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STABILITY ANALYSIS OF ROTAVIRUS-MALARIA CO-EPIDEMIC MODEL WITH VACCINATION

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ABSTRACT: This study proposes a model that describes the dynamics of rotavirus and malaria co-epidemics with vaccination using systems of nonlinear ordinary differential equations. We first study the sub-model of rotavirus-only in order to gain insights into how vaccination impacts on transmission dynamics of rotavirus separately, thereafter we study the full model. The basic reproduction numbers of the sub-models of rotavirus-only and malaria-only are determined and used to establish the existence and analyze the stabilities of equilibria. The model is extended to explore the effects of rotavirus and its vaccination on rotavirus-malaria co-infection dynamics. Results show that the rotavirus-only model is globally asymptotically stable when the reproduction number, R_r is less than one while the co-infection model is found to exhibit a backward bifurcation. Further analysis indicate rotavirus vaccination would effectively reduce co-infections with malaria. We carry out numerical simulations to illustrate the potential impact of the vaccination scenarios and to support our analytical findings.

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1. INTRODUCTION

Malaria and rotavirus co-infection continues to pose public health burden worldwide and is endemic in developing countries [2]. Malaria is a vector-borne infectious disease that is caused by the protozoa *plasmodium* transmitted to vertebrates by an infected female genus Anopheles mosquito [14]. The infected female genus Anopheles mosquito ingests gametocytes (parasites) from a malaria infected person when it feeds on human blood. There are four species of parasites that account for most human malaria infections worldwide, namely; *plasmodium malariae*, *plasmodium falciparum*, *plasmodium ovale* and *plasmodium vivax*. But the one that causes the greatest number of deaths and clinical cases in Africa and the most common cause of malaria in the tropics is *plasmodium falciparum* [15]. Malaria is the highest parasitic killer in the world with around 350 - 500 million episodes of clinical malaria reported and about 700,000 - 2.7 million deaths attributed to it every year, 75% of whom are African children under the age of five [1]. In Kenya, it is the leading cause of mortality and morbidity in children [17]. The disease accounts for 30% to 50% of all outpatient visits, 20% of all hospitalizations and 20% of all deaths in children below the age of five. Malaria symptoms include fever, severe headache, nausea, vomiting, loss of appetite, back pains, increased sweating and chills [19]. The disease is however preventable and curable. Prevention against malaria transmission can be achieved through use of treated mosquito nets and insect repellents in regions where the disease is endemic. Other mosquito control strategies such as draining of stagnant water and spraying of insecticides where mosquitoes breed can also help reduce malaria transmission.

Rotavirus on the other hand is a virus of the gastrointestinal tract that causes acute gastroenteritis infections and diarrhea in children under the age of five [20]. It is an infectious disease that leads in mortality and morbidity among children in developing countries. The disease accounts for 6% of diarrhea cases and 20% of deaths in children globally [21]. Rotavirus causes severe infection which can lead to severe dehydration and electrolyte imbalance, and even death if the situation is not promptly

corrected. Over 2.5% of all children admissions to health facilities worldwide are due to rotavirus infection with over 600,000 deaths caused by it every year[6]. The disease transmission occurs by the fecal-oral route if contact occurs and through contaminated environment to person and possibly by respiratory route [22, 23]. Majority of children globally naturally acquire rotavirus infection once before they turn five, and infection can occur despite good hygiene and clean water supply [14]. In most cases rotavirus infection is diagnosed clinically. 38% of children are protected against any subsequent rotavirus infections once a single natural infection occurs [9]. Studies show that re-infection does occur, though subsequent infections are said to be less severe due to the immunity that develops with each infection [7]. Infants below 3 months old are less likely to be infected due to protection by maternal antibodies while being breastfed [6]. Usually, about 1 to 3 days after exposure to rotavirus infection, symptoms which include fever, vomiting, watery diarrhea, abdominal cramps and nausea do appear which may last eight days [3]. Previous studies show that rotavirus prevention and control may not only be achieved by maintaining high standards of hygiene, water supply or sanitation but also by using recommended rotavirus vaccines to prevent acute infections [20].

Because of the great burden of rotavirus and malaria diseases globally, it is important to understand the biological complexity of their transmission dynamics and to come up with effective measures for their control. Despite the incalculable pain caused and the countless challenges by the coexistence of rotavirus and malaria infections worldwide, very little literature is available on the mathematical models for their co-infection dynamics. Previous works exploring the synergy between rotavirus and malaria in sub-Saharan Africa indicate that infection with malaria contributes to the increase in incidence of rotavirus in the region [14, 3, 7]. Recent research conducted in Ghana showed that out of the 243 children who were examined for rotavirus-malaria infections, 43 were found to be co-infected [24]. There is an increase in susceptibility to bacterial infections in children with malaria especially in malaria endemic areas, and this is due to immunosuppression resulting from acute malarial parasitemia [7]. This synergy between malaria and rotavirus has not been fully explored by the use of mathematical models. Only a handful models exist in the literature that attempted to investigate the dynamics of malaria and rotavirus co-infections.

Recently, Omondi et al. [7] modelled malaria and rotavirus co-infection but ignored a key element of the epidemiology of the two epidemics, basically the inclusion of vaccination for the rotavirus disease. Also, a mathematical model for rotavirus and malaria co-infections was developed in [14] that focused on the estimation of the basic reproduction number. In [3], a mathematical model for rotavirus infection with vaccination was formulated and studied. In an attempt to determine the innate char-

acteristic of rotavirus infection in a population, the authors fitted real data to the model and established that vaccination does control rotavirus infection, and further recommended that vaccination be implemented at birth if possible so as to effectively control the disease. A rotavirus epidemic model was studied in [25] with application of optimal control theory where it was established that multiple control strategies are more effective than a single control strategy. This study is thus aimed at deriving a model for rotavirus-malaria co-infection dynamics with vaccination so as to examine the effects of vaccination in altering population dynamics.

The rotavirus-malaria co-infection model that we analyze in this study is an extension of the equations introduced by Omondi et al. [7] and Mbete et al. [14]. Our model is distinct from the ones discussed in [14, 7] in that we have included vaccination for the rotavirus disease and excluded the direct recovered-to-susceptible recovery that the model of Mbete et. al [14] contains. This assumption is realistic because most infected people recover with temporary immunity from infection before becoming susceptible again. The works by Omondi et al. [7] have included a class for individuals who are latently infected with rotavirus, which in our case is excluded. This is because the incubation period for rotavirus is very short (24 to 72 hours) [3]. Unlike the model presented in [7], the malaria component of our model takes the form of a susceptible-infected-recovered (SIR) model for the human hosts and only susceptible-infected (SI) model for the vector hosts.

The structure of the paper is as follows. In this section we have given a brief background to the study including related previous works and our motivation behind the execution of this study. In the next section we formulate and describe the model. In Section 3, we present the basic properties (invariant region, positivity and boundedness of solutions) of the full model. Dynamics of rotavirus-only sub-model are discussed in Section 4. In Section 5, we carry out an analysis of the full model. Section 6 presents our numerical simulations results and discussions. Finally, we conclude this work in Section 7.

2. MODEL DESCRIPTION AND FORMULATION

The malaria component of the co-infection model derived in this paper follows that of Ross-Lotka model [26] where both human and vector hosts take the form susceptible-infected (SI). We exclude exposure stage for the malaria model because we assume that humans exposed to malaria have a high probability of surviving till infectious state or showing symptoms of infection with malaria. This assumption is viable since malaria-exposed humans are neither infectious nor die as a result of the disease.

We subdivide the total human population, N_h at time t into six distinct sub-populations, namely: susceptible humans to all pathogens, S_h humans vaccinated against rotavirus V_R, humans infectious with malaria I_M, humans infectious with rotavirus I_R, those infectious with both malaria and rotavirus I_{MR} and removed or recovered, R. Our model assumes that infected humans recover with temporary immunity from infection before becoming susceptible again, and so we exclude the direct recovered-to-susceptible recovery in our model. Susceptible humans are infected with malaria after infective bites by malaria infectious female anopheles mosquitoes with force of infection λ_M. Susceptible humans are assumed to acquire rotavirus infection through contact with rotavirus infectious humans with a force of infection λ_R. We exclude the exposure stage for rotavirus infection due to the very short incubation period (24 to 72 hours) of the disease [3]. The model explores the impact of rotavirus vaccination to newborns and vaccination of susceptible population. Some babies may develop some immunity to infection with rotavirus from maternal antibodies because of breastfeeding [27]. We thus have,

$$N_h = S_h + V_R + I_M + I_R + I_{MR} + R \tag{1}$$

Likewise, the mosquito population, N_v at any time t is subdivided into susceptibles S_v, the mosquito population that is not infected with malaria but may if it bites a malaria infectious human and I_v, malaria infectious mosquitoes, those that can infect susceptible humans if they bite them. Again, at any given time, each mosquito exists in only one of the two stated classes. Thus, we have

$$N_v = S_v + I_v \tag{2}$$

Susceptible humans are infected with malaria given that a bite by a malaria infectious mosquito occurs at a force of infection denoted by

$$\lambda_M = \frac{\beta_m b_m I_v}{N_h} \tag{3}$$

where β_m is the probability of transmission for malaria in humans and b_m is the rate at which the infectious female Anopheles mosquito bites. The rate at which susceptible mosquitoes are recruited is Λ_v, and they get infected with malaria after effectively biting malaria infectious humans to progress to infectious mosquito compartment, I_v at a rate

$$\lambda_v = \beta_v b_m \frac{(I_M + \theta_v I_{MR})}{N_h} \tag{4}$$

where β_v is the probability of transmission for malaria in mosquitoes and θ_v models the increased probability of infection of mosquitoes by humans who are infectious with both malaria and rotavirus as opposed to getting infected by those infectious with malaria only [28]. We assume that the dually infectious humans can infect mosquitoes

with malaria parasites only.

Susceptible humans acquire rotavirus infection at a rate

$$\lambda_R = \beta_R \frac{(I_R + \vartheta I_{MR})}{N_h} \tag{5}$$

where β_R is the effective contact rate with humans infectious with rotavirus and the parameter $\vartheta \geq 1$ accounts for the fact that the rotavirus-malaria dually infectious humans are more infectious than those infected with rotavirus only [7].

We assume that disease transmission occurs in an open environment as the human population keeps changing due to immigration and emigration and birth and death that do take place in the population. Therefore, recruitment rate of susceptible humans is given by $(1-\rho)\Lambda_h$, where $0 < \rho < 1$ represents the proportion that is vaccinated at birth. Vaccination of susceptible takes place at a rate γ. Rotavirus vaccinated humans are assumed to be infected with rotavirus via a force of infection $(1-\psi)\lambda_R$, where $0 < \psi < 1$ is the efficacy of the vaccine. Because of waning effect of vaccines [29], vaccinated humans will loose their immunity and become susceptible again at a rate ω. Since, in this model, vaccination is only given against rotavirus, the vaccinated humans are susceptible to malaria and therefore acquire malaria infection through bites by infectious mosquitoes with force of infection λ_M.

