta_R+\gamma_2+\mu_H) > \beta_R(\vartheta_R+\gamma_2+\mu_H+\psi\phi)$, thus $DetA > 0$. The local stability is studied by examining the trace and determinant of the block matrix A. This implies that Routh-Hurwitz condition hold [24]. Therefore, we conclude that the disease free equilibrium is locally asymptotically stable. To prove global stability of E^0, we use Lyapunov function defined by

$$L = (\vartheta_R + \gamma_2 + \mu_H + \phi\psi)L_R + (\mu_H + \psi)\phi I_R \tag{11}$$

If $R_0 \leq 1$, we have

$$\begin{aligned} L' =&(\vartheta_R + \gamma_2 + \mu_H + \phi\psi)\beta_R S_H \left(\frac{L_R + \phi I_R}{N_H}\right) - (\psi + \mu_H)(\vartheta_R + \gamma_2 + \mu_H + \phi\psi)L_R \\ &+ (\mu_H + \psi)\phi L_R - (\mu_H + \psi)(\vartheta_R + \gamma_2 + \mu_H)\phi I_R \\ =&\beta_R \frac{S_H}{N_H}(\vartheta_R + \gamma_2 + \mu_H + \phi\psi)(L_R + \phi I_R) - (\mu_H + \psi)(\vartheta_R + \gamma_2 + \mu_H)L_R - \\ &(\mu_H + \psi)(\vartheta_R + \gamma_2 + \mu_H)\phi I_R \\ \leq\ & [\beta_R(\vartheta_R + \gamma_2 + \mu_H + \phi\psi) - (\mu_H + \psi)(\vartheta_R + \gamma_2 + \mu_H)](L_R + \phi I_R) \\ \leq&(R_0 - 1)[(\mu_H + \psi)(\vartheta_R + \gamma_2 + \mu_H)](L_R + \phi I_R) \\ \leq& 0 \end{aligned} \tag{12}$$

Since all the parameters in the model are nonnegative, we have $L' \leq 0$ for $R_0 \leq 1$ or when both L_R and I_R are equal to zero. Hence L is a Lyapunov function on Ω. Since Ω is invariant and attracting, singleton $\{E^0\}$ is the largest compact invariant set in $\{(S_H, L_R, I_R) \in \Omega : L' = 0\}$. Lasalle's invariance principle [25], therefore implies that the disease free equilibrium is globally asymptotically stable. □

Theorem 2. *An endemic equilibrium $I_R^* > 0$ exists provided that $R_0 > 1$.*

Proof. At an endemic equilibrium, $E^* = (S_H^*, L_R^*, {I_R}^*)$, from equation (3) of system (7) we get,

$$L_R^* = \left(\frac{\vartheta_R + \gamma_2 + \mu_H}{\psi}\right) I_R^* \tag{13}$$

Adding equations (1-3) of system (7) at equilibrium point E^* and expressing the sum as L_R^* in terms of S_H^* and I_R^* we obtain,

$$L_R^* = \frac{\Lambda_H - \mu_H S_H^* - (\mu_H + \vartheta_R)I_R^*}{\mu_H} \tag{14}$$

Solving for S_H^* by equating equations (13) and (14), we get

$$S_H^* = \frac{\Lambda_H}{\mu_H} - \frac{(\mu_H + \vartheta_R)I_R^*}{\mu_H} - \frac{(\vartheta_R + \gamma_2 + \mu_H)I_R^*}{\psi} \tag{15}$$

Substituting equations (14) and (15) into equation (2) of system (7) get

$$\beta_R \left(\frac{\frac{(\vartheta_R+\gamma_2+\mu_H)I_R^*}{\psi} + \phi I_R^*}{\frac{\Lambda_H}{\mu_H} - \frac{(\mu_H+\vartheta_R)I_R^*}{\mu_H} - \frac{(\vartheta_R+\gamma_2+\mu_H)I_R^*}{\psi} + \frac{(\vartheta_R+\gamma_2+\mu_H)I_R^*}{\psi} + I_R^*} \right) \times$$
$$\left(\frac{\Lambda_H}{\mu_H} - \frac{(\mu_H+\vartheta_R)I_R^*}{\mu_H} - \frac{(\vartheta_R+\gamma_2+\mu_H)I_R^*}{\psi} \right) - (\psi+\mu_H)\left(\frac{(\vartheta_R+\gamma_2+\mu_H)I_R^*}{\psi} \right) = 0$$
$$\beta_R \left(\frac{(\vartheta_R+\gamma_2+\mu_H+\psi\phi)I_R^*}{\frac{\Lambda_H-\vartheta_R I_R^*}{\mu_H}} \right) \times \left(\frac{\Lambda_H}{\mu_H} - \frac{(\mu_H+\vartheta_R)I_R^*}{\mu_H} - \frac{(\vartheta_R+\gamma_2+\mu_H)I_R^*}{\psi} \right)$$
$$- (\psi+\mu_H)\left(\frac{(\vartheta_R+\gamma_2+\mu_H)I_R^*}{\psi} \right) = 0$$
$$\beta_R \left(\frac{\vartheta_R+\gamma_2+\mu_H+\psi\phi}{\psi(\Lambda_H-\vartheta_H I_R^*)} \right) \left(\frac{\psi\Lambda_H - \psi(\vartheta_R+\mu_H)I_R^* - \mu_H(\vartheta_R+\gamma_2+\mu_H)I_R^*}{\psi} \right) -$$
$$(\mu_H+\psi)\frac{(\vartheta_R+\gamma_2+\mu_H)}{\psi} = 0$$
$$R_0 \left(\frac{\psi\Lambda_H - \psi(\vartheta_R+\mu_H)I_R^* - \mu_H(\vartheta_R+\gamma_2+\mu_H)I_R^*}{\psi(\Lambda_H-\vartheta_R I_R^*)} \right) - 1 = 0$$
$$R_0\psi\Lambda_H - R_0\psi(\vartheta_R+\mu_H)I_R^* - R_0(\vartheta+\gamma_2+\mu_H)I_R^* = \psi(\Lambda_H-\vartheta_R I_R^*)$$
$$I^* = \frac{\psi\Lambda_H(R_0-1)}{R_0[\psi(\vartheta_R+\mu_H)+\mu_H(\vartheta_R+\gamma_2+\mu_H)]-\psi\vartheta_R} \tag{16}$$

From equation (16) we see that $I_R^* > 0$ provided that $R_0 > 1$. This completes the proof. □

To prove global stability of the endemic equilibrium, E^* of system (7), we use the method of geometrical approach developed by Li and Muldowney in [26]. For a brief outline of this approach, see [27].

