Mathematical modelling of malaria transmission dynamics with resistant human

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Abstract

Malaria is a life-threatening disease especially among individuals that have little or no resistance to the disease. A mathematical model that incorporates an individual's ability to resist malaria infection is consider to study the dynamics of malaria. Preliminary analyses of the model reveal that the model undergoes backward bifurcation which is induced by the ability of individuals to resist malaria infection. By fitting the model to recorded data on the incidence of malaria in Nigeria, important parameters associated with the disease dynamics are estimated. Using these estimated parameters, the basic reproduction number is calculated, future disease dynamics simulated, and the effect of the ability of individuals to resist malaria infection explored. The results indicate that the possibility of eradicating malaria infection is largely dependent on the ability of individuals to resist malaria infection.

Keywords: Malaria dynamics, stability analyses, bifurcation analysis, basic reproduction number, model fitting, sensitivity analysis.

1. Introduction

Malaria is an ancient parasitic disease of humans caused by a protozoan of the genus *Plasmodium* and it is transmitted through the bite of infected female Anopheles mosquitoes. The four species of *Plasmodium* parasite that infect humans are *Plasmodium falciparum, Plasmodium vivax, Plasmodium malariae*, and *Plasmodium ovale*. Of the four the *Plasmodium* species *P. falciparum* and *P. vivax* are the most deadly [25]. The dominant and the deadliest species of this parasite in Africa as a whole is *P. falciparum*. However, outside of the the sub-Saharan region the dominant species is *Plasmodium vivax* [25, 8]. Approximately 228 million cases were reported and 405,000 deaths globally in 2018, of which 94% were from Africa [26].

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Clinical signs of the disease are headache, chills, and fever. Malaria has considerable adverse effects on the health burden, the economy, and social well-being for the African continent. Infected people are less able to produce wealth, and therefore malaria can increase poverty. Furthermore, there is often a negative feedback effect. For example, malaria-endemic countries have low national economic growth which then reduces malaria control [27, 28].

There is strong evidence that when an animal population is repeatedly exposed to an infectious disease that causes considerable mortality, the progeny of the surviving animals develop an increased resistance to the disease over the course of several generations [29]. This is a procedure for choosing animals with genetic resistance. However, the genetic mechanisms influencing disease resistance are typically complicated and rely on a wide range of genes that regulate antibody formation and other responses. In the case of malaria in humans, the sickle-cell gene (α and β-globin) and the glucose-phosphate dehydrogenase-deficiency gene are known to confer significant host genetic resistance. There is also strong circumstantial evidence that the same is true of other abnormal hemoglobin genes. Patients with severe malaria who have Hb S have less hemolysis and have lower amounts of free hemoglobin [29]. In modern times resistance to malaria can be bolstered through appropriate immunization or vaccination. In what follows resistance to malaria will refer to either or both natural or induced processes.

Mathematical modelling plays an essential role in malaria control programmes. Many researchers have worked on mathematical models describing the features involved in the transmission of malaria. For example see [6, 10, 11, 5, 8, 17]. However, there are less models on malaria that incorporate changes in the individual's ability to resist malaria infection and these are needed for an improved understanding and thus better management of epidemics. To this end, this study presents a deterministic model for monitoring the transmission dynamics for malaria in the presence of the ability of humans to resist malaria. The main objective is to analyse the epidemiological impacts of building resistance to malaria and how this impact is influenced by the disease evolution. Further, the study presents a rigorous analysis of the resulting model. For this two realistic assumptions which have not been considered in the previous models found in the literature are introduced and are given by

(i) Classes S_r and I_r represent individuals that have a high resistance to malaria infections. Individuals in these classes do not easily get infected when exposed to the disease. They include genetically resistant humans.

(ii) Classes S_s and I_s denote individuals that have a low resistance to malaria infections. These individuals

are more easily infected if exposed to the disease.

The rest of this paper is organized as follows: Section 2 is devoted to model development. Theoretical results are presented in section 3. Numerical experiments are conducted in section 4. A discussion is presented in section 5.

2. Model Development

The detail formulation of the proposed mathematical model that takes into consideration humans resistance to malaria infection is presented in this section. Let N_h and N_v represent the total population of humans and mosquitoes at time t, respectively. Since our interest is on human resistant to malaria disease, new variables that represents population of humans with high or low resistance to malaria are incorporated into the proposed model. The total human population N_h is sub-divided into mutually-exclusive population compartments, which differ according to infection type (high resistance including genetically resistant or low resistant individuals who are referred to as sensitive to malaria) as follows: susceptible humans that have high resistance to malaria, S_r, susceptible humans that have low resistance (sensitive) to malaria, S_s, infected humans that have high resistance to malaria, I_r, infected humans that are sensitive to malaria, I_s, recovered or immune humans , R. The total population of mosquitoes is partition into susceptible mosquito, X and infected mosquito Y. Thus, $N_h = S_r + S_s + I_r + I_s + R$ and $N_v = X + Y$.

Susceptible humans with a high resistance to malaria S_r and susceptible humans with a low resistance (sensitive) to malaria S_s each have a total influx of $\rho\mu N_h$ and $(1-\rho)\mu N_h$, respectively, where ρ denotes the fraction of humans that have a high resistance to malaria and μ represents the natural birth/mortality rate of humans. Susceptible humans (S_r and S_s) contract the disease through the bite of infected mosquitoes at rates β_r and β_s, respectively. Humans with high resistance are placed in a high resistance class and these can move to a low resistance class as their capacity to resist malaria deteriorates or vice versa. This is taken into consideration using the parameters δ_{rs}, δ_{sr}, l_{rs}, l_{sr} which each denote the rate of change between classes; I_r to I_s and S_r to S_s, as resistance deteriorates, I_s to I_r and S_s to S_r, as resistance improves. Infected individuals I_r and I_s recover at a rate γ_r and γ_s, respectively. The recovered individuals can becomes susceptible as the immune systems wanes at a rate ω.

The mosquitoes population has a total influx of ηN_v, where η denoted the natural birth/death of mosquitoes. Susceptible mosquitoes X become infected at a rate α_r after biting an infected human with resistant I_r or α_s after biting an infected human without resistant I_s. The number of female Anopheles mosquitoes per human

host is denoted by m. The reduction of the infection rate due to the use of a mosquito nets is denoted by c. Based on these assumptions and formulations, (1) is the resulting system of differential equations (ODEs) consistuting our model. A schematic diagram depicting this malaria model is presented in Figure 1. Tables 1 and 2 summarize and define the variables and parameters that are used.

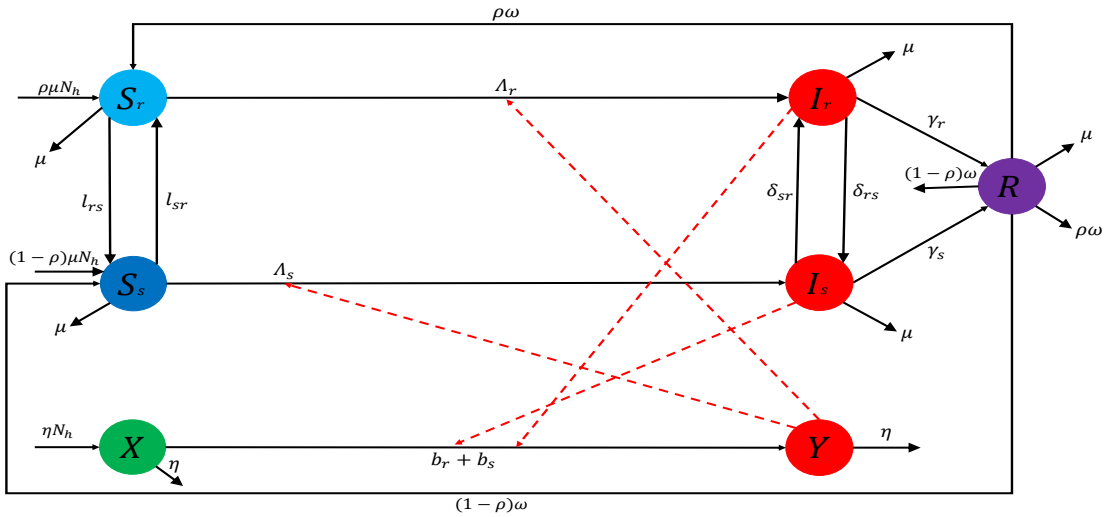

Figure 1: Schematic diagram depicting the malaria model. The model describe the transmission dynamics of malaria that incorporate new variables of human resistance. The bottom row represents mosquitoes compartments divided into Susceptible and Infected.

