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A Mathematical Model for Malaria Transmission Dynamics in the Population with Different Immune Status

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Abstract

Malaria is a febrile illness affecting a large population worldwide. Even though malaria is curable and preventable it continues to pose a significant health risk, economic effects, and social effects in the population. This study formulates a mathematical model to study the transmission dynamics of malaria in a population with different immune status. By dividing the population based on immune status, the model provides insights into how immunity influences the interaction between hosts and malaria parasites, particularly in terms of infection rates, immune responses, and propose appropriate control for effective elimination. The basic reproduction number is computed using the next-generation matrix approach. The analysis shows that the model can undergo forward bifurcation when the basic reproduction number $R_0 > 1$, thus, the condition of $R_0 < 1$ *is* necessary and sufficient for malaria elimination. The numerical simulation results indicate that non-immune individuals play a more significant role in malaria transmission compared to semi-immune individuals. This is because non-immune individuals, lacking strong immunity, are more susceptible to malaria infection. Moreover, the results highlight the effect of mosquito biting rates on the susceptible and infectious population. The findings underscore the importance of considering immune heterogeneity within the population when developing strategies to control and eventually eradicate malaria.

Keywords: Non-immune, Semi-immune, Reproduction number, Bifurcation analysis.

Introduction

Malaria is the deadliest disease caused by the parasite of the genus *Plasmodium* which is transmitted between humans and mosquitoes through a bite from an infected female *Anopheles* mosquito. Despite the efforts to control, eradicate, and eliminate the disease, malaria remains a major health problem in sub-Saharan Africa. In 2021 there were approximately 247 million malaria cases and 619,000 malaria deaths worldwide (WHO 2022). In areas with high prevalence children below five years, pregnant women, and non-immune adults are more vulnerable to malaria infection and they are at high risk of malaria mortality (WHO 2022).

Several factors can affect malaria's transmission dynamics, including an individual's immune status. An individual's immune status helps determine the body's ability to fight against pathogens. To accurately study malaria transmission dynamics, it is essential to categorize the human host by immune status (Mwanga et al. 2015). However, he did not include immune status in his age-structured model. The immune status of hosts, including their levels of innate, naturally, or artificially acquired immunity, significantly influences the spread

of infectious diseases within a population. As malaria parasites develop in the host, they trigger the activity of immune cells, leading to an immune response aimed at combating the infection. This response can either prevent the reinvasion of merozoites or increase the death rate of infected erythrocytes (Tumwiine et al. 2008, Woldegerima et al. 2018, Cai et al 2019). Therefore, designing effective control measures for malaria prevalence should be guided by a thorough understanding of human immune status, particularly for non-immune individuals who are most vulnerable to malaria infection, where we have non-immune and semi-immune individuals. Non-immune individuals are those who have never got malaria infection and thus have not developed clinical immunity. Since they have not acquired immunity against malaria, they are at high risk of suffering from or dying of malaria (Keegan and Dushoff 2013). On the other hand, semi-immune individuals are those who have acquired immunity during their lifetime (Ducrot et al. 2009).

Various mathematical models have been developed to assess the impact of immunity on malaria transmission dynamics, including Cai et al. (2019) formulated a compartmental whereby the human population is assumed to have a susceptible population, infectious humans with immune status and temporarily immune classes; Bakary et al. (2018), formulated a mathematical model of malaria transmission dynamics which considered immune status in human population, however, the focus of the study was in age structure for the vector population and a periodic biting rate of female anopheles mosquitoes. Ducrot et al. (2009) considered two types of hosts within the human population: non-immune individuals, who have never acquired immunity against malaria, and semi-immune individuals. An explicit expression for the reproduction number was derived as a function of the transmission weight between semi-immune individuals and mosquitoes, as well as between non-immune individuals and mosquitoes. However, neither of the studies considers the critical role that immune status plays in determining malaria prevalence and transmission. Therefore, this paper addresses an interesting question of how differences in host immune status affect the transmission of malaria in the absence of control.

Materials and Methods

The flow diagram (Figure 1), is used to describe the movement of human and mosquito populations from one class to another depending on their disease status. The model flow diagram is designed to facilitate the formulation of a mathematical model for populations with different immune status.

Model Formulation

A mathematical model for malaria transmission dynamics in the population with different immune status is formulated by modifying the model by Ducrot et al. (2009) which studied the dynamics of malaria in the presence of differential susceptibility, exposure, and infectivity of the human host. To study the transmission dynamics of malaria, we divide the human population into two major groups; the non-immune individuals who have never got malaria infection and are vulnerable to malaria infection (Ducrot et al. 2009), and semi-immune individuals who already have immunity at least once in their lifetime (Ducrot et al., 2009). The classes are classified with subscript *n* for non-immune and *s* for semi-immune individuals respectively. The non-immune population is divided into susceptible class S_n, (those who are not infected but they are more vulnerable to malaria infection), exposed class E_n, (those already infected but not infectious because the infection is still at a dormant liver stage), and infectious class I_n, (those who can infect susceptible mosquitoes). Similarly, the semi-immune population is divided into susceptible S_s, exposed E_s, and infectious I_s, classes respectively. Hence, the total human population at any time *t* is given by;

$$N_h = S_n + E_n + I_n + S_s + E_s + I_s.$$

The mosquito population is divided into two compartments which are the susceptible S_m, and infectious I_m. Therefore, the total

mosquito population at any time t is given by;

$$N_m = S_m + I_m.$$

Non-immune and semi-immune individuals are recruited through birth at a rate $\theta\Lambda$ and (1-θ)Λ respectively, for $\theta \in [0,1]$. The susceptible non-immune and semi-immune individuals get malaria infection when bitten by an infectious mosquito at rates λ_n and λ_s respectively. The forces of infections λ_n and λ_s are given as;

$$\lambda_n = \frac{ab_{mn}I_m}{N_h}, \quad \lambda_s = \frac{ab_{ms}I_m}{N_h} \qquad (1)$$