Lemma 1. *The system* (7) *is uniformly persistent and satisfies assumptions* (H_1), (H_2) *and* (H_3) *as defined in [26]*

For an assumption (H_3), we have shown in Theorem 2 that indeed $E^* = (S_H^*, L_R^*, I_R^*)$ is the only endemic equilibrium of system (7) and it exits whenever $R_0 > 1$. Assumptions (H_1) and(H_2) also hold since by using the persistence property by [28], it can be verified that the solution of system (7) is uniformly persistent. Let $P = E^0$, Theorem 1. implies that when $R_0 > 1$, P^s is an isolated in Ω and is contained in the $S - axis$ in the boundary of Ω. When $R_0 > 1$, system (7) satisfies condition by [29]. Therefore, we conclude that system (7) is persistent in Ω when $R_0 > 1$.
Since we have shown that all the assumptions are satisfied, we therefore, apply Theorem 3.3 and Theorem 3.4 of [27] to prove the following theorem:

Theorem 3. *If* $R_0 > 1$ *and* $N_H \leq \frac{\psi}{2\beta_R}$, *then the unique positive endemic equilibrium,* E^* *of system* (7) *is globally asymptotically stable.*

Proof. The Jacobian matrix of system (7) associated with the general solution (S_H, L_R, I_R)is given by

$$J = \begin{bmatrix} A_{11} & A_{12} & A_{13} \\ A_{21} & A_{22} & A_{23} \\ A_{31} & A_{32} & A_{33} \end{bmatrix}, \tag{17}$$

where

$$\begin{aligned} A_{11} &= -\frac{\beta_R(L_R + \phi I_R)(L_R + I_R)}{N_H^2} - \mu_H \\ A_{12} &= \frac{-\beta_R S_H(S_H + I_R) + \beta_R \phi I_R S_H}{N_H^2} \\ A_{13} &= \frac{-\phi\beta_R S_H(S_H + L_R) + \beta_R L_R S_H}{N_H^2} + \gamma_2 \end{aligned}$$

$$\begin{aligned} A_{21} &= \frac{\beta_R(L_R + \phi I_R)(L_R + I_R)}{N_H^2} \\ A_{22} &= \frac{\beta_R S_H(S_H + I_R) - \beta_R \phi I_R S_H}{N_H^2} - (\psi + \mu_H) \end{aligned}$$

$$\begin{aligned} A_{23} &= \frac{\phi\beta_R S_H(S_H + I_R) - \beta_R L_R S_H}{N_H^2} \\ A_{31} &= 0 \\ A_{32} &= \psi \\ A_{33} &= -(\vartheta_R + \gamma_2 + \mu_H). \end{aligned}$$

The second compound additive matrix of (17) is given as

$$J^{[2]} = \begin{bmatrix} A_{11} & A_{12} & A_{13} \\ A_{21} & A_{22} & A_{23} \\ A_{31} & A_{32} & A_{33} \end{bmatrix}, \tag{18}$$

where

$$
\begin{aligned}
A_{11} &= -\beta_R \frac{(L_R + \phi I_R - S_H)}{N_H} - (2\mu_H + \psi) \\
A_{12} &= \beta_R S_H \frac{(\phi N_H - (L_R + \phi I_R))}{N_H^2} \\
A_{13} &= \beta_R S_H \frac{(\phi N_H - (L_R + \phi I_R))}{N_H^2} - \gamma_2 \\
A_{21} &= \psi \\
A_{22} &= -\beta_R \frac{(N_H - S_H)(L_R + \phi I_R)}{N_H^2} - (2\mu_H + \vartheta_R + \gamma_2) \\
A_{23} &= -\beta_R S_H \frac{(N_H - (L_R + \phi I_R)}{N_H^2} \\
A_{31} &= 0 \\
A_{32} &= \beta_R \frac{(N_H - S_H)(L_R + \phi I_R)}{N_H^2} \\
A_{33} &= \beta_R S_H \frac{(N_H - (L_R + \phi I_R))}{N_H^2} - (2\mu_H + \vartheta_R + \gamma_2 + \psi).
\end{aligned}
$$

Set matrix

$$
P(S_H, L_R, I_R) = \operatorname{diag}\left(1, \frac{L_R}{I_R}, \frac{L_R}{I_R}\right).
$$

Then

$$
P_f P^{-1} = \operatorname{diag}\left[0, \frac{L_R'}{L_R} - \frac{I_R'}{I_R}, \frac{L_R'}{L_R} - \frac{I_R'}{I_R}\right].
$$

Matrix $PJ^{[2]}P^{-1}$ is given as

$$
PJ^{[2]}P^{-1} = \begin{bmatrix} A_{11} & A_{12} & A_{13} \\ A_{21} & A_{22} & A_{23} \\ A_{31} & A_{32} & A_{33} \end{bmatrix}, \tag{19}
$$

where

$$A_{11} = -\beta_R \frac{(L_R + \phi I_R - S_H)}{N_H} - (2\mu_H + \psi)$$
$$A_{12} = \frac{I_R}{L_R}\left[\beta_R S_H \frac{(\phi N_H - (L_R + \phi I_R))}{N_H^2}\right]$$
$$A_{13} = \beta_R S_H \frac{(\phi N_H - (L_R + \phi I_R))}{N_H^2} - \gamma_2$$
$$A_{21} = \psi \frac{L_R}{I_R}$$
$$A_{22} = -\beta_R \frac{(N_H - S_H)(L_R + \phi I_R)}{N_H^2} - (2\mu_H + \vartheta_R + \gamma_2)$$
$$A_{23} = -\beta_R S_H \frac{(N_H - (L_R + \phi I_R)}{N_H^2}$$
$$A_{31} = 0$$
$$A_{32} = \beta_R \frac{(N_H - S_H)(L_R + \phi I_R)}{N_H^2}$$
$$A_{33} = \beta_R S_H \frac{(N_H - (L_R + \phi I_R))}{N_H^2} - (2\mu_H + \vartheta_R + \gamma_2 + \psi).$$