Malaria-infected humans can be infected with rotavirus at a rate $\tau\lambda_R$, and transfer

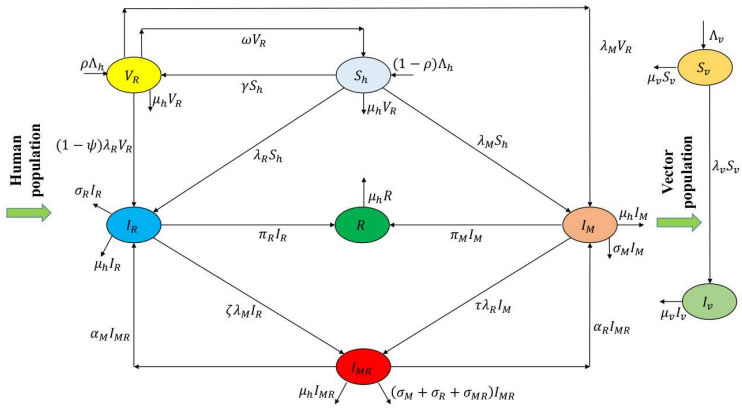


Figure 1: A schematic of the co-infection model for malaria and rotavirus diseases with vaccination.

to the co-infection compartment I_{MR}. The parameter, $\tau > 1$, models the expected increase in becoming susceptible to infection with rotavirus for humans with malaria, especially young children. This is due to the fact that malaria infection has a de-

pressant effect on the immune system. In malaria endemic areas, children may suffer from severe bacterial infections (or protozoal diseases) as either super-infections or co-infections due to immunosuppression resulting from acute malarial parasitemia [30]. Similarly, humans with rotavirus can be infected with malaria at a rate $\zeta\lambda_M$. Hence, they move to the class of humans with dual infection, I_{MR}. The parameter, $\zeta > 1$, is assumed to account for the increased susceptibility to infection as a result of low immunity due to rotavirus disease. It is assumed that the co-infected humans recover from malaria only at a rate α_M and transfer to the compartment of humans who are infectious with rotavirus only, I_R. Likewise, the co-infectious humans recover from rotavirus only at a rate α_R and move to the compartment of humans who are infectious with malaria only, I_M. Our model assumes that infected humans recover with temporary immunity from malaria and rotavirus infections respectively, at the rates π_M and π_R and move to the recovered or removed compartment, R. Natural mortality is assumed to occur in all human and mosquito subpopulations at the rates μ_h and μ_v, respectively irrespective of their infectious status, and that mosquitoes only die naturally. Disease induced death rates for malaria, rotavirus and dual infections are given by σ_M, σ_R and σ_{MR}, respectively.

The state variables in the compartmental model are given in Table 1 while the parameter values used in the model are displayed in Table 2. The flow diagram presented in Fig. 1 summarizes all the assumptions made for simplicity in formulating our model, which include the following:

(i) the model has no vertical transmission, all recruitments are healthy births with no disease and no infective immigrant, and all parameters are nonnegative.

(ii) susceptible human population is general population that is at risk of getting malaria infection at a rate proportional to the density of malaria infected humans and susceptible mosquito population is at risk of acquiring malaria infection at a rate proportional to density of infected mosquitoes.

(iii) susceptible humans cannot at the same time acquire malaria and rotavirus infection as the transmission mechanics of the two diseases are different.

(iv) the dually-infected humans cannot simultaneously recover from malaria and rotavirus.

(v) a person in the co-infectious compartment, I_{MR} can transmit both diseases.

Applying the above assumptions, definitions and parameters, the model which describes the dynamics of malaria-rotavirus co-infection with vaccination is written as

Table 1: State variables of model (6).

Symbol	Description
S_h	Susceptible humans
V_R	Vaccinated humans against rotavirus
I_M	Malaria infected humans
I_R	Rotavirus infected humans
I_{MR}	Humans co-infected with both rotavirus and malaria
R	Recovered or removed humans
S_v	Susceptible mosquitoes
I_v	Infected mosquitoes

follows:

$$\left.\begin{aligned}
\frac{\mathrm{d}S_h}{\mathrm{d}t} &= (1-\rho)\Lambda_h + \omega V_R - \lambda_M S_h - \lambda_R S_h - (\gamma+\mu_h)S_h \\
\frac{\mathrm{d}V_R}{\mathrm{d}t} &= \rho\Lambda_h + \gamma S_h - \lambda_M V_R - (1-\psi)\lambda_R V_R - (\mu_h+\omega)V_R \\
\frac{\mathrm{d}I_M}{\mathrm{d}t} &= \lambda_M S_h + \lambda_M V_R + \alpha_R I_{MR} - \tau\lambda_R I_M - (\pi_M+\mu_h+\sigma_M)I_M \\
\frac{\mathrm{d}I_R}{\mathrm{d}t} &= \lambda_R S_h + (1-\psi)\lambda_R V_R + \alpha_M I_{MR} - \zeta\lambda_M I_R - (\pi_R+\mu_h+\sigma_R)I_R \\
\frac{\mathrm{d}I_{MR}}{\mathrm{d}t} &= \tau\lambda_R I_M + \zeta\lambda_M I_R - (\alpha_M+\alpha_R+\mu_h+\sigma_M+\sigma_R+\sigma_{MR})I_{MR} \\
\frac{\mathrm{d}R}{\mathrm{d}t} &= \pi_M I_M + \pi_R I_R - \mu_h R \\
\frac{\mathrm{d}S_v}{\mathrm{d}t} &= \Lambda_v - \lambda_v S_v - \mu_v S_v \\
\frac{\mathrm{d}I_v}{\mathrm{d}t} &= \lambda_v S_v - \mu_v I_v.
\end{aligned}\right\}. \tag{6}$$

with

$S_h(0) = S_{h0} > 0$, $V_R(0) = V_{R0} \geq 0$, $I_M(0) = I_{M0} \geq 0$, $I_R(0) = I_{R0} \geq 0$, $I_{MR}(0) = I_{MR0} \geq 0$, $R(0) = R_0 \geq 0$, $S_v(0) = S_{v0} \geq 0$ and $I_v(0) = I_{v0} \geq 0$.

3. BASIC PROPERTIES OF THE CO-INFECTION MODEL

Here, we determine the feasibility of the co-infection model (6), that is, its invariant region, positivity and boundedness of the solutions.

3.1. POSITIVITY AND BOUNDEDNESS OF SOLUTIONS

For the co-infection model (6) to be mathematically meaningful and well-posed, we must prove that all the state variables are non-negative for all $t > 0$.

Lemma 1. *Let the initial data set be* $\{(S_h, S_v)(0) > 0, (V_R, I_M, I_R, I_{MR}, R, I_v)(0) \geq 0\} \in \Omega$. *Then, the solution set* $\{S_h, V_R, I_M, I_R, I_{MR}, R, S_v, I_v\}(t)$ *of model* (6) *is positive and bounded for all time,* $t > 0$.

Proof. From equation one of model (6), we have

$$\frac{dS_h}{dt} = (1-\rho)\Lambda_h + \omega V_R - (\gamma + \lambda_M + \lambda_R + \mu_h)S_h$$
$$\geq -(\gamma + \lambda_M + \lambda_R + \mu_h)S_h \tag{7}$$

Integrating equation (7) with respect to t yields

$$S_h(t) \geq S_h(0)e^{-\int(\gamma+\lambda_M+\lambda_R+\mu_h)dt} \geq 0,$$

since

$$(\gamma + \lambda_M + \lambda_R + \mu_h) > 0. \tag{8}$$

If we let the initial data $S_h(0) > 0$, then $S_h(t) > 0$.

From the second equation of model (6), we have

$$\frac{dV_R}{dt} = \rho\Lambda_h + \gamma S_h - (\lambda_M + \psi\lambda_R + \mu_h + \omega)V_R$$

$$\geq -(\lambda_M + \psi\lambda_R + \mu_h + \omega)V_R. \tag{9}$$

Integrating (9) with respect to t yields,

$$V_R(t) \geq V_R(0)e^{-\int(\lambda_M+\psi\lambda_R+\mu_h+\omega)dt} \geq 0,$$

since

$$(\lambda_M + \psi\lambda_R + \mu_h + \omega) > 0. \tag{10}$$

If we let the initial data $V_R(0) > 0$, then $V_R(t) > 0$.

From the second last equation of model (6), we have

$$\frac{dS_v}{dt} = \Lambda_v - (\lambda_v + \mu_v)S_v \geq -(\lambda_v + \mu_v)S_v.$$

Integrating equation (11) with respect to t yields

$$S_v(t) \geq S_v(0)e^{-\int(\lambda_v+\mu_h)dt} \geq 0,$$

since

$$(\lambda_v + \mu_v) > 0. \tag{11}$$

If we let the initial data $S_v(0) > 0$, then $S_v(t) > 0$.

Following the same procedure, it can be shown that the remaining state variables are also positive for all time, $t > 0$. □

Lemma 2. *Solutions of model* (6) *are bounded in the region* $\Omega = \Omega_h \times \Omega_v$.

Proof. We show that all the feasible solutions are uniformly bounded in Ω. We do that by splitting model (6) into both the human component (N_h) and the mosquito component (N_v) given by equations (1) and (2), respectively.

Let

$$(S_h, V_R, I_M, I_R, I_{MR}, R) \in \Re^6_+ \tag{12}$$

be any solution of the system with nonnegative initial conditions. Then, the time derivative of N_h along a solution path of model (6) gives

$$N_h^{'} < \Lambda_h - \mu_h N_h. \tag{13}$$

We employ Birkhoff and Rota's theorem on differential inequality [31] as $t \to \infty$ and obtain

$$0 \leq N_h \leq \frac{\Lambda_h}{\mu_h} + N_h(0)e^{-\mu_h t} \tag{14}$$

where $N_h(0)$ is the value of (1) computed at the initial values of each variable. Therefore, as $t \to \infty$, we have

$$0 \leq N_h \leq \frac{\Lambda_h}{\mu_h}. \tag{15}$$

Thus, all possible solutions of the human-only component of model (6) enter the region

$$\Omega_h = \left\{ (S_h, V_R, I_M, I_R, I_{MR}, R) : N_h \leq \frac{\Lambda_h}{\mu_h} \right\}. \tag{16}$$

Similarly, if we let

$$(S_v, I_v) \in \Re^2_+. \tag{17}$$

By using same procedure in (13) and (14), it can be shown that

$$0 \leq N_v \leq \frac{\Lambda_v}{\mu_v} + N_v(0)e^{-\mu_v t} \tag{18}$$

where $N_v(0)$ is the value of (2) calculated at the initial values of the each variable. Thus, as $t \to \infty$, we have

$$0 \leq N_v \leq \frac{\Lambda_v}{\mu_v}. \tag{19}$$

Therefore, all possible solutions of the mosquito-only component of model (6) enter the region

$$\Omega_v = \left\{ (S_v, I_v) : N_v \leq \frac{\Lambda_v}{\mu_v} \right\}. \tag{20}$$

Hence, it follows from equations (16) and (20) that all possible solutions of model (6) will enter the region

$$\Omega = \Omega_h \times \Omega_v. \tag{21}$$

Thus, Ω is positively invariant under the flow induced by model (6). We can use the theory of permanence [43] to show that all solutions on the boundary of Ω enter the interior of Ω and that the existence, uniqueness and continuation results hold for model (6) [44]. Hence, the model is mathematically well-posed and makes biological sense, and it is sufficient to analyze model (6) in Ω. □

In order to lay foundation for comprehensive analysis of the impact of vaccination on rotavirus-malaria co-infections, we first study rotavirus-only sub-model to enable us understand how vaccination impacts on rotavirus transmission dynamics separately, then we study the full co-infection model.

4. ROTAVIRUS-ONLY SUB-MODEL

We obtain the rotavirus-only sub-model by setting the malaria infectious and co-infectious states equal to zero in model (6). Thus,

$$\left.\begin{aligned}
\frac{\mathrm{d}S_h}{\mathrm{d}t} &= (1-\rho)\Lambda_h + \omega V_R - \beta_R \frac{I_R}{N_h} S_h - (\gamma + \mu_h) S_h \\
\frac{\mathrm{d}V_R}{\mathrm{d}t} &= \rho\Lambda_h + \gamma S_h - (1-\psi)\beta_R \frac{I_R}{N_h} V_R - (\mu_h + \omega) V_R \\
\frac{\mathrm{d}I_R}{\mathrm{d}t} &= \beta_R \frac{I_R}{N_h} S_h + (1-\psi)\beta_R \frac{I_R}{N_h} V_R - (\pi_R + \mu_h + \sigma_R) I_R \\
\frac{\mathrm{d}R}{\mathrm{d}t} &= \pi_R I_R - \mu_h R
\end{aligned}\right\}. \tag{22}$$

where $N_h = S_h + V_R + I_R + R$.