$$
\begin{aligned}
\frac{dS_r(t)}{dt} &= \rho\mu N_h(t) - \frac{(1-c)m\beta_r S_r(t)Y(t)}{N_v(t)} - \mu S_r(t) + l_{sr}S_s(t) - l_{rs}S_r(t) + \rho\omega R(t),\\
\frac{dS_s(t)}{dt} &= (1-\rho)\mu N_h(t) - \frac{(1-c)m\beta_s S_s(t)Y(t)}{N_v(t)} - \mu S_s(t) + l_{rs}S_r(t) - l_{sr}S_s(t) + (1-\rho)\omega R(t),\\
\frac{dI_r(t)}{dt} &= \frac{(1-c)m\beta_r S_r(t)Y(t)}{N_h(t)} - (\gamma_r+\mu)I_r(t) + \delta_{sr}I_s(t) - \delta_{rs}I_r(t),\\
\frac{dI_s(t)}{dt} &= \frac{(1-c)m\beta_s S_s(t)Y(t)}{N_h(t)} - (\gamma_s+\mu)I_s(t) + \delta_{rs}I_r(t) - \delta_{sr}I_s(t),\\
\frac{dR(t)}{dt} &= \gamma_r I_r(t) + \gamma_s I_s(t) - (\omega+\mu)R(t),\\
\frac{dX(t)}{dt} &= \eta N_v(t) - \frac{(1-c)\alpha_r X(t)I_r(t)}{N_h(t)} - \frac{(1-c)\alpha_s X(t)I_s(t)}{N_h(t)} - \eta X(t),\\
\frac{dY(t)}{dt} &= \frac{(1-c)\alpha_r X(t)I_r(t)}{N_h(t)} + \frac{(1-c)\alpha_s X(t)I_s(t)}{N_h(t)} - \eta Y(t).
\end{aligned}
\tag{1}
$$

The meaning of variables and parameters of model (1) can be found in Tables 1 and

Table 1: Variables for model (1)

Variables	Meaning
$N_h(t)$	Total human population at time t
$S_r(t)$	Population of susceptible humans that are resistant to malaria at time t
$S_s(t)$	Population of susceptible humans that are non-resistant (sensitive) to malaria at time t
$I_r(t)$	Population of infected humans that are resistant to malaria at time t
$I_s(t)$	Population of infected humans that are sensitive to malaria at time t
$R(t)$	Population of recovered/immune humans at time t at time t
$N_v(t)$	Total female anopheles mosquito population at time t
$X(t)$	Susceptible female anopheles mosquitoes at time t
$Y(t)$	Population of infected female anopheles mosquitoes at time t

Table 2: Parameters for model (1)

Variables	Meaning	Unit
β_r	Infection rate from mosquitoes to resistant human	day^{-1}
β_s	Infection rate from mosquitoes to sensitive human	day^{-1}
α_r	Infection rate from $I_r(t)$ to mosquitoes	day^{-1}
α_s	Infection rate from $I_s(t)$ to mosquito	day^{-1}
μ	Natural birth/mortality rate of humans	day^{-1}
ρ	Fraction of humans that are resistant to malaria	Dimensionless
c	Reduction of infection rate due to use of mosquito nets	Dimensionless
γ_r	Recovery rate of $I_r(t)$	day^{-1}
γ_s	Recovery rate of $I_s(t)$	day^{-1}
ω	Wanning immunity rate of $R(t)$	day^{-1}
η	Natural birth/death rate of mosquitoes	day^{-1}
l_{sr}	Rate of change from $S_s(t)$ to $S_r(t)$ as the capacity for individuals to resist malaria improves	day^{-1}
l_{rs}	Rate of change from $S_r(t)$ to $S_s(t)$ as the capacity for individuals to resist malaria deteriorate	day^{-1}
δ_{sr}	Rate of change from $I_s(t)$ to $I_r(t)$ as the capacity for individuals to resist malaria improves	day^{-1}
δ_{rs}	Rate of change from $I_r(t)$ to $I_s(t)$ as the capacity for individuals to resist malaria deteriorate	day^{-1}

3. Model Analysis

3.1. Transformation of the ODEs

Since humans and mosquitoes have different measurement units, a model with dimensionless variables is required. To non-dimensionalize the model (1), we scale the variables using the total population of either humans or mosquitoes where appropriate: $s_r(t) = \frac{S_r(t)}{N_h(t)}$, $s_s(t) = \frac{S_s(t)}{N_h(t)}$, $i_r(t) = \frac{I_r(t)}{N_h(t)}$, $i_s(t) = \frac{I_s(t)}{N_h(t)}$, $r(t) = \frac{R(t)}{N_h(t)}$, $x(t) = \frac{X(t)}{N_v(t)}$, $y(t) = \frac{Y(t)}{N_v(t)}$, with $m = \frac{N_v(t)}{N_h(t)}$ a constant. The parameter m denotes the number of female Anopheles mosquitoes per human host. Using these scaled variables the dimensionless version of model (1) becomes

$$
\begin{aligned}
\frac{ds_r(t)}{dt} &= \rho\mu - (1-c)m\beta_r s_r(t)y(t) - \mu s_r(t) + l_{sr}s_s(t) - l_{rs}s_r(t) + \rho\omega r(t),\\
\frac{ds_s(t)}{dt} &= (1-\rho)\mu - (1-c)m\beta_s s_s(t)y(t) - \mu s_s(t) + l_{rs}s_r(t) - l_{sr}s_s(t) + (1-\rho)\omega r(t),\\
\frac{di_r(t)}{dt} &= (1-c)m\beta_r s_r(t)y(t) - (\gamma_r+\mu)i_r(t) + \delta_{sr}i_s(t) - \delta_{rs}i_r(t),\\
\frac{di_s(t)}{dt} &= (1-c)m\beta_s s_s(t)y(t) - (\gamma_s+\mu)i_s(t) + \delta_{rs}i_r(t) - \delta_{sr}i_s(t),\\
\frac{dr(t)}{dt} &= \gamma_r i_r(t) + \gamma_s i_s(t) - (\omega+\mu)r(t),\\
\frac{dx(t)}{dt} &= \eta - (1-c)\alpha_r x(t)i_r(t) - (1-c)\alpha_s x(t)i_s(t) - \eta x(t),\\
\frac{dy(t)}{dt} &= (1-c)\alpha_r X(t)i_r(t) + (1-c)\alpha_s x(t)i_s(t) - \eta y(t).
\end{aligned} \tag{2}
$$

For the analyses of model (2), the following simplifications are made $\Lambda_r = (1-c)m\beta_r,\ \Lambda_s = (1-c)m\beta_s,\ k_r = \gamma_r+\mu+\delta_{rs},\ k_s = \gamma_r+\mu+\delta_{sr},\ b_r = (1-c)\alpha_r,\ b_s = (1-c)\alpha_s,\ \nu = \omega+\mu,\ \theta_r = \rho\mu, \theta_s = (1-\rho)\mu, \phi_r = \rho\omega,\ \phi_s = (1-\rho)\omega,\ \psi = l_{sr}+l_{rs},\ h_r = \gamma_r+\mu,\ h_s = \gamma_s+\mu.$

3.2. Malaria-free equilibrium

Solving the above equations (2) by setting the first derivatives and all the disease classes (i_r, i_s, r, y) to zero, and using the fact that $s_r^0 + s_s^0 = 1$, the malaria free equilibrium (MFE) ε^0 is obtained as

$$
\varepsilon^0 = (s_r^0, s_s^0, i_r^0, i_s^0, r^0, x^0, y^0) = \Big(\frac{\mu\rho + l_{sr}}{\mu + l_{rs} + l_{sr}}, \frac{l_{rs} + \mu(1-\rho)}{\mu + l_{rs} + l_{sr}}, 0, 0, 0, 1, 0\Big). \tag{3}
$$

3.3. Basic reproduction number

The basic reproduction number is calculated by using the next generation matrix method [30]. There are three compartments carrying the infection, i_r, i_s, y and we will keep them in this order. The rate of new infections is given by

$$
\mathcal{F} = [(1-c)m\beta_r s_r(t)y(t), (1-c)m\beta_s s_s(t)y(t), (1-c)\alpha_r x(t)i_r(t) + (1-c)\alpha_s x(t)i_s(t)]^T. \tag{4}
$$