The matrix $P_f P^{-1} + P J^{[2]} P^{-1}$ as defined in equation (3.7) of [27] can be written in block form as:

$$Q = \begin{bmatrix} Q_{11} & Q_{12} \\ Q_{21} & Q_{22} \end{bmatrix}$$

where,

$$Q_{11} = \frac{-\beta_R(L_R + \phi I_R - S_H)}{N_H} - (2\mu_H + \psi)$$
$$Q_{12} = \left[\frac{I_R}{L_R}\left(\frac{\beta_R S_H(\phi N - (L_R + \phi I_R))}{N_H^2}\right), \quad \frac{I_R}{L_R}\left(\frac{\beta_R S_H(\phi N - (L_R + \phi I_R))}{N_H^2} - \gamma_2\right)\right]$$
$$Q_{21} = \begin{pmatrix} \psi \frac{L_R}{I_R} \\ 0 \end{pmatrix}$$

$$Q_{22} = \begin{bmatrix} A_{11} & A_{12} \\ A_{21} & A_{22}, \end{bmatrix}$$

where

$$A_{11} = \frac{L_R'}{L_R} - \frac{I_R'}{I_R} - \frac{\beta_R(N_H - S_H)(L_R + \phi I_R))}{N_H^2} - (2\mu_H + \vartheta_R + \gamma_2)$$
$$A_{12} = \frac{-\beta_R S_H(N_H - (L_R + \phi I_R))}{N_H^2}$$
$$A_{21} = \frac{\beta_R S_H(N_H - S_H)(L_R + \phi I_R))}{N_H^2}$$
$$A_{22} = \frac{L_R'}{L_R} - \frac{I_R'}{I_R} + \frac{\beta_R S_H(N_H - (L_R + \phi I_R))}{N_H^2} - (2\mu_H + \vartheta_R + \psi).$$

Let the vector norm $|\cdot|$ in $\mathbb{R}^3 \cong \mathbb{R}^{\binom{3}{2}}$ be chosen as

$$|(u,v,w)| = \sup\{|u|, |v|+|w|\},$$

for any vector $(u,v,w) \in \mathbb{R}^3$. We can then estimate the Lozinskii measure $k(B)$ with respect to $|\cdot|$[30] by

$$k(Q) \leq \sup\{g_1, g_2\}$$

with

$$g_1 = k_1(Q_{11}) + |Q_{12}|$$
$$g_2 = |Q_{21}| + k_1(Q_{22})$$

where $|Q_{12}|$ and $|Q_{21}|$ are matrix norms induced by L_1 vector norm and k_1 being the Lozinskii measure with respect to the L_1 norm. Specifically,

$$k_1(Q_{22}) = \frac{L_R'}{L_R} - \frac{I_R'}{I_R} - 2\mu_H - \vartheta_R - \gamma_2 + \sup\left\{\frac{2\beta_R S_H(N_H - (L_R + \phi I_R))}{N_H^2} - \psi, 0\right\}$$

$$g_2 = \frac{L_R'}{L_R} - \frac{I_R'}{I_R} - 2\mu_H - \vartheta_R - \gamma_2 + \sup\left\{\frac{2\beta_R S_H(N_H - (L_R + \phi I_R))}{N_H^2} - \psi, 0\right\} + \psi\frac{L_R}{I_R} \quad (20)$$

From equation (3) of system (7), we have

$$\psi\frac{L_R}{I_R} = \frac{I_R'}{I_R} + (\vartheta_R + \gamma_2 + \mu_H).$$

Substituting this equation into (20), we obtain

$$\begin{aligned} g_2 &= \frac{L_R'}{L_R} - \mu_H - \vartheta_R - \gamma_2 + \sup\left\{\frac{2\beta_R S_H(N_H - (L_R + \phi I_R))}{N_H^2} - \psi, 0\right\} \\ &\leq \frac{L_R'}{L_R} - \mu_H \end{aligned}$$

provided that $N_H \leq \frac{\psi}{2\beta_R}$.

For g_1, we have

$$g_1 = \frac{-\beta_R(L_R + \phi I_R - S_H)}{N_H} - \psi - 2\mu_H + \frac{\beta_R S_H I_R(\phi N_H - (L_R + \phi I_R))}{L_R N_H^2} \quad (21)$$

From equation (2) of system (7), we have

$$\frac{\phi\beta_R I_R S_H}{N_H I_R} = \frac{L_R'}{L_R} - \frac{\beta_R S_H}{N_H} + \psi + \mu_H.$$

Again substituting this equation into (21), we obtain

$$\begin{aligned} g_1 &= \frac{L_R'}{L_R} - \mu_H - \frac{\beta_R(L_R + \phi I_R)}{N_H} - \frac{\beta_R S_H I_R(L_R + \phi I_R)}{L_R N_H^2} \\ &\leq \frac{L_R'}{L_R} - \mu_H \end{aligned}$$

Therefore, $k(Q) \leq \frac{L'_R}{L_R} - \mu_H$.

Since $0 \leq L_R \leq N_H$, there exists $T > 0$ such that when $t > T$, $\frac{\ln L_R(t) - \ln L_R(0)}{t} < \frac{\mu_H}{2}$. As a result

$$\frac{1}{t}\int_0^t k(Q)dt \leq \frac{1}{t}\int_0^t \left(\frac{L'_R}{L_R} - \mu_H\right) = \frac{\ln L_R(t) - \ln L_R(0)}{t} - \mu_H < \frac{-\mu_H}{2},$$

which implies that $\bar{q_2} \leq \frac{-\mu_H}{2} < 0$. Hence, we have shown that the endemic equilibrium E^* of system (7) is globally asymptotically stable in Ω. □

4. ANALYSIS OF CO-INFECTION OF ROTAVIRUS AND MALARIA

4.1. Invariant region

Equation (6) models population whose values will never be negative. We therefore assume that all variables and parameters are non-negative for all time, $t \geq 0$. We analyze (6) in a suitable feasible region obtained as follows:

Lemma 2. *Solutions of the model* (6) *are in the region* $\Psi = \Psi_H \times \Psi_v$.

Proof. To show that all feasible solutions are uniformly bounded in a proper subset Ψ, we split model (6) into both human component (N_H) and the mosquito component (N_v) given by equations (1) and (2) respectively.