4.1. WELL-POSEDNESS OF ROTAVIRUS-ONLY SUB-MODEL

For sub-model (22) to make biological sense and be mathematically well-posed, it is important to show that the associated state variables are nonnegative for all $t \geq 0$ and that the solutions with nonnegative initial data will remain nonnegative for all $t \geq 0$.

Lemma 3. *If $S_h(0), V_R(0), I_R(0)$ and $R(0)$ are nonnegative, then so are $S_h(t), V_R(t)$, $I_R(t)$ and $R(t)$ for all time $t \geq 0$. Moreover, $\limsup_{t\to\infty} N_h(t) = \frac{\Lambda}{h}$. Furthermore, if $N_h(0) = \frac{\Lambda_h}{\mu_h}$, then $N_h(0) = \frac{\Lambda_h}{\mu_h}$.*

Proof. Consider the first equation of the sub-model (22) at time t

$$\frac{dS_h}{dt} = (1-\rho)\Lambda_h + \omega V_R - (\gamma + \lambda_R + \mu_h)S_h$$

then,

$$\frac{dS_h}{dt} \geq -(\gamma + \lambda_R + \mu_h)S_h \tag{23}$$

integrating equation (23) yields,

$$\int \frac{dS_h}{dt} \geq -\int (\gamma + \lambda_R + \mu_h)d(t)$$

$$S_h(t) \geq S_h(0)e^{-\int(\gamma+\lambda_R+\mu_h)d(t)} \geq 0$$

Since

$$\gamma + \lambda_R + \mu_h > 0 \tag{24}$$

we can apply the same procedure and show that all the state variables are positive for all $t > 0$. □

Lemma 4. *The solutions of the sub-model* (22) *are uniformly bounded in the region* Ω_R.

Proof. Let

$$\{(S_h, V_R, I_R, R)(t)\} \in \Re^4_+ \tag{25}$$

be any solution with nonnegative initial conditions. The time derivative of N_h along a solution path of the model (22) gives

$$\frac{dN_h}{dt} < \Lambda_h - \mu_h N_h. \tag{26}$$

The sub-model (22) has a varying human population size $\frac{dN_h}{dt} \neq 0$ and so, a trivial equilibrium is not feasible. Whenever $N_h > \frac{\Lambda_h}{\mu_h}$, then $\frac{dN_h}{dt} < 0$. Since $\frac{dN_h}{dt}$ is bounded by $\Lambda_h - \mu_h N_h$, a standard comparison theorem [31] shows that

$$0 \leq N_h(t) \leq N_h(0)e^{-\mu_h t} + \frac{\Lambda_h}{\mu_h}(1 - e^{-\mu_h t}). \tag{27}$$

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

$$0 \leq N_h(t) \leq \frac{\Lambda_h}{\mu_h}. \tag{28}$$

Hence, N_h is bounded and all the possible solutions of sub-model (22) starting in the region Ω_R approach, enter or stay in the region, where,

$$\Omega_R = \left\{ (S_h, V_R, I_R, R) : N_h(t) \leq \frac{\Lambda_h}{\mu_h} \right\}. \tag{29}$$

□

4.2. STABILITY ANALYSIS OF THE ROTAVIRUS-ONLY SUB-MODEL

In this subsection, we discuss the rotavirus-only sub-model to analyze the stability of its equilibria.

4.2.1. DISEASE-FREE EQUILIBRIUM POINT OF ROTAVIRUS-ONLY SUB-MODEL

We can define the disease-free equilibrium point of a model as the model's steady state solutions in the absence of infection or disease. Since the first three equations of the sub-model (22) have no terms in R, we proceed to analyze the new sub-model (30) shown below.

$$\left.\begin{aligned} \frac{\mathrm{d}S_h}{\mathrm{d}t} &= (1-\rho)\Lambda_h + \omega V_R - \lambda_R S_h - (\gamma + \mu_h) S_h \\ \frac{\mathrm{d}V_R}{\mathrm{d}t} &= \rho\Lambda_h + \gamma S_h - (1-\psi)\lambda_R V_R - (\mu_h + \omega) V_R \\ \frac{\mathrm{d}I_R}{\mathrm{d}t} &= \lambda_R S_h + (1-\psi)\lambda_R V_R - (\pi_R + \mu_h + \sigma_R) I_R \end{aligned}\right\}. \tag{30}$$

Therefore, we set all the infectious compartments of the rotavirus-only sub-model to zero to obtain the disease-free equilibrium. Because the rotavirus vaccine is administered at birth to newborns, it can be shown that $S_h + V_R = \frac{\Lambda_h}{\mu_h}$. Hence, the disease-free equilibrium point of the rotavirus-only sub-model is given by

$$E^{r0} = \left(S_h^0, V_R^0, I_R^0\right) = \left\{ \frac{\Lambda_h[(1-\rho)\mu_h + \omega]}{\mu_h(\mu_h + \gamma + \omega)}, \frac{\Lambda_h(\gamma + \rho\mu_h)}{\mu_h(\gamma + \omega + \mu_h)}, 0 \right\}. \tag{31}$$

4.2.2. THE EFFECTIVE REPRODUCTION NUMBER OF ROTAVIRUS-ONLY SUB-MODEL

Using the next generation matrix method [10] as described in [32], we define the basic reproduction number, R_0, as the number of new infections produced by a single infective human introduced into a completely susceptible population over the duration of his or her infectious period . The effective reproduction number, R_r for the rotavirus-only sub-model, represents the average number of new infections caused by a typical

rotavirus infected human in the presence of rotavirus vaccination in a population where everyone else is susceptible. Employing ideas of Driessche and Watmough [10], we derive the effective reproduction number, R_r for the rotavirus-only sub-model. Thus, if the matrix

$$F = \left(\frac{\Lambda_h \beta_R [(1-\rho)\mu_h + \omega + (1-\psi)(\gamma + \rho\mu_h)]}{N_h \mu_h (\gamma + \omega + \mu_h)} \right),$$

represents the new infection terms and the matrix

$$V = \Big(\pi_R + \mu_h + \sigma_R \Big),$$

the remaining transfer terms, then the effective reproduction number, R_r for the sub-model (22), is given by

$$R_r = \rho \left(FV^{-1} \right),$$

where ρ is the spectral radius of the next generation operator matrix FV^{-1}. Therefore,

$$R_r = \beta_R \Lambda_h \left\{ \frac{\omega + (1-\psi)(\rho\mu_h + \gamma) + \mu_h(1-\rho)}{\mu_h(\sigma_R + \pi_R + \mu_h)(\mu_h + \gamma + \omega)} \right\}. \tag{32}$$

If there is no vaccination in the population, then R_0 is given by

$$R_0 = \frac{\beta_R \Lambda_h}{\mu_h(\sigma_R + \pi_R + \mu_h)}. \tag{33}$$

Using expression (33), the effective reproduction number when there is vaccination, R_r in (32) can be expressed as

$$R_r = R_0 \left\{ \frac{\gamma + \omega + \mu_h - \psi(\gamma + \mu_h\rho)}{\mu_h + \gamma + \omega} \right\}. \tag{34}$$

It follows from (34) that $\frac{\gamma+\omega+\mu_h-\psi(\gamma+\mu_h\rho)}{\mu_h+\gamma+\omega} < 1$ since $(1-\psi) \in [0,1]$, which implies that $R_r < R_0$. In the absence of vaccination, $R_r = R_0$. Thus, from the expression of the effective reproduction number, R_r in (34), it can be concluded that administering vaccines both at birth and to susceptibles will have positive effect on new infections in the population.

4.2.3. GLOBAL STABILITY OF DISEASE-FREE EQUILIBRIUM OF ROTAVIRUS-ONLY SUB-MODEL

In this subsection, we prove the global stability of the disease-free equilibrium, E^{r0} using a suitable Lyapunov function [33] and La Salle's invariant principle [13].

Theorem 1. *The disease-free equilibrium, E^{r0} of the sub-model* (22) *is globally asymptotically stable in Ω_R if $R_r < 1$.*

Proof. We consider the reduced sub-model (30), where $S_h + V_R = \frac{\Lambda_h}{\mu_h}$.

Define $L : \{(S_h, V_R, I_R) \in \Omega_R : S_h, V_R > 0\} \to \Re$ by

$$L : \{(S_h, V_R, I_R) = (\omega + \mu_h) I_R. \tag{35}$$

Then, if $R_0 \leq 1$,

$L^{'} \leq (\omega + \mu_h)[\beta_R I_R S_h + (1 - \psi)\beta_R V_R I_R - (\pi_R + \mu_h + \sigma_R) I_R]$

$\leq (\omega + \mu_h)[\beta_R (S_h + (1 - \psi) V_R) - (\pi_R + \mu_h + \sigma_R)] I_R$

$\leq (\omega + \mu_h)[\beta_R (S_h + V_R) - (\pi_R + \mu_h + \sigma_R)] I_R$

$\leq (\omega + \mu_h)[\frac{\beta_R \Lambda_h}{\mu_h} - (\pi_R + \mu_h + \sigma_R)] I_R$

$\leq (\omega + \mu_h)[R_0 - 1](\pi_R + \mu_h + \sigma_R) I_R$

$\leq (R_0 - 1)(\omega + \mu_h)(\pi_R + \mu_h + \sigma_R) I_R$

$\leq (R_r - 1)(\omega + \mu_h)(\pi_R + \mu_h + \sigma_R) I_R$

since $R_0 > R_r$ in $\psi \in [0, 1]$ from (34).

If $R_r \leq 1$, then $L^{'} \leq 0$. Note that $L^{'} = 0$ iff $S_h = S_h^0$, $V_R = V_R^0$ and $I_R = 0$, or if $R_r = 1$, $S_h = S_h^0$, $V_R = V_R^0$ and $I_R = 0$. Therefore, the largest compact invariant set in $\{(S_h, V_R, I_R) \in \Omega_R : L^{'} = 0\}$ is the singleton $\{E^{r0}\}$, where $\{E^{r0}\}$ is the disease-free equilibrium. La Salle's invariant principle then implies that $\{E^{r0}\}$ is globally asymptotically stable in Ω_R. Theorem 1 is thus proved. □

4.2.4. ENDEMIC EQUILIBRIUM POINT OF ROTAVIRUS-ONLY SUB-MODEL

The disease-endemic equilibrium point of a model is a state where the disease establishes in the population. We apply Theorem (2) to calculate the disease-endemic equilibrium of rotavirus-only sub-model (22).

Theorem 2. *A disease-endemic equilibrium, E^{r*} exists provided that $R_r > 1$.*

Proof. At disease-endemic steady states, the reduced sub-model (30) becomes,

$$(1 - \rho)\Lambda_h + \omega V_R^* - \beta_R \frac{I_R^*}{N_h} S_h^* - (\gamma + \mu_h) S_h^* = 0,$$

$$\rho \Lambda_h + \gamma S_h^* - (1 - \psi)\beta_R \frac{I_R^*}{N_h} V_R^* - (\mu_h + \omega) V_R^* = 0, \tag{36}$$

$$\beta_R \frac{I_R^*}{N_h} + (1-\psi)\beta_R \frac{I_R^*}{N_h} V_R^* - (\pi_R + \mu_h + \sigma_R) I_R^* = 0.$$

Again, because of the limiting value, we substitute $N_h = \frac{\Lambda_h}{\mu_h}$ and only consider the first three equations of the sub-model (22) as they do not contain the term in R^*.