where, b_{mn}, and b_{ms} represent the average mosquito biting rate and the probability of infecting non-immune and semi-immune individuals respectively. After some period, exposed individuals E_n and E_s progress into infectious class I_n and I_s at rates β_n and β_s, respectively. Individuals from every compartment suffer natural mortality at a rate μ_h and individuals from infectious class suffer disease-induced death at rates α_n and α_s for non-immune and semi-immune individuals respectively. The mosquito population is considered to be recruited through birth at a per capita rate Λ_m. The susceptible mosquito gets malaria parasites when bites an infectious non-immune and semi-immune individual at a rate λ_m. The force of infection λ_m. is given as;

$$\lambda_m = \frac{ac_{nm}i_n + ac_{sm}i_s}{N_h} \qquad (2)$$

where a, c_{nm}, and c_{sm} represent the mosquito biting rate, the probabilities of a mosquito to get an infection from an infectious non-immune and semi-immune individual respectively. Following infection, susceptible mosquitoes S_m progress to infectious class I_m. Mosquitoes decrease from the population through natural mortality at a rate μ_m. Moreover, throughout the study, we make the following assumptions: All new recruitment is susceptible to the malaria disease, and all women attend clinic hence, there is no vertical transmission of malaria infection from mother to the baby (Bakary et al., 2018). The disease does not confer immunity hence once an individual is infected with malaria will remain infected provided that there is no treatment. The dynamics of malaria in the population with different immune status is summarized in Figure 1.

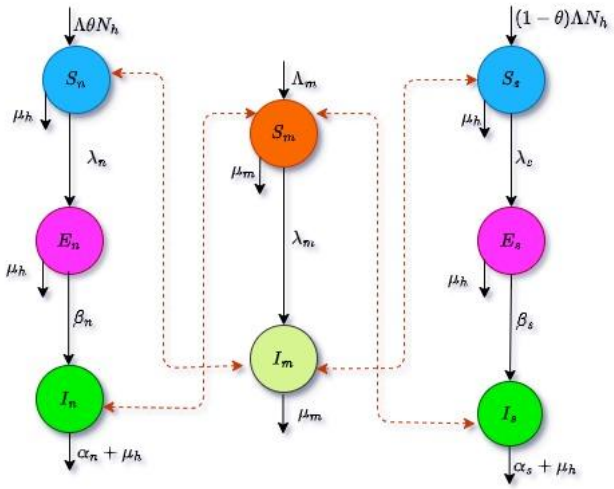

Figure 1: Model Flow Diagram for Malaria Dynamics in the Population with Different Immune Status

Table 1: Description of Model Parameters in the Model

Parameter	Description
θ	The proportion of the human population that joins the susceptible class
Λ	Per capita recruitment rate of the human population
β_n	Progression rate of non-immune individuals from exposed class to an infectious class
β_s	Progression rate of semi-immune individuals from exposed class to an infectious class
b_{mn}	Probability of malaria transmission from an infectious mosquito to susceptible non-immune
b_{ms}	Probability of malaria transmission from an infectious mosquito to susceptible semi-immune
c_{nm}	Probability of malaria transmission from an infectious non-immune to susceptible mosquito
c_{sm}	Probability of malaria transmission from an infectious semi-immune to susceptible mosquito
α_n	Decease-induced death in non-immune individuals
α_s	Decease-induced death in semi-immune individuals
$\lambda_i(n,s,m)$	The infection rate for susceptible non-immune, semi-immune and mosquito
μ_h	Natural mortality rate of the human population
μ_m	Natural death rate mosquito population
g	Vector-human ratio
a	Average mosquito biting rate

The associated system of ordinary differential equations that describes the transmission dynamics of malaria in humans and mosquitoes are given as follows

$$\left.\begin{aligned}
\frac{dS_n}{dt} &= \Lambda\theta N_h - (\lambda_n + \mu_h)S_n(t),\\
\frac{dE_n}{dt} &= \lambda_n S_n - (\beta_n + \mu_h)E_n(t)\,,\\
\frac{dI_n}{dt} &= \beta_n E_n - (\alpha_n + \mu_h)I_n(t)\,,\\
\frac{dS_s}{dt} &= (1-\theta)\Lambda N_h - (\lambda_s + \mu_h)S_s(t),\\
\frac{dE_s}{dt} &= \lambda_s S_s - (\beta_s + \mu_h)E_s(t),\\
\frac{dI_s}{dt} &= \beta_s E_s - (\alpha_s + \mu_h))I_s(t)\,,\\
\frac{dS_m}{dt} &= \Lambda_m N_m - (\lambda_m + \mu_m)S_m(t),\\
\frac{dS_m}{dt} &= \lambda_m S_m(t) - \mu_m I_m(t),
\end{aligned}\right\}, \qquad (3)$$

subject to the initial conditions: $S_n(0) > 0, E_n(0) \geq 0, I_n(0) \geq 0, S_s(0) > 0,$ $E_s(0) \geq 0,\ I_s(0) \geq 0,\ \ S_m(0) > 0,\ \ I_m(0) \geq 0.$

Non-Dimensionalization of the Model

We apply the method used by Kalula et al. (2021) and Chitnis et al. (2008) to rescale the model system (3) by dividing the population in each class by the total population that is $s_n = \frac{S_n}{N_h}, s_s = \frac{S_s}{N_h},\ s_m = \frac{S_m}{N_m}, \ldots,$ etc. Differentiating for *t* we obtain;