Let

$$(S_H, I_M, L_R, I_R, L_{MR}, I_{MR}) \in \mathbb{R}^6_+ \tag{22}$$

be any solution with non-negative initial conditions. Time derivative of N_H along a solution path of the model (6) gives

$$\frac{dN_H}{dt} < \Lambda_H - \mu_H N_H \tag{23}$$

Applying Theorem 8. (Comparison Theorem) on differential inequality by [31], we obtain

$$0 \leq N_H \leq \frac{\Lambda_H}{\mu_H} + N_H(0)e^{-\mu_H t} \tag{24}$$

where $N_H(0)$ is the value of (1) evaluated at the initial values of the respective variables. Therefore, as $t \to \infty$, we have

$$0 \leq N_H \leq \frac{\Lambda_H}{\mu_H} \tag{25}$$

Thus all feasible solutions of the human-only component of model (6) enters the region

$$\Psi_H = \{(S_H, I_M, L_R, I_R, L_{MR}, I_{MR}) : N_H \leq \frac{\Lambda_H}{\mu_H}\} \tag{26}$$

Similarly, if we let

$$(S_V, I_V) \in \mathbb{R}^2_+ \tag{27}$$

by using same steps as in equations (23)-(24) it can be shown that

$$0 \leq N_V \leq \frac{\Lambda_v}{\mu_v} + N_V(0)e^{-\mu_v t} \tag{28}$$

where $N_V(0)$ represents the value of (2) evaluated at the initial values of the respective variables. Thus as $t \to \infty$, we have

$$0 \leq N_V \leq \frac{\Lambda_v}{\mu_v} \tag{29}$$

Therefore all feasible solutions of the mosquito-only component of model (6) enters the region

$$\Psi_v = \{(S_V, I_V) : N_V \leq \frac{\Lambda_v}{\mu_v}\} \tag{30}$$

Thus, it follows from (26) and (30) that all possible solutions of the model will enter the region $\Psi = \Psi_H \times \Psi_v$. □

4.2. Positivity of solutions

Lemma 3. *Let the initial conditions be*

$$\{(S_H, S_V)(0) > 0, (I_M, L_R, I_R, L_{MR}, I_{MR}, I_V)(0) > (0)\} \in \Psi. \tag{31}$$

Then the solution set

$$\{S_H, I_M, L_R, I_R, L_{MR}, I_{MR}, S_V, I_V\}(t) \tag{32}$$

of model (6) is positive $\forall t > 0$.

Proof. From the first equation in model (6), that is

$$\frac{dS_H}{dt} = \Lambda_H - \lambda_M S_H - \lambda_R S_H - \mu_H S_H + \gamma_1 I_M + \gamma_2 I_R + \gamma_3 I_{MR},$$

we have

$$\frac{dS_H}{dt} = \Lambda_H - \lambda_M S_H - \lambda_R S_H + \gamma_1 I_M + \gamma_2 I_R + \gamma_3 I_{MR} - \mu_H S_H \geq -(\lambda_M + \lambda_R + \mu_H) S_H \tag{33}$$

Integrating (33) yields

$$S_H \geq S_H(0)e^{-(\lambda_M + \lambda_R + \mu_H)t} \geq 0 \tag{34}$$

since $\lambda_M + \lambda_R + \mu_H > 0$. □

Applying the same procedure, we can show that the remaining variables are also positive $\forall t > 0$. Hence, Ψ is positively invariant under the flow induced by (6). Existence, uniqueness and continuation results hold for model (6). Thus, model (6) is well-posed mathematically and epidemiologically and it is sufficient to consider solutions in Ψ.

4.3. Disease-free equilibrium point

The disease-free equilibrium (DFE) points of an epidemiological model are its steady-state solutions in the absence of infection or disease. We denote this point by E_1^0 and define the "*diseased*" classes as the human or mosquito populations that are either exposed or infectious. Define the positive orthant in $\mathbb{R}^8$ by $\mathbb{R}^8_+$ and the boundary of $\mathbb{R}^8_+$ by $\partial\mathbb{R}^8_+$.

Lemma 4. *For all equilibrium points on* $\Psi \cap \partial\mathbb{R}^8_+$, $I_M = L_R = I_R = L_{MR} = I_{MR} = I_V = 0$

The positive DFE for human and mosquito populations for the model (6) are

$$N_H^0 = \left(\frac{\Lambda_H}{\mu_H}, 0, 0, 0, 0, 0\right) \text{ and } N_V^0 = \left(\frac{\Lambda_v}{\mu_v}, 0\right). \tag{35}$$

Lemma 5. *The model* (6) *has exactly one DFE,* $E^0 = (\frac{\Lambda_H}{\mu_H}, 0, 0, 0, 0, 0, \frac{\Lambda_v}{\mu_v}, 0)$

Proof. To prove this, we show that E_1^0 is the only equilibrium point of model (6) on $\Psi \cap \partial\mathbb{R}^8_+$. Substituting E_1^0 into (6), we obtain all derivatives as zero, hence E_1^0 is an equilibrium point. From Lemma 4, the only equilibrium point for N_H is $\frac{\Lambda_H}{\mu_H}$ and the only equilibrium point for N_V is $\frac{\Lambda_v}{\mu_v}$. Thus the only equilibrium point for $\Psi \cap \partial\mathbb{R}^8_+$ is E_1^0. □

4.4. Local stability of the disease-free equilibrium

The global dynamics of the model (6) is highly dependent on the basic reproduction number. The basic reproduction number is defined as the expected number of secondary infections produced by an index case in a completely susceptible population[32]. We define the basic reproduction number here, R_{mr} as the number of secondary malaria (or rotavirus) infections due to a single malaria (or a single rotavirus-infective) individual. We determine R_{mr} using the next generation operator approach[21]. The associated next generation matrices are

$$F = \begin{pmatrix} 0 & 0 & 0 & 0 & 0 & \beta_m b_m \\ 0 & \beta_R & \phi\beta_R & \beta_R & \phi\beta_R & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ \beta_v b_m n & 0 & 0 & \beta_v b_m n & \alpha\beta_v b_m n & 0 \end{pmatrix}$$

and

$$V = \begin{pmatrix} h_1 & 0 & 0 & 0 & 0 & 0 \\ 0 & h_2 & 0 & 0 & 0 & 0 \\ 0 & -\psi & h_3 & 0 & 0 & 0 \\ 0 & 0 & 0 & h_4 & 0 & 0 \\ 0 & 0 & 0 & -\epsilon\psi & h_5 & 0 \\ 0 & 0 & 0 & 0 & 0 & \mu_v \end{pmatrix}$$

where $h_1 = \gamma_1 + \vartheta_M + \mu_H$, $h_2 = \psi + \mu_H$, $h_3 = \gamma_2 + \vartheta_R + \mu_H$, $h_4 = \epsilon\psi + \vartheta_M + \mu_H$, $h_5 = \gamma_3 + \delta\vartheta_M + \kappa\vartheta_R + \mu_H$ and $n = \frac{\mu_H \Lambda_v}{\Lambda_H \mu_v}$.