By differentiating $\mathcal{F}$ at the malaria-free equilibrium (ε^0) we obtain

$$
F = \begin{pmatrix} 0 & 0 & (1-c)m\beta_r s_r^0 \\ 0 & 0 & (1-c)m\beta_s s_s^0 \\ (1-c)\alpha_r x^0 & (1-c)\alpha_s x^0 & 0 \end{pmatrix}. \tag{5}
$$

The other transmissions in the system are given by

$$\mathcal{V} = [(\gamma_r + \mu)i_r - \delta_{sr}i_s + \delta_{rs}i_r, (\gamma_s + \mu)i_s - \delta_{rs}i_r + \delta_{sr}i_s, \eta y]^T. \tag{6}$$

Differentiating $\mathcal{V}$ at the malaria-free equilibrium (ε^0) gives

$$V = \begin{pmatrix} (\gamma_r + \mu) + \delta_{rs} & -\delta_{sr} & 0 \\ -\delta_{rs} & (\gamma_r + \mu) + \delta_{sr} & 0 \\ 0 & 0 & \eta \end{pmatrix} = \begin{pmatrix} k_r & -\delta_{sr} & 0 \\ -\delta_{rs} & k_s & 0 \\ 0 & 0 & \eta \end{pmatrix}. \tag{7}$$

Thus,

$$V^{-1} = \begin{pmatrix} \frac{k_s}{h_r h_s + h_r\delta_{sr} + h_s\delta_{rs}} & \frac{\delta_{sr}}{h_r h_s + h_r\delta_{sr} + h_s\delta_{rs}} & 0 \\ \frac{\delta_{rs}}{h_r h_s + h_r\delta_{sr} + h_s\delta_{rs}} & \frac{k_r}{h_r h_s + h_r\delta_{sr} + h_s\delta_{rs}} & 0 \\ 0 & 0 & \frac{1}{\eta} \end{pmatrix} \tag{8}$$

and

$$FV^{-1} = \begin{pmatrix} 0 & 0 & \frac{(1-c)m\beta_r s_r^0}{\eta} \\ 0 & 0 & \frac{(1-c)m\beta_s s_s^0}{\eta} \\ \frac{(1-c)\alpha_r k_s + (1-c)\alpha_s\delta_{rs}}{h_r h_s + h_r\delta_{sr} + h_s\delta_{rs}} & \frac{(1-c)\alpha_r\delta_{sr} + (1-c)\alpha_s k_r}{h_r h_s + h_r\delta_{sr} + h_s\delta_{rs}} & 0 \end{pmatrix}. \tag{9}$$

Therefore, the basic reproduction number $\mathcal{R}_0$ which is the dominant positive eigenvalue of FV^{-1} is

$$\mathcal{R}_0 = \sqrt{\mathcal{R}_0^r + \mathcal{R}_0^s}, \tag{10}$$

where,

$$\mathcal{R}_0^r = \frac{(1-c)^2 m\beta_r s_r^0 (\alpha_r k_s + \alpha_s\delta_{rs})}{\eta (h_r h_s + h_r\delta_{sr} + h_s\delta_{rs})}$$

and

$$\mathcal{R}_0^s = \frac{(1-c)^2 m\beta_s s_s^0 (\alpha_r\delta_{sr} + \alpha_s k_r)}{\eta (h_r h_s + h_r\delta_{sr} + h_s\delta_{rs})}.$$

The quantity $\mathcal{R}_0^r$ can be regarded as the basic reproduction number associated with individuals that have high resistance to malaria while quantity $\mathcal{R}_0^s$ can be regarded as the basic reproduction number associated with individuals that have low resistance to malaria. Both quantities play crucial role on the exact value of the basic reproduction number $\mathcal{R}_0$ as shown in equation (10).

3.4. Local stability of malaria-free equilibrium

The local stability of model (2) about the malaria-free equilibrium is summarized in the theorem below.

Theorem 3.1. *Malaria-free equilibrium, ε^0 is locally asymptotically stable whenever $\mathcal{R}_0 < 1$ and unstable otherwise.*

Proof. The Jacobian matrix of the system (2) evaluated at the malaria-free equilibrium ε^0, is obtained as

$$J(\varepsilon^0) = \begin{pmatrix} -k_1 & l_{sr} & 0 & 0 & \rho\omega & 0 & -(1-c)m\beta_r s_r^0 \\ l_{rs} & -k_2 & 0 & 0 & (1-\rho)\omega & 0 & -(1-c)m\beta_s s_s^0 \\ 0 & 0 & -k_3 & \delta_{sr} & 0 & 0 & (1-c)m\beta_r s_r^0 \\ 0 & 0 & \delta_{rs} & -k_4 & 0 & 0 & (1-c)m\beta_s s_s^0 \\ 0 & 0 & \gamma_r & \gamma_s & -k_5 & 0 & 0 \\ 0 & 0 & -(1-c)\alpha_r & -(1-c)\alpha_s & 0 & -\eta & 0 \\ 0 & 0 & (1-c)\alpha_r & (1-c)\alpha_s & 0 & 0 & -\eta \end{pmatrix}$$

where, $k_1 = \mu + l_{rs}$, $k_2 = \mu + l_{sr}$, $k_3 = \gamma_r + \mu + \delta_{rs}$, $k_4 = \gamma_s + \mu + \delta_{sr}$, $k_5 = \omega + \mu$.
Now, we demonstrate that $J(\varepsilon^0)$ has its all eigenvalues to be negative. Obviously the sixth columns have only the diagonal terms which form the one negative eigenvalues, η, the other six eigenvalues can be obtained from the sub-matrix, $J_1(\varepsilon^0)$, formed by excluding the sixth rows and columns of $J(\varepsilon^0)$.

$$J_1(\varepsilon^0) = \begin{pmatrix} -k_1 & l_{sr} & 0 & 0 & \rho\omega & -(1-c)m\beta_r s_r^0 \\ l_{rs} & -k_2 & 0 & 0 & (1-\rho)\omega & -(1-c)m\beta_s s_s^0 \\ 0 & 0 & -k_3 & \delta_{sr} & 0 & (1-c)m\beta_r s_r^0 \\ 0 & 0 & \delta_{rs} & -k_4 & 0 & (1-c)m\beta_s s_s^0 \\ 0 & 0 & \gamma_r & \gamma_s & -k_5 & 0 \\ 0 & 0 & (1-c)\alpha_r & (1-c)\alpha_s & 0 & -\eta \end{pmatrix}$$

Clearly, the first and second column have the diagonal term which form another two negative eigenvalues, $\mu + l_{rs}$ and $\mu + l_{sr}$, the other four eigenvalues can be obtained from the sub-matrix, $J_2(\varepsilon^0)$, formed by excluding the first and second rows and columns of $J_1(\varepsilon^0)$.

$$J_2(\varepsilon^0) = \begin{pmatrix} -k_3 & \delta_{sr} & 0 & (1-c)m\beta_r s_r^0 \\ \delta_{rs} & -k_4 & 0 & (1-c)m\beta_s s_s^0 \\ \gamma_r & \gamma_s & -k_5 & 0 \\ (1-c)\alpha_r & (1-c)\alpha_s & 0 & -\eta \end{pmatrix}$$

Finally, one sees that the third column have the diagonal term which form another negative eigenvalue, $\omega + \mu$, the other four eigenvalues can be obtained from the sub-matrix, $J_3(\varepsilon^0)$, formed by excluding the third

rows and columns of $J_2(\varepsilon^0)$.

$$J_3(\varepsilon^0) = \begin{pmatrix} -k_3 & \delta_{sr} & (1-c)m\beta_r s_r^0 \\ \delta_{rs} & -k_4 & (1-c)m\beta_s s_s^0 \\ (1-c)\alpha_r & (1-c)\alpha_s & -\eta \end{pmatrix}.$$

The eigenvalues of the matrix $J_3(\varepsilon^0)$ are the roots of the characteristic equation

$$A_3\lambda^3 + A_2\lambda^2 + A_1\lambda + A_0 \tag{11}$$

where,

$$\begin{aligned} A_3 &= 1 \\ A_2 &= \eta + (\gamma_s + \mu + \delta_{sr}) + (\gamma_r + \mu + \delta_{rs}) \\ A_1 &= \delta_{rs}(\gamma_s + \mu + \delta_{sr} + \eta)\mathcal{R}_0^r + \eta(\gamma_r + \mu + \delta_{rs})\delta_{sr}(1 - \mathcal{R}_0) \\ A_0 &= \eta(\gamma_s + \mu + \delta_{sr}) + \delta_{rs}\delta_{sr}\mathcal{R}_0^s + \eta\delta_{rs}\delta_{sr}(1 - \mathcal{R}_0) \end{aligned}$$

Now, we show that the coefficients A_0, A_1, A_2 and A_3 satisfy the Routh-Hurwitz criterion [31]. Clearly, one sees that A_2 and A_3 are positive. Furthermore, A_0 and A_1 are positive whenever the associated basic reproduction number, $\mathcal{R}_0$ is less than unity (i.e., $\mathcal{R}_0 < 1$). □

The implication of this result is that malaria disease can be eliminated whenever $\mathcal{R}_0 < 1$ provided that the initial infected populations is within the neighbourhood of the malaria free equilibrium otherwise the disease persists in the community.