$\frac{ds_n}{dt} = \frac{1}{N_h}\left[\frac{dS_n}{dt} - \frac{dN_h}{dt}\right], \frac{ds_s}{dt} = \frac{1}{N_h}\left[\frac{dS_s}{dt} - \frac{dN_h}{dt}\right], \frac{ds_m}{dt} = \frac{1}{N_m}\left[\frac{dS_m}{dt} - \frac{dN_m}{dt}\right]$. The process is repeated for the remaining variable, $E_n,\ I_n,\ E_s,\ I_s,\ I_m$. We apply the method used by Tumwiine et al. (2007) to solve the derivatives of rescaled variables so that we can have,

$$\left.\begin{aligned}
\frac{ds_n}{dt} &= \Lambda(\theta - s_n) - (agb_{mn}i_m)s_n + (\alpha_n i_n + \alpha_s i_s)\, s_n \\
\frac{de_n}{dt} &= agb_{mn}i_m s_n - (\beta_n + \Lambda)e_n + (\alpha_n i_n + \alpha_s i_s)e_n \\
\frac{di_s}{dt} &= \beta_n e_n - (\alpha_n + \Lambda))i_n \ + (\alpha_n i_n + \alpha_s i_s)\, i_n \\
\frac{ds_s}{dt} &= ((1-\theta) - s_s)\Lambda - (agb_{ms}i_m)s_s + (\alpha_n i_n + \alpha_s i_s)s_s \\
\frac{de_s}{dt} &= agb_{ms}i_m s_s - (\beta_s + \Lambda)e_s + (\alpha_n i_n + \alpha_s i_s)\, e_s \\
\frac{di_s}{dt} &= \beta_s e_s - (\alpha_s + \Lambda))i_s \ + (\alpha_n i_n + \alpha_s i_s)\, i_s \\
\frac{ds_m}{dt} &= \Lambda_m(1 - s_m) - (ac_{nm}i_n + ac_{sm}i_s)s_m \\
\frac{di_m}{dt} &= (ac_{nm}i_n + ac_{sm}i_s)s_m - \Lambda_m i_m
\end{aligned}\right\}, \qquad (4)$$

subject to the conditions; $s_m + i_m = 1$, and $s_n + e_n + i_n + s_s + e_s + i_s = 1$, where, $g = \frac{N_m}{N_h}$ is the vector-human ratio.

Model Analysis

For the model system (4) to be mathematically and epidemiologically meaningful, it is important to show that all model solutions are positive and bounded.

Positivity of Model Solutions

From the first equation in the model system (4) for susceptible non-immune humans, we have:

$$\begin{aligned}
\frac{ds_n}{dt} &= \Lambda\theta - (agb_{mn}i_m + \Lambda)s_n + (\alpha_n i_n + \alpha_s i_s)\, s_n(t), \\
&\Rightarrow \frac{ds_n}{dt} \geq -(ab_{mn}i_m(t) + \Lambda)s_n(t)\ , \\
&\Rightarrow \tfrac{ds_n}{s_n(t)} \geq -(ab_{mn}i_m(t) + \Lambda)dt, \qquad (5) \\
s_n(t) &\geq s_n(0)e^{\int_0^t -(ab_{mn}i_m(s)+\Lambda)ds} \geq 0, \forall t \geq 0.
\end{aligned}$$

Using the same approach for the remaining equations, it can be shown that,

$$e_n \geq 0;\ i_n \geq 0;\ s_s \geq 0;\ e_s \geq 0;\ i_s \geq 0;\ s_m \geq 0;\ i_m \geq 0.$$

Therefore, all solutions of model system (2) are positive for all $t \geq 0$.

Invariant region

To prove the boundedness of model solutions, we apply the method used by Irunde et al. (2016). By considering the total human population $n_h(t) = s_n(t) + e_n(t) + i_n(t) + s_s(t) + e_s(t) + i_s(t)$, we have:

$$\begin{aligned}
\tfrac{dn_h(t)}{dt} &= \Lambda - \Lambda n_h(t) + \alpha_n i_n(t) + \alpha_s i_s(t), \\
\Rightarrow \tfrac{dn(t)}{dt} &\leq \Lambda - \Lambda n_h(t).
\end{aligned}$$

Using integrating factors, it can be shown that:

$$n_h(t) \leq \big(n_h(0)\big)e^{-\Lambda t} + (1 - e^{-\Lambda t}),$$

Applying the limit as $t \to \infty$, it follows that:

$$\lim_{t\to\infty} sup\ n_h \leq 1 \tag{6}$$

where, $n_h(0) = s_n(0) + e_n(0) + i_n(0) + s_s(0) + e_s(0) + i_s(0)$.

Using the same approach, it can be shown that the population of mosquitoes is given as

$$n_m(t) \leq n_m(0)e^{-\Lambda_m t} + (1 - e^{-\Lambda_m t}), \tag{7}$$

where, $n_m(0) = s_m(0) + i_m(0)$.

Hence,

$$\varphi_t = max\{1,\ n_h(0)\}, \tag{8}$$

$$\varepsilon_t = max\{1, n_m(0)\}. \tag{9}$$

Therefore, the model system (2) is positive invariant in the region

$$\Gamma = \{(s_n, e_n, i_n, s_s, e_s, i_s, s_m, i_m) \epsilon \mathbb{R}_+^8 : 0 \leq n_h(t) \leq \varphi_t; 0 \leq n_m(t) \leq \varepsilon_t\},$$

where, φ_t and ε_t are defined in equations (8) and (9) respectively.

Therefore, the model system (4) is both mathematically, epidemiologically, and biologically meaningful, thus we can consider the flow generated by the model system (4) for the analysis.

Malaria-Free Equilibrium and the Basic Reproduction Number R_0

Malaria-Free Equilibrium Point

The malaria-free equilibrium point (MFE) is a point where the population is free from malaria disease. As a result, at the malaria-free equilibrium point, all infectious classes within the model system (4) are set to zero, yielding the representation of the model system (4) as follows.

$$\left.\begin{aligned} &\Lambda(\theta - s_n) = 0 \\ &\Lambda((1-\theta) - s_s) = 0 \\ &\Lambda_m(1 - s_m) = 0 \end{aligned}\right\} \tag{10}$$

Solving for s_n, s_s, and, s_m into equation (10) above, we have;

$$E^0(s_n, e_n, i_n, s_s, e_s, i_s, s_m, i_m) = (\theta,\ 0, 0, (1-\theta), 0,\ 0,\ 1, 0). \tag{11}$$