The basic reproduction number R_{mr} is the spectral radius of the matrix FV^{-1}. The non-zero eigenvalues of the matrix FV^{-1} are

$$R_r = \frac{\beta_R}{\psi + \mu_H} + \frac{\phi\beta_R\psi}{(\gamma_2 + \vartheta_R + \mu_H)(\psi + \mu_H)}$$

and

$$R_m = \sqrt{\frac{b_m^2 \beta_m \beta_v \mu_H \Lambda_v}{\Lambda_H \mu_v^2 (\gamma_1 + \vartheta_M + \mu_H)}}.$$

Therefore R_{mr} is given by

$$R_{mr} = \max\{R_r, R_m\}. \tag{36}$$

R_m is a measure of the average number of secondary malaria infections in human or mosquito population caused by a single infective human or mosquito introduced into an entirely susceptible population. The expression R_m is biologically meaningful. It comprises of the term $\frac{\beta_v b_m}{\mu_v}$ which represents the number of secondary malaria infections in human caused by a single infected mosquito, while the term $\frac{\beta_m b_m \mu_H \Lambda_v}{\Lambda_H \mu_v^2 (\gamma_1 + \vartheta_M + \mu_H)}$ represents the number of secondary malaria infections in mosquitoes caused by a single infected human. Similarly, in R_r, the term $\frac{\beta_R}{\psi + \mu_H}$ is a measure of the average number of secondary rotavirus infections in humans caused by a single latently infected human, while the term $\frac{\phi\beta_R\psi}{(\gamma_2 + \vartheta_R + \mu_H)(\psi + \mu_H)}$ is a measure of the average number of secondary rotavirus infections in humans caused by a single symptomatically infected human introduced into an entirely susceptible population. The following lemma follows from Theorem 2 of [21].

Lemma 6. *If condition set in Theorem 3 holds and* $(\gamma_1 + \vartheta_M + \mu_H) > \beta_v b_m (\frac{\mu_H \Lambda_v}{\Lambda_H \mu_v^2})$, *then the disease-free equilibrium* E_1^0 *of the model* (6) *is locally asymptotically stable whenever* $R_{mr} < 1$.

Proof. The Jacobian matrix of model (6) at the disease free equilibrium is given as:

$$J_{E_1^0} = \begin{bmatrix} -\mu_H & \gamma_1 & -\beta_R & \gamma_2 - \phi\beta_R & -\beta_R & \gamma_3 - \phi\beta_R & 0 & -\beta_m b_m \\ 0 & -K_1 & 0 & 0 & 0 & 0 & 0 & \beta_m b_m \\ 0 & 0 & K_2 & \phi\beta_R & \beta_R & \phi\beta_R & 0 & 0 \\ 0 & 0 & 0 & -K_3 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & -K_4 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & \epsilon\psi & -K_5 & 0 & 0 \\ 0 & -\beta_v b_m p & 0 & 0 & -\beta_v b_m p & -\alpha\beta_v b_m p & -\mu_v & 0 \\ 0 & \beta_v b_m p & 0 & 0 & \beta_v b_m p & \alpha\beta_v b_m p & 0 & -\mu_v \end{bmatrix}, \tag{37}$$

where $K_1 = \gamma_1 + \vartheta_M + \mu_H$, $K_2 = \beta_R - (\psi + \mu_H)$, $K_3 = \vartheta_R + \gamma_2 + \mu_H$, $K_4 = \epsilon\psi + \vartheta_M + \mu_H$, $K_5 = \delta\vartheta_M + \kappa\vartheta_R + \gamma_3 + \mu_H$ and $p = \frac{\mu_H \Lambda_v}{\Lambda_H \mu_v}$.

The eigenvalues of the Jacobian matrix (37) is given as

$$(\lambda + \mu_H)(\lambda - K_2)(\lambda + K_3)(\lambda + K_4)(\lambda + K_5)(\lambda + \mu_v)[(\lambda + K_1)(\lambda + \mu_v) - \beta_v b_m p] = 0.$$

If assumption $\beta_R < (\psi + \mu_H)$ holds, then the first six eigenvalues are all negatives. The remaining two eigenvalues are obtained from the equation below.

$$\lambda^2 + (\mu_v + \gamma_1 + \vartheta_M + \mu_H)\lambda + \mu_v(\gamma_1 + \vartheta_M + \mu_H) - \beta_v b_m(\frac{\mu_H \Lambda_v}{\Lambda_H \mu_v}) = 0.$$

If $(\gamma_1 + \vartheta_M + \mu_H) > \beta_v b_m(\frac{\mu_H \Lambda_v}{\Lambda_H \mu_v^2})$, then these two eigenvalues have negative real part. Thus, the disease-free equilibrium E_1^0 of the model (6) is locally asymptotically stable. □

4.5. Global stability of the disease-free equilibrium of model (6)

We investigate the global asymptotic stability (GAS) of the disease-free equilibrium of the model using the theorem by Castillo-Chavez et.al[33]. We rewrite the model as

$$\begin{aligned} \frac{dX}{dt} &= H(X, Z), \\ \frac{dZ}{dt} &= G(X, Z), G(X, 0) = 0 \end{aligned} \tag{38}$$

where $X = (S_H, S_V)$ and $Z = (I_M, L_R, I_R, L_{MR}, I_{MR}, I_V)$, with the components of $X \in \mathbb{R}^2$ denoting the uninfected population and the components of $Z \in \mathbb{R}^6$ denoting the infected population.
The disease-free equilibrium is now denoted as

$$E_1^0 = (X^0, 0), X^0 = (\frac{\Lambda_H}{\mu_H}, \frac{\Lambda_v}{\mu_v}). \tag{39}$$

The conditions in (40) must be met to guarantee a global asymptotic stability:

$$\begin{aligned} \frac{dX}{dt} &= H(X,0), X^0 \text{ is globally asymptotically stable (GAS)} \\ G(X,Z) &= PZ - \widehat{G}(X,Z), \widehat{G}(X,Z) \geq 0 \text{ for } (X,Z) \in \Omega \end{aligned} \tag{40}$$

where $P = D_z G(X^0, 0)$ is an M-matrix (the off-diagonal elements of P are non-negative) and Ω is the region where the model makes biological sense.