3.5. Existence of endemic equilibrium

Here, we establish the existence of endemic equilibrium in terms of i_s^* and i_r^*. The endemic equilibrium of the model (2) exists and is given by

$$\begin{aligned} x^* &= \frac{\eta}{b_r i_r^* + b_s i_s^* + \eta} \\ y^* &= \frac{b_r + i_r^* + b_s i_s^*}{b_r + i_r^* + b_s i_s^* + \eta} \\ r^* &= \frac{\gamma_r i_r^* + \gamma_s i_s^*}{\omega + \mu} \\ s_r^* &= \frac{\rho\mu + l_{sr} s_s^* + \Phi^*}{\Lambda_r y^* + \mu + l_{rs}} \\ s_s^* &= \frac{\Psi^*(\Lambda y^* + \mu + l_{rs})}{\Lambda y^* + \mu} + \frac{l_{rs}(\rho\mu + \Phi^*)(\Lambda y^* + \mu + l_{rs})}{(\Lambda y^* + \mu + l_{rs})(\Lambda y^* + \mu)} \end{aligned}$$

where,

$$\left.\begin{aligned} i_r^* &= \tfrac{\Lambda_r s_r^* y^* + \delta_{sr} i_s^*}{(\gamma_s+\mu)+\delta_{rs}}, \\ i_s^* &= \tfrac{\eta\mu\rho\omega(1-\rho)\omega(\mu+\omega)(\mathcal{R}_0^2-1)}{\ell} \end{aligned}\right\} \tag{12}$$

and

$$\ell = (\mu+\omega)[(1-c)m\beta_r\rho\mu\mathcal{R}_0^s + (1-c)m\alpha_r(\eta+\eta\rho\mu\mathcal{R}_0^r)] - \mu\eta\rho\omega(1-\rho)\omega\mathcal{R}_0^2,$$

$\Phi^* = \frac{\rho\omega(\gamma_r i_r^* + \gamma_s i_s^*)}{\omega+\mu}$ and $\Psi^* = \frac{(1-\rho)\omega(\gamma_r i_r^* + \gamma_s i_s^*)}{\omega+\mu}$.

Clearly in (12), no positive solution (endemic equilibrium) exists when $\mathcal{R}_0 < 1$ and $\ell > 0$. Whereas, when $\ell > 0$, a unique endemic equilibrium exists when $\mathcal{R}_0 > 1$. It is noteworthy that positive solutions exist for the model (12) if $\ell < 0$ and $\mathcal{R}_0 < 1$. This implies that the disease-free equilibrium coexists with the endemic equilibrium state when $\mathcal{R}_0$ crosses unity, which suggest that the model undergoes a backward bifurcation at this point. To confirm this possibility, a bifurcation analysis of the model is conducted in the next section.

3.6. Bifurcation analysis

The potential of the model (2) equilibria coexisting as $\mathcal{R}_0$ crosses unity (i.e backward bifurcation) is analysed in this section. To achieve this, the Center Manifold Theory [32], which has been employed in several epidemic models [33, 34, 35] is considered in the bifurcation analysis as follows.

Let's write the malaria model (2) in vector $\frac{dX}{dt} = Q(X)$, where $X = (x_1, x_2, x_3, x_4, x_5, x_6, x_7)^T$ and $Q = (q_1, q_2, q_3, q_4, q_5, q_6, q_7)^T$ so that $s_r = x_1$, $s_s = x_2$, $i_r = x_3$, $i_s = x_4$, $r = x_5$, $x = x_6$, $y = x_7$. Then the malaria model (2) becomes

$$\begin{aligned}
\frac{dx_1(t)}{dt} &= \rho\mu - (1-c)m\beta_r x_1(t)x_7(t) - \mu x_1(t) + l_{sr}x_2(t) - l_{rs}x_1(t) + \rho\omega x_5(t) := q_1, \\
\frac{dx_2(t)}{dt} &= (1-\rho)\mu - (1-c)m\beta_s x_2(t)x_7(t) - \mu x_2(t) + l_{rs}x_1(t) - l_{sr}x_2(t) + (1-\rho)\omega x_5(t) := q_2, \\
\frac{dx_3(t)}{dt} &= (1-c)m\beta_r x_1(t)x_7(t) - (\gamma_r+\mu)x_3(t) + \delta_{sr}x_4(t) - \delta_{rs}x_3(t) := q_3, \\
\frac{dx_4(t)}{dt} &= (1-c)m\beta_s x_2(t)x_7(t) - (\gamma_s+\mu)x_4(t) + \delta_{rs}x_3(t) - \delta_{sr}x_4(t) := q_4, \\
\frac{dx_5(t)}{dt} &= \gamma_r x_3(t) + \gamma_s x_4(t) - (\omega+\mu)x_5(t) := q_5, \\
\frac{dx_6(t)}{dt} &= \eta - (1-c)\alpha_r x_6(t)x_3(t) - (1-c)\alpha_s x_6(t)x_4(t) - \eta x_6(t) := q_6, \\
\frac{dx_7(t)}{dt} &= (1-c)\alpha_r x_6(t)x_3(t) + (1-c)\alpha_s x_6(t)x_4(t) - \eta x_7(t) := q_7.
\end{aligned} \tag{13}$$

Let us choose the bifurcation parameter β_s^* so that at $\mathcal{R}_0 = 1$ in (10), we get

$$\beta_s^* = \frac{\eta(h_r h_s + h_r\delta_{sr} + h_s\delta_{rs}) - (1-c)^2 m\beta_r s_r^0(\alpha_r k_s + \alpha_s\delta_{rs})}{(1-c)^2 m s_s^0(\alpha_r\delta_{sr} + \alpha_s k_r)}. \tag{14}$$

The transformed (linearized) matrix of model (2) assessed at β_s^* near the disease-free equilibrium ε^0 is provided as

$$J(\varepsilon^0, \beta_s^*) = \begin{pmatrix} -k_1 & l_{sr} & 0 & 0 & \rho\omega & 0 & -A \\ l_{rs} & -k_2 & 0 & 0 & (1-\rho)\omega & 0 & -B \\ 0 & 0 & -k_3 & \delta_{sr} & 0 & 0 & A \\ 0 & 0 & \delta_{rs} & -k_4 & 0 & 0 & B \\ 0 & 0 & \gamma_r & \gamma_s & -k_5 & 0 & 0 \\ 0 & 0 & -E & -P & 0 & -\eta & 0 \\ 0 & 0 & E & P & 0 & 0 & -\eta \end{pmatrix}$$

where, $A = (1-c)m\beta_r s_r^0$, $B = (1-c)m\beta_s^* s_s^0$, $E = (1-c)\alpha_r$, $P = (1-c)\alpha_s$.

The roots of the characteristic equation are the eigenvalues of $J(\varepsilon^0, \beta_s^*)$ and it is given as

$$K_3\lambda^3 + K_2\lambda^2 + K_1\lambda + K_0. \tag{15}$$

Equation (15) is a three-degree polynomial with all having negative roots except one zero eigenvalue. Let $w = (w^1; w^2; w^3; w^4; w^5; w^6; w^7)^T$ indicate the right eigenvector corresponding to this simple zero eigenvalue, such that $J(\varepsilon^0, \beta_s^*) = 0$. Then there's

$$\left.\begin{array}{rcl} w_1 &=& \frac{l_{sr}P\omega w_4[\gamma_r(\eta\delta_{sr}+AP)+\gamma_s(\eta-AE)]}{(k_1-l_{sr})k_1^2k_5(\eta-AE)} - \sigma_1 + \sigma_2 - \sigma_3 + \sigma_4 - \sigma_5, \\ w_2 &=& \frac{k_1P\omega w_4[\gamma_r(\eta\delta_{sr}+AP)+\gamma_s(\eta-AE)]}{(k_1-l_{sr})k_1k_5(\eta-AE)} - \vartheta_1 + \vartheta_2 - \vartheta_3, \\ w_3 &=& \frac{w_4(\eta\delta_{sr}+AP)}{\eta-AE}, \\ w_4 &=& \frac{\eta(\eta-AE)}{P(\eta-AE)+E(\eta\delta_{sr}+AP)}, \\ w_5 &=& \frac{w_4[\gamma_r(\eta\delta_{sr}+AP)+\gamma_s(\eta-AE)]}{k_5(\eta-AE)} \\ w_6 &=& -w_7, \\ w_7 &=& \frac{w_4(E(\eta\delta_{sr}+AP)+P(\eta-AE))}{\eta(\eta-AE)} \end{array}\right\} \tag{16}$$