Malaria Reproduction Number R_0

The basic reproduction number R_0 is an expected number of secondary infections that may occur as the result of introducing a single infected individual in the whole susceptible population (Diekmann et al., 1990). It determines whether the disease persists or dies. The disease dies when $R_0 < 1$ and persists when $R_0 > 1$. The next-generation matrix method used in van den Driessche and Watmough (2002) is applied to compute the basic reproduction number R_0. Using the infected classes in the model system (4), the vector for new infection in the compartment i and the transfer terms in and out of the compartment i are respectively given by:

$$\mathcal{F}_i = \begin{pmatrix} agb_{mn} i_m s_n \\ 0 \\ agb_{ms} i_m s_s \\ 0 \\ (ac_{nm} i_n + ac_{sm} i_s) s_m \end{pmatrix},\ \nu_i = \begin{pmatrix} (\beta_n + \Lambda)e_n - (\alpha_n i_n + \alpha_s i_s)\ e_n \\ (\alpha_n + \Lambda)i_n - \beta_n e_n - (\alpha_n i_n + \alpha_s i_s)\ i_n \\ (\beta_s + \Lambda)e_s - (\alpha_n i_n + \alpha_s i_s)\ e_s \\ (\alpha_s + \Lambda)i_s - \beta_s e_s - (\alpha_n i_n + \alpha_s i_s)\ i_s \\ \Lambda_m i_m \end{pmatrix}. \tag{12}$$

So that the Jacobian matrices F and V at MFE are given as:

$$F = \frac{\partial \mathcal{F}_i}{\partial x_j}(E^0),\ V = \frac{\partial \nu_i}{\partial x_j}(E^0), \tag{13}$$

The malaria reproduction number R_0 is given by:

$$R_0 = \rho(FV^{-1}). \tag{14}$$

Using equation (13), matrices F and V can be written as;

$$F = \begin{pmatrix} 0 & 0 & 0 & 0 & a_1 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & a_2 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & a_3 & 0 & a_4 & 0 \end{pmatrix} \text{ and } V = \begin{pmatrix} b_1 & 0 & 0 & 0 & 0 \\ -\beta_n & b_3 & 0 & 0 & 0 \\ 0 & 0 & b_4 & 0 & 0 \\ 0 & 0 & -\beta_s & b_6 & 0 \\ 0 & a_3 & 0 & 0 & \Lambda_m \end{pmatrix}, \tag{15}$$

where, $a_1 = agb_{mn}\theta$, $a_2 = agb_{mn}(1-\theta)$, $a_3 = ac_{nm}$, $a_4 = ac_{sm}$, $b_1 = (\beta_n + \Lambda)$, $b_3 = (\alpha_n + \Lambda)$, $b_4 = \beta_s + \Lambda$, $b_6 = \alpha_s + \Lambda$.

The malaria reproduction number R_0 of the model system (2) is given by;

$$R_0 = \sqrt{R_{0n} + R_{0s}} \tag{16}$$

where; $R_{0s} = \frac{a^2 g b_{ms}(1-\theta)c_{sm}\beta_s}{\Lambda_m(\beta_s+\Lambda)(\alpha_s+\Lambda)}$, $R_{0n} = \frac{a^2\theta g\beta_n b_{mn}c_{nm}}{\Lambda_m(\beta_n+\Lambda)(\alpha_n+\Lambda)}$

R_{0n} is the partial reproduction number due to the interaction between non-immune individuals and mosquitoes, whereas R_{0s} is the partial reproduction number due to the interaction between semi-immune and mosquitoes.

The Endemic Equilibrium points

The endemic equilibrium E^* is a steady-state situation where the disease persists in the population. Solving the model system (4) when all infectious classes are not equal to zero, we obtain an endemic equilibrium point $E^* = (s_n^*, e_n^*, i_n^*, s_s^*, e_s^*, i_s^*, s_m^*, i_m^*)$ where;

$s_n^* = \frac{\Lambda\theta}{gab_{mn}\lambda_m^*+(\Lambda-\mathrm{N})(\Lambda_m+\lambda_m^*)}$, $e_n^* = \frac{gab_{mn}\Lambda\theta\lambda_m^*}{(\beta_n+\Lambda-\mathrm{N})(gab_{mn}\lambda_m^*+(\Lambda-\mathrm{N})(\Lambda_m+\lambda_m^*))}$,

$i_n^* = \frac{gab_{mn}\beta_n\Lambda\theta\lambda_m^*}{(\alpha_n+\Lambda-\mathrm{N})(\beta_n+\Lambda-\mathrm{N})(gab_{mn}\lambda_m^*+(\Lambda-\mathrm{N})(\Lambda_m+\lambda_m^*))}$, $s_s^* = \frac{\Lambda(1-\theta)\lambda_m^*}{gab_{mn}\lambda_m^*+(\Lambda-\mathrm{N})(\Lambda_m+\lambda_m^*)}$,

$e_s^* = \frac{gab_{ms}\Lambda(1-\theta)\lambda_m^*}{(\beta_s+\Lambda-\mathrm{N})(gab_{ms}\lambda_m^*+(\Lambda-\mathrm{N})(\Lambda_m+\lambda_m^*))}$, $i_s^* = \frac{\beta_s gab_{ms}\Lambda(1-\theta)\lambda_m^*}{(\alpha_s+\Lambda-\mathrm{N})(\beta_s+\Lambda-\mathrm{N})(gab_{ms}\lambda_m^*+(\Lambda-\mathrm{N})(\Lambda_m+\lambda_m^*))}$,

$s_m^* = \frac{\Lambda_m}{\Lambda_m+\lambda_m^*}$, $i_m^* = \frac{\lambda_m^*}{\Lambda_m+\lambda_m^*}$, where, $N = \alpha_n i_n + \alpha_s i_s$.