To test whether system (38) satisfies conditions of (40), hence globally asymptotically stable whenever $R_{mr} < 1$, we proceed as follows:

From the model system (6) and (38), we have

$$H(X,0) = \begin{pmatrix} \Lambda_H - \mu_H S_H \\ \Lambda_v - \mu_v S_v \end{pmatrix}$$

$$G(X,Z) = PZ - \widehat{G}(X,Z)$$

where

$$P = \begin{pmatrix} -h_1 & 0 & 0 & 0 & 0 & \beta_m b_m \\ 0 & \beta_R - h_2 & \phi\beta_R & \beta_R & \phi\beta_R & 0 \\ 0 & \psi & -h_3 & 0 & 0 & 0 \\ 0 & 0 & 0 & -h_4 & 0 & 0 \\ 0 & 0 & 0 & \epsilon\psi & -h_5 & 0 \\ \beta_v b_m & 0 & 0 & \beta_v b_m & \alpha\beta_v b_m & -\mu_v \end{pmatrix},$$

where $h_1 = \gamma_1 + \vartheta_M + \mu_H, h_3 = \gamma_2 + \vartheta_R + \mu_H$ and $h_5 = \gamma_3 + \delta\vartheta_M + \kappa\vartheta_M + \mu_H$

$$\widehat{G}(X,Z) = \begin{pmatrix} \widehat{G}_1(X,Z) \\ \widehat{G}_2(X,Z) \\ \widehat{G}_3(X,Z) \\ \widehat{G}_4(X,Z) \\ \widehat{G}_5(X,Z) \\ \widehat{G}_6(X,Z) \end{pmatrix} = \begin{pmatrix} \beta_m b_m I_v (1 - \frac{S_H}{N_H}) + \theta\lambda_R I_M \\ \beta_R\{L_R + L_{MR} + \phi(I_R + I_{MR})\}(1 - \frac{S_H}{N_H}) \\ \rho\lambda_M I_R \\ -(\lambda_M L_R + \theta\lambda_R I_M) \\ -\rho\lambda_M I_R \\ \beta_v b_m\{(I_M + L_{MR} + \alpha I_{MR})\}(1 - \frac{S_V}{N_H}) \end{pmatrix}$$

Since $\widehat{G}_4(X,Z) < 0$ and $\widehat{G}_5(X,Z) < 0$, the conditions in (40) are not met. Therefore, E_1^0 is not globally asymptotically stable when $R_{mr} < 1$. However, if maximum protection is provided against the co-infection during an outbreak of rotavirus in a malaria-endemic region, then global stability of disease free equilibrium may be achieved. This is because with such protection $\widehat{G}_4(X,Z) = \widehat{G}_5(X,Z) = 0$, then all conditions in (40) are met. Thus, E_1^0 will be globally asymptotically stable when $R_{mr} < 1$. In other words, the fight against malaria and persistent infections such as rotavirus may be won if co-infection cases are kept at bare minimum.

4.6. Endemic equilibrium of the Model

The endemic equilibrium of the model is studied using the Centre Manifold Theorem [34, 35]. To apply this theorem we make the following change of variables. Let

$S_H = x_1, I_M = x_2, L_R = x_3, I_R = x_4, L_{MR} = x_5, I_{MR} = x_6, S_v = x_7, I_v = x_8$ so that $N_H = x_1 + x_2 + x_3 + x_4 + x_5 + x_6$ and $N_v = x_7 + x_8$. The model (6) can be rewritten in the form $\frac{dX}{dt} = F(x)$ where $X = (x_1, x_2, x_3, x_4, x_5, x_6, x_7, x_8)^T$ and $F = (f_1, f_2, f_3, f_4, f_5, f_6, f_7, f_8)$ as

$$\begin{aligned}
\frac{dx_1}{dt} &= f_1 = \Lambda_H - \lambda_M x_1 - \lambda_R x_1 - \mu_H x_1 + \gamma_1 x_2 + \gamma_2 x_4 + \gamma_3 x_6 \\
\frac{dx_2}{dt} &= f_2 = \lambda_M x_1 - \theta\lambda_R x_2 - \gamma_1 x_2 - \vartheta_M x_2 - \mu_H x_2 \\
\frac{dx_3}{dt} &= f_3 = \lambda_R x_1 - \lambda_M x_3 - \psi x_3 - \mu_H x_3 \\
\frac{dx_4}{dt} &= f_4 = \psi x_3 - \rho\lambda_M x_4 - \vartheta_R x_4 - \gamma_2 x_4 - \mu_H x_4 \\
\frac{dx_5}{dt} &= f_5 = \lambda_M x_3 + \theta\lambda_R x_2 - \epsilon\psi x_5 - (\vartheta_M + \mu_H) x_5 \\
\frac{dx_6}{dt} &= f_6 = \rho\lambda_M x_4 + \epsilon\psi x_5 - (\delta\vartheta_M + \kappa\vartheta_R + \gamma_3 + \mu_H) x_6 \\
\frac{dx_7}{dt} &= f_7 = \Lambda_v - \lambda_v x_7 - \mu_v x_7 \\
\frac{dx_8}{dt} &= f_8 = \lambda_v x_7 - \mu_v x_8
\end{aligned} \tag{41}$$

where $\lambda_M = \frac{\beta_m b_m x_8}{N_H}$, $\lambda_v = \beta_v b_m \frac{(x_2 + x_5 + \alpha x_6)}{N_H}$ and $\lambda_R = \beta_R \frac{x_3 + x_5 + \phi(x_4 + x_6)}{N_H}$.