We solve for S_h^*, V_R^* and I_R^* in (36) and obtain the disease-endemic equilibrium point of rotavirus-only sub-model (22) as,

$E^{r*} = (S_h^*, V_R^*, I_R^*)$,

where,

$$S_h^* = \frac{(\pi_R + \mu_h + \sigma_R)}{\beta} - (1-\psi)\left\{ \frac{\beta\rho\Lambda + \gamma(\pi_R + \mu_h + \sigma_R)}{\beta((1-\psi)\beta I_R^* + \omega + \mu_h + (1-\psi)\gamma)} \right\}. \tag{37}$$

$$V_R^* = \left\{ \frac{\beta\rho\Lambda + \gamma(\pi_R + \mu_h + \sigma_R)}{\beta((1-\psi)\beta I_R^* + \omega + \mu_h + (1-\psi)\gamma)} \right\}. \tag{38}$$

And,

$$I_R^* > 0 \tag{39}$$

or

$$AI_R^{*2} + BI_R^* + C = 0 \tag{40}$$

where,

$A = (1-\psi)\beta^2(\pi_R + \mu_h + \sigma_R)$,

$B = [\gamma(1-\psi)\beta_R(\pi_R + \mu_h + \sigma_R) + \beta_R\omega(\pi_R + \mu_h + \sigma_R) + \mu_h\beta_R(\pi_R + \mu_h + \sigma_R) + (1-\psi)\mu_h\beta_R(\pi_R + \mu_h + \sigma_R) - (1-\psi)\beta^2\Lambda_h]$,

$C = \{\gamma\mu_h(\pi_R + \mu_h + \sigma_R) + \mu_h\omega(\pi_R + \mu_h + \sigma_R) + \mu_h^2(\sigma_R + \mu_h + \pi_R) + \rho\mu_h\beta_R - \beta_R\Lambda_h[\omega + (1-\psi)\gamma + \mu_h + \rho\mu_h(1-\psi)]\}$.

The coefficient A is always nonnegative and C is nonnegative if $R_0 < 1$, respectively. Therefore, we find the sign of C by expressing it as,

$$C = \mu_h[\rho\beta_R\Lambda_h + (\gamma+\omega+\mu_h)(\pi_R+\mu_h+\sigma_R)] - \beta_R\Lambda_h[\omega + (1-\psi)\gamma + \mu_h + \rho\mu_h(1-\psi)]. \tag{41}$$

If $\beta_R\Lambda_h[\omega + (1-\psi)\gamma + \mu_h + \rho\mu_h(1-\psi)] > \mu_h[\rho\beta_R\Lambda_h + (\gamma+\omega+\mu_h)(\pi_R+\mu_h+\sigma_R)]$, then C is negative, and so we express equation (40) as $AI_R^{*2} + BI_R^* - C = 0$ or $AI_R^{*2} + BI_R^* - C = 0$. Thus, there is only one positive root of equation (40) and that implies that $I_R^* > 0$. Hence Theorem 2 is proved. □

4.2.5. GLOBAL STABILITY OF THE DISEASE-ENDEMIC EQUILIBRIUM OF ROTAVIRUS-ONLY SUB-MODEL

We use Lyapunov functionals [13, 33] to investigate the global asymptotic stability of disease-endemic equilibrium, E^{r*} of the rotavirus-only sub-model.

Theorem 3. *The disease-endemic equilibrium of sub-model* (22), $E^{r*} = (S_h^*, V_R^*, I_R^*, R^*)$, *is globally asymptotically stable if* $R_r > 1$.

Proof. To prove the theorem, we begin by constructing a suitable Lyapunov linear and quadratic function of the form:

$$L = \Sigma_{i=1}^{4} U_i(x_i - x_i^* \ln x_i) \tag{42}$$

where U_i is a properly selected constant, x_i is the population of i^{th} compartment, i_i^{th} is the equilibrium value of x_i and $U_i > 0$.

The Lyapunov function denoted by L is continuous and differentiable. We have

$$L(S_h, V_R, I_R, R) = U_1(S_h - S_h^* \ln S_h) + U_2(V_R - V_R^* \ln V_R) + U_3(I_R - I_R^* \ln I_R + U_4(R - R^* \ln R). \tag{43}$$

The global asymptotic stability of the disease-endemic equilibrium holds if $\frac{dL}{dt} \leq 0$.

The time derivative of the Lyapunov function L is given by

$$\frac{dL}{dt} = U_1(1 - \frac{S_h^*}{S_h})\frac{dS_h}{dt} + U_2(1 - \frac{V_R^*}{V_R})\frac{dV_R}{dt} + U_3(1 - \frac{I_R^*}{I_R})\frac{dI_R}{dt} + U_4(1 - \frac{R^*}{R})\frac{dR}{dt}.$$

$$\frac{dL}{dt} = -U_1(1-\frac{S_h^*}{S_h})^2(\gamma+\mu_h)S_h + U_1(1-\frac{S_h^*}{S_h})(\frac{I_R^*}{I_R}\frac{S_h^*}{S_h}-1)\frac{\beta_R}{N_h}S_h I_R - U_2(1-\frac{V_R^*}{V_R})^2(\mu_h+\omega)V_R$$

$$+U_2(1-\frac{V_R^*}{V_R})(\frac{V_R^*}{V_R}\frac{I_{R^*}}{I_R}-1)(1-\psi)\frac{\beta_R}{N_h}V_R I_R - U_3(1-\frac{I_R^*}{I_R})^2(\pi_R+\mu_h+\sigma_R) - U_4(1-\frac{R^*}{R})^2\mu_h R. \tag{44}$$

Applying the approach by McCluskey et. al [34], we have the following expression

$$\frac{dL}{dt} = -U_1(1-\frac{S_h^*}{S_h})^2(\gamma+\mu_h)S_h - U_2(1-\frac{V_R^*}{V_R})^2(\mu_h+\omega)V_R - U_3(1-\frac{I_R^*}{I_R})^2(\pi_R+\mu_h+\sigma_R)$$

$$-U_4(1-\frac{R^*}{R})^2\mu_h R + Z_r(E^r) \tag{45}$$

where,

$$Z_r(E^r) = +U_1(1-\frac{S_h^*}{S_h})(\frac{I_R^*}{I_R}\frac{S_h^*}{S_h}-1)\frac{\beta_R}{N_h}I_R S_h + U_2(1-\frac{V_R^*}{V_R})(\frac{V_R^*}{V_R}\frac{I_{R^*}}{I_R}-1)(1-\psi)\frac{\beta_R}{N_h}I_R V_R \leq 0. \tag{46}$$

$Z_r(E^r)$ is negative if we follow the methods used in [35, 36, 37, 34]. Thus, $Z_r(E^r) \leq 0$ for all $Z_r(E^r) \geq 0$. Hence, $\frac{dL}{dt} \leq 0$ in (E^r) and when $(E^r) = (E^{r*})$. Therefore, the largest invariant set in (E^r) such that $\frac{dL}{dt} \leq 0$ is the singleton (E^{r*}), which is our disease-endemic equilibrium point. By La Salle's invariant principle, we can conclude that the disease-endemic equilibrium, (E^{r*}), is globally stable whenever $R_r > 1$. Proof of Theorem 3 is thus completed. □

5. STABILITY ANALYSIS OF ROTAVIRUS-MALARIA CO-INFECTION MODEL

In order to carry out stability analysis of the equilibria of model (6), we first establish the model's equilibrium point then we calculate its basic reproduction number, R_{mr}.

5.1. DISEASE-FREE EQUILIBRIUM POINT OF THE CO-INFECTION MODEL

To establish the disease-free equilibrium point of model (6), we set the right-hand side of the model equations to zero and then solve for each state variable. Hence, we have

$$E^0 = (S_h^0, V_R^0, I_M^0, I_R^0, I_{MR}^0, R^0, S_v^0, I_v^0)$$
$$= \left\{ \frac{\Lambda_h[(1-\rho)\mu_h + \omega]}{\mu_h(\mu_h + \gamma + \omega)}, \frac{\Lambda_h(\gamma + \rho\mu_h)}{\mu_h(\gamma + \omega + \mu_h)}, 0, 0, 0, 0, \frac{\Lambda_v}{\mu_v}, 0 \right\}. \quad (47)$$

5.1.1. BASIC REPRODUCTION NUMBER OF THE CO-INFECTION MODEL

It is important to note that in this paper we have not discussed the dynamics of malaria-only sub-model as numerous models for malaria sub-model transmission are available in the literature.

We denote the basic reproduction number for malaria epidemic by R_m. It measures the number of new malaria infections in human or mosquito populations caused by a single malaria infectious human (or mosquito) brought in an entirely susceptible human (or mosquito) population during his or its infectious duration. Following the same procedure as implemented in [10], we obtain the next generation matrices for the malaria-sub-model, F and V as

$$F = \begin{pmatrix} 0 & \beta_m b_m \\ \frac{\beta_v b_m \mu_h \Lambda_v}{\mu_v \Lambda_h} & 0 \end{pmatrix}$$

and

$$V = \begin{pmatrix} \pi_M + \sigma_M + \mu_h & 0 \\ 0 & \mu_v \end{pmatrix}.$$

The basic reproduction number, R_m, is the spectral radius of the next generation operator matrix (FV^{-1}). The eigenvalues of (FV^{-1}) are

$$\pm\sqrt{\frac{b_m^2\beta_m\beta_v\Lambda_v\mu_h}{\Lambda_h\mu_v^2(\pi_M+\mu_h+\sigma_M)}}.$$

It follows, therefore, that the basic reproduction number, R_m for malaria-only submodel is given by

$$R_m = \rho(FV^{-1}) = \sqrt{\frac{b_m^2\beta_m\beta_v\Lambda_v\mu_h}{\Lambda_h\mu_v^2(\pi_M+\mu_h+\sigma_M)}}. \tag{48}$$

Note that in vector-host models, the initial transmission of the disease when an infectious human or mosquito is introduced into an entirely susceptible population, the reproduction number is given by R_m^2. The square root in the expression for R_m^2 represents the two 'generations' required for an infectious host or vector to transmit the infection [10].

The term $\frac{\beta_v b_m}{\mu_v}$ in R_m represents the number of new malaria infections in human population generated by a single malaria infectious mosquito, while the term

$$\frac{b_m\beta_m\Lambda_v\mu_h}{\Lambda_h\mu_v^2(\pi_M+\mu_h+\sigma_M)}$$

represents the number of new malaria infections in mosquito population caused by a single malaria infectious human.

From subsection 5.1.1, the basic reproduction number for the rotavirus-only submodel (22) is

$$R_r = \beta_R\Lambda_h\left\{\frac{\omega+(1-\psi)(\rho\mu_h+\gamma)+\mu_h(1-\rho)}{\mu_h(\sigma_R+\pi_R+\mu_h)(\mu_h+\gamma+\omega)}\right\}. \tag{49}$$

Similarly, R_r measures the number of new rotavirus infections in humans caused by a single rotavirus infectious human introduced to a completely virgin population in the presence of vaccination.

It follows therefore that the basic reproduction number for the co-infection model (6), denoted by R_{mr}, is

$$R_{mr} = max\{R_m, R_r\} \tag{50}$$

5.2. LOCAL STABILITY OF THE DISEASE-FREE EQUILIBRIUM

In this subsection, we use the eigenvalues or the trace-determinant of the Jacobian matrix approach to investigate the local stability of the disease-free equilibrium of the co-infection model (6).