Existence of Forward Bifurcation

Forward bifurcation occurs when malaria free equilibrium point loses its stability and a stable malaria equilibrium occurs as the basic reproduction number R_0 increases through one (Chitnis et al., 2006). In this case, if $R_0 < 1$, then the malaria-free equilibrium exists and it is stable, implying that malaria disease will die out. When $R_0 > 1$, then the malaria-free equilibrium becomes unstable resulting in malaria equilibrium, which shows that malaria disease will persist. Normally, when forward bifurcation occurs, then the requirement $R_0 < 1$ is necessary and sufficient for malaria control. Therefore, to prove the existence of forward bifurcation in the model system (4) we adopt the center Manifold theory as applied by Castillo and Chavez et al. (2004). To do so, the state variables are renamed as $y_1 = s_n$, $y_2 = e_n$, $y_3 = i_n$, $y_4 = s_s$, $y_5 = e_s$, $y_6 = i_s$, $y_7 = s_m$, $y_8 = i_m$, such that $y = (y_1, y_2, y_3, y_4, y_5, y_6, y_7, y_8)^T$ where T stands for transpose. The model system (2) can be written in the form of $\frac{dy}{dt} = f(y)$ with, $F = (f_1, f_2, \dots, f_8)$. Thus, the model system (2) becomes

$$\left.\begin{aligned}
\frac{dy_1}{dt} &= f_1 = \Lambda\theta - (agb_{mn}y_8 + \Lambda)\, y_1 + (\alpha_n y_3 + \alpha_s y_6)\, y_1 \\
\frac{dy_2}{dt} &= f_2 = agb_{mn}y_8 y_1 - (\beta_n + \Lambda) y_2 + (\alpha_n y_3 + \alpha_s y_6)\, y_2 \\
\frac{dy_3}{dt} &= f_3 = \beta_n y_2 - (\alpha_n + \Lambda) y_3 + (\alpha_n y_3 + \alpha_s y_6)\, y_3 \\
\frac{dy_4}{dt} &= f_4 = (1-\theta)\Lambda - (agb_{ms}y_8 + \Lambda) y_4 + (\alpha_n y_3 + \alpha_s y_6)\, y_4 \\
\frac{dy_5}{dt} &= f_5 = agb_{ms}y_8 y_4 - (\beta_s + \Lambda) y_5 + (\alpha_n y_3 + \alpha_s y_6)\, y_5 \\
\frac{dy_6}{dt} &= f_6 = \beta_s y_5 - (\alpha_s + \Lambda) y_6 + (\alpha_n y_3 + \alpha_s y_6)\, y_6 \\
\frac{dy_7}{dt} &= f_7 = \Lambda_m - (ac_{nm}y_3 + ac_{sm}y_6 + \Lambda_m) y_7 \\
\frac{dy_8}{dt} &= f_8 = (ac_{nm}y_3 + ac_{sm}y_6) y_7 - \Lambda_m y_8
\end{aligned}\right\} \quad (17),$$

where, $y = y_1 + y_2 + y_3 + y_4 + y_5 + y_6 + y_7 + y_8$. The Jacobian Matrix of Model system (17) at malaria-free equilibrium point is given as

$$J(E^0) = \begin{pmatrix}
-\Lambda & 0 & 0 & 0 & 0 & 0 & 0 & -agb_{mn}\theta \\
0 & -(\beta_n + \Lambda) & 0 & 0 & 0 & 0 & 0 & agb_{mn}\theta \\
0 & \beta_n & -(\alpha_n + \Lambda) & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & -\Lambda & 0 & 0 & 0 & -agb_{ms}(1-\theta) \\
0 & 0 & 0 & 0 & -(\beta_s + \Lambda) & 0 & 0 & agb_{ms}(1-\theta) \\
0 & 0 & 0 & 0 & \beta_s & -(\alpha_s + \Lambda) & 0 & 0 \\
0 & 0 & -ac_{\mathrm{nm}} & 0 & 0 & -ac_{sm} & -\Lambda_m & 0 \\
0 & 0 & ac_{\mathrm{nm}} & 0 & 0 & ac_{sm} & 0 & -\Lambda_m
\end{pmatrix} \quad (18)$$

Choosing a^* as a bifurcation parameter when $R_0 = 1$, we obtain,

$$a^* = \frac{\Lambda_m(\beta_s + \Lambda)(\alpha_s + \Lambda)(\beta_n + \Lambda)(\alpha_n + \Lambda)}{g\beta_s b_{ms}(1-\theta)c_{sm}(\beta_n + \Lambda)(\alpha_n + \Lambda) + g\beta_n b_{mn}\theta c_{nm}(\beta_s + \Lambda)(\alpha_s + \Lambda)} \quad (19)$$

Therefore, the linearized system (18) is transformed by $a = a^*$ which has a simple zero eigenvalue and center Manifold theory is used to analyze the dynamics of the system (18) near to by $a = a^*$. Thus, the Jacobian matrix (18) at the malaria-free equilibrium point E^0 denoted by $J(a^*)$ is given by:

$$J(a^*) = \begin{pmatrix}
-\Lambda & 0 & 0 & 0 & 0 & 0 & 0 & -n_1 \\
0 & -n_2 & 0 & 0 & 0 & 0 & 0 & n_1 \\
0 & \beta_n & -n_3 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & -\Lambda & 0 & 0 & 0 & -n_6 \\
0 & 0 & 0 & 0 & -n_4 & 0 & 0 & n_6 \\
0 & 0 & 0 & 0 & \beta_s & -n_5 & 0 & 0 \\
0 & 0 & -n_7 & 0 & 0 & -n_8 & -\Lambda_m & 0 \\
0 & 0 & n_7 & 0 & 0 & n_8 & 0 & -\Lambda_m
\end{pmatrix}, \quad (20)$$

where $n_1 = a^* g b_{mn}\theta$, $n_2 = \beta_n + \Lambda$, $n_3 = \alpha_n + \Lambda$, $n_4 = \beta_s + \Lambda$, $n_5 = \alpha_s + \Lambda$, $n_6 = a^* g b_{mn}(1-\theta)$, $n_7 = a^* c_{\mathrm{nm}}\Lambda_m$, $n_8 = a^* c_{sm}\Lambda_m$.