The jacobian, $J_{E_1^0}$ of (41) at the disease free equilibrium E_1^0, is given by

$$\begin{pmatrix}
-\mu_H & \gamma_1 & -\beta_R & \gamma_2 - \phi\beta_R & -\beta_R & \gamma_3 - \phi\beta_R & 0 & -\beta_m b_m \\
0 & -K_1 & 0 & 0 & 0 & 0 & 0 & \beta_m b_m \\
0 & 0 & K_2 & \phi\beta_R & \beta_R & \phi\beta_R & 0 & 0 \\
0 & 0 & 0 & -K_3 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & -K_4 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & \epsilon\psi & -K_5 & 0 & 0 \\
0 & -\beta_v b_m p & 0 & 0 & -\beta_v b_m p & -\alpha\beta_v b_m p & -\mu_v & 0 \\
0 & \beta_v b_m p & 0 & 0 & \beta_v b_m p & \alpha\beta_v b_m p & 0 & -\mu_v
\end{pmatrix}$$

where $K_1 = \gamma_1 + \vartheta_M + \mu_H$, $K_2 = \beta_R - (\psi + \mu_H)$, $K_3 = (\vartheta_R + \gamma_2 + \mu_H)$, $K_4 = \epsilon\psi + \vartheta_M + \mu_H$, $K_5 = \delta\vartheta_M + \kappa\vartheta_R + \gamma_3 + \mu_H$, and $p = \frac{\mu_H \Lambda_v}{\Lambda_H \mu_v}$.

To analyze the dynamics of (41), we compute the eigenvectors of the jacobian of (41) at the DFE. It can be shown that this jacobian has a right eigenvector given by $W = (w_1, w_2, w_3, w_4, w_5, w_6, w_7, w_8)^T$, where

$w_3 = w_4 = 0, w_5 = 0, w_6 = 0$ and $w_1 = -\frac{(\gamma_1 + K_1) w_2}{\mu_H}, w_7 = \frac{-\beta_v b_m p w_2}{\mu_v}, w_8 = \frac{K_1 w_2}{\beta_m b_m}, w_2 = w_2 > 0$

and a left eigenvector given by $V = (v_1, v_2, v_3, v_4, v_5, v_6, v_7, v_8)^T$ where

$v_1 = v_3 = v_4 = v_7 = 0$ and $v_5 = \frac{\epsilon\psi v_6}{K_4}$, $v_2 = v_2 > 0$, $v_6 = \frac{\alpha\beta_v b_m p v_8}{K_5}$, $v_8 = \frac{\beta_v b_m v_2}{\mu_v}$.

Consider the case when $R_{mr} = 1$ (assuming that $R_r < R_m$) and choose the transmission probability of malaria in humans $\beta_m = \beta_m^*$ as a bifurcation parameter. Solving for β_m from $R_{mr} = R_m = 1$ gives

$$\beta_m = \beta_m^* = \frac{\Lambda_H \mu_v^2 (\vartheta_M + \gamma_1 + \mu_H)}{b_m^2 \beta_v \mu_H \Lambda_v} \tag{42}$$

It can be shown after some manipulation involving the evaluation of the associated non-vanishing partial derivatives of f that

$$\begin{aligned} s^* &= \frac{2\mu_H}{\Lambda_H}(v_2 w_1 w_8 \beta_m b_m + v_8 w_2 w_7 \beta_v b_m) \text{ and} \\ r^* &= v_2 w_8 b_m > 0. \end{aligned} \tag{43}$$

Thus, the following result follows from item (iv) in the Theorem of Castillo-Chavez et al, see [35].

Lemma 7. *Model* (6) *has a unique endemic equilibrium state which is locally-asymptotically stable (LAS) if* $R_{mr} < 1$ *and unstable if* $R_{mr} > 1$.

Note: Whenever (43) holds, the model may undergo a forward bifurcation. This implies that disease transmission in a population of susceptibles may be contained by a reproduction number less than unity.

5. NUMERICAL SIMULATIONS AND DISCUSSIONS

In order to support the analytical results in this work, we have used Matlab and ODE45 package to conduct numerical simulations for both model (6) and model (7) using parameter values given in Table 1. Figure 2(a) illustrates the global stability of the disease free equilibrium of model (7) when $R_0 = 0.725$. It shows that in a disease free population, both L_R and I_R are equal to zero while S_H goes to the boundary equilibrium as time tends to infinity. Figure 2(b) depicts the global stability of the endemic equilibrium of model (7) when $R_0 = 1.3725$. It shows that there is a rapid decrease in S_H within the first few days of an attack while L_R and I_R are increasing. This calls for immediate attention whenever there is an outbreak of rotavirus. Otherwise, the situation may become endemic. After approximately 100 days, the situation stabilizes and this may be attributed to quick medical intervention, development of the immune system, awareness among the population and short incubation period of the virus.

Figure 3(a) depicts the population co-infected with both malaria and rotavirus. Simulation was done at different initial values but with same parameter values. The figure shows that when $R_{mr} = 0.733$, the outbreak of a co-infection can easily be contained. This can be achieved by use of mosquito nets and improved sanitation. If these two measures are carried out, there are high chances of eliminating disease within the population after a given period of time as illustrated in the figure. Figure 3(b) shows that when $R_{mr} > 1(1.37431)$, the co-infection exists and is likely to be endemic and therefore immediate medical attention is required.

Figure 4(a), depicts population of infected mosquitoes. The figure shows that when $R_{mr} < 1$, the population of infected mosquitoes reduce though at a gradual rate. This may be as a result of their large numbers. To increase the rate of reduction, preventive measures like bush clearing, spray and use of mosquito nets are therefore

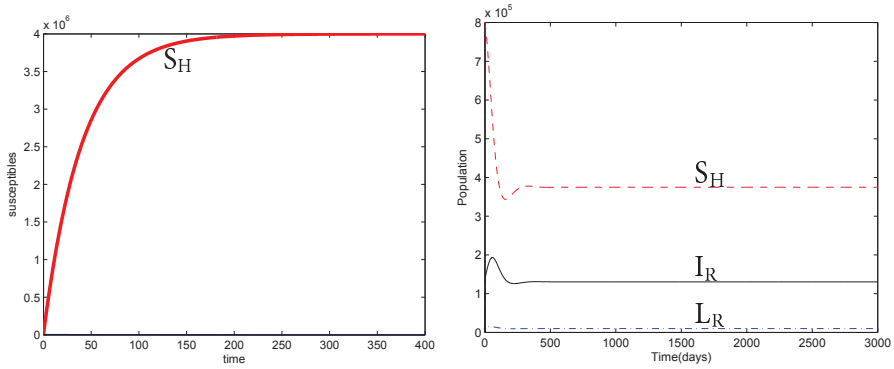
recommended. If a higher rate of reduction is achieved, then the war against co-infection may be won. Thus, the rate of co-infection will be kept at bare minimum resulting into the global stability of the endemic equilibrium of model (6). Figure 4(b) shows that the population L_{MR} reduces at a higher rate and this could be as a result of the incubation period of the two diseases, that is, 14 days for malaria and 2 days for rotavirus. Within this period, most of the population will have moved to the co-infected class resulting into a faster growth rate of I_{MR} as shown in Figure 3(a).