Theorem 4. *The disease-free equilibrium of model* (6) *is locally asymptotically stable if* $R_{mr} < 1$ *and unstable otherwise.*

Proof. The Jacobian matrix of model (6) at disease-free equilibrium is given by

$$J(E^0) = \begin{bmatrix} -(\gamma+\mu_h) & \omega & 0 & -p\beta_R & -p\beta_R\vartheta & 0 & 0 & -p\beta_m b_m \\ \gamma & -(\omega+\mu_h) & 0 & -\beta_R(1-\psi)l & -\beta_R\vartheta(1-\psi)l & 0 & 0 & \beta_m b_m l \\ 0 & 0 & -j_1 & 0 & 0 & 0 & 0 & -\beta_m b_m \\ 0 & 0 & 0 & j_2 & j_3 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & -j_4 & 0 & 0 & 0 \\ 0 & 0 & \pi_M & \pi_R & 0 & -\mu_h & 0 & 0 \\ 0 & 0 & -\beta_v b_m k & 0 & -\beta_v b_m \theta_v k & 0 & -\mu_v & 0 \\ 0 & 0 & \beta_v b_m k & 0 & \beta_v b_m \theta_v k & 0 & 0 & -\mu_v \end{bmatrix} \tag{51}$$

where,

$j_1 = \pi_M + \mu_h + \sigma_M$, $j_2 = \beta_R \left\{ \frac{(1-\rho)\mu_h+\omega+(1-\psi)(\gamma+\rho\mu_h)}{\mu_h+\gamma+\omega} - j_1 \right\}$,
$j_3 = \beta_R \frac{(1-\rho)\vartheta\mu_h+\omega+(1-\psi)(\gamma+\rho\mu_h)}{\mu_h+\gamma+\omega}$, $j_4 = (\alpha_M + \alpha_R + \mu_h + \sigma_M + \sigma_R + \sigma_{MR})$, $k = \frac{\Lambda_v \mu_h}{\mu_v \Lambda_h}$,
$l = \frac{\gamma+\rho\mu_h}{\mu_h+\gamma+\omega}$ and $p = \frac{(1-\rho)\mu_h+\omega}{\mu_h+\gamma+\omega}$.

An equilibrium point is locally asymptotically stable if the Jacobian matrix computed at that point has a negative trace and all eigenvalues with negative real parts or a positive determinant. We calculate the eigenvalues of $J(E^0)$ in (51) using the following expression

$$\{\lambda + (\gamma+\mu_h)\}\{\lambda + (\omega+\mu_h)\}(\lambda+j_1)(\lambda-j_2)(\lambda+\mu_h)(\lambda+\mu_v) \\ \{(\lambda+j_1)(\lambda+\mu_v) - \beta_v b_m \theta_v k\} = 0. \tag{52}$$

Clearly, it follows from equation (52) that the first six eigenvalues are negative if and only if $\frac{(1-\rho)\mu_h+\omega+(1-\psi)(\gamma+\rho\mu_h)}{\mu_h+\gamma+\omega} < (\pi_M + \mu_h + \sigma_M)$. To obtain the other two eigenvalues, we solve the following equation.

$$\lambda^2 + (\mu_v + \pi_M + \mu_h + \sigma_M)\lambda + \mu_v(\pi_M + \mu_h + \sigma_M) - \frac{\beta_v b_m \theta_v \Lambda_v \mu_h}{\mu_v \Lambda_h} = 0. \tag{53}$$

From equation (53), if $\frac{\beta_v b_m \theta_v \Lambda_v \mu_h}{\mu_v \Lambda_h} < \mu_v(\pi_M + \mu_h + \sigma_M)$, then the remaining two eigenvalues have negative real parts. Hence, the disease-free equilibrium of the co-infection model (6) is locally asymptotically stable. □

5.3. GLOBAL STABILITY OF THE DISEASE-FREE EQUILIBRIUM

We examine the global asymptotic stability of the co-infection model (6) using Castillo-Chavez et. al theory [11]. We begin by expressing the system in the form:

$$\begin{aligned} \frac{dX}{dt} &= H(X,Z), \\ \frac{dZ}{dt} &= G(X,Z), G(X,0)=0 \end{aligned} \tag{54}$$

in which $X = (S_h, V_R, S_v)$ denotes the uninfected compartments and $Z = (I_M, I_R, I_{MR}, R, I_v)$ represents the infected compartments.

$$E^0 = (X^0, 0), X^0 = \left(\frac{\Lambda_h[(1-\rho)\mu_h + \omega]}{\mu_h(\mu_h+\gamma+\omega)}, \frac{\Lambda_h(\gamma+\rho\mu_h)}{\mu_h(\gamma+\omega+\mu_h)}, \frac{\Lambda_v}{\mu_v} \right) \tag{55}$$

is the disease-free equilibrium. The conditions, L_1 and L_2 given below must be satisfied to guarantee global asymptotic stability.

L_1 : For $\frac{dX}{dt} = H(X,0), X^0$ is globally asymptotically stable.

$L_2 : G(X,Z) = BZ - \hat{G}(X,Z), \hat{G}(X,Z) \geq 0 for (X,Z) \in \Omega.$

where $B = D_z G(X^0, 0)$ is an M-matrix (that is, the off-diagonal elements of B are nonnegative).

The result state in Theorem 5 below holds if and only if model system (6) meets the the two conditions stated above.

Theorem 5. *The fixed point, $E^0 = (X^0, 0)$ is globally asymptotically stable equilibrium if $R_0 < 1$ and the conditions stated in L_1 and L_2 are met.*

Proof. From model (6), we have,

$$H(X,0) = \begin{pmatrix} (1-\rho)\Lambda_h + \omega V_R - (\gamma + \mu_h S_h) \\ \rho\Lambda_h + \gamma S_h - (\mu_h + \omega)V_R) \\ \Lambda_v - \mu_v S_v \end{pmatrix}$$

$$G(X,Z) = BZ - \hat{G}(X,Z)$$

where,

$$B = \begin{pmatrix} -k_1 & 0 & \alpha_R & 0 & k_2 \\ 0 & k_3 & k_4 & 0 & 0 \\ 0 & 0 & -k_5 & 0 & 0 \\ \pi_M & \pi_R & 0 & -\mu_h & 0 \\ k_6 & 0 & k_7 & 0 & -\mu_v \end{pmatrix}$$

where,
$k_1 = (\pi_M + \mu_h + \sigma_M)$, $k_2 = \beta_m b_m$, $k_3 = \beta_R[\frac{\mu_h(1-\psi\rho)+\gamma(1-\psi)+\omega}{\mu_h+\gamma+\omega}] - (\pi_R + \mu_h + \sigma_R)$, $k_4 = \beta_R\vartheta[\frac{\mu_h(1-\psi\rho)+\gamma(1-\psi)+\omega}{\mu_h+\gamma+\omega}] + \alpha_M$, $k_5 = (\alpha_M + \alpha_R + \mu_h + \sigma_M + \sigma_R + \sigma_{MR})$, $k_6 = \frac{\beta_v b_m \Lambda_v \mu_h}{\Lambda_h \mu_v}$ and $k_7 = \frac{\beta_v b_m \theta_v \Lambda_v \mu_h}{\Lambda_h \mu_v}$

$$\hat{G}(X,Z) = \begin{pmatrix} \hat{G}_1(X,Z) \\ \hat{G}_2(X,Z) \\ \hat{G}_3(X,Z) \\ \hat{G}_4(X,Z) \\ \hat{G}_5(X,Z) \end{pmatrix}$$

$$= \begin{pmatrix} \beta_m b_m I_v\{(1-\frac{S_h}{N_h}) + (1-\frac{V_R}{N_h})\} + \frac{\tau\beta_R(I_R+\vartheta I_{MR})}{N_h} I_M \\ \frac{\beta_R(I_R+\vartheta I_{MR})}{N_h}(1-\frac{S_h}{N_h}) + \frac{(1-\psi)\beta_R(I_R+\vartheta I_{MR})}{N_h}(1-\frac{V_R}{N_h}) + (\frac{\zeta\beta_m b_m I_v}{N_h})I_R \\ -\frac{\tau\beta_R(I_R+\vartheta I_{MR})}{N_h} I_M - (\frac{\zeta\beta_m b_m I_v}{N_h})I_R \\ 0 \\ \frac{\beta_v b_m (I_M+\theta_v I_{MR})}{N_h}(1-\frac{S_v}{N_h}) \end{pmatrix}.$$

It is clear that X^0 is unstable globally as $\hat{G}_3(X,Z) < 0$. It follows that the two conditions, L_1 and L_2 are not met. Therefore, when $R_{mr} < 1$, the disease-free equilibrium of the co-infection model (6) is not globally asymptotically stable. This implies that the model may undergo a bifurcation. □

5.4. DISEASE-ENDEMIC EQUILIBRIUM POINT OF THE CO-INFECTION MODEL

The disease-endemic equilibrium point of model (6) is given by

$$E^* = (S_h^*, V_R^*, I_M^*, I_R^*, I_{MR}^*, R^*, S_v^*, I_v^*). \tag{56}$$

Where,

$$\begin{aligned}
S_h^* &= \frac{(1-\rho)\Lambda_h + \omega V_R^*}{\lambda_M + \lambda_R + \gamma + \mu_h}, \\
V_R^* &= \frac{\rho\Lambda_h + \gamma S_h^*}{\lambda_M + (1-\psi)\lambda_R + \mu_h + \omega}, \\
I_M^* &= \frac{\lambda_M S_h^* + \lambda_M V_R^* + \alpha_R I_{MR}^*}{\tau\lambda_R + \pi_M + \mu_h + \sigma_M}, \\
I_R^* &= \frac{\lambda_R S_h^* + (1-\psi)\lambda_R V_R^* + \alpha_{MR} I_{MR}^*}{\zeta\lambda_M + \pi_R + \mu_h + \sigma_R}, \\
I_{MR}^* &= \frac{\tau\lambda_R I_M^* + \zeta\lambda_M I_R^*}{2\alpha_M + 2\alpha_R + \mu_h + \alpha_{MR}}, \\
R^* &= \frac{\pi_M I_M^* + \pi_R I_R^*}{\mu_h},
\end{aligned}$$

$$S_v^* = \frac{\Lambda_v}{\lambda_v + \mu_v} \quad and \quad I_v^* = \frac{\Lambda_v \lambda_v}{\mu_v(\lambda_v + \mu_v)} \quad with \quad \lambda_M = \frac{\beta_m b_m I_v^*}{N_h},$$
$$\lambda_v = \beta_v b_m \frac{(I_M^* + \theta_v I_{MR}^*)}{N_h^*}$$

$$\lambda_R = \beta_R \frac{(I_R^* + \vartheta I_{MR}^*)}{N_h^*},$$
$$N_h^* = S_h^* + V_R^* + I_M^* + I_R^* + I_{MR}^* + R^* \quad and \quad N_v^* = S_v^* + I_v^*.$$

We adopt Center Manifold Theory [45, 12] to study the disease-endemic equilibrium of model (6) and establish the type of bifurcation the model may undergo. To apply this theory, we first consider the case when $R_{mr} = 1$ and choose the transmission probability for malaria in humans, $\beta_m = \beta_m^*$ and the transmission rate for rotavirus, $\beta_R = \beta_R^*$ as bifurcation parameters. Solving for β_m and β_R from $R_{mr} = R_m = R_r = 1$ gives

$$\beta_m = \beta_m^* = \frac{\Lambda_h \mu_v^2 (\pi_M + \sigma_M + \mu_h)}{b_m^2 \beta_v \Lambda_v \mu_h} \tag{57}$$

and

$$\beta_R = \beta_R^* = \frac{1}{\Lambda_h} \left\{ \frac{\mu_h(\sigma_R + \pi_R + \mu_h)(\mu_h + \gamma + \omega)}{\omega + (1-\psi)(\rho\mu_h + \gamma) + \mu_h(1-\rho)} \right\}. \tag{58}$$