The right eigenvectors associated with zero eigenvalues are given by;

$\psi = (\psi_1, \psi_2, \psi_3, \psi_4, \psi_5, \psi_6, \psi_7, \psi_8)^T$ and the following right eigenvectors are obtained,

$\psi_1 = -\frac{n_1\psi_8}{\mu}$, $\psi_2 = \frac{n_1\psi_8}{n_2}$, $\psi_3 = \frac{n_1\beta_n\psi_8}{n_2 n_3}$, $\psi_4 = -\frac{n_6\psi_8}{\mu}$, $\psi_5 = \frac{n_6\psi_8}{n_4}$, $\psi_6 = \frac{n_6\beta_s\psi_8}{n_4 n_5}$,

$\psi_7 = -\frac{n_1 n_4 n_5 n_7 \beta_s \psi_8 + n_2 n_3 n_6 n_8 \beta_s \psi_8}{\mu_m n_2 n_3 n_4 n_5}$, $\psi_8 = \psi_8 > 0$.

The left eigenvectors are given by;

$\eta_1 = 0$, $\eta_2 = \frac{n_7 \beta_n \eta_8}{n_2 n_3}$, $\eta_3 = \frac{n_7 \eta_8}{n_3}$, $\eta_4 = 0$, $\eta_5 = \frac{n_8 \beta_s \eta_8}{n_4 n_5}$, $\eta_6 = \frac{n_8 \eta_8}{n_5}$, $\eta_7 = 0$, $\eta_8 = \eta_8 > 0$.

Theorem 4.1 in Castillo-Chavez and Song, (2004) is applied to establish conditions for the forward or backward bifurcation. For easy reference, the Theorem is established to demonstrate the regional stability of endemic equilibrium points near $R_0 = 1$.

Theorem 1 *Consider the following general system of ordinary differential equations with a parameter a such that* $\frac{dy}{dt} = f(y, a), f \in \mathbb{R}^n \times \mathbb{R}$ and $f \in \mathbb{C}^2$ $(\mathbb{R}^n \times \mathbb{R})$, *where 0 is an equilibrium point of the model system (4) (that is* $f(o, a) \equiv 0$ *for all* a*) and*

i. $M = N_x f(0,0) = \frac{\partial f}{\partial x_i} f(0,0)$ *is a linearization matrix of the system (16) around equilibrium 0 evaluated at 0.*

Zero is a simple eigenvalue of M and all other eigenvalues of M have negative real parts.

ii. Matrix M has a non-negative right eigenvector ψ *and a left eigenvector* η *corresponding to the zero eigenvalue.*

Let f_k *be the* k^{th}*component of f and*

$$a = \sum_{i,j,k=1}^{n} \eta_k \psi_i \psi_j \frac{\partial^2 f}{\partial x_i \partial x_j}(0,0), \; b = \sum_{i,j,k=1}^{n} \eta_k \psi_i \psi_j \frac{\partial^2 f}{\partial x_i a}(0,0).$$

The local dynamics of the system around the equilibrium point is totally determined by the signs of a and b.

iii. If a > 0 and b > 0, then equilibrium 0 is locally asymptotically stable, and there exists unstable positive equilibrium when β < 0 with |β| << 1. In this case, the direction of bifurcation at β = 0 is backward.

iv. If a < 0, b > 0 and β > 0 with |β| << 1, then equilibrium 0 becomes unstable, and there exists a stable positive equilibrium which is locally asymptotically stable. In this case, the direction of bifurcation at β = 0 is forward.

The non-zero second partial derivatives of f_k at disease-free equilibrium E^0 are given as,

$\frac{\partial^2 f_2}{\partial y_1 \partial y_8} = g a^* b_{mn}$, $\frac{\partial^2 f_5}{\partial y_4 \partial y_8} = g a^* b_{ms}$, $\frac{\partial^2 f_8}{\partial y_7 \partial y_3} = a^* c_{nm}$, $\frac{\partial^2 f_8}{\partial y_7 \partial y_6} = a^* c_{sm}$, $\frac{\partial^2 f_2}{\partial y_1 \partial a} = g b_{mn} \theta$,

$\frac{\partial^2 f_5}{\partial y_4 \partial a} = g b_{ms}(1-\theta)$, $\frac{\partial^2 f_8}{\partial y_7 \partial a} = c_{nm}$, $\frac{\partial^2 f_8}{\partial y_7 \partial a} = c_{sm}$

Thus, we obtain

$$a = -\eta_8 \psi_8 \left(\frac{\beta_n n_1 n_7 g a^* b_{mn}}{n_2 n_3} + \frac{\beta_s n_6 n_8 g a^* b_{ms}}{n_2 n_3} + \frac{\beta_n n_1 (n_1 n_4 n_5 n_7 \beta_n + n_2 n_3 n_6 n_8 \beta_s)}{n_2^2 n_3^2 n_4 n_4} + \frac{\beta_s n_6 (n_1 n_4 n_5 n_7 \beta_n + n_2 n_3 n_6 n_8 \beta_s)}{n_2 n_3 n_4^2 n_5^2} \right) < 0, \quad (21)$$

$$b = \eta_8 \psi_8 \left(\frac{\beta_n n_7 g b_{mn} \theta}{n_2 n_3} + \frac{\beta_s n_8 g b_{mn}(1-\theta)}{n_4 n_5} + \frac{\beta_n n_1 c_{mn}}{n_2 n_3} + \frac{\beta_s n_6 c_{sn}}{n_4 n_6} \right) > 0. \quad (22)$$

Based on the signs of a, and b above, the model system (4) undergoes forward bifurcation. Therefore, when forward bifurcation occurs, then the requirement of $R_0 < 1$ is necessary and sufficient condition for effective disease control and elimination.