where, $\sigma_1 = \frac{l_{sr}k_1Aw_4[E(\eta\delta_{sr}+AP)+P(\eta-AE)]}{(k_1-l_{sr})k_1^2k_5(\eta-AE)}$, $\sigma_2 = \frac{(1-\rho)\omega l_{sr}w_4[\gamma_r(\eta\delta_{sr}+AP)+\gamma_s(\eta-AE)]}{(k_1-l_{sr})k_1^2k_5(\eta-AE)}$,
$\sigma_3 = \frac{l_{sr}k_1BEw_4[(\eta\delta_{sr}+AP)+P(\eta-AE)]}{(k_1-l_{sr})k_2\eta(\eta-AE)}$, $\sigma_4 = \frac{P\omega w_4[\gamma_r\gamma_r(\eta\delta_{sr}+AP)+\gamma_s(\eta-AE)]}{k_1k_5(\eta-AE)}$, $\sigma_5 = \frac{Aw_4[E(\eta\delta_{sr}+AP)+P(\eta-AE)]}{k_1\eta(\eta-AE)}$,
$\vartheta_1 = \frac{k_1Aw_4[E(\eta\delta_{sr}+AP)+P(\eta-AE)]}{(k_1-l_{sr})k_1k_5(\eta-AE)}$, $\vartheta_2 = \frac{(1-\rho)\omega w_4[\gamma_r(\eta\delta_{sr}+AP)+\gamma_s(\eta-AE)]}{(k_1-l_{sr})k_2k_5(\eta-AE)}$, $\vartheta_3 = \frac{k_1BEw_4[(\eta\delta_{sr}+AP)+P(\eta-AE)]}{(k_1-l_{sr})k_2\eta(\eta-AE)}$.

Furthermore, the left eigenvector, $v = (v_1, v_2, ..., v_7)$, which corresponds to the simple zero eigenvalue of

$J(\varepsilon^0, \beta_s^*)$, is calculated as

$$\left.\begin{aligned} v_1 &= 0, \\ v_2 &= 0, \\ v_3 &= \tfrac{(1-c)\alpha_r l_{sr}}{\gamma_r+\mu+\delta_{rs}}, \\ v_4 &= \tfrac{(1-c)\alpha_s l_{rs}}{\gamma_s+\mu+\delta_{sr}}, \\ v_5 &= 0, \\ v_6 &= 0, \\ v_7 &= -\eta(\gamma_r+\mu+\delta_{rs})(\gamma_s+\mu+\delta_{sr}) \end{aligned}\right\} \tag{17}$$

Clearly from (13), one sees that all of the second-order partial derivatives at ε^0 and β_s^* are zero, except for the following:

$$\frac{\partial^2 q_1}{\partial x_1 \partial x_7} = \frac{\partial^2 q_1}{\partial x_7 \partial x_1} = -(1-c)m\beta_r, \frac{\partial^2 q_2}{\partial x_2 \partial x_7} = \frac{\partial^2 q_2}{\partial x_7 \partial x_2} = -(1-c)m\beta_s^*, \frac{\partial^2 q_3}{\partial x_1 \partial x_7} = \frac{\partial^2 q_3}{\partial x_7 \partial x_1} = -(1-c)m\beta_r,$$
$$\frac{\partial^2 q_4}{\partial x_2 \partial x_7} = \frac{\partial^2 q_4}{\partial x_7 \partial x_2} = -(1-c)m\beta_s^*, \frac{\partial^2 q_6}{\partial x_3 \partial x_6} = \frac{\partial^2 q_6}{\partial x_6 \partial x_3} = -(1-c)\alpha_r, \frac{\partial^2 q_6}{\partial x_4 \partial x_6} = \frac{\partial^2 q_6}{\partial x_6 \partial x_4} = -(1-c)\alpha_s,$$
$$\frac{\partial^2 q_7}{\partial x_3 \partial x_6} = \frac{\partial^2 q_7}{\partial x_6 \partial x_3} = (1-c)\alpha_r, \frac{\partial^2 q_7}{\partial x_4 \partial x_6} = \frac{\partial^2 q_7}{\partial x_6 \partial x_4} = (1-c)\alpha_s$$

and

$$\frac{\partial^2 q_2}{\partial x_7 \partial \beta_s^*} = \frac{\partial^2 q_2}{\partial \beta_s^* \partial x_7} = -(1-c)ms_s^0, \frac{\partial^2 q_4}{\partial x_7 \partial \beta_s^*} = \frac{\partial^2 q_4}{\partial \beta_s^* \partial x_7} = (1-c)ms_s^0.$$

The signs of the bifurcation coefficients a and b, calculated from the partial derivatives provided above, define the type of the bifurcation at $\mathcal{R}_0 = 1$, given, respectively, by

$$a = \sum_{k,i,j=1}^{7} v_k w_i w_j \frac{\partial^2 qk}{\partial x_i \partial x_j}(\varepsilon^0, \beta_s^*) = 2v_7(1-c)w_4(\alpha_s+\alpha_r)\left(\frac{l_{sr}P\omega\gamma(\eta\delta_{sr}+AP)}{k_1^2 k_5}\right), \tag{18}$$

and

$$b = \sum_{k,i=1}^{7} v_k w_i \frac{\partial^2 qk}{\partial x_i \partial \beta_s}(\varepsilon^0, \beta_s^*) = \frac{2(1-c)\alpha_r v_7 w_4 + 2(1-c)\alpha_s v_7 w_4}{\eta(\gamma_r+\mu)(\gamma_s+\mu)}. \tag{19}$$

So, $a > 0$ and $b > 0$, the malaria model (2) undergoes a backward bifurcation as the threshold parameter $\mathcal{R}_0$ passes unity. This indicates the coexistence of disease-free and endemic equilibrium, as $\mathcal{R}_0$ slightly less than unity. As a consequence, we have arrived at the following result:

Theorem 3.2. *The malaria model (2) undergoes a backward bifurcation at $\mathcal{R}_0 = 1$.*

The preceding finding implies that lowering $\mathcal{R}_0$ below unity is essential but not sufficient to eliminate the disease. From equation (18), we observe that if $l_{sr} = 0$, then $a = 0$. This implies that if $l_{sr} = 0$, the

model will not undergo backward bifurcation at $\mathcal{R}_0 = 1$. Thus, l_{sr} is the parameter that causes the backward bifurcation. This is illustrated graphically in Figure 2. Therefore, the nature of the dynamics of model (2) especially when $\mathcal{R}_0 < 1$ is determined by the value of l_{sr}. Hence, changes in resistance to malaria l_{sr} should be taken into consideration while developing control measures that can eliminate the disease. This is illustrated numerically in Figure 2. Figure 2(a) show that model (2) undergoes backward bifurcation when for $l_{sr} \neq 0$. On the contrary, when $l_{sr} = 0$, the backward bifurcation disappears and the model undergoes a forward bifurcation. These results illustrate the importance of human resistance on the dynamics of malaria.

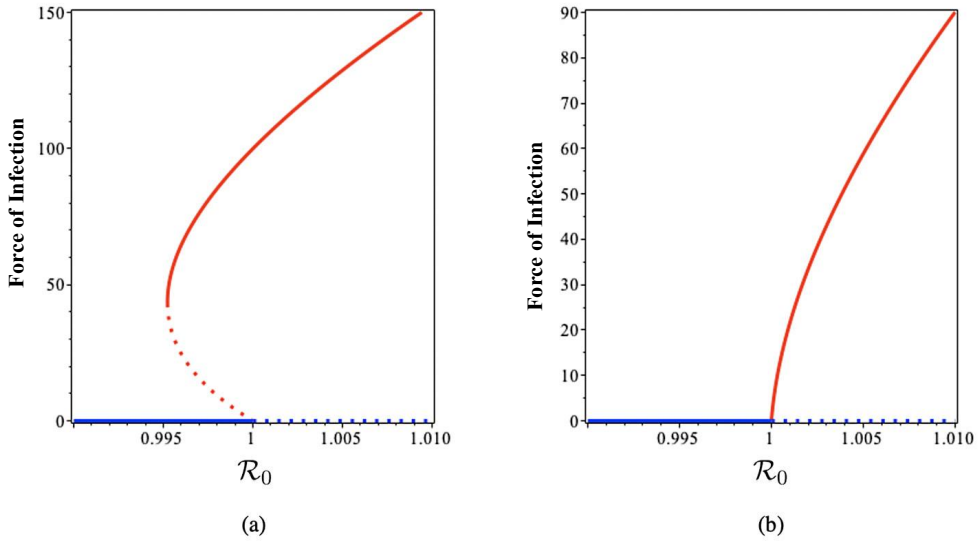

Figure 2: Bifurcation diagrams (a) Backward bifurcation (b) Forward bifurcation..