We then change the variables as follows:

Let $S_h = x_1, V_R = x_2, I_M = x_3, S_h = x_1, I_R = x_4, I_{MR} = x_5, R = x_6, S_v = x_7, I_v = x_8, N_h = x_1 + x_2 + x_3 + x_4 + x_5 + x_6$ and $N_v = x_7 + x_8$. In addition, using vector notation $X = [x_1, x_2, x_3, x_4, x_5, x_6, x_7, x_8]^T$, model (6) can then be rewritten in the form,

$\frac{dx}{dt} = F(X)$, with $F = [f_1, f_2, f_3, f_4, f_5, f_6, f_7, f_8]^T$, as shown in system (59).

$$\left.\begin{aligned}
\frac{dx_1}{dt} &= f_1 = (1-\rho)\Lambda_h + \omega x_2 - \lambda_M x_1 - \lambda_R x_1 - (\gamma + \mu_h)x_1 \\
\frac{dx_2}{dt} &= f_2 = \rho\Lambda_h + \gamma x_1 - \lambda_M x_2 - (1-\psi)\lambda_R x_2 - (\mu_h + \omega)x_2 \\
\frac{dx_3}{dt} &= f_3 = \lambda_M x_1 + \lambda_M x_2 + \alpha_R x_5 - \tau\lambda_R x_3 - (\pi_M + \mu_h + \sigma_M)x_3 \\
\frac{dx_4}{dt} &= f_4 = \lambda_R x_1 + (1-\psi)\lambda_R x_2 + \alpha_M x_5 - \zeta\lambda_M x_4 - (\pi_R + \mu_h + \sigma_R)x_4 \\
\frac{dx_5}{dt} &= f_5 = \tau\lambda_R x_3 + \zeta\lambda_M x_4 - \alpha_M x_5 - \alpha_R x_5 - (\mu_h + \sigma_M + \sigma_R + \sigma_{MR})x_5 \\
\frac{dx_6}{dt} &= f_6 = \pi_M x_3 + \pi_R x_4 - \mu_h x_6 \\
\frac{dx_7}{dt} &= f_7 = \Lambda_v - \lambda_v x_7 - \mu_v x_7 \\
\frac{dx_8}{dt} &= f_8 = \lambda_v x_7 - \mu_v x_8
\end{aligned}\right\}. \tag{59}$$

We evaluate the Jacobian of the transformed system (59) at disease-free equilibrium and obtain,

$$J(E^0) = \begin{bmatrix} -(\gamma+\mu_h) & \omega & 0 & -k_1 & -k_2 & 0 & 0 & -k_3 \\ \gamma & -(\omega+\mu_h) & 0 & -k_4 & -k_5 & 0 & 0 & -k_6 \\ 0 & 0 & -k_7 & 0 & 0 & 0 & 0 & -\beta_m b_m \\ 0 & 0 & 0 & k_8 & k_9 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & -k_{10} & 0 & 0 & 0 \\ 0 & 0 & \pi_M & \pi_R & 0 & -\mu_h & 0 & 0 \\ 0 & 0 & -k_{11} & 0 & -k_{12} & 0 & -\mu_v & 0 \\ 0 & 0 & k_{13} & 0 & k_{14} & 0 & 0 & -\mu_v \end{bmatrix} \tag{60}$$

where,

$k_1 = \beta_R[\frac{(1-\rho)\mu_h+\omega}{(\mu_h+\gamma+\omega)}]$, $k_2 = \beta_R\vartheta[\frac{(1-\rho)\mu_h+\omega}{(\mu_h+\gamma+\omega)}]$, $k_3 = \beta_m b_m[\frac{(1-\rho)\mu_h+\omega}{(\mu_h+\gamma+\omega)}]$, $k_4 = [\frac{(1-\psi)(\gamma+\rho\mu_h)\beta_R}{(\mu_h+\gamma+\omega)}]$,

$k_5 = [\frac{(1-\psi)(\gamma+\rho\mu_h)\beta_R\vartheta}{(\mu_h+\gamma+\omega)}]$, $k_6 = [\frac{\beta_m b_m(\gamma+\rho\mu_h)}{(\mu_h+\gamma+\omega)}]$, $k_8 = \beta_R\{[\frac{(1-\rho)\mu_h+\omega+(1-\psi)(\gamma+\rho\mu_h)}{(\mu_h+\gamma+\omega)}] - (\pi_M+\mu_h+\sigma_M)\}$,

$k_7 = (\pi_M+\mu_h+\sigma_M)$, $k_9 = \beta_R[\frac{(1-\rho)\vartheta\mu_h+\omega+(1-\psi)(\gamma+\rho\mu_h)}{(\mu_h+\gamma+\omega)}]$, $k_{10} = (\alpha_M+\alpha_R+\mu_h+\sigma_M+\sigma_R+\sigma_{MR})$,

$k_{11} = \frac{\beta_v b_m \Lambda_v \mu_h}{\mu_v \Lambda_h}$, $k_{12} = \frac{\beta_v b_m \theta_v \Lambda_v \mu_h}{\mu_v \Lambda_h}$, $k_{13} = \frac{\beta_v b_m \Lambda_v \mu_h}{\mu_v \Lambda_h}$ and $k_{14} = \frac{\beta_v b_m \theta_v \Lambda_v \mu_h}{\mu_v \Lambda_h}$.

The Jacobian, $J(E^0)$ in (60) has a simple zero eigenvalue and other eigenvalues with negative real parts. Therefore, the Center Manifold Theorem can be applied. For this, we start by calculating the right and the left eigenvectors of $J(E^0)$ in (60) at disease-free equilibrium. We obtain the right eigenvector of $J(E^0)|_{(\beta_m=\beta_m^*,\beta_r=\beta_r^*)}$, as $W = [w_1, w_2, w_3, w_4, w_5, w_6, w_7, w_8]^T$ where,

$$w_1 = \frac{k_7 w_3 \left(k_3(\mu_h+\omega)+k_6\omega\right)}{b_m\mu_h\beta_m(\gamma+\mu_h+\omega)}, \quad w_2 = \frac{k_7 w_3 \left(k_6(\gamma+\mu_h)+\gamma k_3\right)}{b_m\mu_h\beta_m(\gamma+\mu_h+\omega)},$$

$$w_4 = 0, \quad w_5 = 0, \quad w_6 = \frac{\pi_m w_3}{\mu_h}, \quad w_7 = \frac{k_{11} w_3}{\mu_v}, \quad w_8 = -\frac{k_7 w_3}{b_m\beta_m}, \quad w_3 = free$$

and the left eigenvector of $J(E^0)|_{(\beta_m=\beta_m^*,\beta_r=\beta_r^*)}$ as $V = [v_1, v_2, v_3, v_4, v_5, v_6, v_7 v_8]^T$, where,

$$v_2 = \frac{v_1(\gamma+\mu_h)}{\gamma}, \quad v_3 = -\frac{k_{13}\left(\frac{k_6 v_1(\gamma+\mu_h)}{\gamma}+k_3 v_1\right)}{k_{13}b_m\beta_m+k_7\mu_v}, \quad v_4 = \frac{v_1\left(k_4(\gamma+\mu_h)+\gamma k_1\right)}{\gamma k_8},$$

$$v_5 = \frac{-\frac{k_7 k_{14} v_1(k_6(\gamma+\mu_h)+\gamma k_3)}{\gamma(k_{13}b_m\beta_m+k_7\mu_v)} + \frac{k_9 v_1(k_4(\gamma+\mu_h)+\gamma k_1)}{\gamma k_8} - \frac{k_5 v_1(\gamma+\mu_h)}{\gamma} - k_2 v_1}{k_{10}},$$

$$v_6 = 0, \quad v_7 = 0,$$

$$v_8 = -\frac{k_7 v_1 \left(k_6 \left(\gamma + \mu_h\right) + \gamma k_3\right)}{\gamma \left(k_{13} b_m \beta_m + k_7 \mu_v\right)}, \quad v_1 = free.$$

We then evaluate the associated partial derivatives (non-zero) of $F(X)|_{J(E^0)}$ and obtain

$$\begin{aligned}
\frac{\partial^2 f_1}{\partial x_1 \partial x_8} &= -\frac{b_m \Lambda_h \mu_h \beta_m \left(\gamma + \rho\mu_h\right)\left(\gamma + \mu_h + \omega\right)}{\left(\Lambda_h \left(\gamma + \mu_h\right) + \omega\right)^2}, \\
\frac{\partial^2 f_1}{\partial x_2 \partial x_8} &= \frac{b_m \mu_h \beta_m \left(\gamma + \mu_h + \omega\right)\left(\omega - (\rho - 1)\Lambda_h \mu_h\right)}{\left(\Lambda_h \left(\gamma + \mu_h\right) + \omega\right)^2}, \\
\frac{\partial^2 f_1}{\partial x_3 \partial x_8} &= \frac{b_m \mu_h \beta_m \left(\gamma + \mu_h + \omega\right)\left(\omega - (\rho - 1)\Lambda_h \mu_h\right)}{\left(\Lambda_h \left(\gamma + \mu_h\right) + \omega\right)^2}, \\
\frac{\partial^2 f_1}{\partial x_6 \partial x_8} &= \frac{b_m \mu_h \beta_m \left(\gamma + \mu_h + \omega\right)\left(\omega - (\rho - 1)\Lambda_h \mu_h\right)}{\left(\Lambda_h \left(\gamma + \mu_h\right) + \omega\right)^2}, \\
\frac{\partial^2 f_2}{\partial x_1 \partial x_8} &= \frac{b_m \Lambda_h \mu_h \beta_m \left(\gamma + \rho\mu_h\right)\left(\gamma + \mu_h + \omega\right)}{\left(\Lambda_h \left(\gamma + \mu_h\right) + \omega\right)^2}, \\
\frac{\partial^2 f_2}{\partial x_2 \partial x_8} &= \frac{b_m \mu_h \beta_m \left(\gamma + \mu_h + \omega\right)\left((\rho - 1)\Lambda_h \mu_h - \omega\right)}{\left(\Lambda_h \left(\gamma + \mu_h\right) + \omega\right)^2}, \\
\frac{\partial^2 f_2}{\partial x_3 \partial x_8} &= \frac{b_m \Lambda_h \mu_h \beta_m \left(\gamma + \rho\mu_h\right)\left(\gamma + \mu_h + \omega\right)}{\left(\Lambda_h \left(\gamma + \mu_h\right) + \omega\right)^2}, \\
\frac{\partial^2 f_3}{\partial x_3 \partial x_8} &= -\frac{b_m \mu_h \beta_m \left(\gamma + \mu_h + \omega\right)}{\Lambda_h \left(\gamma + \mu_h\right) + \omega}, \\
\frac{\partial^2 f_3}{\partial x_6 \partial x_8} &= -\frac{b_m \mu_h \beta_m \left(\gamma + \mu_h + \omega\right)}{\Lambda_h \left(\gamma + \mu_h\right) + \omega}.
\end{aligned} \tag{61}$$