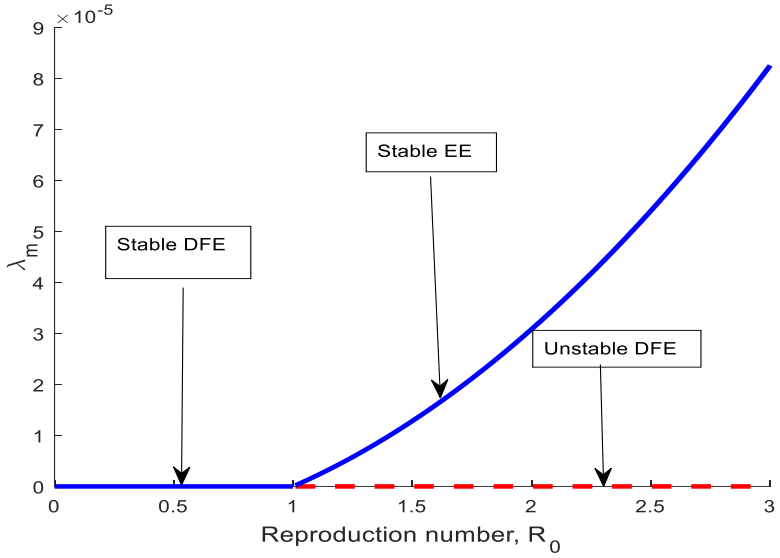

Figure 2: The plot of the basic reproduction number (R_0) against mosquito infection rate

Results and Discussion

The numerical simulation of the model system (4) is carried out to prove the analytical results obtained on the stability of equilibrium points. The model system is simulated using the fourth Runge Kutta in MATLAB. All figures are obtained using parameter values given in Table 2.

Table 2: Parameter values used in the numerical simulations

Parameters	Values	Dimension	Source
Λ	0.00129	Month	Kalula et al. (2021)
Λ_m	0.0498	Month	Mpeshe et al. (2017)
β_n	0.85	Month	Assumed
β_s	0.61	Month	Assumed
a	15	Month	Kalula et al. (2021)
α_n	0.0054	Month	Bakary et al. (2018)
α_s	0.0027	Month	Bakary et al. (2018)
b_{mn}	0.17	Dimensionless	Ducrot et al. (2009)
b_{ms}	0.12	Dimensionless	Ducrot et al. (2009)
c_{nm}	0.45	Dimensionless	Ducrot et al. (2009)
c_{sm}	0.35	Dimensionless	Ducrot et al. (2009)
g	0.129	Dimensionless	calculated

In Figure 3(c), the proportion of infectious mosquito population i_m exhibits an increasing trend with time until when they stabilize after the first 10 months whereas the proportions of infectious humans i_n, and i_s respond positively as a result of the increase in transmission rate and contact rate from infectious mosquitoes. Conversely, the proportion of susceptible mosquito population declines with time until the 10th month when it stabilizes. The proportion of susceptible non-immune individuals declines with time to zero after a 15th month whereas a small portion of semi-immune individuals remain uninfected. This reduction can be attributed to individuals transitioning from the susceptible class to the exposed class upon exposure to the infectious agent and subsequently progressing to the infectious class.

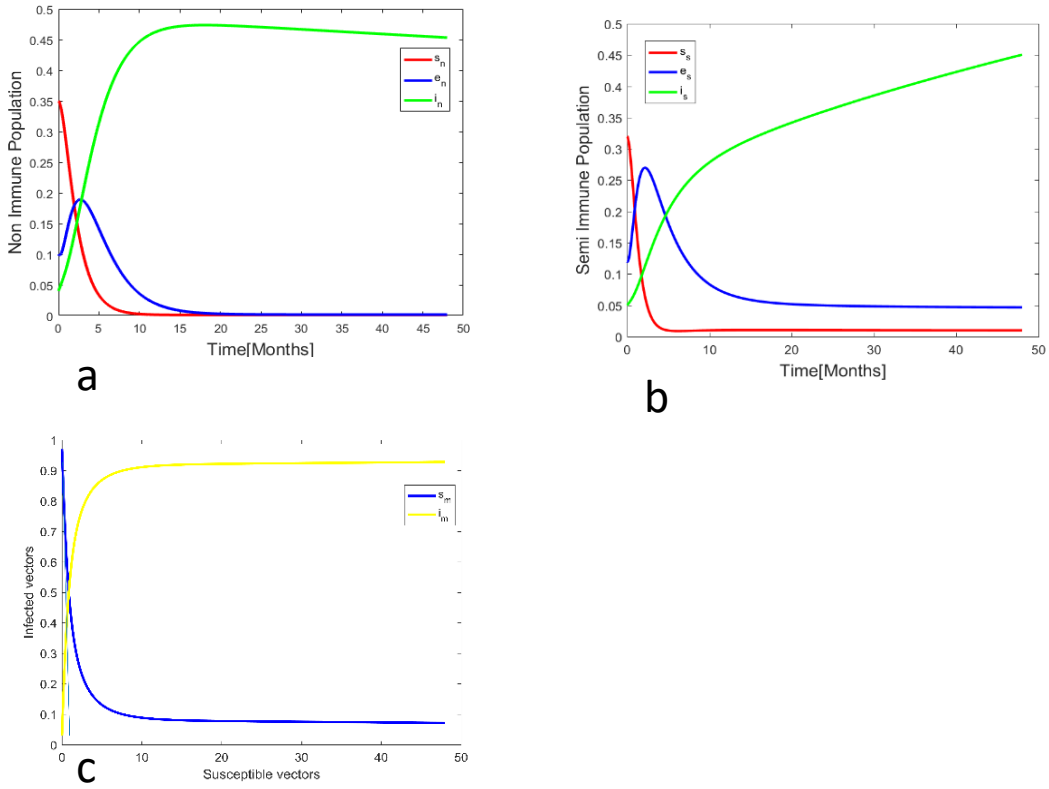

Figure 3: Dynamics of Malaria in Human and Mosquitoes Population

In Figures 4 (a) and 4 (b) it is shown that, as the mosquito biting rate increases, the proportion of susceptible populations also decreases with time. This is expected, as a higher mosquito biting rate led to more frequent exposure to infected mosquitoes, resulting in a higher likelihood of malaria being transmitted. In Figure 4 (c) it can be observed that the proportion of susceptible mosquito population also exhibits a notable response to variations in mosquito biting rates. Susceptible mosquitoes decrease as the mosquito biting rate increases. This is because as mosquito biting rate increases malaria infection in mosquitoes also increases. This results in an elevated potential for malaria transmission to both susceptible non-immune and susceptible semi-immune human populations.