4. Numerical Simulations

In this section, numerical simulations are considered to explore the endemic dynamics of model (2) using a case study of malaria incidence in Nigeria.

4.1. Model fitting and parameter estimation

Malaria has been endemic in Nigeria for many years, so fitting the model (2) to malaria data will be helpful in making future predictions of the malaria disease dynamics. The incidence of malaria can be defined as the number of new cases of malaria per 1,000 of the population at risk in Nigeria. Incidence of malaria in Nigeria from 2000 to 2021 extracted from [24] is used in this study. Model (2) is fit and parameters representing changes in human resistance to malaria are estimated using the data for the incidence of malaria in Nigeria from 2000 to 2021. The other parameter values used for the numerical simulations together with their sources are given in Table 3.

Table 3: Parameter values used for the model simulations

Parameter	Unit	Value	Source
μ	day^{-1}	$\frac{1}{70*365}$	[19, 14]
m	dimensionless	variable	[22, 8]
β_r	day^{-1}	0.0044	[14, 3, 18, 16]
β_s	day^{-1}	0.0066	Estimated
ω	day^{-1}	0.005	[14, 1]
ρ	dimensionless	0.7	[22, 9]
γ_r	day^{-1}	0.00019	[22, 2]
γ_s	day^{-1}	0.0022	[22, 12]
α_r	day^{-1}	0.0044	[14, 3, 18, 16]
α_s	day^{-1}	0.0062	[22]
η	day^{-1}	$\frac{1}{15}$	[14, 16]

Model (2) is non-dimensionalized, therefore to fit the model to the data, the incidence is converted to fractions by dividing it by 1000. The irregular seasonal pattern in the data is taken into consideration by multiplying the transmission rates β_r and β_s by a seasonality factor $(1 + \cos(\frac{\pi t}{12}))$ [14, 8]. Parameter value units in Table 3 that are per day are converted to per year to match the time scale of the data. The parameters in Table 3 are fixed while the remaining parameters especially those that are associated with the changes in human resistance to malaria are estimated using the fitting algorithm.

The algorithm used is a built-in MATLAB least-squares fitting routine fmincon in the optimization tool box. Results of the model fitting given in Figure 3 shows that the model (2) is a reasonable fit for incidence of malaria in Nigeria from 2000 to 2021. Hence, the model is used further for predictions of malaria trends in Nigeria.

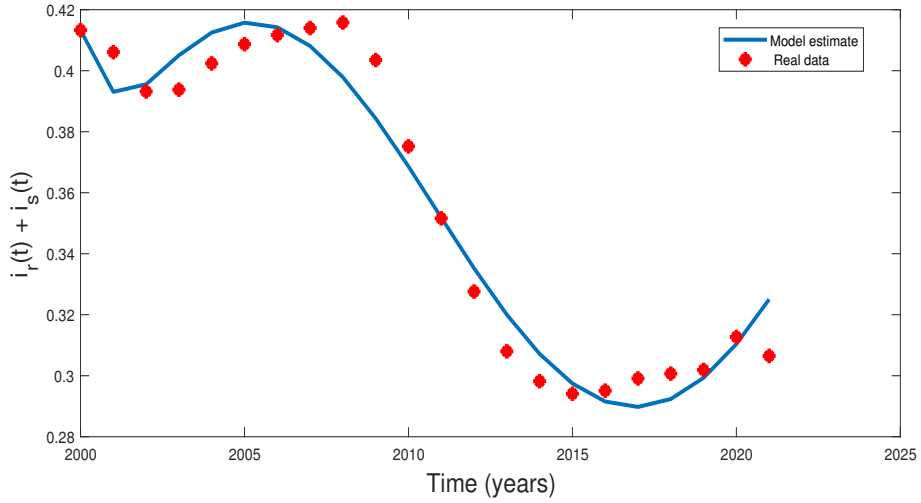

Figure 3: Model fit of the proportion of incidence of malaria per 1,000 population at risk in Nigeria from 2000 to 2021, where bold lines represent the model fit and stars mark the confirm cases.

The parameters values estimated from the model fit are: $c = 0.5978$, $\delta_{rs} = 0.0994$ day^{-1} , $\delta_{sr} = 0.0199$ day^{-1} , $l_{rs} = 0.0434$ day^{-1}, and $l_{sr} = 0.9145$ day^{-1}. Using these estimated parameters together with the parameters in Table 3, the basic reproduction number $\mathcal{R}_0$ is determined by substituting these parameter values into equation (10) to obtain $\mathcal{R}_0 = 1.0376$. This result shows that the probability is high that malaria will remain endemic in Nigeria because $\mathcal{R}_0 > 1$ indicates that a disease is endemic [21]. This results supports previous surveillance report findings that malaria is endemic in Nigeria [23, 8].

4.2. Model predictions

One of the advantages of an epidemiological model is that it can be used to predict the dynamics of the disease which is crucial for the management of the disease. Here model (2) is used together with the estimated parameters to predict further possible dynamics of malaria epidemic in Nigeria.

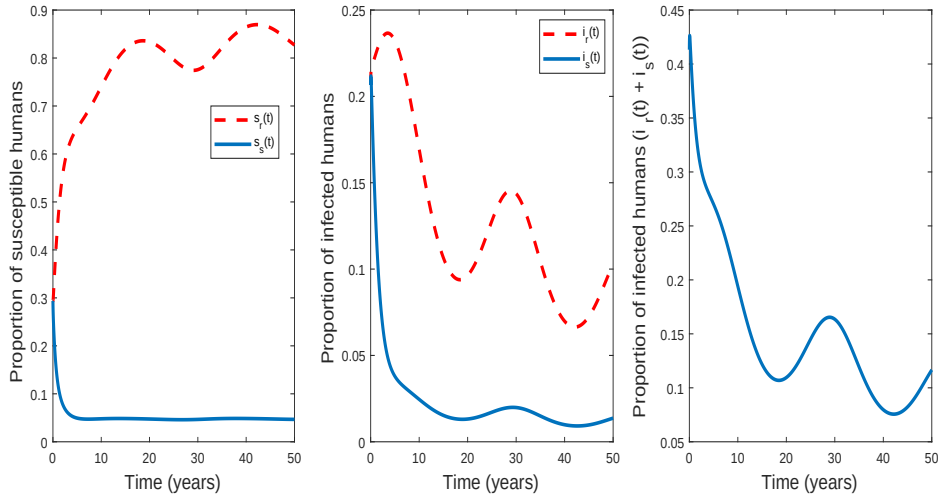

Figure 4: Plot showing a possible long term dynamics of malaria in Nigeria using the estimated parameter values.

The possible long-term dynamics of malaria in Nigeria is determined as shown in Figure 4. From the figure, it can be seen that incidence of malaria remain between 50 and 450 individuals per 1000 at risk of infection for the next three decades. Thus, unless more effective control measures are implemented, malaria is likely to remain endemic in Nigeria for many years. The figure also reveals that susceptible and infected individuals with a greater probability to resist malaria infection dominate. A possible explanation for this could be because many individuals are engaging several (medical) approaches to enhance their capability to resist the malaria infection together with individuals that are already genetically resistant to malaria.

4.3. Effects of changes in human resistance to malaria on the model dynamics

Increasing human resistance to malaria has been shown to result in a backward bifurcation according to our model formulation. In this section, numerical simulations are used to explore further the effects of changes in human resistance to malaria on model dynamics.