From equation (61), the associated bifurcation coefficient a is expressed as follows:

$$\begin{aligned}
a = v_1 w_1 w_8 \frac{\partial^2 f_1}{\partial x_1 \partial x_8} + v_1 w_2 w_8 \frac{\partial^2 f_1}{\partial x_2 \partial x_8} + v_1 w_3 w_8 \frac{\partial^2 f_1}{\partial x_3 \partial x_8} + v_1 w_6 w_8 \frac{\partial^2 f_1}{\partial x_6 \partial x_8} \\
+ v_2 w_1 w_8 \frac{\partial^2 f_2}{\partial x_1 \partial x_8} v_2 w_2 w_8 \frac{\partial^2 f_2}{\partial x_2 \partial x_8} + v_2 w_3 w_8 \frac{\partial^2 f_2}{\partial x_3 \partial x_8} + v_2 w_6 w_8 \frac{\partial^2 f_2}{\partial x_6 \partial x_8} \\
+ v_3 w_3 w_8 \frac{\partial^2 f_2}{\partial x_3 \partial x_8} + v_3 w_6 w_8 \frac{\partial^2 f_2}{\partial x_6 \partial x_8}.
\end{aligned} \tag{62}$$

which can be simplified as

$$a = \sum_{k,i,j=1}^{8} v_k w_i w_j \frac{\partial^2 f_k}{\partial x_i \partial x_j}(0,0). \tag{63}$$

Upon substituting the partial derivatives in (61) and the values of the left and right eigenvectors of $J(E^0)$, we have

$$a = \frac{k_7 v_1 w_3^2}{(\Lambda_h(\gamma + \mu_h) + \omega)^2}[\Delta_P - \Delta_N],$$

where,

$$\begin{aligned}\Delta_P =&\frac{k_7(k_6(\gamma+\mu_h)+\gamma k_3)((1-\rho)\Lambda_h\mu_h+\omega)}{b_m\beta_m}\\&+\frac{k_7(\gamma+\mu_h)(k_6(\gamma+\mu_h)+\gamma k_3)((1-\rho)\Lambda_h\mu_h+\omega)}{\gamma b_m\beta_m}\\&+\frac{k_{13}(\pi_m-\mu_h)(\gamma+\mu_h+\omega)(k_6(\gamma+\mu_h)+\gamma k_3)(\Lambda_h(\gamma+\mu_h)+\omega)}{\gamma(k_{13}b_m\beta_m+k_7\mu_v)}\\&+\pi_m(\gamma+\mu_h+\omega)((1-\rho)\Lambda_h\mu_h+\omega)\end{aligned}$$

$$\begin{aligned}\Delta_N =&\frac{(\Lambda_h\mu_h(\gamma+\mu_h)(\gamma+\rho\mu_h)(\gamma+\mu_h+\omega))(k_7\Lambda_h(\gamma+\rho\mu_h)(k_3(\mu_h+\omega)+k_6\omega))}{\gamma(b_m\beta_m)}\\&+\frac{k_7\Lambda_h(\gamma+\mu_h)(\gamma+\rho\mu_h)(k_3(\mu_h+\omega)+k_6\omega)}{\gamma b_m\beta_m}\\&+\mu_h(\gamma+\mu_h+\omega)((1-\rho)\Lambda_h\mu_h+\omega)\\&+\frac{\pi_m\Lambda_h(\gamma+\mu_h)(\gamma+\rho\mu_h)(\gamma+\mu_h+\omega)}{\gamma}.\end{aligned}$$

We thus have the following cases for values of a.

Case 1: $a>0$ if $\Delta_P>\Delta_N$, Case 2: $a<0$ if $\Delta_P<\Delta_N$.

We repeat the above procedure to obtain the bifurcation coefficient b, which is defined by

$$b=\sum_{k,i=1}^{8}v_kw_i\frac{\partial^2 f_k}{\partial x_i\partial\beta_m^*}(0,0). \tag{64}$$

The basic reproduction number is the maximum of the individual disease reproduction numbers. Therefore, we establish the non-zero derivatives associated with b for R_m and R_r. But since the bifurcation coefficient b is always non-negative, it follows from [12] that the transformed model (59) will exhibit a backward bifurcation if the backward bifurcation coefficient, a is non-negative. This further confirms that the disease-free equilibrium of model (6) is not globally asymptotically stable. The implication is that there will be a disease outbreak in the community and the infection will persist. If $a<0$, then from [12], it follows that there will be no backward bifurcation at $R_m=R_r=1$, only the disease-free equilibrium will exist when $R_m<1$ and when $R_r<1$, which means there will be no infection or disease in the population. We thus, state the following theorem from item (4) in [12] without proof.

Theorem 6. *The co-infection model* (6) *has a unique disease-endemic equilibrium,* $E^*=(S_h^*,V_R^*,I_M^*,I_R^*,I_{MR}^*,R^*,S_v^*,I_v^*)$*, which is locally asymptotically stable if* $R_{mr}<1$ *and unstable otherwise.*

5.5. GLOBAL STABILITY OF THE DISEASE-ENDEMIC EQUILIBRIUM

We investigate global asymptotic stability of the disease-endemic equilibrium point of system (6) using Lyapunov method [33] and La Salle's invariance principle[13]. We present the following stability theorem.

Theorem 7. *The endemic equilibrium of model* (6), $E^* = (S_h^*, V_R^*, I_M^*, I_R^*, I_{MR}^*, R^*, S_v^*, I_v^*)$, *is globally asymptotically stable if* $R_{mr} > 1$.

Proof. We begin by constructing a suitable Lyapunov function of the form:

$$L = \Sigma_{i=1}^{8} A_i(x_i - x_i^* \ln x_i) \tag{65}$$

where A_i is a properly selected constant, x_i is the population of i^{th} compartment, i_i^{th} is the equilibrium value of x_i and $A_i > 0$. The Lyapunov function denoted by L is continuous and differentiable. We have:

$$\begin{aligned} L(S_h, V_R, I_M, I_R, I_{MR}, R, S_v, I_v) &= A_1(S_h - S_h^* \ln S_h) + A_2(V_R - V_R^* \ln V_R) \\ &+ A_3(I_M - I_M^* \ln I_M) + A_4(I_R - I_R^* \ln I_R) + A_5(I_{MR} - I_{MR}^* \ln I_{MR}) \\ &+ A_6(R - R^* \ln R) + A_7(S_v - S_v^* \ln S_v) + A_8(I_v - I_v^* \ln I_v). \end{aligned} \tag{66}$$

The global stability of the disease-endemic equilibrium, $E^* = (S_h^*, V_R^*, I_M^*, I_R^*, I_{MR}^*, R^*, S_v^*, I_v^*)$, holds if $\frac{dL}{dt} \leq 0$. The time derivative of the Lyapunov function L is given by

$$\begin{aligned} \frac{dL}{dt} &= A_1(1 - \frac{S_h^*}{S_h})\frac{dS_h}{dt} + A_2(1 - \frac{V_R^*}{V_R})\frac{dV_R}{dt} + A_3(1 - \frac{I_M^*}{I_M})\frac{dI_M}{dt} + A_4(1 - \frac{I_R^*}{I_R})\frac{dI_R}{dt} \\ &+ A_5(1 - \frac{I_{MR}^*}{I_{MR}})\frac{dI_{MR}}{dt} + A_6(1 - \frac{R^*}{R})\frac{dR}{dt} + A_7(1 - \frac{S_v^*}{S_v})\frac{dS_v}{dt} + A_8(1 - \frac{I_v^*}{I_v})\frac{dI_v}{dt}. \end{aligned} \tag{67}$$

$$\begin{aligned} \frac{dL}{dt} &= -A_1(1 - \frac{S_h^*}{S_h})^2(\gamma + \mu_h)S_h + A_1(1 - \frac{S_h^*}{S_h})(\frac{I_v^*}{I_v}\frac{S_h^*}{S_h} - 1)\frac{\beta_m \beta_v}{N_h} I_v S_h \\ &+ A_1(1 - \frac{S_h^*}{S_h})(\frac{I_R^*}{I_R}\frac{S_h^*}{S_h} - 1)\frac{\beta_R}{N_h} I_R S_h \\ &- A_2(1 - \frac{V_R^*}{V_R})^2(\mu_h + \omega)V_R + A_2(1 - \frac{V_R^*}{V_R})(\frac{I_v^*}{I_v}\frac{V_R^*}{V_R} - 1)\frac{\beta_m \beta_v}{N_h} I_v V_R \\ &+ A_2(1 - \frac{V_R^*}{V_R})(\frac{V_R^*}{V_R}\frac{I_{R^*}}{I_R} - 1)\frac{(1-\psi)\beta_R}{N_h} I_R V_R \\ &- A_3(1 - \frac{I_M^*}{I_M})^2(\mu_h + \sigma_M + \pi_M)I_M + A_3(1 - \frac{I_M^*}{I_M})(\frac{I_M^*}{I_M}\frac{I_{R^*}}{I_R} - 1)\frac{\tau \beta_R}{N_h} I_R I_M \end{aligned}$$

$$-A_4(1-\frac{I_R^*}{I_R})^2(\mu_h+\sigma_R+\pi_R)I_R+A_4(1-\frac{I_R^*}{I_R})(\frac{I_v^*}{I_v}\frac{I_R^*}{I_R}-1)\frac{\zeta\beta_m\beta_v}{N_h}I_vI_R$$
$$-A_5(1-\frac{I_{MR}^*}{I_{MR}})^2(\alpha_M+\alpha_R+\mu_h+\sigma_M+\sigma_R+\sigma_{MR})I_{MR}-A_6(1-\frac{R^*}{R})^2\mu_hR$$
$$-A_7(1-\frac{S_v^*}{S_v})^2\mu_vS_v+A_7(1-\frac{S_v^*}{S_v})(\frac{I_M^*}{I_M}\frac{S_v^*}{S_v}-1)\frac{\beta_vbm}{N_h}I_MS_v-A_8(1-\frac{I_v^*}{I_v})^2I_v\mu_v. \quad (68)$$

By adopting the approach by [34], we have the following expression:

$$\frac{dL}{dt}=-A_1(1-\frac{S_h^*}{S_h})^2(\gamma+\mu_h)S_h-A_2(1-\frac{V_R^*}{V_R})^2(\mu_h+\omega)V_R-A_3(1-\frac{I_M^*}{I_M})^2(\mu_h+\sigma_M+\pi_M)I_M$$
$$-A_4(1-\frac{I_R^*}{I_R})^2(\mu_h+\sigma_R+\pi_R)I_R-A_5(1-\frac{I_{MR}^*}{I_{MR}})^2(\alpha_M+\alpha_R+\mu_h+\sigma_M+\sigma_R+\sigma_{MR})I_{MR}$$
$$-A_6(1-\frac{R^*}{R})^2\mu_hR-A_7(1-\frac{S_v^*}{S_v})^2\mu_vS_v-A_8(1-\frac{I_v^*}{I_v})^2I_v\mu_v+Z(E^0) \quad (69)$$

where,

$$Z(E^0)=+A_1(1-\frac{S_h^*}{S_h})(\frac{I_v^*}{I_v}\frac{S_h^*}{S_h}-1)\frac{\beta_m\beta_v}{N_h}I_vS_h+A_1(1-\frac{S_h^*}{S_h})(\frac{I_R^*}{I_R}\frac{S_h^*}{S_h}-1)\frac{\beta_R}{N_h}I_RS_h$$
$$+A_2(1-\frac{V_R^*}{V_R})(\frac{I_v^*}{I_v}\frac{V_R^*}{V_R}-1)\frac{\beta_m\beta_v}{N_h}I_vV_R+A_2(1-\frac{V_R^*}{V_R})(\frac{V_R^*}{V_R}\frac{I_{R^*}}{I_R}-1)\frac{(1-\psi)\beta_R}{N_h}I_RV_R$$
$$+A_3(1-\frac{I_M^*}{I_M})(\frac{I_M^*}{I_M}\frac{I_{R^*}}{I_R}-1)\frac{\tau\beta_R}{N_h}I_RI_M+A_4(1-\frac{I_R^*}{I_R})(\frac{I_v^*}{I_v}\frac{I_R^*}{I_R}-1)\frac{\zeta\beta_m\beta_v}{N_h}I_vI_R$$
$$+A_7(1-\frac{S_v^*}{S_v})(\frac{I_M^*}{I_M}\frac{S_v^*}{S_v}-1)\frac{\beta_vbm}{N_h}I_MS_v\leq 0. \quad (70)$$

$Z(E^0)$ is negative by following the approaches implemented in [36, 37, 34]. Thus, $Z(E^0)\leq 0$ for all $Z(E^0)\geq 0$. Hence, $\frac{dL}{dt}\leq 0$ in (E^0) and when $(E^0)=(E^*)$. Hence the largest invariant set in (E^0) such that $\frac{dL}{dt}\leq 0$ is the singleton (E^*), which is our disease-endemic equilibrium point. We can conclude that the disease-endemic equilibrium, (E^*), is globally stable if $R_{mr}>1$. □

6. NUMERICAL SIMULATIONS AND DISCUSSION

In this section, we present some numerical results of model (6) to support our analytical results obtained above using the set of parameter values listed in Table 2.