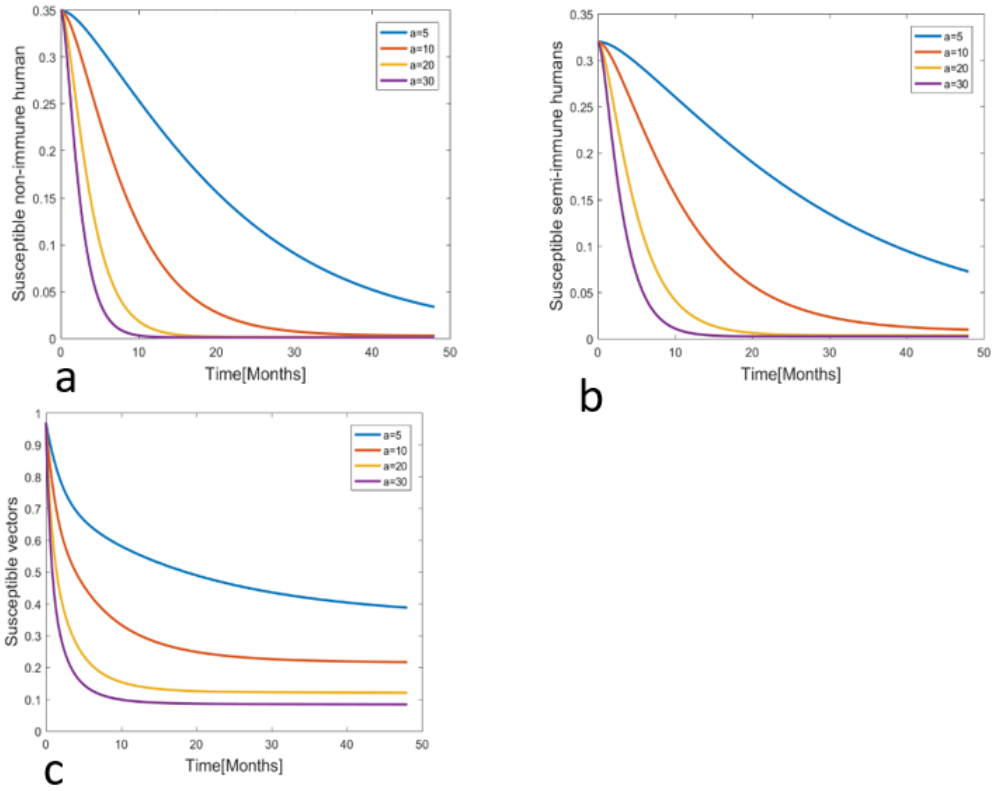

Figure 4: Variation of biting rate in susceptible classes for human and mosquito population

In Figures 5 (a) and 5 (b) it is shown that, as the mosquito biting rate increases, the proportion of infectious populations also increases with time. This is expected, as a higher mosquito biting rate led to more frequent exposure to infected mosquitoes, resulting in a higher likelihood of malaria to be transmitted.

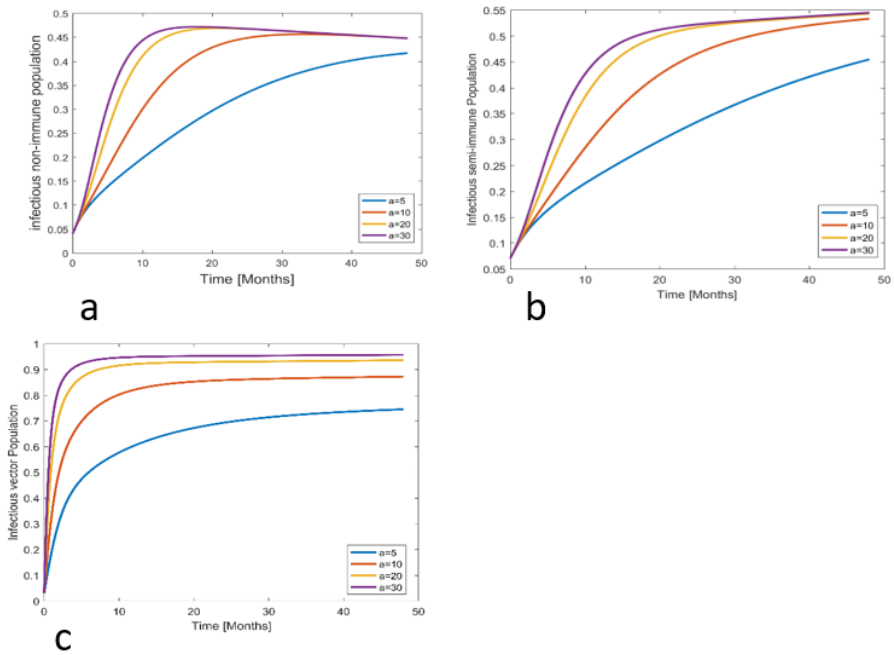

Figure 5: Variation of biting rate in infectious classes for human and mosquito population

Conclusion

In this paper, a mathematical model for the transmission dynamics of malaria in populations with different immune status is formulated and analyzed. The model is well-posed since all model solutions are positive and bounded. The basic reproduction number R_0 is computed using the next-generation matrix method. The malaria-free and endemic equilibrium points exist and their stability is analyzed. The existence of malaria-free and endemic equilibrium is analyzed numerically and indicates that the model incorporating immune status undergoes forward bifurcation which necessitates the requirement of $R_0 < 1$ to control malaria transmission. Furthermore, it can be seen that non-immune individuals are more affected by malaria parasites compared with semi-immune this is due to the differences in the immune status. Moreover, the results show that the mosquito biting rate is the key factor in malaria transmission. This result is more expected in the areas with high malaria transmission as reported by Ductrot et al. (2009). However, even in areas with low transmission non-immune individuals are most vulnerable to malaria infections this is because they have no immunity built in their body. Therefore, to control malaria, individuals should emphasize the use of treated bed nets since the contact rate between humans and mosquitoes will be minimized and thus there will be minimal chance of malaria being transmitted, also the use of indoor residual spraying will increase mosquito mortality rate and result into the decrease of disease prevalence.

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Declaration

The authors declare that there is no conflict of interest.

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