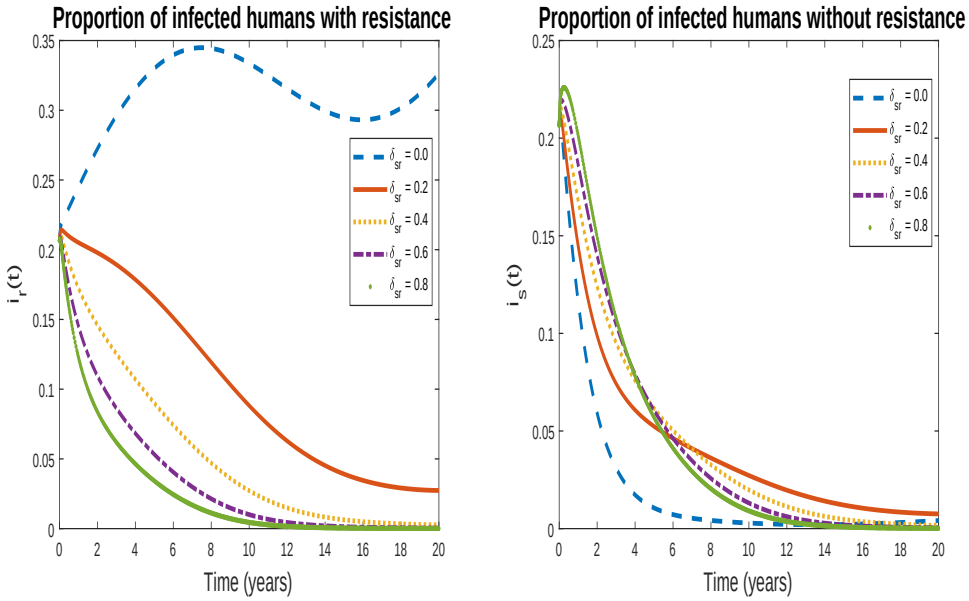

Figure 5: Plot showing the effects of changes in human resistance to malaria (δ_{sr}).

The changes in human resistance to malaria δ_{sr} which shifts individuals from from $I_s(t)$ to $I_r(t)$ as the capacity for individuals to resist malaria improves are shown in Figure 5. The figure shows that improving the capacity to resist malaria leads to a decrease in the number of infected individuals such that the disease is eliminated in the entire community. The entire population can be eliminated both individuals that are infected with high resistance and those with low resistance. Therefore, improving the capacities to resist malaria through vaccination etc are strongly recommended for eradication of malaria in endemic areas.

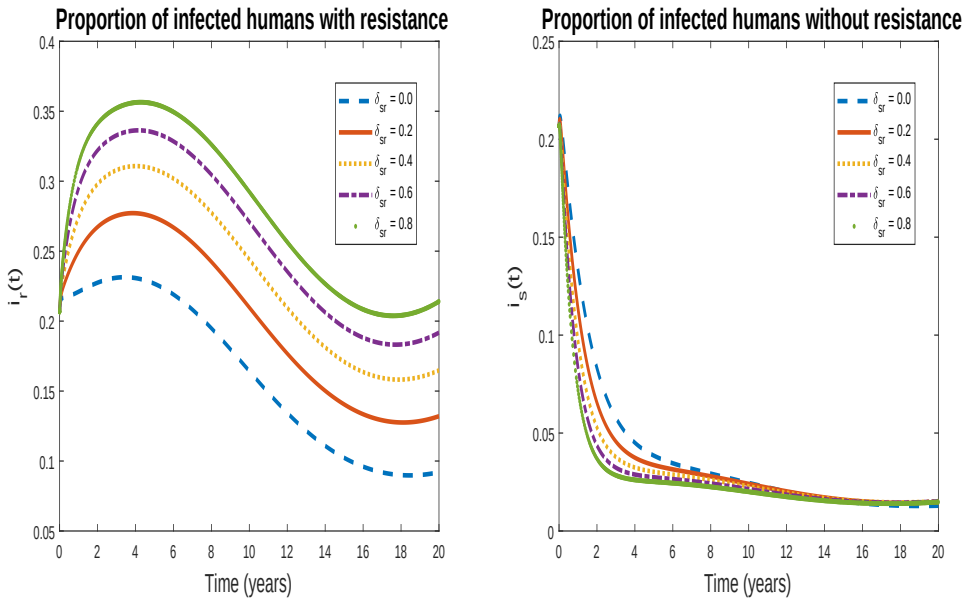

Figure 6: Plot showing the effects of changes in human resistance to malaria (δ_{rs}).

The effects of changes in human resistance to malaria δ_{rs} which shifts individuals from $I_r(t)$ to $I_s(t)$ as capacity to resist malaria deteriorates are presented in Figure 6. The figure shows that as the capacity to resist malaria deteriorates, the number of infected individuals increases such that the malaria becomes endemic in the community. Based on these results, we recommended that any practice that can lead to a decrease in the capacity for individuals to resist malaria should be avoided. Some of the common practices that result in a decrease in the capacity for individuals to resist malaria include: negligence with respect to vaccinations, the use of fake medicines, and incomplete treatment of infected individuals, etc.

The basic reproduction number is an important quantity in epidemiological models. Analysing the effects of changes in human resistance to malaria, δ_{sr}, δ_{rs}, l_{sr} and l_{rs} on the basic reproduction number are considered to improve our understanding of the model dynamics which can assist in the management of the disease. The parameters for human resistance to malaria are varied simultaneously. This method agrees with realistic scenarios where various parameters representing different aspect of the disease dynamics change simultaneously.

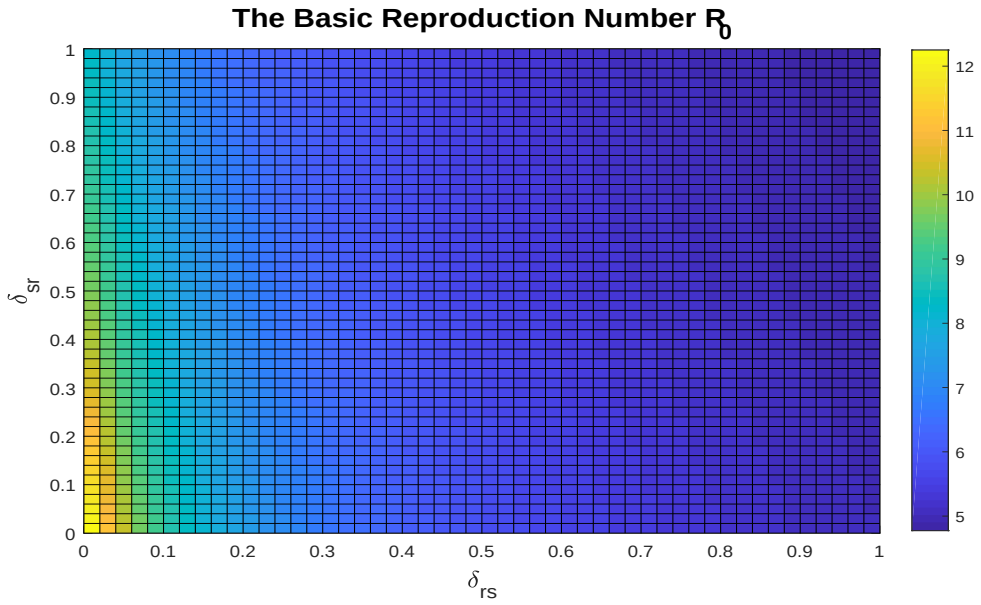

Figure 7: Plot showing the effects of changes in human resistance to malaria (δ_{sr} and δ_{rs}) on the basic reproduction number.

The effects of changes in human resistance to malaria (δ_{sr} and δ_{rs}) on the basic reproduction number $\mathcal{R}_0$ are presented in Figure 7. From the figure, it is observed that as changes in human resistance to malaria (δ_{sr} and δ_{rs}) are varied, the basic reproduction number also varies. Since our main interest is to determine the range of values for changes in human resistance to malaria (δ_{sr} and δ_{rs}) that results in the minimum or maximum value for $\mathcal{R}_0$, we find that for $0.0 < \delta_{sr} < 1.0$ and $0.2 < \delta_{rs} < 1.0$, $\mathcal{R}_0$ tends to a minimum value. On the other hand, for $0.0 < \delta_{sr} < 0.7$ and $0.2 < \delta_{rs} < 1.0$, $\mathcal{R}_0$ tends to a maximum value. Understanding how to determine the range of parameters that leads to a minimum basic reproduction number is necessary for better management of malaria epidemic.