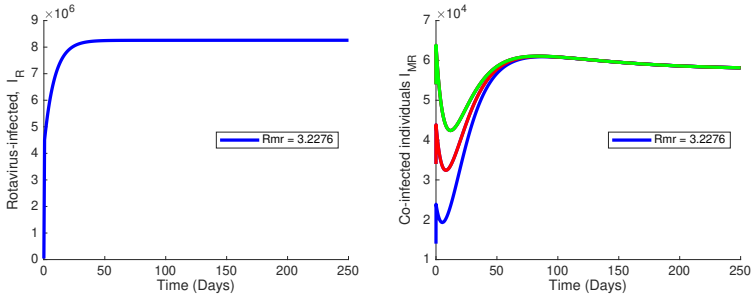
Figure 2 depicts local stability of disease-endemic equilibrium of rotavirus-infected, Fig. 2a and co-infected populations, Fig. 2b, respectively of the co-infection model (6) plotted at various initial values with $R_{mr}=3.2276$. From the figures we observe

Table 2: Parameter values for the malaria-only and rotavirus-only sub-models with vaccination.

Parameter	Symbol	Value	Source
The recruitment rate of humans	Λ_h	$9.6274 \times 10^{-5} day^{-1}$	[39]
The recruitment rate of mosquitoes	Λ_v	$7.1 \times 10^{-2} day^{-1}$	[40]
Natural mortality rate of humans	μ_h	$2.537 \times 10^{-5} day^{-1}$	[39]
Natural mortality rate of mosquitoes	μ_v	$4.0 \times 10^{-5} day^{-1}$	[55]
Malaria-induced mortality rate for humans	σ_M	$4.49312 \times 10^{-4} day^{-1}$	[41]
Rotavirus-induced mortality rate for humans	σ_R	$4.466 \times 10^{-4} day^{-1}$	[6]
Mortality rate of humans from co-infection	σ_{MR}	$6.0 \times 10^{-3} day^{-1}$	Assumed
The probability of transmission of malaria infection in humans	β_m	$0.06 - 0.27$	[49]
The probability of transmission of malaria infection in mosquitoes	β_v	$7.2 \times 10^{-2} day^{-1}$	[50]
The per capita biting rate of female Anopheles mosquito	b_m	$4.0 \times 10^{-1} day^{-1}$	[51]
The effective contact rate for infection with rotavirus	β_R	$0.00160 - 0.050$	Variable
The rate of recovery from malaria infection for humans	π_M	$7.808 \times 10^{-1} day^{-1}$	[52]
The rate of recovery from rotavirus infection for humans	π_R	$2.0 \times 10^{-1} day^{-1}$	[53, 54]
The rate of recovery from co-infection (rotavirus)	α_R	$5.75 \times 10^{-4} day^{-1}$	Assumed
The rate of recovery from co-infection (malaria)	α_M	$1.56 \times 10^{-3} day^{-1}$	Assumed
The recruitment rate of vaccinated humans	ρ	$1.884 \times 10^{-3} day^{-1}$	[42]
The rate of vaccination for susceptible humans	γ	$1.884 \times 10^{-3} day^{-1}$	[42]
The effectivity of the vaccine-induced protection	ψ	$0 - 1.0$	Variable
The vaccine efficacy waning rate	ω	$2.778 \times 10^{-3} day^{-1}$	[29]
Modification parameters	$\vartheta, \zeta, \tau, \theta_v$	$1.5, 1.5, 1.5, 1.5$	Assumed

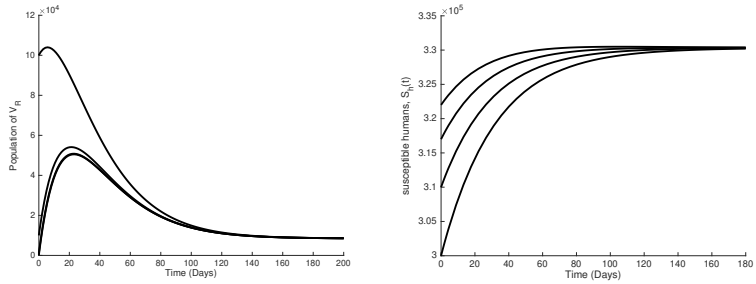
an outbreak of rotavirus infection in the population, which has also affected the co-infected population. This could be attributed to the fact that there is an increased susceptibility to infection with malaria for humans infected with rotavirus because of the compromised immunity [7]. Therefore, rotavirus vaccination should be implemeted immediately to prevent further infections.

In Fig. 3, we plot global stability of disease-free equilibrium of co-infection model (6) for (3a) the vaccinated population and (3b) the rotavirus-malaria co-infected humans with $R_{mr} = 0.1860$. From the figures, we observe that the vaccinated population goes to the boundary equilibrium at disease-free equilibrium as $t \to \infty$ while the susceptible population rapidly increases then comes down to a stable equilibrium after some days. This implies that there is still no infection in the population and so vaccination



(a) (b)

Figure 2: Local stability of disease-endemic equilibrium with $R_{mr} = 3.2276$ for: (2a) rotavirus infected population, (2b) co-infected population at various initial values. Used parameter values are available in Table 2.

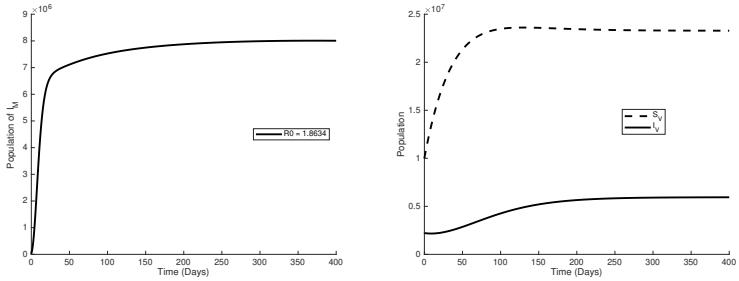


(a) (b)

Figure 3: Simulations of model (22) showing global stability of disease-free equilibrium with $R_r = 0.1860$ for (3a) vaccinated population and (3b) susceptible population. Used parameters are given in Table 2.

is not necessary. The figures also indicate that in a disease-free population, susceptible population increases as all other compartments approach or are equal to zero as $t \to \infty$ irrespective of the initially infected population and the disease eventually dies out. This result confirms our theoretical findings.

Figure 4 shows global asymptotic stability of the disease-endemic equilibrium when $R_{mr} = 1.8634$ for (4a) malaria-infected humans and for (4b) susceptible and infected mosquito populations. From the figures, we observe an outbreak of malaria in the community. As the population of susceptible mosquitoes increases, we note many people are getting infected with malaria. Also, in Fig. 4b, it can be seen that there are fewer infectious mosquitoes than susceptible ones. Therefore, we recommend implementation of control interventions to help eliminate the large number of mosquitoes



(a) (b)

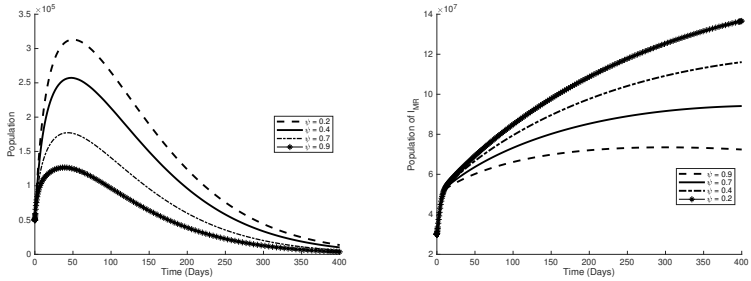
Figure 4: The disease-endemic equilibrium of model (6) with $R_{mr} = 1.8634$. (4a): Plot for malaria infected human population. (4b): Plot for susceptible and infected mosquito population. Used parameter values are in Table 2.

in the population, which will as a result reduce the number of new malaria infection cases in the community. When malaria infection is considered independently of rotavirus in Fig. 4a, we note that vaccination does not greatly change the number of new malaria episodes in the community but it does change disease dynamics such that when we increase the vaccination rate then there can be slight delay in disease prevalence over time but it will not affect the infection duration Fig. 2b.

In Fig. 5, we simulate the rotavirus-malaria model by varying the vaccination rate, $\psi = 0.2, 0.4, 0.7, 0.9$, to see its effects on rotavirus-malaria co-infected populations when there is no disease in the population, $R_{mr} = 0.1476$ (Fig. 5a) and when the disease is established in the population, $R_{mr} = 1.8634$ (Fig. 5b). The figures indicate key interactions between rotavirus vaccination rate and the co-infections. From the figures, we note a reduction in the number of rotavirus-malaria co-infected humans as the vaccine effectivity increases. Hence, we can conclude that vaccination positively impacts on the co-infections, and therefore recommend increasing the availability of efficacious vaccines for rotavirus as they will help contain rotavirus dynamics and also aid reduce acute co-infections with malaria.

7. CONCLUSION

This paper aimed at deriving a model for rotavirus-malaria co-infection dynamics with vaccination involved so as to examine the effects of vaccination in altering population dynamics, especially in developing countries where rotavirus-malaria coexistence is endemic. The model was extended to explore malaria prevalence as a result of rotavirus infection and vice versa. We further investigated the effects of rotavirus



(a) (b)

Figure 5: Effectivity of rotavirus vaccine on the co-infections. (5a): new rotavirus infection cases as a function of time for $\psi = 0.2, 0.4, 0.7, 0.9$ with $R_{mr} = 0.1860$. (5b): number of new co-infection cases as a function of time for $\psi = 0.2, 0.4, 0.7, 0.9$ with $R_{mr} = 1.8634$. Other parameters are as displayed in Table 2.

vaccination on malaria infections and the role vaccination plays in altering transmission dynamics. We recommend continued efforts in increasing access to rotavirus vaccination, strengthening the awareness and education campaigns and emphasizing on the importance of clearing bushes and draining stagnant water around homes and use of treated mosquito nets as a means of fighting effects of rotavirus and malaria co-infections.

Finally, in this paper we considered an SIR model and SI model for the malaria component of the full model, with vaccination for rotavirus disease only. However, it would be interesting to see the results when the model is improved to capture other features of malaria transmission for example incorporating incubation period/exposed class for the malaria model and so we leave that for our future works. Other future goals include application of optimal control theory to the model with control measures for both diseases considered. The model assumed homogeneous mixing, however, human contact process in real world is not uniform collision as different people contact persons may be unique each time. We propose to incorporate into the model complex networks [46, 47, 48] which consider disease transmission dynamics in big social and biological networks with unique heterogeneities, and so we leave that for our future research too.

AUTHORS' CONTRIBUTIONS

RAN and GOL designed the study and formulated the model. RAN analyzed the model, wrote and edited the paper. MOO and TOO performed numerical simulations. All authors proofread and approved the final paper.

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

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