Table 1: Parameter values

Parameter	Symbol	Value	Source
Recruitment rate of humans	Λ_H	$9.6274 \times 10^{-5}\text{day}^{-1}$	[36]
Recruitment rate of mosquitoes	Λ_v	0.071day^{-1}	[37]
Natural death rate of humans	μ_H	$2.537 \times 10^{-5}\text{day}^{-1}$	[36]
Natural death rate of mosquitoes	μ_v	0.1429day^{-1}	[38]
Malaria-induced death rates	ϑ_M	$4.49312 \times 10^{-4}\text{day}^{-1}$	[39]
Rotavirus-induced deaths	ϑ_R	$4.466 \times 10^{-5}\text{day}^{-1}$	[9]
Transmission probability for malaria in human	β_m	0.8333day^{-1}	[38]
Transmission probability for malaria in mosquitoes	β_v	$0.00050 - 0.0025$	Variable
Progress rate of humans from L_R to I_R	ψ	$9.25 \times 10^{-4}\text{day}^{-1}$	Assumed
Biting rate of mosquitoes	b_m	$(0.125, 1)$	Assumed
Modification parameters	α, ϕ, ϵ	$1.0172, 1.01251.025$	Assumed
Effective contact rate	β_R	$0.00160 - 0.030$	Variable
Recovery rates from malaria	γ_1	0.00156	Estimate
Recovery rates from rotavirus	γ_2	0.00095	Estimate
Recovery rates from co-infection	γ_3	0.00575	Estimate
Modification parameters	κ, δ, θ	$1.025, 1.085, 1.0125$	Assumed

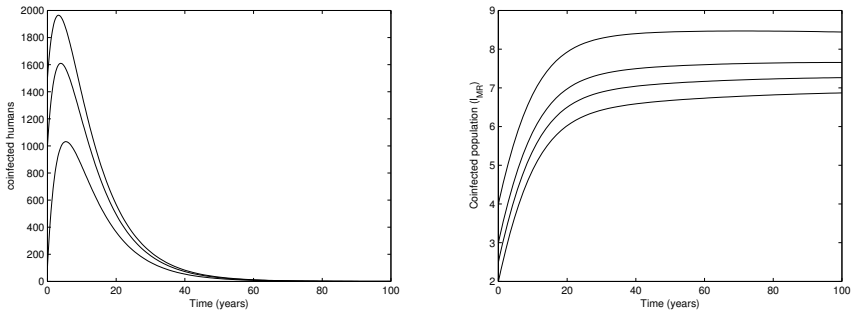
6. CONCLUSION

In conclusion, we have formulated a co-infection model for malaria and rotavirus. We have done elaborate mathematical analysis for both rotavirus only model and the co-infection model. It has been shown that rotavirus only model has a disease free equilibrium and a unique positive endemic equilibrium which are both globally stable when $R_0 < 1$ and $R_0 > 1$ respectively. The disease-free equilibrium of the co-infection model is shown to be locally stable provided the co-infection reproduction number is less than unity. This equilibrium is not globally stable due to co-infection. However, we observe that maximum protection against co-infection during an outbreak of rotavirus infection in a malaria-endemic region may help achieve this stability. In other



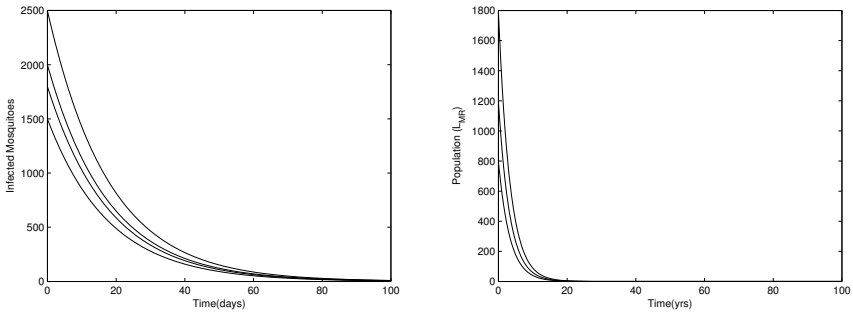
(a) (b)

Figure 2: Simulations of model (7) showing (a) global stability of disease free equilibrium with $R_0 = 0.725, \Lambda_H = 0.000096274, \beta_R = 0.00875, \phi = 1.125, \mu_H = 0.00575, \gamma_2 = 0.00008, \psi = 1.05, \vartheta_R = 0.00013$, (b) global stability of the endemic equilibrium of model (7) with $\Lambda_H = 0.000096274, \beta_R = 0.0925, \phi = 1.0625, \mu_H = 0.000325, \gamma_2 = 0.000925, \psi = 1.0125, \vartheta_R = 0.0753$ and $R_0 = 1.3725$.



(a) (b)

Figure 3: Simulations of model (6) with various initial values showing plots for (a) individuals co-infected with both rotavirus and malaria (I_{MR}), with $R_v = 0.733, \beta_R = 0.00125, \beta_v = 0.000925$ (b) population co-infected with both rotavirus and malaria (L_{MR}) with $R_{mr} = 1.3431, \beta_R = 0.00175$; and $\beta_v = 0.00125$;. Other parameters remain as in Table1.



(a) (b)

Figure 4: Simulations of model (6) with various initial values showing (a) plot for mosquitoes infected with malaria (I_M), (b) population latent with both rotavirus and malaria (L_{MR}) with $R_{mr} = 0.733, \beta_R = 0.0275$ and $\beta_v = 0.02$ with same parameter values as used in Figure 3

words, the fight against malaria and persistent infections such as rotavirus may be won if co-infection cases are kept at a bare minimum. Analysis of the endemic equilibrium, using the Center manifold theorem, indicates that the model may undergo a forward bifurcation. This suggests that at the endemic state, disease spread may be kept under check if the reproduction number can be brought below unity.

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