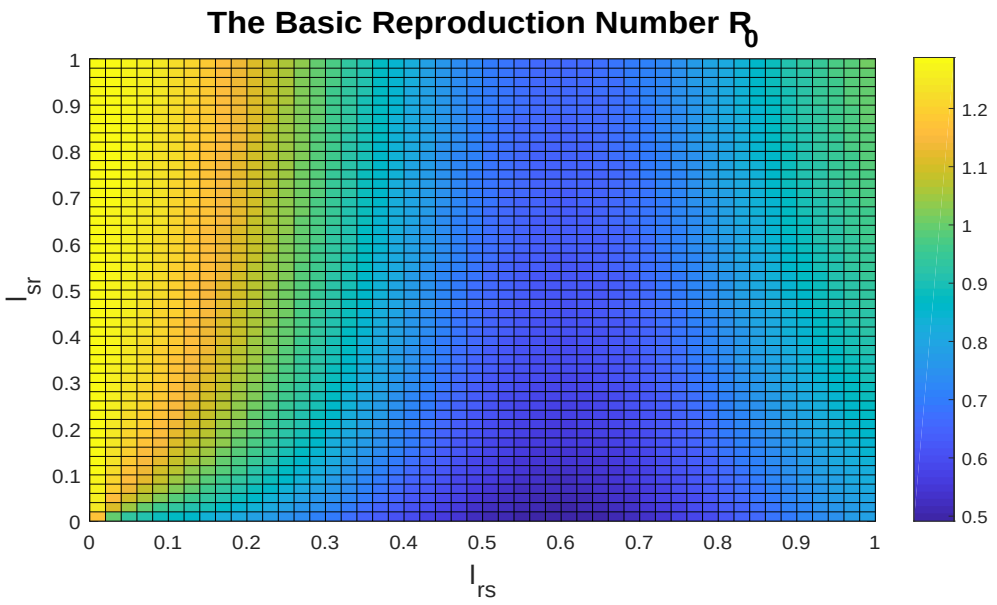

Figure 8: Plot showing the effects of movement rates (l_{sr} and l_{rs}) on the basic reproduction number.

The effects of changes in human resistance to malaria (l_{sr} and l_{rs}) on the basic reproduction number $\mathcal{R}_0$ are presented in Figure 8. From the figure, we discover that for $0.0 < l_{sr} < 1.0$ and $0.4 < l_{rs} < 0.8$, $\mathcal{R}_0$ tends to a minimum value. On the other hand, for $0.0 < l_{sr} < 1.0$ and $0.0 < l_{rs} < 0.2$, $\mathcal{R}_0$ tends to a maximum value. Understanding how to determine these range of parameters that leads to minimum basic reproduction number is crucial for better management of malaria epidemic.

4.4. Sensitivity Analyses

Sensitivity analyses are used to determine the extent to which a parameter value influences disease dynamics [5]. Here sensitivity analyses are used to determine which parameters have a significant effect on $\mathcal{R}_0$. The Latin Hypercube Sampling Method (LHSM) is used. From results of the LHSM, the partial rank correlation coefficients (PRCCs) of $\mathcal{R}_0$ are calculated. The magnitude and sign of the PRCC determine the effect of a parameter on $\mathcal{R}_0$.

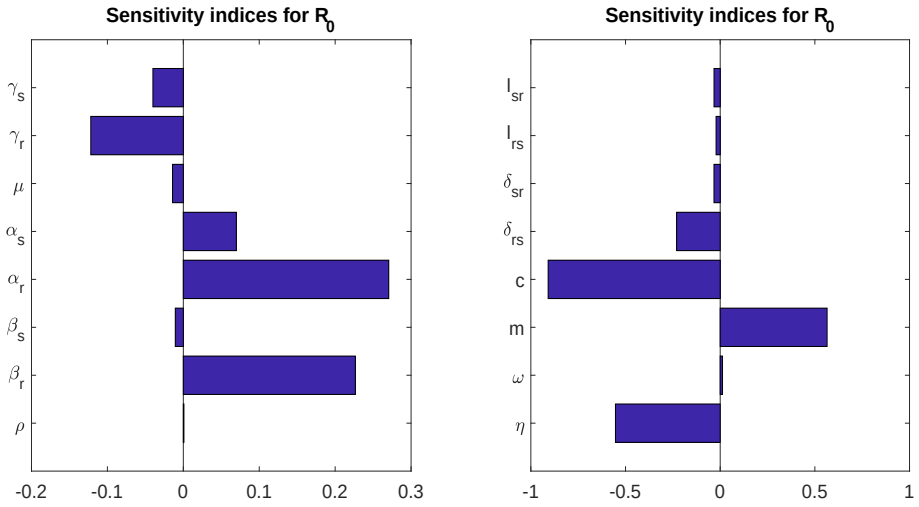

Figure 9: Tornado plot showing the sensitivity indices for $\mathcal{R}_0$.

The sensitivity index of $\mathcal{R}_0$ (based on the PRCC values) are presented as tornado plots in Figure 9. From the figure, the most sensitive parameter is c, followed by m and η. The figure also shows that the sensitivity index of $\mathcal{R}_0$ with respect to the parameters that are associated with individuals that have high resistance to malaria dominates. For instance, the sensitivity index of $\mathcal{R}_0$ with respect to β_r dominates that of β_s, α_r dominates α_s and γ_r dominates γ_s. This shows that parameters associated with individuals that have a high resistance to malaria are more sensitive and therefore should be taken into greater consideration when developing control measures for better management of a malaria epidemic.

5. Discussion

Malaria is a major health problem currently affecting humans, especially in Africa (south of the Sahara). Although it is curable, effective management of the malaria is still a major challenge especially in communities where the disease is endemic. Understanding the complex nature of the disease dynamics is important for managing the disease. A major factor that affects these dynamics is the ability of each individuals to resist malaria infection. The resistance to malaria can be natural (genetically resistant humans like sickle cell patient) or acquired through appropriate immunization or vaccination. Therefore, the ability to resist malaria needs to be taken into consideration for a better understanding of the infection dynamics.

A mathematical model that takes into consideration an individual's ability to resist malaria is formulated

to study the dynamics. Preliminary analyses of this model are assessed qualitatively. For instance, the basic reproduction number of the model is computed and equilibrium points of the model (both the disease free equilibrium and endemic equilibrium) determined. The disease free equilibrium is shown to be locally asymptotically stable when the basic reproduction number is less than unity, suggesting that the disease can be eliminated if the basic reproduction number is less than one and provided that the initial infected population is in the neighbourhood of the disease free equilibrium. On the other hand, the endemic equilibrium is shown to be locally asymptotically stable when the basic reproduction number is greater than unity, suggesting that the disease will persist if the basic reproduction number is greater than one and provided that the initial infected population is in the neighbourhood of the endemic equilibrium.

Importantly, it is also shown that the model trajectories undergo a backward bifurcation as the basic reproduction number cross unity. This implies that reducing the basic reproduction number below unity is necessary but not sufficient to eradicate malaria. Further analyses show that changes in the extent that individuals are able to resist malaria is the cause of the backward bifurcation.

The model dynamics appear realistic. To further validate the model it is fit to data for a recorded epidemic in Nigeria. The parameters of interest, relating to ability to resist malaria, were estimated using model fitting. The resulting fit shows that the model is a reasonable representation of the malaria epidemic. The model is then used to predict the possible future dynamics of malaria in Nigeria.

Using the estimated parameters, the effects of an individual's capacity to resist malaria were explored further. Improving human capability to resist malaria is shown to decrease the number of infected individuals such that the disease can be eliminated in an entire community. Therefore, improving an individual's capability to resist malaria through vaccination etc is strongly recommended for possible eradication of malaria in endemic areas. Further analyses show that as an individual's capability to resist malaria deteriorate, the number of infected individuals increases such that the malaria can become endemic in the population. Thus, any practice that can lead to decreases in the capabilities to resist malaria should be avoided.

The range of values for model parameters for the capability to resist malaria that result in a minimum or maximum value for the basic reproduction number are determined. Knowledge of this range can assist in developing control measures that lead to better management of malaria epidemics.

Finally, sensitivity analysis are considered to consider the importance of each of the model parameters using the Latin Hypercube Sampling Method (LHSM). For this the basic reproduction number $\mathcal{R}_0$ is used as the measure. Parameters that are associated with individuals that have higher resistance to malaria dominate. Specifically, β_r dominates β_s, α_r dominates α_s and γ_r dominates γ_s. This shows that parameters associated

with individuals that have higher resistance to malaria are more sensitive and therefore should be taken into greater considerations while developing control measures for better management of a malaria epidemic.

Overall, the importance of malaria resistance has been shown for the control of malaria. With the advent of new vaccination protocols for the prevention of malaria [13], such as the R21 vaccine, knowledge of the effects of human resistance on malaria dynamics, as shown here, should assist in management of this disease.

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